ICE/CSE 2016
BEIJING, CHINA

17th International Congress of Endocrinology
15th Annual Meeting of Chinese Society of Endocrinology

第十七届国际内分泌大会
暨中华医学会第十五次全国内分泌学学术会议

August 31-September 4, 2016
Beijing, China

PROGRAM BOOK
会议指南

ICE/CSE 2016

Organized by:

Chinese Medical Association

Chinese Society of Endocrinology

International Society of Endocrinology

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西维尔

SELENIOUS YEAST
硒酵母片

低硒状态与人群甲状腺病患病率增加相关

结 果:

来自富硒地区的3038人和低硒地区的3114人的数据是完整可靠的，他们血硒浓度的中位数有近两倍的差距（103.6[79.7，135.9]VS57.4[39.4，82.1]μg；P=0.01）。在富硒地区人群甲状腺疾病（甲减，亚甲减，自身免疫甲状腺炎和甲状腺肿）的患病率显著低于低硒地区人群（18.0%vs30.5%；P<0.001）。高血清硒对三种甲状腺疾病有保护作用，如对自身免疫性甲状腺炎的OR（0.47；[0.35，0.65]）；对亚甲减的OR（0.68；[0.58，0.93]）；甲减（0.75；[0.63，0.90]），对甲肿的OR（0.75；[0.59，0.97]）。

结 论:

低血清硒状态与甲状腺疾病患病危险增加相关。增加硒摄入可以减少低硒地区人群患病风险，这不仅在中国如此，在世界其他很多地方也相似。

（临床内分泌代谢杂志 100：0000-0000，2015）

西维尔(硒酵母片)，咀嚼后服用更有利于人体对硒的吸收。

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Contents

Welcome Address

Dear friends and colleagues,

We are honored to welcome you to Beijing for the 17th International Congress of Endocrinology in collaboration with the 15th Annual Meeting of the Chinese Society of Endocrinology (ICE/CSE 2016).

A world-renowned faculty of professors and researchers will share their experience with us at this congress. An exciting scientific program will include the most important cutting-edge development in basic research and the latest advances of clinical management in the field of endocrinology.

The Conference provides international and local experts with an opportunity to present lectures and workshops, covering a range of topics and important issues which affect us all from the laboratory to the clinic. In addition to the scientific program the ICE/CSE 2016 will offer abundant choices of networking events.

We are sure you will have an amazing experience exploring the most rapidly developing city of Beijing, enjoying the Chinese culture in all aspects including history, religion and fine cuisine.

We hope you enjoy your time in the vibrant city of Beijing.

Guang Ning
President
17th International Congress of Endocrinology
15th Annual Meeting of Chinese Society of Endocrinology

Dear friends and colleagues,

We are excited to partner with the Chinese Society of Endocrinology (CSE) to host the first ever International Congress of Endocrinology (ICE) in China!

The collaboration promotes the International Society of Endocrinology's (ISE) long-term commitment to supporting endocrinology across the globe, especially in developing nations.

Our local and international experts developed an unmissable program of the highest scientific standard appealing to the full spectrum of endocrinologists around the globe – discovery scientists, clinician scientists, practicing endocrinologists and of course, our ongoing commitment to trainees.

Held jointly with the CSE annual meeting, ICE/CSE 2016 will to be a rich and fulfilling educational event with the opportunity to learn from experts, colleagues and peers based around the world in a diverse and colourful environment, unique only to ICE!

Having further developed the CSE's relationship with the ISE, I am personally very enthusiastic in welcoming you all to the exciting location of Beijing, our host city, for this landmark event. It promises to be a memorable experience!

Paul Stewart
Secretary Treasurer
International Society of Endocrinology

Dear friends and colleagues,

It is a privilege to welcome you to the 17th International Congress of Endocrinology in collaboration with the 15th Annual Meeting of the Chinese Society of Endocrinology, taking place from August 31st to September 4th here in Beijing. This international, comprehensive conference will be co-hosted by the International Society of Endocrinology (ISE), the Chinese Medical Association (CMA) and the Chinese Society of Endocrinology (CSE).

Leading endocrinologists from around the world have been invited to give plenary lectures, deliver symposia, and discuss the latest clinical cases. A wide range of continuing education lectures have also been included. We will promote both the study of the causes of domestic endocrine metabolic disease and the development of clinical research, and we will provide a high quality academic platform for those doctors engaged in the study of the disease and related fields.

It's a great pleasure to host the 17th International Congress of Endocrinology here in Beijing. Strong support has been received both within China and from overseas. We are confident that the conference will fully achieve its goals. On behalf of the Chinese Society of Endocrinology, thank you very much for your interest and support.

We extend a very warm welcome to our visitors from all over the world. Your contribution to advancing the development of endocrine metabolic disease research in China is deeply appreciated. Enjoy your stay in Beijing.

Yiming Mu, MD., Ph.D.
President
Chinese Society of Endocrinology
Local Organizing Committee

Committees

International Society of Endocrinology Executive Committee (2014-2016)

Margaret Shupnik	*University of Virginia Medical School, United States*	*Chairperson*
Paul Stewart	*University of Leeds, United Kingdom*	*Secretary Treasurer*
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Oscar Bruno	*University of Buenos Aires, Argentina*	*FELAEN*
Takashi Akamizu	*Wakayama Medical University*	*JAPAN*
Nor Azmi Kamaruddin	*Universiti Kebangsaan Malaysia*	*AFES*
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Guang Ning	*Medical College of Shanghai Jiaotong University, China*	*At Large*
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International Chairman
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Kathryn Tan, Hong Kong, China
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Nanwei Tong, China
Weiqing Wang, China
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Jiajun Zhao, China

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Tien-Shang Huang, Taiwan, China	Tao Huang, China	Shih-Ming Huang, Taiwan, China
Nobuya Inagaki, Japan	Warrick Inder, Australia	Hiroshi Itoh, Japan
Tjin-Shing Jap, Taiwan, China	Linong Ji, China	Weiping Jia, China
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Nor Azmi Kamaruddin, Malaysia	Olle Kämpe, Sweden	Tomoyuki Kawamura, Japan
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Benjamin Leder, United States	Ka Fai Lee, Hong Kong, China	Kok Onn Lee, Singapore
Peter CK Leung, Canada	Jon Levine, United States	Yuxiu Li, China
Guangwei Li, China	Qifu Li, China	Jing Li, China
Hong-Da Lin, Taiwan, China	Jianmin Liu, China	Chao Liu, China

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Margaret McCarthy, United States	Michael McClung, United States	Robert McLachlan, Australia
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Lars C. Moeller, Germany	Yiming Mu, China	Hermann Müller, Germany
Lynette Nieman, United States	Guang Ning, China	Eijun Nishihara, Japan
Yoshihoro Ogawa, Japan	Augustine E. Ohwovoriole, Nigeria	Henrik Oster, Germany
Changyu Pan, China	Simon Pearce, United Kingdom	Yongde Peng, China
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Vincent Prévot, France	Jie Qiao, China	Marcus Quinkler, Germany
Laura Raimondi, Italy	Frank Rauch, Canada	Lars Rejnmark, Denmark
Gail Risbridger, Australia	Ann Robinson, Australia	Mike Rogers, Australia
Johannes A. Romijn, The Netherlands	Ron Rosenfeld, United States	Amy Rothberg, United States
Elisabeth Rutten, Belgium	Richard Santen, United States	Angela Sarabdjitsingh, The Netherlands
Fumitoshi Satoh, Japan	Janet Schlechte, United States	Christof Schöfl, Germany
Lutz Schomburg, Germany	Mary Schooling, Hong Kong, China	Anna Schwartz, United States
David Scott, Australia	Robert Scragg, New Zealand	Susumu Seino, Japan
Stephanie Seminara, United States	Stephen Shalet, United Kingdom	Zhongyan Shan, China
Boyong Shen, China	Lisa Shepherd, United Kingdom	Bingyin Shi, China
Dolores Shoback, United States	Youngkee Shong, Korea	Margaret Shupnik, United States
Evan Simpson, Australia	Natalie Sims, Australia	Isaac Sinay, Argentina
Isabelle Steineck, Sweden	Paul Stewart, United Kingdom	Bronwyn Stuckey, Australia
Qing Su, China	Tingwei Su, China	Hidetaka Suga, Japan
Fukang Sun, China	Kathryn Tan, Hong Kong, China	Lizhi Tang, China
Helena Teede, Australia	Manuel Tena Sempere, Spain	Weiping Teng, China
Ei Terasawa, United States	Massimo Terzolo, Italy	Rajesh Thakker, United Kingdom
Dang Tran Ngoc Thanh, Vietnam	David Thomas, Australia	Wayne Tilley, Australia
Anli Tong, China	Nanwei Tong, China	Peter Trainer, United Kingdom
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Chao Wang, China	Christina Wang, United States	Guixia Wang, China
Qin Wang, China	Weiqing Wang, China	Len Wartofsky, United States
Wilmar M. Wiersinga, The Netherlands	Graham R. Williams, United Kingdom	Kevin Williams, United States
Teresa Woodruff, United States	Jie Wu, China	Xueyan Wu, China
Weibo Xia, China	Hailing Xiao, China	Xinhua Xiao, China
Zhongjian Xie, China	Ming-Zhao Xing, United States	Aimin Xu, Hong Kong, China
Shunichi Yamashita, Japan	Chaoli Yan, China	Tao Yang, China
Huixia Yang, China	Polina Yarova, United Kingdom	Chris Yedinak, United States
Phillip Yeoh, United Kingdom	Williann Yeung, Hong Kong, China	Chun-Xia Yi, The Netherlands
Morag Young, Australia	William F. Young, United States	Oh Youngman, United States
Xuefeng Yu, China	Zhengpei Zeng, China	Maria-Christina Zennaro, France
Junqing Zhang, China	Yong Zhao, China	Jiajun Zhao, China
YingXia Zhou, China	Mei Zhu, China	Sophia Zoungas, Australia

History of ICE

The International Congress of Endocrinology (ICE) is the most widely attended medical conference of its field. The rich, diverse and colourful content of the event coupled with its global perspective make it a congress not to be missed by academics, clinicians, researchers and industry partners from across the globe.
The inaugural ICE was held in Denmark in 1960 and historically held every four years. To facilitate more frequent and geographically diverse scientific exchange the ISE now partner with a Member Society Annual Meeting every two years to host ICE in regional rotation across The Americas-Europe/Africa-Asia/Oceania.

Years	Dates	Venue
1st	1960 July 18-23	Copenhagen (Denmark)
2nd	1964 August 17-22	London (UK)
3rd	1968 June 30 - July 5	Mexico DF (Mexico)
4th	1972 June 18-24	Washington City (USA)
5th	1976 July 18-24	Hamburg (Germany)
6th	1980 February 10 - 16	Melbourne (Australia)
7th	1984 July 1 -7	Quebec City (Canada)
8th	1988 July 17 - 23	Kyoto (Japan)
9th	1992 August 30 - September 5	Nice (France)
10th	1996 June 12 - 15	San Francisco (USA)
11th	2000 October 29 - November 2	Sydney (Australia)
12th	2004 August 31 - September 4	Lisbon (Portugal)
13th	2008 November 8 - 12	Rio de Janeiro (Brazil)
14th	2010 March 26 - 30	Kyoto (Japan)
15th	2012 May 5 - 9	Florence (Italy)
16th	2014 June 21 - 24	Chicago (USA)
17th	2016 August 31 - September 4	Beijing (China)

Registration Information

Registration Fee

Categories	Early Registration *before July 15, 2016*	Regular Registration *before August 15, 2016*	Late Registration/On-site *before September 4, 2016*
ISE Member	600 USD	700 USD	900 USD
Nonmember	750 USD	850 USD	1050 USD
In-Training Member/Nurse	300 USD	400 USD	500 USD
Accompanying person	100USD	100USD	100USD

***Registration fee includes:** *Participation in scientific sessions and sponsored symposia, registration packet, Conference bag, program and abstract book, all printed material of the Conference, exhibition, certificate of attendance, coffee breaks and lunches when provide.*

Registration Desk
The registration desk is located in the Lobby of the China National Convention Center (CNCC) Entrance C3. Please be sure to complete registration procedures before participating in any of the official congress sessions and events.

Date	Opening Hours
Wednesday, August 31	09:00-18:30
Thursday, September 1	08:00-19:00
Friday, September 2	08:00-18:00
Saturday, September 3	08:00-18:00
Sunday, September 4	08:00-12:00

Badges

A badge is required for admittance to all official congress sessions and events. Each participant is asked to present their badge in order to gain access to the congress. The badge must be worn and clearly displayed at all times. Upon losing the badge, duplication will be provided at the Registration desk at an additional cost of $100.

Yellow Lanyard	Staff
Blue Lanyard	Participant
Green Lanyard	Exhibitor/Accompanying Person
Red Lanyard	Invited Guest/Faculty

Speaker Ready Room

Location: Room 308, Level 3, CNCC

Wednesday, August 31, 2016	10:00 -17:30
Thursday, September 1, 2016	08:00 -17:30
Friday, September 2, 2016	08:00 -17:30
Saturday, September 3, 2016	08:00 -17:30
Sunday, September 4, 2016	08:00 -11:30

Guidelines for Speakers and Chairpersons

For Speakers

- ✓ Speakers are kindly requested to use MS PowerPoint in English for their presentations;
- ✓ Please submit PowerPoint files to the Congress Speaker Ready Room at least SIX HOURS before the scheduled presentation time in order to allow verification and transfer to the allocated meeting rooms;
- ✓ Each presentation should be strictly time-limited followed by 5 minutes of question and answer;
- ✓ Please also bring your presentation data on a media (USB flash memory) as a backup file;
- ✓ Please read the following instructions before building the PowerPoint presentations.

PowerPoint Instructions

- ✓ Please use the Microsoft PowerPoint 2007 or 2010* (*.ppt) or (*pptx), to guarantee it can be opened successfully on an on-site PC;
- ✓ Movies: Please take steps to compress your videos (Less than 500Megabytes). Uncompressed videos will take longer to upload. We can only accept movies created as **WMVs** or **AVI** formats;
- ✓ If you cannot convert the files or have a considerable number of MOV files, please check with a technician in the Speaker Ready Room who can make arrangements to convert the videos for you.

Considerations for Keynote Software Users

- ✓ Please export your presentation as a PowerPoint (*.ppt or *.pptx) since keynote is not compatible with the conference's presentation management system;
  If you are having any issues, please notify our on-site support for additional help.

For Chairpersons

Please be seated in the chairpersons' seats located at the front of your session room at least 10 minutes prior to your session starts.

General Information

Congress Dates & Venue

Wednesday, August 31 – Sunday, September 4, 2016
China National Convention Center (CNCC), Beijing, China
No. 7 Tianchen East Road, Chaoyang District, Beijing 100105, China
+86-10-8437 2008
Website: http://www.cnccchina.com

Official Language

English

Business Center

Located on Level 3 of the CNCC

WIFI

The CNCC provides free WI-FI.
CNCC Wi-Fi Name: CNCC-FREE

PPT Review & Cyber Station

Located on Level 3 of the CNCC
Presentation slides with the speakers' authorization can be reviewed here.

Accommodation

ComtecMed Limited has been appointed as the official international hotel accommodation agent for ICE/CSE 2016 and will handle all related arrangements. ComtecMed Limited can be contacted via their desk at the registration area in the lobby of the CNCC.

Meals and Coffee Breaks

Complimentary coffee breaks will be available during scheduled breaks throughout the congress from the E1, E2 Hall in the CNCC, on September 1-3, 2016 as per the timetable. A packed lunch is included in the registration fee and will be available for delegates on September 11-3, 2016 from the commercial satellite symposia rooms and the Exhibition Hall No. 5 at the CNCC.

CME Accreditation and Certificates

All registered participants will need to complete their CME Accreditation Feedback Form online (www.ice-cse2016.org) by logging in to their registration portal after the congress ends. Once the CME Feedback Form is completed and submitted online, your EACCME Certificate will be available for download.

Exhibition

A commercial exhibition will be held in E1, E2 Hall in the CNCC, on September 1-3, 2016.

Date	Opening Hours
September 1-3, 2016	09:00-16:30

Optional Tours

Special tours and excursions have been arranged exclusively for the delegates and accompanying persons at ICE/CSE 2016 for individual purchase. CTS M.I.C.E Service CO., LTD has been appointed as the official tour booking agent for ICE/CSE 2016 and will handle all related arrangements. CTS M.I.C.E Service CO., LTD can be contacted via their desk at the registration area in the lobby of the CNCC.

Shuttle Bus Service to/from CNCC to ICE/CSE 2016 Hotels

From Hotels to the CNCC:
Route A: (September 1-4, 2016)
1st stop 7:00am: Courtyard by Marriott Northeast
2nd stop 7:20am: Radisson Blu
3rd stop 8:00am: Marco Polo Parkside Beijing

Route B: (September 1-4, 2016)
1st stop 7:15 am: Traders
2nd stop 7:20 am: China World Summit Wing

From the CNCC to Hotels:
September 1-3, 2016, 18:45pm: Return shuttles to ICE/CSE 2016 hotels
September 4, 2016, 12:45pm: Return shuttles to ICE/CSE 2016 hotels

ICE/CSE 2016 Abstracts

Abstracts are accessible online at www.ice-cse2016.org.

ISE Office

VIP Room 3-1, Level 3, CNCC

ISE General Council Meeting

17:00-18:30, Friday, September 2, 2016, Room 202AB, Level 2, CNCC

International Society of Endocrinology Travel Fellowship Awards

ISE have awarded over 100 fellowship support grants to bring young researchers from all over the world to present their research at the landmark first ICE in China.
These prestigious grants are awarded to young endocrinologists and/or endocrinologists from developing countries who have demonstrated effectiveness in endocrine research.
Congratulations to our successful awardees who are invited to attend an informal fellows reception and collect their award as follows:

ISE Travel Grant Reception

12:00-13:00, Saturday, September 3, 2016, Ballroom A, Level 1, CNCC
Invitation Only.

Social Programs

Opening Ceremony

18:00-18:30, Wednesday, August 31, 2016, Plenary Hall A, Level 4, CNCC
All delegates are invited.

Welcome Reception

18:40-20:00, Wednesday, August 31, 2016, Ballroom A, Level 1, CNCC
Invitation Only (Invitation can be available at the registration area for individual purchase at the cost of $100)
Please dress in formal.

Closing Ceremony

12:00-12:30pm, Sunday, September 4, 2016, 309AB, Level 3, CNCC
All delegates are invited.

Follow ICE/CSE 2016

Wechat

Mobile APP

Website

www.ice-cse2016.org

Poster Guidelines

Location: E1,E2 Hall in the China National Convention Center (CNCC)

Setup Time

Thursday, September 1, 2016 09:00-10:00	PTx-01-xx
Friday, September 2, 2016 09:00-10:00	PTx-02-xx
Saturday, September 3, 2016 09:00-10:00	PTx-03-xx

Note:

1. Posters presenters are asked to place their posters at the designated space and to follow the schedule above.
2. Poster Number Explanations: PT1-01-01
- PT: Poster Tour
- 1: Each Category is represented by a number.
- 01 / 02 / 03: Presentation date.
- 01: Poster Number.

The assigned poster number contains the date of presentation for each poster presenter. Please follow the scheduled date strictly.

Poster Discussion Time

Thursday, September 1, 2016 13:00-14:00	PTx-01-xx
Friday, September 2, 2016 13:00-14:00	PTx-02-xx
Saturday, September 3, 2016 13:00-14:00	PTx-03-xx

Poster Removal Time

Thursday, September 1, 2016 17:00-17:30	PTx-01-xx
Friday, September 2, 2016 17:00-17:30	PTx-02-xx
Saturday, September 3, 2016 17:00-17:30	PTx-03-xx

Poster Presentation

Poster presenters are expected to be ready and stand in front of their poster panel at least 15 minutes prior to the Poster Tour Session.

Sponsors

Merck Serono Co, Ltd	107	SteriLance Medical (Suzhou) Inc	113
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MSD	104	Medisound (Beijing) Medical Apparatus Co, Ltd	115
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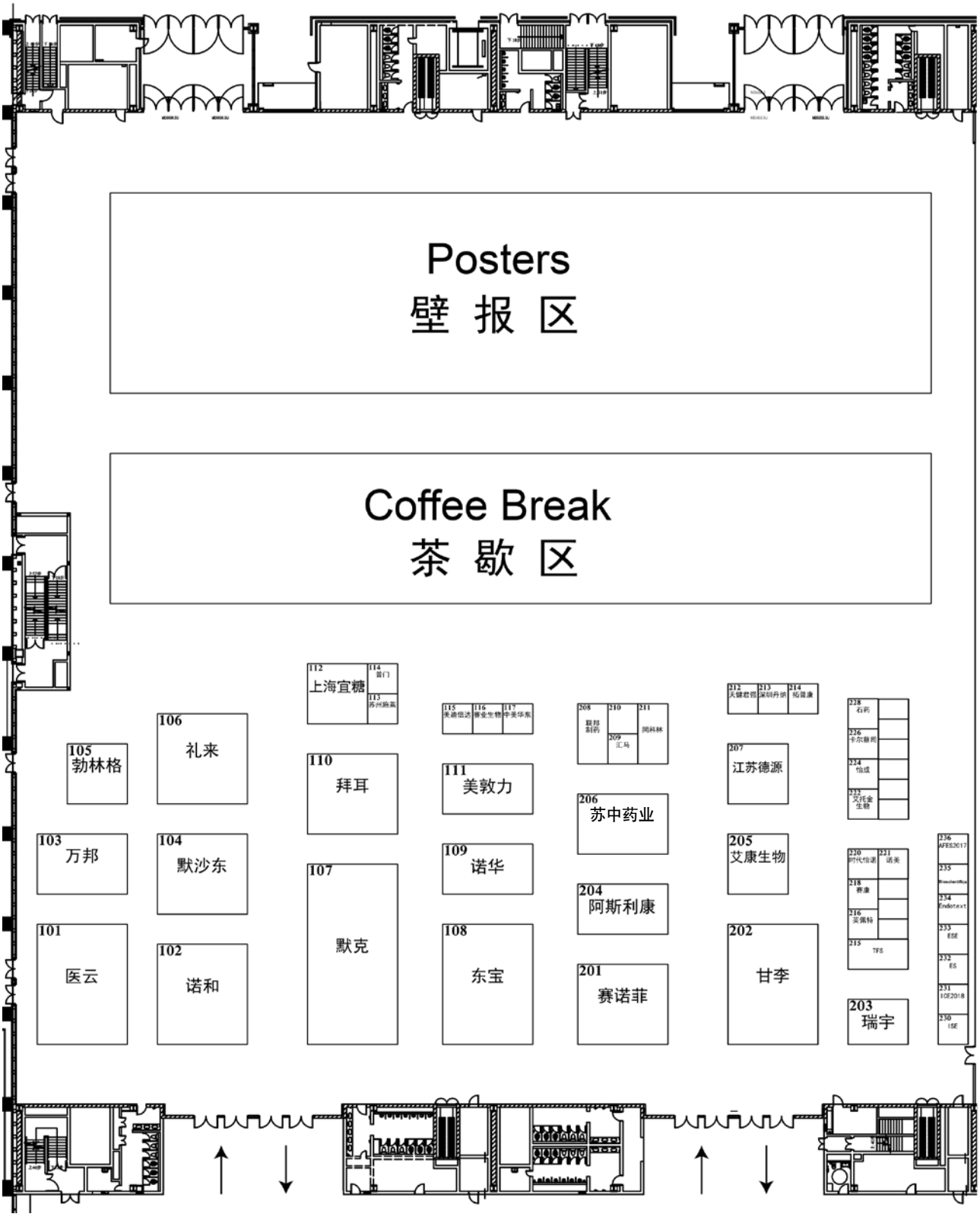
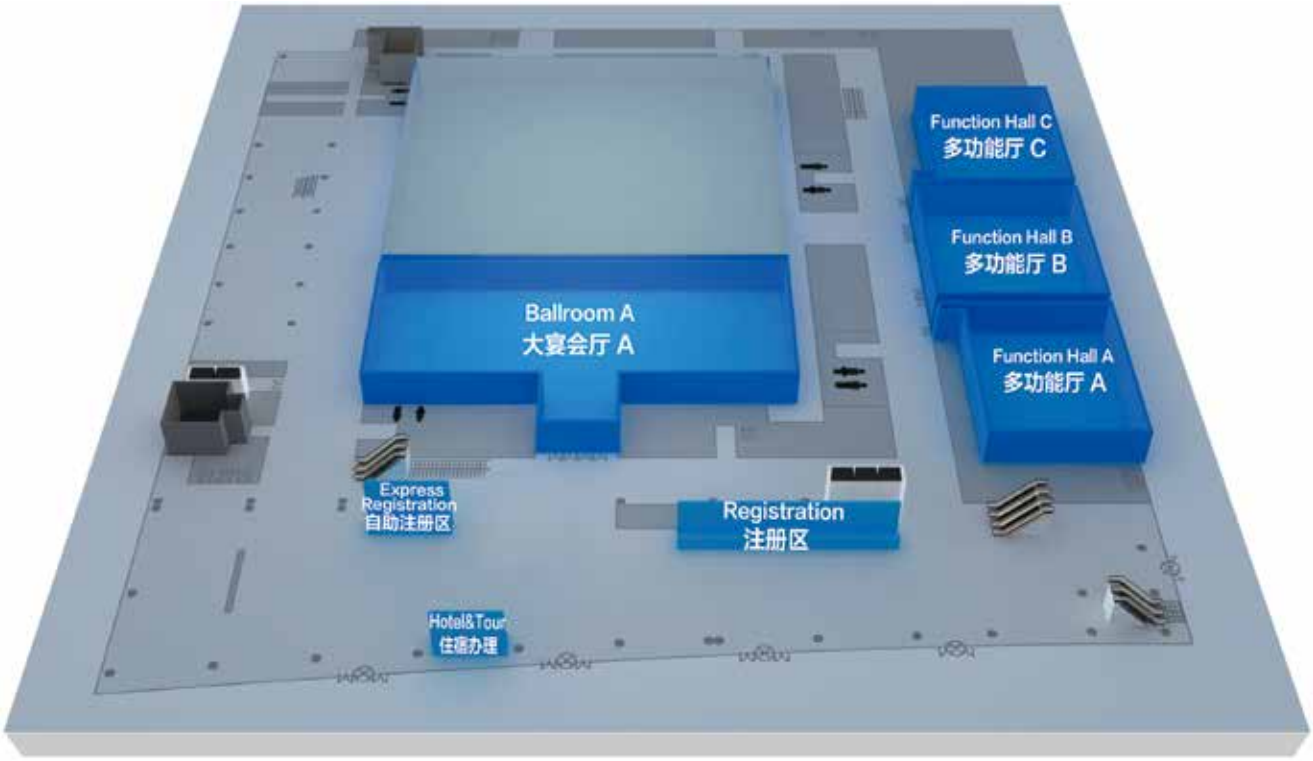
Exhibition Floorplan



CNCC Floorplans



国家会议中心一层平面图

Floorplan of Level 1

China National Convention Center

CNCC Floorplans

国家会议中心三层平面图

Floorplan of Level 3

China National Convention Center

国家会议中心四层平面图

Floorplan of Level 4

China National Convention Center

Program at a Glance

Opening Ceremony: 18:00-18:30, Wednesday August 31, 2016, Plenary Hall A, Level 4, CNCC

		Plenary Hall	Function Hall C	Function Hall B	Function Hall A	Auditorium	309A	309B	310	311A	311B	306	307	301	302	303	401	402A	402B	403	405	406	407
1/9/2016	07:30-08:15									美敦力	诺和诺德												
	08:30-09:00	**PL 1** | Hormones and Cancer-New Insights																					
	09:00-09:15																						
	09:15-10:00	**PL 2** | Diaomics-Diabetes and Metabolic Disorders																**MTE 1a** | Management of Craniopharyngioma	**MTE 2a** | Clinical Usefulness of TSH Receptor Antibody Measurement	**MTE 3a** | Vitamin D	**MTE 4a** | Premature Ovarian Insufficiency	**MTE 5a** | New Genes in Pituitary Tumor and Implications for Management	**MTE 6a** | Optimizing Treatment for Congenital Adrenal
	10:00-10:15	Coffee Break																					
	10:15-11:00					**S 61** | Global Symposium on Obesity	**S 1** | Subclinical Adrenal Diseases	**S 2** | Adrenal Cancer	**S 3** | Thyroid: From Fetal Life to Adulthood	**S 4** | Treatment of Thyroid Cancer	**S 5** | Calcium Sensing Receptor - Basic Biology and Clinical Implications	**S 6** | Off Target Effects of Osteoporosis Therapies in	**S 7** | Kisspeptin Neurons: The Central Reproductive Relay	**S 8** | Polycystic Ovary Syndrome	**S 9** | Understanding Growth	**S 10** | The Gut Nutrient Sensing in Energy Metabolism							
	11:00-11:45																	**MTE 7a** | Primary Hyperaldosteronism	**MTE 8a** | Clinical Management of Thyroid Nodules	**MTE 9a** | Managing Osteoporosis in Under-Served Clinical Groups Transitioning to Adult Care	**MTE 10a** | Genetics of Hypothalamic-Pituitary-Gonadal Function	**MTE 11a** | Insulin Pump	**MTE 12a** | Acromegaly
	11:45-12:00																						
	12:00-12:45				诺和诺德		甘李	默沙东	赛诺菲	东宝	默克	礼来	拜耳										
	13:00-14:00	Poster Guided Tour					Poster Guided Tour		赛诺菲 12:50-13:35	Poster Guided Tour													
	14:00-15:00				专题 1：降糖药物心血管结局研究	专题 2：糖尿病综合管理	**S 11** | Adrenal Insufficiency	**S 12** | Pheochromocytoma	**S 13** | Target Therapy for Thyroid Cancer	**S 14** | Incidence of Thyroid Cancer	**S 15** | Peak Bone Mass and Osteoporois in Young People	**S 16** | Hot Topics and Bone	**S 17** | Controversies in Testosterone Replacement	**S 18** | Novel Endometrial Signalling Pathway and Fertility	**S 19** | New Treatment for Lipid Disorders			**MTE 1b** | Management of Craniopharyngioma	**MTE 2b** | Clinical Usefulness of TSH Receptor Antibody Measurementt	**MTE 3b** | Vitamin D	**MTE 4b** | Premature Ovarian Insufficiency	**MTE 5b** | New Genes in Pituitary Tumor and Implications for Management	**MTE 6b** | Optimizing Treatment for Congenital Adrenal
	15:00-16:00						**OR 11**	**OR 12**	**OR 13**	**OR 14**	**OR 15**	**OR 16**	**OR 17**	**OR 18**	**OR 19**								
	16:00-16:15	Coffee Break																					
	16:15-18:15	**PL 3** | Primary Aldosteronism-Past, Present, and Future								中青年英文演讲比赛（会场一）	中青年英文演讲比赛（会场二）							**MTE 7b** | Primary Hyperaldosteronism	**MTE 8b** | Clinical Management of Thyroid Nodules	**MTE 9b** | Managing Osteoporosis in Under-Served Clinical Groups Transitioning to Adult Care	**MTE 10b** | GGenetics of Hypothalamic-Pituitary-Gonadal Function	**MTE 11b** | Insulin Pump	**MTE 12b** | Acromegaly
2/9/2016	08:30-09:00	**PL 4** | Iodine and Thyroid Disorders in China																					
	09:00-09:15		09:00-10:00 会见教授：如何早期鉴别甲状腺结节的良恶性		09:00-10:40 糖尿病与精准医学	09:00-10:00 大会报告		09:00-10:00 大会报告（309B）	09:00-10:00 大会报告	09:00-10:00 大会报告	09:00-10:00 大会报告		09:00-10:00 大会报告					**MTE 13a** | Primary Adrenal Insufficiency	**MTE 14a** | Thyroid disease in elderly patients: What to do and what to avoid	**MTE 15a** | Managing Osteoporosis in Post Menopausal Women	**MTE 16a** | Dopamine Agonists: When To Use, What To Choose & Safety Issues	**MTE 17a** | Preservation of Fertility in Cancer Patients	
	09:15-10:00	**PL 5** | Mechanisms of Cell Signaling in Insulin Secretion																					
	10:00-10:15	Coffee Break	10:00-11:00 大会报告			Coffee Break																	
	10:15-11:00					**S 20** | Pituitary Tumorigenesis	**S 21** | Primary Aldosteronism	**S 22** | Graves Orbitopathy	**S 23** | Hypothalamus and Energy Homeostasis	**S 24** | Diabetes and Bone	**S 25** | Vitamin D - Myths and Facts		**S 26** | Neuroestrogens and Brain Function	**S 27** | The Timing of Puberty: Neuroendocrine and Genetic Factors	**S 28** | Prolactin: What's New?	**S 29** | Diabetic Complications							
	11:00-11:45		11:00-11:45 口头发言		10:40-11:45 口头发言													**MTE 18a** | Osteoporosis in Men	**MTE 19a** | Testosterone Replacement Therapy	**MTE 20a** | Approach to the Patient with Relapse Hyperthyrodism after Previous ATD Therapy: How Useful are Anti-Thyroid Drugs	**MTE 21a** | Cushing's Syndrome	**MTE 22a** | Treatment of Type 1 Diabetes at Diagnosis and During Remission	
	11:45-12:00																						
	12:00-12:45				诺和诺德	勃林格		诺华	医云	东宝	默克		宜糖										
	13:00-14:00	Poster Guided Tour						诺华 12:50-13:30					Poster Guided Tour										
	14:00-15:00		14:00-15:40 妊娠甲状腺疾病专题		14:00-15:50 糖尿病与肿瘤	**S 30** | Bioinformatics Meets Acromegaly: Insight from Registries	**S 31** | Thyroid Hormone Derivatives	**S 32** | Endocrine Signalling in Phosphate Metabolism-Role of FGF23	**S 33** | Parathyroid Disorders-An Update	**S 34** | Hormonal Determinants of Human Embryo Implantation	**S 35** | GHRH, Growth Hormone and IGF Throughout Life		14:00-15:00 脂肪性肝病与代谢专题					**MTE 13b** | Primary Adrenal Insufficiency	**MTE 14b** | Thyroid disease in elderly patients: What to do and what to avoid	**MTE 15b** | Managing Osteoporosis in Post Menopausal Women	**MTE 16b** | Dopamine Agonists: When To Use, What To Choose & Safety Issues	**MTE 17b** | Preservation of Fertility in Cancer Patients	
	15:00-16:00					**OR 30**	**OR 31**	**OR 32**	**OR 33**	**OR 34**	**OR 35**	**S 92** | Nurses Symposium Program	15:00-16:00 辩论 NAFLD 是否应当干预										
	16:00-18:15	**PL 6** | Mechanisms of thyroid hormone action during skeletal development and bone maintenance	15:50-17:15 口头发言		15:50-17:15 口头发言	肾上腺专题	16:15-18:15	性腺疾病专场（309B）	下丘脑 - 垂体疾病专场	骨代谢专场	肥胖专题及口头发言		16:00–18:15 口头发言					**MTE 18b** | Osteoporosis in Men	**MTE 19b** | Testosterone Replacement Therapy	**MTE 20b** | Approach to the patient with relapse hyperthyrodism after previous ATD therapy: How useful are anti-thyroid drugs?	**MTE 21b** | Cushing's Syndrome	**MTE 22b** | Treatment of Type 1 Diabetes at Diagnosis and During Remission	
3/9/2016	08:30-09:00	**PL 7** | Genetic strategies to understand physiological pathways regulating body weight.	09:00-11:00 甲状腺领域年度进展及病例讨论：不同类型甲亢的治疗		09:00-10:20 特殊人群的血糖管理	09:00-10:00 大会报告		09:00-10:00 大会报告（309B）	09:00-10:00 性腺疾病专场	09:00-10:00 大会报告	09:00-10:00 热点辩论：甲状腺癌过度诊断和治疗了吗							**MTE 23a** | Adrenocortical Cancer	**MTE 24a** | Absolute Fracture Risk and Bone Quality	**MTE 25a** | Management of Disorders of Sex Development	**MTE 26a** | Hypoglycemia Does it Matter?	**MTE 27a** | Thyroid and Pregnancy	**MTE 28a** | Update on Long Acting Growth Hormone
	09:00-09:15																						
	09:15-10:00	**PL 8** | Surprising Origins of Sex Differences in the Brain																					
	10:00-10:15	Coffee Break				Coffee Break																	
	10:15-11:00				10:20-11:45 口头发言	**S 63** | Practical Publishing Advice	**S 36** | Growrh After Cancer Treatment	**S 37** | Cardio-Metabolic Effects of Corticosteroids	**S 38** | Thyroid and Pregnancy	**S 39** | TSH Receptor	**S 40** | Osteoporosis Therapies - What is on the Horizon?	**S 41** | Interactions of Bone and Muscle with Aging	**S 42** | Activin, Folistatin and Ovarian Development				**MTE 29a** | Therapy of Differentiated Thyroid Cancer	**MTE 30a** | Genetic Tests-What the Clinical Endocrinologist Should Know	**MTE 31a** | Treatment in Older People with Type 2 Diabetes	**MTE 32a** | Pheochromocytoma	**MTE 33a** | Modern Management of Hypoparathyroidism	**MTE 34a** | Hormone Therapy in Menopause	**MTE 35a** | Pregnancy and Diabetes
	11:00-11:45		11:00-11:45 口头发言																				
	11:45-12:00																						
	12:00-12:45																						
	13:00-14:00	Poster Guided Tour																					
	14:00-15:00		14:00-15:40 转化医学专场	14:00-16:20 高尿酸血症和痛风专题	14:00-16:00 优秀论文汇报	14:00-15:40 肾上腺专题	**S 43** | Cortisol, Pulsatility and Clocks	**S 44** | Emerging Therapeutic Potential of FGF21	**S 45** | Cushing: Genetic to Clinical	**S 46** | Hypopituitarism	**S 47** | Endocrine Related Cancer	**S 48** | Biology of Aging: Therapeutic Implications	**S 49** | Membrane Signaling and Cancer	**S 50** | New Frontiers in Metabolic Surgery	**S 51** | New Insights into Gonadotropin Synthesis and Secretion			**MTE 23b** | Adrenocortical Cancer	**MTE 24b** | Absolute Fracture Risk and Bone Quality	**MTE 25b** | Management of Disorders of Sex Development	**MTE 26b** | Hypoglycemia: Does it Matter?	**MTE 27b** | Thyroid and Pregnancy	**MTE 28b** | Update on Long Acting Growth Hormone
	15:00-16:00					15:40-16:15 会见教授：疑难肾上腺疾病诊治经验	**OR 43**	**OR 44**	**OR 45**	**OR 46**	**OR 47**	**OR 48**	糖尿病口头发言										
	16:00-16:15	Coffee Break					Coffee Break							Coffee Break									
	16:15-17:00	**PL 9** | Nuclear Receptors and Development: From Drugs to Embryos and Back Again	15:40-17:40 甲状腺炎专题	16:20-17:15 辩论：痛风石的处理内科治疗还是外科治疗好	16:00-17:15 性腺专题	16:15-17:15 口头发言		性腺疾病专场	下丘脑 - 垂体疾病专场	骨代谢专场	脂代谢专题		骨代谢口头发言					**MTE 29b** | Therapy of Differentiated Thyroid Cancer	**MTE 30b** | Genetic Tests: What the Clinical Endocrinologist Should Know	**MTE 31b** | Treatment in Older People with Type 2 Diabetes	**MTE 32b** | Pheochromocytoma	**MTE 33b** | Modern Management of Hypoparathyroidism	**MTE 34b** | Hormone Therapy in Menopause	**MTE 35b** | Pregnancy and Diabetes
	18:00-18:15								口头发言														
4/9/2016	08:30-09:15	**PL 10** | Recent Advances in Polycystic Ovarian																					
	09:00-09:15	Syndrome		中国之声 总结闭幕式																			
	09:15-10:00	**PL 11** | Roles of the Endocrinologist in facing the issue of Endocrine Disrupting Chemicals																					
	10:00-10:15	Coffee Break				Coffee Break																	
	10:15-11:00							**S 53** | Thyroid Hormone Transport and Action	**S 54** | Gene-Linked Hypogonadotropic Hypogonadism	**S 55** | The Future Treatment of Acromegaly	**S 56** | Type 1 Diabetes	**S 57** | Novel Therapies for Metabolic Diseases	**S 58** | Emerging Determinants of Obesity	**S 59** | Islet Endocrinology	**S 60** | Estradiol Production and Metabolism in Breast Cancer	**S 52** | Monogenic Endocrinopathies and Tumor Syndromes							
	11:00-11:45																						
	11:45-12:00																						
	12:00-12:30						Closing Ceremony																

Chinese Sessions | **Chinese Satellite Symposia** | **PL-Plenary Sessions** | **S-Symposia** | **MTE-Meet the Experts** | **OR-Oral Presentations**

Thursday, September 1, 2016

Plenary Hall

08:30-09:15 **Plenary Session 1: Hormones and Cancer-New Insights**

Moderator: William F. Young, *United States*

08:30-09:15
PL-01 Sex Steroid Receptor Action in Breast and Prostate Cancer: New Insights and Therapeutic Implications
Wayne Tilley, *University of Adelaide, Australia*

09:15-10:00 **Plenary Session 2: Diaomics-Diabetes and Metabolic Disorders**

Moderator: Paul M. Stewart, *United Kingdom*

09:15-10:00
PL-02 Diaomics - Diabetes and Metabolic Disorders
Guang Ning, *Shanghai Institute of Endocrine and Metabolic Diseases, China*

16:15-17:00 **Plenary Session 3: Primary Aldosteronism-Past, Present, and Future**

Moderator: Andre Lacroix, *Canada*

16:15-17:00
PL-03 Primary Aldosteronism - Past, Present and Future
John Funder, *MIMR - PHI Institute (formerly Prince Henrys Institute), Australia*

Auditorium

10:15-11:45 **S61: You Might Think you Know, But Why do we Actually Have an Obesity Pandemic?**

Moderator: Aart Jan Van der Lely, *The Netherlands*

10:15-10:45
S61-01 Epigenetic role in obesity spread around the globe
Felipe F Casanueva, *Universidad de Santiago de Compostela, Spain*

10:45-11:15
S61-02 You might think you know, but why do we actually have an obesity pandemic?
Amy Elizabeth Rothberg, *University of Michigan, United States*

11:15-11:45
S61-03 The impact of the obesity epidemic in China
Yiming Mu, *General Hospital of PLA, China*

Room 309A

10:15-11:45 S01: Subclinical Adrenal Diseases

Moderator: Brian Walker, *United Kingdom* and Xiaohui Guo, *China*

10:15-10:45
S01-01 Diagnosis and Treatment of Subclincial enlargement of the adrenal gland
Yiming Mu, *General Hospital of PLA, China*

10:45-11:15
S01-02 Subclinical cushings disease
Massimo Terzolo, *University of Turin, Italy*

11:15-11:45
S01-03 Subclinical tertiary hypoadrenalism
Rachel Crowley, *St. Vincents University Hospital, Ireland*

14:00-16:00 S11: Adrenal Insufficiency

Moderator: Olle Kämpe, *Sweden* and Guixia Wang, *China*

14:00-14:30
S11-01 Novel therapies in adrenal insufficiency
Gudmundur Johannsson, *Department of Endocrinology, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Sweden*

14:30-15:00
S11-02 Adrenal crisis
Marcus Quinkler, *Charlottenburg, Germany*

15:00-15:15
OR11-01 Prevalence, patterns and predictors of hypocortisolism, hypogonadism and thyroid dysfunction in patients with HIV infection and acquired immunodeficiency syndrome in India
Deep Dutta, *PGIMER & Dr RML Hospital, India*

15:15-15:30
OR11-02 ARMC5 mutations in Primary Bilateral Macronodular Adrenal Hyperplasia and Nonfunctional Bilateral Adrenal Nodules
Liping Yu, *Peking University First Hospital, China*

15:30-15:45
OR11-03 Validation Of Hair Cortisol Measurement By An Authomated Method. Utility As A Chronic Stress Biomarker
Bibiana Fabre, *Facultad de Farmacia y Bioquimica. Universidad de Buenos Aires, Argentina*

15:45-16:00
OR11-04 Management of glucocorticoid replacement therapy by continuous glucose monitoring in adult patients with primary and secondary adrenal insufficiency
Takuya Watanabe, *Gunma University Graduate School of Medicine, Japan*

Room 309B

10:15-11:45 S02: Adrenal Cancer

Moderator: Richard Auchus, *United States* and Weiqing Wang, *China*

10:15-10:45
S02-01 The PI3K/AKT/mTOR Signaling Pathway Is Overactivated in Primary Aldosteronism
Fukang Sun, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

10:45-11:15
S02-02 Personalized medical therapy in adrenal cancer
Felix Beuschlein, *Medizinische Klinik und Poliklinik IV, Klinikum der Universitaet Muenchen, Germany*

11:15-11:45
S02-03 Future and new therapies on adrenal cancer
Gary Hammer, *Endocrine Oncology Program, Comprehensive Cancer Center, University of Michigan, United States*

14:00-16:00 S12: Pheochromocytoma

Moderator: William F. Young, *United States* and Tianpei Hong, *China*

14:00-14:30
S12-01 Genetics of pheochromocytoma
Anne-Paule Gimenez-Roqueplo, *INSERM, France*

14:30-15:00
S12-02 Management of malignant pheochromocytoma
Zhengpei Zeng, *Peking Union Medical College Hospital, China*

15:00-15:15
OR12-01 Adrenal Venous Sampling in Patients With Positive Screening but Negative Confirmatory Testing for Primary Aldosteronism
Hironobu Umakoshi, *Clinical Research Institute, Kyoto Medical Center, National Hospital Organization, Japan*

15:15-15:30
OR12-02 The synthesis of 18-oxocortisol can be influenced by expression of CYP11B1 and CYP11B2 in aldosterone-producing adenoma.
Yuta Tezuka, *Tohoku University Hospital, Japan*

15:30-15:45
OR12-03 Clinical study of aldosterone- and cortisol-co-secreting adrenal adenoma
Lili Li, *The First Affiliated Hospital of Zhengzhou University, China*

15:45-16:00
OR12-04 Different diagnostic cut-off values of plasma catecholamines for diagnosis of pheochromocytoma in patients with adrenal masses
Yumin Chen, *West China Hospital of Sichuan University, China*

Room 310

10:15-11:45 **S03: Thyroid: From Fetal Life to Adulthood**

Moderator: Chunxia Yi, *The Netherlands* and Zhongyan Shan, *China*

10:15-10:45
S03-01 Generation of functional thyroids in a dish
Sabine Costagliola, *Université Libre Bruxelles, IRIBHM, Belgium*

10:45-11:15
S03-02 Personalized medical therapy in adrenal cancer Molecular diagnosis and treatment of congenital hypothyroidism
Heiko Krude, *University Medicine Berlin, Germany*

11:15-11:45
S03-03 Therapy of subclinical hypothyroidism
Ying Gao, *Peking University First Hospital, China*

14:00-16:00 **S13: Target therapy for Thyroid Cancer**

Moderator: Francesca Carlomagno, *Italy* and Weiping Teng, *China*

14:00-14:30
S13-01 Mechanism-based therapies for thyroid cancer
James Alexander Fagin, *Memorial Sloan Kettering Center, United States*

14:30-15:00
S13-02 TERT promoter mutations in thyroid cancer
Mingzhao Xing, *Johns Hopkins University School of Medicine, United States*

15:00-15:15
OR13-01 MiR-20b Displays Tumor Suppressor Functions in Papillary Thyroid Carcinoma by Regulating MAPK/ERK Signaling Pathway
Shubin Hong, *The first Affiliated Hospiatal of Sun Yat-Sen University, China*

15:15-15:30
OR13-02 TAZ induction directs differentiation of thyroid follicular cells from human embryonic stem cells
Risheng Ma, *Cahn School of Medicine at Mount Sinai, United States*

15:30-15:45
OR13-03 Thyroid nodule sizes influence the diagnostic performance of TI-RADS and ultrasound patterns of 2015 ATA guidelines: a multicenter retrospective study
Xiao Wu, *The First Hospital affiliated to Nanjing Medical University, China*

15:45-16:00
OR13-04 Follicular Variant of Papillary Thyroid Carcinoma: An Intermediate Clinical Entity
Tom Edward Lo, *Philippine General Hospital, Philippines*

Room 311A

10:15-11:45 **S04: Treatment of Thyroid Cancer**

Moderator: Fereidoun Azizi, *Iran* and Ka Fai Lee, *Hong Kong, China*

10:15-10:45
S04-01 Low and high dose radioiodine therapy in thyroid cancer
Hankui Lu, *Shanghai Sixth People's Hospital, China*

10:45-11:15
S04-02 Surgery
Tao Huang, *Wuhan Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, China*

11:15-11:45
S04-03 New drug - Small molecule inhibitors of mutated kinases
Francesca Carlomagno, *University of Naples Federico II, Italy*

14:00-16:00 **S14: Incidence of Thyroid Cancer**

Moderator: Josef Koehrle, *Germany* and Yan Gao, *China*

14:00-14:30
S14-01 Impact of Chernobyl and Fukushima nuclear accidents
Shunichi Yamashita, *Nagasaki University, Japan*

14:30-15:00
S14-02 Management of thyroid cancer-update
Young Kee Shong, *Asan Medical Center, Korea*

15:00-15:15
OR14-01 Ultrasound-guided percutaneous microwave ablation of benign thyroid nodules: a 12-month follow-up in 395 patients
Shuhang Xu, *Jiangsu Research Institute of Traditional Chinese Medicine, China*

15:15-15:30
OR14-02 The Circulating Epithelial Cells for Detecting Recurrent or Persistent Disease in Patients of Papillary Thyroid Carcinoma with Positive Anti-thyroglobulin Antibody
Yan-Rong Li, *Chang Gung Memorial Hospital, Linkou, Taiwan, China*

15:30-15:45
OR14-03 Clinicopathological Risk Factors Predicting Central Lymph Node Metastasis in Papillary Thyroid Microcarcinoma
Xuejia Song, *The Affiliated Hospital Of Medical College Qingdao University, China*

15:45-16:00
OR14-04 Ultrasound and TIRADS can reduce The needed number of Fine Needle Aspiration?
Sandro Augusto Goncalves Ribeiro, *Governo Estado Rondonia, Brazil*

Room 311B

10:15-11:45 **S05: Calcium Sensing Receptor - Basic Biology and Clinical Implications**

Moderator: Claudia Sedlinsky, *Argentina* and Jianmin Liu, *China*

10:15-10:45
S05-01 Calcium sensing receptor in bone-therapeutic insights
Dolores Shoback, *Univerity of California, San Francisco, United States*

10:45-11:15
S05-02 Genetics of the calcium sensing receptor signaling pathway
Rajesh Thakker, *University of Oxford, United Kingdom*

11:15-11:45
S05-03 Calcium sensing receptor beyond calcium disorders
Polina Yarova, *Cardiff University, United Kingdom*

14:00-16:00 **S15: Bone Mass and Bone Disorders in Young People**

Moderator: Peter Ebeling, *Australia* and Tjin Shing Jap, *Taiwan, China*

14:00-14:30
S15-01 Treating Osteogenesis Imperfecta
Frank Rauch, *Shriners Childrens Hospital, Montreal, Canada*

14:30-15:00
S15-02 Optimizing peak bone mass in adolescence
Qin Wang, *West China Hospital of Sichuan University, China*

15:00-15:15
OR15-01 Gene mutation spectrum and genotype-phenotype correlation in Chinese osteogenesis imperfecta patients revealed by targeted next generation sequencing
Yi Liu, *Peking Union Medical College Hospital, China*

15:15-15:30
OR15-02 Identification of a novel LEMD3 Y871X mutaiton in a three-generation family with osteopoikilosis
Ping Jin, *The Third Xiangya Hospital of Central South University, China*

15:30-15:45
OR15-03 Hip fractures in young adults: a missed opportunity for intervention
Michael Wang, *Monash University, Australia*

15:45-16:00
OR15-04 Exendin-4 protects vascular endothelial cells from advanced glycation end products-induced apoptosis through regulating autophagy flow via SIRT1/FoxO1 pathway
Xiao Wu, *The First Hospital affiliated to Nanjing Medical University, China*

Room 306

10:15-11:45 S06: Off Target Effects of Osteoporosis Therapies in Cancer

Moderator: Natalie Sims, *Australia* and Zhongjian Xie, *China*

10:15-10:45
S06-01 Anti-tumor actions of bisphosphonates
Michael Rogers, *Garvan Institute Medical Research, United Kingdom*

10:45-11:15
S06-02 Effects of vitamin D signaling in cancer
David Feldman, *Stanford University School of Medicine, United States*

11:15-11:45
S06-03 RANK Ligand signaling and giant cell tumor of bone: A model for treating benign tumors
David Thomas, *Director, The Kinghorn Cancer Centre; Head, Cancer Research Division and Laboratory Head, Genomic Ca, Australia*

14:00-16:00 S 16: Hot Topics and Bone

Moderator: Lars Rejnmark Nielsen, *Denmark* and Decai Chen, *China*

14:00-14:30
S16-01 Androgens in men - what should we know?
Christina Wang, *Clinical and Translational Science Institute, Harbor-UCLA Medicla Center, United States*

14:30-15:00
S16-02 How are messages transmitted between osteoclasts and osteoblasts?
Natalie Sims, *St. Vincent's Institute and The University of Melbourne, Australia*

15:00-15:15
OR16-01 Glucagon-like peptide-1 receptor agonist Liraglutide has anabolic bone effects in ovariectomized rats without diabetes
Nan Lu, *Renji Hospital of Shanghai Jiao Tong University School of Medicine, China*

15:15-15:30
OR16-02 The bone-preserving effects of exendin-4 in ovariectomized rats
Hanxiao Sun, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

15:30-15:45
OR16-03 Geometry Parameters and the Impact Factors of the Hip in Type 2 Diabetes Mellitus:Implications for Fracture Risk?
Shidi Hu, *The Third Hospital Affiliated to South Medical University, China*

15:45-16:00
OR16-04 The evolution of untreated hypothyroidism in adults - implications in dento-maxillary pathology
Eduard Circo, *Constanta County Hospital, Romania*

Room 307

10:15-11:45 S07: Kisspeptin Neurons: The Central Reproductive Relay

Moderator: Jon E. Levine, *United States* and Yanyun Gu, *China*

10:15-10:45
S07-01 Estrogen permits neurotransmitter signals to kisspeptin neurons
Allan Herbison, *University of Otago, New Zealand*

10:45-11:15
S07-02 In utero development of kisspeptin/GnRH circuitry
Ulrich Boehm, *University of Hamburg, Germany*

11:15-11:45
S07-03 Synchronous activation of gonadotropin-releasing hormone gene transcription and secretion by pulsatile kisspeptin stimulation
Kyungjin Kim, *Daegu Gyeongbuk Institute of Science and Technology (DGIST) and Korea Brain Research Institute (KBRI), Korea*

14:00-16:00 S17: Controversies in Testosterone Replacement

Moderator: Robert McLachlan, *Australia* and Yongde Peng, *China*

14:00-14:30
S17-01 Irrational exuberance in testosterone prescribing: When will the bubble burst?
Bradley Anawalt, *University of Washington, United States*

14:30-15:00
S17-02 Testosterone and cardiovascular risk
Mary Schooling, *University of Hong Kong, Hong Kong, China*

15:00-15:15
OR17-01 Cardiometabolic consequences of polycystic ovary syndrome; a population based cohort study with 15 years of follow up.
Fahimeh Ramezani Tehrani, *Shahid Beheshti University of Medical Sciences, Tehran, Iran*

15:15-15:30
OR17-02 Visceral fat dysfunction is positively associated with hypogonadism in Chinese men
Ningjian Wang, *Shanghai Ninth People's Hospital, China*

15:30-15:45
OR17-03 Serum Vitamin D concentration is independently associated with anti-Mullerian hormone level and obesity measures in Hong Kong Chinese women with polycystic ovary syndrome
Hang Wun Raymond Li, *The University of Hong Kong, Queen Mary Hospital, Hong Kong, China*

15:45-16:00
OR17-04 Serum GDF-8 levels change dynamically during controlled ovarian hyperstimulation in patients undergoing IVF/ICSI-ET
Lanlan Fang, *The First Affiliated Hospital of Zhengzhou University, China*

Room 301

10:15-11:45 **S08: Polycystic Ovary Syndrome**

Moderator: Constance Chik, *Canada* and Jie Hong, *China*

10:15-10:45
S08-01 Family-based analysis of eight susceptibility loci in polycystic ovary syndrome
Zijiang Chen, *Center of Reproductive Medicine, Shandong University, China*

10:45-11:15
S08-02 Pubertal origins of PCOS
John Marshall, *Center for Research in Reproduction, Div Endocrinology, Dept Medicine. University of Virginia, United States*

11:15-11:45
S08-03 Metabolic risk in PCOS: Phenotype and adiposity impact
Helena Teede, *Monash University, Australia*

14:00-16:00 **S18: Novel Endometrial Signaling Pathway and Fertility**

Moderator: Teresa Woodruff, *United States* and Fen-Yu Tseng, *Taiwan, China*

14:00-14:30
S18-01 Altered notch signaling contributes to progesterone resistance in the utopic and ectopic endometrium
Asgi T. Fazleabas, *Department of Obstetrics, Gynecology & Reproductive Biology Michigan State University, United States*

14:30-15:00
S18-02 AKT pathway in uterine diseases
Ji-Yong Julie Kim, *Northwestern University, United States*

15:00-15:15
OR18-01 The effect of thyroid hormone on the expression of kisspeptin in hypothalamus and its related mechanisms
Junping Wen, *Fujian Provincial Hospital, China*

15:15-15:30
OR18-02 Outcome of in vitro fertilization in women with subclinical hypothyroidism
Yunying Cai, *The first people's Hospital of Yunnan Province, China*

15:30-15:45
OR18-03 The analysis of the changes of maternal thyroid autoantibodies during early pregnancy
Xiaoguang Shi, *First Affiliated Hospital of China Medical University, China*

15:45-16:00
OR18-04 Effect of mild hypothyroidism identified in 4-8 weeks on pregnancy outcome
Yan Li, *First Affiliated Hospital of China Medical University, China*

Room 302

10:15-11:45 **S09: Understanding Growth**

Moderator: Kok-Onn Lee, *Singapore* and Xueyan Wu, *China*

10:15-10:45
S09-01 Daqing children study: What makes children grow fat?
Yanyan Chen, *Fu Wai Hospital, China*

10:45-11:15
S09-02 Genes and short stature
Gerhard Binder, *University Childrens Hospital, Germany*

11:15-11:45
S09-03 Epigenetics and fetal growth
Jie Qiao, *Peking University Third Hospital, China*

14:00-16:00 **S19: New Treatment for Lipid Disorders**

Moderator: Paolo Pozzilli, *Italy* and Karen Lam, *Hong Kong, China*

14:00-14:30
S19-01 New treatment for diabetic dyslipidemia
Jianping Weng, *The Third Hospital Affiliated to Sun Yat-Sen University, China*

14:30-15:00
S19-02 HDL functionality - Coming of age?
Kathryn Tan, *University of Hong Kong, Hong Kong, China*

15:00-15:15
OR19-01 Adipocyte SIRT1 deletion impaired endothelial function via reducing brown fat phenotype in perivascular adipose tissue
Ping Gu, *Nanjing General Hospital of Nanjing Military Area Command, China*

15:15-15:30
OR19-02 TSH increases synthesis of hepatic ATP-binding cassette subfamily A member 1 in hypercholesterolemia
Tiantian Zhang, *Shandong Province Hospital, China*

15:30-15:45
OR19-03 The impact of thyroid-stimulating hormone and fasting insulin level on lipid profiles and serum PCSK9 concentration in euthyroid subjects: a population-based cross-sectional study
Yingyun Gong, *the First Affiliated Hospital of Nanjing Medical University, China*

15:45-16:00
OR19-04 Potential Harmful Correlation Between Homocysteine and Low-density Lipoprotein Cholesterol in Patients with Hypothyroidism
Xuejie Dong, *Beijing Chaoyang Hospital, China*

Room 303

10:15-11:45 S10: The Gut Nutrient Sensing in Energy Metabolism

Moderator: Yoshihiro Ogawa, *Japan* and Xin Gao, *China*

10:15-10:45

S10-01 Gut lipid sensing and energy homeostasis
Tony Lam, *University Health Network, Canada*

10:45-11:15

S10-02 Intestinal taste receptors and gut hormone signalling
Inge Depoortere, *University of Leuven, Belgium*

11:15-11:45

S10-03 Control of GIP secretion
Nobuya Inagaki, *Kyoto University, Japan*

Room 402A

09:00-10:00 and 14:00-15:00

MTE01 Management of craniopharyngioma
Hermann L Müller, *Klinikum Oldenburg, Medical Campus University Oldenburg, Germany*

11:00-12:00 and 16:15-17:15

MTE07 Primary hyperaldosteronism
Fumitoshi Satoh, *Tohoku University Graduate School of Medicine, Japan*

Room 402B

09:00-10:00 and 14:00-15:00

MTE02 Clinical usefulness of TSH receptor antibody measurement
Eijun Nishihara, *Kuma Hospital, Center for Excellence in Thyroid Care, Japan*

11:00-12:00 and 16:15-17:15

MTE08 Clinical management of thyroid nodules
Shih-Ming Huang, *Medical College and Hospital, National Cheng-Kung University Tainan, Taiwan, China*

Room 403

09:00-10:00 and 14:00-15:00

MTE03 Vitaman D is a multifunctional hormone
Roger Bouillon, *KU Leuven, Belgium*

11:00-12:00 and 16:15-17:15

MTE09 Managing Osteoporosis in under-served clinical groups, including those transitioning to adult care
Frances Milat, *Hudson Institute of Medical Research, Australia*

Room 405

09:00-10:00 and 14:00-15:00

MTE04 Premature ovarian insufficiency
Jie Wu, *The First Hospital affiliated to Nanjing Medical University, China*

11:00-12:00 and 16:15-17:15

MTE10 Genetics of hypothalamic-pituitary-gonadal function
Stephanie Seminara, *Harvard, United States*

Room 406

09:00-10:00 and 14:00-15:00

MTE05 New genes in pituitary tumor and implications for management
Marta Korbonits, *Barts and the London School of Medicine, United Kingdom*

11:00-12:00 and 16:15-17:15

MTE11 Insulin Pump
Tomoyuki Kawamura, *Osaka City University Graduate School of Medicine, Japan*

Room 407

09:00-10:00 and 14:00-15:00

MTE06 Optimizing treatment for congenital adrenal
Richard Auchus, *University of Michigan, United States*

11:00-12:00 and 16:15-17:15

MTE12 Acromegaly
Christof Schofl, *Division of Endocrinology and Diabetes, Department of medicine I, University Hospital Erlangen, Frei, Germany*

Friday, September 2, 2016

Plenary Hall

08:30-09:15 **Plenary Session 4: Iodine and Thyroid Disorders in China**

Moderator: Takashi Akamizu, *Japan*

08:30-09:15
PL-04 Iodine and Thyroid Disorders in China
Weiping Teng, *Institute of Endocrine Research, China Medical University, China*

09:15-10:00 **Plenary Session 5: Cell Signaling in Insulin Secretion and its Clinical Implications**

Moderator: Leon Bach, *Australia*

09:15-10:00
PL-05 Cell signaling in insulin secretion and its clinical implications
Susumu Seino, *Division of Molecular and Metabolic Medicine Kobe University Graduate School of Medicine, Japan*

16:15-17:00 **Plenary Session 6: Mechanisms of Thyroid Hormone Action During Skeletal Development and Bone Maintenance**

Moderator: Janet Schlechte, *United States*

16:15-17:00
PL-06 Mechanisms of thyroid hormone action during skeletal development and bone maintenance
Graham R. Williams, *Imperial College London, United Kingdom*

Auditorium

10:15-11:45 **S20: Pituitary Tumorigenesis**

Moderator: Hermann L Muller, *Germany* and Hongwei Gao, *China*

10:15-10:45
S20-01 Natural history of non-functional pituitary adenoma
Warrick Inder, *Princess Alexandra Hospital, Australia*

10:45-11:15
S20-02 Differentiation of pluripotent stem cells into hypothalamic and pituitary cells
Hidetaka Suga, *Nagoya University Graduate School of Medicine, Japan*

11:15-11:45
S20-03 Insights from Molecular Pathology
Sylvia L Asa, *University Health Network, University of Toronto, Canada*

14:00-16:00 S30: Bioinformatics Meets Acromegaly: Insight from Registries

Moderator: Paul M. Stewart, *United Kingdom* and Hong-Da Lin, *Taiwan, China*

14:00-14:30
S30-01 Acromegaly registry, the Taiwanise experience
Fen-Yu Tseng, *National Taiwan University Hospital, Taiwan, China*

14:30-15:00
S30-02 Acromegaly registry, lessons learned in Germany
Christof Schofl, *Division of Endocrinology and Diabetes, Department of medicine I, University Hospital Erlangen, Frei, Germany*

15:00-15:15
OR30-01 Effect of Autologous Marrow Stem Cell Transplantation on Patients with Diabetic Peripheral Neuropathy
Dexue Liu, *The First Affiliated Hospital of Nanyang Medical College, China*

15:15-15:30
OR30-02 Regulation of vascular BK channels by Nrf2 signaling in diabetes mellitus
Hon-Chi Lee, *Mayo Clinic, United States*

15:30-15:45
OR30-03 Growth hormone therapy benefits pituitary stalk interruption syndrome patients with short stature: a retrospective study of 75 Han Chinese
Cheng Wang, *General Hospital of PLA, China*

15:45-16:00
OR30-04 The impact of cancer on the survival of acromegaly in Taiwan
Jen-der Lin, *Chang Gung Memorial Hospital, Linkou, Taiwan, China*

Room 309A

10:15-11:45 S21: Primary Aldosteronism

Moderator: Fumitoshi Satoh, *Japan* and Anli Tong, *China*

10:15-10:45
S21-01 New genes for a 50-year old disease
Maria-Christina Zennaro, *Paris Cardiovascular Research Center, Paris, France*

10:45-11:15
S21-02 Prevalence and risk factors for primary aldosteronism
Weiqing Wang, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

11:15-11:45
S21-03 Implications for essential hypertension
Richard Auchus, *University of Michigan, United States*

14:00-16:00 **S31: Thyroid Hormone Derivatives**

Moderator: Josef Koehrle, *Germany* and Haipeng Xiao, *China*

14:00-14:30
S31-01 3, 5-Diiodothyronine treatment: Risk an benefit
Denise Pires de Carvalho, *Institute of Biophysics Carlos Chagas Filho Federal University of Rio De Janeiro, Brazil*

14:30-15:00
S31-02 Biosynthesis and action of thyronamines
Carolin Hoefig, *Charité University Hospital Berlin, Germany*

15:00-15:15
OR31-01 Free thyroxin variations is associated with incident metabolic syndrome in adults, Tehran Thyroid Study
Ladan Mehran, *Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Iran*

15:15-15:30
OR31-02 Study on thyroid function and metabolism changes of Wistar rats during long-term partial sleep deprivation
Han Liang, *Tianjin Medical University, China*

15:30-15:45
OR31-03 The analysis of the causes of maternal thyroid dysfunction during early pregnancy
Cheng Han, *First Affiliated Hospital of China Medical University, China*

15:45-16:00
OR31-04 Gestation-specific changes in maternal thyroglobulin during pregnancy and lactation in an iodine-sufficient region in China: A longitudinal study
Xiaowen Zhang, *First Affiliated Hospital of China Medical University, China*

Room 309B

10:15-11:45 **S22: Graves Orbitopathy**

Moderator: Josef Kohrle, *Germany* and Jiajun Zhao, *China*

10:15-10:45
S22-01 Clinical management of GO patients: Experiences from EUGOGO
Willem M. Wiersinga, *Academic Medical Center, University of Amsterdam, The Netherlands*

10:45-11:15
S22-02 Novel approaches in detection of auto-antibodies in GO
Lutz Schomburg, *Charite Berlin, Germany*

11:15-11:45
S22-03 Therapy of Graves Orbitopathy
Simon Pearce, *Newcastle University, United Kingdom*

14:00-16:00 S32: Endocrine Signaling in Phosphate Metabolism-Role of FGF23

Moderator: Rajesh Thakker, *United Kingdom* and Junqing Zhang, *China*

14:00-14:30
S32-01 FGF23, bone and mineral metabolism
Seiji Fukumoto, *Tokushima University, Japan*

14:30-15:00
S32-02 Tumor induced osteomalacia
Weibo Xia, *Peking Union Medical College Hospital, China*

15:00-15:15
OR32-01 Two PHEX gene mutations identified in two Chinese X-linked hypophosphatemic rickets pedigrees
Ranran Shi, *Shandong Provincial Hospital, China*

15:15-15:30
OR32-02 FGF23 mediated hypophosphatemic osteomalacia due to multiple iron infusions
Elissa McNamara, *Eastern Health, Australia*

15:30-15:45
OR32-03 The relationship between 25(OH)D, FGF23 levels with bone metabolism in patients with Graves' disease
Zhongshu Ma, *General Hospital of Tianjin Medical University, China*

15:45-16:00
OR32-04 Interleukin-6 Gene Knockout Antagonizes High Fat -Induced Trabecular Bone Loss
Chunyu Wang, *West China Hospital of Sichuan University, China*

Room 310

10:15-11:45 S23: Hypothalamus and Energy Homeostasis

Moderator: Jon E. Levine, *United States* and Weijun Gu, *China*

10:15-10:45
S23-01 Hypothalamic inflammation in obesity and diabetes
Chunxia Yi, *Academic Medical Center (AMC), University of Amsterdam (UvA), The Netherlands*

10:45-11:15
S23-02 TRH neurons as metabolic/stress integrators
Patricia Joseph-Bravo, *Universidad Nacional Autonoma de Mexico, Mexico*

11:15-11:45
S23-03 Hunger-driving hypothalamic circuits
Kevin Williams, *The University of Texas Southwestern Medical Center, United States*

14:00-16:00 **S33: Parathyroid Disorders-An Update**

Moderator: Maria Luisa Brandi, *Italy* and Jianming Ba, *China*

14:00-14:30
S33-01 Guildelines for the treatments of hypoparathyrodism in adults
Lars Rejnmark Nielsen, *Aarhus University, Denmark*

14:30-15:00
S33-02 Whats new in primary hyperparathyroidism?
John Bilezikian, *College of Physicians & Surgeons, Colombia University, United States*

15:00-15:15
OR33-01 Accelerometer-derived Vigorous Physical Activity is associated with Higher Hip Bone Mineral Density in Community-Dwelling Older Adults
Lachlan McMillan, *Monash University, Australia*

15:15-15:30
OR33-02 Significantly negative correlation between vasculopathy and bone mineral density in T2DM
Ni Zhong, *Department of Endocrinolgy and Metabolism, Shanghai Tenth People's Hospital, Tongji University School of Medicine, China*

15:30-15:45
OR33-03 Is waist circumference an independent risk factor of vertebral fracture? Results from REACTION study
Gang Chen, *Fujian Provincial Hospital, China*

15:45-16:00
OR33-04 The chloride/phosphate ratio combined with alkaline phosphatase as a valuable predictive marker for primary hyperparathyroidism in Chinese individuals
Li Wei, *Shanghai Sixth People's Hospital, China*

Room 311A

10:15-11:45 **S24: Diabetes and Bone**

Moderator: Dolores Shoback, *United States* and Yuxiu Li, *China*

10:15-10:45
S24-01 Assessing fracture risk in diabetes
Ann Schwartz, *University of California, San Francisco, United States*

10:45-11:15
S24-02 Effects of advanced glycation products on bone
Antonio Desmond McCarthy, *Laboratorio de Osteopatias y Metabolismo Mineral (LIOMM) Universidad Nacional de La Plata - Argentina, Argentina*

11:15-11:45
S24-03 Effect of diabetes drugs on bone metabolism
Lorenz Hofbauer, *Diabetes and Metabolic Bone Diseases Technical University of Dresden , Germany*

14:00-16:00 S34: Hormonal Determinants of Human Embryo Implantation

Moderator: Asgi T. Fazleabas, *United States* and William Shu Biu Yeung, *Hong Kong, China*

14:00-14:30
S34-01 Control of human trophoblast invasion by activin
Peter CK Leung, *University of British Colombia, Canada*

14:30-15:00
S34-02 Molecular and hormonal regulation of embryo distribution and location during early pregnancy
Enkui Duan, *Institute of Zoology of Chinese Academy of Sciences, China*

15:00-15:15
OR34-01 Neonatal thyrotropin concentration and iodine nutrition status of mothers: A systematic review and meta-analysis
PANTEA NAZERIKAHGANI, *Research Institute for Endocrine Sciences, Iran*

15:15-15:30
OR34-02 Placental 11β-HSD2 and cord plasma cortisol levels, metabolic and cardiovascular health indices in infants
Lu Chen, *Xinhua Hospital Affiliated to Shanghai Jiaotong University Medicine School, China*

15:30-15:45
OR34-03 Levothyroxine Treatment in pregnant women with autoimmune thyroid disease: prenatal and neonatal outcomes.
Fahimeh Ramezani Tehrani, *Shahid Beheshti University of Medical Sciences, Tehran, Iran*

15:45-16:00
OR34-04 Maternal Hypothyroxinemia induces Autism in Rat Offspring by Inhibition of mTOR Signaling Pathway
Aihua Liu, *First Affiliated Hospital of China Medical University, China*

Room 311B

10:15-11:45 S25: Vitamin D - Myths and Facts

Moderator: Roger Bouillon, *Belgium* and Mei Zhu, *China*

10:15-10:45
S25-01 Vitamin D status and disease risk: results from observational studies
Robert Scragg, *University of Auckland, New Zealand*

10:45-11:15
S25-02 Does vitamin D treatment improve health outcomes - data from trials
Rolf Jorde, *University Hospital of North Norway, Norway*

11:15-11:45
S25-03 Reconciling observational studies of vitamin D with randomized control trials - Why the Difference?
Kevin Cashman, *University College Cork, Ireland*

14:00-16:00 **S35: GHRH, Growth Hormone and IGF Throughout Life**

Moderator: Peter Trainer, *United Kingdom* and Jiajun Zhao, *China*

14:00-14:30
S35-01 GHRH throughout life
Aart Jan van der Lely, *Erasmus University MC, The Netherlands*

14:30-15:00
S35-02 Growth hormone throughout life
Jens Otto Lunde Jorgensen, *Aarhus University Hospital, Denmark*

15:00-15:15
OR35-01 Genetic determinants of Growth Hormone and GH-related phenotypes
Erik Hallengren, *Lund University, Sweden*

15:15-15:30
OR35-02 A hybrid Fc-fused human growth hormone, GX-H9, shows a potential for semi-monthly administration in clinical studies
Eun Jig Lee, *Yonsei University, Korea*

15:30-15:45
OR35-03 Causes of sex differences in fetal growth and insulin sensitivity
Danli Zhang, *Xinhua Hospital Affiliated sto Shanghai Jiaotong University Medicine School, China*

15:45-16:00
OR35-04 Effect of GH treatment on coagulation parameters in children with growth hormone deficiency
Feneli Karachaliou, *P & A Kyriakou Childrens Hospital, Greece*

Room 306

09:15-17:00 **S62: Federation of International Nurses in Endocrinology Symposium Program**

Moderator: Yingxia Zhou, *China*, Christine Yedinak, *United States* and Phillip Yeoh, *United Kingdom*

09:15-09:45
S62-01 Collaborative care of T2D compared with usual care at community and hospital: A pilot study in Shanghai
Yingxia Zhou, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

09:45-10:15
S62-02 Pre and Post-Operative Pheochromocytoma/paraganglioma
Karen Adams, *National Institutes of Health, United States*

10:30-11:00
S62-03 Crunchie or violet crumble: What's diabetes got to do with bone health? Diabetes and osteoporosis
Ann Robinson, *Gold Coast Health, Australia*

11:00-11:30
S62-04 Strategies to help Vietnamese patients with diabetes to overcome barriers to self-care
Dang Tran Ngoc Thanh, *Vietnam*

11:30-12:00
S62-05 Western approach of the home care educational program for patients with Acromegaly: crucial role of the nurse for improved patient satisfaction and adherence to the therapy
Els Rutten, *University Hospital of Ghent, Belgium*

12:45-13:15
S62-06 Nurses role and impact in diagnosis and management of adrenal insufficiency
Lisa Shepherd, *Heart of England NHS Foundation Trust, United Kingdom*

13:15-13:45
S62-07 Competency Framework for Adult Endocrine Nursing: How is it developed & put to use in clinical setting
Phillip Yeoh, *The london Clinic, United Kingdom*

13:45-14:15
S62-08 The Insulin Tolerance Test – A New Angle on How to Improve Safety
Julie Hetherington, *Royal Prince Alfred Hospital Sydney, Australia*

14:15-14:45
S62-09 The Education of Paediatric Endocrine Nurses / Advanced level Practice in the UK
Kate Davies, *London South Bank University, United Kingdom*

14:45-15:15
S62-10 Persistent Obesity and Diabetes, hypertension and Sleep dysfunction after Treatment for Cushing's Disease
Christine Yedinak, *Oregon Health & Sciences University, United States*

15:15-16:30 Panel Discussion: Competency Framework for Adult Endocrine Nurses and Advanced level Practice
Moderator: Christine Yedinak, Phillip Yeoh
Panel Discussion: Yingxia Zhou, Lisa Shepherd, Ann Robinson, Dang Tran Ngoc Thanh, Karen Adams

Room 307

10:15-11:45 S26: Neuroestrogens and Brain Function
Moderator: Margaret McCarthy, *United States* and Tien-Shang Huang, *Taiwan, China*

10:15-11:00
S26-01 Estrogen rapidly modulates spinogenesis in the hippocampus
Suguru Kawato, *University of Tokyo, Japan*

11:00-11:45
S26-02 Neuroestrogens and the regulation of GnRH release
Ei Terasawa, *University of Wisconsin-Madison, Japan*

Room 301

10:15-11:45 S27: The Timing of Puberty: Neuroendocrine and Genetic Factors

Moderator: Oscar Bruno, *Argentina* and Yiming Mu, *China*

10:15-10:45
S27-01 Upstream regulators of GnRH in the control of puberty: Kisspeptin and beyond
Ursula Kaiser, *Brigham and Women's Hospital, United States*

10:45-11:15
S27-02 Using Genetic Approaches in a Rare Human Disease Model to Define the Neuroendocrine Control of Human Reproduction
Stephanie Seminara, *Harvard, United States*

11:15-11:45
S27-03 MicroRNAs, GnRH release, and GnRH neuronal development
Vincent Prévot, *Inserm, University of Lille, France*

Room 302

10:15-11:45 S28: Prolactin: Whats New?

Moderator: Maria Fleseriu, *United States* and Jianling Du, *China*

10:15-10:45
S28-01 Prolactin and Cancer
Vincent Goffin, *University Paris Descartes and Inserm U1151, Belgium*

10:45-11:15
S28-02 Prolactinomas and MEN1
Marta Heckenast Korbonits, *Barts and the London School of Medicine, United Kingdom*

11:15-11:45
S28-03 Treatment of prolactinomas: Whats new?
Xueyan Wu, *Peking Union Medical College Hospital, China*

Room 303

10:15-11:45 S29: Diabetic Complications

Moderator: Urd Kielgast, *Denmark* and Weiping Jia, *China*

10:15-10:45
S29-01 Epigenetics in metabolic kidney disease
Hiroshi Itoh, *Keio University School of Medicine, Japan*

10:45-11:15

S29-02 Insulin Pump therapy and cardiovascular mortality
Isabelle Isa Kristin Steineck, *Department of Endocrinology Copenhagen University, Hvidovre Hospital, Sweden*

11:15-11:45

S29-03 Rising tide of early onset diabetes in Asia — Clinical pathophysiological and etiological characteristics and management challenges
Linong Ji, *People's Hospital of Peking University, China*

Room 402A

09:00-10:00 and 14:00-15:00

MTE13 Primary adrenal insufficiency
Marcus Quinkler, *Charlottenburg, Germany*

11:00-12:00 and 16:15-17:15

MTE18 Osteoporosis in men
Benjamin Leder, *Mass General Hospital, Havard University, United States*

Room 402B

09:00-10:00 and 14:00-15:00

MTE14 Thyroid disease in elderly patients: What to do and what to avoid
Kristien Boelaert, *University of Birmingham, United Kingdom*

11:00-12:00 and 16:15-17:15

MTE19 Testosterone replacement therapy
Bradley Anawalt, *University of Washington, United States*

Room 403

09:00-10:00 and 14:00-15:00

MTE15 Managing osteoporosis in post menopausal women
Michael Roy McClung, *Oregon Osteoporosis Center, United States*

11:00-12:00 and 16:15-17:15

MTE20 Approach to the patient with relapse hyperthyrodism after previous ATD therapy: How useful are anti-thyroid drugs?
Bingyin Shi, *The First affiliated Hospital of Xian Jiaotong University, China*

Room 405

09:00-10:00 and 14:00-15:00

MTE16 Dopamine agonists: When to use, what to choose and safety issues
Johannes A. Romijn, *University of Amsterdam, The Netherlands*

11:00-12:00 and 16:15-17:15

MTE21 Cushing's syndrome
Lynnette Kaye Nieman, *NIH, United States*

Room 406

09:00-10:00 and 14:00-15:00

MTE17 Preservation of fertility in cancer patients
Teresa Woodruff, *Northwestern University, United States*

11:00-12:00 and 16:15-17:15

MTE22 Treatment of type 1 diabetes at diagnosis and during remission
Paolo Pozzilli, *University Campus Bio-Medico, Italy*

Saturday, September 3, 2016

Plenary Hall

08:30-09:15 **Plenary Session 7: Genetic strategies to understand physiological pathways regulating body weight**

Moderator: Guang Ning, *China*

08:30-09:15
PL-07 Genetic Strategies to Understand Physiological Pathways Regulating Body Weight
Sedaf Farooqi, *University of Cambridge, United Kingdom*

09:15-10:00 **Plenary Session 8: Surprising Origins of Sex Differences in the Brain**

Moderator: Margaret Shupnik Barrett, *United States*

09:15-10:00
PL-08 Surprising Origins of Sex Differences in the Brain
Margaret McCarthy, *Department of Pharmacology, Program in Neuroscience and Program in Molecular Medicine, University of Maryland School of Medicine, United States*

16:15-17:00 **Plenary Session 9: Nuclear Receptors and Development: From Drugs to Embryos and Back Again**

Moderator: Emanuel Christ, *Switzerland*

16:15-17:00
PL-09 Nuclear Receptors and Development: From Drugs to Embryos and Back Again
Vincent Laudet, *Observatoire Oceanologique de Banyuls-sur-Mer / UPMC, France*

Auditorium

10:15-11:45 **S63: Practical Publishing Advice**

Moderator: William F. Young, *United States*

10:15-10:45
S63-01 How to publish your paper
Leonard Wartofsky, *Endocrine Society, United States*

10:45-11:15
S63-02 Publishing ethics
Sof Andrikopoulos, *Australia*

11:15-11:45
S63-03 Responding to reviewer comments
Josef Köehrle, *Charite-Universitaetsmedizin Berlin, Germany*

Room 309A

10:15-11:45 S36: Growth After Cancer Treatment

Moderator: Jens Otto Lunde *Jorgensen*, Denmark and Chao Liu, *China*

10:15-10:45
S36-01 Growth hormone for short stature after cancer treatment
Xiaoping Luo, *Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, China*

10:45-11:15
S36-02 Is growth hormone safe in cancer treated patients?
Ron Rosenfeld, *Oregon Health & Science University, United States*

11:15-11:45
S36-03 Delayed effects of Cancer Treatment
Stephen Shalet, *Christie Hospital, United Kingdom*

14:00-16:00 S43: Cortisol, Pulsatility and Clocks

Moderator: Marcus Quinkler, *Germany* and Jingtao Dou, *China*

14:00-14:30
S43-01 The importance of glucocorticoid pulsatility for stress sensitivity and synaptic plasticity
Angela Sarabdjitsingh, *Brain Center Rudolf Magnus, University Medical Center Utrecht, The Netherlands*

14:30-15:00
S43-02 Interaction of clock stress systems: implications for metabolism
Henrik Oster, *University of Lübeck, Germany*

15:00-15:15
OR43-01 Rock around the choroid plexus clock
Telma Quintela, *Health Sciences Research Centre - CICS - UBI, Portugal*

15:15-15:30
OR43-02 The Effects of Maternal Protein Restriction and Postweaning High-fat Feeding on Offspring Metabolic Health and POMC Gene Methylation
Jia Zheng, *Peking Union Medical College Hospital, China*

15:30-15:45
OR43-03 Anti-inflammatory role of estrogen in the hippocampus: regulation of inflammasome complex via PELP1
Roshni Thakkar, *Augusta University, India*

15:45-16:00
OR43-04 Characterisation of a novel species-restricted putative hydroxysteroid dehydrogenase called HSD1L in the pituitary-gonadal axis
Timothy James Cole, *Monash University, Australia*

Room 309B

10:15-11:45 S37: Cardio-Metabolic Effects of Corticosteroids

Moderator: Massimo Terzolo, *Italy* and Zhengpei Zeng, *China*

10:15-10:45
S37-01 Glucocorticoids, fat and bone
Mark Cooper, *University of Sydney, Australia*

10:45-11:15
S37-02 Effect of tissue-specific glucocorticoid action on cardiovascular and metabolic disease
Brian Walker, *Centre for Cardiovascular Science, University of Edinburgh, United Kingdom*

11:15-11:45
S37-03 The cardiomyocyte mineralocorticoid receptor as a mediator of cardiac fibrosis
Morag Young, *Hudson Institute of Medical Research, Australia*

14:00-16:00 S44: Emerging Therapeutic Potential of FGF21

Moderator: Karen Lam, *Hong Kong, China* and Guang Ning, *China*

14:00-14:30
S44-01 Clinical aspects of FGF21
Weiping Jia, *Shanghai Sixth People's Hospital, China*

14:30-15:00
S44-02 FGF21 and atherosclerosis
Aimin Xu, *University of Hong Kong, Hong Kong, China*

15:00-15:15
OR44-01 The Predictive Role of Serum High-Sensitivity C-Reactive Protein in Nephropathy Development and Progression among Chinese patients with Type 2 Diabetes
Chi Ho Lee, *University of Hong Kong, Hong Kong, China*

15:15-15:30
OR44-02 1Gestational diabetes mellitus predicts abnormal glucose metabolism in the majority at long term follow up
Jeanette Wahlberg, *Linkoping University, Linkoping, Sweden*

15:30-15:45
OR44-03 Human adipose tissue-derived mesenchymal stem cells facilitate white adipose tissue browning and limit obesity via the activation of M2 macrophages
Zongyan Xie, *General Hospital of PLA, China*

15:45-16:00
OR44-04 The role of established obesity-related loci in Chinese pediatric leptin levels highlights a neuronal influence on body weight regulation
Junling Fu, *Peking Union Medical College Hospital, China*

Room 310

10:15-11:45 S38: Thyroid and Pregnancy

Moderator: Kristien Boelaert, *United Kingdom* and Haixia Guan, *China*

10:15-10:45
S38-01 Gestational thyroid function and offspring brain development: clinical evidence on cognition and behavior
Tim Korevaar, *Erasmus University Medical Center, The Netherlands*

10:45-11:15
S38-02 Impact of trace element status on pregnancy outcome
Zhongyan Shan, *First Affiliated Hospital of China Medical University, China*

11:15-11:45
S38-03 Management of anti thyroid drug therapy in pregnancy
Fereidoun Azizi, *Shahid Beheshti University of Medical Sciences, Iran*

14:00-16:00 S45: Cushing: Genetic to Clinical

Moderator: Lynnette Nieman, *United States* and Guangwei Li, *China*

14:00-14:30
S45-01 New genes for the adrenal cushing syndrome
Felix Beuschlein, *Medizinische Klinik und Poliklinik IV, Klinikum der Universitaet Muenchen, Germany*

14:30-15:00
S45-02 ACTH independent cushing syndrome: Potential therapeutic targets
Yanan Cao, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

15:00-15:15
OR45-01 Serum cortisol and the risk of osteoporosis in nigerians on medroxyprogesterone acetate
Olayiwola Akanji Popoola, *Achievers University, Nigeria*

15:15-15:30
OR45-02 IKKε/TBK1 inhibitor amlexanox induced nephrotic diabetes insipidus by decreasing AQP2 and VR2 expression in kidney
Qian He, *The People Affiliated Hospital, Three Gorges University, China*

15:30-15:45
OR45-03 Monthly pasireotide LAR reduces urinary free cortisol (UFC) and provides clinical benefit in patients with Cushing's disease: a 12-month, randomized, multicenter, Phase III study
Feng Gu, *Peking Union Medical College Hospital, Beijing, China,*

15:45-16:00
OR45-04 Ectopic corticotropin-releasing hormone (CRH)syndrom from Medullary Thyroid Carcinoma
Jianping Xu, *Peking Union Medical College Hospital, China*

Room 311A

10:15-11:45 S39: TSH Receptor

Moderator: Sabine Costagliola, *Belgium* and Qing Su, *China*

10:15-11:00
S39-01 Small molecule drugs targeting TSH receptor
Gerd Krause, *Leibniz-Institut fuer molekulare Pharmakologie, Germany*

11:00-11:45
S39-02 TSH and lipid metabolism
Jiajun Zhao, *Shandong Provincial Hospital, China*

14:00-16:00 S46: Hypopituitarism

Moderator: Gudmundur Johannsson, *Sweden* and Tingwei Su, *China*

14:00-14:30
S46-01 Rare causes of hypopituitarism, ipilimumab, drugs and snake bites
Paula Bruna Mattos Coelho Araujo, *Diagnosticos da America S.A. (DASA) and Universidade Federal do Rio de Janeiro (UFRJ), Brazil*

14:30-15:00
S46-02 Update on trauma and hypopituitarism
Marianne Christina Klose, *Copenhagen University Hospital, Denmark*

15:00-15:15
OR46-01 Somavaratan (VRS-317) Treatment for Pediatric Growth Hormone Deficiency (GHD): Results at 2 Years (NCT02068521)
George Bright, *Versartis, Inc., Canada*

15:15-15:30
OR46-02 Treatment Adherence with Weekly, Twice-Monthly and Monthly Dosing of Somavaratan (VRS-317), a Long-Acting Growth Hormone Treatment for Children with Growth Hormone Deficiency (GHD), After 18 Months of At-Home Dosing
Eric Humphriss, *Versartis, Inc., United States*

15:30-15:45
OR46-03 HbA1c over Two Years of Treatment with Somavaratan (VRS-317) in Children with Growth Hormone Deficiency (GHD)
Will Charlton, *Versartis, Inc.,Canada*

15:45-16:00
OR46-04 Compound mutations in pituitary-related pathways are engaged in pituitary stalk interruption syndrome: A whole exome sequencing study of Han Chinese
Qinghua Guo, *General Hospital of PLA, China*

Room 311B

10:15-11:45 S40: Osteoporosis Therapies - What is on the Horizon?

Moderator: Nor Azmi Bin Kamaruddin, *Malaysia* and Weibo Xia, *China*

10:15-10:45
S40-01 Cathepsin K inhibition and fracture reduction
Bente L Langdahl, *Aarhus University Hospital, Denmark*

10:45-11:15
S40-02 Inhibition of sclerostin and effects on bone
Michael Roy McClung, *Oregon Osteoporosis Center, United States*

11:15-11:45
S40-03 Novel PTH/PTHrP based anabolic approaches to the treatment of PMO
Benjamin Leder, *Mass General Hospital, Havard University, United States*

14:00-16:00 S47: Endocrine Related Cancer

Moderator: James Fagin, *United States* and Brian Lang, *Hong Kong, China*

14:00-14:30
S47-01 Bone Marrow Cancers and Bone Health
Matthew Drake, *Mayo Clinic, United States*

14:30-15:00
S47-02 Prostate cancer: How can we treat therapy-resistant tumours?
Gail Risbridger, *Monash University, Australia*

15:00-15:15
OR47-01 A new therapeutic strategy to enhance radioiodide uptake into breast cancer cells
Vikki Poole, *University of Birmingham, United States*

15:15-15:30
OR47-02 The epigenome landscape of prostate cancer stroma reinforces the pro-tumourigenic actions of estrogen receptor α
Mitchell Lawrence, *Monash University, Australia*

15:30-15:45
OR47-03 The dual inhibition of RNA Pol I transcription and PIM kinase as a new therapeutic approach to treat advanced prostate cancer
Luc Furic, *Monash University, Australia*

15:45-16:00
OR47-04 Transcriptome profiling of single prostate cancer cells in the castrate setting
Ashlee Clark, *Monash University, Australia*

Room 306

10:15-11:45 S41: Interactions of Bone and Muscle with Aging

Moderator: Matthew Drake, *United States* and Lulu Chen, *China*

10:15-10:45
S41-01 Defining and managing sarcopenia in 2016
Roger Fielding, *Tufts University, United States*

10:45-11:15
S41-02 Sarcopenia and mortality
Ching-Lung Cheung, *Hong Kong University, Hong Kong, China*

11:15-11:45
S41-03 Obesity and sarcopenia role of intra- and inter-muscular adipose tissue (IMAT)
David Scott, *Monash University, Australia*

14:00-16:00 S48: Biology of Aging: Therapeutic Implications

Moderator: Leon Bach, *Australia* and Qifu Li, *China*

14:00-14:30
S48-01 Hormones and aging
Andrew Hoffman, *Stanford University, United States*

14:30-15:00
S48-02 Mitochondrial function and Aging
Pinchas Cohen, *University of Southern California, Leonard Davis School of Gerontology, United States*

15:00-15:15
OR48-01 Oral hypoglycemic drugs in the intervention of aging, report from drosophila melanogaster
Yumin Zhang, *First Hospital of Jilin University, China*

15:15-15:30
OR48-02 Oral hypoglycemic drugs in the intervention of drosophila melanogasters' aging
Yumin Zhang, *First Hospital of Jilin University, China*

15:30-15:45
OR48-03 Xanamem: a novel 11beta-HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer's disease
Brian Walker, *Centre for Cardiovascular Science, University of Edinburgh, United Kingdom*

15:45-16:00
OR48-04 Is exposure to famine in different life stages associated with phenotype of obesity: Results from REACTION study
Gang Chen, *Fujian Provincial Hospital, China*

Room 307

10:15-11:45 S42: Activin, Follistatin, and Ovarian Development

Moderator: Peter CK Leung, *Canada* and Christopher Hon Ki Cheng, *Hong Kong, China*

10:15-10:45
S42-01 Activin A accelerates the progression of fetal oocytes through meiosis and early oogenesis in mouse
Yong Zhao, *Institute of reproductive science, Qingdao Agricultural University, China*

10:45-11:15
S42-02 Follistatin regulation of germ cell development
Chao Wang, *China Agricultural University, China*

11:15-11:45
S42-03 Signaling pathways in granulosa cells
Teresa Woodruff, *Northwestern University, United States*

14:00-15:00 S49: Membrane Signaling and Cancer

Moderator: Vincent Goffin, *France* and Linong Ji, *China*

14:00-14:30
S49-01 IGF/IGFBP signalling and cancer
Youngman Oh, *Department of Pathology, School of Medicine, Virginia Commonwealth University, Richmond, Virginia, United States*

14:30-15:00
S49-02 Autocrine actions of growth hormone in cancer
Peter Lobie, *National University of Singapore, Singapore*

Room 301

14:00-15:00 S50: New Frontiers in Metabolic Surgery

Moderator: Augustine Ohwovoriole, *Nigeria* and Ming Liu, *China*

14:00-14:30
S50-01 Patient selection for metabolic and bariatric surgery
Felipe Casanueva, *Universidad de Santiago de Compostela, Spain*

14:30-15:00
S50-02 Long term metabolic effects of bariatric surgery
Boyong Shen, *Shanghai Jiao Tong University School of Medicine, China*

Room 302

14:00-15:00 S51: New Insights into Gonadotropin Synthesis and Secretion

Moderator: Ulrich Boehm, *Germany* and Xinhua Xiao, *China*

14:00-14:30

S51-01 Redirecting intracellular trafficking patterns of FSH & LH
Tunuguntla R. Kumar, *University of Colorado Denver-Anschutz Medical Campus, United States*

14:30-15:00

S51-02 The central roles of the Tet enzymes in regulation of luteinizing hormone b-subunit gene expression
Philippa Melamed, *Technion-Israel Institute of Technology, Israel*

Room 401

11:00-12:00 and 16:15-17:15

MTE29 Therapy of differentiated thyroid cancer
James Fagin, *Memorial Sloan Kettering Center, United States*

Room 402A

09:00-10:00 and 14:00-15:00

MTE23 Adrenocortical cancer
Xavier Bertagna, *Institut Cochin, Faculté de Médecine Paris Descartes, Université Paris 5, France*

11:00-12:00 and 16:15-17:15

MTE30 Genetic tests: What the clinical endocrinologist should know
Maria Luisa Brandi, *University of Florence - Department of Surgery, Italy*

Room 402B

09:00-10:00 and 14:00-15:00

MTE24 Absolute fracture risk and bone quality
Didier Hans, *University of Lausanne, Switzerland*

11:00-12:00 and 16:15-17:15

MTE31 Treatment in older people with type 2 diabetes
Isaac Sinay, *Advisor of the Diabetes Unit in The Cardiovascular Institute of Buenos Aires, Argentina*

Room 403

09:00-10:00 and 14:00-15:00

MTE25 Management of congenital adrenal hyperplasia
Deborah Merke, *National Institutes of Health Clinical Center, United States*

11:00-12:00 and 16:15-17:15

MTE32 Genetics of pheochromocytoma
Anne-Paule Gimenez-Roqueplo, *INSERM, France*

Room 405

09:00-10:00 and 14:00-15:00

MTE26 Hypoglycemia: Does it matter?
Sofia Zoungas, *Monash University, Australia*

11:00-12:00 and 16:15-17:15

MTE33 New concepts in hyperparathyroidism
John Bilezikian, *College of Physicians & Surgeons , Colombia University, United States*

Room 406

09:00-10:00 and 14:00-15:00

MTE27 Thyroid and pregnancy
Tim Korevaar, *Erasmus University Medical Center, The Netherlands*

11:00-12:00 and 16:15-17:15

MTE34 Hormone therapy in menopause
Bronwyn Stuckey, *Sir Charles Gairdner Hospital, Australia*

Room 407

09:00-10:00 and 14:00-15:00

MTE28 Update on long acting growth hormone
Jens Otto Lunde Jorgensen, *Aarhus University Hospital, Denmark*

11:00-12:00 and 16:15-17:15

MTE35 Pregnancy and diabetes
Huixia Yang, *Peking University First Hospital, China*

Sunday, September 4, 2016

Plenary Hall

08:30-09:15 Plenary Session 10: Recent Advances in Polycystic Ovarian Syndrome

Moderator: Oscar Bruno, *Argentina*

08:30-09:15
PL-10 Recent Advances in Polycystic Ovary Syndrome
Andrea Dunaif, *Northwestern University Feinberg School of Medicine, United States*

09:15-10:00 Plenary Session 11: Roles of the Endocrinologist in facing the issue of Endocrine Disrupting Chemicals

Moderator: Nor Azmi bin Kamaruddin, *Malaysia*

09:15-10:00
PL-11 Roles of the Endocrinologist in Facing the Issue of Endocrine Disrupting Chemicals
Jean-Pierre Bourguignon, *CHU Liège Neuroendocrinology Unit, GIGA Neurosciences, Belgium*

Room 303

10:15-11:45 S52: Monogenic Endocrinopathies and Tumor syndromes

Moderator: Felix Beuschlein, *Germany* and Yufang Bi, *China*

10:15-10:45
S52-01 The role of AIRE in tolerance and autoimmune disease
Georg Hollander, *University of Oxford, United Kingdom*

10:45-11:15
S52-02 Autoantigens in APS1, diagnostic utility and lessons learned about physiology
Olle Kämpe, *Karolinska Institutet, Sweden*

11:15-11:45
S52-03 Multiple Endocrine Neoplasia: The Pandora Vase of Endocrinology
Maria Luisa Brandi, *University of Florence - Department of Surgery, Italy*

Room 309AB

10:15-11:15 S53: Thyroid Hormone Transport and Action

Moderator: Graham Williams, *United Kingdom* and Jing Li, *China*

10:15-10:45
S53-01 Non-classical thyroid hormone action mediated by thyroid hormone receptor
Lars C Moeller, *Universität Duisburg-Essen, Germany*

10:45-11:15
S53-02 Central effects of thyronamines and thyroacetic acids
Laura Raimondi, *University of Florence, Italy*

Room 310

10:15-11:45 S54: Gene-Linked Hypogonadotropic Hypogonadism

Moderator: Deborah Merke, *United States* and Lulu Chen, *China*

10:15-10:45
S54-01 Genetics of kallmann syndrome
Weijun Gu, *General Hospital of PLA, China*

10:45-11:15
S54-02 Reversible Reproductive Dysfunction in Hypogonadotropic Hypogonadism
Manuel Tena-Sempere, *University of Cordoba, Spain*

11:15-11:45
S54-03 FGFR mutations in congenital hypogonadotropic hypogonadism
Nelly Pitteloud, *University of Lausanne, Switzerland*

Room 311A

10:15-11:15 S55: The Future Treatment of Acromegaly

Moderator: Stephen Shalet, *United Kingdom* and Changyu Pan, *China*

10:15-10:45
S55-01 New somatostatin analogues
Maria Fleseriu, *Oregon Health Science University, Northwest Pituitary Center, Poland*

10:45-11:15
S55-02 Antisense oligonucleotide therapy for acromegaly
Peter Trainer, *The Christie NHS Foundation Trust, United Kingdom*

Room 311B

10:15-11:45 S56: Type 1 Diabetes

Moderator: Troels Krarup Hansen, *Denmark* and Tao Yang, *China*

10:15-10:45
S56-01 Adjunct therapy with GLP-1 analogues in type 1 diabetes
Urd Kielgast, *Zealand University Hospital, Denmark*

10:45-11:15
S56-02 Diagnosis of type 1 diabetes across all ages: implications on management
Paolo Pozzilli, *University Campus Bio-Medico, Italy*

11:15-11:45
S56-03 Generating β Cells from pluripotent stem cells
Hongkui Deng, *School of Life Science, Peking University, China*

Room 306

10:15-11:15 S57: Novel Therapies for Metabolic Diseases

Moderator: Isaac Sinay, *Argentina* and Zhaoli Yan, *China*

10:15-10:45
S57-01 FGF21 Analogues
Alexei Kharitonenkov, *College of Arts and Sciences, Indiana University Bloomington, United States*

10:45-11:15
S57-02 Effect of berberine on glucose and lipids in diabetes
Jie Hong, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

Room 307

10:15-11:15 S58: Emerging Determinants of Obesity

Moderator: Isaac Sinay, *Argentina* and Zhaoli Yan, *China*

10:15-10:45
S58-01 Gut microbiota
Yanyun Gu, *Ruijin Hospital Affiliated to Shanghai Jiaotong University Medcine School, China*

10:45-11:15
S58-02 Virus-induced obesity
Richard Atkinson, *Virginia Commonwealth University School of Medicine, United States*

Room 301

10:15-11:15 S59: Islet Endocrinology

Moderator: Augustine Ohwovoriole, *Nigeria* and Nanwei Tong, *China*

10:15-10:45
S59-01 PPAR beta/delta in beta cell apoptosis
Lizhi Tang, *West China Hospital of Sichuan University, China*

10:45-11:15
S59-02 Beta-to-PP cell dedifferentiation as a mechanism of pancreatic beta-cell failure in type 2 diabetes
Yoshio Fujitani, *Institute for Molecular and Cellular Regulation, Gunma University, Japan*

Room 302

10:15-11:45 S60: Estradiol Production and Metabolism in Breast Cancer

Moderator: Margaret Shupnik, *United States* and Shih-Ming Huang, *Taiwan, China*

10:15-10:45
S60-01 Obesity and breast cancer: role of inflammation and aromatase
Evan Simpson, *Hudson Institute of Medical Research, Melbourne, Australia*

10:45-11:15
S60-02 Estrogen metabolites and breast cancer
Richard Santen, *University of Virginia, United States*

Plenary Sessions

PL-01

Sex Steroid Receptor Action in Breast and Prostate Cancer: New Insights and Therapeutic Implications

Wayne Tilley

Dame Roma Mitchell Cancer Research Laboratories, School of Medicine, University of Adelaide, Adelaide SA 5005, Australia.

The estrogen receptor-α (ER), androgen receptor (AR) and progesterone receptor (PR) are ligand-activated transcription factors that bind DNA and interact with a host of other nuclear proteins to regulate gene expression. The cognate hormones and their receptors are structurally and functionally related. Progesterone is a precursor hormone for androgen, which is converted to estrogen; ERα is the prototype from which AR and then PR evolved. The action and interaction between these receptors underpins reproductive organ development and maturation in men and women. Accordingly, they also have important roles in diseases of these tissues, including breast and prostate cancer in which ER and AR, respectively, are key drivers and therapeutic targets. My laboratory has been investigating steroid receptor action in breast and prostate cancer for over 30 years. In the breast cancer space, we have been exploring cross-talk between ER and AR, or more recently PR, to explain disease heterogeneity, response to target therapies, and disease outcomes, with view to forging new possibilities for therapeutic targeting. All three receptors have historically been targeted in the treatment of breast cancer, so a wide range of old and new generation drugs are available, offering the opportunity for drug re-purposing and a faster track to clinical translation compared to new drugs that have never been tested in people. In the prostate cancer space, we have been focussing on how to better target the AR, which remains the key driver of disease at all stages of progression. On the horizon are new targeting strategies aimed to outsmart known adaptive mechanisms, particularly in terms of targeting regions of the receptor that lie outside of the ligand binding domain. While these new strategies hold great promise for more effective AR inhibition, historical experience of employing androgen deprivation therapy raises a key question: will more effective AR silencing lead to more durable disease regression and significantly extend life for men with metastatic prostate cancer or will it reveal yet unknown treatment-induced adaptations that allow the disease to persist A similar problem exists in the field of ER-positive breast cancer, in which more effective inhibition of ER has led to more aggressive forms of treatment resistant disease. There is much to be learned from studying these hormone-driven cancers in parallel, with discoveries in one field informing the other.

PL-02

Diaomics - Diabetes and Metabolic Disorders

Guang Ning

Shanghai Institute of Endocrine and Metabolic Diseases, China

Guang Ning is the academicians of Chinese Academy of Engineering, Chair of Chinese Society for Clinical Endocrinologists, Chief Editor of the Journal of Chinese Endocrinology. He is receiver of the National Science Fund for Distinguished Young Scholars, "Changjiang" Professor, "973" project chief scientist. He is also member of the Executive committee of International Endocrine Society.

He has been working in the field of endocrine & metabolic diseases for years and mainly achieved in endocrine tumor and diabetes. He has been supported by more than 20 grants, including Sector Funds of Ministry of Health, the National Key Technology R&D Program, NSFC innovation research group and the National Basic Research Program (973 Program). He has published 250 papers in peer-reviewed journals, including Science, JAMA, Nat Genet, Nat Cell Biol, J Am Coll Cardiol and. He was winner of the National Science and Technical Progress Awards (2nd class) in 2008, 2010 and 2012 respectively (two rank first place and one rank second place). He was winner of Chinese Physician Award, Wu Jieping Medicine Innovation Prize, International Endocrinology Award from American Association of Clinical Endocrinologists, Lifetime Achievement Award from Israel Diabetes Association and Ministry of Health.

The prevalence of type 2 diabetes (T2DM) is rapidly increasing worldwide. In 2010, China nationwide survey indicated that the prevalence of diabetes in Chinese adults is 11.6% and China become the country with largest number of adults with T2DM. As a highly heterogeneous disease, T2DM could be induced by genetics and environmental factors including diet, sedentary life style, experimental pollution, gut microbiota, and their interactive nature. This raises enormous challenges to diabetic research. Until 2014, genetically, around 70 susceptibility T2DM loci have been identified, and environmentally, factors like sedentary behavior, endocrine disruptors have also been demonstrated as risks for T2DM. As the development of systems biology and innovation of new techniques, diabetes research also enters a new era, that we called DiaOmics which could include phenomics, exposomics, genomics, transcriptomics, proteomics, metabolomics, lipidomics, and Metagenomics. Most multi-omics studies on T2DM are cross sectional and longitudinal follow-up studies are required with detailed phenotyping and bio-banks incorporating multiple omics data and animal studies. This strategy enables to find new mechanisms, new biomarker and new treatments for diabetes. In the past decade, our center has established several cohort studies for diabetes and metabolic diseases, including National Diabetes Survey, Community study and "REACTION" study, recruiting more than 400,000 cases.

We have also conducted genetic study of obesity in Chinese Youngs (GOCY) involving a case-control cohort of 1500 young obese subjects (BMI > 30Kg/m2; age, 18-30 yrs), and 1500 well matched normal weight controls ((BMI: 18-23.9 Kg/m2). In addition, we have implemented several clinical trials that have been designed to investigate the metabolic benefits of certain oral antidiabetic drugs (OADs) and traditional Chinese medicine and to explore the potential mechanisms by means of multi-omics study. Based on these cohorts and GCP trials with biobank, we have gained data from high throughput whole exom sequencing, gut metagenomics and blood metabolomics. With aid of bioinformatics study, we could delineate how human genetics, gut microbiome and other environmental factors affect the pathogenesis of obesity and T2DM. With that, we could develop new algorithms to explore potential drug targets and deepen the understandings of metabolic diseases, in the hope to discover a novel strategy for the omics study of other complex diseases.

PL-03

Primary Aldosteronism—Past, Present and Future

John Funder

MIMR-PHI Institute (formerly Prince Henrys Institute

Professor John W. Funder AC, Hudson Institute of Medical Research

In the late 1960s, after graduating in medicine and basic clinical training, John Funder wrote his MD thesis on "The control of aldosterone secretion" and his PhD thesis on "Corticosteroid hormones and hypertension". Over the past 40 years, he has published more than 500 scientific papers in the field, and given over 200 invited presentations at international meetings. In the wake of the 1999 RALES Trial, he has pioneered a reconsideration of the pathophysiological roles of mineralocorticoid receptors in cardiovascular medicine, and of the roles of aldosterone, cortisol and spironolactone as mineralocorticoid receptor ligands. In 2008 he chaired the Endocrine Society Task Force which published Guidelines for the Diagnosis and Management of Primary Aldosteronism; a revised edition of these Guidelines was published in May 2016.

In 2008 he received the prestigious Novartis Award for his contributions to hypertension, in 2013 the Robert Williams Award for Outstanding Leadership in Endocrinology from the Endocrine Society, and in 2014 the Lifetime Achievement in Hypertension Award from the International Society for Hypertension. Most recently, in 2016 he has been awarded the Ipsen Prize, for his contributions to Cardiovascular Endocrinology.

Now in active retirement, he no longer has a laboratory, fellows or students, but a series of collaborations within and outside Australia; in addition he has continued to write reviews, position papers and editorial commentaries in cardiovascular endocrinology and other areas. He has honorary professorial appointments at Monash and Melbourne Universities and the University of

Queensland and is a Distinguished Scholar at the Hudson Institute. In the past he has chaired the Australian Society for Medical Research, the Endocrine Society of Australia, the International Society of Endocrinology, SANE (Australia), the Victorian Health Promotion Foundation, the Victorian Breast Cancer Consortium, the Victorian Hospitals Admission Risk Program and from 1990-2001 was Director of the Baker Medical Research Institute. In January 2015 he was made a Companion of the Order of Australia (AC) for his contributions across a wide range of fields. . He and his wife Valerie live on a small vineyard in the Yarra Valley, 50 km east of Melbourne, where they grow and others make excellent chardonnay and cabernet. Together they enjoy sport (as spectators, alas), reading, cooking and the company of friends, particularly over food and wine.

PL-04

Iodine and Thyroid Disorders in China

Weiping Teng

Institute of Endocrinology, China Medical Univiersity

Dr. Teng is a Professor of Medicine at Institute of Endocrinology and Department of Endocrinology, The First Hospital of China Medical University, in Shenyang. He is the Chief of Institute of Endocrinology of China Medical University and the Chief of State Key Laboratory (Cultivation Base) for Endocrine diseases.

Currently, Dr. Teng is the Predecessor President of Chinese Society of Endocrinology (CSE) . He is also vice-president of AOTA (Asia and Oceania Thyroid Association), the member of ATA (American Thyroid Association) and TES (The Endocrine Society) and the member of editorial board of Thyroid. Dr. Teng graduated from China Medical University in 1976. He completed his postdoctoral fellowship training in endocrinology at University of Cambridge, United Kingdom (1988-1990) and University of Toronto, Canada (1994-1995).

His key research orientation is thyroid diseases, especially in the fields of epidemiology, the relationship between iodine excess and thyroid diseases, genetics of Graves' disease, autoimmune thyroid diseases, thyroid disorders in pregnancy , the effects of thyroid hormone on brain development. He has published more than 210 articles including in peer-reviewed journals. The representative article is the one titled "Effect of iodine intake on thyroid diseases in China", published in《New England Journal of Medicine》.

Iodine is an essential nutrient for human-being which is main component of thyroid hormone and provide a micro environment for the thyroid cells. Both of iodine deficiency and iodine excess could result in thyroid disorders . In 1996, USI policy was introduced in China and Chinese people had exposed to excessive iodine intake for 6 years and more than adequate iodine intake for 10 years. Now MUI of China is 240μg/L. These are the six epidemic studies conducted by our group and the last one (TIDE study) is going on at the moment which will get 31 provinces data about iodine status and thyroid disorders. ① Hyperthyroidism: The hyperthyroidism related to iodine is called iodine-induced thyrotoxicosis (IIT) which is related to the level of iodine deficiency before prophylaxis and to the amount of iodine intake during prophylaxis. Comparing the data between 1999 and 2011, the prevalence of hyperthyroidism in our study were not increase, however were decreased. That indicate IIT does not occur in iodine sufficient area though long-term supplementation of iodine; ② Hypothyroidism: prevalence of overt hypothyroidism: ③ times higher in more than adequate iodine intake, 6.7 times higher in excessive iodine intake; subclinical hypothyroidism showed 3.2 times and 6.8 times higer in more than adequate iodine intake. The cumu-

lative incidence of subclinical hypothyroidism was 13 times in more than adequate and 14.5 times higer in excessive iodine intake. There was no difference in incidence of clinical hypothyroidism, probably due to it occurs after a latent time. ④ Serum TSH level: It was found in our study that TSH median were markedly higher in ten city study of China which resulted in a very high prevalence (16.7%) of subclinical hypothyroidism. Compared with American HANES- = 3 * ROMAN III study, 70% higher in TSH median and 6.92 vs 4.6mU/L at upper limit in reference interval. When we compare our data from 1999, 2007 and 2010, It is found that the median of TSH showed an gradually increase with an increasing MUI. TSH median 1.25mIU/L (1990) , 1.62mIU/L (2007), 1.96mIU/L (2010) with MUI 143μg/L ,206μg/L and 1.96μg/L. We speculated that the high TSH probably resulted from long-term iodine supplementation; ⑤ autoimmune thyroiditis: the prevalence of autoimmune thyroiditis (Hashimoto thyroiditis and atrophic thyroiditis) increased with the increase of iodine intake. (3.4 times and 5.6 times) though there were no difference in Graves disease; The incidence rate of autoimmune thyroiditis in area of more than adequate iodine intake and area of excessive iodine intake was 5 times and 6.5 times higher. Again no difference in Graves disease; In euthyroid subjects with positive thyroid antibodies at baseline, the incidence of supranormal TSH increased with increasing iodine intake. ⑥ Thyroid Cancer: there is no sufficient evidence for the relationship between thyroid cancer and iodine intake though that thyroid cancer were induced by iodine deficiency was consistently reported in animal study. The elevated TSH level may be associated with development of thyroid cancer. The conclusion: iodine intake should be controlled in a safe limits which is quite narrow (UIC 100-200μg) in order to avoid hypothyroidism and thyroid autoimmunity.

PL-05

Cell signaling in insulin secretion and its clinical implications

Susumu Seino

Division of Molecular and Metabolic Medicine Kobe University Graduate School of Medicine

Insulin secretion from pancreatic β-cells plays the central role in the maintenance of glucose homeostasis; its impairment contributes to the pathogenesis and pathophysiology of diabetes and is a target for treatment of the disease. Glucose-induced insulin secretion (GIIS) is the primary mechanism of insulin secretion, in which glucose metabolism in β-cells is prerequisite. GIIS comprises two pathways: the triggering pathway and the metabolic amplifying pathway. The former involves closure of the ATP-sensitive K+ channel (KATP channels) by increased ATP concentration due to glucose metabolism, which is followed by Ca2+ influx through opening of the voltage-dependent Ca2+ channels leading to insulin granule exocytosis. The latter involves amplification of the effects of the triggering pathway by metabolic signals other than ATP evoked by glucose metabolism, but the mechanism remains poorly understood. The closure of the KATP channel is essential in GIIS and antidiabetic sulfonylurea-induced insulin secretion. In 1995, we found that the KATP channel is composed of two subunits, the K+ channel member Kir6.2 and the sulfonylurea receptor SUR1. This discovery was of fundamental importance to our understanding of the metabolic regulation of insulin secretion and led to many important basic and clinical discoveries, including the findings that loss of function mutations lead to persistent hypoglycemia and hyperinsulinemia of infancy and that activating mutations in these subunits are a cause of permanent neonatal diabetes. Mutations in these subunits also cause transient neonatal diabetes, later-onset diabetes, and diabetes with developmental delay and epilepsy, among other syndromes. The patients with diabetes due to mutations in the KATP channel who were treated with insulin may therefore be better treated by oral sulfonylureas.

In addition to GIIS, neuro-hormonal amplification of insulin secretion is also critical in normal regulation of insulin secretion. Most of the hormones and neurotransmitters modulate insulin secretion by G-protein coupled receptor (GPCR)-mediated signals including cAMP, diacylglycerol (DAG), and inositol 1,4,5-triphosphate (IP3). The gut hormone incretins such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide 1 (GLP-1), which are released from enteroendocrine cells in response to meal ingestion, potentiate insulin secretion through cAMP signaling in pancreatic β-cells. Identification of the glucose-dependent action of the incretins in insulin secretion has paved the way for recently developed incretin-based anti-diabetic drugs, which are currently in use worldwide. In the course of our KATP channel studies, we found that the cAMP binding protein cAMP-GEFII (also called Epac2), which interacts with SUR1, mediates cAMP-induced insulin granule exocytosis in a protein kinase A (PKA)-independent manner. This discovery unveiled a novel action of cAMP, clarifying the pathway integrating Gs-protein coupled receptor signaling to insulin granule exocytosis, as cAMP had long been thought to induce insulin secretion by a PKA-dependent mechanism. It is now known that incretin/cAMP signaling potentiates insulin secretion by Epac2-dependent as well as PKA-dependent mechanisms. We also found that Epac2 is a direct target of sulfonylureas, thereby highlighting a novel mechanism of sulfonylurea action in addition to its effect on the KATP channels, further enhancing our understanding of sulfonylurea actions and their better use in treatment of diabetes. Recently, we demonstrated that β-cell glutamate produced through the malate-aspartate shuttle in glucose metabolism acts as a key signal in incretin/cAMP-induced insulin secretion by linking glucose metabolism to incretin/cAMP action in insulin granule exocytosis. This finding could underlie the impaired incretin-induced insulin secretion seen in type 2 diabetes and provide new approaches for treating patients who are unresponsive to incretin therapies.

In this lecture, the interplay of these cell signals in insulin secretion and its clinical implications will be discussed.

PL-06

Mechanisms of thyroid hormone action during skeletal development and bone maintenance

Graham Richard Williams

Imperial College London

PL-07

Genetic Strategies to Understand Physiological Pathways Regulating Body Weight

Sedaf Farooqi

University of Cambridge

PL-08

Surprising Origins of Sex Differences in the Brain

Margaret Merryl McCarthy Ball

Department of Pharmacology, Program in Neuroscience and Program in Molecular Medicine, University of

Margaret M. McCarthy, PhD
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Margaret (Peg) McCarthy received a BA and MA in Biology from the University of Missouri - Columbia and a PhD from the Institute of Animal Behavior at Rutgers University, Newark NJ. She received postdoctoral training at Rockefeller University from 1989 to 1992 and spent one year at NIH as a National Research Council Fellow. Peg joined the faculty of the University Of Maryland School Of Medicine in 1993 and was a professor in the Department of Physiology for 18 years before becoming the Chair of the Department of Pharmacology in 2011. She continues to hold secondary appointments in the Departments of Physiology and Psychiatry. Peg was the Director of Graduate Education for the Program in Neuroscience from 2002 – 2005 after which she served as an Associate Dean with responsibility for the Graduate Program in Life Sciences which oversees the training of 400 MS and PhD students and 350 postdoctoral fellows. She has received numerous awards and recognition for her mentoring of graduate students.

Peg has a long standing interest in the cellular mechanisms establishing sex differences in the brain. She uses a combined behavioral and mechanistic approach in the laboratory rat to understand both normal brain development and how these processes might go selectively awry in males versus females. She has published over 170 peer-reviewed manuscripts on these topics. Her research has been continuously funded by the NIH since 1994 and that same year she received the Frank A. Beach Award in Behavioral Neuroendocrinology. Dr. McCarthy now stands among the country's most pre-eminent scientific investigators, advising the NIH on guidelines governing a new policy, which states that sex must be accounted for, controlled for, and incorporated into all preclinical research funded by NIH, one of the agency's most sweeping research policy shifts in more than a decade. She is a previous Editor at Endocrinology and is currently an Associate Editor at the Journal of Neuroscience and on the Advisory Board for eNeuro. She is a former Associate Editor of Hormones and Behavior, past Secretary of the Society for Behavioral Neuroendocrinology, President-elect of the Organization for the Study of Sex Differences and was named one of Maryland's Top 100 Women in 2009. In 2015, Dr. McCarthy was awarded Researcher of the Year by the University of Maryland for her cumulative accomplishments and contributions to the university.

PL-09

Nuclear Receptors and Development: From Drugs to Embryos and Back Again

Vincent Laudet

Observatoire Oceanologique de Banyuls-sur-Mer / UPMC

Nuclear Hormone Receptors (NRs) are mediators of physiological responses to very important hormones and active molecules. Thyroid hormones, estrogens, corticoids, androgens but also retinoic acids or fatty acids are acting through these receptors. They form a welldefined superfamily of transcription factors that are activated by ligand binding and therefore provide a direct link between small molecules and transcriptional regulation. Nuclear receptors are major drug targets and we considered that up to 10% of current drugs are acting via NRs. In addition, despite the difficulties associated with their pleiotropic action and the presence of numerous side effects, NRs are still scrutinized in order to develop new drugs, specially tackling the modern plagues that are the metabolic diseases such as atherosclerosis, diabetes and obesity. In addition to their very important role in adult, nuclear receptors are very important for embryonic development. If this importance has long been recognized for some of them such as RARs that mediate the action of retinoic acid that are morphogens critical for many key aspects of embryonic development, this is not the case for many of them. Indeed the developmental role of steroid receptors for example has long been relatively neglected. Not only the analysis of mutant animals and in particular of knock-out mice but also the data gathered in small model organisms such as zebrafish and xenopus have nevertheless shown that NRs are deployed quite early on during development and appear critical for many developmental processes. I will present several examples of the importance of nuclear receptors during development, from morphogenesis of complex organs such as teeth to the post-embryonic effects of some hormones such as thyroid hormones. The importance of these receptors in development will also be highlighted by studying their regulation by endocrine disruptors.

PL-10

Recent Advances in Polycystic Ovary Syndrome

Andrea Dunaif[1], M. Geoffrey Hayes[1], Richard S. Legro[2], Margrit Urbanek[1]

1. Northwestern University Feinberg School of Medicine,Charles F Kettering Professor of Endocrinology & Metabolism Director, Northwestern University Specialized Center of Research on Sex Differences (P50 HD044405)
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Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders with global prevalence rates of 5-15% of reproductive-age women, depending on the diagnostic criteria applied. It is characterized by hyperandrogenism, chronic anovulation and polycystic ovarian morphology. PCOS is the leading cause of anovulatory infertility. Further, it is associated with profound defects in insulin action and secretion conferring substantially increased risk for type 2 diabetes (T2D). The syndrome is now recognized as a major metabolic disorder with adverse health outcomes across the lifespan. The etiology of PCOS remains unknown. However, it demonstrates non-Mendelian familial aggregation characteristic of a complex genetic disease resulting from the interaction between susceptibility genes and environmental factors. Male as well as female relatives have reproductive and metabolic features of the syndrome consistent with a genetic susceptibility to these phenotypes. Testosterone levels are elevated in the daughters of affected women prior to menarche suggesting that androgen exposure during critical developmental windows plays a role in the development of PCOS.

Recent major advances in our understanding of PCOS have come from the application of modern genetic approaches. Genomewide association studies (GWAS) in Han Chinese and European PCOS have implicated gonadotropin secretion and action, ovarian androgen biosynthesis, insulin resistance, body weight and sex hormone binding globulin in the development of PCOS. European women with the NIH and Rotterdam phenotypes as well as those with self-reported PCOS have some gene regions in common, such as chromosome 11p14.1 region containing the FSH B polypeptide gene, suggesting shared genetic susceptibility. Several chromosomal signals are significant in both Han Chinese and European PCOS cohorts suggesting that the susceptibility genes in these regions are evolutionarily conserved.

Analogous to other complex genetic diseases/traits, only a small amount of the heritability of PCOS is accounted for by the common susceptibility variants mapped so far. We have exciting new findings from the application of next generation sequencing. We have identified rare, deleterious variants in PCOS candidate genes in a subset of affected women. Further, family-based approaches have identified additional rare, likely to be deleterious, variants associated with androgen levels in genes that are plausible candidate genes as well as in genes that are in linkage disequilibrium with common variants in PCOS GWAS susceptibility loci.

PL-11

Roles of the Endocrinologist in Facing the Issue of Endocrine Disrupting Chemicals

Jean-Pierre Bourguignon

CHU Liège Neuroendocrinology Unit, GIGA Neurosciences, Univ

Jean-Pierre Bourguignon MD, PhD
Developmental Neuroendocrinology, GIGA Neurosciences, University of Liège (ULg)
Liège, Belgium

Jean-Pierre Bourguignon is Professor of Paediatrics Emeritus at the University of Liège, where he was head of the paediatric diabetology-endocrinology unit and vice-chairman of the Department of Paediatrics. He also headed the Developmental Neuroendocrinology Unit, and chaired the Institute of Training and Research in Higher Education. He received his diploma as a Doctor in Medicine, Surgery, and Obstetrics in 1974. From that time, Professor Bourguignon has been involved in many university- and hospital-related duties, including research and teaching. He obtained his higher education teaching certification (Agrégation) from the University of Liège in 1984. Beginning in 1993, he taught several courses at the ULg, including courses in semiology and internal paediatric pathology, normal and disordered growth in children and adolescents, and promotion of health in children and adolescents. He contributed to the implementation of problem-based learning in the Faculty of Medicine, beginning in 2000. Professor Bourguignon has also served as a visiting professor and lecturer at a number of universities in Belgium and in Hershey, Pennsylvania, United States.

Professor Bourguignon is a paediatric endocrinologist and has been the founding president of the Belgian Study Group for Paediatric Endocrinology. He is a translational scientist with the neuroendocrine mechanism of puberty and neuroendocrine disruption as main research interest. He also carries out research in the area of education, in relation to the development of the capacity for clinical reasoning. Professor Bourguignon has served on the editorial boards of several well-known journals in the field of endocrinology, and has authored more than 200 peer-reviewed articles and numerous book chapters. He is co-chairing Endocrine Society policy task forces on endocrine disrupters. He has received several national and international awards including in 2014, the prestigious Andrea Prader prize of the European Society for Paediatric Endocrinology, a life time recognition and, this year 2016, the outstanding Public Service award of the Endocrine Society.

Meet the Experts

MTE01

Management of Craniopharyngioma

Hermann L

Klinikum Oldenburg, Medical Campus University Oldenburg

MTE02

Clinical usefulness of TSH receptor antibody measurement

Eijun Nishihara

Kuma Hospital, Center for Excellence in Thyroid Care

Eijun Nishihara, MD, PhD, is Associate Director at the Department of Internal Medicine, Center for Excellence in Thyroid Care, Kuma Hospital, Kobe, Japan. He was graduated from the School of Medicine, Nagasaki University in 1994 and obtained PhD in 1999. He was engaged in a research as a Postdoctoral Fellow at the Department of Molecular and Cellular Biology, Baylor College of Medicine, United States and became an Assistant Professor, Department of Physiology, Nagasaki University in 2002. He has been working in the Department of Internal Medicine, Kuma Hospital since 2004.
Dr. Nishihara's academic interests include improved diagnostics for thyroid dysfunction caused by autoimmune or hereditary disorders.
Dr. Nishihara is an active member of Japan Thyroid Association, Asia & Oceania Thyroid Association and The Endocrine Society (USA). He has been awarded with Young Investigator Award and Shichijo's Prize from Japan Thyroid Association.

Graves' disease is the most common cause of hyperthyroidism in iodine sufficient regions. The incidence of Graves' disease is reported to be 1 to 2 cases per 1,000 population per year, especially frequent in women aged 30 to 40 years. Since Graves' disease is characterized by an autoimmune disease producing antibodies against the TSH receptor (TRAb), commercially available assays which detect their ability to interfere with the binding of TSH or M22 to the receptor, have been introduced over the past 3 decades. Current third-generation assays have high sensitivity and specificity (97% and 99%, respectively) for detection of TRAb in patients with untreated Graves' disease.
Transient thyrotoxicosis due to gestational hyperthyroidism and postpartum thyroiditis often occurs and anti-thyroid drug therapy is not needed. Radioactive iodine uptake and scanning have been used as a gold standard for the differential diagnosis of hyperthyroidism, but this examination is contraindicated in the patients during pregnancy and nursing. Therefore, combined evaluation of serum TRAb levels, T3/T4 ratio, and thyroid blood flow using ultrasonography has a high priority in the differential diagnosis during this time.
TRAb can be classified as stimulating, blocking, or neutral depending on their bioactivity, which better characterizes clinical pictures in Graves' disease. The presence of TRAb is critical to the diagnosis of euthyroid Graves' disease. Meanwhile, thyroid-stimulating antibodies show more significant association with clinical features of Graves' orbitopathy than TRAb. Graves' disease results in hypothyroidism in about 20% of patients who enter remission after anti-thyroid drug therapy. In the spectrum of autoimmune thyroid diseases, hypothyroidism appears to be caused by two different mechanisms: an inhibitory effect on TSH receptor activity due to the presence of blocking antibodies, and thyroid tissue destruction by the autoimmune process of Hashimoto's thyroiditis. Furthermore, we have reported that a new clinical entity of IgG4 thyroiditis also affects Graves' disease evolving rapidly to hypothyroidism and persistent thyroid enlargement.
We sometimes encounter hyperthyroid patients who present with negative TRAb and diffuse uptake of radioactive iodine in the thyroid. It is most likely to be the early stage or near remission of Graves' hyperthyroidism. However, nonautoimmune hyperthyroidism which is caused by constitutively activating germline mutations of the TSH receptor gene is another etiology in this condition. Neonatal hyperthyroidism can be caused by transplacental passage of maternal TRAb in Graves' disease, and this hyperthyroidism is self-limiting and subsides within a few months because of the disappearance of TRAb in the baby during this time. In contrast, neonatal onset of nonautoimmune hyperthyroidism leads to abnormality of bone structure and impaired neuronal function by inadequate treatment with anti-thyroid drugs. If some neonates whose mothers have no history of Graves' disease present with persistent hyperthyroidism without autoimmunity, the genetic analysis of the TSH receptor gene is essential for the diagnosis. Immediate diagnosis and initiation of ablative therapy without delay is indispensable to avoid the irreversible complications. In addition, absence of orbitopathy is also suggestive of nonautoimmune hyperthyroidism.?
Here, I would like to show several interesting cases mentioned above and verify the clinical utility of TRAb for the differential diagnosis among thyrotoxic diseases and the follow-up of Graves' disease.

MTE03

Vitamin D is a multifunctional hormone

Roger Bouillon

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The vitamin D endocrine system (D-endo) is essential for calcium and bone homeostasis. Absence of a functional VDR or CYP27B1 creates a severe rachitic bone phenotype in humans and mice as in severe vitamin D deficiency. The intestine is the key target for VDR. The intestine is the key target for VDR as a high calcium intake or selective VDR rescue in the intestine restores a normal bone and growth plate phenotype. Selective absence of VDR in osteoblasts does not create a bone phenotype when calcium intake is normal. Tissue specific deletions of VDR or cyp27b1 have now better defined the role of vitamin D in different tissues. Indeed, the vitamin D endocrine system already exist early in the evolution of vertebrates and its primary role is to maintain a normal serum calcium homeostasis, whereas optimal mineralization of bone and teeth is the second role for this endocrine system. The implications for humans are multiple: rickets is still endemic in different parts of the world and milder forms of vitamin D deficiency is present in more than a billion people worldwide so that appropriate large scale strategies are needed to correct this situation.
VDR is ubiquitously expressed and about 3% of the mouse or human genome is regulated by D-endo. All cells of the immune system ex-

press VDR. A large number of immune-related genes are coherently controlled by 1,25(OH)2D. The native immune system is stimulated by 1,25(OH)2D whereas the acquired immune system is suppressed. The generation of T regulator cells is enhanced via direct and indirect effects. Therefore, the native immune defense system is activated by D-endo but VDR or vitamin D deficiency leads to increased sensitivity to autoimmune diseases such as inflammatory bowel disease or autoimmune diabetes after exposure to predisposing factors. A low vitamin D status is associated with an increased risk for all types of infections and especially pulmonary infections and tuberculosis. Intervention studies however are equivocal. The link between vitamin D and autoimmune diseases is suggested in human genetic studies, and in many animal models of autoimmune diseases like type 1 diabetes and multiple sclerosis. In man, epidemiological studies confirm such associations, but intervention studies till now fail to show preventive effects. Prospective and intervention studies are needed and ongoing as to define the optimal vitamin D status for global health. Based on a critical analysis of all existing data from randomized controlled trial, we suggest that serum 25OHD concentrations should be 50 nmol/l (20 ng/l) in all adults. However the mean 25OHD found in normal adults around the world (n > 500 publications) is hardly higher than 50 nmol/l, indicating the widespread presence of mild to severe vitamin D deficiency. Some areas around the world are more prone to severe vitamin D deficiency such as the Middle East and Gulf States, Northern India and China (Mongolia being the worst of all). Populations needed the highest attention are infants, the very elderly (oldest-old) and people with habitual low sun exposure for whatever reason. For these subjects a systematic approach to assure vitamin D supplementation is needed.

While waiting for the results of ongoing clinical intervention studies, optimal vitamin D status should be largely based on evidence based medicine dealing with calcium and bone homeostasis.

Based on a critical analysis of all existing data from randomized controlled trial, we suggest that serum 25OHD concentrations should be 50 nmol/l (20 ng/l) in all adults. However the mean 25OHD found in normal adults around the world (n > 500 publications) is hardly higher than 50 nmol/l, indicating the widespread presence of mild to severe vitamin D deficiency. Some areas around the world are more prone to severe vitamin D deficiency such as the Middle East and Gulf States, Northern India and China (Mongolia being the worst of all). Populations needed the highest attention are infants, the very elderly (oldest-old) and people with habitual low sun exposure for whatever reason. For these subjects a systematic approach to assure vitamin D supplementation is needed.

The highest priority should be given to systematic vitamin D supplementation as general rule for all children till at least 3 years of age. All elderly subjects should also receive vitamin D supplementation up to about the equivalent of 800 IU of vitamin D3 per day keeping serum 25OHD levels above 20 ng/ml or 50 nmol/l.

We call upon all member countries represented in the WHO to ask the WHO to formulate and implement a vitamin D supplementation strategy as to eradicate vitamin D (and or calcium) deficiency rickets.

MTE04

Premature ovarian insufficiency

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2006-2008, Visiting Professor, Yale University School of Medicine, United States
2003-2006, Ph.D. , Nanjing University School of Medicine, Nanjing, CHINA
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1993-1996, MS. Nanjing Medical University, Nanjing, CHINA
1981-1986 MD, Nanjing Medical University, Nanjing, CHINA
Field of research:

Professor Wu has been engaged in the clinic, scientific research, and the education of Obstetrics and Gynecology for almost 30 years, and has focused on Gynecological Endocrinology. Dr. Wu's major research contributions have been in gynecological and reproductive endocrinology, particularly in menopause, polycystic ovary syndrome (PCOS), and premature ovarian failure (POF). Her research projects have resulted in the publication of about 100 papers, and she has obtained a lot of awards and grants in her research field.

Premature ovarian insufficiency (POI) is a complex disorder characterized by cessation of ovarian-ovulation function in women before 40 years of age. The condition is defined as the absence of normal menses for at least 4 months, serum follicle-stimulating hormone (FSH) concentrations exceeding 25 IU/L at least one month apart, resulting in infertility, cardiovascular diseases, neurological disorders, and osteoporosis. POI affects 1% and 0.1% of women by the age of 40 and 30, respectively. Multiple causes contributing to POI include genetic background, autoimmunity, iatrogenic factors. However, the cause of POI remains undetermined in most cases (idiopathic POI). Concerning the treatment of POI patients, whether or not they desire pregnancy, should be treated with combination estrogen and progesterone hormone replacement therapy (HRT) to minimize bone loss and decrease the risk of cardiovascular events, relieve the vasomotor flushes and vaginal dryness. Besides, women with POI extremely rarely ovulate and achieve pregnancy spontaneously, so infertility is an important issue in POI patients. Numerous treatment protocols for follicular development and ovulation induction have been tested in patients with POI, none have been shown to be effective. Therefore, POI/POF remains a clinically challenging entity because IVF with donor oocytes is currently the only treatment known to be effective. Fortunately, the natural cycle IVF may be promising for the POI patients in the future.

MTE05

New genes in pituitary tumor and implications for management

Marta Heckenast Korbonits

Barts and the London School of Medicine

MTE06

Optimizing treatment for congenital adrenal

Richard Auchus

University of Michigan

Richard J. Auchus, MD, PhD, FACE
Dr. Richard Auchus earned his bachelor's degree in Chemistry from the Massachusetts Institute of Technology and his M.D. and Ph.D. in Pharmacology at Washington University. He trained in internal medicine at the University of Iowa and completed his endocrinology fellowship at Wilford Hall USAF Hosptial/UTHSC San Antonio, where he also served in the US Air Force Medical Corps. He performed postdoctoral research and served on the faculty in Pediatrics and Internal Medicine at the University of California, San Francisco. He was an assistant, associate, and full professor at the University of Texas Southwestern Medical Center at Dallas and was acting chief of the Division of Endocrinology and Metabolism and the Division of Translational Research prior to his relocation to the University of Michigan in 2011. He is currently Professor of Pharmacology and Internal Medicine in the Division of Metabolism, Endocrinology, and Diabetes and Director of the Endocrinology Fellowship Program.
Dr. Auchus has authored over 250 journal articles or book chapters, holds two patents, and has presented at a diverse range of national and international conferences.
He is an Associate Editor for Endocrinology and a member of the Editorial Board for Clinical Endocrinology and the Journal of Steroid Biochemistry and Molecular Biology.
His group is active in research projects ranging from basic chemical principles of steroid biosynthetic enzymes to clinical and translational investigation in disorders of the pituitary, adrenals, ovaries, and testes that cause hypertension, infertility, and obesity.
His group also collaborates widely with investigators to study steroid biology in prostate cancer, hypertension, and stress response. Over the last 5 years, his laboratory has focused on steroid mass spectrometry for the diagnosis and management of endocrine disorders and to better understand steroid biochemistry and physiology. His clinical interests also focus on adrenal, pituitary, and reproductive diseases that involve disorders of steroid production, particularly in the care of adults with genetic disorders of steroid biosynthesis and action. He is also active in physician training and education, as well as efforts to improve the health of patients with endocrine diseases.
Dr. Auchus lives in Ann Arbor with his wife of 25 years, Dr. Mary Louise Auchus, who is a hematologist-oncologist, and their three children Nadia, Gabriella, and Gregory. Dr. Auchus is also an avid triathlete who trains and competes with the Ann Arbor Masters Swimming Team. When not doing endocrinology or science, he enjoys skiing, fishing, cooking, and racing.

The two main goals of treatment for congenital adrenal hyperplasia (CAH) due to classic 21-hydroxylase deficiency are to replace the deficient hormones (cortisol and aldosterone) and to dampen the adrenorcorticotropin (ACTH) drive for adrenal androgen excess. Glucocorticoids are the mainstay of CAH treatment, with or without fludrocortisone acetate, but available glucocorticoid preparations do not meet the clinical need entirely. It is important to distinguish which doses of glucocorticoid are used to replace the cortisol deficiency and which are used to lower the androgen excess. Hydrocortisone remains the preferred agent for cortisol replacement into adulthood, but hydrocortisone requires 3 daily doses and is only weakly effective in managing severe androgen excess and testicular adrenal rest tumors (TARTs). More potent synthetic glucocorticoids more effectively treat the androgen excess and TART, but these drugs (prednisone, prednisolone, methylprednisolone, dexamethasone) cause more side effects and iatrogenic Cushing syndrome. Combination therapy with daytime hydrocortisone and a small dose of bedtime prednisolone is a good compromise regimen. Recent literature includes two basic approaches to improving disease control: improved glucocorticoid delivery and adjunct therapies to directly reduce androgen production. Modified-release oral hydrocortisone and continuous subcutaneous hydrocortisone pumps have been studied. Abiraterone acetate has been shown to effectively lower androgens when given with replacement hydrocortisone in a phase 1 study. A corticotropin-releasing hormone-receptor antagonist has also been studied in a phase 1 trial to directly lower ACTH andadrenal androgens. More agents are being developed for future studies.

MTE07

Primary Hyperaldosteronism

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MTE08

Clinical management of thyroid nodules

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MTE09

Managing Osteoporosis in under-served clinical groups, including those transitioning to adult care

Frances Milat

Hudson Institute of Medical Research

Osteoporosis in young adults with complex medical comorbidities remains poorly understood with an absence of evidence-based treatment strategies. Clinical research and therapeutic trials for osteoporosis have largely focused on understanding the pathophysiology and management of postmenopausal osteoporosis. Young adults with transfusion-dependent haemoglobinopathies, chronic neurological conditions including cerebral palsy, renal disease, transplantation and premature menopause are particularly underserved by conventional therapeutic guidelines and evidence. This session will explore current knowledge and new developments in the management of metabolic bone disease in these clinical groups through case-based discussion.
The management of thalassemia major with regular transfusion therapy and iron chelation has significantly improved life expectancy for patients. However, bone disease and fracture have emerged as major therapeutic challenges in this condition; there are significant gaps in our knowledge regarding mechanisms of disease and management. Likely risk factors in thalassemia bone disease include hormonal deficiencies, genetic factors, marrow expansion, skeletal dysmorphism, iron toxicity, chelators and increased bone turnover. Bisphosphonates have been used in the treatment of low BMD and fracture but optimal frequency and duration of bisphosphonate administration is not known. In addition, the optimal dose and route of application of sex hormone therapy for bone preservation remains to be established. Recent insights into the renal-bone axis have also added to the complexity of management, with a high prevalence of hypercalciuria, renal calculi and low BMD in this condition1. The clinical case highlights these challenges and discusses renal-bone disease in thalassemia.
Cerebral palsy (CP) is the most common motor disorder among children, affecting 2 to 3.5 per 1000 live births. It increases fracture risk through diminished ambulation, nutritional deficiencies and anticonvulsant medication use. Improvements in medical care have seen increases in life-expectancy, but studies examining bone mineral density (BMD) and fracture beyond childhood are limited. Recent work in adults with CP suggests that fragility fractures are common with predominant ankle, vertebral and rib fractures2. These osteoporotic-related atraumatic fractures are occurring at a younger age in adults with CP than in the general population. In addition, hypogonadism has recently been shown to be highly prevalent in adults with CP, particularly in those with more severe motor dysfunction2. In the context of bone and muscle disease, this clinical finding is worthy of further research and has implications in the management of osteoporosis in CP. Contributing factors to low bone mineral density in CP will be discussed.
Renal transplantation is the gold standard treatment for patients with end stage renal disease, with reversal of many of the mineral disturbances seen in chronic renal failure. However, bone disorders and fractures remain significant complications post-transplantation. Hip fracture rates post-renal transplantation exceed even those on dialysis, with increased mortality in this group compared to transplant patients without fracture3,4. Risk factors contributing to fracture including increasing age, diabetes, glucocorticoid exposure and the degree of graft function5. The case of a young adult with renal transplantation transitioning to adult care will be presented, highlighting important aspects of endocrine care.
Premature menopause is defined as menopause occurring in women <40 years of age and may occur spontaneously (encompassing premature ovarian insufficiency) or secondary to medical treatment including bilateral oophorectomy or chemotherapy. Spontaneous premature ovarian insufficiency affects 1% of women, with medically induced PM affecting up to 10% of women6,7. Premature menopause places women at increased risk of cardiovascular disease and osteoporosis, yet there is a paucity of literature examining optimal management of these important complications. Clinical issues arising from management of bone disease in women who have premature menopause will be discussed.

MTE10

Genetics of hypothalamic-pituitary-gonadal function

Stephanie Seminara

Harvard

Appointments at Hospitals/Affiliated Institutions
1994-1997 Clinical/Research Fellow Endocrinology Massachusetts General Hospital
1998- Assistant in Medicine Medicine Massachusetts General Hospital

MTE11

Insulin Pump

Tomoyuki Kawamura

Osaka City University Graduate School of Medicine

The insulin pump therapy (Pump) in type 1 diabetes has been spreading in the western countries. The spreading situation of Pump in each country depends on the two aspects. One is the financial situation of medical expense in each country. When the health insurance covers the expense of Pump, Pump may be easy to spread. The other is the understanding of the medical staff about Pump. For the good handling of Pump, the deep understanding about Pump is needed. In Japan, 70% of the medical cost for Pump is covered by the national insurance system. However, Pump dose not spread enough in Japan. In our clinic, 230 (58%) among 430 type 1 diabetes is using Pump.I am a pediatrician. My diabetes treating team was composed by only three pediatricians. We have no diabetes nurse and educator in our clinic. However, we treat all age (0-77 years old) of type 1 diabetes patients, I experienced to introduce Pump to many patients from the infants and the aged patients by myself. I am managing their Pump every month for 20 years. The sensor augmented pump

(SAP) was also introduced to more than 100 patients in my clinic since October 2014. Many of Pump and SAP was stated in our out-patient clinic without the admission.In this session, I will show my experience on Pump and SAP during 20 years in my clinic. The discussion about the financial situation, the easy way of introduction, and the advanced handlings for Pump and SAP will be held with the attendees.

MTE12

Acromegaly

Christof Schöfl

Division of Endocrinology and Diabetes, Department of medicine I, University Hospital Erlangen, Frei

Dr. Christof Schöfl is Professor of Endocrinology and Diabetes at the Friedrich-Alexander-University of Erlangen-Nuremberg, Germany and Head of the Division of Endocrinology and Diabetes at the Department of Medicine I, University Hospital Erlangen since 2010. He received his M.D. and Ph.D. from the Albrecht-Ludwigs-University Freiburg, Germany and trained in Internal Medicine, Endocrinology, Diabetes and Metabolism at Hannover Medical School, Germany. In 2004 he was appointed Professor of Endocrinology and Vice-Director of the Department of Endocrinology, Diabetes and Nutrition at Charité-University-Medicine Berlin, Germany. In 2006 he became Professor of Neuroendocrinology at the FAU Erlangen-Nuremberg, Germany.

One of his current clinical and research activities include pituitary disorders with a special focus on metabolic aspects of acromegaly and Cushing´s disease. Since 2008 he serves as chairman of the German Acromegaly Registry and is board member of the section of neuroendocrinology of the German Endocrine Society. Other clinical and research activities concentrate on the calcium-sensing receptor (CaSR) in diseases of calcium metabolism.

Dr. Schöfl is involved in many national professional bodies and has been a member of the Executive Board of the German Endocrine Society for more than 6 years. Dr. Schöfl has published more than 100 peer-reviewed journal articles and book chapters.

MTE13

Primary Adrenal Insufficiency

Marcus Dr Quinkler

Endocrinology in Charlottenburg, Berlin, Germany

Definition Adrenal crisis (AC) is a life-threatening emergency in patients with adrenal insufficiency (AI). It is defined as major impairment of general health with at least two of the following signs (hypotension, nausea or vomiting, severe fatigue, fever, somnolence, hyponatremia, hypoglycaemia) and the parental glucocorticoid administration followed by clinical improvement (1). AC is weighted in four grades: outpatient care only (grade 1), hospital care on general ward (grade 2), intensive care unit (grade 3), and death from AC (grade 4).

Incidence Retrospective analysis of 444 patients with primary or secondary AI revealed a frequency of 6.3 AC/100patients (2), and 5.7 AC/100patients in patients with congenital adrenal hyperplasia (3). A postal survey of the UK Addison group revealed 8 AC/100patients (4). A recent analysis of a large German health insurance database even suggested even 14-17 AC/100patients (5). The first prospective study in Germany found an incidence of 8.3 AC/100patients. AC was fatal in 6.3% of cases (6), which converts into an excess mortality rate from AC of 0.5/100 patient years (1). Extrapolating this to the population of 507 million in the European Union this would be 5.500 to 10.500 expected deaths from AC in the coming decade (1). The most common precipitating factors of AC are gastrointestinal infection and other infectious diseases but also emotional stress (6).

Pathophysiology The exact mechanisms are hardly known, however it is hypothesized that the lack of increased cortisol concentrations during infection enhances pro-inflammatory cytokine release and sensitivity to toxic effects of these cytokines (e.g. tumour necrosis factor alpha), and those may impair glucocorticoid receptor function aggravating glucocorticoid deficiency (1).

Treatment If AC is suspected immediate therapy is necessary. Treatment is easy and consists of parental glucocorticoid (e.g. 100mg hydrocortisone as bolus intravenously) and isotonic saline (1000ml 0.9% sodium chloride within the first hour) to correct hypovolemia. Additional therapeutic actions should be taken to treat the precipitating factors (e.g. antibiotics). Following the initial treatment, 200mg hydrocortisone/day should be given as continuous infusion or frequent i.v. (or i.m.) boluses (50mg) every 6h (1). Further fluid administration should be assessed clinically or by central venous pressure. Close monitoring preferably on intensive care unit including measurement of serum electrolytes is recommended.

Prevention The major point is that valuable time should not be lost between the sudden onset of increased cortisol need (in stressful situations e.g. infections) and the application of additional hydrocortisone doses. A recent German study revealed a much too long time span between the doctor´s arrival in the case of emergency and the glucocorticoid administration by the doctor (7). This emphasizes the need for a better training of the medical personal, a better identification of patients who are in need of emergency injections in stressful situations, as well as a better patient education to early recognize symptoms of AC and to facilitate parenteral hydrocortisone self-administration.

Current education concepts are not sufficiently effective, and therefore a structured standardized teaching in small patient groups (including one relative per patient) should be implemented with duration of 2-3h (8) and repetition every 6 to 12 months. One key aspect of this training should be the practical learning of self-administration of the hydrocortisone ampoule. The aim of the crisis prevention teaching should be: The well-informed patient (or his/her relative) guides the poorly informed health-care professional!

In addition, every patient should carry emergency cards (a national and an international one) (9-11). It is an important issue to standardize emergency cards to avoid failed recognition by medical personal. Each patient should be equipped with an emergency kit consisting of additional hydrocortisone tablets, glucocorticoid suppositorium, and a hydrocortisone ampoule and syringes for self-injection.

MTE14

Thyroid disease in elderly patients: What to do and what to avoid

Kristien Boelaert

University of Birmingham

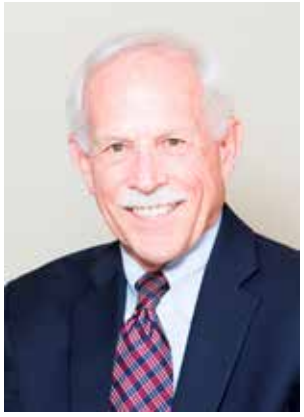
Kristien is a Reader in Endocrinology at the University of Birmingham and a Consultant Endocrinologist at the Queen Elizabeth Hospital in Birmingham. Kristien obtained her MD from the Catholic University Leuven, Belgium and her Wellcome Trust-funded PhD from the University of Birmingham. Subsequently, she was successful in obtaining a prestigious MRC Clinician Scientist Fellowship in 2007. Her clinical research interests include the management of thyroid dysfunction, thyroid nodules and endocrine disorders in pregnancy. Her laboratory research programme focuses on the pathogenesis of goitre and thyroid cancer. Kristien's contribution to the field of thyroid disease has been recognised by awards from several national and international societies and by regular invitations to speak at national and international meetings. She held a Visiting Clinician Fellowship at the Mayo Clinic in 2011 and was the RCP representative on the recent national UK thyroid cancer guidelines committee (2014). Kristien's research continues to attract funding from major grant awarding bodies and is evidenced by a rapidly growing list of peer-reviewed research papers, reviews and book chapters. Kristien is a Senior Editor for Endocrine Connections and serves on the Editorial Boards of Lancet Diabetes & Endocrinology, Thyroid and the Journal of Endocrinological Investigation as well as on the British Thyroid Association Executive Committee and the RCP Specialist Certificate Examination Board.

MTE15

Managing osteoporosis in post menopausal women

Michael McClung

Oregon Osteoporosis Center



Michael McClung, MD, FACP
Director, Oregon Osteoporosis Center
Dr. Michael McClung is the founding director of the Oregon Osteoporosis Center. He graduated from Rice University in Houston and from the University of Texas Southwestern Medical School in Dallas. After his training in Internal Medicine at Parkland Hospital in Dallas, he completed a fellowship in Endocrinology at the National Institute of Health in Bethesda, Maryland. For many years, he was on the faculty at the Oregon Health Sciences University and in the Department of Medical Education at Providence Portland Medical Center where he was actively involved in the training of young physicians.
At the Oregon Osteoporosis Center, Dr. McClung has had an active clinical practice, taken part in multiple educational initiatives and has been the principal investigator in many clinical trials evaluating the utility of tests for diagnosis and monitoring osteoporosis and effects of therapeutic agents for that disease. These activities have resulted in more than 250 scientific and clinical publications. He is frequently invited to speak at national and international society meetings and is the recipient of several teaching and service awards from those societies, including, in 2015, the President's Award from the International Osteoporosis Foundation, the Dr. John P. Bilezikian Global Leadership Award of the International Society for Clinical Densitometry and the Leon Speroff Award for Excellence in Education from the North American Menopause Society. Dr. McClung serves on the editorial board of several journals in the bone field. He has been an active member of the IOF Council of Scientific Advisors since 1999. Dr. McClung served on the WHO Fracture Risk Assessment Task Force that led to the implementation of the FRAX fracture risk assessment tool, and he has been involved in the development of clinical guidelines for several national osteoporosis societies.

MTE16

Dopamine Agonists: When To Use, What To Choose & Safety Issues

J.A Romijn

University of Amsterdam

MTE17

Preservation of fertility in cancer patients

Teresa Woodruff

Northwestern University

Northwestern University
Feinberg School of Medicine
Department of Obstetrics and Gynecology
Division of Reproductive Science in Medicine
Division of Fertility Preservation

MTE18

Osteoporosis in Men

Benjamin Leder

Mass General Hospital, Havard University

In the treatment of postmenopausal osteoporosis, currently available antiresorptive and anabolic therapies increase bone mineral density modestly and reduce fractures in specific populations, but cannot restore skeletal integrity in most patients with established disease. Anabolic therapy theoretically has this potential but currently available anabolic agents and regimens are limited by their duration of action and concomitant pro-resorptive properties. Presently, the parathyroid hormone analog, teriparatide, is the only anabolic agent being used to treat postmenopausal osteoporosis though several drugs are in late-stage development. This session will focus on new therapeutic approaches targeting the parathyroid hormone and parathyroid hormone related-protein receptor (PTHR). Specifically, we will review the proposed mechanism and available data surrounding the parathyroid hormone-related protein analog, abaloparatide. Though much of the abaloparatide anti-fracture efficacy data remains unpublished, initial published studies suggest that abaloparatide may stimulate both bone formation and resorption less than teriparatide and may preferentially increase bone mineral density at anatomic sites comprised of significant cortical bone. The session will also focus on the use of PTHR-targeted therapies in combination with antiresorptive agents. Initial studies investigating the combination of parathyroid hormone and bisphosphonates have generally not shown an additive effect on bone mineral density. In contrast, in the DATA study, we recently reported that the combination of teriparatide and the nuclear factor-κB inhibitor, denosumab, increases bone mineral density at the hip, spine and distal radius, improves peripheral bone microarchitecture, and increases estimated bone strength at the radius and tibia more than either drug alone. Moreover, denosumab, unlike bisphosphonates, appears to fully inhibit the pro-resorptive effects of teriparatide (while allowing for continued osteoblast activity). The session will conclude with a discussion of the optimal sequence of anabolic and antiresorptive agent administration in light of new data and examine how this knowledge can help optimize the long-term therapeutic course in patients with severe disease.

MTE19

Testosterone replacement therapy

Bradley Anawalt

University of Washington

Dr. Bradley D. Anawalt is the Chief of Medicine at the University of Washington Medical Center and Professor and Vice Chair of the University of Washington Department of Medicine. He is an endocrinologist who sees a broad range of patients including men with low testosterone levels, sexual dysfunction and infertility. His research interests include the physiologic effects of testosterone on bone, muscle, and the brain in men. He also has spent the past twenty years collaborating on research in male hormonal contraception ("the male pill"). He is the chair of the Hormone Foundation of the Endocrine Society and is a member of the Therapeutic Use Exemption Committee for the United States Anti-Doping Agency. Dr. Anawalt also serves on the editorial board of two international journals: Clinical Endocrinology and the Journal of Clinical Endocrinology and Metabolism. He loves to teach, and he has received the Beeson Teaching Award for Excellence from the internal medicine residents and the Outstanding Teacher Award from the Endocrinology fellows at the University of Washington.

MTE20

Approach to the patient with relapse hyperthyrodism after previous ATD therapy: How useful are anti-thyroid drugs?

Bingyin Shi

The First Affiliated Hospital of Xi'an Jiaotong University

MTE21

Cushing's Syndrome

Lynette Nieman

Dr. Lynnette Nieman is a Senior Investigator at the NIH Clinical Research Center and head of the Endocrine Consult service. She also directs the Office of Human Subjects Research Protections for intramural NIH. Dr. Nieman attended Smith College (A.B.) and SUNY Buffalo Medical School (M.D.). Her internal medicine residency and one year of endocrinology fellowship were done at SUNY Buffalo. In 1982 she joined the NIH as an endocrinology fellow. From 1991 to 2001 she served as the Clinical Director of intramural NICHD, overseeing the clinical care of the institute's patients and ensuring compliance with human subjects research regulations. Dr. Nieman is an active clinical investigator, with eleven active protocols and special expertise in disorders of hypercortisolism. She has authored more than 250 publications and sponsored three investigational new drug applications, one of which was licensed in the US and Europe. Dr. Nieman served as an associate editor for the Journal of Clinical Endocrinology and Metabolism and is a past member of the Endocrinology and Metabolism subcommittee of the American Board of Internal Medicine. She has received the NIH Director's Award, NIH Clinical Teacher of the Year Award and the Endocrine Society's Distinguished Physician award. She has provided Congressional testimony. She is a past Vice President for Clinical Science of the Endocrine Society and Chaired the Society's 2012 annual meeting. Dr. Nieman is currently the President-elect of the Endocrine Society.

MTE22

Treatment of type 1 diabetes at diagnosis and during remission

Paolo Pozzilli

University Campus Bio-Medico

MTE23

Adrenocortical Cancer

Xavier Bertagna

Institut Cochin, Faculté de Médecine Paris Descartes, Université Paris 5

MTE24

Absolute fracture risk and bone quality

Didier Hans

University of Lausanne

Prof. Didier Hans, Ph.D., MBA. is in one hand the Head of Research and Development in the Bone and Joint Department at the Center of Bone Disease at Lausanne University Hospital and in another hand the Founder, Chairman and CEO of medimaps group. In his academic role, he is involved in a range of clinical, research and teaching activities. Pr. Hans has over 27 years of experience working in the musculoskeletal field, with particular emphasis on DXA, microarchitecture and ultrasound imaging techniques. As a medical expert with radiology expertise, Pr. Hans has served as a co-investigator for several clinical trials involving imaging for some of the world's top pharmaceutical companies as well as in scientific advisory board of diagnostic companies.

Pr. Hans teaches courses in DXA, Bone microarchitecture techniques, ultrasound, body composition and osteoporosis and lectures around the world. In addition, he is a certified full clinician faculty and full technologist faculty for the International Society of Clinical Densitometry Bone Densitometry course. Pr. Hans served as the 1st non North American International Society of Clinical Densitometry (ISCD) President and remained an active member of the ISCD Board of Directors as well as a member of the scientific advisory committee of the International Osteoporosis Foundation (IOF). He has authored more than 210 articles, over 20 book chapters and serves as a reviewer and/or member of the editorial board for 10 international scientific journals including Osteoporosis International, Journal of Bone and Mineral Research, Journal of Clinical Densitometry, Osteoporosis International and Bone. As a musculoskeletal expert, Pr. Hans has been invited to present at over 400 conferences and events on topics including osteoporosis, bone quality and bone fractures, among other subjects.

Pr. Hans was the recipient of the Dr. John P. Bilezikian ISCD Global Leadership Award (2013) as well as the ISCD clinician of the year award (2006) for distinguished services to the field of bone densitometry amongst other distinctions. As President of ISCD, Pr. Hans actively worked toward the reconciliation between ISCD and IOF which led, under his presidency, to strategic alliance for the common osteoporosis courses worldwide: "Osteoporosis Essentials".

Prior his current position, Pr. Hans was during 10 years the Head of the R&D in the Radiology Department, Bone and Body composition laboratory at University of Geneva, Switzerland. Previously, he was the Director of the Quality Assurance Center for Clinical Research and the associate director of R&D for the ultrasound unit at the Osteoporosis and Arthritis Research Group (OARG) at UCSF, San Francisco, United States (directed by Prof Harry K. Genant). At earlier stage, he was the director of both Bone Densitometry and New Technologies Department and Quality Assurance Center at the Centre d'Epidémiologie des Ostéoporoses in Lyon, France (directed by Profs Pierre J. Meunier and Pierre D. Delmas).

Pr. Hans earned a Ph.D. in Human Biology and Medical Physics with honours from Claude Bernard University in Lyon, France. He also earned his Masters of Science degree with honours in the area of Acoustic, Signal and Image Processing and Ultrasound from Claude Bernard University. He completed recently his expertise with a Master Business Administration in Entrepreneurship from HEC in Geneva Switzerland.

MTE25

Management of congenital adrenal hyperplasia

Deborah Merke

National Institutes of Health

Congenital adrenal hyperplasia (CAH) is most commonly due to 21-hydroxylase deficiency.? Early detection and early treatment have resulted in improved survival.? Therefore, the treatment of adults with CAH is of great importance. The management of CAH patients changes over the lifespan and is inherently age- and sex- specific. During childhood, management is aimed at achieving normal growth and development; while management of the adult is aimed at optimizing fertility, minimizing the virilization of females, and preventing long-term consequences such as osteoporosis, metabolic syndrome and tumor formation.? Clinical symptoms in CAH are due to a combination of disease-related and treatment-related side effects.? Both short-term and long-term complications may arise related to glucocorticoid and/or androgen excess. Laboratory evaluation should guide, not define, treatment.? The desire for fertility, the presence of testicular adrenal rest (males) or female virilization, bone mineral density, and BMI help guide therapy. The goal is to treat with the lowest possible glucocorticoid dose and to optimize the risk/benefit ratio for each

patient. Optimal therapeutic regimens are often difficult to achieve, and the transition from pediatric to adult care is a recognized challenge. This session will focus on management strategies, especially during the transition of the CAH patient to adulthood.

MTE26

Hypoglycemia: Does it matter?

Sofia Zoungas

Monash University

Professor Sophia Zoungas
Professor Zoungas (MBBS (Honours), FRACP, PhD) is a leading clinician scientist as recognised by her appointments to Chair of Diabetes, Vascular Health and Ageing and Deputy Director of the Monash Centre for Health Research and Implementation, School of Public Health and Preventive Medicine, Monash University, NHMRC Senior Research Fellow, Professorial Research Fellow George Institute for Global Health and Senior Staff Specialist in Endocrinology/Diabetes/Vascular Medicine at Monash Health, Victoria. Her research focus is on the generation and implementation of the best evidence for the prevention, screening and management of diabetes and vascular diseases, and the impact of these on the ageing population. In addition to a strong record of publications (overall 126, total citations over 4700, 1113 citations in 2015, first or senior author of 57, first author of 2 published in the New England Journal of Medicine, 27 with over 50 citations, 6 with over 200 citations and 1 with over 670 citations, H index 33) and grant success (more than 8 million peer reviewed in the last 5 years including funding from the NHMRC, International Diabetes Federation, Diabetes Australia Research Trust, Australian Diabetes Society and commercial sources), Professor Zoungas has made over 50 presentations at major national and international meetings in the last 5 years and received significant awards including Henry Burger Prize for the best research publication, Monash Health rising star award and Monash University mid-career research award.
Research leadership: Professor Zoungas has brought together international and national teams to complete work on cardiovascular, metabolic and kidney health related projects, including leading large collaborative projects. She leads the NHMRC funded STAREE clinical trial which is examining the effect of statin therapy on survival and major cardiovascular events in over 10,000 healthy and independent living elders over 70 years. She is the international director of the ADVANCE-ON study (the post-trial observational follow up of cardiovascular and mortality outcomes in over 10,000 individuals with type 2 diabetes) and the international scientific coordinator of the Collaborators on trials of glucose lowering project. She leads a NHMRC funded partnership project with health care networks and advocacy groups examining models of health care in patients with diabetes and kidney disease.

MTE27

Thyroid and Pregnancy

Tim Korevaar

Erasmus University Medical Center

During medical school, Tim Korevaar started his research career at the Oxford Center for Diabetes, Endocrinology and Metabolism with Niki Karavitaki and Ashley Grossman. After finishing his MD, he started his PhD at the Rotterdam Thyroid Center with Robin Peeters and Theo Visser and obtained a Master's degree in Clinical Epidemiology. His main interest is to translate thyroid physiological aspects into clinically relevant epidemiological studies. His focus has particularly been on determinants of gestational thyroid function (including hCG, iodine and endocrine disrupting chemicals) and the association of gestational thyroid function with the risks on adverse pregnancy and child development outcomes (including preterm birth, pre-eclampsia and offspring neurocognition). For his studies on these topics, Dr. Korevaar has received the British Thyroid Award and Best Oral Communication Award (BES 2014), an Outstanding Abstract Award (ENDO 2015) and a Poster Prize and Young Investigator Award (ECE 2015, 2016). In this context he has been involved in the EUthyroid Collaboration and has co-initiated international collaborations that combine studies on gestational thyroid function and the role of endocrine disruptors.

MTE28

Update on long acting growth hormone

Jens Otto Lunde Jorgensen

Aarhus University Hospital

Professor of Medicine, Centre Chair, DMSc, Aarhus University and Aarhus University

MTE29

Therapy of differentiated thyroid cancer

James Alexander Fagin

Memorial Sloan Kettering Center

James A. Fagin is Chief of the Endocrinology Service and a Member of the Human Oncology and Pathogenesis Program at MSKCC and a Professor of Medicine at Weill Medical College of Cornell University in New York City, N.Y. He specializes in the treatment of patients with thyroid cancer. His laboratory focuses on thyroid cancer genomics and on understanding the biology of these tumors, in order to identify specific therapies directed at key thyroid oncoproteins, and on understanding mechanisms of response and resistance to targeted therapies. He is a recipient of various awards, the Merck Prize of the European Thyroid Association, the Sidney H. Ingbar Distinguished Lectureship Award of the American Thyroid Association, the Clinical Endocrinology Trust Lectureship of the Society of Endocrinology in the UK and the Clinical Investigator Award of the Endocrine Society in 2014. He is also a past-president of the American Thyroid Association.

MTE30

Genetic Tests: What the Clinical Endocrinologist Should Know

Maria Luisa Brandi

University of Florence - Department of Surgery

BRANDI, MARIA LUISA
Brandi, Maria Luisa Full Professor of Endocrinology, University of Florence, Medical School, Florence, Italy
Education/Training Positions: MD, University of Florence, Florence, Italy, 1977; School of Specialization in Endocrinology, University of Florence Hospital, 1977-1980; National Institutes of Health (NIH) Visiting Scientist in Metabolic Diseases, Metabolic Diseases Branch, NIH, Bethesda, Maryland, United States, 1984-1990; Ph.D. in Cell Biology, University of Rome, 1988; Assistant, Associate and Full Professor of Endocrinology, University of Florence, 1990-to present; Director, Regional Center on Hereditary Endocrine Tumors, University Hospital of Florence, 1998-to present; Director Clinical Unit on Metabolic Bone Disorders, University Hospital of Florence, 2007-to present; Delegate, Italy/USA Academic Interactions, Florence University, 2000-2003; Director of the University Master on Metabolic Bone Disease: From the Gene to the Cure, University of Florence, 2004-to present; Scientific Director, DeGene Spin-off, University of Florence, 2005-2009; President, Fondazione Italiana Ricerca sulle Malattie dell'Osso (F.I.R.M.O.), 2006 - to present; Consultant for the Tuscany Region on Osteoporosis 2008 - to present; Member of the Commission for Osteoporosis of the Italian Ministry of Health 2009 – 2011; Scientific Attaché for the City of Florence 2015 - to present.

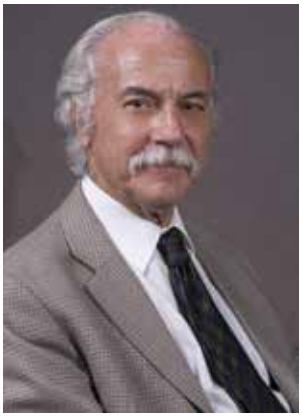
Rare endocrine-metabolic diseases (REMD) represent an important area in the field of medicine and pharmacology. The rare diseases of interest to endocrinologists involve all fields of endocrinology, including rare diseases of the pituitary, thyroid and adrenal glands, paraganglia, ovary and testis, disorders of bone and mineral metabolism, energy and lipid metabolism, water metabolism, and syndromes with possible involvement of multiple endocrine glands, and neuroendocrine tumors.
The total number of rare endocrine diseases in the adult is 166 main disorders, 338 including all various and subtypes. In the future, the creation of registries of rare endocrine diseases to collect data on cohorts of patients and the development of common and standardized diagnostic and therapeutic pathways for each rare endocrine disease is advisable. The need for educational program in clinical endocrinology for the correct prescription of genetic tests is ugently felt.

MTE31

Treatment in older people with type 2 diabetes

Isaac Sinay

Advisor of the Diabetes Unit in The Cardiovascular Institute of Buenos Aires, Argentina



This presentation will be the case of a women, 74 years old, duration of diabetes three years, with hypertention and dislipidemia, with inadequate response to metformin.. Without another comorbidities
The discussion of the medicine to add ("second step") will be in the frame of some International and National guidelines
The age, phenotype, risk profile and availability will conduct to the decision proposed and the alternatives to it.

MTE32

Genetics of pheochromocytoma

Anne-Paule Gimenez-Roqueplo[1,2,3]

1. Inserm, Umr970, Paris-Centre De Recherche Cardiovasculaire, F-75015, Paris, France
2. Université Paris Descartes, Pres Sorbonne Paris Cité, Faculté De Médecine, F-75006 Paris, France
3. Assistance Publique-Hôpitaux De Paris, Hôpital Européen Georges Pompidou, Service De Génétique, F-75015 Paris, France

Paragangliomas and pheochromocytomas (PPGL) are neuroendocrine tumors with a very strong genetic component. A germline mutation in one of the different susceptibility genes identified so far explains about 40% of all cases. Genetic testing is recommended in every affected patient and next-generation sequencing (NGS) is the ideal technology to screen the high number of PPGL susceptibility genes. The interpretation of genetic variants identified by NGS can be guided by the

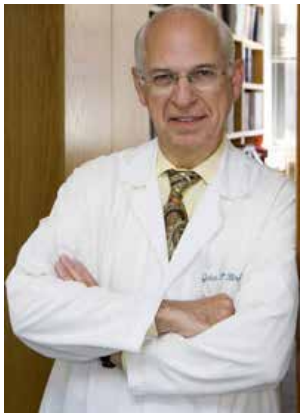
clinical presentation as well as by the secretory phenotype and by the immunohistochemical analysis of tumors. The diagnosis of an inherited form drives clinical management and tumor surveillance of the patient and relatives1.

While whole-exome sequencing studies showed that PPGL is characterized by a low mutation rate of 0.3 mutations per megabase similar to other neural crest-derived tumors, the first integrative genomic analysis of a large collection of 202 PPGL, carried out by the French COMETE network, demonstrated that mutation status in PPGL susceptibility genes is strongly correlated with multi-omics data and revealed the crucial role of predisposing mutations as being the main drivers of PPGL2. PPGL subtypes can be defined by a set of unique genomic alterations that represent different molecular entities. Transcriptomic studies identified two main molecular pathways, activating either the hypoxic pathway (cluster C1) or the MAPkinase/mTOR signalling (cluster C2). This comprehensive analysis further illustrated the functional interdependence between genomic and epigenomic dysregulations. Indeed, DNA methylation profiling uncovered a hypermethylator phenotype specific to the tumors related to a mutation in one of the PPGL susceptibility genes encoding for a protein of the tricarboxylic cycle. Besides, we demonstrated that succinate is acting as an oncometabolite, inhibiting 2-oxoglutarate-dependent dioxygenases, such as HIF prolyl-hydroxylases and histone/DNA demethylases, explaining noradrenergic secretory and metastatic phenotypes of PPGL classified in cluster 1A3. Finally, 'omics' data suggested new therapeutic targets for patients with a metastatic PPGL as well as novel diagnostic and prognostic biomarkers. New 'omics'-based tests for PPGL are likely to be transferred from research laboratories to clinical practice in order to give the access to a precise molecular classification of every PPGL, after surgery, to practicing clinicians with the goal of establishing a personalized medical management of affected patients.

MTE33

New Concepts in Hypoparathyroidism

John Bilezikian



John P. Bilezikian, M.D.

Dr. Bilezikian, the Dorothy L. and Daniel H. Silberberg Professor of Medicine and Professor of Pharmacology at the College of Physicians & Surgeons, Columbia University is Vice Chair of the Department of Medicine for International Education and Research and Chief, Emeritus, of the Division of Endocrinology. He is Director of the Metabolic Bone Diseases Program at Columbia University Medical Center. Dr. Bilezikian received his undergraduate training at Harvard College and his medical training at the College of Physicians & Surgeons. He completed four years of house staff training (internship, residency and Chief Residency) on the Medical Service at Columbia Presbyterian Medical Center. Dr. Bilezikian received his training in Metabolic Bone Diseases and in Endocrinology at the NIH in the Mineral Metabolism Branch under the tutelage of Dr. Gerald Aurbach. He belongs to a number of professional societies including the ASBMR, of which he served as President, 1995-1996 and the ISCD, of which he served as President, 1999-2001. He is a member of the Endocrine Society, the American Federation for Clinical Research, the American Society for Clinical Investigation, the Association of American Physicians, the American Association of Clinical Endocrinologists, the American Society for Pharmacology and Experimental Therapeutics, and the American College of Endocrinology that has designated him Master. He served on the Board of Governors of the International Osteoporosis Foundation (1999-2015) and is a current member of its Committee of Scientific Advisors. He is Chair of the Endocrine Fellows Foundation. He served as Editor-in-Chief of the Journal of Clinical Endocrinology and Metabolism and as Senior Associate Editor of the Journal of Bone and Mineral Research. He is Executive Advisory Editor of Bone Research. His books include Editor-in-Chief of The Parathyroids [1994, 2001, 2014], and co-editor of The Aging Skeleton (1999), Dynamics of Bone and Cartilage Metabolism (1999, 2006), Principles of Bone Biology (1996, 2002, 2008) and Osteoporosis in Men (2010). He is Editor-in-Chief of the Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism (2016-). He has been on numerous panels, including serving as Chair of the NIH Consensus Development Panel on Optimal Calcium Intake (1994), Co-chair of the last three International Workshops on Primary Hyperparathyroidism (2002, 2008, 2013) and of the first International Workshop on Hypoparathyroidism (2015). He is a major national and international spokesperson for the field of metabolic bone diseases. Dr. Bilezikian's major research interests are related to the clinical investigation of metabolic bone diseases, particularly osteoporosis,primary hyperparathyroidism and hypoparathyroidism. He is the recipient of the Distinguished Physician Award of the Endocrine Society, the Frederic C. Bartter Award of the ASBMR for Excellence in Clinical Research, the First Annual Global Leadership Award of the ISCD, and Lifetime Achievement Awards of the Armenian American Medical Society of California and the Armenian American Health Professionals Organizations. In 2009, he received the Gideon A. Rodan Excellence in Mentorship Award from the ASBMR. He received the Laureate Distinguished Educator Award of The Endocrine Society in 2014. In 2014, he was made honorary member of the Brazilian Society of Endocrinology and Metabolism. In 2015, he received the Oscar Gluck Humanitarian Award of the International Society of Clinical Densitometry and the Inaugural Global Educator of the Year Award from McMaster University in Canada. His publications, which number over 750, speak to his active original investigative initiatives as well as his authorship of many reference sources of endocrinology and metabolic bone diseases.

Information about the parathyroid disorders has been dominated over the past several decades by primary hyperparathyroidism, a relatively common endocrine disorder. Its counterpart, namely hypoparathyroidism, has received much less attention due, in part, to the fact that, in contrast to primary hyperparathyroidism, it is a rare disorder. The average endocrinologist sees well under 5 patients per year with hypoparathyroidism. Its etiology is usually due to the consequences of prior anterior neck surgery that may have occurred in the recent or distant past. Hypoparathyroidism can also be caused by autoimmune destruction of the parathyroid glands. The presenting symptoms are generally related to hypocalcemia and its attendant neuromuscular irritability. Patients also classically complain of a set of neurocognitive features best described as "brain fog." Treatment has been limited, until recently, to supplemental calcium and vitamin D. Thiazides can be helpful when there is marked hypercalciuria. The amount of supplemental calcium and vitamin D required to maintain normal calcium levels can be monumentally large, giving rise to concerns about ectopic calcifications. Soft tissue calcifications may be as much due to accompanying hyperphosphatemia as to the calcium-phosphate product. Calcifications in the basal ganglia and other intracerebral sites are common as are renal stones and nephrocalcinosis. Bone density typically is above average but recent insights into skeletal microstructure in

hypoparathyroidism have raised questions as to whether bone quality is good, despite the bone density measurements. The approach to the management of hypoparathyroidism is changing because of the availability in the United States of recombinant, human parathyroid hormone [rhPTH(1-84]). In several clinical trials, including the pivotal clinical trial that led to its registration in the United States, rhPTH(1-84) was shown to reduce significantly supplemental calcium and vitamin D requirements while maintaining serum calcium levels. In other studies, it has been shown that the use of rhPTH(1-84) improves quality of life. Changes in bone mineral density have also been reported. The MTE session will focus on the epidemiology, clinical presentation, and therapeutic approaches to hypoparathyroidism.

MTE34

Hormone therapy in menopause

Bronwyn Stuckey

Sir Charles Gairdner Hospital

MTE35

Pregnancy and Diabetes

Huixia Yang

Peking University First Hospital

S01-01

Diagnosis and Treatment of Subclincial enlargement of the adrenal gland

Yiming Mu

Chinese PLA General Hospital

Yiming Mu is Professor and Chief of the Department of Endocrinology, Chinese PLA General Hospital, in Beijing. He also holds the post of the President of Chinese Society of Endocrinology (CSE), Vice President of the Chinese Endocrinologist Association and President of the Chinese PLA Endocrine Association.

Professor Mu completed his basic medical education in China and then went to Japan to hone his skills on the principles of molecular research and obtained a Ph.D from the Kyushu University in Japan. His broad research interests are reflected in more than 250 publications to date in diverse fields including diabetes, glucose metabolism and pancreatic beta-cell biology and stem cell biology.

Education:

1979-1984: Second Military Medical University, Shanghai, P.R. China

1988-1991: Military Post-graduate Medical School, Beijing, P.R. China

1996-2001: Faculty of Medicine, Kyushu University, Fukuoka, Japan

Employment:

2001-present: Professor and Director, Department of Endocrinology, Chinese PLA General Hospital, Beijing;

1994-2001: Associate Professor, Department of Endocrinology, Chinese PLA General Hospital, Beijing;

1991-1994:Assistant Professor in Residence, Department of Endocrinology, Chinese PLA General Hospital, Beijing;

1984-1991: Residency: Internal Medicine, Chinese PLA General Hospital, Beijing;

1983-1984: Internship: Internal Medicine,Shanghai 4th Hospital, Shanghai.

Adrenal incidentalomas are common since the widely application of noninvasive imaging methods, including ultrasound, CT and MRI. Except the non-functioning adrenal adenomas, subclinical adrenal diseases account for the main part of adrenal incidentalomas, which represent subclinical Cushing's syndrome (5%-10%), subclinical primary aldosteronism (1%-2%) and pheochromocytoma (1%-11%), respectively. Since the subclinical adrenal diseases do not cause classical clinical signs and symptoms of hormone excess syndromes, diagnosis are made after hormone evolution about the affected adrenal glands by related laboratory tests.

Biochemical features of subclinical Cushing's syndrome include suppressed ACTH (<5 or <10 pg/ml), increased urine-free cortisol, suppression of cortisol to greater than 5.0 mg/dl (or 1.8 mg/dl) after dexamethasone 1 mg, elevated late night serum or salivary cortisol, and/or suppressed DHEAS. To screen for normotensive primary aldosteronism, we recommended that PAC and PRA should be measured in normotensives with hypokalaemia and/or an adrenal incidentaloma. Then, suppression testing, including the captopril suppression test, the oral sodium loading test, the intravenous saline infusion test or the fludrocortisone suppression test, are necessary to confirm a diagnosis of primary aldosteronism. For patients with subclinical pheochromocytoma, plasma metanephrines is considered as the first-line diagnostic test due to its excellent diagnostic sensitivity and convenience. Patients with elevated plasma metanephrines within three to four times the upper limit of normal need to proceed further with measurement of 24-h urine metanephrines.

Once diagnosed as the subclinical diseases mentioned above, it's significant to choose the suitable therapeutic strategy for patients, and surgery is indicated for most secretory tumors. Patients in whom with metabolic markers, such as insulin resistance or cardiovascular risks, are more likely to benefit from surgery. However, other strategies would be referred to patients with subclinical Cushing's syndrome and progressively worsening patterns of excess cortisol secretion, that is, an increasing number of abnormal HPA tests, because the more abnormal tests present the higher the risk for postsurgical adrenal insufficiency indicating significant preoperative hypercortisolism and hence an increased tendency to develop complications and higher mortality. For patients with subclinical adrenal aldosteronism, it sometimes may be better treated with a mineralocorticoid receptor antagonist or adrenalectomy even before hypertension develops. All tumors with subclinical pheochromocytoma should undergo surgery.

It is noteworthy that patients undergoing bilateral adrenalectomy should receive appropriate glucocorticoid cover, and the patients with postoperative hypoadrenalism should be with a long-term management and follow-up.

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S01-02

Should we treat sub-clinical cushing's syndrome?

Massimo Terzolo

Internal Medicine 1, Department of Clinical and Biological Sciences, University of Turin, Italy

Head of the Division of Internal Medicine 1 at the University Hospital San Luigi Gonzaga since 2009.

Deputy Director of the Department of Clinical and Biological Sciences, University of Turin since 2012.

Sub-clinical Cushing's syndrome is an ill-defined condition whose most frequent clinical scenario is characterized by 3 major features: 1) presence of an adrenal incidentaloma, 2) in a patient who does not present classic Cushingoid signs, 3) with a work-up of the HPA axis suggesting adrenal autonomy and low grade cortisol excess. Although a classic Cushing phenotype is not apparent, diseases potentially linked to cortisol excess, such as hypertension, diabetes and obesity, may be present. There are currently many definitions in use to define the condition and the controversy in terminology reflects uncertainty in securing the diagnosis, since many diagnostic algorithms have been proposed with different cutoffs to qualify positive test results. Despite heterogeneity in defining the condition, there is evidence linking progressively increased cortisol levels following the 1-mg overnight dexamethasone test to higher mortality, particularly due to cardiovascular events. Thus, the greater is cortisol autonomy from pituitary control the larger is the clinical effect. Intervention studies suffer from methodological limitations but quite consistently show amelioration of blood pressure and glucose levels following removal of the adrenal adenoma, that is to say surgical treatment of sub-clinical Cushing's syndrome. There is evidence showing that the benefit of surgery is greater in patients showing higher degrees of cortisol autonomy. It is likely hat the same factors influencing the outcome of surgical treatment of overt Cushing's syndrome, such as patient age, duration of comorbidities, established target organ damage, may influence also results of treatment of sub-clinical Cushing's syndrome. To conclude, our approach to sub-clinical Cushing's syndrome should not differ from overt adrenal Cushing's syndrome and surgery has to be considered as the primary treatment modality.

S01-03

Subclinical tertiary hypoadrenalism

Rachel Crowley

University College Dublin

Dr Rachel Crowley graduated from the Royal College of Surgeons in Ireland and completed specialty training including an MD in Ireland before moving to the University of Birmingham in 2012. At UoB and University Hospitals Birmingham she worked with Profs Paul Stewart, Jeremy Tomlinson and Weibke Arlt on a number of projects related to steroid hormones, adrenal disease and bone metabolism. In 2014 she returned to Ireland to take up a position at St Vincent's University Hospital and University College Dublin. Dr Crowley is an active clinician and maintains a research interest in bone and electrolyte metabolism, adrenal and pituitary disease.

S02-01

The PI3K/AKT/mTOR Signaling Pathway Is Overactivated in Primary Aldosteronism

Fukang Sun

Ruijin Hospital of Shanghai Jiaotong University

Professional position
Chief physician of Urology department, Ruijin Hospital, School of Medicine, Shanghai Jiaotong University.
Master tutor
Professional societies
Member of prostate Group, Shanghai urology association
Member of quality control group, Shanghai urology association
Member of Shanghai cancer council
External reviewer of CAUJ and International Journal of Experimental Pathology
Educational experience
Further studied in the urology department of Johns Hopkins University of the United States
Specialized field
Be expert in basic medical research of adrenal diseases, and also in minimally invasive surgical management of complicated and critical adrenal diseases and giant adrenal masses, including traditional laparoscopic surgery and robot-assisted laparoscopic surgery.
Be adept in basic medical research and comprehensive treatment of prostatitis, and have accumulated rich experience in preoperative assessment, surgery and combined treatment of prostatic cancer.
Publications
Have published more than forty papers in international journals and Chinese Medicine Series journals in recent years.
Funding information
Be responsible for a National Nature Science Foundation project, two Shanghai Science and Technology Committee projects and a Shanghai Education Commission project.

Honors and prizes: Have won the second prize of national scientific and technological progress award, the first prize of Education Ministry scientific and technological advance award, the first prize of Chinese medical scientific and technological advance award, the first and the third prize of Shanghai medical scientific and technological advance awards.

Background: To date, the available non-invasive remedies for primary aldosteronism are not satisfactory in clinical practice.The phosphoinositide 3-kinase (PI3Ks)/protein kinase B (PKB or AKT)/mammalian target of rapamycin (mTOR) signaling pathway is essential for tumorigenesis and metastasis in many types of human tumors, including renal cancer, adrenal carcinoma and pheochromocytoma. The possibility that this pathway is also necessary for the pathogenesis of primary aldosteronism has not yet been explored. To answer this question, we investigated the activity of the PI3K/AKT/mTOR signaling pathway in normal adrenal glands (NAGs), primary aldosteronism (PA) patients and NCI-H295R cells.
Methodology/Principal Findings: Between January 2005 and December 2011, we retrospectively reviewed the records of 45 patients with PA. We compared clinical characteristics (age, gender and biochemical data) and the expression of phospho-AKT (p-AKT), phospho-mTOR (p-mTOR), phospho-S6 (p-S6) and vascular endothelial growth factor (VEGF) by immunohistochemical staining and western blotting, analyzing 30 aldosterone-producing adenomas (APAs), 15 idiopathic hyperaldosteronism (IHA) tissues and 12 NAGs following nephrectomy for renal tumors (control group). Compared with the control group, most of the PA patients presented with polydipsia, polyuria, resistant hypertension, profound hypokalemia, hyperaldosteronemia and decreased plasma renin activity. Compared with normal zona glomerulosa, the levels of p-AKT, pmTOR, p-S6 and VEGF were significantly upregulated in APA and IHA. No significant differences were found between APA and IHA in the expression of these proteins. Additionally, positive correlations existed between the plasma aldosterone levels and the expression of p-AKT and p-mTOR. In vitro studies showed that mTOR inhibitor rapamycin could inhibit cell proliferation in NCI-H295R cells in a dose- and time-dependent manner. Furthermore, this inhibitor also decreased aldosterone secretion.
Conclusions: Our data suggest that the PI3K/AKT/mTOR signaling pathway, which was overactivated in APA and IHA compared with normal zona glomerulosa, may mediate aldosterone hypersecretion and participate in the development of PA.

S02-02

Personalized medical therapy in adrenal cancer

Felix Beuschlein

Medizinische Klinik und Poliklinik IV, Klinikum der Universitaet Muenchen

• *Current positions*
since 10/11 Head of Endocrine Outpatient Clinic
since 06/06 Head of Endocrine Research, University of Munich (W2 Professorship)

Among patients with adrenal masses, adrenocortical carcinoma (ACC) are found with a low incidence but very unfavorable prognosis: ACC has an estimated prevalence ranging from 4 to 12 per million with a predominance of female patients. In pre-selected patient cohorts on which adrenal tumor surgery had been performed, the proportion of ACC may be as high as 12%. The clinical outcome of ACC is poor with a 5-year survival of only 15-35%. Mitotane is the only approved drug and current first-line therapy for ACC. Mitotane therapy is complicated by poor tolerability, low efficacy, and difficulty in reaching therapeutic blood levels. Virtually all patients develop adrenal insufficiency that is difficult to replace due to drug side effects. There are no randomized trials on efficacy, but several studies indicate that the median progression free survival in advanced ACC on mitotane is about two months. In patients with extended disease poly-chemotherapy regiments including cisplatin, etoposide and doxorubicin have been established as first line treatment. However, response rates and overall survival in this patient group is particularly poor. Therefore, search for better therapeutic options for ACC patients is a long-standing challenge. Following molecular characterization, targeted therapies involving the insulin-like growth factor system have been tested. However, while pre-clinical studies have provided promising results the outcome of randomized clinical trials have been disappointing. Currently, standard histological studies as well as sophisticated molecular analyses are applied to identify markers with prognostic power that will also guide in personalized treatment decisions. When these will be applicable in the routine clinical setting remains an open question.

S02-03

Future and new therapies on adrenal cancer

Gary Hammer

Endocrine Oncology Program, Comprehensive Cancer Center, University of Michigan

Gary D. Hammer, M.D., Ph.D. is a Professor in the Departments of Internal Medicine (Metabolism, Endocrinology & Diabetes), Cell & Developmental Biology, and Molecular & Integrative Physiology at the University of Michigan (UofM). Before arriving in Michigan in 1999, he obtained his M.D. and Ph.D. in Neuroscience from Tufts University and completed his residency in Internal Medicine followed by a clinical fellowship in Endocrinology and a postdoctoral fellowship with Holly Ingraham at the University of California – San Francisco. He currently serves as the Director of the Endocrine Oncology Program in the Comprehensive Cancer Center at UofM where he holds the Millie Schembechler Professorship in Adrenal Cancer. He has brokered the recent renaissance of the current Michigan team of adrenal scientists that includes a who's who in the clinical and basic study of adrenal disease. He received the UofM Jerome Conn Award for Outstanding Research in Internal Medicine, the Endocrine Society Edwin B. Astwood Award for Outstanding Research in Endocrinology and is a member of the American Society for Clinical Investigation and Association of American Physicians. He is the editor of three textbooks: Adrenocortical Carcinoma: Basic Science and Clinical Concepts (Springer 2011), Pathophysiology of Disease: An Introduction to Clinical Medicine (Harper Row, 2014) and Genetics Steroid Disorders (Elsevier, 2014). In addition to being a founding organizer of the biennial International Adrenal Cancer Symposium, he also is a member of the coordinating team of the biennial International Adrenal Meetings and has served in numerous capacities across the tripartite constituencies of the Endocrine Society including Chair of the Student Affairs Committee, Chair of the Mentoring Task Force, Basic Science Chair of the Annual Meeting

Trainee Day, Council Member at Large and Society Ambassador to King Edward Memorial Hospital in Mumbai India as part of the inaugural Endocrine Society Ambassador Exchange Program. Most recently he has served as the Clinical Research Chair of the 2016 Endocrine Society Annual Meeting and will be the Overall Chair of the 2017 Annual Meeting. Research projects in his own laboratory are aimed at elucidating the mechanisms by which growth factor signaling and transcriptional programs initiate adrenal-specific growth and
differentiation with an emphasis on dysregulated adrenocortical stem cells in development and cancer. He is a cofounder of the company MILLENDO that focuses on therapies for adrenal cancer. Collaborative work with colleagues has led to the development of new national and international therapeutic trials with biological-based therapies for adrenal cancer that target the molecular defects in cancer while sparing normal tissue.

S03-01

Generation of functional thyroids in a dish

Sabine Costagliola

Université Libre Bruxelles, IRIBHM

Sabine Costagliola Short CV
Sabine Costagliola is FNRS Senior Researcher and principal investigator at IRIBHM, Université Libre de Bruxelles (ULB), Belgium.
She obtained a Ph.D in Immunology in 1991 at AIX-Marseille University in France and a Ph.D in Biomedidal Sciences in 2000 at ULB in Belgium.
She is Member of the European Thyroid Association (ETA), Member of the Endocrine Society, board member of the Belgian Society for Stem Cells Research (BeSSCR) and board member of the Belgian Society for Cell and Developmental Biology (BSCDB).
She is laureate of several prizes for her contribution to thyroid and endocrine research: Haarington De Vischer Prize 2001 awarded by the European Thyroid Association; Alvarenga Prize 2004 from the Royal Academy of Medicine, Belgium; Gaetano Salvatore Prize 2005, from the Academia dei Lincei, Roma, Italy; Laureate of European Journal of Endocrinology Prize, from the European Endocrine Society, 2006, Merck Serono Prize 2013.
Sabine Costagliola is author of more than 50 peer-reviewed articles in international Journals as first or last author in Endocrinology/thyroid/reproduction and co-author of more than 100 peer-reviewed articles in international Journals.
The main focus of her research is the molecular dissection of signaling mechanisms that control morphogenetic processes and gene networks involved in thyroid organogenesis. A crucial aspect of the working strategy is the combination of various experimental models including Zebrafish and embryonic stem cells to delineate the molecular basis of thyroid morphogenesis.

S03-02

Personalized medical therapy in adrenal cancer Molecular diagnosis and treatment of congenital hypothyroidism

Heiko Krude

University Medicine Berlin

S03-03

Therapy of subclinical hypothyroidism

Ying Gao

Peking University First Hospital

Dr. Ying Gao is Chief Physician and Professor in the department of Endocrinology in Peking University First Hospital in Beijing, China. Dr. Gao received her MD degree from Peking University health and science center, China, in 2004. She completed her training in Internal Medicine and Endocrinology at Peking University First Hospital. In 2004, Dr. Gao joined the department of Endocrinology at the same hospital. Her clinical activities focus on patients with thyroid dysfunction and autoimmune thyroid diseases. Her research interests focus on the pathogenesis of autoimmune thyroid diseases. Dr. Gao is a member of thyroid group of Chinese Society of Endocrinology. She has published more than 50 manuscripts in the field of endocrinology.

Subclinical hypothyroidism (SCH) is defined biochemically as serum TSH levels above the upper limit of the reference range, in the presence of normal concentrations of free T4. It may occur in the presence or absence of mild symptoms of hypothyroidism. SCH can be further classified into a milder condition with TSH levels between the upper limit of the reference range and 10.0 mIU/l (mild-SCH) and a severe form with TSH >10.0 mIU/l (severe-SCH).
SCH is common, which increases with age. Since serum TSH levels can be transiently increasing, TSH should be measured repeatedly after about three months to confirm the diagnosis of SCH. There is considerable controversy regarding who should be treated with SCH. Thyroxine treatment should be started in patients with TSH levels ≥10 mU/L, to prevent progression from SCH to overt hypothyroidism. Evidence on the association of mild-SCH and cognitive dysfunction, mood disorders, cardiovascular events and dyslipidemia is conflicting, thus treatment for patients with serum TSH <10 mIU/l should be made on the basis of the age of the patient, associated risk factors and comorbid conditions, such as the symptoms suggestive of hypothyroidism, or high titers of thyroid peroxidase antibodies. Its is uncertain whether treatment is more beneficial than harmful, especially in the elderly, since some patients receiving treatment will have inadvertent overtreatment.
For pregnant women, increasing TSH levels should be defined using trimester-specific TSH reference ranges. The data have also shown increased risk of adverse pregnancy outcomes in patient with SCH, with some benefits of thyroxine treatment.
More randomized controlled trial of thyroxine treatment for SCH will guide future clinical practice.

S04-01

Low and high dose radioiodine therapy in thyroid cancer

Hankui Lu

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Hankui Lu, MD, Prof.
Director of Nuclear Medicine Research,Associate-Director of Medical Imaging Research Institute, Shanghai Jiaotong University,
Associate Editor-in-Chief of Chinese J of Nuclear Medicine and Molecular Imaging,Standing Committee Member of Thyroid Cancer Division of China Anti-Cancer Association.
Prof. Lu, physician on Nuclear Medicine, has participated in the clinical practice and research works in thyroid diseases for nearly 30 yrs. His personal medical experience has been enriched with more than 5000 patients with thyroid diseases, most of them with differentiated thyroid cancers. He has also accomplished several research works and published more than 40 scientific papers related to the thyroid disorders.

Radioiodine-131 (^{131}I, RAI) therapy has long been used as an integrated part for the management of patients with differentiated thyroid cancer (DTC), with three evolving therapeutic targets as remnant ablation, adjuvant therapy or treatment for inoperable persistent disease (residual or distant metastases). Typically, low dose (30 mCi or any single dose less than 100 mCi) ^{131}I was administrated for simple ablation in low risk patients, high dose (≥100 mCi, usually 100~200 mCi) for adjuvant therapy in patients with intermediate or indeterminate risks, much higher doses (150~250 mCi, even more somewhere) for high risk patients and repeated higher dose therapy for radioiodine-avid distant metastases.

It has long been debatable whether low dose ^{131}I or high dose ^{131}I should be adopted for remnant ablation or adjuvant therapy. Recent studies, especially some well designed randomized clinical trials comparing low-dose (30 mCi, 50 mCi, etc.) and high-dose (100 mCi) ^{131}I in combination with thyrotropin alfa (rhTSH) or thyroid hormone withdrawal for TSH elevation, suggested that low dose ^{131}I was generally favored with the obvious advantages such as almost equal successful remnant ablation rates, simple out-clinic utility, and with less side effects, etc., as compared to high dose ^{131}I. However, limited long term data on the impact of various doses for ablation or adjuvant therapy are available. Our primitive clinical data using 30 mCi (questionable) for ablation suggested that, though the outcomes were acceptable, more than 10% DTC patients needed second ablation dose (100 mCi) and some others were found unexpectedly with distant metastases in the post-therapeutic ^{131}I WBS (whole body scan). Given the varieties of follow-up strategies among the field doctors and stricter sanctions against out-patients treatment with low dose ^{131}I in China, collection of reliable long term follow-up data poses challenges to validate the role of low dose ^{131}I for ablation or adjuvant therapy.

It is also worth note that there is tendency to question the actual clinical significance of ^{131}I ablation for reducing the recurrence and facilitating the follow-up after thyroidectomy for the primary management of low and intermediate risk DTC patients. If, future research evidence collectively turns out that, against former beliefs, remnant thyroid tissue after thyroidectomy is unrelated with increasing recurrence and distant metastases, and serum Tg level also be reliably used for post-thyroidectomy evaluation and equally an important monitoring mark without ^{131}I ablation, then, the strategy without ^{131}I ablation may serve better for most DTC patients.

High dose ^{131}I therapy indicated for DTC patients with radioiodine-avid metastases or other high risk factors remains almost undisputed, though the dose selection range and accumulative dose limits are still defined as "empiric" with source references out of observation data. High dose empiric ^{131}I therapy for patients with serum Tg-positive but diagnostic ^{131}I WBS negative has been a clinical option, but in those cases, significant ^{131}I-avid metastases are scarcely found from post-therapeutic ^{131}I -WBS and long term benefits from this treatment are uncertain. Repeated higher dose ^{131}I therapy with limited cumulative administered activities can be regarded as reasonably safe, but dose related early and late-onset complications as salivary damage, dental cares, weakness, etc. are not uncommon. Second malignancy and leukemia after high dose ^{131}I therapy are actually rare and may well be taken as a clinical warning.

It is ideal but a pending issue how to pre-determine the radioiodine avid and radiation sensitive DTC lesions and thus to set up a reliable formula for ^{131}I dose calculation and qualification instead of empiric dose approximation. Also, mechanism of self-repairing and healing process from high dose ^{131}I damages on the patients' radio-sensitive normal tissues and immunological system has not been well understood. More, the evolving role of high dose ^{131}I therapy in the initial re-classification of risk status and further dynamic stratifications for the long term management for DTC patients, presently individually varied, would be better defined with more evident clinical data assembled.

S04-02

Surgery

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S04-03

New drug - Small molecule inhibitors of mutated kinases

Francesca Carlomagno

University of Naples Federico II

Associate Professor of General Pathology at the Medical Shool, Dipartimento di Biologia e Patologia Cellulare e Molecolare, Universita' degli Studi di Napoli Federico II

S05-01

Calcium Sensing Receptor in Bone-Therapeutic Insights

Dolores Shoback

Univerity of California, San Francisco

S05-02

Genetics of the calcium sensing receptor signaling pathway

Rajesh Thakker

Professor R V Thakker, May Professor of Medicine, Academic Endocrine Unit, University of Oxford, Radcliffe Department of Clinical Medicine, OCDEM, Churchill Hospital, Headington, Oxford, OX3 7LJ

Rajesh Thakker is the May Professor of Medicine at the University of Oxford, and a Fellow of Somerville and Harris Manchester Colleges, Oxford. His main research interests include the molecular basis of disorders of calcium homeostasis. He is a Consultant Endocrinologist who provides expertise in the fields of neuroendocrine tumours (NETs), and disorders of calcium and phosphate metabolism. He was previously Professor of Medicine at The Royal Postgraduate Medical School, The Hammersmith Hospital, London, until 1999, when he took up his present position in Oxford. He has served on the MRC Physiological Medicine and Infections Grants Committee (1994-1997), the MRC Clinical Training and Career Development Panel (1997-2000), the MRC Physiological Medicine and Infections Board (2000-2005), as Secretary to the Forum on Academic Medicine for the Royal College of Physicians (UK) and the Academy of Medical Royal Colleges (2002-2005), and on the Council for the Society for Endocrinology (2003-2006). He is currently Chairman of the National Institute of Health Research (NIHR) / MRC Efficacy and Mechanisms Evaluations (EME) Board. He has been the recipient of many prizes which include Young Investigator Award from the ASBMR (USA), the Raymond-Horton Smith Prize (Cambridge University, United Kingdom), the Society for Endocrinology (UK) medal, the European Journal of Endocrinology Prize (EFES), the Graham Bull Prize from the Royal College of Physicians (UK), the Parathyroid Medal from the Fondazione Raffaella Becagli (F.I.R.M.O.), the Jack W. Coburn Endowed Lectureship from the American Society of Nephrology, and the Louis V Avioli Founder's Award from the American Society for Bone and Mineral Research (USA). Professor Thakker was elected to the Fellowship of the Royal Society (FRS) in 2014.

The extracellular calcium-sensing receptor (CaSR) is a 1,078 amino acid G-protein coupled receptor (GPCR) encoded by the CaSR gene located on chromosome 3q21.1. The CaSR is predominantly expressed in the parathyroids and kidneys, where it allows regulation of parathyroid hormone (PTH) secretion and renal tubular calcium reabsorption appropriate to the prevailing extracellular calcium concentration. The CaSR is also expressed in other tissues that include the thyroid, intestine, bone, bone marrow, brain, skin, lens epithelium, pancreas, lung and heart, where its function remains to be defined. Ligand binding by the CaSR results in G-protein dependent stimulation, via Gαq/11, of phospholipase C (PLC) activity causing an accumulation of inositol 1,4,5 – trisphosphate (IP3) and rapid release of calcium ions from intracellular stores [Ca++] i is followed by an influx of extracellular calcium ions [Ca++]0. The increase in [Ca++]i results in activation of protein kinase C (PKC), which in turn activates the mitogen-activated protein kinase (MAPK) pathway. The CaSR can also activate the MAPK pathway via an isoform of Gi that inhibits adenylate cyclase and that activates Src-family tyrosine kinases.

Much has been learnt about the key role of the CaSR in the regulation of extracellular calcium homeostasis by the identification of CaSR mutations in human disorders. Thus, loss-of-function CaSR mutations result in familial (benign) hypocalciuric hypercalcaemia (FBHH), neonatal severe primary hyperparathyroidism (NSHPT) and adult primary hyperparathyroidism (AHPT). However, some individuals with loss-of-function CaSR mutations remain normocalcaemic. Gain-of-function CaSR mutations result in autosomal dominant hypocalcaemia (ADH) which may be accompanied by hypercalciuria, and also sometimes with Bartter-like syndrome (Bartter-syndrome type V). CaSR auto-antibodies have been found in FHH patients who did not have loss-of-function CaSR mutations, and in patients with an acquired form (ie. autoimmune) of hypoparathyroidism. Thus, abnormalities of the CaSR are associated with 4 hypercalcaemic and 3 hypocalcaemic disorders.

However, loss-of-function CaSR mutations are found in ~65% of FHH, referred to as FHH type 1 (FHH1), and gain-of-function CaSR mutations occur in ~70% of ADH, referred to as ADH type 1 (ADH1) patients. This indicates that other genes may be involved in the aeitology of FHH and ADH, and genetic heterogeneity has been established for FHH, with the FHH2 and FHH3 loci being mapped by genetic linkage studies to chromosomes 19p and 19q13, respecively. In a hypothesis-driven approach FHH2 was shown to be due to loss-of-function Gα11 mutations. It was postulated that Gα11, encoded by the GNA11 gene, may cause FHH2 because: GNA11 is located on chromosome 19p13 (the location of the FHH2 locus); CaSR signals via Gα11 and Gαq to PLC; and mice with parathyroid specific deletions of Gα11 and Gαq develop hypercalcaemia. Investigations of FHH patients without CaSR mutations identified some patients to have Gα11 mutations that diminished the sensitivity of CaSR-expressing cells to extracellular calcium, consistent with a loss-of-function. In addition, ADH patients, without CaSR mutations were found to have gain-of-function Gα11 mutations. These functional abnormalities caused by the FHH2- and ADH2-associated Gα11 mutations can be rectified, in vitro, by CaSR allosteric drugs that are calcimimetics (e.g., cinacalcet) and calcilytic drugs, respectively.

The gene causing FHH3, which had been mapped to a <4Mb interval containing >110 genes on chromosome 19q13, was identified by a hypothesis-generating approach that used whole exome sequencing. This revealed that mutations of the adaptor-protein 2 sigma subunit (AP2σ) which involved only the Arg15 residue, and comprised Arg15Cys, Arg15Leu and Arg15His, occurred in >20% of FHH patients, without CaSR or Gα11 mutations. AP2σ forms a heterotetrameric complex with α, β and μ subunits to yield AP2 which is pivotal in clathrin-mediated endocytosis, and the AP2σ mutations were found to decrease the senstivity of CaSR expressing cells to extracellular calcium alterations, by disrupting clathrin-mediated endocytosis of CaSR. AP2σ mutations have not been identified in ADH patients. These studies have revealed new insights into the CaSR signalling pathway and its role in regulating extracellular homeostasis and the eitology of parathyroid diseases.

S05-03

Calcium sensing receptor beyond calcium disorders

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All living organisms are able to sense and respond to the fluctuations of environmental composition of nutrients, gases and ions. One of the most abundant metals in our planet's crust, calcium, is also among the principal ions in the bodies of living organisms. Calcium plays pivotal roles in numerous of processes, starting from bone and teeth formation, to being an indispensable intracellular second messenger. Its additional role as an extracellular, first messenger became more apparent since early 1990 when the receptor for calcium ion, namely the calcium-sensing receptor (CaSR), was molecularly identified from the parathyroid gland (Brown et al., 1993). In humans, CaSR detects fluctuations in free ionised calcium concentrations in extracellular fluid, and suppresses release of parathyroid hormone (PTH) from parathyroid chief cells, which in turn acts on its target tissues, namely the kidney, intestine, and bone. Mutations of CaSR result in hypercalcemic or hypocalcemic disorders that can be life threatening.

Recent findings, however, indicate an important role of CaSR beyond the calcium metabolism. The CaSR was found to be expressed in mammalian brain, gut, blood vessels and airways. In addition to its classical agonist, calcium, CaSR could be activated by a plethora of molecules, such as mono- and polyvalent ions, amino acids, polyamines, and polycationic proteins, concentrations of which changes in health and disease.

CaSR expressed in the gastrointestinal tract participates in taste formation, hormone release, epithelial differentiation, and fluid movement across the gut wall (Brennan et al., 2014, Geibel and Hebert, 2009). The CaSR plays an important role in neuronal development (Liu et al., 2013, Vizard et al., 2008) and regulation of synaptic transmission (Phillips et al., 2008). The CaSR can also be found in vascular smooth muscle cells, endothelium and perivascular nerves, where it senses changes in local calcium concentration and contributes to modulation of vascular tone (Smajilovic et al., 2006, Schepelmann et al., 2016). CaSR expression is also found in the human and mouse airway epithelium and smooth muscle (Yarova et al., 2015). Its physiological role there becomes apparent from the early stages of life as the CaSR regulates fetal lung development through activation of the cystic fibrosis transmembrane conductance regulator (Brennan et al., 2016). Local elevations in extracellular calcium concentration, which occur in inflammation, can also activate CaSR expressed in blood monocytes and play the major role in recruitment and triggering of immune response in these cells (Olszak et al., 2000, Rossol et al., 2012).

Despite CaSR plays prominent roles in normal body functions, changes in its expression or function also contributes to the development of several pathophysiological processes that are not directly linked to calcium homeostasis, such as cancer, neurodegeneration and development of chronic pro-inflammatory disorders. E.g., CaSR signalling contributes to neuroblastoma and breast cancer growth, bone metastasis, and is down-regulated in colon and gastric cancers (Kim et al., 2016, Rodriguez-Hernandez et al., 2016, Tae et al., 2016, Chakrabarty et al., 2003). In the brain, expression of CaSR increases after injury (Mudo et al., 2009), and amyloid-β peptides were shown to activate CaSR (Ye et al., 1997). Moreover, loss of CaSR in the vasculature is associated with vascular calcification (Alam et al., 2009), whilst increase of CaSR expression in pulmonary arteries contributes to pulmonary hypertension (Tang et al., 2016).

There is a rising body of evidence that altered CaSR also plays a critical role in the molecular pathogenesis of a spectrum of pro-inflammatory diseases, such as gastro-intestinal inflammation (Owen et al., 2016), rheumatoid arthritis (Sejourne et al., 2016), and chronic pro-inflammatory airway disorders (Yarova et al., 2015, Yarova et al., 2016). In the latter, local elevations in extracellular calcium, polyamines and polycationic proteins that occur during asthma and chronic obstructive pulmonary disease (Kurosawa et al., 1992, North et al., 2013, Yarova et al., 2015) may behave as a danger-associated molecular pattern via activation of CaSR linked to NLRP3 inflammasome (Lee et al., 2012, Rossol et al., 2012) that is key to airway inflammation (Hosseinian et al., 2015). Furthermore, CaSR expression is increased in smooth muscle cells of asthmatic patients and in mouse models of allergic asthma, and its activation leads to airway hyperresponsiveness (Yarova et al., 2015).

Drugs targeting CaSR therefore could be a promising tool for treatment of multiple disorders. In the gut, CaSR modulators have been proposed for the treatment of secretory diarrhoea, metabolic acidosis and colorectal cancer (Aggarwal et al., 2015). In the brain, calcilytics have been shown to produce a promising result for treatment of neuroblastoma (Rodriguez-Hernandez et al., 2016) and Alzheimer's disease (Armato et al., 2013). In vitro studies showed that calcimimetic treatment reduces vascular calcification (Alam et al., 2009). Finally, calcilytics could provide a novel therapeutic avenue for the treatment of asthma and potentially other inflammatory lung disorders (Yarova et al., 2015, Yarova et al., 2016).

S06-01

Anti-tumor actions of bisphosphonates

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Bisphosphonate drugs (BPs) rapidly target the skeleton and are the gold standard treatment to inhibit bone destruction in patients with osteoporosis and metastatic bone disease. However, BPs also have anti-cancer effects outside bone; in some mouse models they reduce tumour growth and metastasis and there is some evidence that the addition of adjuvant BP therapy to standard treatment increases survival in post-menopausal women with breast cancer. The exact mechanisms underlying these anti-cancer effects are unknown since BPs are considered to only affect bone-resident osteoclasts in vivo. To address this, we determined the cell types capable of internalising fluorescently-labelled BP in mice bearing 4T1 mammary tumours. Within minutes of tail vein injection, intravital 2-photon imaging revealed the diffusion of BP into tumour tissue from the leaky, disorganised tumour vasculature. BP then appeared to bind to small, granular microcalcifications within the tumour tissue. Intravital imaging revealed that tumour-associated macrophages (TAMs) rapidly internalised BP by

pinocytosis and by engulfing these BP-coated microcalcifications. Flow cytometric analysis of the tumours 24hr later confirmed that uptake occurred predominantly in TAMs and not tumour epithelial cells. We also identified a patient with breast cancer in which the BP 99mTc-MDP (used for SPECT/CT bone scintigraphy) localised to the primary mammary carcinoma. Histological analysis of the resected tumour revealed the presence of granular microcalcifications similar in appearance to those in the mouse 4T1 tumours, and some of which were closely associated with CD68+ TAMs. These studies provide clear evidence that BP can be rapidly internalised by macrophages outside the skeleton. The leaky vasculature of tumours facilitates the local diffusion of BP, where it binds to microcalcifications within the tumour that are engulfed by TAMs. Given the important role of TAMs in promoting tumour progression and metastasis, our studies suggest that any anti-tumour activity of BPs in cancer patients and mouse models occurs indirectly via effects on these cells, rather than any direct effect on tumour cells.

S06-02

Effects of vitamin D signaling in cancer

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Vitamin D is routinely administered in the treatment of osteoporosis, often in addition to other drugs. However, data are accumulating to indicate that vitamin D also has many extra-skeletal effects that benefit diseases such as cancer, immune diseases, inflammation, diabetes and cardiovascular diseases among others. In this study we examined the potential benefits of vitamin D dietary supplements and calcitriol for breast cancer (BCa) in a mouse model of obesity. We chose anobesity model since obesity is an established risk factor for postmenopausal BCa, insulin resistance and diabetes. Obesity is also associated with vitamin D deficiency and contributes to increased synthesis of mammary estrogen, the driver of estrogen receptor-positive (ER+) BCa growth. To assess whether obesity exerted adverse effects on BCa growth and whether vitamin D could reduce these unfavorable effects, we employed a diet-induced obesity (DIO) model in ovariectomized C57BL/6 mice. Breast tumor cells originally from syngeneic Mmtv-wnt1transgenic mice were implanted into the mammary fat pads of lean and obese mice. DIO accelerated the initiation and progression of the mammary tumors. Treatment with either calcitriol or dietary vitamin D reduced the adverse effects of obesity causing a delay in tumor appearance and inhibiting continued tumor growth. Beneficial actions of vitamin D treatments on BCa tissue and surrounding adipose included: repression of ER, CYP19 (aromatase) and Cox-2 expression, decreased tumor derived estrogen and prostaglandin PGE2 synthesis and reduced expression of leptin receptors and increased adiponectin receptors. In summary, we showed that vitamin D treatments reduced BCa growth and improved multiple interrelated pathways contributing to an overall decrease in local estrogen synthesis in the obese mice as well as decreased insulin resistance. We conclude that dietary vitamin D or calcitriol treatment mitigates obesity enhanced BCa growth in the postmenopausal setting.

S06-03

RANK Ligand signaling and giant cell tumor of bone: A model for treating benign tumors

David Thomas

Director, The Kinghorn Cancer Centre; Head, Cancer Research Division and Laboratory Head, Genomic Ca

Professor David Thomas is an NHMRC Senior Research Fellow, and a medical oncologist specialising in sarcomas. In June 2014, he was appointed as Director of The Kinghorn Cancer Centre and Head of the Cancer Division at the Garvan Institute of Medical Research, Sydney. Dr Thomas has a particular focus on the impact of genomics on cancer medicine. His current basic research interests include quantitative evolutionary genetics in cancer cell populations, mapping a cancer neochromosome at single nucleotide resolution, and understanding the in vivo biology of osteosarcoma. His work has had significant translational impact. Dr Thomas led an international clinical trial of denosumab in Giant Cell Tumor of bone, which has led to a new therapeutic option for patients with advanced disease. He established a national infrastructure for clinical research into sarcomas, the Australasian Sarcoma Study Group. As Director of the statewide adolescent and young adult cancer service, onTrac@PeterMac, Dr Thomas played a significant national and international role in the development of adolescent and young adult oncology.

S07-01

Estrogen permits neurotransmitter signals to kisspeptin neurons

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University of Otago

Allan is currently Director of the Centre for Neuroendocrinology (CNE) and Professor of Physiology at the University of Otago, Dunedin New Zealand. After graduating with an intercalated degree in medicine and neuroscience from the University of Otago, and time in clinical practice, Allan received a Commonwealth Scholarship to undertake a PhD in Neuroendocrinology at the University of Cambridge, United Kingdom. Allan then spent a further 12 years as a Principal Investigator at The Babraham Institute and Fellow of Pembroke College, University of Cambridge before returning in 2002 to the University of Otago supported by the Wellcome Trust as Professor of Neuroendocrinology. Allan has received multiple fellowships and prizes including the Lister-Jenner Fellowship of the Lister Institute UK, Mortyn Jones Prize from the British Society for Neuroendocrinology, Benoit Prize from the French Society for Neuroendocrinology Liley Medal from the NZ Health Research Council, Triennial Medal of the Physiological Society of NZ and the Distinguished Research Medal of the University of Otago. Allan was elected Fel-

low of the Royal Society of New Zealand in 2007. Allan has always be interested in adapting the latest neuroscience approaches to the study of neuroendocrine circuits and has pioneered the use of genetically-manipulated rodent models at molecular, cellular, and whole animal levels to interrogate the neuronal network controlling fertility. His studies continue to address the neural mechanisms underlying episodic GnRH secretion, puberty onset, and the mechanisms through which gonadal steroids modulate these neurons. He has published over 200 reviews and research papers and has an H-index over 60.

S07-02

In utero development of kisspeptin/GnRH circuitry

Ulrich Boehm

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S07-03

Synchronous activation of gonadotropin-releasing hormone gene transcription and secretion by pulsatile kisspeptin stimulation

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Pulsatile secretion of hypothalamic gonadotropin-releasing hormone (GnRH) is pivotal for pituitary gonadotrope function. The physiological importance of pulsatile GnRH secretion has been well recognized, but the mechanism underlying GnRH pulse generation remains elusive. We demonstrated rhythmic GnRH gene transcription in single GnRH neurons in coronal slices of the hypothalamic tissue prepared from transgenic mice (postnatal 5-7 days) expressing a GnRH promoter-driven destabilized luciferase reporter (GnRHp-dsLuc). GnRH promoter activity was monitored by a real-time bioluminescence device and GnRH secretion was determined in media collected at 15 min intervals by radioimmunoassay. The basal GnRH promoter activity in each GnRH neuron exhibited irregular and episodic, oscillation, but GnRH neuronal population showed partially synchronized bursts of GnRH transcriptional activity with ~2 hr intervals under the basal condition. Intermittent administration of kisspeptin (10nM, 15 min-on, 45 min-off), a potent GnRH secretagogue, evoked dramatic synchronous activation of GnRH gene transcription together with robust stimulation of pulsatile GnRH secretion. Kisspeptin-evoked GnRH transcription was attenuated in the presence of 15a (GPR54 antagonist) or Go6983 (protein kinase C inhibitor). In summary, synchronous burst of kisspeptin-evoked GnRH transcription in hypothalamic neuronal networks appear to be important for GnRH pulse generation.

S08-01

Family-based analysis of eight susceptibility loci in polycystic ovary syndrome

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Director of National Research Center for Assisted Reproductive Technology and Reproductive Genetics, China.
Prof. Chen focuses on reproductive endocrinology, reproductive genetics and assisted reproductive technology: PCOS, POF/POI, RSA, IVF/ICSI, PGD/PGS, etc. She has more than 300 publications on journals such as Nat Genet, Am J Hum Genet, PNAS, Nature Communication, Hum Reprod Update, Fertil Steril, Hum Reprod, etc.
Prof. Chen serves as Assistant Secretary General of International Federation of Fertility Societies (IFFS), Executive Member of Asia Pacific Initiative on Reproduction(ASPIRE, 2014-2016), Board Member of Preimplantation Genetic Diagnosis International Society (PGDIS), Board Member of PGDSIG at ASRM, Director of Chinese Gynecological Endocrinology of OB/GYN Society.
Contributions to the Journals including Associate Editor: Human Reproduction Update, Gynecologic and Obstetric Investigation; International Consultant: American Journal of Obstetrics and Gynecology; Editorial Board Member: Asia Journal of Andrology; Guest Editor: British Journal of Obstetrics and Gynaecology; Deputy Editor-in-Chief: Chinese Journal of Obstetrics and Gynecology(Chinese), etc.

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder that is proposed to have a genetic basis. A recent genome-wide association study (GWAS) identified eight new risk loci that are independently associated with PCOS. To further validate the findings, a total of 321 case-parent trios (963 participants) who had a proband affected with PCOS were recruited for the family-based study. The transmission disequilibrium test (TDT) was used to analyze associations between PCOS and ten single nucleotide polymorphisms (SNPs) mapped to eight new susceptibility loci. Significant differences in transmission were observed for the SNPs rs2349415 (located in the FSHR gene, $P = 0.0001$) and rs3802457 (located in the C9orf3 gene, $P = 0.0001$), even after correction for multiple testing bias. The present data provides further evidence for an association between two susceptibility loci, 2p16.3 and 9q22.32, and PCOS. Follow-up functional studies on the FSHR and C9orf3 genes are required to understand their roles in PCOS development.

S08-02

Pubertal Origins of PCOS

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PCOS is a disorder of uncertain etiology associated with hyperandrogenemia, anovulation, obesity and the metabolic syndrome. The disorder is first manifest clinically in adolescence. Despite the elevated androgens, plasma LH and GnRH/LH pulse frequency are elevated and maintain testosterone secretion, as testosterone levels fall if LH is suppressed by a GnRH antagonist. The rapid GnRH/LH pulse frequency reflects testosterone impairment of progesterone inhibition of the GnRH pulse generator and is first seen during puberty and adolescence. During pubertal maturation, sleep related GnRH/LH pulse frequency remains constant, but daytime frequency increases by mid-puberty extending the duration of GnRH stimulation of the pituitary. Progesterone preferentially inhibits daytime LH pulses, an action impaired in the presence of elevated testosterone. 65% of obese girls during pubertal maturation (Tanner 1-5) are hyperandrogenemic. The elevated testosterone is of adrenal (early puberty) and ovarian (late puberty) origin. In these girls daytime GnRH/LH pulse frequency increases earlier in puberty, advancing pubertal maturation. Administration of testosterone, at levels present in obese girls, to prepubertal monkeys results in elevated GnRH/LH pulse frequency during subsequent puberty. Thus the presence of hyperandrogemia in early puberty modifies normal steroidal regulation of GnRH secretion. The impaired progesterone inhibition of the GnRH pulse generator results in a rapid GnRH/LH pulse drive. As a result plasma LH is not suppressed and maintains the hyperandrogenemia throughout adolescence and into adulthood.

S08-03

Metabolic risk in PCOS: Phenotype and adiposity impact

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Prof Teede is a senior reproductive endocrinologist at Monash Health. She is also Professor of Women's Health at Monash University focused on reproductive and metabolic health in reproductive aged women. As a funded Australian National Health and Medical Research Council (NHMRC) Practitioner Research Fellow, she leads an integrated multidisciplinary team conducting research from mechanistic studies, large scale clinical intervention trials, implementation and epidemiological research. She supervises 12 PhD students and has over 250 peer reviewed publications, whilst together with her direct team she currently holds $20M in grant funding. Prof Teede also has a leading role in translation of research including evidence synthesis, international guidelines including with the World Health Organization, co-design of new models of care, implementation and scale-up as well as holding policy advisory roles. She sits on the national NHMRC Research Committee, is on National NHMRC Faculty for Research Translation committees in obesity (member) and diabetes (Chair). Professor Teede is also President of the Endocrine Society of Australia and President Elect of the international Androgen Excess and Polycystic Ovary Syndrome Society. She is Executive Director of Monash Partners Academic Health Sciences Centre and Director of the Monash Centre for Health Research and Implementation, School of Public Health, Monash University. Her interests include reproductive and metabolic health in women including Polycystic Ovary Syndrome, the interaction between lifestyle, obesity and reproductive health, preconception and pregnancy health including gestational weight gain and gestational diabetes prevention and management.

S09-01

Daqing children study: What makes children grow fat?

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Professor Chen is from Fuwai Hospital, Chinese Academy of Medical Science. She is the director of department of Endocrinology, and also the vice director of Center for Endocrinology and Cardiovascular Disease.
She also has some titles in academic social organizations. She is the Vice Chief of Diabetes Research Center of Chinese Academy of Medical Science, the Standing Committee Member of Geriatric Endocrinology and Metabolism Committee, Chinese Association Geriatric Research and Committee Member of Chinese Association Geriatric Research. Her titles also include: Committee Member of Beijing Society of Endocrinology, China Medical Association; Committee Member of Cardiopulmonary Resuscitation Committee, Beijing Association of Rehabilitation Medicine; Committee Member of Beijing Diabetes Prevention and Treatment Association and Editorial Board Member of Chinese Journal of Endocrinology and Metabolism, Chinese Drug Evaluation.
Prof. Chen graduated from China Medical School in 1993 and got her master degree in Peking Union Medical College. From 2008-2009 she visited National University of Singapore as Visiting Scholar Sponsored by CSC, Chinese Scholarship Council.
Her Research interest includes epidemiology and related genes on Insulin Resistance and Obesity in children, and Metabonomics Study of diabetes and cardiovascular diseases. Her research work has been funded by the National Natural Science Foundation of China, Janssen Scientific Research Funding Committee, Chinese Medical Association and Chinese Academy of Medical Sciences-Novo Nordisk Union Diabetes Research Talent Fund.

Childhood and adolescent obesity is of great concern around the world. In China, the prevalence of obese children has been increasing over the last 20 years. It is associated with adult-onset diabetes, hypertension, dyslipidemia and coronary heart disease. A

number of factors lead to obesity in children---genetic, behavioral and environmental factors. The Daqing children study is a longitudinal observational study of the factors associated with childhood obesity. We have identified TV viewing time, hyperinsulinemia and susceptibility genes (Nuclebindin 2 and FTO gene). Our study also explored the effects of excessive weight gain during childhood on the development of metabolic disease risk factors.

605 children in Daqing city were recruited when they were 5 years of age and followed up for 5 years. 424 children completed full data collection from 5 to 10 years of age. Birth weight, TV viewing time at 5 years of age, and blood pressure, anthropometric measurements, fasting plasma insulin, glucose and triglycerides were measured at 5 and 10 years. Blood sampling was also performed for DNA extraction.

The results revealed that TV viewing time was associated with a higher risk of being overweight. An increase of 5 hours/week of TV viewing time led to 1.1 kg/m^2 increase of BMI over the 5 years of age. We also found the top positive change of percentage of ideal weight for height (WFH) group had significantly higher fasting insulin, HOMA-IR index, systolic blood pressure, diastolic blood pressure and triglycerides. Otherwise, when we focused on the effect of hyperinsulinemia to obesity in childhood, the results showed the children who were in the highest insulin quartile group at 5 years of age had the largest change in weight, BMI and WFH in the subsequent 5 years. After adjustment for gender, birth weight, TV viewing time and weight at baseline, fasting insulin at 5 years of age predicted weight gain over 5 years. By contrast, the initial weight at 5 years of age did not predict change of insulin level 5 years later.

The variants of Nuclebindin 2(NUCB 2) gene which is a precursor of nesfatin-1 were examined in Daqing cohort children. Genotyping for C.1012C>G (q338E) showed that the GG genotype had lower BMI and WFH at 5 and 8 years of age. This may indicate that the GG genotype is a protective factor to against excessive weight gain. We also examined the FTO gene rs9939609 polymorphism for association with weight gain in Daqing children. The AA genotype had significant greater weight gain from 5 to 10 years of age than the TT genotype after adjustment for gender and TV viewing time.

In summary, the mechanism for childhood obesity is complex, and comprise of interactive effects of gene, in uterus and environmental factors. Higher fasting insulin and certain susceptibility genes are important factors. However, life style intervention may help, and Children at early age should increase activity time instead of having prolonged TV viewing time. This may prevent the development of childhood obesity and the subsequent accumulated of metabolic syndrome risk factors in adult life.

S09-02

Genes and short stature

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Professional Career:
1992-1993 Basic research fellowship, Department of Endocrine Laboratory Diagnostics (Prof. Gupta), University of Tuebingen, Germany
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S09-03

Epigenetics and fetal growth

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As Chief Scientist responsible for the Ministry of Science " reproductive and developmental major projects" , the Yangtze River scholar Professor in Ministry of Education, chief expert of National Natural Science Fund for Creative Research Groups " germ cell development ", she has been engaged in obstetrics and gynecology and reproductive health related clinical and basic research work, studying on early embryo development mechanism of human conduct in-depth research from genetics, epigenetic perspective, the basic research results successfully applied to the front of the clinical implantation genetic diagnosis, revealing the pathogenesis of infertility , optimizing assisted reproductive technology and improving the treatment success rate of infertility patients. " As the first or corresponding author, she published SCI articles about 118 in well-known international magazine such as "Nature" and "Cell".

The discipline of epigenomics represents the merged science of epigenetics and genomics. The ultimate aim of this field is to map and unravel the biological and biomedical significance of epigenetic phenomena. Today, epigenetics is typically defined as inherited phenotypic changes that are not due to changes in gene sequence.

The transcriptome and DNA methylome landscapes of human migrating and gonadal PGCs are in general similar to those of mouse PGCs at comparable stages. At the same time, human PGCs also show unique features different from mouse PGCs. Our work paves the way to elucidating the complex relationship of DNA methylation and the gene expression network during the global epigenetic reprogramming process of human PGCs.

The epigenetic regulation of spatiotemporal gene expression is crucial for human development. We also present whole-genome chromatin immunoprecipitation followed by high throughput DNA sequencing (ChIP-seq) analyses of a wide variety of histone markers in the brain, heart, and liver of early human embryos shortly after their formation. Our work illustrates the potentially critical roles of tissue-specific and developmental stage-specific epigenomes in regulating the spatiotemporal expression of developmental genes during early human embryonic development.

S10-01

Intestinal taste receptors and incretin signaling

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Recent progress in unraveling the nutrient-sensing mechanisms in the taste buds of the tongue has prompted studies on the existence and role ofchemosensory cells in extra-oral tissues. The gut, which is the key interface between food and the human body, "tastes" what we eat in much the same way as the lingual system through the use of similar taste receptors. These receptors sense the luminal content via the epithelium and transmit signals that regulate nutrient transporter expression and nutrient uptake but also the release of gut hormones from enteroendocrine cells. Several anorexigenic (GLP-1, PYY3-36) and orexigenic (ghrelin) gut hormones are released from the gut mucosa, in accordance to the fed or fasted state and play an important role in regulating short-term food intake. Hence, nutrient sensors play a prominent role in the communication between the lumen, epithelium, afferent nerve fibers and the brain to trigger adaptive responses that affect gastrointestinal function, food intake and glucose metabolism. During my talk, I will focus on how sweet, bitter and amino acid taste receptors throughout the gut play a distinct role during the process of digestion and absorption. The proximal stomach is the major site of the production of the hunger hormone ghrelin. The ghrelin cell expresses amino acid taste receptors that are involved in the sensing of protein breakdown products to mediate the postprandial decline in plasma ghrelin levels. Furthermore, they activate the release of two important regulators of pepsinogen and acid secretion: gastrin (G-cells) and somatostatin (D-cells). Next, food is emptied from the stomach into the small intestine, the major site of digestion and absorption. In the duodenum, fat, protein hydrolysates and amino acids stimulate the secretion of cholecystokinin (CCK) which is known to induce satiation and to inhibit gastric emptying. Carbohydrates are mainly sensed by the L-cells and the K-cells in the jejunum-ileum to induce the secretion of glucagon like-peptide (GLP-1) and glucose- dependent insulinotropic polypeptide (GIP), respectively. These are two important incretin hormones that regulate glucose-induced insulin secretion. The mechanisms by which L-cells couple glucose detection to GLP-1 secretion are controversial, but both sweet taste receptors and glucose transporters seem to be involved. Furthermore, there is some evidence that sweet taste receptors dysregulation in patients with type 2 diabetes may potentially increase the risk of postprandial hyperglycemia. In addition, the rerouting of nutrients to more distal regions in the gut during gastric bypass surgery may affect the expression of nutrient sensors and hence contribute to the altered gut hormone release involved in the metabolic reprogramming after RYGB surgery. Finally, food residues are stored in the colon where mucus is secreted and the remaining water and electrolytes are absorbed from the food residue before defecation. The intestinal flora performs fermentation reactions that produce short chain fatty acids (SCFA) that are sensed by free fatty acid receptors on L-cells. Short-chain fatty acid receptors in the colon and in peripheral tissues are considered as a therapeutic target for the treatment of obesity, diabetes and inflammatory disorders and can be targeted by dietary fibers. It is suggested that sensing of toxic bitter tastants by bitter taste receptors on enteroendocrine cells throughout the gut is important to prevent further ingestion of toxic food and to expel ingested toxins before being absorbed in the circulation. Targeting extra-oral taste receptors with functional foods or taste receptor (anta)agonists may offer new and exciting therapies for the treatment of diseases such as obesity or diabetes.

S10-02

Gut lipid sensing and energy homeostasis

Tony Lam

University of Toronto

S10-03

Control of GIP secretion

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Single fat ingestion stimulates GIP secretion from K-cells, and chronic high-fat diet (HFD) loading enhances GIP secretion and induces obesity in mice in a GIP-dependent manner. However, the mechanisms of fat-induced GIP secretion from K-cells in acute and chronic conditions are not well known. To understand them, we generated GIP-GFP knock-in mice in which K-cells are labeled by enhanced GFP (EGFP). Microarray analysis of isolated K-cells from GIP-GFP heterozygous knockin (GIPgfp/+) mice and wild-type (GIP+/+) mice revealed that both fatty acid-binding protein (FABP) 5 and GPR120 are highly expressed in K-cells. Single oral administration of fat resulted in significant reduction in GIP secretion in both FABP5- and GPR120-deficient mice, demonstrating that both FABP5 and GPR120 are involved in acute fat-induced GIP secretion. In addition, in vitro and in vivo experiments suggested coexistence of bile is critical in acute fat-induced GIP secretion. Furthermore, we identified that the transcriptional factor regulatory factor X6 (Rfx6) is expressed exclusively in K-cells. In vitro experiments using mouse intestinal cell line STC-1 showed that GIP mRNA levels are regulated by Rfx6. Expression levels of Rfx6 mRNA as well as GIP mRNA were augmented in the K-cells of HFD-induced obese GIPgfp/+ mice in which GIP content in small intestine is increased compared to the mice fed by normal

control diet. These results suggested that Rfx6 is involved in hypersecretion of GIP in HFD-induced obese conditions by increasing the expression levels of GIP mRNA. Finally, we will show our up-to-date data comparing the effects of medium-chain and long-chain triglycerides on GIP secretion and obesity.

S11-01

Novel therapies in adrenal insufficiency

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Patients with diagnosed and treated adrenal insufficiency (AI) have increased morbidity and mortality. The endogenous cortisol secretion and tissue exposure follows a specific diurnal pattern and is markedly influenced by various stressors. The challenge in glucocorticoid replacement is therefore to target the diurnal cortisol time exposure profile as well as to respond to increased need during physical and mental stress. Novel therapies for cortisol replacement have recently been developed in order to improve the management and outcome of patients with AI. A dual release hydrocortisone (DR-HC) oral formulation was developed in order to achieve a more physiological cortisol exposure-time profile.

The DR-HC has an outer layer of immediate release HC allowing a peak cortisol concentration early morning after intake, and an inner core with modified release HC mimicking the reduction in serum cortisol concentration throughout the day and evening. This together produces a unique diurnal serum cortisol concentration profile with peaks in morning and physiological through cortisol concentrations at midnight. In the pivotal trial comparing DR-HC with three times daily conventional HC tablets (TID) in patients with Addison's disease mean body weight, systolic- and diastolic blood pressure were all reduced after DR-HC compared with TID. In 11 patients with concomitant diabetes mellitus a reduction in HbA1c was observed with DR-HC as compared with TID. A prospective open labelled 24-month safety trial using DR-HC showed that the median number of intercurrent illness episodes ranged from 1.0 to 2.0 during each 3-month period and the median number of days per episode ranged from 2.0 to 3.1. The study concluded that the safety data were stable both in terms of reported adverse events and increased HC use due to intercurrent illnesses.

Another novel strategy to improve the serum cortisol profile in patients with AI is to use a sc. infusion pump. In a prospective trial comparing treatment with TID oral HC vs HC pump infusion, the pump therapy brought ACTH and cortisol toward normal circadian level]. Another development targeting CAH patients is a modified release oral formulation administered before bedtime and in the morning in order to achieve a higher night time cortisol exposure and a more physiological serum cortisol profile has been studied in adults with CAH.

In summary, novel therapies have been introduced in order to achieve a more physiological cortisol replacement therapy in patients with AI. Outcome data from the DR-HC studies strongly support that a more circadian-based serum cortisol profile improves metabolism and cardiovascular risk factors, and that long-term management is safe.

S11-02

Adrenal crisis

Marcus Quinkler

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Definition

Adrenal crisis (AC) is a life-threatening emergency in patients with adrenal insufficiency (AI). It is defined as major impairment of general health with at least two of the following signs (hypotension, nausea or vomiting, severe fatigue, fever, somnolence, hyponatremia, hypoglycaemia) and the parental glucocorticoid administration followed by clinical improvement (1). AC is weighted in four grades: outpatient care only (grade 1), hospital care on general ward (grade 2), intensive care unit (grade 3), and death from AC (grade 4).

Incidence

Retrospective analysis of 444 patients with primary or secondary AI revealed a frequency of 6.3 AC/100patients, and 5.7 AC/100patients in patients with congenital adrenal hyperplasia. A postal survey of the UK Addison group revealed 8 AC/100patients. A recent analysis of a large German health insurance database even suggested even 14-17 AC/100patients. The first prospective study in Germany found an incidence of 8.3 AC/100patients. AC was fatal in 6.3% of cases, which converts into an excess mortality rate from AC of 0.5/100 patient years. Extrapolating this to the population of 507 million in the European Union this would be 5.500 to 10.500 expected deaths from AC in the coming decade. The most common precipitating factors of AC are gastrointestinal infection and other infectious diseases but also emotional stress.

Pathophysiology

The exact mechanisms are hardly known, however it is hypothesized that the lack of increased cortisol concentrations during infection enhances pro-inflammatory cytokine release and sensitivity to toxic effects of these cytokines (e.g. tumour necrosis factor alpha), and those may impair glucocorticoid receptor function aggravating glucocorticoid deficiency.

Treatment

If AC is suspected immediate therapy is necessary. Treatment is easy and consists of parental glucocorticoid (e.g. 100mg hydrocortisone as bolus intravenously) and isotonic saline (1000ml 0.9% sodium chloride within the first hour) to correct hypovolemia. Additional therapeutic actions should be taken to treat the precipitating factors (e.g. antibiotics). Following the initial treatment, 200mg hydrocortisone/day should be given as continuous infusion or frequent i.v. (or i.m.) boluses (50mg) every 6h. Further fluid administration should be assessed clinically or by central venous pressure. Close monitoring preferably on intensive care unit including measurement of serum electrolytes is recommended.

Prevention

The major point is that valuable time should not be lost between the sudden onset of increased cortisol need (in stressful situations e.g. infections) and the application of additional hydrocortisone doses. A recent German study revealed a much too long time span between the doctor´s arrival in the case of emergency and the glucocorticoid administration by the doctor. This emphasizes the need for a better training of the medical personal, a better identification of patients who are in need of emergency injections in stressful situations, as well as a better patient education to early recognize

symptoms of AC and to facilitate parenteral hydrocortisone self-administration.
Current education concepts are not sufficiently effective, and therefore a structured standardized teaching in small patient groups (including one relative per patient) should be implemented with duration of 2-3h and repetition every 6 to 12 months.
One key aspect of this training should be the practical learning of self-administration of the hydrocortisone ampoule. The aim of the crisis prevention teaching should be: The well-informed patient (or his/her relative) guides the poorly informed health-care professional! .
In addition, every patient should carry emergency cards (a national and an international one). It is an important issue to standardize emergency cards to avoid failed recognition by medical personal. Each patient should be equipped with an emergency kit consisting of additional hydrocortisone tablets, glucocorticoid suppositorium, and a hydrocortisone ampoule and syringes for self-injection.

S12-01

Genetics of pheochromocytoma

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Anne-Paule Gimenez-Roqueplo (MD, specialized in Endocrinology, PhD in Genetics) is Full Professor in Genetics (Paris Descartes University. She is the leader of an academic research team entitled "Pheochromocytomas and paragangliomas (PCC/PGL), from genetics to molecular targeted therapies" within the INSERM Unit 970 at the Paris Cardiovascular Center at HEGP (PARCC@HEGP), Paris, France. Her group established the genetic testing recommendations for patients with PCC/PGL, demonstrated that the identification of a germline SDHB mutation is the first high risk factor of malignancy and of poor prognosis and showed that SDHx-related PCC/PGL are characterized by a stimulation of the hypoxia-angiogenesis pathway and by an hypermethylator phenotype.
Her group develops an integrative genomic approach and different animal and cellular experimental models of malignant PCC/PGL.
She is the past chairman of the Pheochromocytoma-Paraganglioma Research Support Organization (PRESSOR), the Head of the PCC/PGL working group of the European Network for the Study of Adrenal Tumors (ENS@T) and member of the ENS@T steering committee. She coordinates the National French registry for SDH-related paraganglioma (PGL.R).
Anne-Paule Gimenez-Roqueplo is an editorial board member of the J Clin Endocrinol Metab.

Paragangliomas and pheochromocytomas (PPGL) are neuroendocrine tumors with a very strong genetic component. A germline mutation in one of the different susceptibility genes identified so far explains about 40% of all cases. Genetic testing is recommended in every affected patient and next-generation sequencing (NGS) is the ideal technology to screen the high number of PPGL susceptibility genes. The interpretation of genetic variants identified by NGS can be guided by the clinical presentation as well as by the secretory phenotype and by the immunohistochemical analysis of tumors. The diagnosis of an inherited form drives clinical management and tumor surveillance of the patient and relatives1.
While whole-exome sequencing studies showed that PPGL is characterized by a low mutation rate of 0.3 mutations per megabase similar to other neural crest-derived tumors, the first integrative genomic analysis of a large collection of 202 PPGL, carried out by the French COMETE network, demonstrated that mutation status in PPGL susceptibility genes is strongly correlated with multi-omics data and revealed the crucial role of predisposing mutations as being the main drivers of PPGL2. PPGL subtypes can be defined by a set of unique genomic alterations that represent different molecular entities. Transcriptomic studies identified two main molecular pathways, activating either the hypoxic pathway (cluster C1) or the MAPkinase/mTOR signalling (cluster C2). This comprehensive analysis further illustrated the functional interdependence between genomic and epigenomic dysregulations. Indeed, DNA methylation profiling uncovered a hypermethylator phenotype specific to the tumors related to a mutation in one of the PPGL susceptibility genes encoding for a protein of the tricarboxylic cycle. Besides, we demonstrated that succinate is acting as an oncometabolite, inhibiting 2-oxoglutarate-dependent dioxygenases, such as HIF prolyl-hydroxylases and histone/DNA demethylases, explaining noradrenergic secretory and metastatic phenotypes of PPGL classified in cluster 1A3. Finally, 'omics' data suggested new therapeutic targets for patients with a metastatic PPGL as well as novel diagnostic and prognostic biomarkers. New 'omics'-based tests for PPGL are likely to be transferred from research laboratories to clinical practice in order to give the access to a precise molecular classification of every PPGL, after surgery, to practicing clinicians with the goal of establishing a personalized medical management of affected patients.

S12-02

Management of malignant pheochromocytoma

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Pheochromocytoma (PCC) and paraganglioma (PGL) are rare catecholamine -producing neuroendocrine tumors (NET) and a surgically treatable cause of hypertension. The tumors arise from chromaffin tissue in the adrenal medulla (PCC) or from extra-adrenal chromaffin cells (PGL). Most PCC are located in the adrenal glands and only approximately 10% PGL are extra adrenal. Malignancy is defined only as the presence of metastases in non-chromaffin sites, or when invasion of neighboring tissue is seen, the prevalence varies 10-17%. The rate of malignancy is much higher in patients with PGL who have mutations in the succinate dehydrogenase subunit B (SDHB). The average 5-year survival with metastases is approximately 50%.
The treatment of malignant PCC/PGL includes advanced surgery, nuclear medicine, chemotherapy, radiotherapy and, experimentally, new biologically targeted drugs. The most effective treatment remains surgical resection. Treatment with high dose 131I-MIBG is an effective and safe therapy for patients with malignant, recurrent or irremovable PCC/PGL. However, it is not useful if MIGB scintigraphy is negative, and toxicity may sometimes limit the use of this modality. Treatment with radiolabeled somatostatin receptor ligands may be of benefit to patients showing a high uptake on octreotide scintigraphy. Chemotherapy is generally considered of limited effect and is usually reserved to treat advanced or aggressive disease. Cyclophosphamide,Vincristine and Dacarbazine (CVD) which have shown to produce symptomatic and hormonal improvement, but often transient and with minimal tumor shrinkage. mTOR inhibitors (everolimus, temsirolimus) and some of these targeted drugs, including sunitinib and temozolamide., are currently under investigation in clinical trials.
Total 1320 cases (1244 inpatients, Male 633 and Female 611, aged 42±14 years old , 7-85 yrs) of PCC/PGL were diagnosed and management from 1939 to 2015 in Peking Union Medical College Hospital (PUMCH), Beijing CHINA. About 100 cases of PCC/PGL per year come to PUMCH in recent three years. 195 patients (M 111, F 84) were diagnosed as malignant PCC/PGL (15.7%). Total 130 individuals with malignant, recurrent or irremovable PCC/PGL had been treated with 131I-MIBG in Beijing 401 Hospital in the last 10 years. Efficacy and safety of 131I-MIBG therapy were evaluated by retrospective analysis. We would share our experience on clinical diagnosis and treatment of malignant PCC/PGL in PUMCH.

S13-01

Mechanism-based therapies for thyroid cancer

James Alexander Fagin

Memorial Sloan Kettering Center

S13-02

Molecular approaches in thyroid cancer and metastasis

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Thyroid cancer is the most common endocrine malignancy. Exciting progress has occurred in the area of molecular-based management of thyroid cancer. This discussion will specifically focused on genetic marker-based risk stratification of thyroid cancer. In this context, several oncogenic mutations are particularly promising, which is best exemplified by BRAF B600E and TERT promoter mutations. The association of BRAF B600E with aggressive clinicopathological outcomes of thyroid cancer and hence its prognostic value for poor prognosis of thyroid cancer has been extensively studied. Its synergism with conventional aggressive clinicopathological factors and mutations in the promoter of the gene for telomerase reverse transcriptase (TERT) in affecting clinical outcomes of thyroid cancer has become particularly recognized in recent years. TERT plays a critical role in maintaining and protecting the length of chromosomes by adding telomers to their ends, hence promoting cell survival. TERT is now known to also play an important role in several other fundamental biological functions, such as cell proliferation, cell division, and tumor growth. In recent years, two somatic mutations, chr5:1,295,228C>T and chr5:1,295,250C>T (termed here as C228T and C250T, respectively), have been discovered in the TERT promoter in many human cancers, including thyroid cancer. These mutations confer TERT promoter increased transcriptional activities and up-regulate the expression of the TERT gene, thus promoting tumorigenesis. In thyroid cancer, TERT promoter mutations occur progressively more commonly from low-grade to high-grade tumors, being about 10-12% in differentiated thyroid cancer and about 40-50% in poorly and undifferentiated thyroid cancers. Many recent studies demonstrated that TERT promoter mutations were highly associated with aggressive pathological characteristics

and poor clinical outcomes, including thyroid cancer recurrence and patient mortality. TERT promoter mutations are significantly associated with BRAF V600E mutation. Coexisting BRAF V600E and TERT promoter mutations are particularly associated with aggressive behaviors of thyroid cancer and sharply increased cancer recurrence and patient mortality. Thus, following this past one decade of remarkable achievements in the BRAF research on thyroid cancer, we are now entering a new exciting era of TERT in thyroid cancer research, which, like BRAF, will likely have an important impact on the management thyroid cancer.

S14-01

Impact of Chernobyl and Fukushima nuclear accidents

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S14-02

Management of thyroid cancer-update

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Under this topic, recent increase in the incidence of thyroid cancer in Korea will be discussed. Recently thyroid cancer incidence increased all over the world, however, astonishingly rapid increase in Korea was noteworthy. Recent rapid increase in thyroid cancer like epidemic during the lase decades seems certainly due to overdiagnosis of indolent micropapillary carcinoma, however, there are sound evidence that thyroid cancer may be slowly increasing during the last several decades and this slow but steady increase may be masked by rapid increase due to overdiagnosis. First incidence of thyroid cancer was increasing slowly since early 1980's when ultrasound and other imaging modality to detect thyroid cancer was not widely used. At that time only palpable nodule was evaluated by manual aspiration. Recent rapid increase in thyroid cancer is mostly increase in the small papillary carcinoma, but there are also slow increase in large cancers and other types of thyroid cancers such as follicular and medullary carcinomas, which are not easily diagnosed during the screening procedures. Thyroid cancer incidence began to increase not in the metropolitan area where income is higher and various medical resources are concentrated but in the rural southwestern costal area where income is relatively low and medical resource is sparse. Incidence of thyroid cancer in children is also increasing and most of the patients with childhood thyroid cancer did not ever undergo screening procedure. Number of thyroid cancer specific death remains stable due to the detection of early stage cancers with negligible mortality. All these evidence suggest that there might be true slow increase in thyroid cancer which is masked by rapid increase of thyroid cancer due to overdiagnosis. Another factor is the mistake from the healthcare authorities. They launched the so-called national cancer screening program to detect various cancers in early stage in everybody living in Korea from the budget of government driven health insurance. After preliminary pilot course, this program started from 2002 and at first comprised screening of stomach, liver, breast and uterine cervix but other screening procedures were encouraged at the patients' own expense. Since cost for ultrasonography was kept very low and ultrasonography was recommended by government for breast cancer detection when mammography was not conclusive, ultrasonographic screening for thyroid became popular with small added cost and this policy opened Pandora's box.

S15-01

Treating Osteogenesis Imperfecta

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S15-02

Optimizing peak bone mass in adolescence

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Doctor degree of Philosophy in 2010 from Sichuan University. She is the Associated Professor of Medicine at West China Hospital of Sichuan University. As an endocrinologist, Dr. Wang Qin specializes in skeletal health across the life, osteoporosis and other metabolic bone disease. Up to now she has published 16 academic papers in international academic journals, such as the Journal of Bone and Mineral Research (the top journal in bone research area), Bone, and Cochrane Database of Systematic Reviews et al. She served as a young committee member of Osteoporosis and Bone Mineral Committee of Chinese Medical Society, and the associated chairman of young committee of Osteoporosis and Bone Mineral Committee of Sichuan provincial Medical Society. She is also the peer reviewer of musculoskeletal group of Cochrane collaboration, Evidence-Based Complementary and Alternative Medicine, and other academic journals.

Bone mass reaches the maximal amount at the end of adolescence, designated as peak bone mass (PBM), with about half of them gained during adolescence. Building the highest possible PBM during adolescence helps to reserve better skeletal health and reduce fractures later in life. Bone development during adolescence are characterized by huge linear growth, intensive mineralization and large gain in bone mass. Proper hormone levels and mechan-

ical stimulus, and adequate nutrients are essential to initiate and optimize bone growth and quality during adolescence. The controllable factors, such as calcium and vitamin D intake, physical activity and weight can be modified to optimize PBM. Calcium, as a bone-building nutrient, is extremely important for the rapid bone growth and calcium accretion, and vitamin D is essential for calcium absorption and utilization. Dietary calcium intake and vitamin D status affect bone mass acquisition and affect fracture risk in adulthood. Diary products are good sources of calcium. Skin synthesis by sunlight, natural dietary resources and vitamin D fortified foods are good resources of vitamin D. The effectiveness of calcium supplement in gaining bone mass is controversial, so the emphasis should be on establishing healthy dietary behaviors. Vitamin D supplements are recommended for children who are unable to obtain adequate vitamin D or have vitamin D deficiency. Mechanical stimulus by weight-bearing physical activities is associated with increased bone mass accrual, more favorable geometric adaptations of bones, and enhanced bone strength. But excessive high-intensity exercise is not recommended since it increases fracture risk. A healthy body weight and composition during adolescence are also recommended to optimize PBM, for body mass index and lean body mass are positively correlated with bone mineral density, and increased adiposity increases fracture risk. Behaviors associated with decreased bone health in adult like smoking, excessive caffeine and alcohol intake should also be avoided in adolescence.

S16-01

Androgens in men - what should we know?

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Androgens are used mainly for the treatment of male hypogonadism. The questions that physicians need to know are: who to treat?; what are the potential benefits versus risks?; what are the contraindications to treatment?; what preparations of testosterone (T) or other agents should be used?; and how do we monitor response? Diagnosis of male hypogonadism is based on symptoms, the most common symptoms in both older and younger men are sexual dysfunction symptoms including decreased in sexual desire, activity and erectile problems. Signs of low T varied according to the age at presentation. These symptoms are not specific and must be used with the measurement of serum T. Serum T must be measured both accurately and precisely by validated assays that are harmonized to a standard. Generally total T can be used for diagnosis but free and bioavailable T should be measured when SHBG levels are high (e.g. aging) or low (e.g. obesity). Reference ranges are being developed for the international community. The known benefits of T replacement in male hypogonadism include improvement in sexual function (more in younger than older men with other co-morbidities), increase in lean mass and bone mineral density and decrease in fat mass notably visceral fat. The more controversial benefits may include improvements in vitality and mood, and muscle strength, and ability to perform daily activities in older men. Elevated hematocrit and hemoglobin to high levels may increase thromboembolism risk but the increase in erythrocytosis may benefit unexplained anemia in older men. It is unlikely that androgens are responsible for BPH or prostate cancer but long term interventional studies are lacking. Whether androgen replacement increases cardiovascular disease risk is controversial and cannot be resolved until a long term controlled intervention study is performed yielding evidence based results. Selection of the type of T delivery system and other agents to increase endogenous T production depends on the patient's needs and preferences. Monitoring includes serum T levels at the initiation and during therapy, improvement of symptoms, and assessment for adverse effects. If used carefully and judiciously for younger and older men with appropriately diagnosed hypogonadism, T replacement is beneficial and safe.

S16-02

How are messages transmitted between osteoclasts and osteoblasts?

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Assoc. Prof. Natalie Sims directs the Bone Cell Biology and Disease Unit at St. Vincent's Institute and is an NHMRC Senior Research Fellow and Principal Research Fellow at The University of Melbourne. She completed her PhD in 1995 at the University of Adelaide, and started her own laboratory in Melbourne in 2001 after postdoctoral studies at the Garvan Institute (Sydney) and Yale University. She defined the roles of Oncostatin M, Cardiotrophin 1, and Leukemia Inhibitory Factor on the development and maintenance of the skeleton, using genetically altered mouse models and in vitro systems. She has worked closely with Prof TJ Martin on developing theories of bone cell communication, particularly with respect to the concept of "coupling". Her current work continues to focus on paracrine control of the skeleton, particularly the way parathyroid hormone, IL-6 and STAT1/3 signalling influence bone formation and destruction. She has >100 publications and review articles. Dr Sims is a board member of the American Society for Bone and Mineral Research. She is a Senior Editor of the journal Bone. Her work has been recognised by the ASBMR Fuller Albright Award (2010) and the International Bone and Mineral Society Herbert A Fleisch Award (2013).

S17-01

Irrational exuberance in testosterone prescribing: When will the bubble burst?

Bradley Anawalt

University of Washington

S17-02

Testosterone and cardiovascular risk

C Mary Schooling

University of Hong Kong

Rates of cardiovascular disease are rising in some settings, such as China, and are higher in men than women, even at the same level of established cardiovascular disease risk factors. To gain new insights cardiovascular disease is now being considered within the well-known evolutionary biology paradigm of growth and reproduction trading off against longevity with trials of dietary restriction mimetics underway. However dietary restriction has not been as successful as expected in primates because it is increasingly realized that effects on the reproductive axis may also be needed, which raises the question of the effect of sex hormones on major causes of death, such as cardiovascular disease.

Randomized controlled trials in men (Coronary Drug Project) and women (Women's Health Initiative) have already established that estrogen, at best, has a neutral effect on mortality. In contrast, the role of androgens in cardiovascular disease has been much less extensively investigated, particularly in men. Despite its limitations the current body of evidence has resulted in Health Canada and the US Food and Drug Administration recently advising of the cardiovascular risk of testosterone, with Health Canada specifically mentioning that testosterone raises blood pressure and might cause blood clots.

Nevertheless, observationally low endogenous testosterone among men is associated with higher mortality and higher risk of cardiovascular disease, although biases due to confounding by ill-health cannot be ruled out. This association does not extend to other measures of endogenous androgens, where a positive association has been observed. Testosterone prescription has been associated with a neutral or increased risk of cardiovascular disease, although potential biases by indication, unmeasured confounding, and "immortal time" make interpretation uncertain. Meta-analyses of randomized controlled trials of testosterone in men give estimates in the direction of increased cardiovascular disease risk, but often have confidence intervals consistent with no effect, although testosterone may reduce waist circumference and improve insulin resistance, but raises hematocrit, lowers high density lipoprotein-cholesterol, lowers adiponectin and increases venous thromboembolism. The plausibility of any potential physiological pathways linking androgens with cardiovascular disease, such as via hematocrit or coagulation factors, will be considered.

Reflections on this diverse evidence base concerning testosterone and cardiovascular risk, the gaps in evidence and new means of augmenting the evidence base will be provided. Finally, in the light of reproduction trading off against longevity, and hence most likely cardiovascular disease, novel implications for the prevention and treatment of cardiovascular disease will be given.

S18-01

Altered notch signaling contributes to progesterone resistance in the utopic and ectopic endometrium

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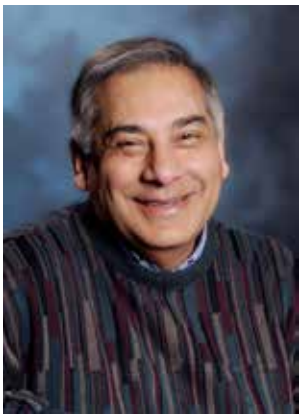

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Dr. Asgi Fazleabas received his PhD in Reproductive Physiology from the University of Illinois at Urbana-Champaign and his post-doctoral training in Biochemistry and Molecular Biology from the University of Florida in Gainesville. He was appointed to the faculty at the University of Illinois at Chicago until his move to Michigan State University in 2009 where he currently serves as Professor and Associate Chair of Research in the Department of Obstetrics, Gynecology and Reproductive Biology as well as the Director for the Center for Women's Health and Co-Director of the Reproductive and Developmental Sciences Program. His laboratory has been funded continuously by the National Institutes of Health, primarily NICHD since 1986 for studies using the baboon as a model for reproductive research. His laboratory was the first to demonstrate that chorionic gonadotropin acts directly on the uterus in vivo and using this "simulated pregnancy model" went on to demonstrate that the early luteotrophic signal from the primate embryo is critical for initiating the decidualization response and remodeling the luminal epithelium to enhance trophoblast invasion. The translational significance of this signaling mechanism has been further validated in women undergoing controlled ovarian hyperstimulation in a clinical trial the results of which have been accepted for publication in Human Reproduction. His laboratory has also published extensively on morphological changes associated with early placental development and the interaction between placental attachment and endometrial transformation. These initial studies have led to the more recent extensive studies related to embryo implantation and maternal fetal interactions and have focused specifically on the role of Notch 1 during the process of decidualization. In addition to studies in the non-human primate and in stromal cells from women, his laboratory has also developed novel transgenic models which have cell specific gain of function and loss of function properties to study the role of

Notch signaling in decidualization and endometriosis. In addition to the basic fundamental role that Notch1 plays in initiating the decidualization process, recent data from the laboratory also suggests that altered Notch signaling as a consequence of endometriosis, which is a disease that affects 176 million women worldwide, has a significant impact on an aberrant decidualization response in the eutopic endometrium and promotes lesions development at ectopic sites. The focus of these studies are to understand the fundamental mechanisms by which Notch1 interacts with FOXO1 and progesterone to promote decidualization and the implications of altered Notch1 signaling in contributing to the pathophysiology of endometriosis. In conjunction with the studies on the role of Notch signaling in the pathophysiology of endometriosis, his laboratory has also identified specific microRNA's that are altered in both the ectopic and eutopic tissues of baboons and women with endometriosis. These studies have specifically focused on target genes that are regulated my microRNA's 451, 29c and 21 which in turn contribute to enhanced proliferation, suppression of apoptosis, development of progesterone resistance and fibrosis, which are all hallmarks of endometriosis related pathologies. He has over 200 peer reviewed publications and has authored multiple book chapters and reviews.

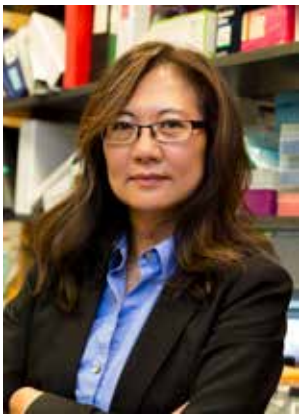
The Notch family of transmembrane receptors (NOTCH1-4) transduces extracellular signals responsible for cell survival, cell-to-cell communication, and differentiation, which are all fundamental processes associated with decidualization. In women and non-human primates, NOTCH1 has a dual role during the window of uterine receptivity. Initially, NOTCH1 mediates a survival signal in the uterine endometrium in response to chorionic gonadotropin (CG) from the implanting blastocyst and progesterone (P), thereby promoting cell survival and aversion of apoptosis. Subsequently, NOTCH1 down-regulation is critical for the completion of the transition of a stromal fibroblast to a decidual cell which is essential for the establishment of a successful pregnancy. We have shown that progesterone increases the cleavage and subsequent activation of transcriptionally competent NOTCH1, serving as a regulator of Notch signaling during decidualization. Using a (progesterone receptor-cre) Pgrcre/+Notch1flox/flox (Notch1d/d) mouse model, we further demonstrated that the pre-implantation uterus relies on Notch signaling to inhibit apoptosis of stromal fibroblasts and regulate cell cycle progression, which together promote successful decidualization.
Endometriosis is a common gynecological disease affecting 1 in 10 women of reproductive age and is a major cause of pelvic pain and impaired fertility. Endometrial stromal cells of women with endometriosis exhibit a reduced response to in vitro decidualization. NOTCH1 is critical for decidualization of both mouse and human uterine stromal cells. To determine whether decidualization failure in women with endometriosis is a consequence of impaired Notch signaling, we investigated expression levels of Notch signaling components in the endometrium of women and baboons with or without endometriosis. We identified NOTCH1 regulated genes during decidualization of Human Uterine Fibroblast (HuF) cells by microarray and quantified their expression levels in in vitro decidualized endometrial stromal cells isolated from women with or without endometriosis. Our data demonstrate that: 1) Notch signaling receptors NOTCH1 and NOTCH4, ligands JAGGED2 and DLL4, as well as direct target genes HES5 and HEY1 were decreased in the eutopic endometrium of women and baboons with endometriosis. 2) Notch signaling was decreased in stromal cells isolated from women with endometriosis, which was associated with impaired in vitro decidualization. 3) Genes that were down-regulated by NOTCH1 silencing in decidualized HuF cells were also decreased in decidualized endometrial stromal cells of women with endometriosis and 4) FOXO1 acts as a downstream target of Notch signaling and endometriosis is associated with decreased expression of NOTCH1-regulated, FOXO- responsive genes during decidualization. Lesion development is difficult to study in women with endometriosis because of the significant delays in diagnosis as well as variability in disease progression. Understanding the mechanisms that regulate the development and progression of ectopic lesions at the onset of the disease will result in new opportunities for targeted therapies to prevent and/or treat endometriosis. Notch signaling controls multiple cell fate decisions such as proliferation, survival and immune modulation. NOTCH1, which targets IL-6 and phosphorylates STAT3 is overexpressed in endometriotic lesions in both baboons and women with endometriosis suggesting that the NOTCH1 signaling pathway actively promotes endometriotic lesion development. We propose that the inflammatory peritoneal environment induces the aberrant expression of NOTCH1 to up regulate IL-6 and phosphorylate STAT3 which in turn promotes endometriotic lesion development by controlling cell proliferation, invasion and epithelial-mesenchymal transformation (EMT). To further evaluate the consequences of Notch overexpression, we generated a Notch gain of function transgenic mouse transgenic by conditionally overexpressing Notch1 intracellular domain (N1ICD) in reproductive tract driven by progesterone receptor-cre. Overexpression of N1ICD in the uterus results in complete infertility as a consequence of multiple developmental and physiological defects including the dysregulation of progesterone and estrogen signaling. The inhibition of progesterone signaling is due to hyper-methylation of its receptor Pgr by over-activation of Notch signaling via the transcription factor PU.1 and DNA methyltransferase Dnmt3b. The increase in PU.1 was also confirmed in ectopic endometriotic lesions which suggests that Notch signaling contributes to the epigenetic silencing of progesterone receptor in endometriosis. Our data provides compelling evidence that NOTCH1 plays a central role in the pathophysiology of endometriosis. As an arbiter of decidualization, the decrease in the eutopic endometrium compromises this process in endometriosis. In contrast, the increase in NOTCH1 expression in ectopic tissues promotes and sustains lesion development. (Supported by NIH HD 042280).

S18-02

AKT pathway in uterine diseases

J. Julie Kim

Northwestern University



The PI3K/AKT signaling pathway is often overactive in uterine diseases. Its role in promoting growth and survival is evident in endometriosis, endometrial cancer and uterine fibroids. Importantly, AKT blunts progesterone signaling in endometrial cancer and endometriosis resulting in suboptimal progesterone response in these diseases. The molecular mechanisms underlying AKT's influence on the progesterone receptor (PR) involve direct post-translational modification of the receptor itself, as well as altering the cofactors that are needed for PR to enhance gene expression. As progesterone plays an essential role in the remodeling of the endometrium in preparation for embryo implantation, aberrant action of this hormone can have dire consequences on endometrial growth and fertility. Understanding how AKT influences disease processes in the uterus is critical in order to consider its potential as a target for therapy.

S19-01

New treatment for diabetic dyslipidemia

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Professor Jianping Weng is professor of the Department of Endocrinology at the Third Affiliated Hospital, Sun Yat-Sen University of Medical Sciences, Guangdong, China. He is the director of Guangdong Provincial Key Laboratory of Diabetology.
Professor Jianping Weng received his PhD and Master degree at the Sun Yat Sen University of Medical Sciences. He was a research fellow of the Department of Endocrinology at the MalmÖ University Hospital of Lund in Sweden.
Professor Jianping weng's research interests focus on endocrinology, metabolic disease and genetics in diabetes. He has published over 100 scientific articles in peer review journals including Lancet, Molecular Endocrinology, Endocrinology, Human Genetics, Diabetes, Diabetes Care and JCEM. He is the Editor-in-Chief of Chinese Journal of Diabetes Mellitus. He is Associate Editor-in-Chief of Chinese Medical Journal. He is board editor of Diabetes, Journal of Internal Medicine.
Professor Jianping Weng is the President of Chinese Diabetes Society 2012-2015.
Professor Jianping Weng is winner of Outstanding Young Scholars, National Natural Science Foundation of China, 2010. He is CHEUNG KONG Scholar professor, Ministry of Education, 2012. He is also the winner of Canton Talents, 2013.

More precise target for the treatment of dyslipidemia: focusing on the LDL-C and downgrading the importance of TG. Patients with type 2 diabetic mellitus (T2D) are known as with high risk of atherosclerotic cardiovascular disease (ASCVD). The characteristics of the dyslipidemia in T2D patients include normal/mild elevated LDL-C, elevated TG and decreased HDL-C. Meanwhile, the number of sdLDL particles which with more atherogenic effect increase. So far, the therapies which aimed at decreasing TG or increasing HDL-C on top of statins had been proved ineffective. (the key studies include the ACCORD-LLA in 2010, the AIM-HIGH in 2011, the HPS2-THRIVE in 2014, the ILLUMINATE in 2007, the Dal-OUTCOMES in 2012, and the ACCELERATE in 2016.) Therefore, the treatment of dyslipidemia in patients with T2D should aim at LDL-C.
International guidelines emphasize dyslipidemia management for the patients with T2D. And the LDL-C goal gets lower and stricter. International guidelines/consensuses have shown a common trend to emphasize the importance of treating dyslipidemia based on risk stratification, and the targets have become stricter. It is still controversial whether a target value is necessary. However, an LDL-C target value is still recommended by the CCEP and the Chinese guideline for Management of dyslipidemia 2016.
Statin is the cornerstone for dyslipidemia treatment. And the IMPROVE-IT study proved ezetimibe could bring more benefits for the T2D patients on top of stains. Statin is the cornerstone of dyslipidemia treatment. Multiple large-scale clinical trials (HPS, 4S) showed that statins could bring cardiovascular benefits for the T2D patients. However, with the target becoming stricter, high doses of statins are usually needed. But this would bring the safety issues. Ezetimibe inhibits the cholesterol absorption from intestine by selectively combining the protein NPC1L1. And the level of LDL-C may drop remarkably with combination therapy due to the complimentary mechanisms. And It has also been reported that expression of NPC1L1 gene in T2D patients had been upgraded, which made the cholesterol absorption increased in these patients. IMPROVE-IT study enrolled 18144 ACS patients, with a median follow-up period of 6 years, was published in 2015. This study got the positive primary endpoints and proved ezetimibe plus simvastatin compared simvastatin alone could statistically reduce CV risk. The subgroup analysis showed even more prominent benefits for patients with T2D.
Brief introduction of other lipid regulators under R&D: The following studies are ongoing: the phase III study focusing on the ASCVD outcomes of PCSK9 inhibitors; the REVEAL study for Anacetrapib, which is the CETP inhibitor aims at increasing the HDL-C; and there are more new targets for lipid regulation emerging, but the safety profile and the efficacy are still needed to be proved. The drugs focused on cholesterol lowering remain the mainstream therapy in a few years.

S19-02

HDL functionality - Coming of age?

Kathryn Tan

University of Hong Kong

An inverse relationship between high-density lipoprotein cholesterol (HDL-C) concentration and cardiovascular risk has been consistently shown in clinical and epidemiological studies and low level of HDL-C is an important cardiovascular risk factor. Although there are strong experimental and epidemiologic data supporting a protective role for HDL in atherosclerosis, the "HDL hypothesis" has recently been challenged by negative findings from large-scale human genetic studies and failed cardiovascular outcome trials with HDL-C raising agents. Experimental data have suggested that HDL has multiple protective functions against atherosclerosis. HDL particles are highly heterogeneous and consist of multiple forms, and it is important to recognize that the heterogeneity in HDL structure is intrinsically related to their functional diversity. Measurement of the cholesterol content of HDL does not reflect the distribution or overall abundance of HDL subspecies and structure-function analyses have shown that HDL-C is a rather poor indicator of the functionality of HDL. Clinical measures to determine the different aspects of HDL function are being developed and evaluated in a number of research laboratories. The most widely-studied and well-characterized function of HDL is its cholesterol efflux capacity. It has been shown that HDL-C levels only explain a fraction of the variance in the cholesterol efflux capacity of HDL, and recent studies have demonstrated that HDL cholesterol efflux capacity is predictive of prevalent and incident coronary heart disease independent of HDL-C. Measures of HDL functionality rather than the cholesterol content of HDL is more robustly associated with clinical outcomes, and evaluation of HDL function rather than HDL mass such as HDL-C is much more informative. Hence, whether improvement in HDL function will translate into clinical benefit deserves further investigation.

S20-01

Natural history of non-functional pituitary adenoma

Warrick Inder

Princess Alexandra Hospital

Associate Professor Warrick Inder MBChB, MD, FRACP
Biographical Sketch
Dr Inder graduated from the University of Otago, NZ in 1988. He obtained his MD examining the effects of opioid peptides on ACTH secretion, before spending 2 years in the Neuroendocrine Unit of the Massachusetts General Hospital, Boston USA on a post-doctoral fellowship researching pituitary adenomas. He has worked as consultant Endocrinologist at Christchurch Hospital, NZ and St Vincent's Hospital, Melbourne and is currently a senior staff specialist at Princess Alexandra Hospital, Brisbane, associate professor with the University of Queensland and member of the Translational Research Institute. He is the President-elect of the Endocrine Society of Australia and chair of the Advanced Training Committee in Endocrinology for the Royal Australasian College of Physicians. His major clinical and research interests are pituitary and adrenal disease.

Non-functional pituitary adenomas account for approximately 30% of pituitary adenomas. They may present with symptoms of mass effect such as visual field defects and headaches, pituitary hypofunction or as an incidental finding when neuroimaging is requested for another indication. The Endocrine Society have formulated guidelines for the investigation and management of pituitary "incidentaloma" – essentially this recommends surgical intervention of a non-functional lesion if it is causing visual compromise or other neurological disturbance. The remainder are followed conservatively with serial MRI scanning, at 6 months for a macroadenoma and 12 months for a microadenoma, then annually for 3 years (every 1-2 years for a microadenoma) and "less frequently after that". Surgery should be considered where there has been clinically significant growth, loss of endocrine function, a lesion close to the optic apparatus in a woman considering pregnancy or when there is unremitting headache. As a result, a substantial number of patients with non-functional pituitary adenomas are subjected to frequent imaging and pituitary function testing. This has allowed longitudinal follow-up to ascertain the natural history of conservatively managed pituitary adenomas.

When a patient with a non-functional adenoma is surgically managed, complete resection is achieved in less than 50% of cases, with a high degree of variation depending on case mix and local surgical expertise. Therefore, it is important to take into account the natural history of operated patients. By definition, they have generally had larger, more aggressive adenomas to have had surgery in the first place. It is well established that post-operative radiotherapy markedly reduces the risk of tumour regrowth and recurrence, but contemporary practice involves selective rather than routine use of this treatment modality. Therefore we have a number of series where post-operative radiotherapy has not been routine, allowing the opportunity to follow the natural history of operated non-functional adenomas.

Microadenomas discovered incidentally rarely grow to the extent of requiring intervention. On the other hand, a significant number of macroadenomas ultimately require surgery. Baseline size correlates with subsequent growth, suggesting larger lesions have already shown a propensity to increase. Growth rate particularly over the first 2 years following diagnosis is highly predictive of requirement for surgery or absolute increase in size of ≥20%. Recent data using volumetric analysis rather than maximal diameter allows a better estimate of change in size.

In operated patients, young age and the presence of residual tumour in the first post-operative scan are the major risk factors for subsequent regrowth/recurrence. Similar to the conservatively managed adenomas, the growth rate over the first 3 years post-operatively is highly predictive of requiring further intervention (repeat surgery or radiotherapy). Some but not all series suggest that the site of the residual tumour is important (more likely if suprasellar residual). Silent corticoptroph tumours may demonstrate more aggressive recurrence but not increased recurrence rates. Both recurrence of a lesion considered totally resected and regrowth of stable residual disease, can occur after >10 years of follow-up.

These data potentially allow refinement of current guidelines in the management and follow-up of non-functional pituitary adenomas. Microadenomas could be imaged at less frequent intervals. It is suggested that an initial scan at 2 years and if stable 5 years would suffice. Only lesions growing significantly in size over that time frame would need later imaging. For conservatively managed macroadenomas, the current recommendations for imaging over the first 3 years allow for the determination of growth rate by volumetric analysis. Those which have not significantly changed across that period could be safely imaged less frequently, with the suggested frequency at 5, 7 and 10 years and then every 5 years thereafter. Lesions whose growth rate by 3 years predicts the need for intervention should undergo surgery, which is likely to reduce the problem of age-related co-morbidities and improve surgical outcome. In the post operative setting, patients should be imaged as per the recommended frequency for conservatively managed macroadenomas. Significant growth of residual tumour over the first 3 years, particularly in a young patient, suggests the need for a second intervention.

In conclusion, there has been a considerable increase in recent knowledge regarding the natural history of both conservatively managed and operated non-functional pituitary adenomas. This allows clinicians to avoid unnecessary tests, focusing on identification and treatment of those patients who exhibit a higher risk of requiring intervention.

S20-02

Differentiation of pluripotent stem cells into hypothalamic and pituitary cells

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The hypothalamic-pituitary system is essential for maintaining homeostasis and life by controlling systemic hormones. We have established a technique that allows the generation of functional adenohypophysis from mouse and human embryonic stem (ES) cells. Pluripotent stem cells, such as ES cells and induced pluripotent stem (iPS) cells, differentiate into neuroectodermal progenitors when cultured as floating aggregates under serum-free conditions. Recent results have shown that strict removal of exogenous patterning factors during the early differentiation peri-

od induces efficient generation of rostral hypothalamic-like progenitors from mouse ES cell-derived neuroectodermal cells. During early embryonic development, the hypothalamus position in the cerebral nervous systems is characterized by the most rostral and most ventral. Hypothalamic differentiation is inhibited by many signals in differentiation medium. Hence, the use of growth factor-free, chemically defined medium (gfCDM) was critical for this induction. The ES cell-derived hypothalamic-like progenitors generated rostral-dorsal hypothalamic neurons, in particular magnocellular vasopressinergic neurons, which release hormones upon stimulation.

We subsequently reported efficient self-formation of adenohypophysis tissues in three-dimensional (3D) aggregate cultures of mouse ES cells. Based on the gfCDM culture mentioned above, we modified the differentiation method from the perspective of positional information. As a result, we have succeeded in inducing both ventral hypothalamic and oral ectodermal tissues simultaneously. The ES cells were stimulated to differentiate into the two tissues in adjacent layers within the aggregate, followed by treatment with a Sonic Hedgehog agonist. Self-organization of Rathke's pouch-like structures occurred at the interface of the two epithelia in vitro. Subsequently, after long culture, various endocrine cells including corticotrophs and somatotrophs were produced from the Rathke's pouch-like structures. The induced corticotrophs efficiently secreted adrenocorticotropic hormone (ACTH) in response to corticotropin-releasing hormone (CRH). In addition, we found that, in vitro-generated corticotroph cells were able to rescue hormone levels, physical activity levels and survival when grafted into pituitary-resected hypopituitary mice. Thus, we have generated a useful methodology for the production of functional human pituitary tissue that will benefit future studies in both disease research and regenerative medicine.

Our latest study aimed to prepare hypothalamic and pituitary tissues from human pluripotent stem cells and establish effective transplantation techniques for future clinical applications. We succeeded in establishing the differentiation method using human ES/iPS cells. The culture method is characterized by replication of stepwise embryonic differentiation. Therefore, these methods could potentially be used as developmental and disease models, as well as for future regenerative medicine.

S20-03

Insights from Molecular Pathology

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The pathogenesis and pathophysiology of pituitary tumors is highly variable, reflecting the multiplicity of diseases comprising these lesions. While clinically, pituitary tumors are classified according to the clinical syndrome that they cause, pathology has achieved a subclassification of tumor types that is both prognostic and predictive. Molecular analysis has identified that some of these various subgroups have specific alterations underlying tumor development, and therefore have implications for therapeutic decision making. While growth hormone (GH) hypersecretion resulting in acromegaly and/or gigantism is thought to represent a single clinical entity, morphologic examination of pituitary tumors underlying this disorder has provided evidence of at least 4 tumor types responsible. The most common type, the densely granulated (DG) somatotroph tumor, is associated with activation of cyclic adenosine monophosphate (cAMP) signaling, as has been shown by the identification of sporadic GNAS mutations in these lesions. Mammosomatotroph tumors, which resemble DG somatotrophs but also express prolactin, occur in situations also associated with cAMP activation, such as McCune-Albright and Carney complex. It is therefore not surprising that these tumors, both composed of cells resembling their normal counterparts, respond well to somatostatin analogues. In contrast, sparsely granulated somatotroph tumors, although derived from the same cells, have a completely different morphology that has no normal counterpart and have been shown to have AIP mutation, epigenetic silencing of AIP, GHR mutation or other causes of altered STAT activation. As expected of tumors that are not dependent on cAMP, they do not respond well to somatostatin inhibition and instead require pegvisomant to control the effects of GH excess. More primitive tumors, including the plurihormonal tumors of Pit-1 lineage, tend to behave in a more aggressive fashion but are rare and have not been examined systematically at the molecular level.

USP8 mutations underlie DG corticotroph tumors associated with Cushing disease; they are usually small tumors causing florid corticotropin excess. These tumors have been shown to be responsive to pasireotide. In contrast, SG corticotroph tumors tend to be larger and more invasive, diagnosed later because of the more subtle features of hormone excess. The rare Crooke cell tumors are a manifestation of complete loss of feedback inhibition of cell proliferation and they tend to be highly aggressive neoplasms.

The molecular pathogenesis of prolactin-producing tumors has remained enigmatic, possibly because the majority of these tumors respond well to dopamine agonists, therefore they do not require surgery and tissue is not available for analysis. Autopsy studies and surgical specimens of these tumors have shown that they are comprised of SG lactotrophs that resemble normal lactotrophs. In contrast, tumor that do not respond to dopamine agonists tend to be composed of atypical DG lactotrophs or of more primitive cells, known as acidophil stem cells.

Although genetic mutations have not been identified in the majority of surgically resected adenohypophysial tumors, the clinically non-functioning gonadotroph tumors, epigenetic alterations have been identified that may be implicated in tumor development and progression. It appears that environmental and other epigenetic factors ae implicated in activation of growth factors and their receptors that is a feature of some of these lesions.

A large number of other tumors comprise the family of pituitary tumors; these include hormone- and transcription factor-negative proliferation of unclassified adenohypophysial cells known as "null cells", as well as tumors with divergent differentiation by activation of multiple transcription factors. Tumors of Rathke's cleft, craniopharyngiomas, have been shown to have mutations reflective of their morphology; BRAFV600E mutation is associated with papillary variants and beta-catenin mutation resulting in nuclear translocation found in adamantinomatous variants. The molecular basis of tumors of the posterior lobe, the various typesof pituicytoma (including oncocytic and granular cell tumors) remains to be elucidated.

The application of additional biomarkers such as proliferation indices (Ki-67) provides further information in morphologically stratified pituitary tumors.

Integration of predictive information about tumor type and prognostic data from such biomarkers with radiologic information about residual tumor will allow structured management approaches ranging from active surveillance to aggressive multimodal targeted therapies.

S21-01

New genes for a 50-year old disease

Maria-Christina Zennaro

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Maria-Christina Zennaro is INSERM Research Director, head of team 14 "Genetic mechanisms of aldosterone related disorders" at the Paris Cardiovascular Research Center and associated investigator at the Genetics Department of the European Hospital Georges Pompidou in Paris (France).

She received her MD and board certification in Endocrinology at the University of Padova (Italy) and completed her PhD in Molecular Endocrinology at the University Pierre et Marie Curie in Paris (France). Her research team has developed a genome-wide strategy to explore the genetics and genomics of pseudohypoaldosteronism type 1 and primary aldosteronism, in order to generate knowledge translatable to patient's care. She coordinates the genetic investigations on PHA1 at the laboratory of genetics at HEGP, which is the French referral center for the genetic diagnosis of the disease. She is coordinator of an ANR-DFG funded French-German research network on the genetics of primary aldosteronism and coordinator of the EU H2020 funded program ENS@T-HT. Her team has recently been appointed by the Fondation pour la recherché médicale as FRM Team.

Maria-Christina Zennaro has been awarded for her work by the Italian Societies of Internal Medicine, Hypertension, Endocrinology, the French Society of Nephrology and the International Aldosterone Conference. She is head of the APA working group of the European Network for the Study of Adrenal Tumors (ENS@T), president of the European Section of Aldosterone council (ESAC)-France, member of the Executive Committee of the International Aldosterone Conference, working group leader of the European COST action ADMIRE and member of the European Society of Hypertension - Centre of Excellence for Hypertension at HEGP-Paris. She has been invited as 15th Richard Underwood Memorial Visiting Professor at the University of Harvard in 2014.

She serves a reviewer for multiple national and international funding organizations and journals and is member of the Editorial Board of the journal Endocrinology.

S21-02

Genetics of primary hyperaldosteronism. Alternative: Prevalence of and risk factors for primary

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Currently, she is the Vice president of the Chinese Endocrine Society, Chief Executive of Chinese Endocrinologist Association, Chair of Shanghai Endocrine Society, vice-president of Shanghai Diabetes Rehabilitation Society. She is the associated-chief-editor of Journal of Diabetes. She has received more than 10 national and local grants and more than 100 peer-reviewed SCI publications, including JAMA and Science. She was winner of the National Science &Technology Progress Awards in 2008, 2010 and 2012 respectively (2nd class), winner of Shanghai Science& Technology Progress Awards/Shanghai Medical Science &Technology Awards/Awards/Shanghai Medical Science &Technology Promotion Awards (1st class, rank 1st place)

Recent studies indicate that primary aldosteronism (PA) is a much more common cause of hypertension than had been demonstrated historically. In patients with resistant hypertension, the prevalence of PA from different clinics worldwide is about 10-20%. As has been no such data in China, we launched a large-scale, hospital-based national survey and enrolled 1656 patients with resistant hypertension finally. Serum aldosterone and plasma renin activity were measured in every subject and ARR (aldosterone-to-renin ratio) was calculated to screen PA. Positive patient ARR>20 underwent intravenous saline infusion test, and diagnosis of PA was established if post-saline aldosterone was above 8ng/dl. Among 1656 patients with resistant hypertension, 494 (29.8%) were screened positive on the basis of ARR>20 and underwent intravenous saline infusion. The diagnosis of PA was established in 118 (7.1%) subjects according to an unsuppressed post-saline aldosterone (>8 ng/dl). Adrenal venous sampling(AVS) was performed in 70 of 118 patients, 39 were diagnosed as unilateral PA and 31 were bilateral PA. Generalized additive regression analysis revealed that among all the factors investigated (age of hypertension onset, BMI, family history of hypertension, cigarette smoking, alcohol consumption, diabetes, serum potassium, hyperlipidemia, and creatinine), only age of hypertension onset and serum potassium were independently associated with the presence of PA. Prevalence of PA decreases with aging and so do aldosterone and renin activity level. Data show no significant gender difference in prevalence, however, women intrinsically have lower PRA level and thus higher ARR, due to which some screening strategies may require further modification. The prevalence of primary aldosteronism in Chinese patients with resistant hypertension is relatively lower compared with previously reported data from other ethnic populations. The screen on PA should be on those with early onset of hypertension and/or hypokalemia.

S21-03

Implications for essential hypertension

Richard Auchus

University of Michigan

Numerous studies in several settings from primary care to hypertension clinics throughout the world have established that primary aldosteronism (PA) is present in 5-13% of hypertension and up to 20% of patients with resistant hypertension. Paradoxically, estimates conclude that Much has been learned about the pathogenesis of PA in the last 5 years, including the demonstration that potassium and calcium channel mutations are responsible for some genetic forms of PA and for many aldosterone-producing adenomas. This information has led to consideration of the pathogenesis of PA, which might begin with clusters of aldosterone-producing cell clusters. This model suggests that PA might evolve through several stages, which include a 'pre-clinical' PA state.

Although a major goal of the PA evaluation is to identify surgically curable disease, mineralocorticoid receptor antagonist (MRA) therapy with spironolactone or eplerenone is equally effective in blood pressure control and amelioration of complications. MRA therapy is also uniquely effective in the treatment of resistant hypertension. These facts raise the need for greater awareness of PA, its pathogenesis, and broader use of MRA therapy.

S22-01

Clinical management of GO patients: Experiences from EUGOGO

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Wilmar M. Wiersinga, MD, PhD

Wilmar M. Wiersinga MD, PhD is Professor-Emeritus of Endocrinology at the University of Amsterdam in The Netherlands. He was chair of the Division of Endocrinology & Metabolism in the Academic Medical Center from 1995 to 2008. He is past president of the Dutch Endocrine Society and the European Thyroid Association, and served on the Executive Committee of the European Society of Endocrinology. He has been European editor of Clinical Endocrinology and member of the Editorial Board of JCEM; currently he is editor-in-chief of the European Thyroid Journal. He was member or chair of several program organizing committees of the annual European Congress of Endocrinology, and chaired that of the International Thyroid Congress in 2010; he also served on program committees of the annual meetings of the American Thyroid Association and the Endocrine Society. He is a honorary member of the European Society for Endocrinology, the Hellenic Endocrine Society and the German Endocrine Society. His research interests are autoimmune thyroid diseases in particular Graves' ophthalmopathy (he was one of the founders of EUGOGO), nonthyroidal illness syndrome, amiodarone and thyroid hormone replacement.

Guidelines for the management of Graves' Orbitopathy (GO) have been published in 2016 by the European Thyroid Association/European Group on Graves' Orbitopathy (EUGOGO)1. 45% of GO patients is restricted in daily activities, 36% is on sick leave, 28% is disabled, 5% went into early retirement and 3% lost their job. A patient-focussed approach is thus recommended, which encompasses the effects of the disease and its treatment on quality-of-life (QoL) and psychosocial well-being. Therefore the disease-specific and validated GO-QoL questionnaire is recommended in routine clinical practice. The GO-QoL is available in sixteen languages (www.eugogo.eu). Activity and severity of GO should be assessed according to standardized criteria. GO should be categorized as active or inactive (clinical activity score CAS ≥3 and <3 respectively), and as mild, moderate-to-severe or sight-threatening (dysthyroid optic neuropathy DON and/or corneal breakdown). Mild GO usually has lid retraction <2mm, mild soft tissue involvement, exophthalmos <3 mm above normal for race and gender, no or intermittent diplopia, and corneal exposure responsive to lubricants. Moderate-to-severe GO usually has ≥2 of the following items: lid retraction ≥2 mm, moderate or severe soft tissue involvement, exophthalmos ≥3 mm above normal, inconstant or constant diplopia. Moderate-to-severe GO and DON occur in about 5% of all patients with Graves' hyperthyroidism. GO patients –except for the mildest cases- should be referred to combined thyroid-eye clinics or specialized centers providing endocrinological and ophthalmological expertise. The 2009 Amsterdam Declaration on Graves' Orbitopathy has been signed by many international and national learned societies and patient associations. Its goal is to increase awareness of GO and to increase the quality of care delivered to GO patients, e.g. by shortening the time to diagnosis of GO and shortening the time between diagnosis and treatment. GO patients referred to EUGOGO centers had less active and less severe disease in 2012 than in 2000.

S22-02

Novel approaches in detection of auto-antibodies in GO

Lutz Schomburg

Charite Berlin

S22-03

Therapy of Graves Orbitopathy

Simon Pearce

Newcastle University

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Management of Graves' orbitopathy (GO) can be considered in the following 6 categories:

• Management of risk factors, particularly cigarette smoking should be encouraged at all times.

• Control of thyroid status is essential for the optimal management of GO. Antithyroid drugs are the mainstay of therapy for hyperthyroidism, although hypothyroidism should be strictly avoided either by use of block-replace regimens combining antithyroid drug and levothyroxine, or by regular monitoring of serum thyroid function. If hyperthyroidism can't be controlled or there is massive goitre, then total thyroidectomy should be undertaken. Hypothyroidism should also be controlled carefully to maintain TSH in the lower part of the reference range.

• Mild to moderate GO with or without inflammatory features

should be managed symptomatically with lubricating eye drops. Selenium supplementation (sodium selenite 100mcg daily) has also been shown to be effective in ameliorating mild to moderate thyroid eye disease.

• Moderate to severe active GO with functional consequences to vision (eg. diplopia) or severe soft-tissue inflammation should be treated with anti-inflammatory therapy in the form of glucocorticoids. Intravenous methylprednisolone 500mg weekly for 6 weeks, followed by 250mg weekly for a further 6 weeks strikes a balance between efficacy and side-effects of steroid therapy. Orbital radiotherapy has been shown to effective and is suitable for older patients. There is a little evidence for efficacy of other immunomodulatory treatments including ciclosporine, rituximab and tocilizumab.

• Dysthyroid optic neuropathy requires urgent treatment with intravenous steroid; methylprednisolone 500mg or 1g daily on 3 consecutive days. About 50% of patients make a good response, however if visual acuity or colour vision remain reduced, then emergency orbital decompression focused on the medial orbital wall is necessary to preserve vision.

• Residual proptosis, strabismus or eyelid abnormality. After the active phase of the GO has 'burned out': usually 12 to 18 months following the initial presentation, rehabilitative surgery should be offered. Orbital decompression surgery can reduce proptosis, muscle recession may correct strabismus and symmetrical appearance may be improved by eyelid surgery.

S23-01

Hypothalamic inflammation in obesity and diabetes

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Despite numerous educational interventions and medical efforts, modern society continues to suffer from obesity and its associated metabolic diseases, such as type 2 diabetes mellitus, and these diseases show little sign of abating. The brain, and in particular the hypothalamus, continues to gain attention as an important central target for the treatment of metabolic disease. However, most of the pharmaceutical approaches directly targeting the brain largely have failed, this might be due to an incomplete understanding of hypothalamic function in control of energy metabolism. Our recent studies on pathophysiology in obesity and diabetes discovered hypothalamic inflammation-like processes that is mainly driven by reactive microglia and the associated pro-inflammatory factors, result in a vicious cycle of cellular destruction ending with a loss of the appetite-curbing neurons and ultimately cumulating into the development of obesity and type 2 diabetes. Building on a considerable body of preliminary data, we have applied an array of advanced technologies to develop a functional understanding of the impact of major pathophysiological changes in reactive hypothalamic microglia. First of all, we discovered that consumption of high-carbohydrate, high-fat (HCHF) diets, but not of low-carbohydrate, high-fat diets, increases microgliosis as well presence of N(e)-(Carboxymethyl)-Lysine (CML), a major advanced glycation end product (AGE), in hypothalamic neurons in control of appetite. On a HCHF diet, mice lacking CML receptors RAGE and ALCAM displayed less microglial reactivity and less neovasculature formation in the mediobasal hypothalamus, and this was associated with significant improvements of metabolic disorders induced by the HCHF diet. We conclude that combined overconsumption of fat and sugar, but not the overconsumption of fat per se, leads to excessive CML production in hypothalamic neurons, which in turn stimulates hypothalamic inflammatory responses that eventually leads to neuronal dysfunction in the control of energy metabolism. We then found that in HCHF diet-induced obese mice, TNFalpha produced by persistently activated microglia stimulates mitochondrial stress in appetite regulating neurons. Disruption of specific TNF downstream signals in the mediobasal hypothalamus of diet-induced obese mice reverses mitochondrial stress and reduces obesity. These data suggest that in a hypercaloric environment, persistent elevation of microglial reactivity and TNFalpha production induces mitochondrial stress in hypothalamic neurons that contributes to the development of obesity. In our future study, more detailed understanding of the complex interactions between cellular and intracellular players involved in diet induced hypothalamic inflammation-like processes may hold opportunities for novel ways to effectively target obesity, diabetes and their comorbidities.

S23-02

TRH neurons as metabolic/stress integrators

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Thyroid hormones and glucocorticoids are crucial participants in energy homeostasis, dependent on two neuroendocrine axes: hypothalamus-pituitary-thyroid (HPT:TRH-TSH-T4/T3) and HP-adrenal (HPA; CRH-ACTH-corticosterone). Paraventricular-hypothalamic TRH and CRH neurons decode metabolic, neuronal and environmental signals. *Trh* expression and HPT axis are activated by energy demanding situations (cold, exercise) and inhibited by negative energy balance (fasting). At the median eminence, released TRH may be inactivated before reaching the thyrotrophs by TRH degrading ectoenzyme (*Trhde)* expressed in tanycytes and modulated by nutritional status. CRH neurons are activated by acute or chronic stress; increased corticosterone activates the glucocorticoid receptor (GR). Glucocorticoids (Gc) control HPT axis at distinct levels including *Trh* transcription. We searched for the mechanism of Gc interference on the neuronal-induced activation of *Trh* expression. In vivo, corticosterone injection blunted cold-induced stimulation of CREB phosphorylation in TRH-PVN neurons,

TRH and TSH synthesis and release. In hypothalamic cultured cells, dexamethasone (Dex) curtailed cAMP-induced increase of Trh mRNA level and CREB phosphorylation, so as pCREB and GR binding to Trh-gene promoter. Simultaneous incubation with forskolin-Dex decreased nuclear translocation of catalytic PKA or of GR compared with forskolin or Dex alone; PKAc co-immunooprecipitated with GR. We propose that Gc repress neuronal-induced transcriptional activation of Trh by protein:protein interaction between GR and PKAc.
Finally, the susceptibility of HTP axis to insults is extended to postnatal stress; maternal separation (MS) affected HPT axis programming in a gender-specific manner. Trh expression increased in MS females and TRHde in males. Response to fasting was partially blunted in adult males which could affect their adaptive response to negative energy balance. TRH neurons act thus as energy sensors, but are vulnerable to stress. (CONACYT 180009)

S23-03

Hunger-driving hypothalamic circuits

Kevin Williams

The University of Texas Southwestern Medical Center

The brain plays a critical role in regulating food intake, body weight and blood glucose levels. Dysfunction of this regulation results in obesity and diabetes. To develop new treatments, it is first necessary to unravel the brain pathways regulating energy balance. Key signals act on collection of neurons within the hypothalamus to regulate food intake and body weight and glucose homeostasis. However, the inherent complexity of these circuits has made it extremely difficult to identify the key neurons that regulate these processes. Over the past several years the ability to manipulate gene expression in a neuron-specific fashion has become feasible. We will describe some our recent findings using mouse models that allow neuron-specific manipulation of genes regulating energy balance and glucose homeostasis. It is our hope that these studies have provided insights into the mechanisms through which the brain controls food intake, body weight and blood glucose levels.

S24-01

Assessing fracture risk in diabetes

Ann Schwartz

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Both type 1 and type 2 diabetes are associated with higher risk of hip fracture. Type 2 diabetes affects an increasing proportion of older adults, the population that is also at elevated risk of fracture. Paradoxically, type 2 diabetes is also associated with higher bone density. As a result standard tools for fracture prediction, BMD T-score and FRAX, tend to underestimate fracture risk in diabetic patients, an important challenge for clinical care. Factors that may contribute to reduced bone strength in diabetes include accumulation of advanced glycation endproducts in bone collagen, increased cortical porosity, and deficits in bone microvasculature. Additional studies are needed to determine if measurement of these factors can improve fracture risk assessment in diabetic patients. Diabetes-specific risk factors for fracture include poor glycemic control, longer duration of diabetes, presence of diabetic complications, and use of specific diabetes medications. These factors can aid in the identification of diabetic patients at high risk of fracture.

S24-02

Effects of advanced glycation products on bone

Antonio Desmond McCarthy

Laboratorio de Osteopatias y Metabolismo Mineral (LIOMM) Universidad Nacional de La Plata - Argentina

Dr. Antonio Desmond McCarthy holds a degree in Biochemistry (1990) and a Ph.D. in Biochemical Sciences (2001), from the National University of La Plata, Argentina. He additionally completed a three-year Ministry of Health Hospital Residency in Clinical Biochemistry (1993). His main areas of expertise are: (a) Education (1994-present): he is currently Professor of Human Anatomy and Histology and a member of the board of Directors of the Faculty of Exact Sciences, National University of La Plata. He is also a member of the board of Directors of the Instituto de Cultura Itálica de La Plata. (b) Clinical biochemistry and research (1990-present): he is currently Director of the Clinical Biochemistry Laboratory in the "Horacio Cestino" General Hospital. The ground-breaking results of his clinical research projects contributed to modify screening procedures for Gestational Diabetes mellitus in Argentina, which used to be selective but are now universal. (c) Basic research (1994-present): he is currently co-director of LIOMM (Mineral Metabolism and Osteopathy Research Laboratory), National University of La Plata. Together with co-workers, Dr. McCarthy has established that the accumulation of AGEs on bone collagen (a characteristic of Diabetes mellitus) can induce a decrease in bone turnover and quality. He also investigates the secondary effects on bone of anti-diabetic drugs, and participates in the development of biomaterials for bone tissue engineering.

S24-03

Effect of diabetes drugs on bone metabolism

Lorenz Hofbauer

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S25-01

Vitamin D status and disease risk: results from observational studies

Robert Scragg

University of Auckland

Interest in vitamin D has expanded substantially over the last 15 years with a three-fold increase in the number of scientific vitamin D publications from 2000 to 2015. Traditionally, the main disease group linked to vitamin D deficiency has been bone disease, particularly rickets. However, the growth in vitamin D research has been driven by epidemiological studies linking vitamin D status to a wide range of other diseases.
The diseases linked to vitamin D deficiency include cardiovascular diseases (coronary heart disease, heart failure, hypertension, stroke) [1], diabetes (both type 1 and type 2 [2]), cancer (colorectal [3], breast, prostate) , respiratory infections (TB, pneumonia) and lung function (asthma), musculoskeletal diseases (osteoporosis, fractures [4], skeletal muscle weakness) and other diseases (eg. multiple sclerosis, dementia). Increased risk of all-cause mortality, the most important outcome of all, is also linked to vitamin D deficiency [5].
The conduct of these epidemiological studies has been facilitated by the development since the 1970s of a range of assays to measure in blood the concentration of the main vitamin D metabolite, 25-hydroxyvitamin D, which is used as a marker of vitamin D status. The epidemiological evidence comes from all the three main observational study designs – cross-sectional, case control and cohort studies. The latter, where blood samples to measure vitamin D status are collected at baseline and then linked with disease risk during follow-up, provide the strongest evidence for causation, aside from interventions studies of vitamin D supplementation.
The evidence from observational studies fulfil many of the Bradford-Hill criteria for causation. These include:
Temporality, with evidence from cohort studies showing that exposure to low vitamin D status at baseline precedes the onset of disease during follow-up; Consistency, as meta-analyses of cohort studies show convincingly that when studies are combined, low baseline vitamin D status significantly predicts increased risk of many of the above diseases during follow-up; Strength of association, with meta-analyses reporting moderate 2-3 fold increases in disease risk associated with very low vitamin D status (25-hydroxyvitamin D dose-response relationship, with disease risk increasing as vitamin D status decreases, although recent evidence suggest the association between vitamin D status and disease risk may be non-linear; Biological plausibility, as laboratory research has identified both the presence of the vitamin D receptor in many tissues of the body and also biological mechanisms to explain the associations between vitamin D status and disease risk.
The above evidence from observational studies will be reviewed. However, one critical criterion of causation remains to be met: evidence of reversibility from intervention studies of vitamin D supplementation, which will be covered by another presentation in this symposium on vitamin D.

S25-02

Does vitamin D treatment improve health outcomes - data from trials

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Rolf Jorde is Professor of Internal Medicine, UiT – the Arctic University of Norway. He is a specialist in endocrinology with vitamin D as main research focus. Rolf Jorde is leader of Tromsø Endocrine research group which has performed several large RCTs with vitamin D on a number of clinical endpoints.

There is no question that vitamin D is important for bone health, with vitamin D deficiency in childhood leading to rickets and in adults to osteomalacia. In recent years supplementation with vitamin D has also by many been advocated for the prevention and/or treatment of a number of diseases, included cancer, cardiovascular diseases, diabetes and infections. The reason for this is the observation that for all of these diseases there is a negative cross-sectional and longitudinal association with vitamin D status as evaluated by the serum levels of 25-hydroxyvitamin D (25OHD).
However, associations are no proof of a causal relation. For vitamin D this is particularly important, since there is a high likelihood of reverse causality, with the low serum 25OHD levels being the result and not the cause of disease. Thus, subjects in ill health probably stay more indoors, get less sun exposure and accordingly have less vitamin D produced in the skin.
Accordingly, the only way to determine whether supplementation with vitamin D improves health is to do randomized clinical trials (RCT) where one group is randomized to vitamin D and another to placebo and the groups followed for a sufficient length of time for the effects to be detected (1).
A number of such RCTs in a multitude of clinical settings have been performed during the last decade, hundreds of reviews and meta-analyses have been published, and even a meta-analysis of the meta-analyses (umbrella review) has appeared (2). In general, the results have been negative.
As an example, there is a strong negative correlation between serum 25OHD levels and blood pressure. This is compatible with the observation that subjects with vitamin D deficiency have greater plasma renin activity, and there is increasing evidence that vitamin D regulates the angiotensin – renin axis. One could therefore expect that supplementation with vitamin D would decrease blood pressure. However, in a systematic review and meta-analysis based on 4541 individual patient data from 46 trials, no effect on blood pressure was found (3).
There could be several reasons for this lack of effect. First of all, most of the RCTs have included subjects who probably were not vitamin D deficient, and therefore no effect of vitamin D supplementation were to be expected. In this regard it should be mentioned that we do not know what is a sufficient (not say optimal) 25OHD level and the current recommendations are not based on adequate RCT data. Given the almost universal lack of effect of vitamin D supplementation in populations with serum 25OHD levels > 40 nmol/L, the definitions of vitamin D insufficiency might need revision. In future RCTs one should therefore only include subjects with low serum 25OHD levels (probably < 25 – 30 nmol/L) to

avoid type 2 errors.
Another explanation for the lack of effect could be the dosing regimens used. Thus, giving vitamin D as weekly, monthly or annual doses may not be physiological and will result in short-lived serum vitamin D peaks and longer-lived 25OHD peaks. If the mother compound vitamin D has effects of its own through intracellular hydroxylation in peripheral tissues then studies with large dose intervals may have left the subjects intermittent intracellular vitamin D deficient in spite of adequate serum 25OHD levels.
Results from several large vitamin D intervention studies like the ViDA study from New Zealand with 5110 participants, the VITAL study from the US with 25,875 participants, and the Australian D-Health Study, which has recruited over 20,000 participants, will appear within the near future and hopefully settle the questions on beneficial effects of vitamin D supplementation. However, vitamin D deficiency has not been an inclusion criterion in these studies, but hopefully the large number of participants will allow for subgroup analyses. If not, we have to start all over again, and do the proper RCTs in vitamin D deficient populations.

S25-03

Reconciling observational studies of vitamin D with randomized control trials - Why the Difference?

Kevin Cashman

University College Cork

Vitamin D is an essential nutrient, albeit an unusual one with a key component of its supply being ultraviolet B (UVB) sunlight-induced synthesis in the skin as well as dietary supply. Dietary Reference Values (DRV) for vitamin D, which are estimates of the dietary requirements for vitamin D, are crucial from a public health perspective in providing a framework for prevention of vitamin D deficiency and optimizing vitamin D status of individuals. There have been at least 6 different agencies internationally who revised their DRV for vitamin D in the last 5 years and all concluded that the role of vitamin D in bone health is unquestionable, but their suggested threshold of serum 25-hydroxyvitamin D [25(OH)D] (which supports different components of bone health) are variable. A serum 25(OH)D concentration <25 to 30 nmol/L increases risk of rickets in children and osteomalacia in adults (1,2), but some agencies have proposed that a serum 25(OH)D concentration of 50 nmol/L is required to protect nearly all on the population in terms of bone health. While still growing, the evidence-base behind the role of vitamin D status in non-skeletal disease is much more ambiguous, which has meant agencies have not used these to define their recommendations.
Establishment of DRV relies heavily on data from randomized controlled trials (RCT) as top tier evidence, but also from longitudinal cohort studies as the next highest level of evidence. In this respect, the conflict in the data from observation and RCT studies in terms of the role of vitamin D in skeletal and non-skeletal health outcomes has created uncertainties for these regulatory agencies. Some of the reasons for why the RCT and observational data may disagree will be discussed in this presentation but also in the two presentations in the session which will overview the observational and the RCT evidence, respectively. The weaknesses of both types of studies will be discussed, and also how data from a number of large RCTs may help resolve some, but probably not all, of the disagreement. The type of analyses or indeed new studies that might be needed will be highlighted.
Even while we await these new data, and using the current and recently established DRV, it is clear that many in the population have 'low vitamin D status', whether one chooses the more conservative serum 25(OH)D <30 nmol/L or the growing consensus threshold of <50 nmol/L. As just one example, in Europe one in eight individuals may have serum 25(OH)D <30 nmol/L, while four in ten have serum 25(OH)D <30 nmol/L (5). This requires some public health response in terms of addressing low status, and the options which include UVB exposure, vitamin D supplementation and food fortification will be briefly discussed, including their pros and cons.
References:

S26-01

Estrogen rapidly modulates spinogenesis in the hippocampus

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Objective Can nuclear receptors of estrogen act through not only classical/slow genomic pathways but also non-genomic rapid signaling pathways? Can hippocampus synthesize estradiol (E2) locally from cholesterol? Many labs have challenged to solve these difficult problems for recent 15 years. The answer?is Yes.
Methods and Results By using confocal microscopic analysis of fluorescently labeled dendritic spines, we demonstrated that E2 rapidly increased the spine density in hippocampal glutamatergic neurons, upon incubation of hippocampal acute slices (<0.5 nM E2) with 1 or 10 nM E2 for 2 h. To investigate the rapid E2-signaling in spinogenesis, we applied selective inhibitors of kinases which play important role in synaptic plasticity. The participation of Erk MAPK, LIMK, PKA, PKC, PI3K and p38 MAPK was observed in E2-signaling. Activation of Erk MAPK may promote polymerization of actin filaments via cortactin, leading to increase of the spine density.?Activation of LIMK may inhibit de-polymerization of actin filaments via cofilin, leading to increase of the spine density. PKA, PKC, PI3K may act in a similar manner to Erk MAPK. The participation of ERalpha, but not ERbeta, to the rapid E2-signaling was indicated by using agonists and antagonists. ERalpha in dendritic spines (= post-synapses) participated in the spinogenesis. The synaptic expression of ERalpha was observed by immunogold electron-microscopic investigations, in addition to their expression in nuclei. Study of ERalpha KO mouse and ERbeta KO mouse also showed the selective participation of ERalpha in the rapid spinogenesis. GPR30 may not act as a membrane receptor of E2, due to very low affinity to E2.?The hippocampus synthesizes E2 locally from cholesterol. All the mRNAs and proteins of enzymes, necessary for E2 synthesis, were found in the hippocampal neurons. From 3H-steroid metabolism analysis of hippocampal slices, it was observed that hippocampal neurons?synthesize sex-steroids, including E2, testosterone (T) and dihydrotestosterone (DHT) from cholesterol. Mass spectrometric analysis was used to determine the sex-steroid levels. The levels of steroids are different between male hippocampus (8 nM E2, 17 nM

T and 6 nM DHT) and female hippocampus (0.1-1 nM E2, 1 nM T, 0.5 nM DHT). Local steroid synthesis is dependent on neuronal activity, including Ca influx through NMDA type glutamate receptors. The pulsed local synthesis of E2, rather than circulating E2, is probably?useful for rapid synaptic modulation.

Conclusion Mechanisms of non-genomic E2 signaling depend on kinase networks, synaptic estrogen receptors and locally synthesized E2 in the hippocampus. Activation

S26-02

Neuroestrogens and the regulation of GnRH release

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The concept that the female reproductive cycle is regulated by ovarian estradiol (E2) through its negative and positive feedback effects on GnRH and gonadotropin secretions is a well-established principle. However, a series of studies in this lab using female rhesus monkeys has led to a new concept that neuroestradiol, synthesized and released in the hypothalamus, also contributes to the regulation of GnRH release. First, we found that unlike E2 benzoate (EB) administered systemically, a brief (20 min), direct infusion of EB into the median eminence (ME) of the hypothalamus in ovariectomized (OVX) female monkeys rapidly stimulated release of GnRH and E2 in the ME in a pulsatile manner. Second, this EB-induced pulsatile GnRH and E2 release was blocked by simultaneous infusion of the aromatase inhibitor, letrozole, indicating that stimulated release of E2 is of hypothalamic origin. Third, a prolonged EB infusion in the ME for 7 hours continuously stimulated release of GnRH and kisspeptin in OVX females, in contrast to their inhibition by s.c. EB injection. Fourth, the LH surge induced by s.c. injection of EB was 50% reduced in the presence of letrozole in OVX females. Finally, E2 levels in the ME of prepubertal female monkeys, in which GnRH and LH levels were low, were quite elevated, whereas in early pubertal females E2 levels in the ME decreased when GnRH and LH start to increase, suggesting neuroestradiol is an inhibitory substrate for low GnRH release during the juvenile period. Collectively, neuroestradiol in the hypothalamus appears to play an important role in regulation of GnRH release.

S27-01

Upstream regulators of GnRH in the control of puberty: Kisspeptin and beyond

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The hypothalamic-pituitary-gonadal (HPG) axis controls puberty and reproduction and is tightly regulated by a complex network of excitatory and inhibitory factors. Delayed or absent activation of the HPG axis results in delayed puberty or hypogonadotropic hypogonadism, whereas early activation results in central precocious puberty (CPP). In recent years, many genes have been identified in this complex network, providing insight into the regulation of GnRH secretion. These advances were heralded by the discovery of the kisspeptin system as a critical component for the activation of GnRH secretion, and followed by the discovery of the tachykinin, neurokinin B, and its role in pubertal activation, in turn, through regulation of kisspeptin secretion.? More recently, we identified loss-of-function mutations in the MKRN3 gene, encoding makorin ring finger protein 3, as an important cause of CPP. MKRN3 is an imprinted gene on chromosome 15q11.2 in the Prader-Willi Syndrome critical region, with expression only from the paternally inherited allele. MKRN3 is expressed at high levels in the mouse hypothalamus prepubertally and decreases prior to puberty onset, suggesting that it acts as a 'brake' on GnRH secretion. To date, MKRN3 is the first factor to be identified that likely has an inhibitory role on puberty in humans. The discovery of this new genetic link to early puberty will help to diagnose the cause of precocious puberty or to identify children at risk for developing precocious puberty, and the elucidation of the mechanisms by which MKRN3 regulates GnRH secretion will bring new insights into reproductive physiology.

S27-02

Using Genetic Approaches in a Rare Human Disease Model to Define the Neuroendocrine Control of Human Reproduction

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Experimental, clinical and epidemiological evidence support a role for prolactin (PRL) in various cancers including breast, prostate, endometrial, ovarian, gastrointestinal and hematological cancers (Goffin and Touraine, Expert Opinion in Therapeutic Targets 2015). In addition to circulating PRL, whose levels have been shown in some instances to correlate to cancer risk (breast, gastrointestinal, hematological), locally-produced PRL is also suspected to participate in tumorigenesis via autocrine/paracrine signaling in almost all of the tissues mentioned above. These findings have boosted academic and industrial groups to develop therapeutic compounds targeting the prolactin receptor (neutralizing antibodies, antagonists, small molecules). Despite encouraging pre-clinical results, we are still awaiting evidence that therapeutic inhibition of PRL signaling has clinical benefit in any cancer.

After a general introduction covering the general aspects of PRL pathobiology, I will focus my talk on the results recently obtained by our group regarding PRL actions in mouse prostate tumorigenesis. Strikingly, our studies have highlighted a role for PRL in regulating prostate stem/progenitor cells. First, we showed that over-activation of the PRL/Stat5 cascade led to the amplification of the prostate basal/stem cell compartment (Rouet et al, PNAS 2010). More recently, we showed that this pathway also led to the emergence of a so-far unidentified prostate cell population containing luminal progenitors (Sackmann Sala et al, Am. J. Pathol 2014). Of interest, not only are stem/progenitor cells believed to participate in prostate cancer initiation, but also to trigger recurrence, owing to their capacity to survive androgen-deprivation. Thus, the fact that PRL signaling leads to the amplification of prostate stem/progenitor cells provides a possible mechanism for the pro-tumorigenic role of PRL/Stat5 signaling in prostate cancer (Goffin et al, Nat Rev Urol 2011, Sackmann Sala et al, Adv. Exp. Med. Biol 2015).

Prolactin has been reported to regulate the pool of adult stem cells in

various other tissues, e.g. the breast and the brain (Sackmann Sala et al, Mol Endocrinol 2015). In the breast, extensive functional studies using genetically-modified mouse models have revealed that PRL can act in concert with progesterone to stimulate RANKL production which in turn acts on progenitor cells by paracrine mechanisms. Unfortunately, the mechanisms by which PRL regulates stem/progenitor cells in other tissues are poorly elucidated. This is in part linked to the fact that expression of the PRL receptor by these cells is not clearly established due to the lack of reliable antibodies (especially in the mouse). In the prostate, by using in vitro prostasphere assays, we were able to show that prostate basal/stem cells were insensitive to PRL stimulation (Sackmann Sala et al, Gen & Comp Endocrinol 2015). These data were confirmed by RT-qPCR experiments showing undetectable levels of PRL receptor expression in basal/stem cells enriched by cell sorting. Similarly, preliminary studies suggest that receptor levels are quite low for the recently discovered luminal progenitor population. Together, these data suggest that, as in the breast, paracrine factors downstream of PRL/Stat5 signaling may be involved in regulating the pool of prostate stem/progenitor cells. The identification of those factors/pathways represents a major challenge and is one of our current research goals.

S27-03

MicroRNAs, GnRH release, and GnRH neuronal development

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It is known that a timely postnatal increase in GnRH expression is essential for sexual maturation and the normal hypothalamic-pituitary-gonadal (HPG) functioning; yet, the underlying molecular mechanisms have remained largely unexplored.
Here we show that a dramatic switch in miRNA expression patterns in infantile GnRH neurons inverts the balance between inductive and repressive signals, triggering increased hypothalamic GnRH expression and controlling the crucial transition from the early infantile phase, when its levels are low, to the GnRH-fuelled run-up to puberty. This switch operates during the infantile "critical period", lasting just a few days and corresponding to the first centrally-driven gonad-independent activation of the HPG axis and resulting surge in gonadotropin levels (on postnatal day 10-16 in mice). This phenomenon, known as "mini-puberty" in humans, is the first of three activational periods that primes the HPG axis for puberty and adult fertility, setting in motion, for example, the growth of the first wave of ovarian follicles that will ovulate at puberty in females and the development of the testes in males. We show that during this critical period, a switch in miRNA expression in turn flips a switch in a multilayered array of GnRH gene activators and repressors, permitting the sustained increase of the neurohormone required for subsequent sexual maturation. We found that two miRNA species act as the linchpins of this process: the miR-200/429 family, which is not only upregulated during this critical period but selectively enhanced in GnRH neurons, and miR-155, which appears to act on other hypothalamic cell types as well, and mediates, for example, the effects of a concomitant release of nitric oxide upstream of GnRH neurons.
We have identified several genes targeted directly or indirectly by miR-155 and miR-200/429, whose repression (e.g. Cebpb and Zeb1) or activation (e.g. Pou2f1 and Meis1, which are both targets for Zeb1) is required for normal increase of GnRH expression from "mini-puberty" on. Selectively blocking in the hypothalamus miR-200/429 binding onto the 3'UTR of Zeb1 transcript during the infantile period (between P7 and weaning) suppresses GnRH promoter activity at the cellular level and causes alterations in puberty onset. Interestingly, our data also suggest that the miRNA-gene micronetworks sustaining the postnatal increase in GnRH expression are also at work during adulthood, since blockade in the hypothalamus of miR-200/429/Zeb1 binding blunts estrous cyclicity in adult female mice. ?

S28-01

Prolactin and Cancer

Vincent Goffin

University Paris Descartes and Inserm U1151

Vincent Goffin graduated in Biology at the University of Liège (Belgium). He trained as a biochemist during his doctoral studies in Joseph Martial's laboratory at the University of Liège then as a molecular endocrinologist during his post-doctoral fellowship in Paul Kelly's laboratory at Inserm, Paris. His first paper published in 1992 in Molecular Endocrinology opened the road towards the identification of the residues involved in prolactin binding to its receptor. During the next fifteen years, he performed cutting-edge structure-function studies to elucidate the molecular bases of the prolactin-receptor interaction. Beyond their cognitive outcome, these studies also nourished i) the development of pure prolactin receptor antagonists that are currently in preclinical development for various indications in Oncology, and ii) the identification of the first gain-of-function mutation of the prolactin receptor in humans. Vincent Goffin has developed translational studies to address the role of prolactin signaling in various human diseases including hormone-dependent cancers. Currently, one of his main research interests relates to the regulation of prostate stem/progenitor cells by prolactin signaling in mouse models, which may provide a rationale for the oncogenic activity of this pathway in human prostate cancer. As a leader in the prolactin field, he also participates in multiple collaborative networks to explore the role of this hormonal system in many other pathophysiological contexts (e.g. skin, pituitary, pancreas, pain, osmoregulation, etc). He was chairman/founder of the inaugural FASEB Science Research Conference "The GH/PRL family in biology and diseases" held in 2012 in Colorado, and also acts as consultant for various companies on prolactin-related research programs.

Experimental, clinical and epidemiological evidence support a role for prolactin (PRL) in various cancers including breast, prostate, endometrial, ovarian, gastrointestinal and hematological cancers (Goffin and Touraine, Expert Opinion in Therapeutic Targets 2015). In addition to circulating PRL, whose levels have been shown in some instances to correlate to cancer risk (breast, gastrointestinal, hematological), locally-produced PRL is also suspected to participate in tumorigenesis via autocrine/paracrine signaling in almost all

of the tissues mentioned above. These findings have boosted academic and industrial groups to develop therapeutic compounds targeting the prolactin receptor (neutralizing antibodies, antagonists, small molecules). Despite encouraging pre-clinical results, we are still awaiting evidence that therapeutic inhibition of PRL signaling has clinical benefit in any cancer.

After a general introduction covering the general aspects of PRL pathobiology, I will focus my talk on the results recently obtained by our group regarding PRL actions in mouse prostate tumorigenesis. Strikingly, our studies have highlighted a role for PRL in regulating prostate stem/progenitor cells. First, we showed that over-activation of the PRL/Stat5 cascade led to the amplification of the prostate basal/stem cell compartment (Rouet et al, PNAS 2010). More recently, we showed that this pathway also led to the emergence of a so-far unidentified prostate cell population containing luminal progenitors (Sackmann Sala et al, Am. J. Pathol 2014). Of interest, not only are stem/progenitor cells believed to participate in prostate cancer initiation, but also to trigger recurrence, owing to their capacity to survive androgen-deprivation. Thus, the fact that PRL signaling leads to the amplification of prostate stem/progenitor cells provides a possible mechanism for the pro-tumorigenic role of PRL/Stat5 signaling in prostate cancer (Goffin et al, Nat Rev Urol 2011, Sackmann Sala et al, Adv. Exp. Med. Biol 2015).

Prolactin has been reported to regulate the pool of adult stem cells in various other tissues, e.g. the breast and the brain (Sackmann Sala et al, Mol Endocrinol 2015). In the breast, extensive functional studies using genetically-modified mouse models have revealed that PRL can act in concert with progesterone to stimulate RANKL production which in turn acts on progenitor cells by paracrine mechanisms. Unfortunately, the mechanisms by which PRL regulates stem/progenitor cells in other tissues are poorly elucidated. This is in part linked to the fact that expression of the PRL receptor by these cells is not clearly established due to the lack of reliable antibodies (especially in the mouse). In the prostate, by using in vitro prostasphere assays, we were able to show that prostate basal/stem cells were insensitive to PRL stimulation (Sackmann Sala et al, Gen & Comp Endocrinol 2015). These data were confirmed by RT-qPCR experiments showing undetectable levels of PRL receptor expression in basal/stem cells enriched by cell sorting. Similarly, preliminary studies suggest that receptor levels are quite low for the recently discovered luminal progenitor population. Together, these data suggest that, as in the breast, paracrine factors downstream of PRL/Stat5 signaling may be involved in regulating the pool of prostate stem/progenitor cells. The identification of those factors/pathways represents a major challenge and is one of our current research goals.

S28-02

Prolactinomas and MEN1

Marta Heckenast Korbonits

Barts and the London School of Medicine

Multiple Endocrine Neoplasia type 1 is an autosomal dominant condition with over 90% overall penetrance by the age of 50. The pituitary component has a penetrance of 46% in females and 30% in males. Pituitary adenomas can present from childhood to 70s; the current guidance document suggest screening from the age of 5 years in carrier subjects. Pituitary adenomas can be the first presentation of the syndrome in 15-20% of the cases. There is strong intrafamilial heritability of pituitary adenomas of 64%, suggesting higher chance of this tumour type in carrier family members of an MEN1 patient with pituitary adenoma. While some studies found predominantly prolactinomas, a large surgical series and a recent prospective screening study found no tumour type predominance. Adenomas are more often plurihormonal, can be multiple, are larger and behave more aggressively, especially in boys, although no significantly elevated Ki67 can be found. Responsiveness to cabergoline has been reported as normal or poor. While somatotroph adenomas are well described in MEN1 patients, acromegaly or acromegalic gigantism can also be due to a GHRH-secreting neuroendocrine tumour, usually from a pancreatic source. MEN1 is a tumour suppressor gene located on 11q13 and loss of heterozygosity due to deletion of the wild-type copy of the gene is the most common "2nd hit" mechanism, although the presence of a second single-nucleotide mutation or overexpression of an inhibitory microRNA is also a possibility. Patients with young onset prolactinomas have 14% chance to harbor a mutation in either the AIP or in the MEN1 gene, both located at 11q13. Loss of chromosome 11 in sporadic prolactinomas is associated with more aggressive behaviour.

Menin has several functions in transcriptional regulation, genome stability, cell cycle control, apoptosis and epigenetic regulation. Menin influences transcription regulation via JunD, NF-kB, pem, SIN3A, HDAC, Smad1, Smad3, Smad5, Runx2, mixed lineage leukemia protein (MLL) and oestrogen receptor-α. Menin activates the transcription of CDKN1B (encoding p27) and CDKN1C (encoding p18) by recruiting the histone methyltransferase MLL protein to the promoters of these genes. CDKN1B and CDKN1C are predominantly expressed in endocrine organs, which can explain, at least in part, the selectivity of MEN1 tumorigenesis. Menin interacts with activin in normal pituitary, negatively regulating cell proliferation and secretion of prolactin. Additionally, menin act as a repressor of telomerase activity through its interaction with the human telomerase reverse transcriptase and can increase or decrease gene expression by epigenetic regulation via histone methylation or acetylation.

MEN4 is a recently established entity describing patients with multiple endocrine neoplasia due to mutation in CDKN1B. These patients typically have somatotroph adenomas, but prolactinomas and non-functioning pituitary adenomas have also been described. The affected organ spectrum is slightly different from classical MEN1: while primary hyperparathyroidism is present in
all reported MEN4 cases, pancreatic neuroendocrine tumours, uterine neoplasms, adrenocortical and thyroid tumours as well as meningiomas have all been described. A few MEN1-like syndrome patients cases have also been described with mutation in other cell cycle inhibitors: a mutation in CDKN1A (coding p21) was described in two sisters with a MEN1-like syndrome of primary hyperparathyroidism and macroprolactinoma. Mutations in CDKN2B (p15) and CDKN2C (p18) have also been detected in the context of multiple endocrine neoplasia, but these cases have?not included pituitary tumours as part of the syndrome.

In summary, MEN1 is an endocrine tumour predisposition syndrome with significant percentage of the carriers affected by pituitary disease. Hormonal and imaging screening might help to avoid severe complications of tumour growth and hormonal abnormalities.

S28-03

Treatment of prolactinomas: Whats new?

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Focused on reproductive endocrinology research and clinical practice more than 20 years, published more than 100 papers in medical science and participated in writing more than ten medical textbooks. He is expert in the diagnosis and treatment of disorders of sex differentiation.

Prolactinomas are among the most frequently occurring pituitary adenomas. In women, it presented with amenorrhea/oligomenorreha, anovulation and galactorrhea, whereas in men, it may manifest as diminished libido and erectile dysfunction. Macroprolactinomas can also present with symptoms and signs of mass effect of the tumor, such as headaches and visual field defects.
Most patients respond favourably to medical therapy with dopaminergic drugs leading to normoprolactinaemia, recovery of hypogonadism and regression of adenoma size. But when dopamine agonist treatment has been unsuccessful in lowering the serum prolactin concentration or size of the macroadenoma, and symptoms or signs due to hyperprolactinemia or adenoma size persist during treatment, transsphenoidal surgery is suggested. Dopamine agonist withdrawal may be safely undertaken after two years in patients who have achieved normoprolactinemia and significant tumor volume reduction. But recurrence after withdrawal may occur, long-term surveillance is needed.

S29-01

Epigenetics in metabolic kidney disease

Hiroshi Itoh

Keio University School of Medicine

In several clinical trials, "memory phenomenon" or "legacy effect" has been proposed by the evidence to show that after the cessation of the study, the superiority of one treatment persists. Follow-up of UKPDS revealed that past intensive glucose control in type 2 diabetes resulted in persistent reduction of cardiovascular events in the follow up period. In hypertension and its renal/vascular complications, we reported that "memory phenomenon" was observed in hypertensive experimental animals (JASN 2006, Hypertension 2009, Kid Int 2011). TROPHY study demonstrated that transient renin-angiotensin system (RAS) inhibition in the stage of prehypertension reduced the risk of transition from prehypertension to hypertension. We demonstrated that the alteration of clinical course of hypertension was possible by inhibiting RAS transiently (STAR CAST study) (Am J Hypertens 2013).
We recently reported that persistent "hypertensive" phenotype is acquired by transient high salt intake in hypertensive rats ("salt memory")(Hypertension 2014). We further demonstrated that transplanting the kidney of hypertensive rats with "salt memory" to normotensive animals resulted in the development of hypertension. The result indicated that the kidney contains "salt memory." The cardio-metabolic memory can "reside" in the organ, and we call it as "organ memory". "Salt memory" for hypertension is "erased" by the transient combination treatment of a calcium channel blocker and an angiotensin receptor blocker.
One of the significant elements responsible for "organ memory" is epigenetic gene regulation. We reported that epigenetic changes occurred in human kidneys of glomerulonephritis, including diabetic nephropathy. We reported that decrease of Sirt1, NAD-dependent deacetylase, in proximal renal tubules is the first trigger for diabetic nephropathy under epigenetic regulation (Nat Med 2013). We also demonstrated that the expression of the transcription factor, KLF4 was reduced in podocytes in diabetic and other glomerular diseases. The reduced expression of KLF4 in podocytes leads to increased methylation level of nephrin promoter, decreases nephrin expression and causes proteinuria (J Clin Invest 2014). We further reported that angiotensin II, the crucial mediator for diabetic nephropathy, suppressed KLF4 expression to modulate long-term epigenetic status of nephrin gene (Kid Int 2015).
Thus, blockade of RAS at the appropriate time can modulate "organ memory" to exert long-standing efficient suppression of occurrence and progression of diabetes/hypertension and their complications.

S29-02

Insulin Pump therapy and cardiovascular mortality

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I will in this talk give you a brief overview of research about insulin pumps and highlight recent advances in this field. After this I will tell you how insulin pumps are associated with cardiovascular mortality.
Objective To investigate the long-term effects of insulin pump therapy on cardiovascular diseases and mortality in people with type 1 diabetes.
Design Observational study.
Setting Swedish National Diabetes Register, Sweden 2005-12 linked to other population-based registers by means of personal-identity numbers unique for each Swedish citizen.
Participants 18 168 people with type 1 diabetes, 2441 using insulin pump therapy and 15 727 using multiple daily insulin injections.
Main outcome measures Cox regression analysis was used to estimate hazard ratios for the outcomes, adjusted for propensity scores including clinical characteristics, risk factors for cardiovascular disease, treatments, and previous diseases.
Results Follow-up was a mean of 6.8 years until December 2012, with 114 135 person years observed. With multiple daily injections as reference, the adjusted hazard ratios for insulin pump treatment were significantly lower: 0.55 (95% confidence interval 0.36 to 0.83) for fatal coronary heart disease, 0.58 (0.40 to 0.85) for fatal cardiovascular disease (coronary heart disease or stroke), and 0.73 (0.58 to 0.92)

for all-cause mortality. Hazard ratios were lower, but not statistically significantly so, for fatal or non-fatal coronary heart disease and fatal or non-fatal cardiovascular disease. Unadjusted absolute differences were 3.0 events of fatal coronary heart disease per 1000 person years; corresponding figures were 3.3 for fatal cardiovascular disease and 5.7 for all-cause mortality. When lower body mass index and previous cardiovascular diseases were excluded, results of subgroup analyses were similar to the results from complete data. A sensitivity analysis of unmeasured confounders in all individuals showed that an unmeasured confounders with hazard ratio of 1.3 would have to be present in >80% of the individuals treated with multiple daily injections versus not presence in those treated with pump therapy to invalidate the significantly lower hazard ratios for fatal cardiovascular disease. Data on patient education and frequency of blood glucose monitoring were missing, which might have influenced the observed association.

Conclusion This is the first large study from a population based setting that documents the relation between insulin pump treatment and cardiovascular mortality. We studied individuals with type 1 diabetes during a mean follow-up period of 6.8 years. Among 2441 of those treated with insulin pump therapy and 15 727 treated with multiple daily injections, insulin pump treatment was associated with a reduction of 45% for fatal coronary heart disease, 42% for fatal cardiovascular disease, and 27% for all-cause mortality. We evaluated the patient who used insulin pump therapy and do not know if the observed effect is attributable to continuous infusion of insulin or that some, if not all, of the effect is attributable to intensified glucose monitoring, increased motivation to control blood glucose, or a better knowledge about having diabetes type..

S29-03

Rising tide of early onset diabetes in Asia — Clinical pathophysiological and etiological characteristics and management challenges

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Former president of Chinese Diabetes Society
Vice President of China Stroke Society
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Chief editor of the Chinese Journal of Diabetes and a member of editorial board of Journal of Diabetes, Diabetes Research and Clinical Practice, Metabolism, Diabetes Technology & Therapeutics, Metabolism, International Journal of Diabetes
Member of IDF-WPR diabetes policy Group and a World Health Organization Consultant on the Definition, Diagnosis and Classification of Diabetes Mellitus

S30-01

Acromegaly registry, the Taiwanise experience

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S30-02

Acromegaly registry, lessons learned in Germany

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S31-01

3, 5-Diiodothyronine treatment: Risk an benefit

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Recent data report the beneficial effects of 3,5-diiodothyronine (3,5-T2) in preventing and treating liver steatosis that develops in animals fed a high fat diet. These interesting results prompted us to evaluate whether the chronic administration of 3,5-T2 could interfere with the pituitary-thyroid axis. Daily 3,5-T2 administration for ninety days to adult male Wistar rats led to a reduction in body mass gain and retroperitoneal fat compartment, accompanied by higher resting metabolic rate. In accordance to previous data showing that 3,5-T2 exerts important

metabolic effects, we have found a significant increase in oxygen consumption of rats treated with 50 ?g of 3,5-T2/100 g b.w. for 90 days. It is important to note that these animals had significantly lower serum T4 and T3 levels, which are the main regulators of energy metabolism. Thus, 3,5-T2 itself functions as a chronic stimulator of resting metabolic rate, increasing oxygen consumption just like T3 does. Decreased body mass gain in 3,5-T2-treated rats was not dose-dependent, and a maximal effect was already obtained with 25 ?g of 3,5-T2/100 g b.w., however, one could speculate that the decrease in serum T4 and T3 might in some way compensate for the increase in the dose of T2. Besides the beneficial effects of 3,5-T2 on body mass gain and adiposity, aged rats treated with 3,5-T2 had an improvement in the glucose tolerance test by more than 10%, when compared to control animals. This finding suggests that 3,5-T2 may increase insulin responsiveness, either directly or due to the decreased adiposity seen in the treated animals. These results are in accordance with the fact that 3,5-T2 was shown to prevent insulin resistance in skeletal muscle of rats fed a high-fat diet, increasing GLUT4 protein expression and insulin-induced Akt phosphorylation. Regardless of reduced serum T4 and T3, TSH was significantly lower in 3,5-T2 treated animals. Other authors had previously shown that 3,5-T2 reduces TSH secretion by the rat pituitary fragments stimulated by TRH, and also found a reduction in serum T4 levels after 90 days of treatment with 25 ?g of 3,5-T2/100 g b.w., what is in accordance with the results obtained by our group. The thyroid hormone receptor (TR) beta is the main mediator of thyroid hormone negative feedback, and TRbeta 2 binds 3,5-T2 more avidly than the other TR isoforms, which could well explain the effectiveness of 3,5-T2 in suppressing TSH secretion. Based on our results, we cannot explain why serum thyroid hormones are already decreased with the lower dose of 25 ?g/ 100 g b.w. of 3,5-T2, while serum TSH levels is in the normal range, suggesting that this hormone could be less bioactive in T2 treated animals. In the thyroid gland, we found a reduction in the thyroid D1, NIS and TPO activities, as well as their respective mRNA levels. Iodide uptake is a fundamental step and TPO is the key enzyme of thyroid hormone biosynthesis, so the decreased serum T4 levels is at least in part secondary to the decreased NIS function and TPO activity. TSH receptor protein and mRNA levels were increased in the thyroid of 3,5-T2-treated rats, probably due to the reduced serum TSH levels, which is a negative regulator of its own receptor. Besides the central regulation of thyroid-responsive genes, hepatic and kidney D1 activities were significantly increased in rats treated with 3,5-T2 despite significantly reduced serum T3 levels. Since T3 is the main stimulator of hepatic and kidney D1 activities through genomic actions, our results reinforce the idea of a T3-like genomic effect of 3,5-T2 on D1 regulation, rather than a non-genomic action. The regulation of D1 gene by T3 is mediated by the TRbeta isoform, since T3 induction of hepatic and renal D1 is severely blunted in TRbeta1-null mice, but is normal in TRalpha1-null mice. Thus, confirming that 3,5-T2 binds and activates TRbeta. On the other hand, D2 activity was increased in both hypothalamus and pituitary of rats treated with 3,5-T2, despite the thyromimetic effects of 3,5-T2. Since T4 levels are reduced in 3,5-T2-treated rats, this could explain the increment of D2 activity in these animals. Altogether, our results show that 3,5-T2 significantly down regulates thyroid function. In conclusion, chronic 3,5-T2 administration reduced body mass gain and retroperitoneal fat compartment and increased resting metabolic rate, regardless of decreased serum thyroid hormone levels, besides improving insulin responsiveness during aging in ad libitum fed male Wistar rats. The reduction in thyroid hormone levels seem to be secondary to the decreased TSH action and secretion, which lead to reduced NIS, thyroid D1 and TPO activities and expression. These data support the idea that exogenous 3,5-T2 leads to central hypothyroidism. Thus, future studies on the possible deleterious effects of hypothyroidism in tissues where 3,5-T2 might not act as a thyromimetic agent is of great importance. Financial Support: CNPq, CAPES, FAPERJ.

S31-02

Biosynthesis and action of thyronamines

Carolin Hoefig

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Thyronamines (3-T1AM, T0AM) are endogenous compounds probably derived from T4 or its intermediate metabolites previously detected in vivo. Evidence has been presented that combined activities of deiodinases and ornithine decarboxylase generate 3-T1AM in vitro in a mouse intestinal sac model and after incubation with human recombinant ornithine decarboxylase. Alternatively, 3-T1AM might directly be formed by the thyroid gland and secreted into the blood. 3-T1AM and T0AM concentrations have been determined by liquid chromatography–tandem mass spectrometry analysis in tissues of several animals, rodent and human serum. However, large variations of 3-T1AM serum concentrations in humans were reported by different groups compared to immunoassay data based on a monoclonal antibody. These differences might be caused by strong binding of the highly hydrophobic 3-T1AM to apolipoprotein B100. Pharmacological administration of 3-T1AM by various routes results in dose-dependent reversible effects on body temperature, cardiac function, energy metabolism and neurological functions such as pain sensation, learning behavior and memory. The physiological relevance of these actions is unclear, but some of them, particularly the metabolic and neurological ones, occur at tissue concentrations close to the estimated endogenous concentrations. Some of the central nervous actions ascribed to 3-T1AM might be exerted by its metabolites T0AM or TA1. This talk will summarize current insights and open questions of 3-T1AM research topics.

S32-01

FGF23, bone and mineral metabolism

Seiji Fukumoto

Tokushima University

FGF23 is a hormone that decreases serum phosphate by inhibiting proximal tubular phosphate reabsorption and intestinal phosphate absorption through reducing 1,25-dihyroxybitamin D level. Excessive actions of FGF23 result in several kinds of hypophosphatemic diseases including tumor-induced osteomalacia and X-linked hypophosphatemic rickets (XLH) with impaired proximal tubular phosphate reabsorption. On the contrary, deficient actions of FGF23 cause hyperphosphatemic familial tumoral calcinosis characterized by enhanced tubular phosphate reabsorption and high 1,25-dihydrox-

yvitamin D. XLH is the most prevalent cause of genetic hypophosphatemic rickets and caused by mutations in phosphate-regulating gene with homologies to endopeptidases on the X chromosome (PHEX). While phosphate and active vitamin D have been used for patients with XLH, these medications are known to be associated with several adverse events such as hypercalciuria, secondary-tertiary hyperparathyroidism and diarrhea. Now that it was shown that excessive actions of FGF23 cause XLH, several methods that inhibit FGF23 actions have been considered to be possible new therapeutic measures for XLH. We have examined effects of anti-FGF23 antibodies in Hyp mice. Hyp mouse is a murine homologue of XLH and was shown to have a mutation in Phex gene. Anti-FGF23 antibodies corrected several phenotypes of Hyp mice such as hypophosphatemia, impaired phosphate reabsorption, disorganized growth plate, increased osteoid and reduced muscle power. Based on these preclinical results, effects of humanized anti-FGF23 antibody on patients with XLH have been tested in clinical trials. In this symposium, I would like to discuss about physiological and pathophysiological roles of FGF23.

S32-02

Tumor induced osteomalacia

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Dr.Xia is interested in bone and mineral disease. He did the study on epidemiological trends of osteoporosis and osteoporotic fracture in China. He conducted many new agents evaluation on osteoporosis in clinical trials. To better understand the pathophysiology of osteoporosis, He carried out some genetic studies in Chinese osteoporotic populations. His research also focused on other metabolic diseases, such as the rickets and osteomalacia, especially on hypophosphatemic rickets, tumor induced osteomalacia, vitamin D deficient rickets and vitamin D dependent rickets. Hypoparathyroidism and hyperparathyroidism are also involved in his research fields. As a co-editor-in-chief, he conducted "The Chinese Guidline of Primary Hyperparathyroidism" in 2014. As author or Co-author, he has published over 200 scientific papers, including more than 60 SCI papers

Tumor-induced osteomalacia (TIO), which is usually associated with benign mesenchymal neoplasms, is a kind of metabolic bone disease characterized by hypophosphatemia, low serum 1,25-dihydroxyvitamin D concentrations and bone demineralization. The clinical and biochemical manifestations of TIO are similar to those of patients with autosomal-dominant hypophosphatemic rickets (ADHR), X-linked hypophosphatemic rickets (ARHR). The pathophysiology of TIO is the overproduction of fibroblast growth factor 23(FGF23) from tumor which suppress renal brush border membrane sodium-dependent phosphate transporter and reduce the activity of renal 1α-hydroxylase causing renal phosphate wasting and hypophosphatemia. The clinical manifestations often include bone pain, muscle weakness and skeletal deformities. TIO often manifests itself as nonspecific hypophosphatemia so that misdiagnosis and missed diagnosis often occur. Because of the small size, slow growth rate, wide distribution and nonspecific imaging manifestations, the localization of the responsible tumors is challenging. Fortunately, the employment of octreotide scintigraphy increase the detection rate of TIO greatly. And we successfully use the method to locate tumors in Peking Union Medical College Hospital. The most common cause of TIO is phosphaturic mesenchymal tumor (PMT) which is of bone (50%) or soft tissue (50%) origins. The casuative tumors are more frequently located in lower extremities, craniomaxillofical (mandile and maxilla, nasal sinus) and thorax region. Histopathologically, PMTs are composed of spindle-shaped or stellate cells with low nuclear grade embedded in a mesenchymal myxoid with "grungy" calcification. Bone-like structure and cartilage-like tissue is a frequent finding and the tumors are rich in prominent vascularity notably. To date, however, the genetic mechanisms underlying the pathogenesis of PMT remain obscure. Recent study demonstrate that FN1-FGFR1 fusion gene play an important role in tumorigenesis. And 20-60% FN1-FGFR1 fusion gene was identified in PMT. Complete surgical resection of causative tumors is the definitive treatment of TIO. After tumor resection, FGF23 level decreased, serum phosphorus level normalized and symptoms relieved. For patients without tumor complete resection or fail to localization of the tumors, medical therapy consisting of phosphorus supplementation and calcitriol is essential. In addition, the recently developed FGF23 antibody has the potential to normalize serum phosphorus level and relieve osteomalacia.

S33-01

Guildelines for the treatments of hypoparathyrodism in adults

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Recent studies have revealed hypoparathyroidism to be a disease associated with an increased risk of a number of co-morbidities including seizures, renal diseases, and infections as well as an impaired muscle function and quality of life. In the summer of 2015, the first international guideline on treatment of hypoparathyroidism in the adults was published by the European Society of Endocrinology. The guideline is based on a systematic literature search for which available evidence was synthesized in order to assess: what is the best treatment for adult patients with chronic HypoPT? The Guideline suggest to treat patients with active vitamin D analogues (alfacalcidol or calcitriol) and calcium supplements in order to maintain serum calcium levels in the lower part or slightly below the lower limit of the reference range (target range) with patients being free of symptoms or signs of hypocalcaemia. Additional goals of treatment are to keep 24-h urinary

calcium excretion within the sex-specific reference range, to avoid hyperphosphatemia, and to maintain the serum calcium–phosphate product below 4.4 $mmol^2/L^2$ (55 mg^2/dL^2). Patients should also have serum magnesium levels within the reference range and an adequate vitamin D status. The clinical importance of archiving these goals is, however, only poorly documented. Only sparse data exist on whether risk of complications is reduced in response to optimization of treatment. It is therefore of major importance that treatment is personalized with focus on the overall well-being and quality of life of patients. Aims to archive the biochemical targets should not impede the well-being of patients. In the future, replacement therapy with parathyroid hormone may become an alternative to conventional treatment as studies have suggested an improved QoL with a reduction in urinary calcium and serum phosphate level in response to PTH treatment.

S33-02

What's new in primary hyperparathyroidism?

John Bilezikian

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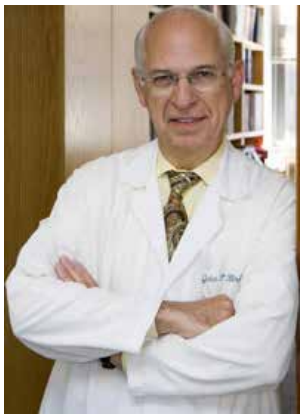

The past several decades have witnessed a plethora of observations regarding the various clinical and subclinical manifestations of primary hyperparathyroidism (PHPT).They vary greatly from asymptomatic to symptomatic, and from normocalcemic to hypercalcemic, its classical biochemical trademark. The skeletal manifestations range from overt fractures to selective reduction in bone density. Recent observations have helped not only to confirm an increased risk of fractures in PHPT but also the microarchitectural abnormalities that help to account for that increase in fracture risk. The predilection of parathyroid hormone to be catabolic for bone when present in excess and continuously in the circulation has given rise to a more proactive approach to identifying individuals at risk for skeletal disease. The other major target organ for complications of PHPT is the kidneys. While overt renal stones are still the most common clinical complication of PHPT, recent observations have indicated that nephrolithiasis and nephrocalcinosis are more commonly appreciated than before. These new observations have led to a more proactive approach to identifying individuals with PHPT at risk for renal complications. The relationship of vitamin D insufficiency to the target organ manifestations of PHPT has helped to account for why there is such global variability in the disease. Vitamin D deficiency appears to provide further stimulation to poorly controlled PTH secretory dynamics in PHPT, which leads, in turn, to more active disease. One of the more vexing aspects of PHPT is the so-called neurocognitive features of the disease. Patients complain often of weakness, easy fatigability, difficulty concentrating, and generally reduced quality of life. What has made this set of complaints particularly problematical is the point that they are also found in a variety of endocrine and other chronic disorders. Moreover, it is not clear or consistently observed that such complains remit after successful parathyroid surgery. It has been difficult to conduct carefully controlled clinical studies to investigate this conundrum. Advances in our understanding of the clinical manifestations of PHPT, along with greater insights into its natural history with or without parathyroid surgery, have all given rise to a new set of guidelines to the management of this disorder. The presentation will summarize these new advances as well as the guidelines for management of PHPT.

S34-01

Control of human trophoblast invasion by activin

Peter CK Leung

University of British Colombia

Peter C.K. Leung, PhD, FCAHS, FRSC

Dr. Leung is Professor of Obstetrics and Gynaecology, and former Associate Dean in the Faculty of Medicine at the University of British Columbia. He received his PhD degree from the University of Western Ontario, and postdoctoral training at the University of California at Los Angeles and Laval University. To date, Dr. Leung has published over 350 papers and supervised more than 100 research trainees. He has received numerous honours and awards, including a Distinguished Scholar Award from the Michael Smith Foundation for Health Research, President of the Canadian Fertility and Andrology Society. Dr. Leung is a Fellow of the Royal Society of Canada, and Fellow of the Canadian Academy of Health Sciences.

S34-02

Molecular and hormonal regulation of embryo distribution and location during early pregnancy

Enkui Duan*, Ying Zhang

State Key Lab of Stem Cell and Reproductive Biology, Institute of Zoology, Chinese Academy of Science

Dr. DUAN received a PhD in Embryo Engineering from Northwest Agricultural University, China and then worked as a visiting scientists for research on reproductive immunology and embryo implantation at University of New England, Australia (1995-1996) and at University of Kansas Medical Center, United States (1998). Dr. Duan is a Professor in State Key Lab of Stem Cell and Reproductive Biology, IOZ. He had been a vice chair of Expert Committee for Developmental and Reproductive Program in The Minister of Science and Technology (MOST) from 2006.10-2014.06. He is also a member of Journal Editorial Board in J Biol Chem, Endocrinology as well as an associate editor in Current Zoology. He received a National Award for Science and Technology progress in Population and Reproductive Science, First prize (2011) and the 7th "China Population Prize in Science and Technology" for his great contribution in promoting basic and translational reproductive research in China (2011). Dr. DUAN's research focuses on embryo implantation, skin-derived stem cells and sperm tsRNAs.

The distribution and location of intrauterine embryo site(s) show

conserved patterns in most mammalian species (in humans the embryo tends to implant in the uterine fundus while in rodents, embryos evenly distribute along the uterine horns). These long-term evolved embryo location pattern bears great significance for disruption of these pattern have adverse effects on pregnancy outcome. In the past ten years, we used different mouse models to study hormonal and molecular regulation of embryo distribution. We revealed β2-adrenoceptor regulated uterine peristalsis is essential for intrauterine embryo location as well as embryo implantation. Then we identified two water channel (aqp5 and aqp8) which regulated uterine fluid homeostasis is responsible for embryo distribution and location, especially in hyper-estrogen mice. We also found a transducer of Notch signaling, Rbpj is required for embryonic-uterine orientation via Notch independent pathway by interacting with ERα. These work will provide evidences for further understanding of embryo distribution and location in early pregnancy, which will open opportunities for the development of therapeutic approaches for IVF-ET treatment.

S35-01

GHRH throughout life

AJ van der Lely

Erasmus University MC, Rotterdam, The Netherlands

GHRH is released from neurosecretory nerve terminals of arcuate neurons, and is carried by the hypothalamo-hypophyseal portal system to the anterior pituitary gland, where it stimulates growth hormone (GH) secretion by stimulating the growth hormone-releasing hormone receptor. GHRH is released in a pulsatile manner, stimulating similar pulsatile release of GH. In addition, GHRH also promotes slow-wave sleep directly. It's critical role became apparent, when the group of Gerry Baumann described the dwarfism of Sindh.

It demonstrates the absolute requirement of GHRH signaling for pituitary GH secretion and postnatal growth in humans, and its relatively minor (but discernible) biological importance in extrapituitary sites. But already GHRH seems to play a role in the crosstalk between the fetus and the mother as the identification of TRH, CRF, LHRH and GHRH in human suggests that the placenta is also contributing to the development of fetuses. In acromegaly, GHRH has regained the interest of the scientific field after the description of the X-linked acrogigantism (X-LAG). X-LAG is a new syndrome of pituitary gigantism, caused by microduplications on chromosome Xq26.3, encompassing the gene GPR101, which is highly upregulated in pituitary tumors.

There is a widespread presence of GHRH-R in hyperplastic and adenomatous tissue in X-LAG subjects. Such a presence of GHRH-R would seem to be a pre-requisite for a GHRH-driven disease, particularly as local pituitary GHRH sources cannot be found. In sleep, secretion of GH has a marked non-rapid-eye-movements-sleep (NREMS)-associated component suggesting an activation of GHRH during deep NREMS. GHRH promotes NREMS after various routes of administration in every species tested (rat, rabbit, mouse, human). Acute inhibition of endogenous GHRH causes decreases in NREMS. Also, activation of the GHRH inhibiting negative feedback mechanisms within the somatotropic system results in inhibition of NREMS. Moreover, hypothalamic GHRH displays diurnal and sleep-related variations. Interestingly, GH and IGF-1 are not involved in the NREMS promoting activity of GHRH. Finally, in HIV-related lipodystrophy, tesamorelin, a GHRH(1-44) analogue, significantly decreases visceral adiposity and concomitant dyslipidemia, without worsening overall glucose tolerance, in HIV-infected patients. In conclusion, GHRH is a bit a forgotten hormone.

However, it has intriguing properties and is on it's way back. It's again one of the suspects in the causes of acromegaly. It has a role in body composition and sleep patterns and, therefore, it needs more attention as we might be in for more surprises.

S35-02

Growth hormone throughout life

Jens Otto Lunde Jorgensen

Aarhus University Hospital

S36-01

Growth hormone for short stature after cancer treatment

Xiaoping Luo

Tongji Hospital, Tongji Medical College of HUST

Dr. Xiaoping Luo is the Professor and Chairman of the Department of Pediatrics, Tongji Hospital, Director of the Center for the Diagnosis of Genetic Metabolic Diseases, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Dr. Luo is now the Vice President of the Chinese Pediatric Society (CPS), President of the Chinese Society of Pediatric Endocrinology and Metabolism (CSPEM). He is also the past president for the Asia Pacific Paediatric Endocrine Society (APPES), Executive Committee member of the Global Pediatric Endocrinology and Diabetes (GPED), Board of Directors for the Asian Society for Inherited Metabolic Diseases (ASIMD). His main interests are pediatric endocrinology and metabolism, and neonatal/perinatal medicine. Dr. Luo's research was funded by the National Natural Science Foundation of China, the Ministry of Health, the Ministry of Education, and the Ministry of Science and Technology of China, and the World Diabetes Foundation, etc. He has published 48 book chapters and over 320 peer reviewed articles, and served as editor or reviewer for 42 domestic and international medical journals.

Survival for childhood cancer has increased dramatically over the last 40 years with 5-year survival rates now approaching 80%. An increase in the number of survivors of childhood cancer has heightened the appreciation of the late complications caused by the disease and its treatment. Related adverse health outcomes include pulmonary, auditory, endocrine-reproductive, cardiac, and neurocognitive dysfunction, etc. The most common long-term sequelae

of therapy for childhood cancer were impaired reproductive capacity and abnormal growth. Growth hormone deficiency, delayed or precocious puberty and hypopituitarism can all occur in childhood cancer survivors, hypothalamic dysfunction being the most common abnormality seen after cranial irradiation. Nearly 40% of childhood brain cancer survivors were below the 10th percentile for height. The strongest risk factors for adult short stature were young age at diagnosis, radiation treatment involving the hypothalamic-pituitary axis (HPA), and brain surgery in the central brain district where the pituitary locates.
Childhood cancer survivors are commonly treated with GH for GH deficiency and other condition-related short stature that develop either as a result of primary malignancy or its treatment. Over the last 25 years, an overall improvement in final height has been achieved in children treated with GH for GHD after therapy for brain tumors. These improvements are attributable to refinements in GH dosing schedules, increased use of GnRH analogues for radiation-induced precocious puberty, and a reduced time interval between completion of irradiation and initiation of GH therapy.
The safety of using GH for treatment of short stature after cancer treatment is confirmed by multiple studies. There was no statistically significant increased overall risk of the occurrence of a CNS-second neoplasm (SN) ass

S36-02

Is growth hormone safe in cancer treated patients?

Ron Rosenfeld

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Concerns about the long-term safety of growth hormone (GH) therapy remain, despite the fact that it has been in use for 50 years. In particular, questions about potential cancer risk remain incompletely resolved. GH and, especially, insulin-like growth factor-I (IGF-I) are known mitogens and stimulate cell proliferation and inhibit apoptosis. Signal transducer and activation of transcription (STAT)-5 has been shown to be constitutively phosphorylated in cancer cells and has become the target of a number of anti-cancer therapies. The same is true for the IGF-I receptor. Several epidemiologic studies have suggested a link between elevated serum IGF-I concentrations and prostate, breast, colon and lung cancers. A variety of animal models of severe GH and/or IGF-I deficiency have indicated a reduced lifetime cancer risk. The cumulative effect of these factors and studies is to underline the importance of assessing GH safety.
Survivors of childhood cancer have been shown to be at risk for both tumor recurrence and, in some cases, development of secondary tumors. Since patients who have received cranial radiation to the hypothalamus are prone to develop GH deficiency, the possible role of GH therapy is tumor recurrence or development of secondary neoplasms is of particular concern. This has proven to be a difficult issue to resolve, as concomitant therapies, including radiation, alkylating agents and other chemotherapeutic drugs may also place the patient at risk. We will review past and ongoing studies of childhood cancer survivors in an effort to determine whether GH exposure is an independent risk factor for the development of recurrent or secondary neoplasms.

S36-03

Delayed effects of Cancer Treatment

Stephen Shalet

Delayed Impact of Cancer Treatment on Hypothalamic-Pituitary Function---The Road Ahead
S M Shalet, Emeritus Professor of Medicine, Christie Hospital, Manchester, United Kingdom

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The delayed impact of cancer treatment on childhood growth primarily refers to the impact of conventional radiotherapy (XRT) on the hypothalamic-pituitary axis (HPA). Deficiency of one or more anterior pituitary hormones may occur following therapeutic cranial XRT for primary brain tumours, tumours involving the HPA, nasopharyngeal tumours, tumours of the base of the skull, and solid tumours of the face and neck, as well as following prophylactic cranial XRT for acute lymphoblastic leukaemia (ALL) and total body XRT prior to bone marrow transplantation.
The extent and speed of onset of the hypopituitarism are dose-dependent. Thus after lower XRT doses, isolated growth hormone (GH) deficiency ensues, while higher XRT doses may produce panhypopituitarism. Similarly the higher the radiobiological dose to the HPA then the earlier the onset of pituitary hormone deficiency.
There is evidence that the hypothalamus is more radiosensitive than the pituitary and is damaged by lower doses of XRT. This observation has implications with respect to dynamic assessment of pituitary function following XRT; thus in the first 6 years after XRT to the HPA axis there may be discordant GH responses to an ITT (subnormal) versus Arginine plus GHRH (normal) reflecting hypothalamic damage but subsequently beyond 6 years the same individuals will show subnormal GH responses to both types of provocative tests reflecting both hypothalamic and pituitary dysfunction.
ACTH deficiency is less common than GH deficiency after cranial XRT but of greater consequence to the patient, and it may not appear until many years have elapsed post-XRT. Thus in the first 5 years after cranial XRT (18-24 Gy) for ALL, ACTH deficiency is rarely seen, however, ACTH deficiency has been reported in 38% of all such patents 20 years post-XRT.
XRT-induced hypopituitarism may not only be delayed by many years but it is also irreversible, with a significant impact on health in adult life if left untreated. There is good evidence that the impairment in quality of life in GH deficient adult survivors of childhood cancer responds favourably to GH replacement and yet at the same time insufficient numbers of these patients are offered GH replacement.
Therefore a regular annual screening programme to determine pituitary function is required in all survivors who received XRT that included the HPA. By 2010 one in 250 of the adult population was a long-term survivor of all childhood cancers and therefore the list of patients requiring screening is long and continually growing. More recently proton beam therapy has been introduced to replace

conventional external XRT for children with brain tumours. This modality of therapy spares healthy tissues outside the target volume. However the early report (Yock et al. Lancet Oncology 2016) of a Single Centre Phase 2 trial in 59 patients with a median follow-up of 7 years following treatment of medulloblastoma showed non-inferior 5 year progression-free survival compared with conventional XRT data and no cardiac, pulmonary or gastro-intestinal late effects. Nonetheless there was a cumulative incidence of 63% with endocrine deficits including 55% with GH deficiency. Thus there is much work ahead for the Endocrine Community, both paediatric and adult, if the health of this patient population is to remain optimal.

S37-01

Glucocorticoids, fat and bone

Mark Cooper

University of Sydney

Cushing's syndrome has dramatic effects on fat and bone resulting in central fat accumulation and osteoporosis. These adverse effects have traditionally been believed to be due to direct effects on adipocytes and osteoblasts (bone forming cells). The role of endogenous glucocorticoids in normal fat and bone metabolism (and the clinical states of obesity and osteoporosis) is less clear. Some studies have linked circulating cortisol levels to regional fat mass, osteoporosis and fracture risk, particularly with ageing, but results have not been consistent and the direction of causality of any associations has difficult to establish.

It is now clear that many of the effects of glucocorticoids are determined at a 'pre-receptor' level through expression and activity of glucocorticoid metabolising enzymes. The most well studied of these is the 11beta-hydroxysteroid dehydrogenase type 1 (11b-HSD1) enzyme which primarily converts inactive cortisone to active cortisol (and dehydrocorticosterone to corticosterone in rodents). 11b-HSD1 is highly expressed in adipocytes and osteoblasts in addition to other metabolically relevant tissues such as liver and muscle. Recent work suggests that 11b-HSD1 is an important determinant of adiposity and bone density both in response to glucocorticoid treatment and during normal ageing. Pharmacological inhibition of 11b-HSD1 activity has a modest weight reducing effect and protects against hepatic steatosis and transgenic global deletion of 11b-HSD1 in mice protects against diet induced fat accumulation.

Studies selectively targeting tissue glucocorticoid action are beginning to give insights about the mechanisms by which glucocorticoids exert their effects on fat and bone. Interestingly, blockade of cortisol action exclusively in osteoblasts protects mice against many of the adverse metabolic effects of glucocorticoids. This phenotype is partially recovered when the bone specific protein osteocalcin is expressed heterotopically. This suggests that glucocorticoid signalling in bone can have significant impacts on fat metabolism through bone derived factors. These mice also demonstrate protection against age related obesity indicating that physiological levels of glucocorticoids can impact on fat indirectly through their effects on bone. The extent to which these findings apply in humans and how effectively these findings can be utilised therapeutically is currently under investigation.

S37-02

Effect of tissue-specific glucocorticoid action on cardiovascular and metabolic disease

Brian Walker

Centre for Cardiovascular Science, University of Edinburgh, United Kingdom

Glucocorticoids are essential in mediating adaptive stress responses of metabolism, inflammation, and cardiovascular regulation. However, in Cushings syndrome, prolonged glucocorticoid excess becomes maladaptive, accelerating the risk factors and progression of atheromatous cardiovascular disease. Recent data from prospective cohort studies and genome wide association studies by the cortisol NETwork (CORNET) consortium suggest that, in the otherwise healthy population, higher plasma cortisol is a causative risk factor for metabolic syndrome and cardiovascular disease. These findings implicate activation of the hypothalamic-pituitary adrenal (HPA) axis as a key mechanism contributing to cardiovascular risk. In addition, however, there are complex tissue-specific mechanisms which determine intracellular glucocorticoid concentrations and glucocorticoid action. These mechanisms - operating in cardiometabolic target tissues for glucocorticoids such as adipose, liver and vascular wall - may lend themselves to therapeutic intervention to reduce cardiovascular risk and improve outcome of cardiovascular disease. Glucocorticoids are inactivated by several enzymes including 5α-reductases, and regenerated by 11β-HSD1. 11β-HSD1 is dysregulated in patients with cardiovascular risk factors. Inhibition of 11β-HSD1 lowers cortisol concentrations in tissues and induces modest improvements in glycaemic control and other cardiovascular risk factors amongst patients with type II diabetes. In addition, deletion or inhibition of 11βHSD1 improves recovery following myocardial infarction in mice, putatively by promoting angiogenesis following tissue ischaemia. Conversely, deletion or inhibition of 5α-reductase type 1 increases the risk of liver steatosis, insulin resistance and type II diabetes.

Glucocorticoids are trafficked across cell membranes by members of the ATP binding cassette (ABC) transporter family. De Kloet and colleagues have shown that ABCB1 exports cortisol, but not the less abundant endogenous glucocorticoid corticosterone, from the brain; this mechanism renders the brain more sensitive to corticosterone than to cortisol. We have documented recently that ABCC1 exports corticosterone but not cortisol from adipose tissue; this renders adipose tissue differentially sensitive to cortisol rather than corticosterone. As a result, relative deficiency of corticosterone may impair the negative feedback signal to the HPA axis, driving hypercortisolaemia which in turn may act disproportionately in adipose tissue, driving obesity and associated cardio metabolic risk. This may explain the association of obesity with genetic variation in CYP17A1, encoding the 17α-hydroxylase which determines corticosterone/cortisol balance. Moreover, it suggests that corticosterone may be a useful alternative to cortisol in glucocorticoid replacement therapy, especially when suppression of ACTH is desirable as in congenital adrenal hyperplasia, since corticosterone should achieve ACTH suppression at concentrations which are less likely to induce obesity than cortisol.

In summary, cortisol action is determined by an interplay between the HPA axis and local control of tissue cortisol. Dysregulation of either is plausibly implicated in cardiometabolic disease, and un-

derstanding tissue-specific control of glucocorticoid action provides opportunities for new therapies.

S37-03

The cardiomyocyte mineralocorticoid receptor as a mediator of cardiac fibrosis

Morag Young

Hudson Institute of Medical Research

Dr Morag Young is a leading authority on the role of steroid hormone signalling in cardiovascular disease. She completed a CJ Martin Postdoctoral Fellowship at the University of Texas Southwestern Medical Centre, United States and the Baker Institute of Medical Research and joined PHI in 2002 and established the Cardiovascular Endocrinology Laboratory in 2005.

Her work has redefined the role of the mineralocorticoid receptor (MR) in cardiac disease in particular and has brought about a major shift in the understanding of MR pathophysiology by identifying a fundamental role for the MR in the control of inflammation, heart disease and hypertension. Her work has been validated by several large clinical trials but the use of MR antagonists is limited by significant renal side effects (hyperkalaemia).

Dr Young received the Best Basic Research Paper published in Hypertension in 2009 from the American Heart Association for her work on identifying the role MR in macrophages and regulation of cardiac remodelling and blood pressure control. Ongoing studies have also identified unique roles for MR signalling in cardiomyocytes and endothelial cells in the regulation of cardiac inflammation, fibrosis and in the heart, the functional recovery to ischemia reperfusion injury. She has also contributed a series of studies identifying novel coregulator proteins for the MR, which demonstrated ligand and cell dependent activities. Dr Young's work has been supported by NHMRC of Australia, the National Heart Foundation as well as by Industry and philanthropic organisations.

S38-01

Gestational thyroid function and offspring brain development: clinical evidence on cognition and behavior

Tim Korevaar

Erasmus University Medical Center

S38-02

Impact of trace element status on pregnancy outcome

Zhongyan Shan

First Hospital; Chinese Medical University

Professor Zhongyan Shan, MD, PhD.
Education backgroud:

• Graduated from China Medical University, MD, PhD
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Academic Positions:
• Chief Director of Endocrinology Dept., The First Hospital of China Medical University
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• Standing Committee member of Chinese Endocrinologist Association
• Former President of Liaoning Diabetes Society
Research Interests, Thyroid Diseases during pregnancy

Iodine is the essential trace elements of the human body,which is the main raw material for the synthesis of thyroid hormones. If the iodine deficiency to some degreecan lead to low thyroid hormone levels in pregnancy, thus affects the fetal brain development andpregnancy outcome. Iodine deficiency in pregnancy as a chief cause of maternal hypothyroidism is under investigationby endocrinologists.However, we investigated the relationship betweenmaternal thyroid dysfunction and UIC in 7190 women inthe stages of early pregnancy in an iodine-sufficient region.We found the upper limit of iodine intake forearly pregnancy in iodine-sufficient regions should not exceedUIC 250 g/L, because this is associated with a significantly high risk of subclinical hypothyroidism andUICs that exceed 500 g/L is associated with a significantlyhigh risk of isolated hypothyroxinemia.Further investigation indicated that mild iodine deficiency in early pregnancy increased incidence of gestational diabetes and premature birth.Iodine intervention could reduce the incidence of gestational diabetes and premature birth.

Iron deficiency (ID) is the most prevalent of all micronutrientdeficiencies worldwide, which can impair thyroid hormone synthesis andmetabolism. It decreases plasma T4 and T3 concentrations by impairing two initial steps catalyzed by heme-dependentthyroid peroxidase (TPO) enzyme in thyroid hormonessynthesis. Pregnantwomen are highly vulnerable to ID. They have an increased demand for iron to expand their erythrocyte massand generate the iron supply to the growing fetus. Therefore, we investigated whether maternal ironnutrition deficiency can affect thyroid status of women inthe first trimester of pregnancy. We found a definite association between IDand isolated hypothyroxinemia in pregnant women duringthe first trimester. ID maybe a pathogenic factorfor isolated hypothyroxinemia, even in women during thefirst trimester of pregnancy.

S38-03

Management of anti thyroid drug therapy in pregnancy

Fereidoun Azizi

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Hyperthyroidism is one of the most common endocrine disorders

in pregnancy. Graves' disease is the most common cause of autoimmune hyperthyroidism among pregnant women, accounting for 0.1 to 1% (0.4% clinical and 0.6% subclinical) of all pregnancies. It may be diagnosed for the first time in pregnancy, may present as a recurrent episode in a woman with past history of hyperthyroidism, or in a women on antithyroid drugs (ATD). Less common, non autoimmune causes include multinodular goiter, toxic adenoma, and factitious hyperthyroidism. More frequent than Graves' disease as the cause of hyperthyroidism is the syndrome of gestational hyperthyroidism defined as "transient hyperthyroidism", limited to the first half of pregnancy and characterized by elevated FT4 and suppressed or undetectable serum TSH, in the absence of serum markers of thyroid autoimmunity.

The obstetrical and medical complications are directly related to control of hyperthyroidism and duration of the euthyroid state in pregnancy. Poor control of thyrotoxicosis is associated with miscarriages, pregnancy-induced hypertension, prematurity, low birth weight, intrauterine growth restriction, stillbirth, thyroid storm and maternal congestive heart failure. Antithyroid drugs are the preferred treatment for hyperthyroidism during pregnancy. They reduce both iodine organification and the coupling of monoiodothyrosine and diiodothyrosine, resulting in inhibition of thyroid hormone synthesis. Both methimazole (MMI) and propyltiouracil (PTU) cross the placenta and are equally effective in the treatment of hyperthyroidism. Side effects occur in a 3-10%, of patients taking thionamide drugs. The greatest concern in the use of ATD in pregnancy is related to its teratogenic effects. Exposure to MMI may produce several congenital malformations, mainly aplasia cutis and the "methimazole embryopathy" syndrome that includes choanal or esophageal atresia, omphalocele and omphalomesentric duct anomalies. These complications have rarely been reported with the use of PTU. However, other complications such as birth defects of the circulatory or urinary system and dysmorphic face may also occur with PTU. It has been recommended that the use of PTU be limited to the first trimester of pregnancy because of hepatotoxicity, which may occur at any time during PTU treatment, without warning. Considering the more severe birth defects associated with MMI, PTU is preferred in the first trimester. In women with hyperthyroidism planning pregnancy MMI should be replaced by PTU before pregnancy. Following the first trimester, PTU should be switched to methimazole. Equivalent doses of PTU to MMI are 10:1 to 15:1 (100 mg PTU= 7.5-10 mg MMI). The initial dose of ATDs depends on the severity of the symptoms and degree of hyperthyroxinemia. It is recommended that the use of ATD in early pregnancy should be limited and new ATDs with the fewer side effects be developed. Pregnant women taking ATDs, FT4 and TSH should be monitored every 2-6 weeks. The primary goal is a serum FT4 at or moderately above the normal range.

The combination of ATD plus levothyroxine is not recommended in the management of hyperthyroidism in pregnancy. Adrenergic beta blocking agents, such as propranolol 20-40 mg every 6-8 hours may be used for controlling hyper-metabolic symptoms. In the vast majority of cases the drug could be discontinued in 2 to 6 weeks. Long term treatment with propranolol has been associated with intrauterine growth restriction, fetal bradycardia and neonatal hypoglycemia. Thyroidectomy should be considered in cases of allergies to both ATDs, in women requiring large doses of ATDs and in the occasional patient who is not adherent to drug therapy. If surgery is indicated, the second trimester is the most optimal time. A determination of serum TRAb titers is mandatory at the time of surgery in order to assess the potential risk of fetal hyperthyroidism. Preparation with beta-blocking agents and a short course of potassium iodine solution (50-100 mg a day) are recommended. Serum TRAb should also be determined by 24-28 weeks gestation in all pregnant women with presence or history of hyperthyroidism, and a value over 3 times the upper limits of normal is an indication for close follow up of fetus and future neonate.

It is concluded that overt hypothyroidism is rather common during pregnancy, influencing the health of mother, fetus and the infant. Effective evidence based strategies for both detection and management should be developed for the benefit of both mother and child. At the present ATDs are the mainstay of treatment of hyperthyroidism in pregnancy. Careful attention to teratogenic effects, alongwith careful use of these drugs, to minimize their complications and to avoid both hypo- and hyperthyroidism could dramatically improve the pregnancy outcome and ensure health promotion of mother and infant.

S39-01

Small molecule drugs targeting TSH receptor

Gerd Krause

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S39-02

TSH and lipid metabolism

Jiajun Zhao

Shandong Provincial Hospital

1983 Prof. Dr. Jiajun Zhao graduated from department of. Medical Taishan MedicalCollege, Taian, P. R. China 1979.07-1983.07:1989 he became a graduate student in Shanghai Second Medical University, Shanghai, P. R. China. He is also tutorial teacher in Endocrinology for the postgraduate students of Shandong University. Dr. Zhaos research has focused on effects of thyroid diseases and type 2 diabetes on lipids, and has received more than 20 grants from China government, published a lots of scientific papers such as Journal of Clinical Endocrinology and Metabolism, Endocrinology, Hepatology, J Hepatology, Clinical Endocrinology, Endocrine, European Journal of Endocrinology, JAMA Prof. Zhao has published more than 300 papers in journals and holds 30 China patents, co-written 4 books. His main research field is in the chromatography-related research and the metabolomics applications in disease biomarker discovery, traditional Chinese medicines and food safety.

President, Shandong Diabetes Society, Elect-President, Chinese Endocrine Society

Jiajun Zhao, male, born in May 1961. In 1994, he graduated from Shanghai Second Medical University (Shanghai Jiaotong University now) as PhD in endocrine metabolic disease. Now he is Vice President of Provincial Hospital affiliated to Shandong University, Director of Institute of Endocrinology and Metabolic Diseases of Shandong Academy of Clinical Medicine and Director of Department of Endocrinology of Provincial Hospital Affiliated to Shandong University. He is also a professor of Shandong University, a doctoral supervisor and a postdoctoral mentor.

Elect-President of Chinese Society of Endocrinology, Chairman of Shandong Diabetes Society, and Vice Chairman of Shandong Endocrinology Society. Deputy Editor-in-Chief of Chinese Journal of Endocrinology, Editorial Board Member of Chinese Journal of Diabetes, Associate Editor-in-Chief of Diabetes Issue of the Inter-

national Medical BBS (electronic), Editor of The Lancet (Chinese version) and Nat Rev Endocrinol (Chinese version) , Associate Editor-in-Chief of JCEM (Chinese version) and Editorial Board Member of APS. Advanced Worker of the National Health System, Young and Middle-aged Expert with Outstanding Contribution of the Ministry of Health, National Excellent Scientific and Technical Worker, Medical Leading Talent of Shandong Province, and Expert of Mount Tai Climbing Scholar Program.
He has been engaged in clinical work and basic research on endocrine and metabolic diseases more than 30 years and attended annual conferences of The Endocrine Society, American Diabetes Association, European Association for the Study of Diabetes and American Thyroid Association as a member of the research to introduce the advances and progress of research and exchange experience with other experts annually. Many of his students received awards from the conferences.
He has published plenty of research papers, many of which are included in Hepatology, Endocrinology, Hum Mol Genet, JCEM and JCMM, etc.

Thyroid-stimulating hormone (TSH) is a kind of glycoprotein derived from anterior pituitary, acting on thyroid gland and regulating the synthesis and secretory of thyroid hormones. In recent years, TSH was found to play an important role in all major metabolic pathways, especially lipid metabolism.
Clinically, TSH was positively associated with serum lipid profiles independent of thyroid hormones. In patients with newly diagnosed coronary heart diseases, we found that compared with the euthyroid subjects, the prevalence of hypercholesterolemia was significantly higher in the patients with subclinical hypothyroidism. Even in the euthyroidism subjects, serum total cholesterol (TC) and triglyceride (TG) levels were gradually elevated following TSH concentrations increasing.
We further investigated the complicated molecular mechanism by which TSH regulated lipid metabolism. First, TSH was identified to regulate both the synthesis and transformation of cholesterol in liver, suggesting a potential role in the pathogenesis of hypercholesterolemia. On one hand, TSH promoted the expression and activity of 3-hydroxy-3-methyl-glutaryl coenzyme A reductase (HMGCR), a rate-limiting enzyme in cholesterol synthesis, by acting on the TSH receptor in hepatocyte membranes and stimulating the cyclic adenosine monophosphate/protein kinase A/cyclic adenosine monophosphate-responsive element binding protein (cAMP/PKA/CREB) signaling system. On the other hand, TSH repressed the bile acid synthesis from cholesterol via sterol regulatory element-binding protein 2/ hepatocyte nuclear factor 4α/ Cholesterol 7α-hydroxylase (SREBP-2/HNF-4α/CYP7A1) axis. Second, TSH triggered hepatic sterol regulatory element-binding protein 1c (SREBP-1c) activity via the cyclic adenosine monophosphate/protein kinase A/ peroxisome proliferator-activated receptor α (cAMP/PKA/PPARα) pathway associated with decreased AMP-activated protein kinase (AMPK), which further increased the expression of the genes associated with lipogenesis and finally increased hepatic triglyceride content which resulting in the development of non-alcoholic fatty liver disease (NAFLD). Third, in adipose tissues, we found that TSH promoted preadipocyte differentiation, as well as acted as a previously unrecognized master regulator of adipogenesis via AMP-activated protein kinase/ peroxisome proliferator-activated receptor γ/glycerol-3-phosphate-acyltransferase 3 (AMPK/PPARγ/GPAT3) axis, resulting in obesity.
Based on the above research, we performed an open-label, randomized, controlled trial to investigate the effect of L-thyroxine on lipid profiles, NAFLD and obesity in mild subclinical hypothyroidism patients. After the 15-month follow-up, serum TC concentrations, the prevalence of NAFLD and body mass index were all improved in the intervention group with L-thyroxine replacement therapy. A long-term, prospective, randomized, controlled trial is necessary in future to investigate the effects of L-thyroxine replacement therapy on cardiocerebrovascular events.

S40-01

Cathepsin K inhibition and fracture reduction

Bente L Langdahl

Aarhus University Hospital

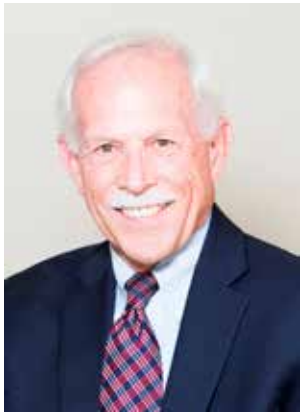
Cathepsin K (CatK) is a cysteine protease and is highly and almost exclusively expressed by osteoclasts. CatK very efficiently degrades type I collagen, the major organic component of bone matrix. Preclinical studies have consistently demonstrated that CatK inhibition increases bone mass, improves bone microarchitecture and strength. Inhibition of CatK decreases bone resorption, but increases the number of osteoclasts, which in-turn maintains the signals to bone formation and perhaps even increases bone formation on some cortical surfaces. Several inhibitors of CatK have been investigated for the treatment of osteoporosis, but currently only Odanacatib (ODN) is being investigated in clinical trials. ODN is a potent and highly selective oral CatK inhibitor dosed once-weekly in humans. In a phase 2 clinical trial, post-menopausal women treated with ODN had sustained reductions of bone resorption markers, while bone formation markers after an initial decrease returned to baseline levels. Bone mineral density increased continuously at both spine and hip for up to 5 years. Efficacy of ODN in improving bone mineral density has also been demonstrated in postmenopausal women with osteoporosis pretreated with alendronate and in men with osteoporosis. ODN is currently in a worldwide phase III fracture outcome trial for the treatment of postmenopausal osteoporosis with interim results supporting its anti-fracture efficacy at vertebrae, hip and non-vertebral sites.

S40-02

Inhibition of sclerostin and effects on bone

Michael McClung

Oregon Osteoporosis Center



S40-03

Novel PTH/PTHrP based anabolic approaches to the treatment of PMO

Benjamin Leder

Mass General Hospital, Havard University

In the treatment of postmenopausal osteoporosis, currently available antiresorptive and anabolic therapies increase bone mineral density modestly and reduce fractures in specific populations, but cannot restore skeletal integrity in most patients with established disease. Anabolic therapy theoretically has this potential but currently available anabolic agents and regimens are limited by their duration of action and concomitant pro-resorptive properties. Presently, the parathyroid hormone analog, teriparatide, is the only anabolic agent being used to treat postmenopausal osteoporosis though several drugs are in late-stage development. This session will focus on new therapeutic approaches targeting the parathyroid hormone and parathyroid hormone related-protein receptor (PTHR). Specifically, we will review the proposed mechanism and available data surrounding the parathyroid hormone-related protein analog, abaloparatide. Though much of the abaloparatide anti-fracture efficacy data remains unpublished, initial published studies suggest that abaloparatide may stimulate both bone formation and resorption less than teriparatide and may preferentially increase bone mineral density at anatomic sites comprised of significant cortical bone. The session will also focus on the use of PTHR-targeted therapies in combination with antiresorptive agents. Initial studies investigating the combination of parathyroid hormone and bisphosphonates have generally not shown an additive effect on bone mineral density. In contrast, in the DATA study, we recently reported that the combination of teriparatide and the nuclear factor-κB inhibitor, denosumab, increases bone mineral density at the hip, spine and distal radius, improves peripheral bone microarchitecture, and increases estimated bone strength at the radius and tibia more than either drug alone. Moreover, denosumab, unlike bisphosphonates, appears to fully inhibit the pro-resorptive effects of teriparatide (while allowing for continued osteoblast activity). The session will conclude with a discussion of the optimal sequence of anabolic and antiresorptive agent administration in light of new data and examine how this knowledge can help optimize the long-term therapeutic course in patients with severe disease.

S41-01

Defining and managing sarcopenia in 2016

Roger Fielding

Tufts University

Roger A. Fielding, Ph.D. is Director and Senior Scientist of the Nutrition, Exercise Physiology, and Sarcopenia (NEPS) Laboratory at the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. He is also Professor of Nutrition at the Friedman School of Nutrition Science and Policy and Professor of Medicine at Tufts University School of Medicine. Currently, he serves as the Associate Director of the Boston Claude D. Pepper Older Americans Independence Center. Dr. Fielding is an internationally known researcher who studies the underlying mechanisms contributing to the age-associated decline in skeletal muscle mass, the resultant impact on function, and the potential role of exercise, nutrition, and physical activity on attenuating this process. He has extensive experience in the conduct of randomized controlled trials of exercise, nutrition, and pharmacologic therapies in older adults. Dr. Fielding has a strong record of extramural funding including support from the NIH, USDA, private foundations, and industry. He serves as associate editor of the Journal of Gerontology Medical Sciences, and Calcified Tissues International and Musculoskeletal Research.

S41-02

Sarcopenia and mortality

Ching-Lung Cheung

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Sarcopenia is a prevalent condition worldwide and associated with limited mobility, poor quality of life, and increased morbidity and mortality. The prevalence of sarcopenia is expected to continue to rise due to the rapid aging in the worlds population. According to the World Health Organization, it was estimated that the number of people aged 60 years or older will rise from 900 million in 2015 to 2 billion in 2050. Thus, sarcopenia becomes an important topic in medical research.

Despite various definitions of sarcopenia have been proposed by professional bodies, it is generally agreed that sarcopenia refers to reduced muscle mass, strength, and/or function. Thus, lean mass, gait speed, and grip strength are commonly used to define sarcopenia. Sarcopenia is well documented to be associated with increased all-cause and several disease-specific mortality. However, the strength of association between each component of sarcopenia and mortality varies. For example, we recently showed that low lean mass and slow gait speed were associated with increased death with a hazard ratio of 1.72 and 2.32, respectively (Cheung et al., 2016). However, an earlier study from the Health ABC study showed that low grip strength, but not low lean mass, was associated with mortality (Newman et al., 2006). Moreover, the mechanism underlies the association between sarcopenia and mortality remains largely unknown. In this seminar, I will first summarize evidence about associations between sarcopenia and mortality, and then discuss the mechanism how sarcopenia is associated with increased mortality based on current evidences.

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Newman AB, Kupelian V, Visser M, Simonsick EM, Goodpaster BH, Kritchevsky SB, Tylavsky FA, Rubin SM, Harris TB (2016) J Gerontol A Biol Sci Med Sci.;61(1):72-7.

S41-03

Obesity and sarcopenia role of intra- and inter-muscular adipose tissue (IMAT)

David Scott

Monash University

Obesity epidemics and improved life expectancies in developing countries have resulted in large populations of obese older adults internationally. The growing population of obese older adults presents numerous public health and economic challenges, as these individuals are likely to accumulate substantial numbers of years with lost independence and excess health care costs. Obese older adults have over two-fold increased risk of disability compared with non-obese counterparts, and also demonstrate faster rates of decline in physical function and increased rates for falls.

"Sarcopenia" is the term used to describe the loss of skeletal muscle mass and function during ageing, and this condition is also associated with increased disability, falls, fractures and mortality in older adults. Over one-quarter of obese older adults may demonstrate sarcopenia, depending on the definition applied. There is increasing interest in the implications of co-occurring sarcopenia and obesity, or "sarcopenic obesity", during ageing. The combination of high amounts of fat mass and low amounts of skeletal muscle mass (the largest insulin sensitive tissue in the body accounting for up to 80% of glucose uptake) likely has significant impact on the metabolic health of older adults, and potentially increase the risk for type 2 diabetes and cardiovascular disease. Furthermore, given that both conditions are associated with poor physical function, sarcopenia and obesity may also interact to exacerbate functional decline during ageing. Indeed, we have observed increased falls and fracture rates in sarcopenic obese older adults compared to non-sarcopenic and non-obese controls.

When sarcopenia was initially described over 25 years ago it was considered to represent the excessive loss of skeletal muscle mass only. In recent years expert groups have proposed criteria for sarcopenia case-finding which reflect the now widely-accepted multi-component definition of sarcopenia, incorporating age-related declines in both muscle mass and function. The inclusion of poor muscle function as a component of sarcopenia followed research findings demonstrating that the declines in skeletal muscle mass with age are not the primary cause of muscle function deficits. In fact, loss of strength exceeds the rate of loss of muscle mass by up to five-fold during ageing, and even those older adults who are able to maintain muscle mass during later life will experience muscle strength declines. The loss of muscle function not attributable to declines in skeletal muscle mass is attributable to declines in muscle quality during ageing, including changes to components of the neuromuscular system such as decreased activation of motor neurons and changes in skeletal muscle composition. Muscle quality may be particularly compromised in obese older adults who, despite generally having higher absolute muscle mass and function, have significantly poorer specific force (strength relative to muscle mass) compared with non-obese older adults, and even compared with frail non-obese older adults.

One component of the age-related decline in muscle quality which is particularly relevant in obesity is the increasing infiltration of fat depots in skeletal muscle, known as inter- and intra-muscular adipose tissue (IMAT). IMAT levels in skeletal muscle increase by as much as three-fold from young adulthood to old age and are two-fold higher in obese compared to normal weight older adults. IMAT adipocytes may increase local secretion of pro-inflammatory factors with significant impacts on skeletal muscle metabolism and insulin sensitivity, and high levels of IMAT have been associated with increased risk for type 2 diabetes. IMAT also reduces the contractile properties of skeletal muscle and thereby leads to functional declines. High levels of lower-limb IMAT have been associated with mobility limitation, poor balance, falls and hip fracture risk, even after adjustment for muscle size. Thus, high IMAT levels are likely an important contributor to the poor physical function of obese older adults, and may also explain in some part why some obese older adults develop sarcopenic obesity.

For the obese older patient, weight loss through caloric restriction and aerobic exercise may be beneficial in reducing body fat and improving cardiometabolic outcomes. However, weight loss may also result in undesirable declines in muscle and bone mass and so weight loss interventions should where possible incorporate progressive resistance training which is targeted at maintaining, if not improving, skeletal muscle mass and function. The combination of aerobic and progressive resistance training also appears to be most effective at reducing IMAT levels, and therefore has the potential to provide significant improvements in physical function and cardiometabolic health for obese older adults.

S42-01

Activin A Accelerates the Progression of Fetal Oocytes through Meiosis and Early Oogenesis in Mouse

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Yong Zhao is a professor in Qingdao Agricultural University. He got his Ph.D. in South Dakota State University (in USA) in September 2008. Then he had worked as research associate in Michigan State University (in USA) from 2008 to 2013. In 2013 he joined Qingdao Agricultural University in China. His research had been focused on the effects of mechanisms of air pollutants on the female reproductive systems, especially the roles of interactions of air pollutants and female hormones in female reproductive development. He has published many publications in Journals like Brest Cancer Research, Toxicological Sciences, Reproductive Toxicology, Free Radical & Biological Medicine, and so on. He is the member of American Chemistry Society, American Association of Pharmaceutical Sciences, Breast Cancer and Environment Research Program

Chromosome segregation in mammalian oocyte meiosis is an error-prone process, and any mistake in this process may result in aneuploidy, which is the main cause of infertility, abortion and many genetic diseases. The mechanisms of regulating the entry into meiosis of germ cell remain incompletely understood. ActA, a member of the TGF-β family, plays an important role in the development of mammals, and its major functions were regulating the prolifiteration and differation of granulosal cells, enhancing the quality of follicle development via promoting the maturation of oocytes and inhibing the follicular atresia and few reports about the early development of ovary.

Immunohistochemistry, RT-qPCR and Western blot were used to detect the expression level and location of the Activin I and II type receptor in the 12.5dpc, 0dpp, 7dpp, 14dpp and 21dpp ovaries. The expression was robust on all days examined especially from 12.5dpc to 7dpp. The in vitro experiment verified that while in vitro culture of 12.5 dpc gonad, at the beginning 14 days absence of ActA, the oocyte diameter, number and quality were decreased ($P<0.05$), 12.5 dpc ovaries treated by ActA after 3 days in vitro culture, the progress of meiosis I was accelerated ($P<0.05$). The meiosis genes Stra8, Dazl, Dmc1 and Scp3 were increased ($P<0.05$) , the levels of meiosis protein STRA8, DAZL and SCP3 also increased ($P<0.05$). We administrated the mouse pregnancy for 10 day, the meiosis progress and related genes in the treatment group were accelerated 4 days later ($P<0.05$). Act A effects the primordial follicle poll establishment and expands the primordial follicle number. The increase of RALDH1 and RARs expression in the mRNA levels lead us study the relation between Act A and RA signaling pathway. Thus we detected the expression levels of CYP26B1 in each group and found that Act A can decrease the Cyp26b1 in mRNA and protein levels. In conclusion, Act A can accelarete the progression of the meiosis prophase I via the RA-STRA8 signaling.

S42-02

Follistatin regulation of germ cell developmen

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State Key Laboratory of Agro-Biotechnology, College of Biological Sciences, China Agricultural University

Chao Wang received his Ph.D. training in Physiology with Guoliang Xia at the China Agricultural University, Beijing, China. He had postdoctoral training with Dr. Jianzhong Shen at the China Agricultural University on Pharmacology. Dr. Wang worked as an associate professor from 2008 to 2014 in the School of Basic Medical Sciences, Capital Medical University, Beijing, China. Dr. Wang works in the College of Biological Sciences, China Agricultural University since 2014. Dr. Wang's research focused on ovarian physiology. His work engaged in defining the molecular mechanisms of meiotic maturation in mammalian oocytes and primordial follicle formation. Currently, he is interested in studying the possible roles of RNA binding proteins in oocytes and ovarian somatic cells during follicle development as well as gonadotropin-induced oocyte maturation. His work has been published in the journals of Scientific Reports, J Cell Sci, Reproduction, J Cell Physiol., Development, Mutation Research, J. lipid Res., PLoS ONE, Mol. Reprod. Dev., Biol. Pharm. Bull., Mol. Cell Endocrinol. , J. Mol. Endoc. and Front. Biosci.

Objective: The transforming growth factor-β (TGF-β) family member activin (ACT) contributes to folliculogenesis. This study is designed to clarify the role of FST288, the strongest ACT-neutralizing isoform of follistatin (FST), during cyst breakdown and primordial follicle formation in the fetal mice ovary.
Methods: Fetal ovaries of mice (17.5 dpc) were in vitro cultured in medium of DMEM/F-12 plus recombinant mouse FST288 at 500 ng/mL, or in medium plus FST288 recombinant human activin A at 100 ng/mL for up to 7 days (equivalent to 5 dpp). After culture, the FST expressed in prenatal and neonatal mouse ovaries were examined through Immunohistochemical analysis. The ovarian germ cells and follicles were quantified. The degree of oocyte apoptosis was measured by terminal deoxynucleotidyl transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL) assay. The expression levels of relative proteins were examined through Western Blotting.
Results: FST was continuously expressed in the oocytes as well as the cuboidal granulosa cells of growing follicles in perinatal mouse ovaries. Treatment with FST288 delayed germ cell nest breakdown, particularly near the periphery of the ovary, and dramatically decreased the percentage of primordial follicles. In addition, there was a dramatic decrease in proliferation of granulosa cells, and somatic cell expression of Notch signaling was impaired.
Conclusion: FST288 impacts germ cell nest breakdown and primordial follicle assembly by inhibiting somatic cell proliferation.

S42-03

Signaling Pathways in Granulosa Cells

Teresa Woodruff

Northwestern University

S43-01

The importance of glucocorticoid pulsatility for stress sensitivity and synaptic plasticity

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Brain Center Rudolf Magnus, University Medical Center Utrecht

Plasma levels of glucocorticoid (GC) stress hormones (cortisol in humans and corticosterone in rodents) rapidly oscillate in approximately hourly hormone bursts released by the adrenal gland. The amplitude of these ultradian pulses increase in anticipation towards to circadian peak to meet the metabolic demands of the active phase. Though the underlying mechanisms are still unclear, dysregulation of GC pulse characteristics has been correlated with stress-related disease (i.e. major depression, Cushing's syndrome) and is considered to enhance vulnerability to psychopathology.
Corticosterone pulses are carried across the blood-brain barrier and bind intracellularly to the mineralocorticoid and glucocorticoid receptor (MR and GR), respectively. These receptors are highly enriched in limbic brain areas such as the hippocampus and act as strong transcriptional regulators of glucocorticoid target genes.

Recent elegant studies have shown that in target tissues (e.g. liver and cultured cells), GC pulsatility keeps transcriptional target gene activity at a dynamic equilibrium via a GR-dependent mechanism (Lightman and Conway-Campbell, 2010). Yet, the physiological relevance of rhythmic GC release for responsiveness to stress and brain function is unknown.

In a series of studies we have used a variety of rodent model systems of GC pulsatility by either interfering with the endogenous corticosterone rhythm or controlling pulsatility prospectively. Specifically, we studied the effect of glucocorticoid pulsatility on 1) HPA axis activity and 2) target tissue responsiveness to stress and 3) synaptic plasticity processes in the brain.

To study the HPA axis response to stress we have combined a novel automated infusion system with automated blood sampling in adrenalectomized rats. This highly controlled experimental design allowed exact timing of the infused corticosterone levels in either continuous or pulsatile corticosterone patters within the daily physiological range. We show that GC pulsatility is essential in maintaining the resilient ACTH response to stress and that this depends on the phase of the ultradian pulse. Additionally, neuronal activation patterns varied in a brain-region-specific manner in the limbic circuit (e.g. hippocampus, amygdala) suggesting an important role of GC pulsatility in the coordination of the stress response.

Previous studies have shown the importance of glucocorticoid rhythms in the maintenance of target gene expression. In a second study we elaborated on this concept by investigated the role of pulsatility in neural target tissue responsiveness to stress. Hereto we effectively disrupted and flattened corticosterone rhythms in adrenally-intact rats by subcutaneous corticosterone pellet implantation. Tissue responsiveness was challenged with a high dose of corticosterone to mimic the stress response. Using molecular markers in the hippocampus (i.e. MR and GR expression, receptor translocation and glucocorticoid target gene expression) we conclude that 1) GC pulsatility prevents desensitization of the GR and that 2) hippocampal responsiveness to glucocorticoids is attenuated when glucocorticoid signaling is interrupted, even within the normal physiological hormone range.

Glucocorticoids are known to be important neuronal regulators of learning and memory processes via glutamatergic neurotransmission and synaptic plasticity. While the impact of a single dose of corticosterone on glutamatergic transmission is well documented, it remains poorly understood how consecutive pulses impact on glutamate receptor trafficking and synaptic plasticity. By using high-resolution imaging and electrophysiological approaches in primary hippocampal cultured cells and ex vivo mouse brain slices, we report that a single corticosterone pulse to hippocampal networks causes synaptic enrichment of glutamate receptors and increased responses to spontaneously released glutamatergic vesicles, collectively abrogating the ability to subsequently induce synaptic long-term potentiation. Strikingly, a second pulse of CORT one hour after the first--mimicking ultradian pulses--completely normalizes all aspects of glutamate transmission investigated. The effect of the second pulse is precisely timed and depends on a nongenomic glucocorticoid receptor-dependent pathway.These data suggests that consecutive GC pulses are necessary to restore the plastic range of the synapse possibly preventing the brain from overshooting during stressful conditions.

In conclusion, the data altogether provide strong evidence that the rapid ultradian fluctuations in corticosterone levels crucially maintain the resilient response in HPA axis activity and target tissue responsiveness to stress and synaptic plasticity. This possibly underlies a mechanism that ensures full responsiveness of the brain and stress system to cope with the stress-related event and facilitate the encoding of new stress-related information. This finding is of importance for understanding the role of glucocorticoid pulsatility in resilience to stress-related disorders.

S43-02

Interaction of clock stress systems: implications for metabolism

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Objective: Endogenous cellular clocks in all tissues regulate 24-h rhythms of physiology and behavior. Under non-stressed conditions hypothalamus-pituitary-adrenal (HPA) endocrine axis activity follows a robust circadian pattern. At the same time glucocorticoids are potent synchronizers of clock gene oscillation in various tissues and cells. How these two systems interact, however, is still poorly understood.

Methods: HPA axis activity and clock gene rhythms were studied in mice with tissue-specific genetic disruption of clock function in the suprachiasmatic nucleus (SCN) pacemaker and the adrenal gland. Pharmacological manipulations were used to alter glucocorticoid rhythms and clock gene expression in target tissues was studied.

Results: Different tissue clocks contribute to the regulation of circadian glucocorticoid rhythms. The central pacemaker of the hypothalamic SCN controls circadian release of vasopressin and corticotropin-releasing hormone (CRH), which together initiate activation of the HPA axis. On the other hand, the SCN regulates clock function in the adrenal cortex via the autonomic nervous system, thus aligning adrenal physiology with the external light-dark cycle. Transplantation and genetic lesion studies suggest that adrenal clock function is essential for the circadian regulation of glucocorticoid release, but recent data from our group challenge this view. Abrogation of glucocorticoid signaling, either by pharmacological or genetic means, destabilizes peripheral clock regulation, thus making the circadian system more vulnerable to external perturbation.

Conclusion: Extensive crosstalk exists at central and peripheral levels between the HPA axis and the circadian clock system, with impact on metabolic, immune, and stress response regulation.

S44-01

Clinical aspects of FGF21

Weiping Jia

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Weiping Jia is now Professor of Division of Endocrinology & metabolism at Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Director of Shanghai Clinical Center for Diabetes, Shanghai Key Laboratory for Diabetes and Shanghai Diabetes Institute. Dr. Jia is now president of Chinese Diabetes Society, and Chief Editor of Chinese Journal of Internal Medicine as well as editorial board members of Lancet Diabetes Endocrinology and Diabetes. Her research interest involved various aspects of diabetes, obesity and metabolic disorders from genetic and molecular biology to disease management, especially the translational research on the

disease. She has published more than 400 papers and over 100 research articles in international scientific journals, including British Medical Journal, Diabetes, Diabetes Care, Diabetologia, JCEM, AJP, and Obesity Review, etc. Her research has been funded by National Natural Science Foundation of China (NSFC), National Basic Research Program of China (973 program), Hi-tech Research and Development Program of China (863 program), and European Association for the Study of Diabetes (EASD). She is the Co-PI of research projects funded by the National Institute of Health (NIH) in USA.

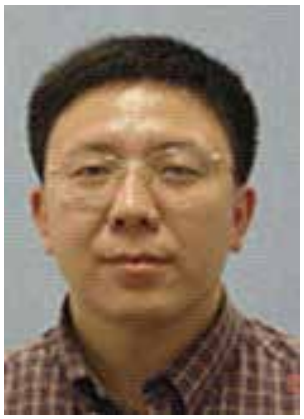
Fibroblast growth factor 21 (FGF21) is a member of the Fibroblast growth factor family. It actually functions as endocrine hormones but not regulates cell growth and differentiation. It is demonstrated that FGF21 acts on multiple tissues to coordinate carbohydrate and lipid metabolism, including enhancing insulin sensitivity, decreasing triglyceride concentrations, causing weight loss, ameliorating obesity-associated hyperglycemia and hyperlipidemia. We found that serum levels of FGF21 are closely related to adiposity, lipid metabolism and biomarkers of liver injury. However, FGF21 level was not correlated with insulin secretion and sensitivity in humans measured by the glucose clamp technique. We also investigated the relationship between serum FGF21 levels and nonalcoholic fatty liver disease (NAFLD). FGF21 levels were significantly higher in patients with NAFLD than those in control subjects. Moreover, FGF21 mRNA expression and protein levels were increased in human liver tissue were increased with the degree of steatosis and were positively correlated with the intrahepatic TG. We next investigated the prospective association of FGF21 with the onset and development of NAFLD in a 3-year prospective study and found that high serum FGF21 level is an independent predictor of the onset of NAFLD. FGF21 level increases in the early stage of adiposity and dyslipidemia and can be a potential biomarker for early detection of NAFLD.

S44-02

FGF21 and atherosclerosis

Aimin Xu

University of Hong Kong



Fibroblast growth factor 21 (FGF21) is an atypical member of the FGF family that functions as an endocrine factor. In obese animals, elevating plasma FGF21 levels by either pharmacological or genetic approaches reduces body weight, decreases hyperglycemia and hyperlipidemia, alleviates fatty liver and increases insulin sensitivity. While the liver is the major site for FGF21 production, adipose tissues appear to be the primary target of FGF21. Our recent work demonstrated that FGF21 acts both in an endocrine and autocrine manner to stimulate the expression and secretion of adiponectin in adipocytes, thereby increasing serum levels of adiponectin. In patients with obesity and type-2 diabetes, therapeutic administration of long-acting forms of FGF21 can also lead to a marked increase in circulating adiponectin. Adiponectin knockout mice are refractory to several therapeutic benefits of FGF21, including alleviation of obesity-associated hyperglycemia, hypertriglyceridemia, insulin resistance, and hepatic steatosis More recently, we have demonstrated that FGF21 acts as a physiological protector against atherosclerosis via two independent mechanisms: inducing the adipocyte production of adiponectin, which in turn acts on the blood vessels to inhibit neointima formation and macrophage inflammation, and suppressing the hepatic expression of the transcription factor Srebp-2, thereby leading to reduced cholesterol synthesis and attenuation of hypercholeseterolemia. These findings support a key role of the FGF21-adiponectin axis in maintaining metabolic and vascular homeostasis, by mediating the crosstalk between liver, adipose tissue and vasculature. However, in obesity and its related cardiometabolic complications, circulating FGF21 levels are increased whereas plasma adiponectin are decreased, suggesting the uncoupling of the FGF21-adiponectin axis as a possible cause of this disease. We have recently uncovered several uncoupling mechanisms, including dysregulated miRNAs and FGF21 resistance caused by downregulation of the FGF21 receptor complex. Restoration of the FGF21-adiponectin axis may represent an effective strategy for prevention of obesity-related medical complications, including atherosclerosis (supported by Hong Kong Collaborative Research Fund C7055-14G and HKU2/CRF/12R) .

S45-01

New genes for the adrenal Cushing syndrome

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The advent of new genetic techniques that allow for high-throughput sequencing in surgical tumor tissues and germline DNA has boosted progress in many fields of biomedical research. The technique has been proven to be particularly fruitful in the area of endocrine tumors with many new driver genes being identified over the last few years that are involved in cell growth but more importantly in hormonal autonomy. Examples account for aldosterone producing adrenal adenomas, insulin producing neuroendocrine tumors, growth hormone producing pituitary adenomas and pheochromocytomas. Also, the field of Cushing's syndrome has been moved forward on several fronts by identifying new genetic and molecular mechanisms that ultimately result in the clinical phenotype of hypercortisolism. This can be highlighted on three distinct disorders that are all associated with Cushing's syndrome:
Following a whole genome sequencing approach in patients with familial cases of bilateral macronodular adrenal hyperplasia the group of Jér?me Bertherat identified germline mutations in the ARMC5 gene together with second hits in adrenal nodules as the cause of the disorder (1). This finding has not only opened the possibility to explore new pathophysiological mechanisms in adrenal steroidogenesis and cellular growth but also has led to the clinical application of genetic testing for case finding and prospective clinical follow-up. Based on exome sequencing from tumor tissue an European consortium was able to pinpoint mutations in the catalytic subunit of PKA (PRKACA) as the underlying genetic event in around one third of cases of cortisol producing adrenal adenomas (2). In addition, genetic duplications of the same gene were identified in a subgroup of patients from the NIH with bilateral micronodular hyperplasia. Interestingly, in the adenoma patients, there was a clear genotype/phenotype correlation with the most severe disease course in mutation carriers. Follow-up genetic studies in adrenal Cushing syndrome patients devoid of any PRKACA mutation suggests genetic heterogeneity, which needs to be explored in more detail in the future.
In summary, the last few years have witnessed significant progress in the elucidation of molecular mechanisms driving the clinical phenotype of endogenous hypercortisolism with all its metabolic

and cardiovascular sequelae. The future will show how these findings will translate into clinically tangible progress.

S45-02

ACTH independent Cushing Syndrome: Potential therapeutic targets

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Cao Yanan, MD, Shanghai Key Laboratory for Endocrine Tumors, Rui-jin Hospital, Shanghai Jiaotong University School of Medicine. Our research focus on the genetics, molecular mechanisms and clinical intervention of neuroendocrine tumors (NETs). We have the establish the endocrine-related tumour bank and databases, animal models and translational research platform. Recent works have been published on Science, Nature Communications and Endocrinology.

Adrenal Cushing's syndrome is caused by excess production of glucocorticoid from adrenocortical tumors and hyperplasias, which leads to metabolic disorders. We performed whole-exome sequencing of 49 blood-tumor pairs and RNA sequencing of 44 tumors from cortisol-producing adrenocortical adenomas (ACAs), adrenocorticotropic hormone–independent macronodular adrenocortical hyperplasias (AIMAHs), and adrenocortical oncocytomas (ADOs). We identified a hotspot in the PRKACA gene with a L205R mutation in 69.2% (27 out of 39) of ACAs and validated in 65.5% of a total of 87 ACAs. Our data revealed that the activating L205R mutation, which locates in the P+1 loop of the protein kinase A (PKA) catalytic subunit, promoted PKA substrate phosphorylation and target gene expression. Moreover, we discovered the recurrently mutated gene DOT1L in AIMAHs and CLASP2 in ADOs. Furthermore, we designed a gene sequencing panels for investigation of cancer gene alterations in neuroendocrine tumors, including adrenocortical tumors. Therapeutically targetable could be analyzed based on the evaluation of genomic alterations.

S46-01

Rare causes of hypopituitarism, ipilimumab, drugs and snake bites

Paula Bruna Mattos Coelho Araujo

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Hypopituitarism is defined as the deficiency of one or more hormones released by the anterior and posterior pituitary gland that is caused by pituitary or hypothalamic disorders. Clinical manifestations are variable and dependent on the degree and severity of hormone deficiency. It is associated with increased mortality, mainly attributable to cardiovascular and respiratory diseases. Most cases of hypopituitarism are caused by benign pituitary tumors, or secondary to its treatment either by pituitary surgery or radiotherapy. Central nervous system disorders involving the hypothalamus, such as craniopharyngioma and germ cell tumor, may also cause hypopituitarism. Pituitary dysfunction following traumatic brain injury, subarachnoid hemorrahage and ischemic stroke may also lead to hypopituitarism, being a frequently overlooked complication in these scenarios.

Besides classical etiologies of hypopituitarism, increasing use of immunologically based treatments in patients with cancer has resulted in a growing number of reports of hypophysitis. In this context, ipilimumab, a monoclonal antibody (mAb) anti-cytotoxic T lymphocyte-associated antigen 4 (anti-CTLA-4), is an agent used as an immunotherapy for metastatic melanoma. With the expanding use of ipilimumab, many immune-related adverse events (IRAEs) have been recorded, including some endocrinopathies, distinctly autoimmune hypophysitis, with an incidence ranging from 0 to 17% of treated melanoma patients. The frequency and severity of hypophysitis in this setting seem to be dose dependent; with fatigue and headache being the most common clinical manifestations, and most cases presents an enlarged pituitary gland at MRI. Also, it is more commonly seen in patients from male sex and older age. Tremelimumab, which has a similar mode of action, has been associated with hypophysitis in about 3% of patients.

The use of interferon, a cytokine that modulates immune signaling, in the treatment of hepatitis C, melanoma and multiple sclerosis, can interfere with the homeostasis of neuroendocrine-immune interaction. Various endocrine dysfunctions in virtually all hormonal axis have been observed with the use of interferon-alpha. However, only single cases of hypopituitarism have been attributed to interferon.

Another recent rare cause of hypopituitarism following snakebite has been recognized. The development of a Sheehan's-like syndrome with chronic hypopituitarism following Russell viper envenomation has been reported from Myanmar, South India and Sri Lanka. People envenomed by these snakes suffer coagulopathy, systemic hemorrhage, shock, neurotoxicity, acute kidney injury and local tissue damage leading to severe morbidity and mortality. This presentation will try to elucidate the phatophysiological mechanisms underlying these recently reported rare causes of hypopituitarism.

S46-02

Update on trauma and hypopituitarism

Marianne Christina Klose

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Marianne Klose, MD, PhD, consultant at the department of Internal medicine and Endocrinology, Copenhagen University Hospital, Rigshospitalet. Her clinical and research interest are on hypothalamo-pituitary diseases. Since 2003 her research has been focussed on traumatic brain injury, and during that period headed a large Danish nationwide study on pituitary insufficiency after traumatic brain injury, a topic she also dealt with during her PhD. Apart from that she has also been involved in studies on sleep patterns in craniopharyngeoma, and adrenal insufficiency after glucocorticoid withdrawal. She participated in the establishment of the Danish association of young endocrinologist where she served as secretary for eight years.

Traumatic brain injury (TBI) is a major public health problem with potentially debilitating consequences for the individual. Hypopituitarism after TBI has received increasing attention over the past decade. While hypopituitarism after TBI was previously considered rare, it is now believed a major cause of treatable morbidity among TBI survivors. A meta-analysis reported hypopituitarism in over 25% of adults after TBI, with similar data found in children. If these data hold true, TBI would be by far the most common cause of hypopituitarism. The disproportion between this proposed incidence and the occasional cases of post-TBI hypopituitarism in clinical practice has left us with the question whether hypopituitarism is often unrecognized in TBI patients or whether data were misinterpreted?
Strikingly, there are considerable differences in the reported prevalence rates of posttraumatic hypopituitarism ranging from negligible to >50%, probably partly attributable to differences in the severity of head trauma in the published series. However, severity cannot unambiguously explain the observed variation, and other explanations seem to weigh higher. In a Danish national study on hypopituitarism in TBI we assessed the potential sources of common methodological bias. The main finding was a significantly lower prevalence of posttraumatic hypopituitarism when local assay and test specific cut-off values were used as compared to those generally recommended in guidelines, and when confirmatory rather than single testing was performed. The results stress the importance of proper control groups and stringent testing, thus increasing the diagnostic accuracy, particularly in cohorts with a low a priori likelihood of hypopituitarism such as TBI. Our results, in line with other very recent studies, question the evidence for recommendations for routine pituitary assessment in patients with moderate or severe TBI, and indicate a need for re-evaluation of guidelines in order to diminish the financial burden of routine pituitary testing in all patients with TBI.
The current recommendations will be discussed in the lines of currently available evidence.

S47-01

Bone Marrow Cancers and Bone Health

Matthew Drake

Mayo Clinic

Matthew Drake, M.D., Ph.D.
Dr. Matthew T. Drake is a Consultant in the Division of Endocrinology, Department of Medicine, and Associate Professor of Medicine at Mayo Clinic in Rochester, Minnesota. Dr. Drake received his A.B. degree from Harvard College and completed his M.D. and Ph.D. degrees at Washington University in St. Louis. His clinical training in Internal Medicine was performed at Duke University Medical Center in Durham, North Carolina. Dr. Drake completed his Endocrinology fellowship training at the Mayo Clinic, where he subsequently joined the staff in 2007. He is board certified in Endocrinology.
Dr. Drake has received numerous awards, including the American Society for Bone and Mineral Research (ASBMR) Young Investigator Award and the Mayo Clinic Department of Medicine New Investigator Award. He currently serves as Chair of the Mayo Clinic Metabolic Bone Disease Core Group, on the editorial boards of Bone, the Journal of Bone and Mineral Research, and the Journal of Clinical Endocrinology and Metabolism, and on the Scientific Advisory Board for the Soft Bones Foundation. In his clinical practice, Dr. Drake is involved in providing care to patients with a variety of metabolic bone diseases. In addition, he performs translational research with areas of interest including understanding the mechanisms underlying age-associated bone loss, the etiology of increased skeletal fragility in patients with diabetes, and the basis by which monoclonal gammopathies [monoclonal gammopathy of undetermined significance (MGUS) and multiple myeloma] induce bone loss and fractures.

Fractures resulting from age-associated bone loss are common and are expected to increase with the aging population. This age-associated increase in fracture risk is paralleled by the increased risk for developing a monoclonal gammopathy, a spectrum of plasma cell disorders marked by the pre-malignant condition monoclonal gammopathy of undetermined significance (MGUS) at one end, and the hematologic malignancy multiple myeloma at the other end of the spectrum. MGUS is a frequent finding identified during routine clinical care. It affects more than 3% of adults aged > 50 years. Further, MGUS increases with age, affecting nearly 8% of adults by age 85. As originally described, the 'undetermined significance' portion of the term MGUS reflected the uncertainty in identifying patients with a benign stable plasma cell disorder from those patients destined to progress to multiple myeloma. However, there is now clear epidemiologic evidence that rather than being a condition of 'undetermined significance', patients with MGUS have a significantly increased fracture risk. Potential etiologies for this increased fracture risk have until recently, however, been poorly understood.
While fracture incidence is increased in MGUS, bone mineral density (DXA) imaging has provided conflicting results as to whether MGUS subjects have decreased bone mass. DXA limitations include the extrapolation of a two-dimensional (areal) measurement of bone mineral content to derive a three-dimensional (volumetric) density, as well as the inability to accurately assess bone structure and to differentiate between cortical and trabecular bone compartments. Recent imaging studies using high resolution peripheral quantitative computed tomography (HRpQCT) clearly show that patients with MGUS have substantial trabecular and cortical microarchitectural deterioration and associated deficits in biomechanical bone strength, factors which are likely important contributors to the increased skeletal fragility seen in these patients. Further, circulating levels at least two cytokines [the osteoclast-activating factor chemokine (C-C motif) ligand 3 (CCL3)/macrophage inflammatory protein-1alpha (MIP-1alpha) and the osteoblast-inhibitory factor Dickkopf-related protein 1 (DKK1)] with well-recognized roles in bone disease in the closely related monoclonal gammopathy multiple myeloma are also increased in patients with MGUS. Collectively, this evolving evidence strongly suggests that care providers need to shift the paradigm from one in which MGUS is considered to be a disorder of 'undetermined significance' to one of 'skeletal significance' in order to ultimately limit skeletal deterioration and fractures in this high-risk population.
While our understanding of bone loss and fracture risk in MGUS is evolving, the bone loss that occurs in multiple myeloma, a cancer characterized by the clonal proliferation of plasma cells within the bone marrow cavity, has been the focus of significantly more research effort. Multiple myeloma accounts for approximately 15% of hematologic cancers, and 1% of all cancers. Like MGUS, the risk for developing multiple myeloma increases with aging. Multiple myeloma is the most common cancer to affect the skeleton, with 80-90% of patients with multiple myeloma having bone involvement. Affected skeletal sites most commonly affected include the spine, skull, pelvis, ribs, humeri, and femora. Complications of this skeletal involvement include pain, pathologic fractures, hypercalcemia, and spinal cord compression. Importantly, the occurrence of a skeletal-related-event significantly increases the risk for death

in multiple myeloma. Due to factors produced by multiple myeloma cells within the bone marrow microenvironment, myeloma bone disease results from both increased osteoclast-mediated bone resorption and simultaneous suppression of osteoblast-mediated bone formation. Current treatment regimens for limiting bone loss and skeletal-related-events in patients with multiple myeloma involve the use of the intravenous bisphosphonates pamidronate and zoledronic acid. Efforts to reduce the risk for developing osteonecrosis of the jaw (ONJ) in patients with multiple myeloma treated with bisphosphonates have primarily focused on preventative measures including routine dental care, maintenance of good oral hygiene, and peri-procedural mouth rinses and/or brief antibiotic courses when invasive dental procedures are performed. Novel pharmacologic approaches to limit bone loss and prevent the development of osteolytic lesions in patients with multiple myeloma are currently under investigation.

All patients with MGUS or multiple myeloma require a pro-active approach to limit their risks for skeletal complications. This should include counseling patients on limiting their risks for falls, providing appropriate lifting recommendations, and ensuring adequate intake of vitamin D and calcium once any initial hypercalcemia has been treated. Pharmacologic treatment is likely warranted in patients with MGUS and low bone mass/osteopenia due to the limitations of DXA to accurately document the amount of bone loss that has already occurred. Pharmacologic treatment with intravenous bisphosphonates is warranted in all patients with multiple myeloma and evidence of bone disease.

S47-02

Prostate cancer: how can we treat therapy-resistant tumours?

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Objective: Prostate cancer patients with advanced disease invariably develop metastatic castrate- resistant prostate cancer (mCRPC). Abiraterone acetate and Enzalutamide only increase patient survival by a few months, before death. There is an immediate need to identify mechanisms of tumour resistance and to test therapies to further control tumour progression.

Methods: Using autopsy specimens from the CASCADE program (Alsop et al Nature Biotech in press, 2016), we established patient derived xenografts (PDX) lines from mCRPC samples from patients who had failed multiple lines of conventional therapies.

Results: The new PDXs expand the limited set of experimental models currently available for prostate cancer research discovery. Most of the PDXs remained hormone-responsive, but exhibited varying sensitivity to different forms of androgen receptor blockade. In a line with high MYC activity, we tested a novel therapy by conducting a proof-of-concept PDX clinical trial (PCT) with a combination of inhibitors of RNA Pol I transcription and PIM kinase. Our results demonstrated preclinical efficacy of targeting the ribosome at multiple levels with this drug combination.

Conclusion: Such evidence of response to new and emerging therapies, paves the way for rapid translation into the clinic by directly informing the development of a novel approach for treatment of mCRPC and the design of subsequent clinical trials.

S48-01

Hormones and aging

Andrew Hoffman

Stanford University

Andrew R. Hoffman, MD

Dr. Hoffman is a Professor and Vice Chair for Academic Affairs in the Department of Medicine at Stanford University School of Medicine and Chief of Endocrinology at the VA Palo Alto Health Care System. He previously served as Chief of Medicine at the VA Palo Alto Health Care System and as Chief of the Division of Endocrinology at Stanford.

His research focuses on examining epigenetic mechanisms of gene expression and on studying the role of insulin-like growth factors (IGF) and growth hormone in normal physiology and in cancer development. His studies have implications for the therapeutic use of growth hormone and IGF in development and in the clinical consequences of aging. He is currently studying the natural history of bone health in elderly men and neuroendocrine function in aging and traumatic brain injury.

Dr. Hoffman received his MD from Stanford in 1976. He completed an internship and his residency in medicine at Massachusetts General Hospital (MGH) in Boston in 1978, and he was a research associate at the National Institute of Mental Health with Julius Axelrod from 1978-80. He was a clinical and research fellow in medicine and in gynecology at MGH from 1980-1982. Dr. Hoffman is a former president of the American Federation for Medical Research, the Association of VA Chiefs of Medicine, and the Western Society for Clinical Investigation. He has been elected to membership in the American Society for Clinical Investigation and the Association of American Professors.

He is a member of the Endocrine Society and the American Association of Clinical Endocrinologists, and serves on the Council of the Growth Hormone Research Society.

Scientists have tried to use hormones and testicular extracts to forestall the decline in libido and the other catabolic aspects of aging for more than one hundred years. The modern day search for an endocrine fountain of youth has centered around growth hormone and sex steroid replacement therapy to restore circulating hormone levels to the young adult range.

The activity of the hypothalamic–GH—IGF axis declines in midlife, leading to decreasing levels of both GH and IGF-I. Since this decline occurs in parallel with many of the catabolic changes seen in normal aging, the term "somatopause" has been used describe the fall in serum GH and IGF-I levels. Over the past 30 years, a significant body of evidence has accumulated that suggests that GH and IGF-I might play a role in several pathological conditions commonly seen during aging, such as atherosclerosis and

cardiovascular disease (CVD), cognitive decline, dementia, sarcopenia and frailty. Some cross sectional studies have shown that low IGF-I levels have been associated with unfavorable CVD risk factors profile. In addition, there is a correlation between declining GH and IGF-I levels and age-related changes in body composition and physical function. However, few studies have documented a precise role of the GH axis in the development of sarcopenia, frailty and poor mobility. While there have been numerous trials of GH replacement therapy for the somatopause, the hopes that GH would restore a healthy, vigorous and anabolic youthful state have not been borne out by carefully controlled studies of healthy or somewhat frail elders. Moreover, a very large body of evidence has been amassed in lower animals, ranging from yeast to flies to mice, that demonstrate that longevity is in fact markedly enhanced in organisms that are deficient in various aspects of GH or IGF/insulin hormone action. Despite the disappointing results from controlled clinical trials, GH is still widely used by anti-aging clinics, and there is a large market for GH "stimulators" that is available through the internet.

When synthetic estrogens became available, they were touted as miracle drugs that would make women "forever young." Although they were widely prescribed for this purpose for many years, the carefully controlled Women's Health Initiative study demonstrated the many risks of this therapy, and estrogens are no longer routinely prescribed to forestall the signs and symptoms of aging.

There is more uncertainty about the use of testosterone replacement therapy in older men.The decline in testosterone secretion, termed "the andropause" develops slowly over several decades in most, but not all, men. Serum total testosterone levels decline at a constant rate from the mid-thirties onward in healthy men. Because many of the catabolic sequelae associated with aging, such as sarcopenia, increased adiposity, and osteoporosis, are similar to those seen in hypogonadal young men, it has been tempting to recommend treating the andropause with testosterone replacement therapy. There is a true paucity of data concerning the safety and even the efficacy of testosterone replacement therapy in the andropause. While some epidemiologic studies suggest that men who receive testosterone have less cardiovascular disease, a number of similar studies have shown just the opposite. Before clinicians begin to prescribe androgen replacement therapy for a large fraction of the elderly male population, it would be ideal if long-term, multicenter, placebo-controlled trials of testosterone therapy were to be initiated. These trials would allow us to learn more about the natural history of the andropause, and to determine whether this therapy has a salutary effect on bone density, muscle strength, and quality of life without exacerbating prostate or cardiovascular disease.

S48-02

Mitochondrial function and Aging

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Mitochondria are critical for organismal function, but are far more sensitive to environmental insults and the aging process than other cellular systems. Strong evidence links mitochondrial damage to a variety of diseases of aging including Alzheimer's and atherosclerosis. Mitochondrial DNA undergoes damage overtime as a result of recurrent oxidative stress and this leads to organ dysfunction. We recently discovered a novel class of Mitochondrial-Derived Peptides that are encoded from within the mtDNA, and serves as signals related to cell and organismal protection and energy expenditure. The first peptide identified, humanin, is encoded from the 16S rRNA region and has broad protective effects in vivo and in vitro. We recently identified six additional peptides encoded from the 16S Region named small humanin-like peptides or SHLPs, that also have potent activities on physiological functions. Another peptide we discovered is called MOTS-c and is encoded from the 12S rRNA region of the mtDNA, and has insulin sensitizing activity and potent weight-loss inducing abilities. In vitro, MDPs, are capable of protecting cells from a host of insults such as amyloid- in neurons and oxidized-LDL in endothelial cells. MDPs have direct and potent effects on mitochondrial function and cellular respiration and are able to increase mitochondrial copy number and regulate oxygen consumption rates. MDPs have been administered to a variety of animal models of disease and have been shown to delay the onset of atherosclerosis in APOE-KO mice, delay the progression of Alzheimer's and ALS, prevent chemotherapy-induced side effects, and importantly, improve insulin sensitivity in the liver through direct central effects on the hypothalamus (in the case if humanin) and in muscle (in the case of MOTS-c). MOTS-c has the remarkable ability to dramatically prevent weight gain in mice fed a high-fat diet by increasing energy expenditure while maintaining muscle mass. The levels of humanin, SHLP2, and MOTS-c are all reduced in older rodents and humans, and humanin levels correlate with endothelial function and the GH-IGF status. In summary, MDPs are a new class of mitochondrial hormones that have diagnostic and therapeutic potential in human disease especially in aging-related disorders.

S49-01

IGF/IGFBP signalling and cancer

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The insulin-like growth factor (IGF) system plays a major role in growth, development and maintenance of homeostasis in normal cells and also contributes towards proliferation of malignant cells. Any disruption in the IGF system has its implications on growth retardation, atherosclerosis, insulin resistance and cancer. The IGF system is comprised of ligands (IGF-I and IGF-II), cognate receptors (IGF-IR and IGF-IIR), IGF-binding proteins (IGFBPs) and IGFBP proteases. IGF-IR is a cell-surface heterotetrameric tyrosine kinase receptor and binds IGF-I and IGF-II with high affinity and subsequently triggering the intracellular second messenger pathways, including the Mitogen activated protein kinase (MAPK) and Phosphoinositide-3-kinase (PI3K) signaling cascades. IGF-IIR is a single chain receptor identical to the cation independent mannose-6-phosphate (M6P) receptor and binds IGF-II and other M6P containing ligands but does not transduce the signal intracellularly. In addition, IGF-IR can hybridize with insulin receptor (IR) to form a heterodimer composed of one alpha-subunit and one beta-subunit of each receptor (IGF-IR/IR hybrid). IGFBPs 1-6 share a high degree of similarity in their primary protein structure, particularly in their N- and C-terminal regions, which are separated by a variable mid-protein segment. IGFBPs bind IGF-I and IGF-II with high affinity and are essential

for transporting IGFs, prolonging their half-lives and regulating the availability of free IGFs for interaction with IGFRs, thereby modulating the effects of IGFs on growth and differentiation.
Recently, the importance of the IGF system in a variety of cancers has been addressed in large prospective studies by demonstrating a strong correlation between high IGF-I/low IGFBP-3 levels in circulation and increased cancer risk. Due to the ubiquitous nature of the components of the IGF system, targeting specific members of the axis has gained attention over the past decades. The most elaborately investigated component as a therapeutic target for cancer in the system is the IGF-IR and studies have been pursued to inhibit IGF-IR by the administration of monoclonal antibodies and tyrosine kinase inhibitors.
In addition, recent studies have revealed that IGFBPs may have specific biological effects in various cell systems, which are not mediated through interaction with IGFs (IGF/IGF-IR-independent actions). Those IGF/IGF-IR independent effects of IGFBPs occur by IGFBP binding to its putative receptor or several IGFBP binding partners on the cell surface as well as in cytoplasmic and nuclear compartments in variety of cancer cells. These non-IGF partners include integrins for IGFBP-1 and -2; the type V TGF-beta receptor (also known as low density lipoprotein receptor-related protein 1) for IGFBP-3, -4 and -5; retinoic acid receptor for IGFBP-3 and -5; vitamin D receptor for IGFBP-3, -5 and -6; and the retinoid X receptor, NUR77 and the molecular chaperone GRP78 for IGFBP-3.
Importantly, IGFBP-3 is the only IGFBP species regulated by tumor suppressor p53, and is a well-documented potent tumor suppressor as well as a potent anti-metastatic factor. Very recently, we have identified a novel IGFBP-3 receptor (IGFBP-3R, also known as TMEM219), which constitutes a novel cell-death receptor that mediates the proapoptotic effects of IGFBP-3 via activation of specific caspases and suppression of tumor-activated NF-kappa B signaling in a variety of human cancers. This newly identified IGFBP-3 cell death receptor provides the avenue for the IGF/IGF-IR-independent antiproliferative and proapoptotic actions of IGFBP-3. Recent publication provides further solid evidence that IGFBP-3R is indispensable for IGFBP-3's antitumor function by showing that knockdown of IGFBP-3R completely abolishes IGFBP-3's antiproliferative and proapoptotic effects. In addition, we have generated a panel of IGFBP-3R agonistic mAbs acting like IGFBP-3, showing antitumor effects in many different types of cancer cells. These findings clearly demonstrate the IGFBP-3/IGFBP-3R system as a new target and the IGFBP-3R agonists (IGFBP-3 and IGFBP-3R agonistic mAbs) as a new therapy for a variety of human cancer including colon, lung and breast cancer.
It is clear that the biology of the IGF system is complex and each component of the system significantly influences the initiation and the progression of cancers. Our better understanding for IGF/IGF-IR-dependent and -independent signaling and subsequent biological functions of IGFBPs in cancer cells would warrant new diagnostic and therapeutic approaches for human cancers.

S49-02

Autocrine actions of growth hormone in cancer

Peter Lobie

National University of Singapore

Peter Lobie obtained a B.Med. Sci. (Distinction) and MBBS (Medicine First Class Honours) from the University of Queensland in Australia. He was awarded the highest accolade from the University in the form of a University Medal. His postdoctoral work was undertaken at the Karolinska Institute in Sweden where he also obtained a PhD. He has consecutively held faculty positions in Singapore and New Zealand. He was also New Zealand's first chair of Breast Cancer funded by the Breast Cancer Research Trust. He is now is Professor and Senior Principal Investigator at the Cancer Science Institute of Singapore within the National University of Singapore. He is author of over 150 publications and his work is focused on molecular mechanisms of hormone action. Recent emphasis in his laboratory has focused on the capacity of hormones or secreted proteins to initiate or progress cancer and thereby evaluation of individual molecules for their potential therapeutic application.
He is the recipient of multiple local and international awards and has been appointed a Fellow (Academician) of the Royal Society of New Zealand. He was recently bestowed the highest honour awarded to foreigners by the Chinese Government for his contributions to social and economic progress. Prof. Lobie is the inventor on a number of patent families and has been associated heavily with industry during his time in Sweden and later served as a consultant for a number of governmental and pharmaceutical entities. He is the founding scientist of Perseis Therapeutics Ltd and Saratan Therapeutics Ltd, two new entities focused on development of therapeutics to novel cancer target molecules. He is also a founding shareholder in Wuhan Long Ke Ltd. He has served on the editorial boards of Endocrinology and Molecular Endocrinology, among a number of other international journals and also served on the Annual Meeting Steering Committee of The Endocrine Society (USA). He has functioned as a reviewer for more than 50 academic journals and more than 15 local and international granting agencies.

Increasing empirical evidence supports a role of locally produced or autocrine/paracrine human growth hormone (hGH) in the initiation and progression of mammary and other human carcinomas. Tumor expression of hGH is associated with various clinicopathologic parameters in both mammary and endometrial carcinoma and with worse relapse free and overall survival of patients with these cancers. Functionally, autocrine hGH has been demonstrated to stimulate mammary carcinoma cell proliferation and survival enhancing xenograft growth; epithelial to mensenchymal transition with concomitant migration, invasion and metastasis; and resistance to chemotherapeutic agents. Paracrine actions of hGH include modulation of endothelial cell behavior producing enhanced tumor angiogenesis. The functional role of hGH expressed in hepatocellular carcinoma will be discussed as will autocrine hGH utilization of specific miRNAs to regulate oncogenic functions.

S50-01

Patient selection for metabolic and bariatric surgery

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S50-02

Long term metabolic effects of bariatric surgery

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BIOGRAPHY

Shen Bai-yong, male, was born in Oct, 1966. He studied in the Shanghai Second Medical University during 1985 to 1991. He majored in Clinical Medicine, and earned his bachelor degree in 1991. He graduated with distinction. Later, he came postgraduate work and residencies at Shanghai Ruijin Hospital. In 1994, he went to Grenoble University hospital in France, as a foreign intern. During 1996 to 1999, he interned again in Beaujon Hospital of Paris 7th University in France. And then to the HuaXi Medical University in Chengdou, where in 2002 he received a master's degree in hygiene management. He was a senior visiting scholar in the transplant center of Pittsburgh University in America during 2002. In 2006, he received his doctoral degree of clinical medicine in Shanghai Jiaotong University.

As a pioneer in the hepatobiliopancreatic field, he participated in the first split liver transplantation of China in 2002 and the first multiple organ transplantation of Asia in 2004. In 2005, he and his colleagues began to launch a living donor liver transplantation program and have successfully performed 47 cases of LDLT with 0% mortality of donors and 87.6% one-year survival rate of recipients till now. He is also committed to the laparoscopic surgery and Robotic surgery. He has achieved more than 200 laparoscopic hepatectomies, 60 laparoscopic pancreatectomies and 400 robotic hepatobiliopancreatic surgeries (220 pancreatic surgeries included), which keeps leading position in China.

As a member of Chinese Medical Association, he earned many distinguished honors in medical science, including Shanghai Science and Technology Award in 2009 & 2013 (First class), Higher colleges Science and Technology Award in 2013 (First class) and National Science and Technology Award in 2010 (Second class).

S51-01

Redirecting intracellular trafficking patterns of FSH & LH

Tunuguntla Rajendra Kumar

University of Colorado Denver-Anschutz Medical Campus

T. Rajendra Kumar, PhD

Dr. T. Rajendra Kumar is an Edgar Makowski Endowed Professor and Vice-Chair of Research in the Department of Obstetrics & Gynecology at the University of Colorado Denver Anschutz Medical Campus, Aurora, Colorado, United States. He received his Masters degree in Biochemistry (Central University of Hyderabad), Master of Philosophy in Reproductive Biology (Central University of Hyderabad), and PhD in Endocrine Biochemistry (University of Delhi) - all from India. He obtained his postdoctoral training in the Vollum Institute of Advanced Biomedical Research at the Oregon Health Sciences University, Portland. He then moved to Baylor College of Medicine in Houston where he continued his research on mouse developmental genetics and reproductive axis development. At Baylor College of Medicine, he rose to the rank of an Assistant Professor in the Department of Pathology. During 2004-2016, he established his laboratory at the Department of Molecular & Integrative Physiology, University of Kansas Medical Center, Kansas City, KS and rose to the rank of a Tenured Full Professor. During 2014-2016, he served as the Director of Center for Reproductive Sciences, Institute of Reproductive Health and Regenerative Medicine, at the KU Medical Center.

Dr. Kumar's current research efforts are focused on gonadotrope development and molecular genetics of gonadotrope tumors, transcriptional and post-transcriptional regulation of gonadotropin subunit gene expression, gonadotropin secretion, pituitary hormone control of gonad and bone development and physiology. He has received support from NIH for his current research work on pituitary and gonad developmental genetics.

Dr. Kumar published over 80 papers including textbook chapters and invited reviews. His research was published in Nature, Nature Genetics, Cell, PNAS, J Clinical Investigation, Molecular and Cellular Biology, Molecular Endocrinology and Endocrinology. He also co-edited a textbook entitled " Transgenics in Endocrinology". He has been an invited speaker at more than 90 national and international symposia/conferences and various universities/institutes. He served as a Chair, Co-Chair at several of these national/international symposia. He has been an ad-hoc manuscript reviewer for over 50 national and international scientific journals and served as a Senior Editor of Journal of Assisted Reproduction and Genetics, Member on Editorial Boards of Biology of Reproduction and Endocrinology. Currently, he is an Associate Editor of Molecular Reproduction and Development, a member of the Board of Reviewing Editors of Biology of Reproduction and an Editorial Board member of Frontiers in Neuroendocrinology.

Dr. Kumar served as a Member on several NIH Study Section and Special Emphasis panels. He taught extensively in several graduate and post-graduate level courses and as an Instructor at the Frontiers in Reproduction course in Woods Hole, MA. He served as a Director of the Reproductive Physiology Advanced Course at the KU Medical Center. He has trained several graduate students, technicians, and postdoctoral fellows and serves as a member on many graduate student thesis committees. Dr. Kumar received the Kansas-IDeA Network of Biomedical Research Excellence (K-INBRE) Faculty Scholar

Award, KU Medical Center Faculty Investigator Research Award and Thomas L. Noffsinger Investigator Award, Outstanding Reviewer Awards from the Endocrine Society and Elsevier Press Journals for Molecule and Cellular Endocrinology.

S51-02

The central roles of the Tet enzymes in regulation of luteinizing hormone b-subunit gene expression

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The Tet enzymes that catalyze the hydrolysis of 5-methylcytosine (5mC) in DNA to 5-hydroxymethyl cytosine (5hmC) play central and complex roles during development. We show that Tet1 expression is markedly down-regulated with gonadotrope differentiation, concordant with the increased expression of the luteinizing hormone b-subunit gene (Lhb). This Tet1 isoform, which is truncated at its N-terminus due to alternative promoter usage, does not catalyze 5hmC and directly represses the Lhb gene promoter. Its expression is facilitated by Tet2-directed demethylation of a novel distal enhancer, and is repressed by GnRH and estradiol acting at the proximal promoter. The down-regulation of Tet1 during gonadotrope differentiation and following hormonal exposure relieves the inhibition of Lhb, and Tet1 is replaced by Tet2 which catalyzes 5hmC of the methylated DNA to facilitate Lhb expression. Although the Tet1 protein is not detected in the fully-differentiated gonadotropes of mature mice, gonadectomy is followed initially by an increase in Tet1 expression in the proliferating gonadotrope population, which express only low levels of Lhb at this stage; as the effects of the removal of the gonadal feedback escalate, Tet1 levels drop and Lhb levels markedly increase. Our work thus reveals novel epigenetic pathways through which reproduction is regulated and defines Tet1 as a central regulator of gonadotrope differentiation through its effects on Lhb.

S52-01

The role of AIRE in tolerance and autoimmune disease

Georg Hollander

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Autoimmunity is caused by an inappropriate immune response directed against self-components of the host. This aberrant reactivity typically results in tissue damage leading to partial or complete loss of organ function. The enormous clinical diversity is reflective of the complex molecular and cellular mechanisms responsible for the establishment and maintenance of immunological tolerance. Consequently, autoimmunity implies a failure of the regulatory mechanisms that normally prevent such destructive responses. Breakdown of immunological tolerance appears to be the result of a complex interplay between genetic polymorphisms that predispose an individual to develop common autoimmune disorders and several environmental factors such as hormones, infections, and therapeutic agents. Many of these genetic and environmental influences highlight a central role of T cells. However, the precise molecular underpinning that allows T cell tolerance to an individual's own tissue (aka self tolerance) to be established and maintained is still incompletely understood.
Recent progress in understanding how T cells develop in the thymus has provided important insight into the cellular and molecular mechanisms that dictate immunological tolerance to self–antigens. The thymus stromal microenvironment is unique as it promotes the development of naïve T cells with a repertoire purged of vital "Self" specificities and poised to react to injurious "Non-Self". Thymic epithelial cells (TECs) constitute an essential component of that environment as they have the unqiue capacity for the promiscuous expression of transcripts that encode proteins which are normally only detected in differentiated organs residing in the periphery (a.k.a. tissue restricted self antigens, TRA). The molecular regulation of this promiscuous gene expression of TRA in TEC is not yet fully understood but in part dependent on the transcriptional activator AutoImmune REgulator (Aire). Mutations in the gene encoding Aire cause the autoimmune polyendocrine syndrome type-1 (APS-1) as the thymus fails to express a normal TRA repertoire of up to several thousand peripheral (i.e. non-thymic) tissue antigens which consequently results in the maturation and export of autoreactive T cells. Recent insight into the molecular and cellular mechanisms that control TEC development and the cell's unique capacity express almost all protein coding genes of an individual will be presented and discussed.

S52-02

Autoantigens in APS1, diagnostic utility and lessons learned about physiology

Olle Kämpe

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Olle Kämpe MD, PhD is professor and senior consultant in endocrinology at the Karolinska Institutet in Stockholm, Sweden. He holds the Torsten and Ragnar Söderberg endowment professorship in clinical endocrinology since 2014 and was before that professor of molecular medicine at Uppsala University between 1999 and 2014. He is a Fellow of the Royal Swedish Academy of Sciences, and a member of the Nobel Assembly at the Karolinska Institutet. He has participated in several EU-projects of which he coordinated one, EurAPS, dealing with APS-1/APECED. He has identified a number of the autoantibodies in clinical use for Addison's disease and APS-1, including autoantibodies against 21-hydroxylase, side-chain cleavage enzyme, tryptophan hydroxylase and transglutaminase 4. He has initiated the Swedish national registries and biobanks for Addison's disease and APS-1/APECED.

S52-03

Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1)

Maria Luisa Brandi

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MEN1 is an autosomal dominant disorder that is due to mutations in the tumor suppressor gene MEN1, which encodes a 610-amino acid protein, menin. Thus, the finding of MEN1 in a patient has important implications for family members because first-degree relatives have a 50% risk of developing the disease and can often be identified by MEN1 mutational analysis. MEN1 is characterized by the occurrence of parathyroid, pancreatic islet, and anterior pituitary tumors. Some patients may also develop carcinoid tumors, adrenocortical tumors, meningiomas, facial angiofibromas, collagenomas, and lipomas. Patients with MEN1 have a decreased life expectancy, and the outcomes of current treatments, which are generally similar to those for the respective tumors occurring in non-MEN1 patients, are not as successful because of multiple tumors, which may be larger, more aggressive, and resistant to treatment, and the concurrence of metastases. The prognosis for MEN1 patients might be improved by presymptomatic tumor detection and undertaking treatment specific for MEN1 tumors. Thus, it is recommended that MEN1 patients and their families should be cared for by multidisciplinary teams comprising relevant specialists with experience in the diagnosis and treatment of patients with endocrine tumors.

S53-01

Non-classical thyroid hormone action mediated by thyroid hormone receptor

Lars C Moeller

Universitat Duisburg-Essen

S53-02

Central effects of thyronamines and thyroacetic acids

Laura Raimondi

University of Florence

S54-01

Genetics of kallmann syndrome

Weijun Gu

The PLA General Hospital

Dr. Gu graduated from the Chinese PLA General Hospital Medical School, and obtained PhD degree in Endocrinology and Metabolism. She is now the deputy chief physician, associate professor and master tutor in the Department of Endocrinology, Chinese PLA General Hospital. Dr. Gu has been engaged in clinical work regarding to pituitary, gonadal, adrenal gland, diabetes and other endocrine and metabolic diseases for long time. Until now, she has published more than 30 papers as the first author, and undertook several projects funded by the Beijing Natural Science Foundation, the Chinese Medical Association, the International Exchange Funds, etc. She is now assigned as the youth deputy director of Chinese Endocrinologist Association (CEA) of Chinese Medical Doctor Association (CMDA), the youth committee member of Diabetes Association of Beijing Medical Association (BMA), the youth editorial board member of International Journal of Diabetes, the editorial board member of Drug Evaluation, and the corresponding editorial board member of Chinese Journal of Endocrinology and Metabolism.

Kallmann syndrome, a form of idiopathic hypogonadotropic hypogonadism, is characterized by developmental abnormalities of the reproductive system and abnormal olfaction. Despite association of certain genes with idiopathic hypogonadotropic hypogonadism, the genetic inheritance and expression are complex and incompletely known. In the present study, seven Kallmann syndrome pedigrees in an ethnic Han Chinese population were screened for genetic mutations. The exons and intron–exon boundaries of 19 idiopathic hypogonadotropic hypogonadism (idiopathic hypogonadotropic hypogonadism)-related genes in seven Chinese Kallmann syndrome pedigrees were sequenced. Detected mutations were also tested in 70 sporadic Kallmann syndrome cases and 200 Chinese healthy controls. In pedigrees 1, 2, and 7, the secondary sex characteristics were poorly developed and the patients' sense of smell was severely or completely lost. We detected a genetic mutation in five of the seven pedigrees: homozygous KAL1 p.R191ter (pedigree 1); homozygous KAL1 p.C13ter (pedigree 2; a novel mutation); heterozygous FGFR1 p.R250W (pedigree 3); and homozygous PROKR2 p.Y113H (pedigrees 4 and 5). No genetic change of the assayed genes was detected in pedigrees 6 and 7. Among the 70 sporadic cases we detected one homozygous and one heterozygous PROKR2 p.Y113H mutation. This mutation was also detected heterozygously in 2/200 normal controls and its pathogenicity is likely questionable. The genetics and genotype–phenotype relationships in Kallmann syndrome are complicated. Classical monogenic inheritance does not explain the full range of genetic inheritance of Kallmann syndrome patients. Because of stochastic nature of genetic mutations, exome analyses of Kallmann syndrome patients may provide novel insights.

S54-02

Reversible Reproductive Dysfunction in Hypogonadotropic Hypogonadism

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Hypogonadotropic hypogonadism (HH) is a condition defined by the concomitant lowering of circulating gonadotropins and gonadal hormones, of either gene-linked or acquired basis. Congenital forms of HH, defined by defective GnRH neuronal development or secretion, are commonly defined by profound phenotypes of lack of puberty and infertility, which were usually thought to be life-long. Clinical evidence, however, has now documented that, despite sharing common genetic determinants with permanent cases, some forms of congenital HH are reversible, often after cessation of hormonal replacement treatments. Yet, the substrate and underlying mechanisms for this phenomenon remain unfolded. Likewise, the determinants for relapse from such reversion, which is often observed, remain unknown. In addition, acquired forms of HH of non-genetic origin exist. These are more frequent than congenital HH and include conditions of central hypogonadism linked to metabolic deregulation, ranging from chronic subnutrition or strenuous exercise to morbid obesity, as well as to hormonal perturbations, such as hyper-prolactinemia. These acquired forms of HH are commonly reversible, as far as the etiological cause is eliminated. While the mechanisms underlying this phenomenon are likely diverse and have not been completely elucidated, solid experimental evidence suggests a major pathophysiological role of the hypothalamic Kiss1 system, an essential up-stream regulator of GnRH neurons, in the generation (and eventual reversion) of acquired forms of HH of metabolic or hormonal origin. The translational relevance of these experimental data, as to explain different forms of HH and their eventual reversibility, will be critically discussed in this presentation.

S54-03

FGFR mutations in congenital hypogonadotropic hypogonadism

Nelly Pitteloud

University of Lausanne

S55-01

New somatostatin analogues

Maria Fleseriu

Oregon Health Science University, Northwest Pituitary Center

Maria Fleseriu, MD, FACE is a Professor of Medicine and Neurological Surgery and Director of the Northwest Pituitary Center at Oregon Health & Science University. Dr. Fleseriu received her medical degree from the University of Medicine and Pharmacy, Timisoara, Romania and completed an endocrinology fellowship with a focus on pituitary disorders. She pursued additional training in the US: a residency in internal medicine at Case Western Reserve University and an endocrinology fellowship at Cleveland Clinic.

Dr. Fleseriu has a long-standing clinical and research interest in the pathophysiology and treatment of pituitary and adrenal disorders. She is a frequent guest speaker at national and international meetings on various topics related to the treatment of pituitary tumours (especially Cushing's disease and acromegaly), is the principal investigator in numerous clinical trials, and has authored over 100 manuscripts and book chapters.

She currently chairs the Endocrine Society Guidelines Committee and the Hypopituitarism task force and she is on the Board of Directors of the Pituitary Society. She is also a member of the Endocrine Society Knowledge Task Force and the Clinical Endocrinology Update Steering Committee, and serves on several committees for the American Association of Clinical Endocrinology. Dr Fleseriu is Consulting Editor for Endocrinology Clinics of North America, Chief Editor of Pituitary Endocrinology for Frontiers in Endocrinology, Senior Editor for Endocrinology, Diabetes and Metabolism CR and a member of the editorial board of many journals, including Pituitary, Endocrine, and Reviews in Endocrinology and Metabolism.

Medical therapy has an increasingly important role in the treatment of patients with acromegaly. Somatostatin receptor ligands (SRLs) are considered the standard medical therapy, either after surgery or as a first-line therapy when surgery is deemed ineffective or is contraindicated. Octreotide and lanreotide are first-generation SRLs and are effective in ~20%-70% of patients. Pegvisomant, a growth hormone receptor antagonist, controls insulin-like growth factor 1 in 65%-90% of cases. Consequently, a subset of patients (nonresponders) requires other treatment options. Drug combination therapy offers the potential for more efficacious disease control. However, the development of new medical therapies remains essential. Here, emphasis is placed on new SRLs to control acromegaly.

Pasireotide, a novel SRL, has high-affinity for sst1, sst2, sst3, and particularly sst5 . A 1- year, phase III study (n=358) demonstrated the superiority of pasireotide 40/60 mg over octreotide 20/30 mg in acromegaly. Biochemical control (normal IGF-1 and GH<2.5 ng/dL) on pasireotide was 35.8% vs. 20.9% octreotide. Interestingly, IGF-1 levels were significantly lower with pasireotide. However, response to both SRL's was overall lower than expected. Lack of dose- uptitration (which was not mandatory) in almost 1/3 of patients not achieving control can partially explain it. Furthermore, control in patients who had surgery has been higher, but remarkably, approximately 60% of patients did not undergo surgery. Pasireotide induced hyperglycemia related AEs were 56.7% versus

21.7% on octreotide. A 24 -weeks study (198 patients) randomized patients resistants to the available SRLs to 40 mg /60 mg of pasireotide or to continue octreotide or lanreotide. 15% of patients in the 40 mg and 20% in the 60 mg group achieved biochemical control. Pasireotide also induced further tumor shrinkage and greater improvements in symptoms, but hyperglycemia related AEs were also double in the pasireotide group with antidiabetics initiated in 38% of patients. Studies in healthy volunteers suggest that pasireotide-associated hyperglycemia is related to decreases in insulin secretion and incretin hormone responses, without changes in hepatic/peripheral insulin sensitivity. Baseline glucose may predict hyperglycemia occurrence after pasireotide treatment, and careful monitoring of glycemic status and appropriate treatment is required. A precise definition of patients with acromegaly who will derive the greatest therapeutic benefit from pasireotide LAR remains to be established. Lastly, new potential delivery modalities (octreotide) and novel therapies and are summarized.

Oral octreotide appears to be an attractive option for patients biochemically controlled with injectable SRLs. A newly developed transient permeability enhancer to improve the absorption of pharmacologically active drug has been shown to increase the intestinal absorption of an oral formulation of octreotide within 1 hour of administration. A large, multicenter, Phase III study showed biochemical normalization in 62% of cases after switching from injectable SRLs (from 88.7% at the baseline visit while on injectable SRLs). The effect was durable, and 85% of subjects initially controlled on oral octreotide maintained the response for ~1 year. GH levels were reduced compared with baseline and acromegaly-related symptoms improved. Approximately half of the patients did require >40 mg to maintain response. Interestingly, the dose of injectable SRLs was not a good predictor of responsiveness. Over 70% of patients on low- or mid-dose injectable SRLs responded to capsules, but half of the patients on high-dose injections were also responders after switching to oral capsules. As expected, the safety profile was similar to that of other SRLs. Most adverse events occurred at the beginning of treatment. Gastrointestinal adverse events were transient and mostly resolved within 2 weeks.

Octreotide fluid crystal (FC) is a long-acting octreotide formulation that is based on a FC delivery system. Octreotide is delivered such that both rapid onset and long-acting release are provided. In healthy volunteers, octreotide FC provided greater bioavailability with a more rapid onset and similar duration of effect compared with octreotide LAR. The FC formulation offered enhanced convenience as it is supplied in a prefilled syringe with a thin needle.

An open label Phase II study of Lanreotide long acting prolonged formulation (PRF) subcutaneous injection is ongoing at doses of either 180mg or 270mg or 360mg.

Somatoprim (COR-005) is a multireceptor SRL that binds sst2, sst4 and sst5. In vivo studies showed an additional 40% response in patients with pituitary adenomas that were resistant to octreotide and less of a hyperglycemic effect since insulin-suppressing activity is less potent. A Phase II study showed lower GH secretion with reduced effects on insulin secretion and glucose levels as compared with octreotide in two single ascending dose in patients with acromegaly

BIM-065, a novel 2nd generation somatostatin-dopamine chimeric compound, 'dopastatin', showed a statistically significant greater ability to suppress GH in tumors from patients partially responsive to SRLs in a dose-related manner compared with either octreotide, or the combination of octreotide and cabergoline.

Treating patients with acromegaly can be extremely challenging, and inadequate disease control may lead to serious consequences. Novel pharmaceutical therapies, as well as new potential delivery modalities, including the first oral octreotide therapy are on the horizon and show early promise.

S55-02

Antisense oligonucleotide therapy for acromegaly

Peter Trainer

The Christie NHS Foundation Trust

Antisense oligonucleotides (ASOs) are single-stranded synthetic oligonucleotides that have been developed as therapeutic agents that block protein synthesis from messenger ribonucleic acid (mRNA) by binding the target mRNA through sequence-specific Watson–Crick base-pair interactions to inhibit gene expression. ATL1103 is a second generation, antisense oligomer targeted at the human GHR. It comprises 20 nucleotides with a phosphorothioate backbone and 2'-O-methoxyethyl modifications of the terminal five nucleotides at each end which in combination increase its plasma half-life and affinity for the mRNA. Post-Hybridisation RNaseH degradation results in inhibition of GHR translation. In pre-clinical primate studies, ATL1103 has been shown to reduce GHR mRNA levels in the liver and serum IGF-I. Phase 1 studies in healthy male volunteers demonstrated a fall in serum IGF-I.

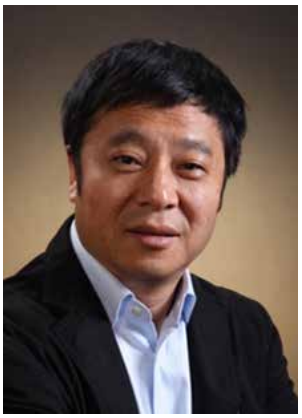
A phase 2, randomised, open-label, parallel group study of the safety, tolerability, and efficacy of subcutaneous administered ATL1103 in adult patients with acromegaly demonstrated it to be well tolerated with mild to moderate injection site reactions being the most common drug-related AE. Four SAEs were reported, of which three occurred in a single patient, but none were felt to be study drug related. There was a significant fall in serum IGF-I of 26% by week 14 with 200 mg twice weekly (577 ± 198 v 411 ± 174 ng/ml (mean ± SD).

S55-03

Generating β Cells from pluripotent stem cells

Hongkui Deng

Stem Cell Research Center, Center for Life Sciences, Peking University



Hongkui Deng is a professor of cell biology and a principal investigator at the Center for Life Sciences at Peking University. He is also the director of the Peking University Stem Cell Research Center.

Biography

Hongkui Deng earned his B. Sc.in Cell Biology from Wuhan University and his Ph.D. in immunology from the University of California, Los Angeles. From 1995 to 1997 he was an Aaron Diamond Postdoctoral Fellow with Dan R. Littman at the NYU School of Medicine's Skirball Institute, where he identified major co-receptors responsible for HIV entry into cells. From 1998 to 2000, Hongkui was the director of molecular biology at Viacell Inc. working on ex vivo expansion of human hematopoietic stem cells.

Hongkui Deng was awarded the prestigious Cheung Kong Scholarship in 2000 and became a professor at Peking University in 2001.

Since 2013, he has been the director of the Peking University Stem Cell Research Center. Professor Deng's research focuses on somatic cell reprogramming and lineage specific differentiation of human pluripotent stem cells. His lab also explores chemical biological approaches for manipulating cell fate and function. His group was the first to report a chemical approach to induce pluripotent stem cells. He has been awarded several awards and honors including the Tan Jiazhen Life Science Award in 2014. He also serves on a number of editorial boards including Cell, Cell Stem Cell, Stem Cell Report, and Cell Research. Professor Deng was elected to the ISSCR Board of Directors in 2010 and re-appointed for a second term in 2013.

Human pluripotent stem cells represent a potentially unlimited source of functional pancreatic endocrine lineage cells. We established a highly efficient approach to induce human embryonic stem (ES) cells and induced pluripotent stem (iPS) cells to differentiate into mature insulin-producing cells in a chemical-defined culture system. The differentiated cells obtained by this approach comprised nearly 50% insulin-positive cells as assayed by flow cytometry analysis, which released insulin/C-peptide in response to glucose stimuli in a manner comparable to that of adult human islets. Most of these insulin-producing cells co-expressed mature beta cell-specific markers such as NKX6-1 and PDX1, indicating a similar gene expression pattern to adult islet beta cells in vivo. In this study, we also identified several signaling pathways that regulate the maturation of pancreatic progenitor cells into functional beta cells. This work provides a new model to study the mechanism of human pancreatic specialization and maturation in vitro, and enhances the possibility of utilizing patient-specific iPS cells for the treatment of diabetes.

S56-01

Adjunct therapy with GLP-1 analogues in type 1 diabetes

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Despite multiple daily insulin injections and improved pharmacokinetic profiles of exogenous insulin, achieving and maintaining good glycaemic control in patients with type 1 diabetes is often challenging. Nevertheless, the only current approved treatment for type 1 diabetes is insulin therapy. Therefore, combination of insulin with other glucoselowering therapies, that are used for treatment of patients with type 2 diabetes, is of great interest in type 1 diabetes.

In type 2 diabetic patients, the combination of GLP-1 receptor agonists with insulin, induce weightloss, reduce insulin dose and improve glycaemic control with no increased risk of hypoglycaemia.

Mechanistic studies have shown, that GLP-1 increases insulin secretion in type 1 patients with residual beta cell function and that glycaemic control is improved through a reduction in glucagon secretion and gastric emptying rate in patients with as well as without residual beta cell function.

In clinical studies however, the effect on glycaemic control is less clear.

Several short term uncontrolled small scale "proof of concept" studies and retrospective analyses, have consistently shown, that treatment with GLP-1 receptor agonists in combination with insulin reduces insulin dose and body weight with reduced or unaltered HbA1c as well as risk of hypoglycaemia. However, two newer placebo controlled, randomised longer term studies showed similar reductions in HbA1c between placebo and liraglutide treated patients and no differences in occurence of hypoglycaemia. Nevertheless, reductions in insulin dose and body weight were reported in both studies.

In the large scale multinational ADJUNCT ONE and TWO studies recently presented, liraglutide treatment gave rise to reductions in HbA1c, insulin dose and body weight and a larger proportion of patients reaching a reduction in HbA1c of > 1.0% with no severe hypoglycaemia. However, liraglutide also increased occurrence of symptomatic hypoglycaemia and hyperglycaemic ketosis which may limit the clinical utility of liraglutide for treatment of type 1 diabetes.

Currently, GLP-1 receptor agonists are therefore not approved for treatment of patients with type 1 diabetes. Further research on the effect of GLP-1 receptor agonists in patients with new onset type 1 diabetes and the effect of short as well as longacting GLP-1 receptor agonists in patients with established disease, are warranted.

S56-02

Diagnosis of type 1 diabetes across all ages: implications on management

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Type 1 diabetes (T1D) is a disease characterised by a different age of onset including insurgence in childhood, adolescence and adulthood. The disease process may differ not only in the age at diagnosis but also in clinical presentation, varying from severe metabolic derangement to simple hyperglycaemia. C-peptide secretion is currently the only available clinical biomarker to measure residual β-cell function in T1D. The natural history of C-peptide decline after diagnosis varies considerably dependent upon several variables. Thus, the shape of C-peptide decline over time from T1D onset in relation to age at diagnosis, the haemoglobin A1c (HbA1c) level and the insulin dose have been investigated in this respect. In a very large series of patients with T1D (n = 3929) we demonstrated that a positive correlation exists between the age at diagnosis and the fasting C-peptide (FCP) with a more rapid decline of β-cell function in the very young patients (< 5 years of age). On the contrary, adults with T1D tend to show higher C-peptide values both at onset and 1 year later, with a decline of C-peptide less rapid when compared to children. We also showed a log-linear decline of FCP following diagnosis. This effect implies a predictable decline in the process that destroys β-cell mass, although it should be noted that patients diagnosed >18 years of age show no decline of FCP in the first year after diagnosis. These data may be instrumental for the design of clinical trials using C-peptide values as the primary end-point for the effect of a given treatment.

Increased body weight and increased insulin demand are relevant parameters associated with a more rapid disease progression after diagnosis in the age group 10–18 years (adolescence). The relationship between body weight and β-cell loss may have clinical implications. The fact that β-cell dysfunction is much more severe in this group of patients and much less severe in the oldest group, suggests

the negative role of counter regulatory hormone secretion associated with puberty in determining β-cell loss. We are not able to define whether insulin resistance or adiposity are the main determinants of the β-cell decline during the first year after diagnosis; however results of our studies may suggest that, especially in individuals diagnosed during adolescence, intervention to reduce insulin resistance or drugs aimed at improving insulin sensitivity may be a possible component of therapy aimed at preventing the loss of β-cells. In addition, if the association between BMI and more rapid C-peptide decline is a result of pro-inflammatory processes associated with obesity, then treatments aimed to reduced inflammation would also be beneficial. These observations have significant consequences for trials investigating novel treatments for T1D at onset. In recent years several treatment modalities have been studied and showed modest results in terms of efficacy on residual β-cell function likely because patients were not carefully selected according to their age of onset and/or C-peptide levels. It is known that subgroups of T1D patients exist who respond differently to immuno-intervention, with those patients diagnosed in the adult age being more responsive to treatment to protect β-cell function.
In conclusion, the observation that the decline of C-peptide after diagnosis varies among different age patient groups and even between males and females, implies that strict age grouping is necessary in patient selection for trials aimed to prevent β-cell loss. It is also of interest that in some T1D patients after a few years of disease progression, C-peptide is still measurable, suggesting that such patients may be still target of an immune intervention to protect residual β-cell function.

S57-01

FGF21 Analogues

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S57-02

Effect of berberine on glucose and lipids in diabetes

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Hong Jie, Female, Ph.D., Doctoral supervisor, Chief physician, Professor, Deputy Director of Department of Endocrine and Metabolic Diseases, Shanghai Jiaotong University Affiliated Ruijin Hospital, Committee Member of the 8th Chinese Medical Association Diabetes Branch, Vice Chairman of the 7th Shanghai Medical Association Diabetes Branch, Committee Member of division of basic science in endocrinology of Shanghai Medical Association, Editorial Board Member of "Chinese Journal of Endocrine and metabolic Diseases", "Shanghai Medical Journal", and "Journal of diabetes" , Editorial Board Corresponding Member of "Chinese Journal of diabetes".
Professor Hong has long been engaged in basic and clinical research of obesity and metabolic syndrome. She took charge of 3 general programs of the National Natural Science Foundation of China, 1 Project of National Science-technology Support Plan, 1 sub-project under Special Research Foundation of the Ministry of Health and 1 "new hundred people" project of Shanghai Health System. In the past five years, Professor Hong has published more than 30 SCI paper as the first or corresponding author in Diabetes Care, International Journal of Obesity and so on. Her research findings has won the 1st prize in Shanghai Medical Science and Technology Award, 2nd prize in Shanghai Science and Technology Progress Award and 3th prize in Chinese Medical Science and Technology Award and other awards.

Berberine, a natural plant alkaloid isolated from the Chinese herb, is usually used for diarrhea as antibiotic and antivirus. Recently its potential glucose and lipid lowering effect has been noted. In our study, we found that, compared with placebo, berberine had a potent glucose-lowering effect by significantly reducing fasting and post load plasma glucose and HbA1c at 3 months. Furthermore, significant reductions of serum total cholesterol, triglycerides and low-density lipoprotein-cholesterol were also observed in these patients. The precise mechanism of berberine in glucose and lipid lowering action has not been fully elucidated. BBR could up-regulate LDLR by activating ERK and inhibiting PCSK9, reduce lipid synthesis and activate the thermogenic of adipose tissue by activating AMPK. It could decrease insulin resistance by inhibiting PTP1B and mTOR. It also acts through gut microbiota regulation. BBR has been shown to reduce glucose and lipid levels by participating in adipose autophagy. Therefore it may have multi-target effects in regulating glucose and lipid metabolism.

S58-01

Gut microbiota

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Postdoc training: Vanderbilt University Medical Center, Nashville, TN, United States
Research Interests: The role of mTORC2 regulates functional β cell mass. Human gut microbiome and host metabolic health. Multiomics study of Type 2 Diabetes .
Awards:
2006 Diabetes Hong Kong Presidential Awards in 4th International HUAXIA (Taiwan Hong Kong & Mainland China) Congress of Endocrinology
2009 69th Scientific Sessions of America Diabetes Association meeting, Young Investigator Travel Grant Award
2012 Young Investigator Award of China Group on Insulin Secretion (CGIS)
Grants and Fellowships:
973 Project co-investigator, 2015
Natural Science Foundation of China 2012,2017
Shanghai Committee of Science and Technology Grant 2013
Shanghai Pujiang Program 2012
Publications: Academic studies published on journals like Endocrinology, Diabetes and Cell Metabolism. In 8 SCI papers, is marked as First and Corresponding Author.

Antidiabetic medication was recently shown to modulate the composition of the gut microbiota, but the biomedical significance is unknown. We conducted a clinical trial on naive type 2 diabetes patients to compare the impact of two oral antidiabetic drugs commonly prescribed in China: Acarbose, an α-glucosidase inhibitor, and a sulfonylurea, Glipizide, on the intestinal microbiota. Deep metagenomic shotgun sequencing showed Acarbose modulated the intestinal microbiota more pronouncedly than Glipizide. Acarbose induced enrichment of Bifidobacterium and Lactobacillus with concomitant depletion of Bilophila wadsworthia and Clostridium bolteae. Acarbose treatment decreases the abundance of genes involved in mucus degradation and formation of secondary bile acids resulting in an increased ratio of plasma primary and secondary bile acids with a concurrent improvement in insulin sensitivity. Importantly, the Acarbose-induced changes in gut microbiota were correlated with host metabolic features that were dependent on the composition of the gut microbiota prior to initiation of treatment. This finding indicates that the gut microbiome may determine the therapeutic effect of oral antidiabetic drugs and that analysis of baseline microbiomes may be used to stratify patients prior to treatment, thereby personalizing diabetes medication.

S58-02

Virus-induced obesity

Richard Atkinson

Richard L. Atkinson, M.D. graduated from the Virginia Military Institute and the Medical College of Virginia, Richmond. He took residency and fellowship training in Endocrine-Metabolism at UCLA Harbor General Hospital, Torrance, California, and fellowship training in Endocrine-Metabolism at Walter Reed Army Hospital. He has been on the faculty of the University of Virginia; University of California, Davis; Eastern Virginia Medical School; and the University of Wisconsin, Madison, where he is Emeritus Professor of Medicine and Nutritional Sciences. He currently is Affiliate Clinical Professor of Internal Medicine at Virginia Commonwealth University; Adjunct Professor of Molecular Medicine and Drug Research, University of Karachi, Pakistan; Visiting Professor of Molecular Medicine, Karolinska Institute, Stockholm, Sweden; Chief Scientific Officer for Obesity PPM, Arlington, VA; Executive Director of the Virginia Obesity Research Institute; Medical Director, Veracis Laboratory; and President of Obetech, LLC, all of Richmond, VA. He is Editor of the International Journal of Obesity and of Nutrition and Diabetes; Past President and Co-Founder of the American Obesity Association, Past President of the North American Association for the Study of Obesity, and Past President of the American Society for Clinical Nutrition. NAASO-The Obesity Society established the annual Richard Atkinson-Judith Stern Public Service Award in 2006 to honor his service to the field of obesity and he received the 2014 Stunkard Lifetime Achievement Award from TOS. Dr. Atkinson has been a consultant to the National Institutes of Health, National Academy of Sciences, US Department of Agriculture, Department of Defense, Department of Veterans Affairs, Food and Drug Administration, Federal Trade Commission, and numerous companies and foundations. He has been involved in obesity research and treatment for over 40 years. He is interested in obesity policy and has advocated for young investigator programs nationally and internationally. His research interests include causes and treatments of obesity, particularly obesity drugs and obesity surgery. Recently, his research has focused on virus-induced obesity. He and his research group demonstrated that a human adenovirus (Adv36) produces obesity in animals and is associated with obesity in humans. Dr. Atkinson has over 200 publications and over 250 abstracts in the medical literature.

The prevalence of obesity began to increase dramatically starting about 1980 in most countries of the world. Environmental factors must be responsible for this epidemic of obesity as genetic factors could not change so quickly. Many clinicians, scientists, government officials, and the lay public believe that changes in behavior, increased portion sizes, fast foods, sugar sweetened beverages, and labor saving devices are responsible. Public policies affecting these factors have been put into place, but sadly, have been ineffective in stopping the rise in obesity. Because this epidemic has occurred in both developed and developing countries and these factors vary dramatically across countries, other explanations for the epidemic are more likely. Eight viruses have been shown to increase adiposity in animals but for human obesity, attention has focused on human adenoviruses (Adv). Adv36, Adv37, and Adv5 have been

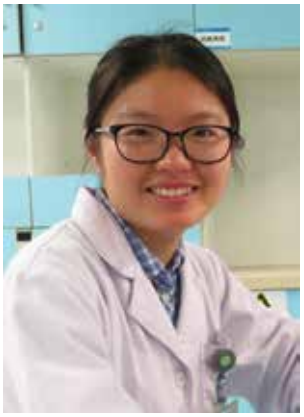
shown to cause obesity in animals, but only Adv36 has been associated consistently with human obesity. Experimental infection of chickens, mice, rats, and monkeys with Adv36 causes obesity in a high percentage of animals, including 100% of monkeys. Visceral or total adipose tissue mass increased 50% to >100% in chickens and mice and about 70% in monkeys. Humans cannot be infected experimentally, but the presence of Adv36 antibodies in serum or Adv36 DNA in tissue are evidence of past infection. Studies in multiple countries by multiple investigators have supported the hypothesis that Adv36 causes human obesity. An average of about 30% of obese adults and children has been shown to have Adv36 antibodies, compared to about 10%-20% of non-obese. However, the prevalence of Adv36 infection varies widely, from only 6% in Belgium/Holland to 65% in Italy. In most studies that have been published, there is a correlation of Adv36 infection and body weight or BMI, or the prevalence of infection has been higher in obese compared to lean individuals. The association of Adv36 infection and obesity is stronger and more consistent in children, perhaps because antibodies decrease over time and may fall below the threshold for a positive assay. Since children likely have been infected more recently, their antibody titers are more likely to still be elevated compared to adults. Almost all of multiple studies involving over 3000 children from China, Czech Republic, Korea, Poland, Sweden, Turkey, and the USA have shown that the prevalence of Adv36 infection in overweight and obese children is greater than in lean children. Gabbert et al found that obese children who were Adv36-positive weighed 16.1 kg more than obese children who were Adv36-negative ($p < .01$). The initial study of Adv36 in adults showed a prevalence of infection of 30% in obese adults and 11% in lean. In the total population, the BMI of infected individuals was 9 BMI units higher than in the non-obese ($p<.001$). Twenty-six twin pairs discordant for Adv36 antibodies were compared and the infected twins had a significantly higher BMI and percent body fat. Although a few studies are negative, two meta-analyses have confirmed that Adv36 is associated with obesity in humans. The mechanisms by which Adv36 causes obesity are not completely identified, but appear to be due to peripheral effects on adipocytes by the E4orf1 gene of Adv36. Adv36 is a upper respiratory virus that produces an intense viremia with exposure of most tissues of the body. Adv36 DNA, but not live virus, may be found in multiple tissues months after infection in animals. In several non-respiratory tissues Adv36 DNA initiates a cascade of molecular changes that enhance production of enzymes and transcription factors particularly in the glucose handling and lipid pathways. Glucose receptors in the cell membrane of adipocytes are up-regulated via the Ras pathway, independent of insulin. Fatty acid synthase (FAS) mRNA also is up-regulated and the combination of increased glucose transport into the cells and production of fatty acids by the FAS leads to accumulation of lipids within the cells. The PPAR-ɣ pathway is stimulated, which results in recruitment of new adipocytes from adult stem cells and preadipocytes in the adipose tissue. Thus, both cell size and cell number are increased. The gene in Adv36 responsible for this effect is the E4orf1 gene. When this gene is blocked, the adiposity effects goes away; and when E4orf1 is cut out and transfected via lentivirus, this reproduces the Adv36 adiposity effect. Currently there are no drugs available for treatment of Adv36-induced obesity, although Rathod et al showed that cidofovir, an injectable, fairly toxic anti-HIV drug, can block Adv36 gene expression. Na et al reported that an Adv36 vaccine prevented the accumulation of adipose tissue in mice. Research is needed to identify anti-viral agents that block Adv36-induced obesity and for commercialization of the vaccine against Adv36.

S59-01

PPAR beta/delta in beta cell apoptosis

Lizhi Tang

West China Hospital of Sichuan University



Lizhi Tang, MD, Ph.D, is an endocrinologist at West China Hospital of Sichuan University and an instructor of Medicine at West China School of Medicine. Dr. Tang received her MD in Clinical medicine from Chongqing Medical University. She received her Ph.D. in endocrinology from Sichuan University and Ph.D training in the Section of Molecular and Cellular Physiology at the Joslin Diabetes Center.

One of the key factors responsible for the development of type 2 diabetes is the free fatty acid-induced lipotoxic apoptosis of β cells. The peroxisome proliferator-activated receptor δ (PPARδ) is a member of the nuclear hormone receptor superfamily and is activated by fatty acids (FAs) and FA derivatives in non-β-cells. All members of the PPAR family are expressed in pancreatic β-cells, but investigations of PPARδ in β cells are rare. Our group found that activation of PPARδ can up-regulated fatty acid oxidation (FAO) and energy uncoupling genes of mitochondria; attenuated palmitate-induced ER stress by promoting fatty acid oxidation; alleviated mitochondrial swelling; reduced basal insulin secretion; therefore protect pancreatic β cells against lipotoxic apoptosis; we also demonstrated that the underlying mechanism can be mediated by raising expression of GLP-1R. These data may ultimately result in the identification of additional therapeutic targets for the use of PPARβ/δ agonists in the treatment of T2D.

S59-02

Beta-to-PP cell dedifferentiation as a mechanism of pancreatic beta-cell failure in type 2 diabetes

Yoshio Fujitani

Institute for Molecular and Cellular Regulation, Gunma University

Yoshio Fujitani, MD, PhD
Professor, Laboratory of Developmental Biology and Metabolism
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Persistent hyperglycemia decreases pancreatic β-cell function and survival. As a possible explanation for the reduced β-cell mass, previous reports suggested that non-β cells are increased in obese diabetic mice, although the origin of these cells remains to be elucidated. In this study, we investigated whether persistent hyperglycemia contributes to the increase in non-β cells, and whether this isdue to the fate conversion of β cells. We employed genetically non-diabetic and lineage traceable mice, and fed them a high fat diet and treated them with a low dose of streptozotocin. The mice became hyperglycemic and obese, and their non-β cells were significantly increased similarly to that of the genetically obese diabetic mice. Interestingly, the increased pancreatic polypep-

tide (PP)-producing cells were found to originate from the pre-existing β cells. The expression of β-cell-specific transcription factors including pancreas duodenum homeobox gene 1 (PDX1), Nkx6.1, and MafA was downregulated in our diabetic mice. By the suppression of PDX1 in insulinoma cells and in heterozygous PDX1 mutant mice, we demonstrate the possibility that persistent hyperglycemia can induce β-to-PP cell transdifferentiation in the adult pancreas by the attenuation of the essential β-cell transcription factor PDX1. We also provide a genetic evidence that PP cell is likely to represent a progenitor of beta cell. Taken together, de-differentiation of beta cells might be a mechanism of beta-cell failure in type 2 diabetes.

S60-01

Dysregulated Metabolism, the Microbiome and Cancer

Evan Simpson[1,2], Kristy Brown[1]

1Hudson Institute of Medical Research, Melbourne
2Centre for Reproductive Health, University of Edinburgh

Professor Evan Simpson is a world leader in the field of estrogen biosynthesis. His work has focused on the study of aromatase, the enzyme responsible for oestrogen biosynthesis. His group was the first to clone the gene encoding aromatase, and to show that tissue-specific regulation was under the control of tissue-specific promoters. His research led to the concept that oestrogen action in post-menopausal women is due to local production in sites such as the breast, bone and brain. This has led to the search for drugs for breast cancer therapy which specifically inhibit aromatase expression in the breast but spare other sites where it serves a critical role, such as in the bone, brain and blood vessels. Professor Simpson's work also led to the creation of the first aromatase knockout (ArKO) mouse, which is a model of oestrogen insufficiency that compares with the phenotype of humans with natural mutations in aromatase. This resulted in the discovery of new and unexpected roles for oestrogens in both males and females. In particular, the role of oestrogens in the maintenance of bone metabolism in men and the role of oestrogens in the regulation of energy homeostasis in both sexes are among these discoveries. His current research is focused on the role of oestrogen in several important health conditions, including obesity, diabetes, osteoporosis and, of course, breast cancer.

There is increasing evidence that metabolic flux is a driver of gene expression rather than a follower, leading Hanahan and Weinberg to state that metabolism should be considered as one of the Hallmarks of Cancer (Cell, 2011). In line with this it is apparent that the dysregulated metabolism which characterises the Metabolic Syndrome gives rise to increased risk of a number of cancers including those of the intestine, endometrium and breast. Thus, for example, a BMI of greater than 30 results in a 2-fold increase in breast cancer in postmenopausal women, and the risk increases with increased obesity. The composition of the gut microbiome is influenced by diet, and consumption of a high-fat diet alters the population of gut bacteria. This gives rise to increased production of local and systemic inflammatory mediators as well as fatty acids, thus driving obesity and increasing the risk of insulin resistance and potentially tumorigenesis. One important product of gut flora metabolism is acetate. Recent studies have indicated that acetate is an important fuel for breast tumor growth, especially under hypoxic conditions (Shug et al. Cancer Cell 27: 57-71, 2015). Acetate is formed primarily by the gut flora, but an important source is also ethanol which is converted to acetate in the liver. Following conversion to acetyl coenzyme A, in addition to serving as a substrate for lipid synthesis, acetate is also potentially important as a co-substrate for acetyl transferases involved in epigenetic modification of histone H3 tails.
Obesity is regarded as a low-grade inflammatory condition associated with increased location of M1-type macrophages to the adipose tissue, giving rise to so-called crown-like structures surrounding the lipid-engorged adipocytes, and formation of inflammatory agents such as TNFα, PGE2, IL-6, and MCP1. The actions of these agents involve mediators such as NFκB, cAMP/CRTCs, STATs and HIF-1α. One consequence of this is increased expression of aromatase in the adipose stromal cells, especially those of the breast, which is driven by several of these mediators, giving rise to increased local production of estrogen. On the other hand factors which have an anti-inflammatory role such as AMPK and p53 are inhibitory of estrogen formation in the breast. Thus the inflammatory state of breast adipose tissue has a major role to play in the growth of breast tumors and the local synthesis of estrogens in the breast is an important player in this process.

S60-02

Estrogen metabolites and breast cancer

Richard Santen

University of Virginia

S61-01

Epigenetic role in obesity spread around the globe

Felipe F Casanueva

Universidad de Santiago de Compostela

FELIPE F. CASANUEVA
• Head of Department of Endocrinology and Nutrition Hospital Universitario de Santiago
• President of the Spanish Foundation for the study of obesity (FSEEDO
• Acting President of Spanish Society for the Study of Obesity (SEEDO)
• Member of the Executive Committee of the Pituitary Society (USA)
• ESE Hormone Medal 2016. Munich 2016

• Honorary Member of the European Society of Endocrinology (ESE). Poland 2014
• Honorary Doctorate in Medicine of the University of Belgrade. Serbia 2014
• Honorary Doctorate in Medicine of the University of Erciyes. Turkey 2013
• Honorary Doctorate in Medicine of the Medical University of Lódz. Poland 2008
• Full member of the Real Academia de Medicina y Cirugia de Galicia (RAMYCGA). Coruña 2013

S61-02

You might think you know, but why do we actually have an obesity pandemic?

Amy Elizabeth Rothberg

University of Michigan

Amy E. Ro*thberg, MD,*
Assistant Professor of Medicine, Division of Metabolism, Endocrinology & Diabetes, Department of Internal Medicine; Assistant Professor of Nutritional Sciences,School of Public Health.

S61-03

The impact of the obesity epidemic in China

Yiming Mu

Chinese PLA General Hospital

Yiming Mu is Professor and Chief of the Department of Endocrinology, Chinese PLA General Hospital, in Beijing. He also holds the post of the President of Chinese Society of Endocrinology (CSE), Vice President of the Chinese Endocrinologist Association and President of the Chinese PLA Endocrine Association.
Professor Mu completed his basic medical education in China and then went to Japan to hone his skills on the principles of molecular research and obtained a Ph.D from the Kyushu University in Japan. His broad research interests are reflected in more than 250 publications to date in diverse fields including diabetes, glucose metabolism and pancreatic beta-cell biology and stem cell biology.
Education:
1979-1984: Second Military Medical University, Shanghai, P.R. China; 1988-1991: Military Post-graduate Medical School, Beijing, P.R. China; 1996-2001: Faculty of Medicine, Kyushu University, Fukuoka, Japan
Employment:
2001-present: Professor and Director, Department of Endocrinology, Chinese PLA General Hospital, Beijing; 1994-2001: Associate Professor, Department of Endocrinology, Chinese PLA General Hospital, Beijing; 1991-1994:Assistant Professor in Residence, Department of Endocrinology, Chinese PLA General Hospital, Beijing; 1984-1991: Residency: Internal Medicine, Chinese PLA General Hospital, Beijing; 1983-1984: Internship: Internal Medicine,Shanghai 4th Hospital, Shanghai.

In past 20 years, along with the country's economic growth, the Chinese population is undergoing lifestyle changes, such as a decreasing level of physical activity and a remarkable increase in excessive caloric intake and sedentary behavior, that may contribute to the progression of obesity, diabetes and hypertension. The prevalences of overweight and obesity, prediabetes and diabetes and prehypertension and hypertension increased rapidly from 2004 to 2012 in adult, children and adolescents in China. This lecture will focus on the possible reasons and the relationship between the rapid increase of obesity and the dramatic increase of diabetes and hypertension in China.

S62-01

Collaborative care of T2D compared with usual care at community and hospital: A pilot study in Shanghai

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Marriage status: Married
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Place of Birth: Shanghai, China
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Educational Background
Sep.1994-Jul.1999 MD. in Nursing, Shanghai Second Medical University
PROFESSIONAL TITLE
Vice Chief Senior nurse
EMPLOYMENT AND EXPERIENCE
Jan.2013-present Deputy director, Diabetes specialized committee of Chinese Nursing Association; Jan.2007-present Vice director, Shanghai Diet Committee; Feb.2006-present Deputy director, Shanghai Academy of Nursing in Diabetes; Jun.2005-present Lecturer in Nursing, Shanghai Jiao-Tong University School of medicine; Jun.2005-present Member of the Shanghai Science Association; May.2003-present Director, Program of diabetes education, Rui-jin Hospital Diabetes Center; Jun.2002-present Head nurse, Department of endocrinology and metabolism, Rui-jin hospital, Shanghai Jiao-Tong University School of Medicine; Oct.2000-Jun.2002 Nurse, Department of endocrinology and metabolism, Rui-jin hospital, Shanghai Jiao-Tong University School of Medicine May.2000-Oct.2000 Nurse, Department of Cardiology, Rui-jin hospital, Shanghai Jiao-Tong University School of Medicine; Jun.1999-May.2000 Nurse, Department of Gastroenterology, Rui-jin hospital, Shanghai Jiao-Tong University School of Medicine

Objective: To evaluate the effect of collaborative care, usual care at community and hospital in T2D control, mainly focus on HbA1c, blood pressure, self-management and pathway of patient care.
Methods: (1) It was a one year cluster-randomized trial in four community clinics and a general hospital in Shanghai. Twelve GPs, two specialists and three diabetes nurses were enrolled in the study. (2) A total of 519 T2Ds were identified by these medical staff, 4 clinics with 415 patients were randomized to two groups, group 1 using collaborative care model (CC, 7 GPs care for 215 patients, 6 community nurses and medical staff gave education and follow-up) . Group 2 was usual care in community (UC, 5 GPs care for 200

patients, 8 community nurses and medical staff gave supporting). 104 patients with T2D were enrolled in group 3(ST), and it was cared by specialist team in outpatient department of the hospital. Inclusion criteria were age 60-80 years, with social health insurance, without serious complications, and these medical sites were followed 12 months. At the endpoint, there are170 patients(CC, 79.1%), 142 patients(UC, 71%) and 62 patients(ST, 59.6%) completed the procedure. (4) At the baseline, no difference was found in age, gender, HbA1cand blood pressure in three groups. (5) The Guideline of Chinese T2D Prevention and Care was served as standardization material. We gave a one day training course to all community medical staff, and they were asked to help their patients with well blood glucose and blood pressure control(HbA1c≤7%, blood pressure<130/80mmHg). (6) There was a consultation in CC-specialists to solve the problem from their patients each month. Two hours education session was held in the community each season, one specialist and two diabetes nurses attended. Internet video conferencing was used in the procedure above. Patients of CC had a free monitoring of pre and post meal blood glucose each month in community clinic. (7) Patients of UC access to existing services at the clinics, including health education resource sponsored by the bureau of health. (8) Patients of ST had a half day education session by diabetes nurses at the first month. Treatment conducted individually at the time of randomization by specialists. A minimal telephone implemented by diabetes nurses to know the control status of patients each three month. (9) The primary outcome was HbA1c. The secondary outcomes included blood pressure, BMI, health eating, exercise, self monitoring and the pathway of patient care. Outcomes were collected at baseline and 12 months.

Results: At the 12 month, HbA1cof CC (6.6+1.13) showed a significant reduction and was better than UC (7,12+1.10) . It was close to ST (6.64+0.96) . sBP of three groups were 134.27+20.40 (ST) ,134.84+19.39 (CC) and 140.51+19.55 (UC) . Health eating and awareness of diabetes in CC and ST both were better than UC obviously. The rate of self monitoring and treatment in community were increased in CC, and it was the best one in three groups. We did not find the statistical difference in dBP, BMI and exercise.

Conclusions: As compared with usual care, a 1-year collaborative care significantly improved control of HbA1cand sBP in T2D at community. It had active effect for patients in health eating, self monitoring and treatment in community.

S62-02

Pre and Post-Operative Pheochromocytoma/paraganglioma

Karen Adams

Research Assistant & Program Coordinator to Karel Pacak, MD. PhD, DSc, National Institutes of Health, Bethesda, Maryland. 01/04-Present.

S62-03

Crunchie or violet crumble: What's diabetes got to do with bone health? Diabetes and osteoporosis

Ann Robinson

Gold Coast Health

S62-04

Strategies to help Vietnamese patients with diabetes to overcome barriers to self-care

Dang Tran Ngoc Thanh

S62-05

Western approach of the home care educational program for patients with Acromegaly: crucial role of the nurse for improved patient satisfaction and adherence to the therapy

Els Rutten

University Hospital of Ghent

Independent Diabetes Educator: Home Care Program Diabetes in West of Flanders (Diabetes Education Program)

S62-06

Nurses role and impact in diagnosis and management of adrenal insufficiency

Lisa Shepherd

Heart of England NHS Foundation Trust

Lisa Shepherd. RN (Adult), MSc, BSc (Hons), Dip H.E, NMP. Endocrinology Advanced Nurse Practitioner, Department of Diabetes & Endocrinology, Heart of England Foundation Trust.
Since 1999, she has worked as the lead Advanced Nurse Practitioner in Endocrinology at Heart of England NHS Foundation Trust. Within the role she supports and case load manages patients with endocrine disorders. She runs nurse led clinics and support other Consultant and multidisciplinary clinics. This includes diagnosis and performing dynamic function tests, treatment, management and education of patients with long term, highly complex needs. Part of this role is the diagnosis, treatment management and education of patients with adrenal insufficiency. She has further developed the service by instigating and running education sessions on adrenal insufficiency which includes intercurrent illness treatment management and emergency injection administration training for these patients, their family and friends.
Her MSc looked at the knowledge and experience of patients with primary adrenal insufficiency and is looking to continue research in this area when undertaking a PhD.
An active member of the Society for Endocrinology Nurse Committee since 2007, and is the current Chair. An inaugural member of the Federation of International Nurses in Endocrinology (F.I.N.E) founded in 2014. She was awarded the Clinical Endocrinology Trust Award for the highest marked Nursing Abstract at the Society for Endocrinology BES in 2015. She has co-authored the first and second edition of the Society for Endocrinology Competency Framework for Adult Endocrine Nursing and has also authored and co-authored 19 published abstracts.

S62-07

Competency Framework for Adult Endocrine Nursing: How is it developed & put to use in clinical setting

Phillip Yeoh

The london Clinic

S62-08

The Insulin Tolerance Test – A New Angle on How to Improve Safety

Julie Hetherington[1,2*], Samantha Hocking[4,3], Albert Hsieh[1,3], Elizabeth Chua[1,3]

1. Department of Endocrinology, Royal Prince Alfred Hospital, Sydney, Australia
2. Sydney Nursing School, University of Sydney, Sydney, Australia
3. Sydney Medical School, University of Sydney, Sydney, Australia
4. Department of Endocrinology, Royal North Shore Hospital, Sydney, Australia

The Insulin tolerance test (ITT) is regarded as the 'gold standard' dynamic test in assessing adult hypothalamic-pituitary-adrenal (HPA) axis and growth hormone deficiency. The intentionally induced hypoglycaemia produces a standard physiological stress that causes adrenocorticotrophic hormone (ACTH) and growth hormone release. However, the rate of change of blood glucose level (BGL) can vary widely between patients, resulting in a rapid and significant hypoglycemic event which requires immediate glucose rescue. Cardiac and neurological adverse events secondary to hypoglycemia have created significant staff anxiety and concern regarding safety during testing.
This has commonly been reported as the reason for choosing an alternative test.
On the other hand, a poor response to insulin, particularly in individuals with insulin resistance, results in failure to reach the hypoglycemia target.
Most of the ITT protocols do not address bedside glucose monitoring techniques. This begs the questions: Can there be a better early intervention guide depending on the rate of change of BGLs during an ITT to improve safety yet ensure success of reaching the target BGL? In this invited lecture, we are introducing an innovative method of predicting and graphing the expected rate of fall of the BGL, the Hetherington/Hocking Insulin Tolerance Test Line - "HHITT Line", which predicts the glucose rate of fall of an individual and identifies when glucose rescue or insulin intervention is needed in a timely manner.

S62-09

The Education of Paediatric Endocrine Nurses / Advanced level Practice in the UK

Kate Davies

London South Bank University

This presentation will give a brief historical view on nursing education in the UK,including the current nursing structure, showing the current position of Clinical Nurse Specialists, Advanced Nurse Practitioners and Nurse Consultants. Opportunities will be described to further and advance nursing practice for children's nurses. A new Bachelors (BSc) and Masters (MSc) degree module will be discussed, purely for paediatric endocrine nurse

specialists, or for children's nurses with an interest within this specialised field, focusing on the module content and assessment.

S62-10

Persistent Obesity and Diabetes, hypertension and Sleep dysfunction after Treatment for Cushing's Disease

Christine Yedinak

Oregon Health & Sciences University

Assistant professor Family Nurse Practitioner, Northwest Pituitary Center ,Department of Neurological Surgery (1.0FTE), OHSU, Portland, OR

S63-01

How to publish your paper

Leonard Wartofsky

Endocrine Society

S63-02

Publishing ethics

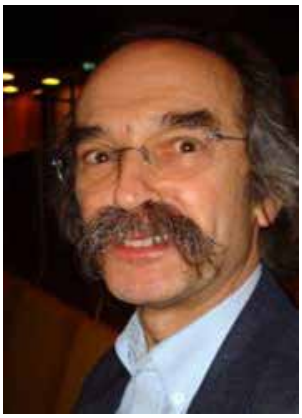
Sof Andrikopoulos

S63-03

Responding to reviewer comments

Josef Köehrle

Charite-Universitaetsmedizin Berlin



2001-University Professor of Molecular Endocrinology and Chairman Institute for Experimental Endocrinology, Medical Faculty Charité
2002- Head Endokrinologisches Forschungszentrum der Charité EnForCé
2010- Board of Directors Master Program ,Molecular Medicine' Charité
2011- 2016 Scientific Director Charité Center 4 Therapeutic Research
2012- Acting Deputy Director Institut für Biometrie und Klinische Epidemiologie
2013- Coopted as member of the Faculty of Biology Free University Berlin

Oral Presentations

OR11-01

Prevalence, patterns and predictors of hypocortisolism, hypogonadism and thyroid dysfunction in patients with HIV infection and acquired immunodeficiency syndrome in India

Deep Dutta*, Adesh Kisanji Gadpayle, Atul Anand, Lokesh Kumar Sharma, Neera Sharma, Bindu Kulshreshtha

PGIMER & Dr RML Hospital

Objective This study aimed to determine prevalence, patterns and predictors of hypocortisolism, hypogonadism and thyroid dysfunction (TD) in Indians with HIV.

Methods Consecutive patients, 18–70 years age, without any severe co-morbidity, having at least 1-year follow-up at anti-retroviral therapy (ART) clinic, underwent clinical and hormone assessment.

Results From initially screened 527, 359 patients (225 males; 134 females; disease duration 61.44±39.42 months), 88.58% on ART, 40.67% having TB history and 89.69% having vit-D insufficiency were analyzed. Morning cortisol <6 mcg/dl (Group-1), 6-11 mcg/dl (Group-2), 11-18 mcg/dl (Group-3) and ≥18mcg/dl (Group-4) was observed in 13, 71, 199 and 76 patients. ACTH stimulation revealed 87 patients (24.23%) to have adrenal insufficiency (AI). AI in Groups 1-4 was 100%, 56.34%, 17.09% and 0%. AI were more likely to be females, longer disease duration (LDD), IRIS, hyperkalemia, lower fasting glucose, DHEAS and vit-D. Morning cortisol and DHEAS were best predictors of AI (P 0.004 and 0.028).39.11% males had testosterone <300ng/dl. Primary, secondary and compensated hypogonadism was observed in 7.56%, 31.56% and 12.44%. Hypogonad males were older, higher opportunistic infections with LDD. Menstrual abnormalities (MA) were observed in 54 (40.3%) females, who were older, had lower CD4, higher TB. Age, CD4 count at diagnosis and vit-D were best predictors of male hypogonadism. Age and increment in CD4 count in first 6-12 months following ART were best predictors of POI. Subclinical hypothyroidism (ScH) was commonest TD (14.76%) followed by sick euthyroid syndrome (5.29%) and isolated low TSH (3.1%). TPOAb was positive in 3.90%. Baseline CD4, TPOAb and TB were best predictors of ScH after adjusting for age, weight, disease duration, opportunistic infections.

Conclusion AI and hypogonadism are significant problem observed in 24% patients, 39% male and 29% females respectively. TD is primarily non-autoimmune, predominantly ScH.

OR11-02

ARMC5 mutations in Primary Bilateral Macronodular Adrenal Hyperplasia and Nonfunctional Bilateral Adrenal Nodules

Liping Yu, Junqing Zhang, Xiaohui Guo, Qian Zhang, Xuesong Li, Qun He

Peking University First Hospital

Objective To investigate ARMC5 mutations in Primary bilateral macronodular adrenal hyperplasia (PBMAH) families, sporadic PBMAH patients and patients with Nonfunctional bilateral adrenal nodules (NFBAN).

Methods (1) The clinical data, peripheral blood samples and adrenal samples of PBMAH family members, sporadic PBMAH and NFBAN patients were collected. (2) DNA was extracted from peripheral blood samples and adrenal samples. ARMC5 gene was amplified and sequenced.

Results (1) ARMC5 pathogenic germline mutations, c.1855C>T (p.Arg619*), c.2290C>T (p.Arg764*) and c.2189C>A (p.Ser730*), were identified in PBMAH family-1, family-2 and family-3 respectively. Secondary ARMC5 somatic mutations, c.2599G>T (p.Glu867*) and c.1851delG (p.His618Thrfs*12), were found in the adrenal nodules of two PBMAH patients from the family-1 and family-2 respectively. ARMC5 mutations, c.2189C>A (p.Ser730*), c.2599G>T (p.Glu867*) and c.1851delG (p.His618Thrfs*12), have not been described previously. (2) PBMAH family members with ARMC5 pathogenic germline mutations displayed various clinical manifestations. (3) ARMC5 novel pathogenic germline mutations, c.1214delG (p.Gly405Alafs*56), c.318delG (p.Ser107Argfs*30), c.2564delT (p.Val855Glyfs*62) and c.622_623insC (p.Gln208Profs*15), were identified in 4 of 20 (20%) sporadic PBMAH patients respectively. (4) No ARMC5 pathogenic germline mutation was detected in the 23 sporadic NFBAN patients.

Conclusion (1) ARMC5 pathogenic germline mutations are common in PBMAH families. Secondary ARMC5 somatic mutations can be found in the adrenal nodules of the PBMAH family members who carry the ARMC5 germline mutations. (2) PBMAH family members with ARMC5 pathogenic germline mutations display various clinical manifestations. ARMC5 gene screening for PBMAH family members can help detect insidious PBMAH patients. (3) ARMC5 pathogenic germline mutations can be identified in sporadic PBMAH patients. (4) No ARMC5 pathogenic germline mutation was detected in sporadic NFBAN patients.

OR11-03

Validation of hair cortisol measurement by an authomated method. Utility as a chronic stress biomarker

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Objectives Hair sample allows a retrospective evaluation of the cortisol levels to which the individual was exposed in the previous three months. The aim of the present study is to validate an automated hair cortisol measurement method to be used in daily laboratory, in order to evaluate the Hypothalamic-Pituitary-Adrenal (HPA) axis.

Methods Hair cortisol levels were measured with Siemens Immulite 2000 automated CLIA analyzer with a brief modification after cortisol methanol extraction. We performed a novel calibration curve from dilutions of standard solutions of cortisol (Cortisol RIA kit, Immunotech Beckman Coulter, in range 2 to 100 nmol/L) with CLIA′s kit diluent recommended by the manufacturer. Limit of blank (LOB), limit of detection (LOD) and limit of quantification (LOQ) were performed according to the EP-17A protocol. The precision profile was determined using four hair extracted samples of different cortisol concentrations (1.6 nmol/L, 3.9 nmol/L, 11.5 nmol/L, 20.0 nmol/L).

In order to evaluate hair cortisol concentration according to stress levels, hair samples were obtained from 74 individuals (50 women and 24 men; 20-30 years), who were students at the Faculty of Pharmacy and Biochemistry. They were classified according to Holmes-Rahe life events scale score and then divided in two groups: stress free (score <300, n=64) and with stress (score >300, n=10).

In order to evaluate the impact of stress reduction techniques, hair samples were obtained from 37 individuals (31 women and 6 men, 24-45 years) who attended to a Stress Coping Program at the Faculty of Pharmacy and Biochemistry. The objective of the program was to teach a variety of stress reduction techniques. Hair samples were obtained at the beginning and at the end of the program (3 months).

Results The LOB for the method was 0.9 nmol/L; the LOD was 2 nmol/L and the LOQ, determined by a graphical method, was 3.4 nmol/L. The precision profile variation coefficientswere 45.7% for 1.6 nmol/L, 16.5% for 3.9 nmol/L, 8.3% for 11.5 nmol/L, and 6.7% for 20.0 nmol/L.

In the studied population, stress free individuals (score lower than 300) presented a hair cortisol median value of 139 pg/mg hair (range 69-251 pg/mg hair), while hair cortisol median value of those individuals who presented stress (score higher than 300) was 380 pg/mg hair (range 280-520 pg/mg; $p<0.001$).

Hair cortisol levels obtained at the end of the stress reduction program were significantly lower than those obtained at the beginning of the program (226.3 (175.2) vs 113.0 (64.3) pg/mg hair; $p = 0.026$).

Conclusions In the current study a novel technique which allows automated hair cortisol measurement is developed. Hair cortisol constitutes a better tool for evaluating chronic stress due to the fact that it allows to evaluate a longer period of time, providing a measure of the integrated hormone concentration during that period. Hair sample provides the possibility of obtaining serial samples in a large number of individuals as it is a non-invasive sample and it also offers a long stability. The results support the possibility to use this method in clinical laboratories for evaluating and monitoring chronic stress on psychosocial studies. These encouraging results allow to project future researches on the evaluation of the clinical application of the measurement of hair cortisol such as job stress, cyclic Cushing syndrome and Addison disease.

OR11-04

Management of glucocorticoid replacement therapy by continuous glucose monitoring in adult patients with primary and secondary adrenal insufficiency

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Objective Adrenal insufficiency is a life-threatening endocrine emergency caused by primary adrenal failure or hypothalamic-pituitary impairments in the corticotropic axis. Daily glucocorticoid replacement therapy is essential for these patients. However, the management of optimal dose continues to be a challenge because of the lack of reliable biological parameters for its assessment. Based on recent studies, the administration of lower glucocorticoid doses (10-20 mg/m2/day hydrocortisone) is recommended. However, these glucocorticoid replacement regimens cannot eliminate a nocturnal hypocortisolemia known as the risk factor of cardiovascular events. In our previous study, some patients considered to be receiving appropriate hydrocortisone replacement exhibited morning fatigue in routine clinical visits in the absence of acute stressful conditions. Thus, unrecognizednocturnal hypoglycemia was speculated to cause morning fatigue in these patients. In the present study, we investigated the usefulness of Continuousglucose monitoring (CGM) for identifying unrecognized hypoglycemia in patients with primary and secondary adrenal insufficiency characteristically exhibiting morning fatigue and also for optimizing hormone replacement therapy to reduce hypoglycemic events and improve their quality of life.

Methods Eleven adult patients exhibiting morning fatigue with primary or secondary adrenal insufficiency were enrolled in this study from our outpatient clinic. The diagnosis of adrenal insufficiency was confirmed by an ACTH stimulation test. Patients complicated with Diabetes Mellitus (DM) or impaired glucose tolerance were excluded. Chief symptoms and physical findings such as body mass index and blood pressure were assessed. Blood tests and urinalyses were performed including fasting blood glucose (FBG), hematocrit, hemoglobin, white blood cell count, serum sodium, serum potasium, creatinin kinase, total cholesterol and daily urinal free cortisol concentrations.

Patients underwent CGM for 24-48 h including at least one night before and after the modification of glucocorticoid replacement regimens. In each case, the mean BG, minimum BG, maximum BG and the mean amplitude of glycemic excursion (MAGE) were analysed. The CGM systems used were MiniMed CGMS-Gold (Medtronic, Northridge, CA) and iPro2 (Medtronic, Northridge, CA). Hypoglycemia was defined as glucose levels less than 70 mg/dL in this study. All group data were expressed as the mean ± standard deviation (SD). Group comparisons in standard or non-standarddistributions were performed by ANOVA and the Student's t-test or the Wilcoxon rank-sum test, respectively, using JMP 5.1.2 software (SAS Institute Inc). All tests for significance and the resulting P values were two-sided with a level of significance of 5%.

Results There were eleven index cases with various etiologies of adrenal insufficiency. Two patients were diagnosed with primary adrenal insufficiency. Other patients were diagnosed with secondary adrenal insufficiency comprising one patient with lymphocytic hypophysitis, 2 with panhypopituitarism caused by pituitary apoplexy, one with panhypopituitarism after surgery of pituitary tumor, 2 with panhypopituitarism after diencephalon surgery, one with congenital panhypopituitarism and 2 with isolated ACTH deficiency. The mean age of the 11 cases was 48 ± 22 years old. Nine patients were treated with hydrocortisone at a dose ranging from 5 to 30 mg/day. Laboratory findings of these patients were not altered before and after modifying hormonal supplementation. The daily urine free cortisol level, which is regarded as another clinical marker useful for hydrocortisone supplementation, was 52 ± 55 mg/day (range: 7.1-173 mg/day). Based on these data, all cases were clinically considered to be taking appropriate amounts of glucocorticoid supplementation; however, most patients exhibited general fatigue, especially in the morning. As anticipated, in 9 out of 11 (82%) patients, CGM identified unrecognized hypoglycemia episodes at midnight and early in the morning suggesting that the evening doses and timing of hydrocortisone supplementation were not appropriate to maintain normal nocturnal glucose levels. In order to reduce hypoglycemic events, we maintained glucocorticoid replacement therapy for each case and re-examined their glucose levels using CGM. After the optimization of hydrocortisonesupplementation, nocturnal hypoglycemia was not observed in 10 patients. Morning fatigue also completely improved. Comparisons of pre- vs. post-modified CGM data revealed that the mean minimum BG was significantly improved (62 ± 11 mg/dL vs. 81 ± 10 mg/dL, $p=0.0032$) and the mean frequency of hypoglycemia events were also significantly reduced (2.1 ± 1.1 vs. 0.1 ± 0.4, $p=0.0091$). On the other hand, the mean BG during CGM (105 ± 10 mg/dl vs. 108 ± 12 mg/dl) and MAGE (44 ± 18 vs. 39 ± 21) were not significantly altered ($p=0.6243$ and $p=0.5286$). The mean maximum BG (160 ± 17 mg/dL) of pre-modification did not differ from the post-modified status (149 ± 24 mg/dL, $p=0.2062$).

Conclusion CGM is a sophisticated method to measure interstitial glucose concentrations day and night and was originally developed for patients with DM in order to detect asymptomatic hypoglycemia events. Our study revealed that CGM may represent a powerful tool for detecting unrecognized nocturnal hypoglycemia and for optimizing supplementary hormones in patients with adrenal insufficiency.

OR12-01

Adrenal Venous Sampling in Patients With Positive Screen-

ing but Negative Confirmatory Testing for Primary Aldosteronism

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Objective Adrenal venous sampling (AVS) is considered to be the most reliable diagnostic procedure to lateralize aldosterone excess in primary aldosteronism (PA). However, normative criteria have not been established partially because of a lack of data in non-PA hypertensive patients. The aim of the study was to investigate aldosterone concentration and its gradient in the adrenal vein of non-PA hypertensive patients.

Methods This retrospective study was conducted as a multi-center collaborative study involving 9 referral centers in Japan (WAVES-J study). The WAVES-J database included clinical and laboratory data of hypertensive patients who underwent AVS between January 2006 and December 2013. Of 550 AVS data in WAVES-J database, we retrospectively studied the results of cosyntropin-stimulated adrenal venous sampling in 40 hypertensive patients who showed positive screening testing but negative results in 2 confirmatory tests/captopril challenge test and saline infusion test. Plasma aldosterone concentration, aldosterone/cortisol ratio, its higher/lower ratio (lateralization index) in the adrenal vein with cosyntropin stimulation were measured.

Results Median plasma aldosterone concentration in the adrenal vein was 25819 pg/mL (range, 5154–69920) in the higher side and 12 953 (range, 1866–36 190) pg/mL in the lower side ($P<0.001$). There was a significant gradient in aldosterone/cortisol ratio between the higher and the lower sides (27.2 [5.4–66.0] versus 17.3 [4.0–59.0] pg/mL per μg/dL; $P<0.001$) with lateralization index ranging from 1.01 to 3.87. The aldosterone lateralization gradient was between 1 to 2 in 32 patients and 2 to 4 in 8 patients. None of the patients showed lateralization index ≥4.

Conclusion The present study demonstrated that plasma aldosterone concentration in the adrenal veins showed significant variation and lateralization gradient even in non-PA hypertensive patients. Adrenal venous sampling aldosterone lateralization gradients between 2 and 4 should be interpreted with caution in patients with PA because these gradients can be found even in patients with negative confirmatory testing for PA.

OR12-02

The synthesis of 18-oxocortisol can be influenced by expression of CYP11B1 and CYP11B2 in aldosterone-producing adenoma.

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Background and Purpose 18-oxocortisol (18-oxoF) is so called "Hybrid steroid" which is a metabolite of cortisol converted by CYP11B2, aldosterone synthetase. In normal adrenal subjects, 18-oxoF could be synthesized from the circulating cortisol, converted from 11-deoxycortisol by CYP11B1, and the amount of production is quite small. However, in primary aldosteronism (PA), it was previously reported that the patients with PA, especially with aldosterone-producing adenoma (APA), had higher plasma and urinary levels of 18-oxoF than the hypertensive patients with essential hypertension. Moreover, recent our studies found the utility of measuring peripheral 18-oxoF concentrations which can distinguish patients with APA from those with bilateral adrenal hyperplasia (Satoh et al. Hypertension 2015). So, measurement of 18-oxoF is expected as a gold-standard method for determining treatment, surgery or medication, instead of?adrenal venous sampling (AVS). However, some patients with APA did have lower plasma levels of 18-oxoF and the reason why these differences existed remained unclear. In order to clarify the status of intra-tumoral 18-oxoF synthesis in APA cases, we examined the association between histopathological and immunohistochemical (IHC) findings of APA and plasma levels of 18-oxoF determined by super sensitive LC-MS/MS instrument.

Material and Method We analyzed 15 patients with surgically proven APA retrospectively, who underwent unilateral adrenalectomy based on the results of AVS at Tohoku University Hospital in 2011. They were diagnosed with PA by blood test at supine position and captopril-challenge test in which the cut-off of aldosterone-to-renin ratio (ARR) was set at 20 after captopril loading (50 mg), and the laterality of aldosterone-producing was determined by AVS using laterality index which cut-off was 2.6. All APAs were confirmed by pathological findings and postoperative biochemical data. Adrenal specimens embedded in paraffin were utilized for IHC analysis with a specific rat and mouse monoclonal antibody against CYP11B1 and CYP11B2, respectively. Halo digital image software v1.90 (Indica Labs; Albuquerque, NM) was used to evaluate the cross-sectional area (CSA) and the percentage of positive area of each enzyme. All analyses performed by Stat Flex version 6.0 (Artech Co Ltd, Osaka, Japan) and statistical significance was set at $P < 0.05$.

Results The mean age of the patients was 48.3 ±11.1 (mean ±SD) years, and the percentage of male was 60.0%. The baseline parameters at the diagnosis were as follows: BMI 25.3 ±4.2 kg/m^2; serum potassium 3.97 ±0.37 mM; plasma renin activity 0.23 ±0.15 ng/ml/hr; plasma aldosterone concentration (PAC) 38.7 ±17.2 ng/dl; ARR 248.2 ±173.8; urinary aldosterone excretion 26.4 ±14.2 μg/day; ACTH 25.3 ±9.8 pg/ml; cortisol 8.6 ±2.3 μg/dl; urinary free cortisol 45.7 ±17.6 μg/day; 18-oxoF 16.3 ±15.6 ng/dl. The maximum diameter (MD), CSA, the percentage of positive area of CYP11B1 (PR-B1) and that of CYP11B2 (PR-B2) in APA were 12.1 ±6.1 mm, 77.50 ±65.63 m2, 16.1 ±8.5% and 21.6 ±9.2%, respectively. Using Spearman's correlation, the plasma peripheral levels of 18-oxoF were positively correlated with PAC ($r = 0.657$, $P < 0.01$), MD ($r = 0.867$, $P < 0.01$), CSA ($r = 0.756$, $P < 0.01$) and PR-B1 ($r = 0.575$, $P < 0.05$), while neither cortisol nor PR-B2 correlated with 18-oxoF significantly. However, the positive area of both CYP11B1 and CYP11B2 were significantly correlated with 18-oxoF ($P < 0.01$). Then, we analyzed the serum cortisol levels at low dose (1 mg) overnight dexamethasone suppression test (DST1) to evaluate the intra-tumoral cortisol production. As the patients could be divided into high 18-oxoF group (7 cases) and low 18-oxoF group (8 cases) based on the cut-off, "6.1" reported by previous study, the

mean serum cortisol level was 1.67 ±0.76 and 0.97 ±0.25 μg/dl, respectively and that in high 18-oxoF group was higher than that in low 18-oxoF group. Although the difference was not significant. it was implied that the intra-tumoral production of cortisol played a key role of 18-oxoF synthesis.

Conclusions In current study, it is postulated that the plasma peripheral 18-oxoF levels can be influenced by tumor size and the expression levels of CYP11B1 and CYP11B2 in APA cases. The intra-tumoral production of cortisol, the precursor of 18-oxoF, may be a key factor of 18-oxoF synthesis in APA.

OR12-03

Clinical study of aldosterone- and cortisol-co-secreting adrenal adenoma

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Objective In recent years,several papers have been published regarding the association of primary aldosteronism (PA) with autonomous secretion of cortisol,that is aldosterone- and cortisol-producing adrenal adenoma (A/CPA) ,many such reports have come from Japan,whereas lacking systematic research on this aspect in China.Because unilateral and autonomous production of cortisol may result in controlateral adrenal suppression,patients with A/CPA are at risk of developing postoperative adrenal crisis and adrenal insufficiency.A/CPA is the subtype of PA,usually presented with PA with subclinical Cushing syndrome(SCS).SCS was defined as an increase in the endogenous secretion of glucocorticoids without clinical manifestations of clinical Cushing syndrome.We reminded that we should think about comorbidity of the two disorders in the clinical work,especially to avoid only paying attention to aldosterone-producing adenoma (APA) ,improper treatment of post-surgical ,and adrenal crisis and adrenal insufficiency occurred.To evaluate the clinical characteristics of aldosterone- and cortisol-co-secreting adrenal adenoma,this article for the data of 197 patients with PA were reviewed retrospecively.

Design Data of 197 patients with PA admitted to the first affiliated hospital of Zhengzhou university between January 2010 and September 2015 were collected,pure aldosterone-producing adrenal adenoma(APA) in 180 cases,combined autonomous secretion of cortisol (A/CPA) in 17cases were reviewed retrospecively.

Results A/CPA patients were significantly (P<0.05) older and had higher serum potassium levels,higher serum cortisol levels and urinary cortisol levels than that of APA patients,while serum aldosterone and plasma ACTH levels were significantly (P<0.05) lower. The tumor size (25.7±6.mm) of A/CPA patients were significantly (P<0.05) larger than that (18.3±7.4) of APA patients .there were no statistical differences between A/CPA patients and APA patients of sex,BMI,blood pressure or basal PRA levels.Postoperative adrenal insufficiency occured in 4 cases of A/CPA patients,none in APA patients.

Conclusion Aldosterone- and cortisol-producing adrenal adenoma is not uncommon,which has more unique clinical features.Postoperative adrenal crisis and adrenal insufficiency may occure in A/CPA patients.Therefore, the screening test for aldosterone and cortisol cosecreting should be performed in patients with primary aldosteronism even if there are no clinical features of Cushing syndrome.It should be noted that hydrocortisone replacement is necessary during and after adrenalectomy.closely following up,and the dosage of hydrocortisone should be adjusted according to the adrenocortical function.

OR12-04

Different diagnostic cut-off values of plasma catecholamines for diagnosis of pheochromocytoma in patients with adrenal masses

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Objective The diagnosis of pheochromocytoma mostly depends on the documentation of catecholamine overproduction, whereas the normal reference ranges of catecholamines are based on the general populations rather than the patients with adrenal masses. Therefore, the aim of our study was to establish valuable thresholds of plasma epinephrine and norepinephrine in patients with adrenal masses to diagnose pheochromocytoma.

Methods We reviewed the medical records of 433 subjects with suspected pheochromocytomas for adrenal incidentalomas in West China Hospital of Sichuan University, whose plasma catecholamine was measured by high-performance liquid chromatography methods before surgery. All patients had pathologically diagnosis. Receiver operating characteristic (ROC) curves were used to determine cut-off values of plasma epinephrine and norepinephrine.

Results The epinephrine levels of pheochromocytomas group were 1.69-fold(P<0.001) and norepinephrine levels were 4.82-fold(P<0.001) higher respectively than non-pheochromocytomas group. The norepinephrine levels in pheochromocytomas group were significantly higher in male subjects compared with females(P<0.001), and similarly higher norepinephrine levels were found in patients with hypertension compared with normotensive patients in pheochromocytomas group(P=0.001). The cut-off values with valuable sensitivity and specificity for plasma epinephrine and norepinephrine were 134.5ng/L and 515.5ng/L respectively. The diagnostic efficacies (defining a positive test as either epinephrine or norepinephrine levels above the cut-off value) were a sensitivity of 88.7% and a specificity of 82.6%. To hypertensive male sudjects, when we applied cut-off values, the sensitivity was 100% and specificity was 88.2%, and in normotensive males, there were 91.7% and 91.4% respectively.

Conclusion The results of our study definitely demonstrated that patients with adrenal masses had different thresholds of plasma catecholamines, which were higher than upper limit of reference values, to diagnose pheochromocytoma. This study clearly shows specific cut-off values of catecholamines may be needed according to the history of hypertension in male patients to diagnose pheochromocytoma.

OR13-01

MiR-20b Displays Tumor Suppressor Functions in Papillary Thyroid Carcinoma by Regulating MAPK/ERK Signaling Pathway

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Objective MicroRNAs (miRNAs) are endogenous, small non-coding RNAs that play important roles in multiple biological processes. MiR-20b has been reported to be dysregulated in papillary thyroid carcinoma (PTC). However, the functional roles are still largely unknown. This study aimed to investigate the biological functions and the underlying molecular mechanisms of miR-20b in PTC.

Method The expression of miR-20b was assessed by quantitative RT-PCR in 47 pairs of PTC and adjacent normal thyroid tissues. The association between miR-20b expression and clinicopathological status of PTC patients were analyzed. MiR-20b was over-expressed in PTC cell lines K1 and TPC-1, and the effects on cell viability, migration and invasion were evaluated. We further searched

for targets of miR-20b and identified the possible molecular mechanisms of miR-20b in PTC cells.
Results We found that miR-20b was markedly down-regulated in PTC tissues compared with their adjacent normal thyroid tissues. The low-level expression of miR-20b was correlated with cervical lymph node metastasis and TNM staging. Up-regulation of miR-20b inhibited cell viability, migration, invasion in K1 and TPC-1 cells. Ectopic over-expression of miR-20b could suppress the mitogen-activated protein kinase/extracellular signal-regulated kinase (MAPK/ERK) signaling pathway through directly targeting son of sevenless homolog 1 (SOS1) and extracellular signal-regulated kinase 2 (ERK2). Furthermore, depletion of SOS1 or ERK2 by siRNAs has similar effects as miR-20b over-expression on cell viability and invasion, whereas rescued SOS1 or ERK2 expression partially reversed the inhibitory effects of miR-20b in TPC cell lines.
Conclusion These results indicate, for the first time, that miR-20b displays tumor suppressor functions in PTC. By targeting SOS1 and ERK2, miR-20b inhibits the activity of MAPK/ERK signaling pathway. Our findings suggest that miR-20b may play an important role in PTC initiation, progression and metastasis, and may provide us a potential therapeutic target for PTC.

OR13-02

TAZ induction directs differentiation of thyroid follicular cells from human embryonic stem cells

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Objective The differentiation program for human thyroid follicular cells (TFCs) relies on the interplay between sequence-specific transcription factors and transcriptional co-regulators. TAZ (transcriptional co-activator with PDZ-binding motif) is a co-activator that regulates several transcription factors, including PAX8 and NKX2-1, which play a central role in thyroid-specific gene transcription. TAZ and PAX8/NKX2-1 are co-expressed in the nuclei of thyroid cells and TAZ interacts directly with both PAX8 and NKX2-1 leading to their enhanced transcriptional activity on the thyroglobulin (TG) promoter and additional genes.
Methods We have studied the use of a small molecule, ethacridine, recently identified as a TAZ activator, in the differentiation of thyroid cells from human embryonic stem (hES) cells. We first derived endodermal cells from hES cells using Activin A followed by induction of differentiation into thyroid cells directed by ethacridine and thyrotropin (TSH).
Results The expression of TAZ was increased in the Activin A derived endodermal cells by ethacridine in a dose-dependent manner and followed by increases in PAX8 and NKX2-1 when assessed by both qPCR and immunostaining. Following further differentiation with the combination of ethacridine and TSH, the thyroid specific genes - TG, TPO, TSHR and NIS were all induced in the differentiated hES cells. When these cells were cultured with extracellular matrix coated dishes we observed thyroid follicle formation and abundant TG protein expression. Furthermore, such hES cell derived thyroid follicles showed a marked TSH induced and dose-dependent increase in radio-iodine uptake and protein-bound iodine accumulation.
Conclusion These data show that fully functional human thyroid cells can be derived from hES cells using ethacridine, a TAZ activator, which induced thyroid-specific gene expression and promoted thyroid cell differentiation from the hES cells. These studies once again demonstrated the importance of transcriptional regulation in thyroid cell development. This approach also yielded functional human thyrocytes, without any gene transfection or complex culture conditions, by directly manipulating the transcriptional machinery without interfering with intermediate signaling?events.

OR13-03

Thyroid nodule sizes influence the diagnostic performance of TI-RADS and ultrasound patterns of 2015 ATA guidelines: a multicenter retrospective study

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Objective To compare the diagnostic value between the thyroid imaging reporting and data system (TI-RADS) and 2015 American Thyroid Association (ATA) guidelines ultrasound (US) patterns in the differentiation of benign and malignant thyroid nodules and to evaluate the impact of sizes on the diagnostic performance of them.
Patients and methods Seven hundred and thirty-four patients with 962 thyroid nodules from eight tertiary hospitals around Jiangsu province in China from Janurary 2014 to November 2014 were recruited for the retrospective study. All nodules were divided into three groups according to the maximal diameter (d< 10 mm, d = 10-20 mm and d > 20 mm). The ultrasound images were categorized based on TI-RADS and ATA ultrasound patterns, respectively. The receiver operating characteristic curves were established to compare the diagnostic value of the two models and the influence of thyroid nodule sizes on them.
Results (1) Of the 962 thyroid nodules, 587 were benign and 375 were malignant. The average age was 46.84 ± 13.09 years old and the mean diameter of the noduleswas 17.73 ± 12.83 mm. (2) A total of 931 (96.8%) and 906 (94.2%) patterns could meet the criteria for TI-RADS categories and the ATA ultrasound patterns. The specificity (79.4%) was significantly higher in ATA guidelines US patterns, while the sensitivity (83.2%) and AUC (0.826) of TI-RADS were higher than that of 2015 ATA guidelines US patterns (77.3%, 0.807), though, not significant. (3) Considering the influence of nodule sizes on the diagnostic value, the AUC and sensitivity of TI-RADS in d = 10-20 mm group were 0.849, 85.3%, respectively, higher than those in d < 10 mm or d > 20 mm group. However, among the three groups, ATA ultrasound patterns had highest AUC (0.839) and specificity (89.8%) in d > 20 mm group. In nodules d > 20 mm, the specificity of ATA ultrasound patterns was significantly higher compared with TI-RADS classification (89.8% vs 80.6%, P = 0.003). For nodules d < 20 mm, the differences between the two models were not significant. (4) Total 31 and 56 nodules were unable to be categorized according to TI-RADS and ATA ultrasound patterns. The malignancy rates of these nodules were 38.7%, 28.6%, respectively. Those nodules beyond the range of TI-RADS categories and ATA patterns had little relation with nodule size.
Conclusion The 2015 ATA guidelines US patterns may yield higher specificity in the differential diagnosis of benign and malignant thyroid nodules, while TI-RADS classification may offer a relatively higher sensitivity and AUC. In addition, thyroid nodule sizes may influence the diagnostic performance of the two models. The TI-RADS shows best value in nodule between 10-20 mm, while ATA patterns have highest value in lesions larger than 20 mm. The ATA patterns may yield higher specificity than TI-RADS, especially in

nodules larger than 20 mm. Both models are less reliable in lesions smaller than 10 mm. A minority of patterns beyond the range of TI-RADS or 2015 ATA guideline US patterns may have intermediate hidden risk of malignancy to some extent.

OR13-04

Follicular Variant of Papillary Thyroid Carcinoma: An Intermediate Clinical Entity

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Objectives With the dramatic increase in thyroid cancer incidence, Follicular variant papillary thyroid cancer (FV-PTC) has also been increasingly diagnosed in recent times. Despite its high incidence, the clinical behaviour, prognosis and outcome of FV-PTC remains controversial and challenging for most physicians. This study aims to determine the disease characteristics of FV-PTC, compare its clinical profile, behaviour and outcomes with classic papillary thyroid cancer (C-PTC) and follicular thyroid cancer (FTC) in a single institution in the Philippines (Philippine General Hospital).
Methods This is a retrospective cohort study of 606 thyroid cancer patients diagnosed as C-PTC (n=440), FV-PTC (n=87) or FTC (n=79) by biopsy seen at the Philippine General Hospital between January 1990 and June 2014. Age at diagnosis, male percentage, tumor size, extrathyroidal extension, multifocality, bilaterality, nodal and distant metastases at presentation, treatment modalities received, recurrence and mortality rates were all tabulated and recorded using a descriptive statistical analysis (mean, standard deviation). Different clinical variables of 3 groups were then compared using a univariate logistic regression analysis.
Results Age at presentation (43-44), male percentage (8.9-16.4%), tumor size at presentation (3.3-3.6 cm) and extrathyroidal extension (5.1-8.7%) were similar across the groups. FV-PTC and C-PTC presented similarly with higher rates of multifocality (25.3% and 22.7% vs 7.6%) and bilateral involvement (20.7% and 17.1% vs 6.3%) as compared to FTC which was usually solitary at presentation. C-PTC (37.7%) presented with high nodal involvement at presentation while both FV-PTC (8.1%) and FTC (7.6%) rarely presented with nodal metastases. Distant metastases was observed highest among the FTC (12.7%) group followed by FV-PTC (5.8%) and rarely in C-PTC (3.4%). Majority of patients underwent complete thyroidectomy and post-surgical radioactive iodine ablative therapy with similar rates across the groups. Recurrence rate was observed to be highest among C-PTC (39.4%) while FV-PTC (18.4%) had the lowest recurrence rate. FV-PTC resulted in almost 50% reduction (HR=0.4934; p-Value=0.007) in recurrence risk as compared with C-PTC. Mortality rate was highest among FTC (2.5%) group while FV-PTC (0%) and C-PTC (0.5%) had a similarly low mortality rate.
Conclusions FV-PTC represents a major sub-type of PTC that represents an intermediate entity between C-PTC and FTC. Although it behaves clinically like FTC presenting with lower lymph node metastases and higher distant metastases than C-PTC, its long-term survival and prognosis is quite similar with that of C-PTC. Treatment recommendations (complete thyroidectomy with ablative radioactive iodine therapy) for C-PTC and FTC can be applied to FV-PTC cases.

OR14-01

Ultrasound-guided percutaneous microwave ablation of benign thyroid nodules: a 12-month follow-up in 395 patients

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Objective Thermal ablation is a minimally invasive method for thermal ablation of benign thyroid nodules. The study aimed to investigate the effectiveness and safety of ultrasound-guided percutaneous microwave ablation (MWA) in the treatment of benign thyroid nodules with a large sample.
Materials and methods A total of 437 benign thyroid nodules in 395 patients underwent microwave ablation from May 2011 to July 2014. Microwave ablation was carried out using microwave antenna (16G) under local anesthesia. Nodule volume, intranodular blood flow, thyroid function and clinical symptoms were evaluated before treatment and at 1, 3, 6 and 12 months. This study was ethics committee approved and its written informed consents were obtained from all patients.
Results All thyroid nodules significantly decreased in size after microwave ablation. A 12-month follow-up was achieved in 437 nodules. The mean reduction in the volume of thyroid nodules was from 5.46±10.40 ml to 0.04±0.20 ml. There were no differences of the volume reduction among the solid nodules, cysts and mixed nodules after a 12-month follow-up. The treatment was well tolerated and no major complications were observed except pain during the ablation.
Conclusions Ultrasound-guided percutaneous microwave ablation seems to be a safe and effective method for the treatment of benign thyroid nodules, including solid and cystic nodules. It should be considered as an option for the management of benign thyroid nodules.

OR14-02

The Circulating Epithelial Cells for Detecting Recurrent or Persistent Disease in Patients of Papillary Thyroid Carcinoma with Positive Anti-thyroglobulin Antibody

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Objective Papillary thyroid carcinoma (PTC) accounts for about 80% of the cases in thyroid cancer. Routine surveillance by serum thyroglobulin (Tg) and medical imaging is the current practice to monitor disease status of the patients. However, serum Tg cannot be a tumor marker in patients with positive anti-Tg antibody. Our recent study implicates that circulating epithelial cell (CEC) testing can supplement the current standard methods for monitoring disease status of PTC. The aim of this pilot study is to evaluate the clinical role of CEC in patients of PTC with positive anti-Tg antibody.
Methods From April 2013 to August 2015, we performed a pilot study with a total of 12 patients of PTC with positive anti-Tg Ab. CECs were enriched from the peripheral blood by the negative selection system PowerMag. Cell populations in leukocyte-depleted cell filtrates were characterized by immunofluorescence staining using anti-epithelial cell adhesion molecule (EpCAM) and anti-thyroid stimulating hormone receptor (TSHR) antibodies. The cut-off point for CEC testing was considered positive for recurrent or persistent disease of PTC when CEC with EpCAM > 22 cells/ml or CEC with TSHR > 33 cells/ml according to our previous publication.
Results The result showed use of CEC counts to identification of disease status in patients of PTC with positive anti-Tg Ab is useful with good specificity (100%) and positive predictive value (100%) and could be a potential tumor marker for patients in PTC with positive anti-Tg Ab.

Conclusion In summary, our preliminary data illustrated CEC testing could be a useful marker to identify the disease status in patients of PTC with positive anti-Tg Ab.

OR14-03

Clinicopathological Risk Factors Predicting Central Lymph Node Metastasis in Papillary Thyroid Microcarcinoma

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Aim The incidence of papillarythyroid microcarcinoma (PTMC) had been rising rapidly. How to optimally manage PTMC is still controversial and a major consideration is how to predict the presence of central lymph node metastasis (CLNM) to determine appropriate surgical treatments.

Methods This was a retrospective study on 917 patients with PTMC treated with surgery from January 2014 to July 2015 in our institution. The relationship between a variety of clinicopathological risk factors and CLNM was analyzed to identify those that couldpredict CLNM.

Results Of the 917 patients, 344 (37.5%) had CLNM. Univariate logistic regression analysis showed that there was a significant association of CLNM with male patient sex and younger age (<45years, positive CLNM on ultrasonography, mulifocality, larger tumor size (>5 mm), tumor bilaterality, and thyroid capsular invasion. Multiple logistic regression analyses showed an independent association between CLNM and male patient sex (OR =1.751, 95%CI 1.172~2.615; P=0.006), younger age (<45years) (OR =1.695, 95%CI 1.205~2.384; P=0.002), positive CLNM on ultrasonography (OR =10.202, 95%CI 5.512~18.883; P<0.001), mulifocality (OR =1.695, 95%CI 1.007~2.852; P=0.047), and larger tumor size (>5 mm) (OR=2.805, 95%CI 2.011~3.911; P<0.001).

Conclusions CLNM in PTMC is significantly associated with several risk factors that are known preoperatively, including male patient sex, younger age (<45years), larger tumor size (>5 mm), mulifocality, and positive CLNM on ultrasonography. Status of these risk factors may help preoperatively predict CLNM and determine the right surgical treatment for patients in appropriate clinical settings.

OR14-04

Ultrasound and TIRADS can reduce The needed number of Fine Needle Aspiration?

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1. Governo Estado Rond?nia
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Objective The prevalence of solid thyroid nodules is very high in the general population. Appropriate selection of cases for surgery is the most important task, when evaluating nodules. The present study wants to see if the use of Thyroid Imaging Reporting and Data System (TIRADS) could decrease the number of needed FNAB procedures.

Material and method 254 nodules evaluated by conventional ultrasound with linear multifrequency probe between january 1, 2012 and january 1, 2016. Prospective all nodules were classified by TIRADS system: ecogeneity (risk hipomogeneity), margins (risk irregular margins), shape (risk irregular shape, taller than wide), calcification (risk micro calcifications), lymph node (risk presence), and increased strain (color map 4, 5, increased strain ration). TIRADS 4A, 4B, and 5 cases were referred also to FNAB. All 254 cases were operated and pathology report was obtained.

Results The Cancer was certified in 49 of the 254 operated thyroid nodules. The number of required punctions would be in 229 cases, if we consider the AACE guidelines. If we apply the TIRADS system (all 4A, 4B, and 5 TIRADs nodules) in selecting the cases for FNAB, the number would decrease significantly up to 74 nodules. The diagnostic quality of TIRADS is very high: using the ROC method, the AUC = 0.95761, confidence limit of 0.8424 - 0.989 (95% LCL and 95% UPL), specificity in diagnostic of cancer was excellent: diagnostic sensitivity, 86.20% with high specificity, 97.24%. with the best accuracy of 95.40%

Conclusion Using TIRADs system, the correct evaluation of the majority of the thyroid nodules is achieved.

OR15-01

Gene mutation spectrum and genotype-phenotype correlation in Chinese osteogenesis imperfecta patients revealed by targeted next generation sequencing

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Objective: Osteogenesis imperfecta (OI) is a group of skeletal diseases characterized by increasing bone fragility and recurrent fractures. The molecular diagnosis of OI is often challenging due to the clinical and genetic heterogeneity of these diseases. This study aims to reveal the gene mutation spectrum, and genotype- phenotype relationship among Chinese OI patients by next generation sequencing (NGS).

Method: We developed a NGS-based panel for targeted sequencing of all exons of 14 genes related to OI, and performed diagnostic gene sequencing for a cohort of 103 Chinese OI patients from 101 unrelated families. Mutations identified by NGS were further confirmed by Sanger sequencing and co-segregation analysis. Genotype and phenotype relationship were analyzed by comparison of bone morphologies among patients with different gene mutations.

Results: Of the 103 patients from 101 unrelated OI families, we identified 79 mutations (15 frameshift, 40 missense, 6 nonsense, 15 splice site and 3 others), including 43 novel (11 frameshift, 17 missense, 5 nonsense, 9 splice site and 1 chromosome translocation) in 90 patients (87.4%). Mutations in genes encoding type I collagen, COL1A1 (n=37) and COL1A2 (n=29), accounts for 73.3% of all molecularly diagnosed patients, followed by IFITM5 (n=9, 10 %), SERPINF1 (n=4, 4.4%), WNT1 (n=4, 4.4%), FKBP10 (n=3, 3.3%), TMEM38B (n=3, 3.3%) and PLOD2 (n=1, 1.1%). This corresponds to 75 autosomal dominant inherited OI patients and 15 autosomal recessive inherited patients. Compared with autosomal dominant (AD) inherited OI patients, autosomal recessive (AR) inherited patients had lower bone mineral density (BMD) at spine (BMD Z score -3.6±2.1 for AR and -2.6±1.9 for AD, P=0.05, respectively) and less frequent blue sclera (71.1% in AD versus 26.7% in AR, P=0.001, respectively). Patients with type I collagen qualitative defects had lower femoral neck BMD Z score (-3.1±2.1 for quantitative and -5.0±3.2 for qualitative, P=0.034, respectively) and were shorter compared with patients with type I collagen quantitative defects (-1.2±4.8 for quantitative and -6.5±8.2 for qualitative, P=0.022, respectively).

Conclusions: We revealed here the gene mutation spectrum in Chinese OI patients by NGS sequencing, and novel mutations identified here expanded the mutation catalogue of OI. Our results demonstrated NGS-panel as an effective method for molecular diagnosis of OI, and provided novel insights into the genotype and phenotype relationships among OI patients.

OR15-02

Identification of a novel LEMD3 Y871X mutaiton in a three-generation family with osteopoikilosis

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Introduction Osteopoikilosis is a rare and benign autosomal dominant genetic disorder, characterized by a symmetric but unequal distribution of multiple hyperostotic areas in different parts of the skeleton. It can occur in isolation or in association with other skin and bone lesions, most notably in Buschke-Ollendorff syndrome-and melorheostosis. Recently, whole-genome linkage analysis of affected individuals showed that loss-of-function mutation in gene LEMD3 (OMIM 607844) at position 12q13 was the cause of osteopoikilosis, irrespective of whether these patients had coexistent BOS or melorheostosis.

Methods We investigated LEMD3 gene in a three-generation family from China, with six patients affected with osteopoikilosis. Peripheral blood samples were collected from family members and 100 healthy controls. All exons of the LEMD3 gene and adjacent exon-intron sequences were amplified by PCR and subsequently sequenced.

Results A novel heterozygous c.2612_2613insA (p.Y871X) mutation in exon 13 of LEMD3 was identified, which resulted in a frame shift predicted to generate a premature stop codon at amino acid position 871. The mutation co-segregates with the osteopoikilosis phenotype and was not found in 100 ethnically matched controls.

Conclusion we have identified a novel insertion mutation in the LEMD3 gene as the cause of osteopoikilosis, which contributes to further understanding of the pathogenesis of this disease. Moreover, our study stresses the importance of early recognition of osteopoikilosis to avoid unnecessary emotional distress and invasive testing.

OR15-03

Hip fractures in young adults: a missed opportunity for intervention

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Objective Hip fractures are a common cause of morbidity, hospitalisation, and death in the elderly, with published standards of care to guide optimal management. In comparison, there is a paucity of data examining hip fractures in young adults (<50 years) with only a limited understanding of related comorbidities and health outcomes. We aimed to characterise risk factors, complications and follow-up of hip fractures in young adults at a single Australian tertiary referral centre.

Methods Medical records of patients aged 15-49 years and hip fractures were identified using ICD-10 codes for the period of January 2009 to June 2015. Fractures were classified as high-impact (HIF) or minimal-trauma (MTF). The primary outcome was to compare co-morbidities, health outcomes and follow-up rates between the MTF and HIF groups, in order to test the hypotheses (established before data collection) that the MTF group have higher rates of co-morbidities and post-operative complications, and inadequate treatment for osteoporosis.

Results 2,512 patients presented with hip fractures, with 2.5% (n=62) aged 15-49. The mean age was 40 years (±9.0) and 56% were male. MTF occurred in 43 individuals (51% male) and HIF in 10 (70% male). Mechanism of injury was unspecified in 7 patients and 2 pathological fractures were excluded. The most common fracture sites were subcapital (32%), trochanteric (15%) and subtrochanteric (12%).

Young adults with MTF hip fractures had significantly higher American Society of Anesthesiologists Physical Status Classification System[1] values compared to those with HIF (MTF 2.44±0.9; HIF 1.43±0.5) (p=0.025). Consistent with this, comorbidities were more common in the MTF group, including chronic endocrine disorders (MTF 35%; HIF 0%; p=0.046) (hypogonadism, thyroid disorders, type 1 or 2 diabetes mellitus, parathyroid disease). Other comorbidities included neurological disease (MTF 36%; HIF 10%) and stage 4/5 chronic renal disease (9%; 0%), but these were not statistically significant. Regular medication use was more common in the MTF group, including use of anticonvulsants (20%; 0%), opioids (20%; 0%) and corticosteroids (16%; 0%).

The MTF group had increased rates of post-operative medical complications (MTF 29.7%; HIF 12.5%) and surgical complications (22.5%; 14.3%), with more frequent readmissions within 6 months (10.8%; 0%), although none of these differences reached statistical significance.

Of the MTF group, Osteoporosis Clinic follow-up was arranged for 35% (15/43), with no osteoporosis follow-up in ~50 % of patients (data not available in 15%). Of those referred to Osteoporosis Clinic, 9/15 patients were commenced on antiresorptive therapy (bisphosphonates n=8,denosumab n=1) and 2/15 were commenced on teriparatide. Patients not commenced on specific osteoporosis therapies at review had complex chronic kidney disease. Further fractures occurred in 5/43 MTF patients (12%) during the study period, including 3 peri-prosthetic fractures, of whom 60% (n=3/5) had not been reviewed in the Osteoporosis Clinic. Mean time to re-fracture was 315 days post-initial fracture.

Conclusions Young adults with MTF of the hip have significantly higher ASA scores and rates of chronic endocrine disease compared to those with HIF. These patients have complex co-morbidities including neurological disease, renal disease and polypharmacy. Further research is required to characterise this vulnerable group. Development of a systematic medical referral pathway for young adults with minimal trauma hip fracture is needed to ensure appropriate follow-up of osteoporosis and its associated complex comorbidities.

OR15-04

Exendin-4 protects vascular endothelial cells from advanced glycation end products-induced apoptosis through regulating autophagy flow via SIRT1/FoxO1 pathway

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Background and aims Dysfunction of vascular endothelial cells (ECs) elicited by advanced glycation end products (AGEs) is the main cause of diabetic vascular complications. Impaired autophagic flux contributed to endothelial dysfunction in patients with diabetes. Exendin-4, besides its insulinotropic action, has been found to exert a direct beneficial effect on endothelial function; however,

the underlying mechanisms remain elusive. The aim of this study is to investigate the effects of Exendin-4 on ECs autophagy and its impact on AGEs-induced ECs apoptosis.

Materials and methods Cultured human aortic vascular ECs (HAECs) were stimulated with AGEs-bovine serum albumin (AGEs-BSA) or BSA, or AGEs-BSA and Exendin-4, respectively. Autophagosomes were observed by electron microscopy. The apoptosis rate was evaluated by flow cytometry. The expression levels of LC3-II, P-62, Rab7, cleaved-caspase-3, Bcl-2, SIRT1, p-SIRT, FoxO1, Ac-FoxO1, p-FoxO1, AKT and p-AKT were determined by western blotting.

Results AGEs induced autophagy of HAECs in a time-dependent manner. For 24h, the LC3-II expression and the number of autophagosomes were gradually increased with no change of P-62, Rab7 expression and apoptotic rates. For 48h, AGEs markedly upregulated LC3-II expression and the number of autophagosomes with increased level of P-62 which indicated the reduced autophagic flux. The apoptotic rates were significantly increased with elevated cleaved-caspase-3 level and declined Bcl-2 expression. The expressions of p-SIRT, Ac-FoxO1, Ac-FoxO1/Atg7 and p-AKT were strikingly increased while p-FoxO1 level was obviously decreased. Inhibition of autophagy with 3-MA could reduce AGEs-induced HAECs apoptosis. When pretreated with Exendin-4 AGEs-induced apoptosis of HAECs was significantly decreased with reduced cleaved-caspase-3 level and elevated Bcl-2 level. The LC3-II expression and the number of autophagosomes were not changed while AGEs-induced accumulation of P-62 was diminished with upregulated Rab7 level. Exendin-4 markedly decreased AGEs-induced expression of p-SIRT1, Ac-FoxO1 and nucleus p-AKT and promoted the phosphorylation of FoxO1 and cytoplasm localization. The SIRT1 inhibitor nicotinamide could reduce the antagonistic effect of exendin-4 on AGEs-induced apoptosis of HAECs.

Conclusions Impaired autophagic flux involves in AGEs-induced ECs apoptosis. Exendin-4 could protect vascular endothelial cells from AGEs-induced apoptosis through regulating autophagy flow via SIRT1/FoxO1 pathway.

OR16-01

Glucagon-like peptide-1 receptor agonist Liraglutide has anabolic bone effects in ovariectomized rats without diabetes

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Aims Recently,a number of studies have demonstrated the potential beneficial role for novel anti-diabetic GLP-1 receptor agonists (GLP-1RAs) in the skeleton metabolism in diabetic rodents and patients. In this study, we evaluated the impacts of the synthetic GLP-1RA Liraglutide on bone mass and quality in osteoporotic rats induced by ovariectomy (OVX) but without diabetes, as well as its effect on the adipogenic and osteoblastogenic differentiation of bone marrow stromal cells (BMSCs).

Methods Three months after sham surgery or bilateral OVX, eighteen 5-month old female Wistar rats were randomly divided into three groups to receive the following treatments for 2 months: (1) Sham + normal saline; (2)OVX+ normal saline; and (3) OVX+Liraglutide (0.6 mg/day).The effects of Liraglutide on osteoblastogenic and adipogenic differentiation in vitro were determined by culturing rat and human BMSCs in different differentiation media with or without 10 nM Liraglutide.

Results As revealed by micro-CT analysis, Liraglutide improved trabecular volume, thickness and number, increased BMD, and reduced trabecular spacing in the femurs in OVX rats; similar results were observed in the lumbar vertebrae of OVX rats treated with Liraglutide. Following in vitro treatment of rat and human BMSCs with 10 nM Liraglutide, there was a significant increase in the mRNA expression of osteoblast-specific transcriptional factor Runx2 and the osteoblast markers alkaline phosphatase (ALP) and collagen a1(Col-1), but a significant decrease in peroxisome proliferator-activated receptor γ(PPARγ).

Conclusion Our results indicate that the anti-diabetic drug Liraglutide can exert a bone protective effect even in non-diabetic osteoporotic OVX rats. This protective effect is likely attributable to the impact of Liraglutide on the lineage fate determination of BMSCs.

OR16-02

The bone-preserving effects of exendin-4 in ovariectomized rats

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Purpose Exendin-4 is a type of glucagon-like peptide-1 (GLP-1) receptor agonist that is beneficial to the skeleton in diabetic rodents.In this study, we assessed the changes of bone in non-diabetic osteoporotic ovariectomized (OVX) rats after treatment with Exendin-4, in addition with the regulatory role of Exendin-4 on osteoblastogenesis and adipogenesis in rat bone marrow stromal cells (BMSCs) and explored the potential underlying signaling pathways.

Methods Three months after sham surgery or bilateral OVX, eighteen 5-month old female Wistar rats were randomly divided into three groups (6 rats per group) and received the following treatment for 8 weeks: (1) Sham + normal saline (Sham); (2) OVX + normal saline (OVX); and (3) OVX+Exendin-4 20 μg/kg/d (OVX+E). Then, Micro-CT and three-point bending test were used to evaluate the BMDs, bone morphometric parameters and biomechanical properties. In vitro, real-time PCR and western blot were performed to measure gene and protein expression after exendin-4 treatment in adipogenesis and osteoblastogenesis of rat BMSCs.

Results Exendin-4 could improve trabecular volume, thickness and number, increase BMD, and reduce trabecular spacing in the lumbar-spine and femur of OVX rats. However, little impact by Exendin-4 was found on the mechanical resistance of femurs to fracture.In vitro, when rat BMSCs were treated with Exendin-4, there was a significant increase in the mRNA expression levels of Runx2, ALP and collagen a1,but a marked decrease in PPARγ and C/EBPα mRNA expression levels. Moreover, Exendin-4 treatment also resulted in increased expression levels of p38, p42/44, and β-catenin proteins.

Conclusions Taken together, our study indicated that Exendin-4 was anabolic to bone in OVX rats and provided evidence that Exendin-4 could facilitate osteoblastogenesis with simultaneous repression of adipogenesis during BMSC lineage differentiation through the MAPK and Wnt signaling pathways.

OR16-03

Geometry Parameters and the Impact Factors of the Hip in Type 2 Diabetes Mellitus:Implications for Fracture Risk?

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Objectives To investigate the variation of geometry parameters and the related impact factors of the Hip in type 2 diabetes mellitus

(T2DM).

Methods The medical records of 305 patients (155 men and 150 women) with T2DM and 332 health controls matched for age and sex in the Second Xiangya Hospital from December 2013 to November 2014 were involved in this retrospective research. The detailed clinical informations of the patients were collected including name, gender, age, weight, height, menstrual history, the history of bone fracture, duration of diabetes, diabetic chronic complications and the blood biochemical indices containing fasting blood glucose (FBG), glycosylated hemoglobin (HbAlc), fasting plasma c-peptide (F-CP), postprandial c-peptide (P-CP), creatinine, calcium, phosphorus. Bone mineral density (BMD), including lumbar spines (L1~L4), the left femoral neck, Troch, Ward's and the total hip, were measured with dual energy X-ray absorptionmetry (DXA). Analyses of hip geometry parameters such as neck shaft angle (NSA), cross sectional area (CSA), cross-sectional moment of inertia (CSMI), sectional modulus (Z), average cortical thickness (CT), bucking ratio (BR) at femoral feck (FN), intertrochanteric (IT), and shaft (FS) were done using the validated Becks method on hip scans from DXA. Correlation analysis was performed by Partial correlation test, and multiple stepwise regression analysis was used to analyse the related impact factors.

Results 1. The prevalence rate of osteoporosis has not been found significance difference between the T2DM and control group. There was no statistical significance for the BMD at lumbar spine and proximal femur regions between the female T2DM and control group. Postmenopausal women with T2DM group showed decreased femoral neck CSA, intertrochanteric BR and femoral shaft BR vs controls (P<0.05) , increased upper neck shaft angle (NSA) and femoral shaft CT vs controls (P<0.05) . In male T2DM group, the BMD at lumbar spine and the total hip regions were significantly higher than those in control group, while the BMD at left femoral neck region was significantly lower than that in control group. Male T2DM group showed decreased femoral neck (CSA, CSMI, BR), intertrochanteric BR, and femoral shaft (CSMI, Z, BR) vs controls (P<0.05) , increased intertrochanteric (Z, CT) and femoral shaft CT vs controls (P<0.05) .

2. Adjusted for age and body mass index (BMI), BMD at proximal femur regions showed a positive correlation with hip geometry parameters (CSA, Z, CSMI, CT) at all three regions, while a negative correlation with BR (P<0.01) . Adjusted for the total hip BMD, the stepwise multiple linear regression showed that the main positive influence factor affecting geometry parameters of the hip was BMI. The negative factor mainly affecting hip geometry parameters was duration of menopause in female T2DM group except that age negatively affected the femoral neck CSMI. All the hip geometry parameters were mostly negatively affected by age in male T2DM group except CT and BR in intertrochanteric and femoral shaft.

3. All T2DM patients were divided into normal weight group (18.5<bmi<24.0< span=""></bmi<24.0<>) , overweight group (24.0≤BMI<28.0) and obesity group (28.0≤BMI) . The BMD at lumbar spine and proximal femur regions in overweight and obesity group were significantly higher than those in normal weight group. The normal weight patients showed higher osteoporosis prevalence rate than that of overweight group while overweight group was higher than that in obesity group. Overweight and obesity group indicated increased hip geometry parameters (CSA, Z, CSMI, CT) at all three regions vs normal weight group (P<0.05) , decreased BR at all three regions vs normal weight group (P<0.05) . In female T2DM obesity group, only hip geometry parameters at femoral shaft (CSA, CSMI, Z) were significantly higher than those in overweight group. In male T2DM obesity group, only hip geometry parameters at femoral neck (CSA, CSMI) and femoral shaft (CSA, CSMI, Z) were significantly higher than those in overweight group. The NSA showed no significant difference in different BMI groups for both male and female.

4. In different duration of diabetes, whether male or female, there was no significant difference in age, age of menopause (women), duration of menopause (women), BMI, FBG, HbAlc, the BMD at lumbar spine and proximal femur regions, osteoporosis prevalence rate, and hip geometry parameters (CSA, Z, CSMI, CT, BR) at all three regions.

Conclusions 1. There were some differences in hip geometry parameters between T2DM patients and health controls, which varied with skeletal site and gender.

2. There was a sexual difference in the related impact factors on hip geometry structure: BMD, BMI and duration of menopause were the main impact factors of hip geometry parameters in female T2DM patients, while BMD, BMI and age in male T2DM patients.

3. FBG, HbA1c, F-CP and duration of diabetes were not found related to the hip geometry parameters in T2DM patients.

OR16-04

The evolution of untreated hypothyroidism in adults - implications in dento-maxillary pathology

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Introduction dento-maxillary system changes are constantly present and differentiated depending on the period of evolution of hypothyroidism, appearing from the stages of its subclinical evolution.

Aim of the study: Evaluating the oro-maxillo-facial changes in patients with hypothyroidism, with characteristics depending on the history of disease evolution.

Methods The study group - 154 patients with myxedema, 132 women and 22 men. The examination of oral cavity was done under parodontal status, the quality of dentition, changes of dento-maxillary dynamics.

Results Facial and lip infiltrative changes present in 98.4% of cases; macroglossia 13%; mucoid infiltration of lingual mucosa and oral cavity submucosa -100% ; gingivitis and chronic marginal periodontitis -100%; pathological tooth mobility - grade 1 (73%) and grade 2 (15%); 12 patients (9.16%) required periodontal abscess drainage - 2 cases of upper premolars (14,15) -10 cases of lower molars (36,47). Modification of occlusion by changing maximum pressure points -72 patients (52%). A total of 61 patients (46.5%) presented vestibular pockets -23 periodontal (17.5%), 25 palatal (19%) and 13 with lingual localization (10%). The average time of evolution of untreated hypothyroidism was

8.3 ± 1.2 months. Dental cavities were present in 77% of patients; partial edentation – in 89.3%; total edentation - 9.16%. Atrophied prosthetic field -4 cases (3%); 8 cases (6%) -process of osteophitic hyperostosis with bosselated, irregular prosthetic field. The mean time of hypothyroidism evolution: 2.4 ± 1.5 months.

Conclusions Periodontal changes are almost constantly found in hypothyroidism. The extent of the thyroid disease without substitution therapy is directly proportional to the severity and a high incidence of parodontal changes and dento-maxillary dinamics.

OR17-01

Cardiometabolic consequences of polycystic ovary syndrome; a population based cohort study with 15 years of follow up.

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Objectives Polycystic ovary syndrome (PCOS) is the common endocrine disorder in women of childbearing age, with a reported prevalence of 4-15% depending on the diagnostic criteria.The trends of cardio-metabolic risks of Polycystic Ovary Syndrome (PCOS) have not been well described. We aimed to compare the trends of these risk factors in PCOS patients and healthy controls in a 15-year prospective population based cohort study with 3-year intervals between follow-ups

Methods Of a subset of 1002 non-menopausal women randomly selected from the Tehran Lipid and Glucose Study, 637 participants were selected for the study groups of the present study including 85 with PCOS diagnosis and 552 as eumenorrheic non hirsute controls. Using the National Institute of Health criteria, we defined PCOS as the presence of ovulatory dysfunction and clinical hyperandrogenism and/or hyperandrogenemia, after exclusion of other known related disorders such as hyperprolactinemia, thyroid and adrenal disorders.Cardio-metabolic risks were assessed at the time of recruitment and three times after that with a 3-year interval. The GEE models were created with an interaction form (follow-up years × study group) to analyze the change in various cardio-metabolic parameters across the time by PCOS status.

Results The prevalence of pre-diabetes and diabetes in PCOS patients at the time of recruitment were 11.9% and 1.5%, respectively; while these amounts for normal subjects were 7.3% and 4.4%, respectively. The prevalence of pre-hypertensive state were 26.5% and 19.7%, and of hypertension were 7.1% and 5.1%, for PCOS patients and normal subjects respectively.There was a significant difference on incidence rates of DM between PCOS women (0.013; 95% CI: 0.007, 0.025), and normal controls (0.004; 95%CI: 0.002, 0.006). However no significant differences was observed on incidence rates for pre-DM between PCOS women with normal controls 0.028 person-year (CI: 0.017, 0.047) and 0.022 person-year (CI: 0.018, 0.027), respectively. There were no significant differences between incidence rates for pre-HTN and HTN of PCOS women and controls during our study; incidence rate for pre-HTN 0.040 (CI: 0.025, 0.066) for PCOS patients and 0.036 (CI: 0.031, 0.044) for normal subjects and for HTN it was 0.015 (CI: 0.008, 0.027) and 0.013 (CI: 0.010, 0.017), respectively.According to GEE analysis, there were no significant correlation between various metabolic parameters and PCOS status, except HOMA-IR and IR that increased in PCOS patients compared to normal ones after adjustment for age, BMI and baseline status of these variables; however their changes' slops were decreased by the time in PCOS women (HOMA-IR: -.063, CI(-.124, -.003), P=0.04; odds ratio of IR: .894, CI(.814, .981), P=0.019).

Conclusion Despite the higher prevalence of CVD risk factors of reproductive aged PCOS women, their adverse cardio-metabolic consequences in future are much lower than initially anticipated.

OR17-02

Visceral fat dysfunction is positively associated with hypogonadism in Chinese men

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Objective Visceral adiposity index (VAI) well mirrors visceral fat dysfunction. No study explored the association between low androgen and VAI. We aimed to determine whether VAI was associated with hypogonadism and sex hormones, and also whether it better predicted hypogonadism than other obesity indices (waist, hip and neck circumference, BMI, waist-hip ratio and body adiposity index).

Methods Our data were collected from 16 sites in East China. 2,759 men were enrolled. Hypogonadism was defined as total testosterone <11.3 nmol/L. VAI was calculated in male: (waist circumference/(39.68 + (1.88 × BMI))) × (triglycerides/1.03) × (1.31/HDL).

Results 484 (17.5%) hypogonadal men had significantly higher VAI. After adjusting for age, smoking, neck and hip circumference, diabetes and hypertension, VAI was inversely associated with total testosterone, estradiol and SHBG (P<0.01). Higher quartiles of VAI were associated with significantly increasing odds of hypogonadism (P for trend <0.01). The fully adjusted odds ratio was 5.88 (95 CI% 4.09, 8.46) for the highest quartile compared with the lowest quartile of VAI. Among all the indices investigated, VAI showed the largest area under the curve (P <0.001).

Conclusion the VAI was significantly associated with a higher prevalence of hypogonadism in Chinese men. VAI also best predicted hypogonadism among obesity indices (waist, hip and neck circumference, BMI, waist-hip ratio and body adiposity index).

OR17-03

Serum Vitamin D concentration is independently associated with anti-Mullerian hormone level and obesity measures in Hong Kong Chinese women with polycystic ovary syndrome

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Objective Polycystic ovary syndrome (PCOS) is one of the commonest reproductive endocrine disorder among women of reproductive age. Vitamin D status has been postulated to be involved in the pathogenesis of PCOS. Increased serum anti-Mullerian hormone (AMH) level, hyperandrogenism and the metabolic syndrome are common endocrine and metabolic characteristics in PCOS. There have been limited and inconsistent data on the relationship between vitamin D status and these parameters. This study aimed at investigating the association of serum vitamin D concentration with serum AMH level and obesity measures in women diagnosed with PCOS as well as non-PCOS healthy women in the Hong Kong Chinese population.

Methods This study was conducted on archival serum samples prospectively collected from 451 women diagnosed with PCOS according to the Rotterdam criteria as well as 242 non-PCOS women who were recruited into another observational clinical study on the metabolic and endocrine profile of PCOS patients in the Hong Kong Chinese population (HK PCOS Study). Vitamin D (25-hydroxycholecalciferal) and AMH were measured on the archival serum samples by chemiluminescent immunoassays on the Access 2 automated platform (Beckman-Coulter Diagnostics). Other clinical and biochemical data were obtained from the HK PCOS Study. Statistical analyses were performed using the Pearson correlation and multiple linear regression.

Results Among PCOS subjects, 114 (25.2%) and 325 (72.1%) were vitamin D-insufficient (20-30 ng/ml inclusive) and vitamin D-deficient (<20 ng/ml) respectively, compared to 78 (32.2%) and 158 (62.7%) of non-PCOS controls who were vitamin D-insufficient and vitamin D-deficient respectively (p>0.05). Serum vitamin D level was significantly higher in both PCOS and non-PCOS subjects recruited during summer (June to August) and autumn (September to November) compared to winter (December to February) and spring (March to May) months; there was a similar significant peak of serum AMH level in PCOS subjects recruited in summer compared to winter and spring months, but no significant seasonal variation in serum AMH was evident in the non-PCOS controls. In the PCOS subjects, serum vitamin D was significantly

correlated with serum AMH (r=0.185, p<0.0005), body weight (r=-0.117, p=0.013), waist circumference (r=-0.111, p=0.018), body mass index (r=-0.138, p=0.001), serum total testosterone (r=0.109, p=0.021), serum androstenedione (r=0.098, p=0.039), sex hormone-binding globulin (SHBG) (r=0.149, p=0.002), insulin (r=-0.121, p=0.011), HOMA-IR (r=-0.126, p=0.008) and QUICKI (r=0.121, p=0.010), but not with fasting glucose nor any of the lipid parameters (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides) (p>0.05). After controlling the confounding effect of BMI by partial correlation analysis, serum vitamin D remained significantly correlated with serum AMH (r=0.160, p=0.001), total testosterone (r=0.111, p=0.023) and androstenedione (r=0.098, p=0.039), but the correlation with other parameters became insignificant, indicating that the association of vitamin D with SHBG and insulin resistance were probably through the effect of obesity. In the non-PCOS control subjects, however, all of the above correlations were not statistically significant (p>0.05). Multiple linear regression analysis revealed that serum AMH (beta=0.135, p=0.012) and BMI (beta = -0.123, p=0.009), but not serum total testosterone, were significant independent factors associated with serum vitamin D in the PCOS subjects.

Conclusion In our population, lower serum AMH level and obesity are significant independent factors that are associated with lower serum vitamin D concentration in women with PCOS. The clinical significance of low vitamin D status on the ovulatory function and long-term cardio-metabolic risk worth further investigations.

OR17-04

Serum GDF-8 levels change dynamically during controlled ovarian hyperstimulation in patients undergoing IVF/ICSI-ET

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Objective To evaluate the expression profile of GDF-8 in serum and whether the level of serum GDF-8 influences pregnancy results for patients treated with in vitro fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET).

Methods All the included patients were treated with a standard long gonadotropin-releasing hormone agonist (GnRH-a) protocol. GDF-8 levels were measured in serum from patients undergoing controlled ovarian hyperstimulation (COH) at different time points:Time point 1, GnRH-a day; Time point 2, initial gonadotropin(Gn) administration day; Time point 3, human chorionic gonadotropin (hCG) administration day; Time point 4, 12 hours after hCG administration; Time point 5, Oocyte pick-up (OPU) day, approximately 36 hous after hCG administration; Time point 6, 48 hours after OPU; Time point 7, 14 days after embryo transfer (ET). These GDF-8 levels were correlated with the pregnancy results. GDF-8 levels were also measured in the patients' follicular fluid. GDF-8 protein levels were measured by an enzyme immunoassay (ELISA).

Results GDF-8 had a dynamic trend during controlled ovarian hyperstimulation (COH) procedure. GDF-8 level in serum increased slightly after GnRH-a administration; however, it decreased greatly after Gn injection, especially at 12 h after hCG administration. Interestingly, serum GDF-8 levels were primarily down-regulated in the early luteal phase, and then they were up-regulated in the late luteal phase. On hCG administration day, patients with a GDF-8 level higher than 4.7 ng/ml had lower progesterone levels and a higher pregnancy rate. From hCG day to oocyte pick-up day, patients with a GDF-8 decrease greater than 1.3 ng/ml had a higher progesterone increase and a higher pregnancy rate. Importantly, the levels of GDF-8 were negatively correlated with progesterone levels.

Conclusion Serum GDF-8 levels change dynamically during COH in patients undergoing IVF/ICSI-ET and GDF-8 plays an important role in ensuring successful pregnancy by regulating progesterone levels

OR18-01

The effect of thyroid hormone on the expression of kisspeptin in hypothalamus and its related mechanisms

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Objective 1. To explore the effect of T3 on the expression of the KISS1 gene and the kisspeptin in GT1-7 cells and figure out the optimal concentration of T3 that can stimulate the exprression of kisspeptin in GT1-7 cells. 2. To investigate the effect of instantaneous lateral intraventricular injection of T3 on the expression of the KISS1 gene and the kisspeptin in hypothalamus of the mice. 3. To study how the chronic injection of T3 by intracerebroventricular cannulation affects the KISS1 gene transcription level and the kisspeptin expression. Explore the pathways and related mechanisms of how T3 intervenes the reproductive function by observing the effect of rapamycin.

Methods 1. In vitro experiment: We cultivated GT1-7 cells in vitro and prepared DMEM with T3 concentration of 2000ng/ml, 200ng/ml, 20ng/ml, 0ng/ml respectively. GT1-7 cells were treated with different concentration of T3 solutions for 24 hours, then collected. We used Realtime PCR to test the gene expression of KISS1 and western blot to detect kisspeptin expression in GT1-7 cells which were treated with different concentrations of T3. So as to figure out the optimal concentration of T3 that can stimulate the expression of kisspeptin in GT1-7 cells. 2. In vivo experiment: acute experiment: 12 mice were randomly divided into control group (N group) and T3 injection group (T group). We performed instantaneous injection of NaOH and T3 respectively by mouse stereotaxic instrument, and observed the expression of KISS1 mRNA and kisspeptin in hypothalamus of mice. We also used immunohistochemical method to compare the differences of the expression of kisspeptin in the arcuate nucleus area between these two groups. Chronic experiment: 24 mice were randomly divided into four groups. Each group contains 6 mice. Group N was set as a normal control group with no intracerebroventricular cannulation and no injection of drugs; With the help of the mouse stereotaxic instrument we implanted catheter into the lateral ventricle and connected the catheter with ALZET capsule osmotic pump which was embedded ubcutaneously. With these sets Group IN were treated with chronic 6injection of NaOH for 7 days. Group IT were treated with chronic injection of T3 for 7 days. Group IR were treated with chronic injection of T3 and rapamycin for 7 days . During the dosing days we take vaginal smears of every mouse to know their estrus cycles. We measured their weights before and after the experiment to observe the effects of drug injection on their body weights. We tested the serum thyroid stimulating hormone (TSH), free thyroid hormones (FT4), luteinizing hormone (LH), and estrogen(E) to compare the effects of different drug intervention in mice. We used realtime PCR to test KISS1 gene mRNA expression and used western blot to measue kisspeptin expression. We also compared hypothalamic arcuate nucleus kisspeptin protein expression among these different treatments groups with immunohistochemical staining.

Results 1. In vivo experiment results: T3 can change KISS1 mRNA and kisspeptin expression in GT1-7 cells. The influence of T3 on the expression of KISS1 gene and kisspeptin expression is a "U" shape curve. Both of the doses that were too low or too high would supressed the expression of KISS1 gene and kisspeptin. The best concentration of T3 on the expression of kisspeptin in GT1-7 cells were 200 ng/ml. In vivo experiment results: acute experiment: Intracerebroventricular injection of T3 instantaneously can increase KISS1 mRNA and kisspeptin expression in mice. The difference was significant (P<0.05) . Immunohistochemical results

were consistent with the results of KISS1 gene and kisspeptin expression. Chronic experiments: One week after lateral ventricle catheter intervention, Compared with Group IN, the mice in Group IT had better appetite and their weights increased significantly, while the mice in Group IR reduced their weights significantly with reduced feeding. The difference was statistically significant ($P < 0.05$). There were no significant difference among these groups in estrus cycles, pathological results of ovaries and uterus. The TSH, FT4 and LH levels in Group IT were significantly lower than the control group, but the level of E was higher than that of the control group. ($P < 0.05$). Compared with Group IN, Group IT decreased the expression of KISS gene and kisspeptin in hypothalamus. The immunohistochemical results of kisspeptin in hypothalamic arcuate nucleus suggested the same trend, The difference was statistically significant ($P < 0.05$). Compared with Group IN, Group IR mice decreased the expression of KISS1 gene and kisspeptin in 7hypothalamus too. ($P < 0.05$). There is no significant difference between Group IT and Group IR.

Conclusion 1. In vitro, thyroid hormone that applied to GT1-7 cells can change the expression of KISS1 gene and kisspeptin in GT1-7 cell. 2. Different concentrations of thyroid hormone on kisspeptin GT1-7 cells had different influence. Either too high or too low concentration of T3 can reduce the expression of kisspeptin. when the concentration of T3 was 200 ng/ml the expression of kisspeptin in GT1-7 cells was the highest . 3. In vivo, instantaneous lateral intraventricular injection of T3 can increase the expression of KISS1 gene and kisspeptin in the hypothalamus..4.In vivo, continued chronic lateral intraventricular injection of T3 can significantly increase body weight in mice, Rapamycin can reverse this kind of effect. 5. T3 chronic lateral intraventricular injection can inhibit hypothalamic KISS1 gene and kisseptin expression. Rapamycin can't reverse this impact, but can make the influence of T3 on the sex hormone levels in mice improved. The influence of thyroid hormone in gonad axis is related with kisspeptin. mTOR may play a pivotal role in the interaction between the thyroid axis and gonad axis .

OR18-02

Outcome of in vitro fertilization in women with subclinical hypothyroidism

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Objective Our aim was to investigate the rate of biochemical pregnancies of in vitro fertilization (IVF) and the change of thyroid function in subclinical hypothyroid (SCH) women substituted with levothyroxine (LT4).

Methods 1. In total, 2463 subfertile women undergoing IVF between June 2015 and October 2015 were enrolled. Serum thyroid-stimulating hormone (TSH) were measured by electrochemiluminescence(ECL) immunoassays before controlled ovarian Hyperstimulation (COH). The rate of biochemical pregnancies were pursued.2. Sixty-three SCH women substituted with LT4 were considered for study entry. They were eligible if serum TSH tested the month preceding the IVF cycle was 0.2-4.2 mIU/L. Thyroid function parameters (TSH and FT4) were tested before the start of controlled ovarian hyperstimulation (COH),at the time of human chorionic gonadotropin (hCG) administration and at 16 days after hCG administration. The rate of biochemical pregnancies were pursued.

Results 1. The prevalence of elevated TSH levels consistent with hypothyroidism/SCH was 3.83% in a cohort of 2463 subfertile women undergoing IVF. The rate of biochemical pregnancies were significantly decreased in women with hypothyroidism/ SCH compared to euthyroid women (35.71% vs 49.31%,x=17.109,p<0.001) .

2. The rate of biochemical pregnancies were similar between SCH women substituted with LT4 and euthyroid women underwent IVF (x=0.793 p=0.373) .

3.The level of serum TSH at basal assessment, at the time of hCG administration, and at 16 days after hCG administration were 1.8mIU/l (0.43,2.57 mIU/L) ,1.05mIU/l (0.366,2.385mIU/L) and 4.625 mIU/l (1.1,6.88 mIU/L) ,respectively. The level of serum FT4 at basal assessment, at the time of hCG
administration, and at 16 days after hCG administration were 19.96 pmol/l (17.39-22.38pmol/l) ,19.05 pmol/l (17.08-21.3pmol/l) and 18.535pmol/l (17.95-20.77 pmol/l) ,respectively.

4. SCH women receiving LT4 replacement with a basal TSH level between 0.2-2.5 mIU/L displayed a similar rate of biochemical pregnancies of IVF compared to women with a basal TSH level between 2.5-4.2 mIU/ L (61.5% vs52.63%, p=0.806) .Serum TSH exceeded the threshold of 2.5 mIU/L in 52.38% SCH women with a basal TSH level between 0.2-2.5mIU/L and 77.78% in SCH women with a basal TSH level between 2.5-4.2 mIU/ L at the time of biochemical pregancies.

Conclusions Hopothyroidism/ SCH has a negative effect on the early outcome of IVF, but this negative influence may be avoided with adequate levothyroxine therapy. Strictly controlled TSH before IVF may have no beneficial effect on the early outcome of IVF, but may be helpful to keep TSH
level on goal after pregnancy.

OR18-03

The analysis of the changes of maternal thyroid autoantibodies during early pregnancy

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Objective To investigate the changes and related factors of maternal thyroid autoantibodies during early pregnancy.

Methods Urinary iodine concentration (UIC), serum thyroid stimulating hormone (TSH), free thyroxine (FT4), thyroid-peroxidase antibody (TPOAb), thyroglobulin antibody (TgAb) concentration were determined in 7,190 pregnant women at 4-8 weeks gestation in an iodine-sufficient region of China. All reported P values were two sided and a $P < 0.05$ was considered to be significant. Analyses were performed using the SPSS software (versions 19.0).

Results The prevalence of TPOAb positivity and TgAb positivity were 8.7% and 12% respectively. The prevalence of overt hypothyroidism and subclinical hypothyroidism were 7.2% (45/623) and 9.8% (61/623) respectively in TPOAb positive group and were 5.3% (46/865) and 8.1% (70/865) respectively in TgAb positive group, which were all significantly higher than group of thyroid antibody negative. The prevalence of TPOAb positivity and TgAb positivity presented a U-shaped curve, ranging from mild iodine deficiency to iodine excess, especially increased significantly in the group with UIC < 100μg/L.

Conclusion Prevalence of thyroid antibodies positivity became higher during early pregnancy. The positive thyroid autoantibodies during pregnancy were significantly associated with maternal hypothyroidism. Both of iodine excess and iodine deficiency were risks of positive thyroid autoantibodies. Screening and treatment of

thyroid autoantibodies positivity was necessary for women during early pregnancy.

OR18-04

Effect of mild hypothyroidism identified in 4-8 weeks on pregnancy outcome

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Objective Thyroid disease during pregnancy is common. However, the effect of subclinical or mild thyroid abnormalities on pregnancy complications is controversial. The purpose of this study is to explore the effect of subclinical hypothyroidism, thyroid peroxidase antibody (TPOAb) positive and hypothyroxinemia on pregnancy complications, to evaluate whether the treatment of L-T4 can improve pregnancy outcome, and to provide clinical evidence for screening and treatment.

Method In this study, 9245 pregnant women during 4-8 weeks were screened for thyroid function, according to thyroid function and their will to intervent, we divided them into different groups, then we followed up their pregnancy outcomes and used SPSS for the statistical analysis.

Result Of 9245 women,342 had subclinical hypothyroidism(the prevalence was 3.70%), 293 had isolated TPOAb positive (the prevalence was 3.17%), 684 had isolated hypothyroxinaemia (the prevalence was 7.40%).Compared with normal thyroid group ,subclinical hypothyroidism had significantly increased incidence of miscarriage (14.29% vs 7.15%, $p<0.05$) . TPOAb positive group had a significantly higher incidence of miscarriage, prematurity, and low birth weight (13.64% vs 7.15%, $p<0.05$; 10.00% vs 3.01% $p<0.05$;7.27% vs 2.90%,$p<0.05$, respectively) .Women with hypothyroxinemia had a significantly increased incidence of macrosomia (14.95% vs 10.27%, $p<0.05$) . Compared with SCH control groups, the incidence of miscarriage decreased in SCH intervention group (9.43% vs 14.29%) ,which was no significant difference with normal thyroid group.Compared with TPOAb positive control group,the incidence of miscarriage, prematurity and low birth weight decreased in TPOAb positive intervention group(9.09% vs 13.64%;2.02% vs 10.00% and 0.00% vs 7.27%, respectively), and all had no significantly difference with normal thyroid group. Compared with hypothyroxinemia control group the incidence of macrosomia decreased in hypothyroxinemia intervention group (9.29% vs 14.95%) , and was no significant difference with normal thyroid group.

Conclusion Mild hypothyroidism identified in 4-8 weeks during pregnancy had adverse effect on pregnancy complications and pregnancy outcome. Screening of thyroid function is necessary,and proper and timely treatment can reduce the risk of pregnancy.

OR19-01

Adipocyte SIRT1 deletion impaired endothelial function via reducing brown fat phenotype in perivascular adipose tissue

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Objectives Perivascular adipose tissue (PVAT) is the fat depot surrounding blood vessels. It has long been regarded as merely structural support for vasculature but evidence has been emerging that PVAT is actually playing indispensible roles in maintaining the normal function of cardiovascular systems. But the underlying mechanism how PVAT achieves its cardio-protective function is unknown. The aim of this study is to investigate whether obesity induces endothelial dysfunction via PVAT and elucidate the underlying mechanisms.

Methods Six weeks old wild type(WT) and adipocyte-specific SIRT1 knockout mice(AKO) were fed with either standard chow or high fat diet for 12 weeks. The obese mice were exposure to cold environment (4 ℃) for 6 days. The aortic rings either without or with PVAT were isolated and the endothelial-dependent relaxation (EDR) of aorta in response to acetylcholine was measured by wire myograph. Expression of the brown adipocyte markers including UCP-1 and PGC1α were evaluated by western blotting, immunohistochemistry and/or qPCR. DHE staining and lucigenin assay were used to measure superoxide levels.

Results Compared to the lean mice, the EDR was significantly impaired in aorta from obese mice in the presence of PVAT. We also found that the browning level of PVAT was significantly decreased in obese mice. Interestingly, mice with SIRT1 deletion in adipocytes suffered from a further decline of PVAT browning and exacerbation of endothelial dysfunction. Furthermore, cold induced upregulation of the browning marker and thereby improved EDR readily observed in PVAT from wildtype mice by reducing superoxide production , but the effect was abolished in SIRT1 knockout mice.

Conclusions Our studies demonstrated that enhanced PVAT browning showed strong superoxide chelating ability and and thereby improves endothelial dysfunction in mice. SIRT1 plays a pivotal role in controlling PVAT browning, which in turn causes decreased superoxide production.

OR19-02

TSH increases synthesis of hepatic ATP-binding cassette subfamily A member 1 in hypercholesterolemia

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Objective In this study, our aim was to determine whether TSH regulated ATP binding cassette subfamily A member 1(ABCA1) expression in the liver, resulting in increased plasma cholesterol levels.

Methods ABCA1 is a member of the ABC superfamily, which induces transfer of intracellular cholesterol to extracellular apolipoprotein. The SCH mouse which is characterized by elevated serum TSH but not thyroid hormone levels and *Tshr* KO mice with normal thyroid hormone levels after thyroid hormone supplementation, were used as the experimental models to determine the influence of TSH on in vivo. We used hepG2, a human hepatoblastoma cell line with a wide range of liver-specific metabolic responses to different types of stimuli, to confirm the direct effect of TSH on hepatocytes.

Results Hepatic total and free cholesterol levels were increased in SCH mice compared with the controls. When TSH failed to act via TSHRs in the liver, *Tshr*-/-mice showed reduced hepatic total and free cholesterol content in contrast to *Tshr*+/+ mice. Higher serum total cholesterol, triglyceride and LDL cholesterol were found in SCH mice compared with control mice. Accordingly, we found an apparent decrease in serum total cholesterol and HDL cholesterol levels in *Tshr*-/- mice compared with *Tshr*+/+mice. The expression of ABCA1 were increased SCH mice compared with that of the control mice and accordingly decreased in *Tshr*-/- mice, compared with that of *Tshr*+/+ mice. A concentration-dependent effect of TSH on the intracellular total, free cholesterol content and ABCA1 expression were also showed in HepG2 cells.

Conclusion TSH upregulated hepatic ABCA1 to promote the efflux of intercellular cumulative cholesterol, resulting in increased plas-

ma cholesterol. These data might partially explain the pathogenesis of hypercholesterolemia in SCH.

OR19-03

The impact of thyroid-stimulating hormone and fasting insulin level on lipid profiles and serum PCSK9 concentration in euthyroid subjects: a population-based cross-sectional study

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Objective Large amounts of recent studies pay attention to the relationship between thyroid-stimulating hormone (TSH) and dyslipidemia, as well as related diseases. Besides, fasting insulin (FINS) level and insulin resistance status are closely related to metabolic disorders. Whether this two endocrine hormones, TSH and insulin, may interact with each other in worsening lipid metabolic disturbance remains unclear.

Methods A total of 1225 middle-aged (55.83±8.49 years, 500 men) euthyroid subjects with FINS within reference range were included from a cross-sectional, population-based study conducted in Gulou district, Nanjing, China during June to December 2011. Participants with any history of myocardial infarction, stroke, coronary heart disease, hypertension, lower extremity arterial disease, hyperlipidemia or retinopathy are excluded. Anthropometrics and plasma biochemical indicators were assessed, and questionnaire survey on personal and family members' health status were also conducted. A 75-g oral glucose tolerance test (OGTT) was performed, and plasma glucose and insulin levels were measured at 0, 30 and 120min. According to the OGTT results, subjects were divided into five subgroups, including normal, impaired fasting glucose, impaired glucose tolerance, impaired fasting glucose with impaired glucose tolerance and diabetes mellitus. Moreover, 270 subjects randomly enrolled from these five groups were measured plasma proprotein convertase subtilisin/kexin type 9 (PCSK9) concentration by a sandwich ELISA method.

Results There are significant differences between male and female groups in some main index. In Pearson correlation analyses, plasma TSH correlated with age (r=0.100, P=0.025) and thyroid volume (r=-0.193, P<0.001) in male, and with TC (r=0.108, P=0.004), LDL-c (r=0.113, P=0.002), fT4 (r=-0.117, P=0.002), thyroid volume (r=-0.105, P=0.005) in female. A multiple stepwise regression analysis showed TSH has an independent and significant association with LDL-c (β=0.118, P=0.002) in female. Moreover, FINS significantly correlated with LDL-c (β=0.021, P=0.010), TG (β=0.023, P=0.006) and thyroid volume (β=-0.018, P=0.027) in female. On the basis of the median of TSH and FINS levels, the 1225 subjects were further classified into $TSH^{lo}INS^{lo}$, $TSH^{hi}INS^{lo}$, $TSH^{lo}INS^{hi}$, and $TSH^{hi}INS^{hi}$ groups in male and female respectively. The LDL-c level in $TSH^{hi}INS^{hi}$ group was significantly higher than $TSH^{lo}INS^{lo}$, $TSH^{hi}INS^{lo}$ and $TSH^{hi}INS^{hi}$ group (3.12 vs 2.89, 2.95, 2.94 mmol/L, P=0.004, 0.038, 0.024, respectively) in female, but not in male. TG concentration differs between the four groups in both genders. Plasma PCSK9 positively correlated with FINS only in female (r=-0.195, P=0.015), but did not have significant correlations with TSH in neither group.

Conclusion In our middle-aged cross-sectional population, TSH correlated with LDL-c level, and FINS level had association with plasma PCSK9 concentration in female, indicating TSH and FINS take active parts in lipid metabolism. The difference in gender needs further investigation. More follow-up studies are warranted to observe their potential role under disease status. What's more, further studies are needed to illustrate the precise mechanism of the impact of TSH and FINS on LDL-c and PCSK9 expression.

OR19-04

Potential Harmful Correlation Between Homocysteine and Low-density Lipoprotein Cholesterol in Patients with Hypothyroidism

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Objective Hypothyroidism (HO) can induce metabolic dysfunctions related to insulin resistance and dyslipidemia. Our previous studies showed that homocysteine (Hcy) impaired the coronary endothelial function and that Hcy can promote chemokine expression and insulin resistance (IR) by inducing endoplasmic reticulum stress in human adipose tissue and hypothyroid patients. The aim of this study was to investigate the potential harmful interaction between plasma Hcy and low-density lipoprotein cholesterol (LDL-C) in patients with HO.

Methods A total of 286 subjects were enrolled. All subjects were divided into the following three groups: an HO group, subclinical hypothyroidism (SHO) group and control group. Statistical analyses were carried out to evaluate the correlation between the plasma levels of Hcy and LDL-C in HO patients. The changes in the plasma Hcy levels and other metabolic parameters were measured before and after levothyroxine (L-T4) treatment. The relationship between the changes in the plasma Hcy level and the LDL-C level was also evaluated after L-T4 treatment.

Results In the patients with hypothyroidism, both the plasma Hcy and LDL-C levels were significantly higher than those of the controls. The plasma levels of Hcy were positively correlated with the LDL-C level in the HO group. L-T4 treatment resulted in a significant decrease in the BMI, total cholesterol (TC), LDL-C, triglycerides (TG), ApoB (Apolipoprotein, B) and Hcy levels. Moreover, the decrease in Hcy (△ Hcy) was positively correlated with decreased LDL-C (△ LDL-C) levels after L-T4 treatment in OH patients.

Conclusions Our results suggest that the increased Hcy level was positively correlated with the LDL-C in the HO group. A potential harmful interaction may exist between Hcy and LDL-C under the HO condition. In addition to reducing the plasma levels of Hcy, L-T4 treatment exerts beneficial effects on patients with HO by improving dyslipidemia, including a decrease in the LDL-C level.

OR30-01

Effect of Autologous Marrow Stem Cell Transplantation on Patients with Diabetic Peripheral Neuropathy

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Object This paper observed the therapeutic result of autologous marrow stem cell transplantation on patients with diabetic peripheral neuropathy (DPN)

Method 112 cases, according to randomly paried design method, divided into control group(n=56) and observation group(n=156), were offered both of them basic treatments such as regular blood glucose adjustment and trophic nerve adjustment, while given the observation group treatment of autologous marrow stem cell transplantation ,with a period of 3 years.All of them as effective rate, average limb nerve conduction velocity(ALNCV),clinical symptom score,side-effect rate and treatment loss rate were as evaluation index.Therapeutic method were as fllowing:provide two groups the regular medicines for adjusting blood glucose and methyleobalamin for trophic nerves, apply autologous marrow stem cell transplantation on the observation group. A symptom evaluation, a test on limb nerve conduction velocity and sensory nerve extraction rate

were conducted one day before the beginning of the therapy and 3 months,6 months,1 year and 3 years after the beginning of the therapy.It was as a clinical endpoint for three years.The main endpoint were effective rate and ALNCV.The minor endpoint were clinical symptom score and side-effect rate.The measurement data was analyzed by single variance and tested by t, while the enumeration data was tested by x^2.

Result The improvement degree of nerve conduction velocity of the treatment group ,clinical symptom score and effective rate are significant compared with the control group.In observation group vers control group(n=56), the effective rate is 91.07% (51/56cases) vers 78.57% (44/56cases) p<0.05.ALNCV before treatment,3 months,6 months,1 year and 3 years after were respectively 40.02,54.21,55.04 ,54.84 and 52.75m/s vers 39.25,49.23 ,47.01, 43.32 and 41.32m/s .The linical symptom score were 8.56,4.32,3.38,3.47 and 4.05 point vers 8.46 ,5.61,5.93,6.8 and 7.79 point.With more longer continuous period,efficacy both of clinical symptoms and ALNCV are better in the observation group than that in the control group.

Conclusion With higher effective rate, longer continuous efficacy and safety, it is a good method of AMSCT for treatment of DPN .

OR30-02

Regulation of vascular BK channels by Nrf2 signaling in diabetes mellitus

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Background The large conductance calcium-activated potassium (BK) channels are major determinants of vasodilation. BK channel function is impaired in diabetes mellitus (DM) due to downregulation of BK-β1 by reactive oxygen species-dependent mechanisms. The upstream mechanism mediating the regulation of BK-β1 is unclear. The nuclear factor E2-related factor-2 (Nrf2) signaling pathway has emerged as a master regulator of cellular redox status but its role on the regulation of BK channels is unknown.

Objective To test the hypothesis that Nrf2 signaling plays a central role in the regulation of vascular BK channel function in DM.

Methods Studies were performed combining cellular, molecular, vascular, and electrophysiological techniques in type 2 diabetic db/db mouse and in cultured human coronary artery smooth muscle cells (HCSMC).

Results In db/db mouse aorta, the protein expression of Nrf2, BK-β1 and heme oxygenase 1 (HO-1), a known Nrf2 downstream target were significantly downregulated while that of muscle ring finger protein 1 (MuRF1), a known E-3 ligase targeting BK-β1, was significantly upregulated. Similar findings were observed in HCASMC cultured in high glucose (HG 22 mM). or by knockdown of Nrf2 in HCSMC in normal glucose, whereas adenoviral transfer of Nrf2 gene in these cells resulted in the downregulation of MuRF1 and upregulation of BK-β1 and HO-1 expression. Further molecular manipulation of Nrf2 by knockdown or overexpression of Keap1, a regulator of Nrf2 activity, confirmed the inverse relationship between the levels of Nrf2, BK-β1, HO-1 expression and those of MuRF1. Activation of Nrf2 by dimethyl fumarate in HG-cultured HCSMC or in db/db mouse coronary arteries preserved BK-β1 expression, BK channel and vascular function.

Conclusions Expression of BK-β1 is closely regulated by Nrf2 and vascular BK channel function can be restored by activation of Nrf2. This should be considered a novel therapeutic target in the treatment of diabetic vasculopathy.

OR30-03

Growth hormone therapy benefits pituitary stalk interruption syndrome patients with short stature: a retrospective study of 75 Han Chinese

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Objective We aim to investigate the long-term benefits of growth hormone (GH) therapy in short stature adolescents and adults with pituitary stalk interruption syndrome (PSIS), which would be beneficial for future clinical applications.

Design and methods In this study, initial height, final height, total height gain and GH treatment history were retrospectively investigated in 75 Chinese PSIS patients. We compared height gain between the GH treated cohort and untreated cohort, and explored the impact of different GH therapy duration to height gain.

Results For all the patients, their final height (SDS) increased from -4.10 ± 1.83 (-9.30~2.03) to -2.15 ± 1.94 (-7.82~3.98) (P < 0.001). GH treated patients had more height gain than the untreated patients (P < 0.05). There was a significant difference between the different GH therapy duration groups (P = 0.01).

Conclusion Adult Chinese PSIS patients with short stature benefitted the most from 12-months of GH therapy. Although patient diagnosis age was lagged behind in the developing countries, GH treatment was still effective for them and resulted in a higher final height and more height gain.

OR30-04

The impact of cancer on the survival of acromegaly in Taiwan

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Over 95% of patients with acromegaly results from chronic hypersecretion of growth hormone (GH) from a GH-secreting pituitary adenoma. The purposes in the management of acromegaly are to reduce morbidity and restore the increased mortality rate compared to normal age and gender adjusted rates. IGF-1 is an important cell growth-stimulating hormone. Different types of cancer have been shown to be associated with acromegaly. Increased risk of mortality in patients with uncontrolled acromegaly has been reported in several studies.

Objective We assessed the impact of co-morbidities and cancer on the survival of patients with acromegaly after long-term treatment and follow-up.

Methods Retrospective analysis was performed for 285 patients with active acromegaly who were admitted to the Chang Gung Memorial Hospital, Taiwan between 1978 and 2012. Clinical presentation, laboratory data, therapeutic modality, and follow-up outcome were coded for analysis.

Results Of the 285 cases, 240 patients underwent surgical treatment. Most of these underwent transsphenoidal adenomectomy of the pituitary tumor. After 1994, stereotactic radiosurgery was performed for residual pituitary tumor with persistently high GH or IGF-1 levels after medical treatment. The diagnostic codes for malignancy were codes 140 to 208.91 of the ICD-9 clinical modification format. Coded data including clinical symptoms and signs, pre-operative and post-operative laboratory and imaging results, surgery results, complications, clinical outcomes of post-operative management, and mortality, were analyzed. The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital. During the follow-up period, 21 patients (7.4%) were diagnosed with cancer with different histological types. DM patients had a higher incidence of malignancy (13.2% vs. 3.8%; p < 0.01). Colon, thyroid and head and neck cancers were the 3 leading cancer types. Malignancy patients had a lower survival rate than

non-malignancy patients (61.1% vs. 94.1%; $p < 0.01$). The survival rate of malignancy patients with DM was 50.0%. DM with acromegaly had a higher incidence of malignancy (13.2% vs. 3.8%; $p < 0.01$). After a mean follow-up of 15.1 ± 0.6 years, age, DM, coronary heart disease, and malignancy were found to be significant factors of mortality. Control of growth hormone and IGF-1 levels also conferred a marginal survival benefit.

Conclusions Malignancy and DM are significantly influence the survival of patients with acromegaly; thus, these patients need close follow-up and appropriate therapy.

OR31-01

Free thyroxin variations is associated with incident metabolic syndrome in adults, Tehran Thyroid Study

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Objective It is not clear whether changes in thyroid hormones are associated with incident of metabolic syndrome(MetS). This study for the first time evaluated the association between thyroid hormone variations and incident of MetS and its components within a 10 years follow- up period (from 1999 to 2009).

Methods Data were analyzed from a prospective population-based Tehran Thyroid Study. Out of 5786 subjects aged ≥20 years, after excluding subjects with MetS (1403), TSH>10 or <0.1 (104), taking thyroid drugs(85), corticosteroids(57), steroid drugs(40), BMI<18.5 and GFR<30 and history of cancer(12) at baseline, 2393 subjects were included in the study. Body weight, waist circumference (WC) and blood pressure (BP) were measured. Serum concentrations of lipids and lipoproteins, fasting blood glucose (FBG), insulin, Free T4 (FT4) and TSH were assayed at baseline and three follow ups every 3 years. Metabolic syndrome was determined by definition of the Joint Interim Statement (JIS) adjusted for the Iranian population.

Results The mean age was 39.9±13.7 and 36.4±11.7 for men and women, respectively. FT4 was associated with lower odds of high WC (OR (95%CI) = 0.49(0.35-0.69) and high TG (OR (95%CI) = 0.57(0.41-0.78)), and higher odds of high BP (OR (95%CI) = 1.35(1.05-1.74)) adjusting for age, sex, smoking, BMI, and HOMA-IR. There were no association of FT4 with high FBS and low HDL-C components. Serum TSH levels were not associated with any of the MetS components. TSH was not associated with odds of MetS.FT4 was associated with lower odds of MetS in crude model, and when adjusting for age, sex, and smoking. After dividing subjects to obese and non-obese, FT4 was associated with incident Mets only in obese subjects.

Conclusion Decrease in serum FT4 values (not TSH), within subclinical and thyroid ranges, is associated with higher odds of incident MetS especially in obese individuals.

OR31-02

Study on thyroid function and metabolism changes of Wistar rats during long-term partial sleep deprivation

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Objective Researches showed that sleep deprivation can induce the physiological function changes, such as immune disorders, cognition disorders and emotion disorders. Preceding studies indicated consecutive six days of sleep deprivation could influence thyroid function. The complexity of this mechanism remains unclear recognition so far. Besides, partial sleep deprivation is more common in the daily life. The aim of this study is to investigate the effects of long-term partial sleep deprivation on function as well as metabolism changes of thyroid and explore its probable mechanism.

Methods Thirty two three-month-old male Wistar rats were randomly divided into four groups: partial sleep deprivation group 1 (SD1 group), partial sleep deprivation group 2 (SD2 group), treatment control group (TC group) and cage control group (CC group), with equal number involved. The Sleep deprivation model was established by flowerpot technique. SD1 group, SD2 group and TC group were all placed in 24-hour proposed lighting environment. Rats in SD1 group were deprived of sleep for 18 hours per day with an intermission for 6 hours, while rats in SD2 group were deprived of sleep for 22 hours per day with an intermission for 2 hours. Rats in CC group were placed in 12 hours light and 12 hours dark environment. After twenty one days, all rats were executed. Thyroid tissues were saved for weight recording and morphology observation; blood from the femoral artery was saved as well for determining the concentrations of total T3(TT3), total T4(TT4), free T3(FT3), free T4(FT4), thyroid stimulating hormone (TSH), thyroglobulin(Tg), anti-thyroglobulin(TgAb) and anti-thyroid peroxidase(TPOAb) in serum among different groups.

Results Compared with CC group, serum TT3 and relative weight of thyroid had a rising trend in SD1 group but they were significantly higher in SD2 group($P<0.05$). The concentrations of TgAb and Tg had a falling trend in SD1 group but were significantly lower in SD2 group($P<0.05$). Compared with CC group(3.06±0.30pmol/L), serum FT3 increased in SD1 group(3.31±0.19pmol/L, $P<0.05$), but remained relatively stable in SD2 group. Serum FT4 in SD1 group was significantly higher(17.26±2.25pmol/L, $P<0.05$) than that in CC group(15.14±1.35pmol/L), but in SD2 group, it was significantly lower(12.30±2.25pmol/L, $P<0.05$). Compared with CC group(62.63±6.36nmol/L), serum TT4 showed a rising trend in SD1 group, but was significantly lower in SD2 group(34.94±4.64nmol/L, $P<0.05$). Serum TSH in SD1 and SD2 groups both had a rising trend compared with CC group. No significant change was found in TPOAb between SD1 group and CC group, and it only had a rising trend in SD2 group.

Conclusions Long-term partial sleep deprivation impairs thyroid function of rats, but still can be partly compensated. Meanwhile, long-term partial sleep deprivation can also influence the immune function. With the extension of the deprivation time, immune level shows a significant reduce.

OR31-03

The analysis of the causes of maternal thyroid dysfunction during early pregnancy

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Objective To investigate the causes of abnormal thyroid function during early pregnancy.
Method Urinary iodine concentration (UIC), serum thyroid stimulating hormone (TSH), free thyroxine (FT4), thyroid -peroxidase antibody (TPOAb), thyroglobulin antibody (TgAb) concentration and body mass index (BMI) were determined in 7,190 pregnant women at 4-8 gestational weeks in Liaoning province of China.
Results On the basis of pregnancy-specific references made by our laboratory, the prevalence of overt hypothyroidism (0.7%), subclinical hypothyroidism (2.4%) and isolated hypothyroxinemia (1.7%) were lowest in the group with UIC 150-249μg/L. Multivariate logistic regression indicated that more-than-adequate iodine intake and excessive iodine intake were associated with a 1.72-fold and a 2.17-fold increased risk of subclinical hypothyroidism respectively. Meanwhile excessive iodine intake was associated with a 2.85-fold increased risk of isolated hypothyroxinemia. TSH was significantly higher in obese group than that of in the overweight group (2.50 mIU/l vs 2.11 mIU/l, $P < 0.008$), and it was also higher in the overweight group than that of in the normal group (2.11 mIU/l vs 1.86 mIU/l, $P < 0.001$). In contrast, the median concentration of FT4 decreased significantly as BMI value increased among all the groups.
Conclusion The criterion of a UIC of 150-249μg/L could be used as an optimal and safe interval. The criterions of a UIC of 250-499μg/L and ≥ 500μg/L are associated with a significantly high risk of subclinical hypothyroidism and isolated hypothroxinemia. For women whose BMI > 24kg/m2, and who are within 8 weeks of pregnancy, thyroid functions should be assessed especially.

OR31-04

Gestation-specific changes in maternal thyroglobulin during pregnancy and lactation in an iodine-sufficient region in China: A longitudinal study

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Background Thyroglobulin (Tg) is a biomarker of iodine status, but the use of Tg as a biomarker for pregnant women is controversial. The aim of this study is to describe the changes in Tg based upon gestational and postpartum concentrations in healthy pregnant women from an iodine-sufficient region in China, and to evaluate the use of Tg as a biomarker for the iodine sufficient pregnant women.
Methods Blood and urine samples were obtained from healthy pregnant women and non-pregnant women. Urinary iodine concentration (UIC) was measured using an ammonium persulfate method. Eighty-five neonates born from these women were also included in this study, and cord blood and heel blood were collected. Serum iodine concentration was measured by inductively coupled plasma mass spectrometry (ICP-MS). Serum and cord thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3), total thyroxine (TT4), total triiodothyronine (TT3), anti-thyroid peroxidase antibody (TPOAb), anti-thyroglobulin antibody (TgAb), and Tg were measured using an electrochemiluminescence immunoassay. Data analyses were performed using SPSS version 20.0 software. Spearman's rank correlation was used to examine the correlation between Tg and UIC, TSH, TT4, TT3, FT4, or FT3. Multiple regression was performed to identify the determinant factors regarding Tg levels.
Results One hundred thirty-three women with uncomplicated pregnancies met the criteria and were recruited into the pregnant group, and one hundred thirty-two non-pregnant healthy women were recruited into the control group. Median Tg was higher in early pregnancy (pregnancy at 8 week vs non-pregnancy: 11.42ng/ml vs 8.8 ng/ml, $p < 0.01$) and maintained a stable level, then increased greatly at the 36th week. After delivery, Tg decreased to non-pregnant levels. Median Tg concentrations for the 8 time points were 11.42 ng/ml, 12.83 ng/ml, 12.18 ng/ml, 13.34 ng/ml, 11.70 ng/ml, 14.86 ng/ml, 9.63 ng/ml, and 11.25 ng/ml, respectively. During pregnancy, maternal Tg was not correlated with thyroid function, UIC, or UI/Cr. After delivery, median Tg reached its nadir with regard to sufficient iodine status, similar to the non-pregnant group. Cord blood Tg was much higher compared to maternal Tg levels (57.34 vs 14.86 ng/ml, $p < 0.001$), and correlated positively with cord FT4 ($r = 0.256$, $p < 0.05$), cord TT4 ($r = 0.263$, $p < 0.05$), and maternal UI/Cr in late 3rd trimester ($r = -0.214$, $p < 0.05$). Cord blood Tg was not correlated with maternal weight during pregnancy, maternal age, gestational age, or with neonatal weight, sex, or delivery method.
Conclusions Our work demonstrates: 1) in iodine-sufficient region, Tg is elevated from early pregnancy, remained a stable level, and increased greatly in late 3rd trimester; 2) Tg is not a good biomarker for the iodine status of pregnant women in an iodine-sufficient region; and 3) cord blood Tg is correlated with maternal iodine status.

OR32-01

Two PHEX gene mutations identified in two Chinese X-linked hypophosphatemic rickets pedigrees

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Objectives X-linked hypophosphatemic ricket (XLH) is a kind of common hereditary hypophosphatemic rickets characterized by mineralization disorder in new synthetic matrix. X-linked dominant hereditary disease (XLHR) is the most common type, which is mainly caused by PHEX gene mutation. The classic clinical characteristics include osteoporosis and bone abnormalities, muscle weakness, short stature, teeth dysplasia, bone pain, multiple fracture, etc. The main biochemical traits of this disease are hypophosphatemia, normal serum calcium level with hypocalciuria, normal or low serum 1,25-(OH)2D3 level and increased ALP(alkaline phosphatase activity). The definite diagnosis of XLH depends on gene detection to find the genetic mutation site. In our study, we performed genetic detection and mutation diagnosis on PHEX gene in two XLHR pedigrees to find the related gene mutation point, at the same time, we also investigated the pathogenesis of this disease to provide more materials for the future clinical research and treatment of this disease to help the clinicians get better understand in this disease.
Subjects and methods Two clinical suspected XLHR families were identified and screened for mutation sites in PHEX gene. The pathogenesis of XLHR was also discussed in this study.
Results The probands of these two XLHR families were both characterized by arcuate deformities of lower extremities, short stature; and proband A also suffered from joint intumescence, bone pain. Biochemical examination displayed that the blood phosphorus level of the two probands were lower, the serum calcium was normal or lower and the serum 1.25-(OH)2D3 level was normal (in the normal lower limit). The parents of the two probands were all not close relatives, and the mother of the proband A also showed the same symptom. The PHEX gene detection of proband A revealed a homozygotic mutation identified in the PHEX gene, and this mutation

was located at the EXON 12 of PHEX gene(c.1363 C>T). This was predicted to cause the mutation between glutamic acid (Glu) and stop codon at the 455 amino acid in PHEX protein (p.E455X). At the same time, the mother of the proband A also showed the same mutation at the same site, but the mutation is heterozygote. While the PHEX gene detection of proband B showed another mutation at the EXON 3 of PHEX gene (c.200 T>G), which was heterozygote and could lead to the mutation between leucine (Leu) and stop codon at the 67 amino acid in PHEX gene (p.L67X). Both of the two mutations were predicted to cause PHEX protein premature, thus affecting its enzyme activity. The probands and the mother of proband A were all treated by supplement of oral phosphorus and vitamin D, and we also performed a 1 year follow-up, which displayed that the symptoms of the patients were improved.

Conclusion In this study, two different PHEX gene mutations were found in the PHEX gene of the two families, respectively, and are all dominant inherited. The mutations are predicted to be the pathogenesis of XLHR in the two families.

OR32-02

FGF23 mediated hypophosphatemic osteomalacia due to multiple iron infusions

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Objective To describe a case of FGF23 mediated hypophosphatemic osteomalacia induced by multiple administrations of iron infusions containing saccharated ferric oxide preparation, and review the current literature on this uncommon adverse response to a common therapy.

Methods A 39-year-old woman presented with eighteen months of widespread bony pain and proximal myopathy. This occurred on a background of eight years of unexplained iron deficiency anaemia for which she had been treated with 2000mg of intravenous iron polymaltose every four to five months for five years prior to presentation.

Further investigation revealed hypophosphatemia, hypocalcemia, elevated alkaline phosphatase, vitamin D deficiency and mildly elevated parathyroid hormone. Imaging studies revealed multiple rib and pelvic fractures, bilateral renal calculi and diffuse osteoblastic bone lesions in the axial and appendicular skeleton. Bone Mineral Densitometry showed generalised osteopenia. Fibroblast growth factor 23 (FGF23) level was elevated. Upon cessation of iron infusions, bone pain and proximal myopathy improved, and biochemical and radiological parameters returned to normal.

Results FGF23 is produced in bone osteocytes, and acts to regulate phosphate and vitamin D homeostasis and metabolism. Tubular reabsorption of phosphate is inhibited by FGF23, in a process that is independent of PTH. Increased levels of FGF23 are seen in several hypophosphatemic conditions, including X-linked hypophosphatemic rickets, tumour-associated osteomalacia, autosomal recessive hypophosphatemic rickets, and some cases of McCune-Albright syndrome. Hypophosphatemic osteomalacia resulting from iron infusions has been described previously in a case series from Japan, and in one case from New Zealand. The mechanism of how parenteral iron infusion upregulates FGF23 remains speculative. It is unclear whether it is the iron itself or the carbohydrate ligand (dextran, sucrose, gluconate or polymaltose) that triggers the elevation of FGF23, although emerging evidence suggests that iron has a direct effect on FGF23 activity and phosphate regulation.

Conclusion Use of iron infusions is widespread in clinical medicine. Iron infusions have been shown to cause hypophosphatemia, and in the setting of repeated infusions, symptomatic hypophosphatemic osteomalacia can result. Clinicians must be aware of this rare, but serious side-effect.

OR32-03

The relationship between 25(OH)D, FGF23 levels with bone metabolism in patients with Graves' disease

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Objective To evaluate the effective of vitamin D status , FGF-23 levels on bone metabolism in patients with GD.

Methods Sixty-nine young adults patients with GD were involved(-male,n=17,age,38.47±6.27;female,n=52, age, 37.50±8.59,menstruation normal) as GD group. In addition, 35 healthy subjects were recruited (male, n=8,age: 37.67±7.35;female, n=27,age: 39.05±7.55 ,menstruation normal) as control group, matched age, sex with GD group. All subjects were detected free thyroid function, blood routine, blood calcium, blood phosphorus, parathyroid hormone, 25 (OH) D and FGF-23. BMD of lumbar vertebra (L1-L4), femoral neck and total hip were measured by dual-energy X-ray absorption. Based on BMD, the patients with GD were divided into the normal bone mass group ,low bone mass group and osteoporosis group; according to the vitamin D levels, the patients with GD were divided into three groups,. Compared the differences of each parameter between GD group and control group.

Results 1. FT3, FT4, P, PTH and FGF-23 in GD group were significantly higher than control group, TSH and 25(OH)D lower than control group ($P<0.05$) . 2. BMD of L1-L4 in female patients with GD were significantly lower than that of the female control group ($P < 0.05$), BMD of L1-L4, femoral neck and total hip in female patients with GD were significantly lower than male patients with GD ($P<0.01$) .3.In with GD, BMI in abnormal bone mass group was significantly lower than normal bone mass group,FT3 and FT4 were higher than normal bone mass group ($P<0.05$) ; 4. In GD patients ,the incidence of low bone mass in female patients (42.31%) was greater than that male (17.65%). 5. In GD patients, the level of 25(OH)D was negatively correlated with the level of FT3, FT4 and PTH ($P < 0.05$) ,there was a significant positive correlation between FGF-23 and serum Pi ($P < 0.01$).

Conclusion 1. Young adults patients with GD was prone to bone loss, especially in female. 2. The level of 25 (OH) D was negatively correlated with FT3 and FT4. There was a positive relationship between the level of serum FGF-23 and serum phosphorus, which indicated that FGF-23 plays an important role in the regulation of the phosphorus homeostasis and increased serum phosphate may be associated with a compensatory rise in circulating FGF-23 level.

OR32-04

Interleukin-6 Gene Knockout Antagonizes High Fat -Induced Trabecular Bone Loss

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Purpose To determine the roles of interleukin-6 (IL-6) in fat and bone communication.

Methods Male wild type (WT) mice and IL-6 knockout (IL-6-/-) mice were fed with either regular diet (RD) or high fat diet (HFD) for 12 weeks. Bone mass and bone microstructure were evaluated by micro-CT. Gene expression related to lipid and bone metabolisms was assayed with real-time qRT-PCR. Bone marrow cells from both genotypes were induced to differentiate into osteoblasts or osteoclasts, and treated with palmitic acid (PA).

Results HFD increased body weight and fat-pad weight and impaired lipid metabolism both in WT and IL-6-/- mice, the dysregulation of lipid metabolism was more serious in IL-6-/- mice. Trabecular bone volume fraction (Tb.BV/TV), trabecular number (Tb.

N) and trabecular thickness (Tb.Th) were significantly down-regulated in WT mice after HFD than those in RD group (P<.05). However, these bone micro-structural parameters increased by 53%, 34% and 40%, respectively in IL-6-/- mice than those in WT mice on the HFD (P<.05). Furthermore, IL-6-/- osteoblasts displayed higher alkaline phosphatase(ALP) activity and higher mRNA levels of Runx2 and Colla1 than those in WT osteoblasts no matter in the control or PA treatment group (P<.05).

Conclusions These findings suggested that IL-6 gene deficient antagonized HFD-induced bone loss. IL-6 might bridge lipid and bone metabolismsand could be a new potential therapeutic target for lipid metabolism disturbance-related bone loss.

OR33-01

Accelerometer-derived Vigorous Physical Activity is associated with Higher Hip Bone Mineral Density in Community-Dwelling Older Adults

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Objectives To determine associations of varying?accelerometer-determined physical activity (PA) intensities with bone mineral?density (BMD) in community-dwelling older adults.

Methods This cross-sectional analysis of the Tasmanian Older Adult Cohort Study included community-dwelling older adults (51% female; mean ± SD age 66 ± 7 years) with complete seven-day accelerometer measures generated via an ActiGraph GT1M hip-worn device. Mean minutes/day of sedentary behaviour, light intensity PA, moderate intensity PA & vigorous intensity PA were estimated via previously established thresholds. BMD at the hip, lumbar spine, and whole body was assessed via dual-energy x-ray absorptiometry (DXA). Relationships of PA intensity and BMD parameters were assessed by Spearman's correlation and multivariable regression analysis.

Results Males spent significantly more time engaged in moderate and vigorous intensity PA (37.5 ± 28.0 minutes vs 28.4 ± 23.2 minutes, p<0.01) than females. There were no associations for sedentary
behaviour or light intensity PA with BMD parameters at any site in unadjusted analyses. Moderate intensity PA was positively correlated with total hip (r=0.09, p=0.02) and whole body BMD (r=0.15 p<0.01). Vigorous PA was also correlated with total hip (r=0.08 p=0.04) and whole body BMD (r=0.161 p<0.01). No associations were observed for any level of PA intensity with lumbar spine BMD (all p>0.05). After adjustment for age, sex, body mass index and other PA intensities, each 10minute/day increase in vigorous intensity PA was associated with 0.03g/cm2 higher BMD at the femoral neck (95% CI 0.01 – 0.05; partial R2 = 0.08), but no association was observed at the total hip, lumbar spine or whole-body. Sedentary behaviour, light PA and moderate PA were not associated with BMD at any site (allp>0.05).

Conclusions Higher amounts of vigorous intensity PA, but not sedentary behaviour, or light or moderate PA, are associated with greater femoral neck BMD in community-dwelling older adults. Higher intensity PA appears to make a relatively small contribution to femoral neck BMD however. Further studies are needed to elucidate the role of other lifestyle factors and exercise modalities on BMD, but clinical interventions targeting an increase in hip BMD in older adults may be most effective if weight-bearing moderate to vigorous intensity PA is included.

OR33-02

Significantly negative correlation between vasculopathy and bone mineral density in T2DM

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Purpose Osteoporosis aggravates with vasculature degeneration and improvement of vasculature could prevent osteoporosis. We, thus, hypothesize that healthy vascular structure and function play an important role in bone health. Type 2 diabetes mellitus (T2DM) patients are vulnerable to vasculopathy, so T2DM were involved in this project to study the correlation between vasculopathy and bone mineral density (BMD).

Methods 2170 patients with type 2 diabetes mellitus (998 males more than 50 years old and 1182 postmenopausal females) were included in our cross-sectional study. Baseline characteristics of the patients were collected, including age, gender, height, weight, body mass index(BMI), course of diseases, systolic blood pressure(SBP) and diastolic blood pressure(DBP). Serum characteristics of the patients were also measured, including the markers of glucose metabolism, bone metabolism, and other physiological and biochemical indexes. BMD were evaluated dual energy X-ray absorptiometry (DXEA, Hologic QDR4500W). Vasculopathy severity markers including both microangiopathy marker 24-hour proteinuria and macroangiopathy marker carotid plaque score. Carotid plaque score (Score 0-4, the score higher, the plaques more sever) according to University of Washington criteria was used to assess the severity of carotid plaques. According to 24-hour proteinuria, subjects were classified as normal albumin (<30mg/24h), microalbuminuria(30-300mg/24h) and macroalbuminuria(≥300mg/24h). BMD at L1-L4, hip and femoral neck and the rate of osteoporosis in 3 groups of 24-hour proteinuria were compared. Logistic regression analysis was used to study the association between bone mineral density and 24-hour proteinuria or carotid plaque score. Statistical analysis using SPSS20.0, $P < 0.05$ was statistically significant.

Results BMD at L1-L4 (males: p=0.041; postmenopausal females: p<0.001), hip (males: p=0.025; postmenopausal females: p=0.002) and femoral neck (males: p=0.014; postmenopausal females: p=0.002) was lowest and the rate of osteoporosis (males: p=0.003; postmenopausal females: p<0.001) was highest in the highest group of 24-hour proteinuria concentration in both male and postmenopausal female T2DM patients. Additionally, after adjusted for age, BMI, course of disease, SBP, DBP, HbA1C, estradiol, testosterone, osteocalcin CTX and 25(OH)VitD, BMD at L1-L4, hip and femoral neck was negatively associated with 24-hour proteinuria in postmenopausal female T2DM patients ($P < 0.001$). And BMD at L1-L4, hip and femoral neck was negatively associated with carotid plaque score in male T2DM patients ($P < 0.001$).

Conclusion The results demonstrate a negative correlation between BMD and carotid plaque score in male T2DM patients, and a negative correlation between BMD and 24-hour proteinuria in postmenopausal female T2DM patients, which supports the hypothesis that vascular structure and function play an important role in maintain skeletal health.

OR33-03

Is waist circumference an independent risk factor of vertebral fracture? Results from REACTION study

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Objective The study was aimed to explore the association of abdominal obesity with bone quality, not just with BMD.
Methods This was a prospective study, in which a total of 2847 participants (1965 women and 882 men) aged 23-87years were included in our analyses at
baseline from 2011 to 2012, and data from 846 individuals (602 women and 244 men) were obtained at follow-up after three years. BMD and bone quality
were measured using the quantitative ultrasound. Abdominal obesity was assessed by waist circumference (WC). Vertebral fracture was identified according to a prospective height loss > 2cm. Multiple regression analyses were applied to explore the associations.
Results 157 women and 51 men were detected with vertebral fracture at 3 year follow-up visit. In women, BMD, broad ultrasound attenuation (BUA), speed of sound (SOS) and quantitative ultrasound index (QUI) decreased as quartiles of WC increased. Multiple linear regression models showed that BMD, BUA, SOS and QUI were inversely associated with WC after adjusting for potential covariates. Compared to women in the lowest quartile, those in the highest quartile of WC had a more than five times increased risk of vertebral fracture (full adjusted OR=5.365, 95% CI, 2.045-14.075). The relationship between WC and BMD or bone quality or fracture risk were found only in the 45 years or over group.
Conclusions Abdominal obesity was inversely related to BMD and bone quality in women, especially in middle-aged and elderly women. WC is an independent risk factor of vertebral fracture.

OR33-04

The chloride/phosphate ratio combined with alkaline phosphatase as a valuable predictive marker for primary hyperparathyroidism in Chinese individuals

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Objectives Recent studies have highlighted a critical relationship between the chloride/phosphate ratio (Cl/PO4) and different types of primary hyperparathyroidism (PHPT). Moreover, alkaline phosphatase (ALP) is maintained at consistently high levels in PHPT. We examined whether Cl/PO4 determination combined with ALP measurement is an alternative method for predicting PHPT in a Chinese population.
Design A cross-sectional retrospective analysis examined 172 patients diagnosed with PHPT at Shanghai Jiao Tong University Affiliated Sixth People's Hospital.
Participants A serum PTH level ≥ 65 ng/L and confirmed parathyroid adenoma.
Measurements:The chloride, phosphorus, and ALP levels were measured using automated techniques. Serum parathyroid hormone (PTH) was measured using an Elecsys autoanalyser.
Results The median Cl/PO4 level was 33.9 [31.7–43.0] in the normocalcaemic primary hyperparathyroidism (NPHPT) group and 43.1 [37.0–47.5] in the hypercalcaemia PHPT group, and were both significantly higher than normal controls (29.9 [27.6–32.3], P<0.05). The median serum levels of ALP were 107.0 [74.0-269.0] in the NPHPT group and 114.0 [79.5-289.5] in the hypercalcemia group with ALP levels in PHPT, significantly higher than in the normal control group (61.5 [55.8-76.3]; P<0.05). Correlation analysis showed that the Cl/PO4 and ALP levels correlated with the PTH and calcium levels (P<0.001). Regression analyses demonstrated that after adjusting for ALP, Cl/PO4 was associated with PHPT only in the hypercalcaemia group (95% CI = 0.850 (0.776–0.931), P<0.001), and not in the NPHPT group (95% CI = 0.507(0.201–1.277), P=0.149). Cl/PO4 combined with ALP (0.913 [95% CI, 0.744–1.000]) increased the AUROC and the diagnostic value in both groups (0.913; 95% CI, 0.744–1.000 and 0.932; 95% CI, 0.897–0.966, respectively).
Conclusions The Cl/PO4 and ALP levels were independently and positively correlated with the PTH and calcium levels. Thus, Cl/PO4 determination combined with ALP level measurement might be a low-cost, available predictive marker of PHPT in Chinese individuals.

OR34-01

Neonatal thyrotropin concentration and iodine nutrition status of mothers: A systematic review and meta-analysis

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Objective The aim of this systematic review and meta-analysis is to explore for the first time the association of neonatal thyrotropin concentration and iodine status of mothers during pregnancy and early postpartum periods.
Materials and methods Data were collected from studies published between 1969 and 2015 through literature searches, using Pub Med, ISI Web, and Cochrane Library, Google Scholar, relevant databases and the reference lists of previous reviews. Mean or median maternal urinary iodine and neonatal thyrotropin concentrations along with other relevant data were extracted from eligible studies. The quality and risk of bias of individual studies were assessed. The random effect model was used in analysis.
Results Of 110 studies identified, 25 were found to be eligible for inclusion in the meta-analysis. Mean (95% confidence interval (CI)) thyrotropin concentrations of neonates born to mothers with iodine deficiency was higher than in those with iodine sufficiency during pregnancy in both heel: 1.79(1.61-1.97) mIU/l vs. 1.75(1.68-1.82) mIU/l and cord: 11.91(6.67-17.14) mIU/l vs. 6.15(4.30-8.01) mIU/l blood samples. There was no significant difference in neonatal thyrotropin concentration of heel samples between mothers with iodine deficiency and sufficiency during early postpartum period: 3.37(2.71-4.02) mIU/l vs. 3.85(2.76-4.94) mIU/l; however, the values of thyrotropin in cord samples in neonates born to mothers with iodine deficiency were significantly higher as compared to those with iodine sufficiency: 11.62(10.47-12.77) mIU/l vs. 7.40(6.21-8.59) mIU/l).
Conclusion Although neonatal thyrotropin constitutes an index of monitoring of iodine status in populations and intervention programs, it can be influenced by several prenatal and postnatal factors. The findings of our meta-analysis reveal that as compared to heel blood samples, neonatal thyrotropin in samples collected from cord were more sensitive to the iodine status of mothers; however, further investigations are still required in this regard.

OR34-02

Placental 11β-HSD2 and cord plasma cortisol levels, metabolic and cardiovascular health indices in infants

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Background/Objective Glucocorticoids may be involved in fetal "programming" of cardiometabolic risk. Placental 11β-hydroxysteroid dehydrogenase 2 (11β-HSD2) can convert cortisol to cortisone to avoid fetal exposure to high cortisol levels. It is not known whether placenta 11β-HSD2 and circulating cortisol levels are related to cardiometabolic health parameters in early life. We sought

to address this question in infants at 1-year of age, and evaluate the influence of gestational diabetic mellitus (GDM).
Methods This was a prospective cohort study of 26 GDM and 249 non-diabetic singleton pregnant women and their infants. Maternal blood samples (24-28 and 32-35 weeks of gestation), umbilical cord blood, placenta tissues and infant blood samples (fasting at 1-year) were collected. Placenta 11β-HSD2, maternal and cord plasma cortisol concentrations were measured. Outcomes included glucose metabolic health biomarkers at birth and 1-year of age, skinfold thickness, blood pressure and carotid intima-media thickness at 1-year.
Results Cord blood cortisol concentrations were significant lower in gestational diabetic vs. non-diabetic pregnancies, while placenta 11β-HSD2 levels were similar. However, there were no significant differences in all observed metabolic and cardiovascular outcomes among infants between GDM and non-diabetic groups. Maternal and cord blood cortisol levels were positively correlated (r: 0.17 to 0.25). Cord blood cortisol levels were negatively correlated with IGF-1 levels (r=-0.14) and beta function indices at birth (r=-0.30, p<0.0001), and negatively correlated to skinfold thickness at 1y. Placental 11β-HSD2 levels were negatively correlated with cord blood cortisol levels (r=-0.14, p=0.03), positively correlated with insulin sensitivity (r=0.16, p=0.04), borderline significantly negatively correlated with systolic blood pressure (r=-0.16, p=0.057), but uncorrelated to carotid intima-media thickness in infants at 1-y.
Conclusions There is some evidence suggesting that placenta 11β-HSD2 and circulating cortisol levels may affect insulin sensitivity and beta cell function in early life.?

OR34-03

Levothyroxine Treatment in pregnant women with autoimmune thyroid disease: prenatal and neonatal outcomes.

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Background Despite some studies indicating that thyroid antibody positivity during pregnancy has been associated with adverse pregnancy outcomes, evidence regarding the effect of levothyroxine (LT4) treatment of euthyroid/subclinical hypothyroid pregnant women with autoimmune thyroid disease on pregnancy outcome is limited. As a result various scientific societies, including the America Thyroid Association (ATA), European Thyroid Association (ETA), and the Thyroid Society report lack of sufficient evidence and clinical trials on effectiveness of levothyroxine treatments of these pregnant women in terms of pregnancy or neonatal outcomes; these societies mostly referred to a single clinical trial conducted by Negro et al. that reported a lower rate of adverse outcomes in TPO antibody-positive women treated with levothyroxine
Objective We aimed to assess whether pregnant women with autoimmune thyroid disease and without overt thyroid dysfunction are affected by a higher rate of adverse pregnancy outcomes. In addition we aimed to explore whether LT4 treatment improves the pregnancy outcome of affected women.
Design: This study consisted of two phases, the first of which was a population based cross sectional study in which 1746 pregnant women, attending prenatal clinics of Shahid Beheshti Medical University, were screened for thyroid dysfunction through collecting data on medical history, clinical examination and measurement of serum concentrations of TSH,T4 (TT4), T-uptake and TPOAb. Three casual morning urine samples (5-10 mL) of each participant were collected on an every other day basis and kept frozen at -20°C until assayed at the end of the study; the median urinary iodine was calculated. Blood samples were also collected at second (20-24 wk gestation) and third (30-34 wk gestation) trimesters and stored at -80°C till end of the study for measurement of thyroid hormones. Serum concentrations of TSH of offspring were measured 3-5 days after delivery.
By excluding those with twin pregnancies, those diagnosed with hyperthyroidism or overt hypothyroidism and those TPOAb- subclinical hypothyroid women, 134 TPOAb+ (euthyroid and subclinical) women and 1092 euthyroid TPOAb- women remained; they were invited for the second phase of the study, of whom 1028 and 131 women accepted, respectively.
Second phase of this study was a double blind clinical trial conducted on TPOAb+ subjects divided into two groups, group A (n = 65), treated with LT4 and group B (n = 66), without treatment; TPOAb-women without any thyroid dysfunction served as the control group (group C) ; all three groups were followed and any adverse outcomes of pregnancy were recorded.
Main Outcome Measures: Primary outcomes were preterm delivery and miscarriage and secondary outcomes included placenta abruption, still birth and neonatal admission.
Results Using the predefined classification, after excluding twins (n=28), 36.4% (626) had thyroid disorders, including 0.8% (n=14) overt hyperthyroidism; 3.5% (n=60) overt hypothyroidism; 1.5% (n=25) subclinical hyperthyroidism; 22.9% (n=393) TPOAb- subclinical hypothyroidism; 7.8% (n=134) euthyroid/ subclinical TPOAb+(group A and B); and 1092 women (63.6%) were euthyroid TPOAb-(group C).The medians (interquartiles) of urine iodine in groups A, B and C were 84.52(58.51, 137.23), 104.78(78.59, 140.24) and 119.70 (78.72, 184, 27) µg/l, respectively, indicating no significant difference between these groups.
Results of phase 2 of the study demonstrated a higher rate of preterm deliveries in group B compared with group A (RR=3.38, 95% CI: 1.18- 9.65, P = 0.0229) and group C (RR= 4.28, 95% CI: 2.53-7.24, P < 0.001). There was no statistically significant difference in rate of preterm labor between groups A and C (RR= 1.27, 95% CI: 0.48- 3.38, P= 0.64). The number needed to treat (NNT) for the preterm birth was 5.9 (95% CI: 3.33- 25.16).The rate of neonatal admission in group B was significantly higher than in groups A and group C [(P = 0.005, RR=5.8, 95% CI: 1.36- 24.73) and (P= 0.001, RR= 2.6, 95% CI: 1.50-4.48), respectively] .The number needed to treat (NNT) for neonatal admission was 5.84(95% CI: 3.48-18.23).
Conclusions Replacement therapy with levothyroxine in TPOAb+ euthyroid pregnant improves pregnancy outcomes and is beneficial in reducing preterm delivery. Number needed to treated (5.9) is reasonable as it can prevent a serious pregnancy outcome (preterm delivery), with adverse effects, not limited to the neonatal period per se but continuing into adulthood.

OR34-04

Maternal Hypothyroxinemia induces Autism in Rat Offspring by Inhibition of mTOR Signaling Pathway

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Context Maternal hypothyroxinemia in pregnancy not only can result in mental and pychomotor development disorders, but also increase the risk of autism of the offsprings. This study intends to discuss the mechanism on autism of the offsprings from the pregnant women with hypothyroxinemia via the established pregnant hypothyroxinemic animal model with PTU.

Methods 1. The pregnant hypothyroxinemic animal model was established by female wistar rats fed with PTU. The hypothyroxinemic offspring pups were defined as the T group, while normal control offsprings were C group. 2. In order to evaluate the possible social skills, repetitive stereotyped behaviors, anxiety, depression, spatial learning and memory ability, the offspring pups would be arranged behavioral experiments, including: three-chamber sociability test, marbels burying, grooming behaviors, elevated plus-maze, open field activity, forced swim test, Morris water maze after the birth of 40th day. 3. Detecting the neurotransmitter level on the prefrontal cortex of the offsprings with high performance liquid chromatography (HPLC) method. 4. On the first day of birth (P0), RT-PCR will be applied to detect the mRNA levels of thyroid hormone response genes Reelin, RC3 and Dendritic development related actors mTOR on prefrontal cortex.
Results 1. In the behavioral experiments which could reflect autistic behaviors, T group showed social disorders. In marble burying test, T group have buried more marbles than C group ($P<0.05$) , also in monitoring the grooming time and grooming frequencies test for 30min, T group showed more grooming time compared with C group ($P<0.05$) , which meant repeat stereotyped behaviors. 2. In forced swimming test which would reflect depression, the T group showed more immobile duration compared with C group ($P<0.05$) ,while less mobile duration ($P<0.05$) , which meant depression. 3. In the behavioral experiments which could reflect anxiety, the time or the percentage of time spent in center zone didn`t have any differencies between the two groups in open field test, while T group spent more time or the percentage of time spent in center zone compared with normal control group ($P<0.05$) in elevated plus-maze test, which meant no anxiety. 4. In Morris water maze test which would reflect spatial learning and memory ability, the escape latency time and the space exploration had no differencies between the two groups. 5. In the mechanism study, compared with C group, the 5 - HT, dopamine levels of T group were significantly lower on prefrontal cortex ($P<0.05$) . While on P0, the mRNA levels of thyroid response genes reelin, RC3 and the dendritic growth related factor mTOR in T group showed decreased expression on prefrontal cortex compared with C group ($P<0.05$) .
Conclusions Thyroid hormones insufficiency leads to the down-regulation of reelin /5-HT/dopamine signaling pathways, and followed inhibition of mTOR signaling pathways, which may be the mechanism of autism in offsprings induced by maternal hypothyroxinemia.

OR35-01

Genetic determinants of Growth Hormone and GH-related phenotypes

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Background Higher levels of Growth Hormone (GH) are associated with cardiovascular disease. Finding genetic determinants of the fasting levels of GH would facilitate future efforts of understanding if the GH-CVD relationship is causal or not.
Objectives To find single nucleotide polymorphisms (SNPs) associated with fasting levels of hs-GH.
Methods We applied two different methods (figure 1), the first a genome-wide association study (GWAS)
in a discovery cohort of 4,134 persons (58% females; age 46 to 68 yrs; subset of Malm? Diet and Cancer study – MDC), linking SNPs to the fasting levels of hs-GH. The top SNPs were replicated in an independent cohort of 5,262 persons (28.9% females; age 56 to 85 yrs; Malm? preventive project – MPP). The best performing SNP from the replication study was selected for further investigation vs GH-related variables in the entire MDC-cohort (n=28,181; 60% females; age 44 to 73 yrs). The second approach was a candidate gene approach where significant
SNPs in the genes for GH1 and GHR in the discovery cohort were analyzed vs hs-GH in MPP and vs GH-related variables in MDC.
Results In the GWAS-approach we discovered a SNP (rs7208736) that was nominally associatiated with lower hs-GH in the discovery cohort (p=5.15*10^-6) and the replication cohort (p=0.005). The GH reducing allele was associated with lower BMI
(P=0.035) and waist (P=0.016). In the candidate gene approach a SNP (rs13153388) in the GHR-gene was associated with elevated GH-levels (P=0.003) and reduced height (figure 2) in the MDC (P<0.001).
Conclusion: Elevation of hs-GH and lower height suggests that the GHR variant identified by the candidate approach leads to reduced GHR ligand sensitivity. In the first GWAS ever for hs-GH, we identify a novel locus on chromosome 17 contributing to hs-GH levels, implying novel biological mechanisms behind GH secretion and GH-related traits.

OR35-02

A hybrid Fc-fused human growth hormone, GX-H9, shows a potential for semi-monthly administration in clinical studies.

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Objective GX-H9 is a hybrid Fc-based long-acting recombinant human growth hormone (hGH). The safety, tolerability, and PK/PD were assessed in a single ascending dose study in healthy volunteers and in a multiple sequential dose study in patients with adult growth hormone deficiency (AGHD). The efficacy of GX-H9 was compared to that of a daily recombinant hGH in AGHD. A Phase 2 study in pediatric GHD (PGHD) is also ongoing to investigate safety, efficacy and PK/PD of GX-H9 in pediatric patients.
Method A double-blind, randomized, placebo-controlled, single ascending dose Phase 1 study of GX-H9 was conducted in 4 groups of healthy subjects (n=32) with four sequential dose levels (0.2, 0.4, 0.8 or 1.6 mg/kg). Currently, a Phase 2, randomized, active-controlled, open-label, sequential dose study of GX-H9 (0.1 mg/kg/weekly, 0.2 and 0.3 mg/kg/semi-monthly) is being conducted in patients with AGHD (n=45). In addition, a Phase 2, randomized, active-controlled, open-label, multiple dose study of GX-H9 with weekly and semi-monthly administrations is being conducted in patients with PGHD (n=48).
Results Single doses of GX-H9 in the range of 0.2 to 1.6 mg/kg were well tolerated at all dose levels. No safety concerns were noted, including absence of any lipoatrophy or anti-drug antibodies. Geometric mean of t1/2 ranged between 69.2 and 138.0 hours. IGF-1 serum concentrations increased in a dose-dependent manner between 0.2 and 1.6 mg/kg. The interim Phase 2 results have indicated that AGHD patients (n=11) receiving the lowest dose of GX-H9 (0.1 mg/kg) weekly for 12 weeks were safe and comparable with those receiving 6 μg/kg of Genotropin daily for 12 weeks (n=2) in the mean increases in IGF-1 (101.3±31.2 ng/mL vs 109.1±45.0 ng/mL, respectively). The administration of higher doses showed a potential for semi-monthly treatment of GX-H9 in AGHD and PGHD.
Conclusions Phase 1 and interim Phase 2 results have demonstrated that GX-H9 is safe and well tolerated in healthy subjects and in

patients with AGHD and PGHD. The data from ongoing Phase 2 studies will be presented in addition to the Phase 1 result.

OR35-03

Causes of sex differences in fetal growth and insulin sensitivity

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Objective Girls have lower birth weight, birth length and insulin sensitivity than boys. The causes of such sex differences are incompletely understood. The present study sought to uncover fetal metabolic hormones related to such sex differences in fetal growth and insulin resistance.
Methods In a prospective singleton pregnancy cohort (n=255), we assessed cord plasma insulin, proinsulin, IGF-1, IGF-2, leptin,adiponectin and ghreline concentrations in relation to gender differences in fetal growth and insulin sensitivity (QUICKI, quantitative insulin sensitivity check index).
Results Adjusting for gestitational age, girls were 92 (95%CI 65.1, 194.8) g lighter in birth weight, 0.83 (0.4, 1.3) cm shorter in birth length, and 0.72 (0.4, 1.0) cm smaller in head circumference, respectively. Further adjusting for leptin concentration, girls growth deficits increased to 144 (44.9, 242.8) g for birth weight, 0.98 (0.5, 1.5) cm for birth length, and 0.78 (0.5, 1.1) cm for head circumference, respectively. Adjusting for IGF-1 concentration, girlsgrowth deficits increased to 141 (53.2, 228.5) g for birth weight, 0.95 (0.5, 1.4)cm for birth length, and 0.79 (0.5, 1.1) cm for head circumference,respectively. Adjusting for proinsulin concentration, girls growth deficits increased to 156 (61.1, 250.8) g for birth weight, 0.97 (0.5, 1.4) cm for birth length, and 0.79 (0.5, 1.1) cm for head circumference, respectively. QUICKI is lower in girls, and the sex difference increased by 10% (1.2%, 18.3%) after adjusting for leptine concentration, 6% (-2.6%,14.6%) after adjusting for IGF-1, respectively. Other hormones were not related to gender differences in fetal growth or insulin sensitivity.
Conclusions Leptin, IGF-1 and proinsulin are related to gender differences in fetal growth. Girls are more IGF-1 and leptin resistance than boys.

OR35-04

Effect of GH treatment on coagulation parameters in children with growth hormone deficiency

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Background Increased fibrinogen levels have been reported in adolescents with growth hormone deficiency (GHD), which were reduced after rhGH treatment. rhGH treatment has also been shown to exert a beneficial effect on the amount of aPAI-1 in children with GHD
Aim To evaluate the effect of GH therapy on coagulation and fibrinolysis related parameters in children with GH deficiency
Methods Fifteen prepubertal children (10 girls and 5 boys) of a mean (sd) age of 9.8 (0.4) yrs and GH deficiency were included in this hospital based prospective study. Serum levels of PT, APTT, fibrinogen, VII, VIII, AT, PC, D-dimers, Plg, and PAI-1 were measured before and after 6-12 months of GH treatment.
Results At baseline all studied parameters were within normal ranges. A significant increase in PT values was noted after a mean (sd) interval of 9.3(0.4) months of treatment : 12.46 (0.77)sec vs 12.1(0.68)sec, p=0.045. A significant decrease in PAI-1 levels (3.04 (0.48)U/ml vs 2.28 (0.71) U/ml, p=0.018) was noted at the same time. No significant changes in the rest of parameters were found during the study period.
Conclusion GH replacement therapy for 6-12 months led to a significant increase in PT values, while fibrinogen levels did not change. Moreover, GH treatment reduced PAI-1 levels in GHD children, suggesting a beneficial effect of GH treatment on possible risk of atherothrombosis. Further evaluation of the clinical significance of these changes is needed.

OR43-01

Rock around the choroid plexus clock

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The suprachiasmatic nucleus (SCN) of the mammalian hypothalamus is considered the master circadian pacemaker. The SCN clockwork is a cell autonomous mechanism consisting of a series of interlocked transcriptional/ post-translational feedback loops. Nevertheless, the SCN is not the only structure in the brain displaying daily rhythms. Olfactory bulb, amygdala, lateral habenula, cerebellum, a variety of nuclei in the thalamus and hypothalamus, and recently choroid plexus (CP), contain the molecular machinery necessary for the generation of the circadian rhythms, that in the case of CP are subjected to circadian regulation in a gender dependent manner. There is a growing recognition that gonadal steroids may exert several stimuli on core clock genes affecting biological rhythms. However, it is not known the effects of steroid hormones on CP circadian rhythmicity or even the possible influence of this new extra-SCN tissue on the regulation of critical physiological circuits. Therefore, using an *in vivo* and *in vitro* approach we studied the effects of estrogens in the regulation of CP clock genes. We observed that estrogen depletion following ovariectomy affects the CP circadian rhythmicity in female rat CP and that *Period 1* and *Period 2* mRNA expression are up-regulated by estradiol (E2) in rat primary CP epithelial cell cultures. In addition, we tested if the E2 circadian modulation of *Period 1* and *Period 2* are caused by a direct effect of estrogen-mediated activation of estrogen receptor in CP, and we provide evidence that this receptor is involved. Moreover, using CP explants cultured from mice carrying the Period-luciferase transgene, we report that CP exhibits endogenous circadian rhythms of PERIOD2::LUCIFERASE expression. Therefore, our study reinforces the importance of estrogens on circadian oscillators and supports the hypothesis that E2 directly controls the molecular clock machinery present in the CP.

OR43-02

The Effects of Maternal Protein Restriction and Postweaning High-fat Feeding on Offspring Metabolic Health and POMC Gene Methylation

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Background Substantial evidence indicated that catch-up growth could increase the susceptibility to obesity, insulin resistance and type 2 diabetes in adulthood. In addition, there is increasing ev-

idence that both brain and epigenetic modifications play critical roles in glucose homeostasis. However, little information is known about the long-term effects and epigenetic programming of candidate genes in hypothalamic neurons of catch-up growth. Given the interactional relationship among epigenetic modifications, diets and glucose matabolism, our objective was to explore the effects of catch-up growth on glucose metabolism and DNA methylation status of hypothalamic feeding-related neuropeptides in the mice offspring.

Methods C57/BL6 mice were fed on either low protein (LP) or normal chow (NC) diet throughout gestation and lactation. Then, the offspring were randomly weaned to either NC or high fat (HF) diet until 32 weeks of age, generating four experimental groups: NC-NC, NC-HF, LP-NC and LP-HF. Metabolic parameters, DNA methylation and gene expressions of hypothalamic proopiomelanocortin (POMC) and melanocortin receptor 4 (MC4R) were determined in the offspring.

Results It showed that the male offspring from maternal NC and LP dams and weaned to HF diet had higher body weight at 16 weeks of age until to termination, compared with the NC-NC offspring ($P<0.05$). The blood glucose levels of the male offspring in the NC-HF and LP-HF groups were significantly higher at 30 min ($P<0.001$), 60 min ($P<0.001$) and 120 min ($P<0.01$) after intraperitoneal glucose administration, compared with those of the NC-NC offspring. Consistently, the blood glucose AUC was significantly greater in NC-HF and LP-HF offspring ($P<0.001$). HOMA-IR of the NC-HF and LP-HF offspring was also significantly higher than NC-NC offspring ($P<0.05$). Serum triglyceride and total cholesterol levels were both significantly elevated in the NC-HF ($P<0.05$ and $P<0.001$, respectively) and LP-HF offspring ($P<0.05$ and $P<0.001$, respectively) at 32 weeks of age. Both the mRNA and protein expressions of POMC and MC4R genes were significantly increased in NC-HF and LP-HF offspring ($P<0.05$). Consistently, hypomethylation of POMC promoter in the hypothalamus occurred in the NC-HF and LP-HF offspring ($P<0.05$), compared with the NC-NC group. However, no differential methylation was detected of MC4R promoter among the four groups ($P>0.05$). Furthermore, POMC-specific methylation (%) was negatively associated with glucose response to a glucose load ($r =-0.361$, $P = 0.02$) in the offspring at 32 weeks of age.

Conclusion In conclusion, catch-up growth predisposed the offspring to POMC promoter hypomethylation, obesity, impaired glucose tolerance, insulin resistance and dyslipidemia. Our study was novel in showing the 'programming' effects of nutrition-induced catch-up growth on glucose metabolism and epigenetic changes in hypothalamic appetite regulatory genes in the adult mice.

OR43-03

Anti-inflammatory role of estrogen in the hippocampus: regulation of inflammasome complex via PELP1

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Objective To study the role ofestrogen (E2) and the estrogen receptor co-regulator, PELP1 in regulating NLRP3inflammasome activation in the hippocampus after global cerebral ischemia.

Methods In the current study, we examined whether E2, acting viaPELP1, can exert anti-inflammatory effects. Three-month old young adult femaleSprague Dawley rats and PELP1 forebrain specific knockout mice wereovariectomized and subjected to global cerebral ischemia (GCI). Animals weregrouped into shams, injury and injury with estrogen treatment and weresacrificed at days 6-7 after injury. Hippocampal tissue was collected for Westernblot, RT-PCR, and immunofluorescence analyses of NLRP3 inflammasome pathwaymolecules.

Results The results showed thatactivation of the NLRP3 inflammasome pathway and expression of its downstreamproducts, cleaved caspase-1, and IL1β, are temporally increased inthe hippocampus after GCI, with peak levels observed at 6-7 days after ischemia-reperfusion.E2 robustly inhibited NLRP3 inflammasome pathway activation, caspase-1 andpro-inflammatory cytokine production after GCI at mRNA as well as proteinlevels. E2 also suppressed the expression of P2X7 receptor, an upstreamactivator of NLRP3. Intriguingly, the ability of E2 to exert all of theseanti-inflammatory effects was lost in PELP1 forebrain-specific knockout mice. Thisfinding suggests a critical role for PELP1 in mediating the anti-inflammatoryeffects of E2 in the hippocampus after GCI.

Conclusions Collectively, our studydemonstrates that E2 signaling via the ER co-regulator, PELP1 exerts robustanti-inflammatory effects in the hippocampus after GCI to regulate inflammasomeactivation and cytokine production. Thus, in addition to its neuroprotectiveactions, E2 can also exert robust anti-inflammatory effects following ischemicinjury to the brain. These preclinical findings provide potential therapeutictargets for managing brain ischemia and inflammation that should be exploredfurther.

OR43-04

Characterisation of a novel species-restricted putative hydroxysteroid dehydrogenase called HSD1L in the pituitary-gonadal axis

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Objective Endocrine steroid hormones including estrogens, androgens, glucocorticoids and mineralocorticoids play clinically important and specific regulatory roles in human development, growth, metabolism, reproduction and brain function. The 11-beta hydroxysteroid dehydrogenase (11-betaHSD) enzymes have key roles in the pre-receptor modification of glucocorticoids, modifications that directly regulate blood pressure, fluid and electrolyte homeostasis, as well as modulating metabolic and brain function. We have recently identified a novel largely uncharacterized 11betaHSD-like gene on human chromosome 19p13.3, a distinct gene from the well characterized 11betaHSD1 and 11betaHSD2 genes. Strikingly, a search in other mammalian genomes has revealed the complete absence of this third 11beta-like HSD gene in the mouse, rat and rabbit genomes. We have characterized this novel member of the HSD/SDR (Short-chain Dehydrogenase-Reductase) enzyme family for expression across 20 tissues of the body and for cell-type specific localization in the pituitary/gonadal axis.

Methods Expression of the HSD1L gene has been assessed by RT-PCR, qPCR and drop-digital PCR in a range of tissues and cell lines across human, non-human primates and the sheep. The tertiary structure of the human HSD1L protein was modeled the program 'Pymol' with the known tertiary structure of 11betaHSD1. Cell-type specific localization in tissue sections was determined by immunohistochemistry in non-human primates and the sheep using two distinct specific antibodies. Intracellular localization was determined by GFP/ds-Red-tagged HSD1L transfected into the human HEK293 and COV74 cell lines.

Results The human HSD11B1L gene is encoded by 9 exons and analysis of EST library transcripts and additional exon-specific PCR analysis indicates the use of two alternate ATG start-sites in exons 2 & 3, and alternative splicing in exon 9. Determination of the predict-

ed tertiary structure of the human HSD1L protein with the protein modeling program 'Pymol' shows a strong structural homology to 11betaHSD1 with all important structural protein fold domains highly conserved. We have detected high expression of this enzyme in human, non-human primate and sheep tissue samples from the brain, ovary, testis and gut. Analysis for cell-type specific expression by immunohistochemistry localizes 11betaHSD1L to the cytoplasm of ovarian granulosa cells, testis leydig and sertoli cells, and the somatotroph cells in the anterior pituitary of non-human primates and the sheep. Co-localization analysis identifies intracellular localization to endoplasmic reticulum compartments. The endogenous substrate of this enzyme is unknown but we demonstrate that it is unlikely to be the steroids cortisol or cortisone.

Conclusion A new species-restricted member of the HSD/SDR family of enzymes has been identified and characterized in human, non-human primates and the sheep. This protein is localized to specific cells of the anterior pituitary, ovary and testis implicating a physiological role in the pituitary-gonadal reproductive axis. A causal role in developmental or reproductive human disease is currently under investigation. The endogenous substrate of this enzyme is currently unknown, is most likely a reproductive steroid or metabolite, and we show that it is unlikely to be the known 11-betaHSD substrates cortisol or cortisone.

OR44-01

The Predictive Role of Serum High-Sensitivity C-Reactive Protein in Nephropathy Development and Progression among Chinese patients with Type 2 Diabetes

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Background The role of serum high-sensitivity C-reactive protein (sCRP) in diabetic nephropathy among Chinese patients has not been clearly defined. Previous studies were either of cross-sectional design or with relatively small sample size. Here we investigate prospectively whether serum sCRP predicts nephropathy development and progression in Chinese patients with type 2 diabetes.

Method Baseline serum sCRP levels were measured in 5,199 Chinese subjects with type 2 diabetes recruited from the Hong Kong West Diabetes Registry. The role of serum sCRP in predicting nephropathy progression, in terms of decline in estimated glomerular filtration rate (eGFR), and nephropathy development, defined as eGFR decline to <60ml/min/1.73m^2 or deterioration of albuminuria category from A1 to A2 or A3, over a median follow-up of 3.5 years was analysed using Cox regression analysis.

Results Amongst 5,199 subjects with baseline eGFR >/= 30ml/min/1.73m^2, serum sCRP levels were significantly higher in those with eGFR decline during follow-up (N=1091) than those without decline (N=4108) (1.5mg/L [0.7-3.9] vs. 1.0 [0.5-2.5]; p<0.001). O multivariable Cox regression analysis, baseline serum sCRP levels were independently associated with nephropathy progression (Hazard ratio [HR] 1.228; 95% confidence interval [CI] 1.174-1.285; p=<0.001). In 2,361 subjects without diabetic nephropathy at baseline, on multivariable Cox regression analysis, baseline serum sCRP also independently predicted nephropathy development (HR 1.072; 95% CI 1.003-1.145; p=0.041).

Conclusions Our findings are supportive of a significant contribution of inflammation in diabetic nephropathy. Serum hsCRP could be usefully employed as a biomarker for predicting both nephropathy development and progression in patients with type 2 diabetes.

OR44-02

Gestational diabetes mellitus predicts abnormal glucose metabolism in the majority at long term follow up

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Background We reported recently in a large questionnaire study from Sweden that 25 % (334/1334) of the women diagnosed with gestational diabetes mellitus (GDM) had developed manifest diabetes mellitus after median 11 years follow up (Wahlberg et al. Diabetes Res Clin Pract. 2016 Apr;114:99-105).

The aim with the present study was to make a careful clinical and biochemical evaluation in the subpopulation of the GDM women living in our regional area to assess the long term risk for all kind of glucose metabolic abnormalities.

Methods Women (n=51) previously diagnosed with GDM by capillary blood glucose ≥9.0mmol/l (≈plasma glucose ≥10.0mmol/l) after a 75g oral glucose tolerance test (OGTT) were included. Median follow up time was 12 yrs. after initial GDM diagnosis. Country of origin was Sweden (n=45; 88%), Europe (n=1; 2%) and outside Europe (n=5; 10%). All invited women underwent a clinical and biochemical evaluation including a new 75g OGTT. Individuals with known type 1-diabetes were excluded from this study.

Results At the clinical follow up had 12/51 (24%) previously diagnosed type 2-diabetes. In addition 4 more patients were diagnosed with diabetes mellitus after the new OGTT, increasing the prevalence of diabetes mellitus to 16/51 patients (31%). Moreover, 22/51 were diagnosed with impaired fasting plasma glucose (IGF) and/or impaired glucose tolerance (IGT), left only 13 (24%) with normal glucose tolerance. In addition 2 of the 51 women had high levels of GAD antibodies and one woman classified as type 2-diabetes was reclassified as type 1-diabetes and the second GAD positive women was diagnosed with IGT.

Conclusions GDM diagnosed as capillary blood glucose >?9.0 mmol/l (plasma glucose >10.0 mmol/l) after a 75g OGTT predicts later development of impaired glucose metabolism in most of the women diagnosed with GDM and our data indicates that all women with prior GDM should be offered regular glucose measurements lifelong. Moreover, type 1-diabetes should be regarded as a diagnostic alternative, at least in Scandinavian women.

OR44-03

Human adipose tissue-derived mesenchymal stem cells facilitate white adipose tissue browning and limit obesity via the activation of M2 macrophages

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Objective Obesity is a chronic metabolic disease characterized by excess accumulation of adipose tissue. Adipose tissue can be divided into two distinctly functional types, white adipose tissue and brown adipose tissue. M2 macrophages in adipose tissue could facilitate white adipose tissue browning and limit obesity. Mesenchymal stem cells (MSCs), which are fibroblast-like stromal cells displayed with self-renewal and multipotent differentiation capacities, have been identified to promote M2 macrophages in epididymal adipose tissue. Therefore, we aimed to investigate whether MSC could facilitate white adipose tissue browning and limit obesity, and also aimed to investigate the origin of M2 macrophages.

Research design and methods Eight-week-old C57/bl6 mice

were given high-fat diet to induce obese model, body weight was detected each week. Sixteen weeks later, 1×10^6 human adipose tissue-derived MSCs (hASC) suspended in 0.2 ml PBS were infused into mice via tail vein, obese group was infused 0.2 ml PBS as control. Two weeks later, indirect calorimetry was performed to assess the oxygen consumption, EchoMRI was performed to analyze the body composition. H.E. staining was conducted to observe the morphology of adipose tissues. Protein UCP-1 was analyzed by western blotting and metabolic associated genes were analyzed by RT-PCR. At the same time, we collected epididymal adipose tissues and isolated stromal vascular fraction (SVF) from adipose tissues to analyze the phenotypes of adipose tissue macrophages by flow cytometry and western blotting. Quantitative real-time PCR analysis was also conducted to assess the inflammation state of the epididymal adipose tissue. The peripheral blood was collected to perform flow cytometry. We used CM-Dil marked hASC to trace their distribution in mice.

Results In obese mice, hASC infusion significantly decreased the fat mass and increased the lean mass, and also increased the oxygen consumption. After hASC infusion, the adipocytes' size was decreased, protein UCP-1 in subcutaneous and epididymal adipose tissue was increased, and also the metabolic associated genes were increased in epididymal adipose tissue. hASC also acted in ATMs, promoting M2 polarization and limiting the expression of genes encoding pro-inflammatory molecules. The percent of $LY6C^-CCR2^-CX3CR1^+$ monocytes was increased by hASC infusion. Few hMSCs were distributed in lungs, liver, pancrease and adipose tissue, most of them were found in the red pulp and marginal zone of spleen and overlapped with macrophages.

Conclusions In conclusion, hASC infusion facilitate white adipose tissue browning and limit obesity, and this effect was partially attributed to directing macrophages into M2 phenotype. hASCs were distributed in spleen to display their immunomodulation effect and increased $LY6C^-CCR2^-CX3CR1^+$ monocytes to promote M2 macrophages.

OR44-04

The role of established obesity-related loci in Chinese pediatric leptin levels highlights a neuronal influence on body weight regulation

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Objective Recent genome-wide association studies have identified multiple variants associated with body mass index (BMI) and obesity, mostly in populations of European ancestry. We aimed to systematically assess the contribution of key loci to obesity and related adipokine profiles, and metabolic traits in a Chinese pediatric population.

Methods 13 single nucleotide polymorphisms (SNPs) at 13 loci, were tested in 3,506 school-aged children (6-18 years, 51% male). The associations between these loci and cardiometabolic parameters and adipokine profiles, including leptin, adiponectin, resistin, fibroblast growth factor 21, and retinol binding protein 4 levels were evaluated.

Results Of the thirteen SNPs : *MC4R*-rs2331841 (P = 2.8E-7), *FTO*-rs1558902 (P = 5.6E-5), *GNPDA2*-rs16858082 (P = 3.4E-4), *PCSK1*-rs261967 (P = 0.001), *MAP2K5*-rs4776970 (P = 0.004), and *SEC16B*-rs516636 (P = 0.004) were found to be significantly associated with obesity, while *ITIH4*-rs2535633 and *BDNF*-rs2030323 were found to be nominal associated with obesity ($P < 0.05$) following adjustment for gender, age, Tanner stage and residence, with odds ratio from 1.133 to 1.421, the same trend was found with BMI, waist circumference, percent body fat and upper arm circumference in the linear regression analysis. Interestingly, the risk alleles of *FTO* (P = 0.002), *MC4R* (P = 0.003), *MAP2K5* (P = 0.003), *GNPDA2* (P = 0.007), *PCSK1* (P = 0.009) and *BDNF* (P = 0.027) yielded association with plasma leptin levels and their cumulative genetic risk score showed strong association with increased leptin levels (P = 6.0E-7). In addition to leptin, the risk alleles of *MC4R* and *BDNF* yielded nominal association with plasma adiponectin levels ($P < 0.05$). No association was observed between these loci and other adipokines levels. When further adjusted for BMI, the risk alleles of *KCNQ1*-rs2237892 (P = 3.7E-4), *GNPDA2* (P = 0.016), and *PCSK1* (P = 0.026) remained associated with lipids, while *MC4R* remained correlated with fasting glucose levels (P = 0.012)

Conclusion Our results reveal that key obesity-associated loci previously reported in Europeans are also associated with obesity risk and/or metabolic quantitative traits in Chinese children and adolescents. These associations coincide with six brain-expressed genes that correlate with leptin levels, thus points to a neuronal influence on body weight regulation in the pediatric setting.

OR45-01

Serum cortisol and the risk of osteoporosis in nigerians on medroxyprogesterone acetate

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Depot-Medroxyprogesterone Acetate (DMPA) is one of the most used contraceptives and it is currently used by more than 30 million women in most of developed and developing countries. The use of Depot-Medroxyprogesterone is associated with Osteoporosis and reduction in bone mineral density. The study was designed to investigate the relationship between serum cortisol and the risk of osteoporosis in Nigerians using Depot-Medroxyprogesterone acetate (DMPA) contraceptive. We investigated 50 women using DPMA and 50 age-matched controls, not on DPMA. Serum cortisol, progesterone, estrogen, estradiol, cathepsin K, calcium and urinary excretion rate of calcium was determined in subjects and controls. Serum cortisol and cathepsin K was significantly higher in women using DPMA Vs controls ($P< 0.01$), we also found a significantly lower estradiol, serum calcium and an increased urinary excretion rate of calcium in subjects using DPMA as compared to controls ($P<0.05$). We found a positive correlation between serum cortisol and serum calcium ($r= 0.553$) ($P< 0.01$), serum cortisol and cathepsin K ($r=0.568$, $P<0.05$). Our study shows that hypercortisolemia may be associated with calcium loss in subjects using DPMA, hence further investigation is required to ascertain if cortisol induced calcium loss is responsible for osteoporosis associated with the use of Depot-Medroxyprogesterone Acetate.

OR45-02

IKKε/TBK1 inhibitor amlexanox induced nephrotic diabetes

insipidus by decreasing AQP2 and VR2 expression in kidney

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Objective Amlexanox is a specific IKKε/TBK1 inhibitor which was reported as drugs to obesity-related metabolic dysfunctions in mice. However, the side effect of amlexanox remains unknown.
Methods This study was carried by method as followed: animal metabolic cage, western blot, quantitative PCR, hematoxylin-eosin (HE) stain and immunohistochemistry.
Results By animal metabolic cage, it was found that amlexanox could induce reversible polyurine (4-5 times than control) and polydipsia in short term (one week) and long term(three months) in mice with normal or with high-fat diet. Urine output was characterized with tripled-quadrupled hypobaric urine output daily, low ions concentration (sodium, calcium, potassium, chlorine, magnesium) in amlexanox group. However, serum ion concentration and renal function (serum creatinine, urea nitrogen) had not been changed in amlexanox group. secretion of urine creatinine and nitrogen also had not been changed in amlexanox group. Injection subcutaneously with desmopressin acetate (dDAVP) could not alter urine output and urine osmotic pressure in amlexanox group. Water deprivation test for 24 hours could not reverse the polyurine and urine hyposmolality in amlexanox group. Amlexanox inhibited IKKε expression in medulla of kidney but not cortex of kidney. Also, Amlexanox decreased aquaporin 2(AQP2) and vasopressin receptor 2 (VR2) mRNA expression in kidney, suggesting its inducible nephrotic diabetes insipidus. Meanwhile, amlexanox increased five times mRNA expression of IKKε and vasopressin (VP) in pituitary. HE stain and immunohistochemistry supported the diabetes insipidus and showed downregulation of IKKε in kidney by amlexanox.
Conclusion This study firstly reported that amlexanox could induce nephrotic diabetes insipidus by decreasing AQP2 and VR2 expression in kidney.

OR45-03

Monthly pasireotide LAR reduces urinary free cortisol (UFC) and provides clinical benefit in patients with Cushing's disease: a 12-month, randomized, multicenter, Phase III study

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Objective Cushing's disease (CD) is a rare, deleteriouscondition of hypercortisolism secondary to an adrenocorticotropic hormone (ACTH)-secretingpituitary adenoma. Owing to the rarity of the disorder, fewlarge prospective studies of medical therapies have been conducted in patientswith CD. Twice-daily,subcutaneous pasireotide (Signifor) a pituitary directed agent that acts to inhibit ACTH secretion is approved inmany countries for the treatment of CD. Here, we present results of the first, randomized,multicenter, Phase III study designed to evaluate the efficacy and safety of aonce-monthly, long-acting release (LAR) formulation of pasireotide LAR inpatients with CD.
Methods Patientswith persistent/recurrent (n=123) or de novo(if not surgical candidates) [n=27] CD and a mean UFC (mUFC) level ≥1.5–5xULN wererandomized (double blind) to monthly pasireotide LAR 10 mg (n=74) or 30 mg (n=76).Randomization was stratified by screening mUFC level (stratum 1: ≥1.5–<2.0xULN;stratum 2: ≥2.0–5.0xULN). Pasireotide LAR dose could be up-titrated(10to 30 mg/30 to 40 mg)at month 4 if mUFC>1.5xULNand/or at months 7, 9, 12 if mUFC>1.0xULN.The primary endpoint was the proportion of patients with mUFC≤ULN after sevenmonths of treatment (month 7), regardless of dose titration. Secondary endpointsincluded: change from baseline in mUFC, plasma ACTH, clinical signs andhealth-related quality of life (HRQoL; measured by CushingQoL questionnaire) overtime; and safety.
Results Primaryefficacy response rates at month 7 were 41.9% (95% CI: 30.5–53.9%) and 40.8% (95%CI: 29.7–52.7%) in the 10 mg and 30 mg arms, respectively. The percentage ofpatients with mUFC≤ULN at month 7 was 52.0% in both the 10 and 30 mg arms instratum 1 (screening mUFC: ≥1.5–<2.0xULN); and 36.7% and 35.3% in stratum 2(screening mUFC: ≥2.0–5.0xULN). Response rates at month12 were 35.1%(95% CI: 24.4–47.1%)and 23.7% (95% CI: 14.7–34.8%)in the 10 mg and 30 mg arms, respectively. Forty-eight (64.9%) and 51 (67.1%)patients in the 10 mg and 30 mg groups,respectively, had ≥1 dose up-titration during the 12-month study; 31(41.9%) and 28 (36.8%), respectively, were dose up-titrated at month 4. Median decreases in mUFC from baseline to month 7 (10mg arm, 47.9% [n=57]; 30 mg arm, 48.1% [n=57]) were maintained through to month12 (10 mg arm, 52.5% [n=50]; 30 mg arm, 50.3% [n=54]). Median plasma ACTHdecreased from baseline to month 12 by 10.2% (n=44) and 14.5% (n=52) in the 10mg and 30 mg arms, respectively.Reductions inmedian mUFC and ACTH levels were accompanied by sustained improvementsin clinical signs and HRQoL. Mean changes from baseline to month 12 in the 10 mgand 30 mg arms were: systolic BP, 4.6 mmHg (n=49) and 5.0 mmHg (n=53); diastolic BP,3.4 mmHg(n=49) and 3.1 mmHg (n=53); weight, 3.4 kg (n=49) and 6.5 kg (n=54); BMI, 1.3 kg/m2 (n=49)and 2.6 kg/m2 (n=54); and HRQoL score, +6.4 (n=47) and +7.0(n=53). Thesafety profile of pasireotide LAR was similar to that of twice-dailypasireotide. Hyperglycemia-related AEs occurred in 72% and 82% of patients inthe 10 mg and 30 mg arms, respectively, although only eight patients (10 mgarm; 5.4%; 30 mg arm, 5.3%) discontinuedbecause of hyperglycemia-related AEs. Mean HbA1c increasedfrom 5.7% in each arm at baseline to 6.9% (10 mg arm) and 7.0% (30 mg arm) atmonth 12. Four patients (10 mg arm, 2.7%; 30 mg arm, 2.6%) experiencedan injection site-related AE.
Conclusions Pasireotide LARnormalized mUFC in ~40% of patients with CD at month 7. Patients with lower mUFClevels at screening were more likely to achieve mUFC≤ULN at month 7. Pasireotide LARprovided sustained improvements in mUFC, clinical signs and HRQoL over 12months, and had a safety profile similar to that of twice-daily pasireotide. These findings show that pasireotide LAR can be aneffective treatment for CD while providing a

convenient monthly administrationschedule.

OR45-04

Ectopic corticotropin-releasing hormone (CRH)syndrom from Medullary Thyroid Carcinoma

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Background Cushing's Syndrome (CS) which is caused by isolated Corticotropin-releasing hormone (CRH)production, rather than adrenocorticotropin (ACTH) production, is extremely rare. Medullary Thyroid Carcinoma seldom present ectopic CRH syndrom,only 0.6 percent have Cushing's syndrome by ectopic ACTH secretion.
Methods We describe the clinical presentation, course, laboratory values and pathologic findings of two patients with isolated ectopic CRH causing CS by Medullary Thyroid Carcinoma. We review the literature of MTC associated with ectopic CRH syndrome and the behavior of these tumors by
endocrine testing. Case1 A 50-year old man was admitted to the PUMCH Endocrine Unit in 2014 complaining of red face four yeas and central obesity two years. Four years ago he appeared flushing, ultrasound found thyroid has many hypoechoic and lobulated nodes with neck lymph node metastatic. Then
he was made near total thyroidectomies with bilateral central neck dissections, the pathology diagnosis is Medullary Thyroid Carcinoma and lymph node metastatic. He used external beam radiation 36 times and calcitonin decreased from 500pg/ml to normal. Then he took L-T4 150ug once per day. Two years before he was admitted he present facial swollen and central obesity and hypertension. Morning serum cortisol was extremely elevated. ACTH was elevated to 171 pg/ml. Octretide imaging scan shows pituitary, lung, pulmonary hila lymph nodes and mediastinum all have metastatic mass. Tumor cells were diffusely immunopositive for calcitonin, carcinoembyonic antigen, ACTH and CRH. So we confirmed this is an ectopic CRH syndrome. We suggest he use vandetanib but he refused and left hospital. Case 2 A 47-year old man was admitted to the Endocrine Unit in september 2014 complaining of neck swollen six years, fatigue and leg weakness of one year. Six years ago, he was diagnosised medullary thyroid carcinoma accomplied with lympy nodes metastatic by thyroid puncture. Immunohistochemical staining showed positive of CEA, Calcitonin. But he did not treatment. One year before he was admitted, he appeared hoarseness with central obesity. Clinical examination revealed a moon and red face. Blood cortisol level was elevated and Serum ACTH elevated to 158.0pg/ml in spite of hypercortisolism, Tumor cells showed immunopositivity for calcitonin ,CEA,ACTH and CRH. Octretide scan showed thyroid express highly , bilateral neck and mediastinum lymph nodes express highly. We suggest he use vedatani but he selected operation,then he made a total thyroidocmy with neck lymph node dissection.After the operation his levels of calcitonin decreased to normal.His ACTH was 13.0pg/ml and cortisol was 7.66ug/dl.
Results Both patients' plasma ACTH levels were high.Tumor cells were diffusely immunopositive for calcitonin.Immunohisochemical stain of biopsy tissue show positivity for both ACTH and corticotropin- releasing hormone (CRH) in scattered cells.Diagnosis Ectopic corticotropin- releasing hormone syndrom from Medullary Thyroid Carcinoma is definite.
Conclusion Medullary Thyroid Carcinoma is rare cause of Cushing's syndrome which can secret ACTH and CRH then causing hypercortisol level. Ectopic CRH syndrome is very rarly.MTC represents 2.2-7.5% of cases with ectopic ACTH-secreting tumors and lesser represents ectopic CRH-secreting tumors. Therapy include several methods. Operation is much effective to decrease CT level. For advance patients vandetanib can be effectively.

OR46-01

Somavaratan (VRS-317) Treatment for Pediatric Growth Hormone Deficiency (GHD): Results at 2 Years (NCT02068521)

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Objective Somavaratan, a novel long-acting recombinant human growth hormone (rhGH) fusion protein with t1/2>100h, previously demonstrated clinically meaningful improvements in height velocity (HV) and IGF-I in pre-pubertal children with GHD in a randomized Phase 1b/2a study initiated in 2013 (Moore JCEM 2016). We present the results for the second year of treatment, completed in December 2015.
Methods 48 patients (pts) participated in a single dose PK/PD study to establish pediatric doses, which were then tested in 64 pts for 6 months at weekly, twice-monthly (TM), and monthly dosing schedules (total 5.0 mg/kg per month); 60 pts entered an ongoing extension study. All pts transitioned to the 3.5 mg/kg TM regimen by start of Year 2, based on growth and IGF-I responses from the first 6-12 months of treatment.
Results Of 24 females and 33 males evaluable in Year 2, mean age was 7.8 years. At baseline, HT-SDS was -2.6±0.6, IGF-I SDS -1.5±0.8, and GHmax 5.3±2.6 ng/mL. During Year 2, IGF-I SDS was 0.59±1.4 at peak (3-5 days postinjection) and -0.47±1.1 at trough (at end of dosing cycle). Eight pts had peak IGF-I SDS >2.0; 2 were >3.0 (range, 2.01-3.67). From Years 1 to 2, mean HV was maintained (8.1±2.2 vs. 7.8±2.3 cm/year), and HT-SDS continued to improve (-2.1±0.6 vs. -1.6±0.7). Over the 2 years, mean bone age (BA) advanced by 2.4 years, mean height age by 2.7 years. The difference in years between chronological age and BA was 1.5±0.8 at screening, 1.4±0.9 at Year 1, and 1.0±1.0 at Year 2. Rates of related AEs declined in Year 2 (n=7 pts). Related AEs were generally mild and transient, and no new types were reported.
Conclusions Somavaratan improved IGF-I and HV through 2 years in pre-pubertal children with GHD, with AE rates declining over time. The 3.5 mg/kg TM dose maintained HV levels similar to that of second-year US NCGS data for daily rhGH. This dose is now being evaluated in a Phase 3 trial in treatment-na?ve GHD children (NCT02339090).

OR46-02

Treatment Adherence with Weekly, Twice-Monthly and Monthly Dosing of Somavaratan (VRS-317), a Long-Acting Growth Hormone Treatment for Children with Growth Hormone Deficiency (GHD), After 18 Months of At-Home Dosing

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Objective Noncompliance to daily subcutaneous (SC) recombinant human growth hormone (rhGH) has been reported in up to 77% of GHD patients and is significantly associated with reduced efficacy. Somavaratan, a novel rhGH fusion protein with t1/2 >100h, previously demonstrated clinically meaningful improvements in height velocity and IGF-I in a randomized Phase 2 study in pre-pubertal

children with GHD (NCT01718041). Treatment adherence to at-home dosing of somavaratan was evaluated in this ongoing, long-term extension study (NCT02068521).

Methods 64 subjects were initially randomized to weekly (W), twice-monthly (TM), and monthly (M) dosing groups for a total of 5.0 mg/kg somavaratan per month for 6 months. Sixty subjects enrolled in the extension study. Injections were administered at home by caregivers during the 18-month observation period (data cutoff: December 2015). All subjects transitioned to 3.5 mg/kg TM by start of the 2nd year, based on growth and IGF-I responses observed in the first 6-12 months of treatment. Treatment adherence was recorded by caregivers using an electronic patient-reported outcome diary (eDiary; Bracket, Inc.).

Results Mean baseline age of subjects in the extension study was 8.3±2.4 years. Over 4000 SC injections were administered with at-home dosing. Injection adherence was 99.5% for W, 99.4% for TM, and 99.1% for the M dosing schedules. Overall dosing adherence was 99.7% across regimens, with 2217 of 2224 intended doses administered.

Conclusions Adherence to somavaratan was nearly 100% over 18 months of therapy, suggesting that long-term adherence may be improved in GHD children receiving somavaratan. These findings are important for validating the reduced burden of GH replacement therapy with longer treatment intervals, including the TM schedule used by all subjects during the final 12 months of the observation period. A Phase 3 trial of TM somavaratan using the eDiary to monitor treatment adherence is ongoing (NCT02339090).

OR46-03

HbA1c over Two Years of Treatment with Somavaratan (VRS-317) in Children with Growth Hormone Deficiency (GHD)

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Objective GHD is associated with dysregulated glucose homeostasis due to loss of GH counterregulation of peripheral and hepatic insulin effects on glucose metabolism. While rhGH-treated GHD adults predisposed to diabetes mellitus (DM) are prone to impaired glucose tolerance (IGT) or overt DM, children on rhGH rarely develop either, but may develop modest insulin resistance. Somavaratan is a long-acting rhGH fusion protein (t1/2>100h) that improved height velocity and IGF-I in pre-pubertal GHD children in a Phase 1b/2a study. To characterize whether somavaratan may have distinct metabolic effects, subjects from the study were evaluated for two years on the effects on glucose metabolism using HbA1c.

Methods 64 subjects received somavaratan for 6 months given as weekly, twice-monthly, and monthly regimens (total 5.0 mg/kg per month). Sixty subjects entered an ongoing extension study; all transitioned to the 3.5 mg/kg twice-monthly dose by the start of Year 2. HbA1c was measured at study entry and yearly (months 6, 18, and 30 of somavaratan exposure).

Results Mean HbA1c was 5.2±0.31% at study entry (n=58), 5.3±0.33% at Year 1 (n=54), and 5.3±0.29% at Year 2 (n=28). Individual subjects showed modest changes in HbA1c over 2 years of treatment, but without a clear pattern: 2/58 subjects with elevated HbA1c at study entry showed improvement in HbA1c; 1 subject showed improvement at Year 1 and HbA1c returned to baseline at Year 2; HbA1c increased in 3 subjects to prediabetes range, and 1 showed increased HbA1c at Year 1 followed by normalization at Year 2. No subjects developed overt DM. There was no significant change in Hba1c in the remaining subjects.

Conclusion Overall, HbA1c was stable in pre-pubertal GHD children treated with somavaratan. Individual subjects showed minor changes in HbA1c over time, and no subjects developed DM. More study is required to further characterize the metabolic effects of somavaratan.

OR46-04

Compound mutations in pituitary-related pathways are engaged in pituitary stalk interruption syndrome: A whole exome sequencing study of Han Chinese

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Context (PSIS) is a rare congenital defect manifesting various degrees of anterior pituitary hormone deficiency. Although mutations have been identified in some familial cases, the underpinning mechanisms of sporadic PSIS patients who are in a vast majority remain elusive, necessitating a comprehensive study using systemic approaches.

Objective We postulate that other genetic mechanisms may be responsible for the sporadic PSIS. To test this hypothesis, we conducted a study in 24 PSIS patients of Han Chinese using whole exome sequencing (WES) and Sanger's sequencing.

Design Whole exome sequencing was performed on samples to 24 typical patients with no family history, bioinformatic analysis was carried out to find out relevant pathways within which regulated genes were significantly enriched.

Results We identified a group of heterozygous mutations in 92% (22/24) of the patients, and these genes are associated with Notch, Shh, Wnt signaling pathways. Importantly, 83% (20/24) of the patients had more than one mutation in those pathways suggesting synergy of compound mutations underpins the pathogenesis of sporadic PSIS.

Conclusion Compromised genetic interactions among multiple signaling pathways likely underpin the pathogenesis of sporadic PSIS.

OR47-01

A new therapeutic strategy to enhance radioiodide uptake into breast cancer cells

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The development of new therapeutic strategies for breast cancer is urgently needed. Exploitation of the uptake of high energy radioiodide by the sodium iodide symporter NIS, which is overexpressed in breast cancer, has been widely proposed as a novel therapeutic strategy. However, radioiodide uptake is insufficient for tumour destruction. We previously demonstrated that the proto-oncogene PBF, which is overexpressed in breast cancer, binds NIS and inhibits its plasma membrane retention. We now show that phosphorylation of PBF at Y174, which is key to NIS interaction, can be switched off via treatment with the Src inhibitor Dasatinib in MCF-7 and MDA-MB-231 breast cells. Mutation of a predicted Src consensus sequence (EEN170-172AAA) abrogated pY174 and radioiodide uptake repression, confirming Src-dependent Y174 phosphorylation. In the presence of Dasatinib-resistant Src (T341I), Dasatinib no longer rescued PBF repression of NIS, indicating that Src specifically mediates PBF phosphorylation. We utilised a new high affinity inhibitor of myristoylation, a post-translational mechanism which modulates the enzyme activity of ~1% of human proteins. N-myristoyltransferase inhibitor 3 (NMTi3), which prevents Src reaching the plasma membrane, significantly increased the radioiodide uptake of MDA-MB-231 cells lentivirally expressing NIS. Critically, combined Dasatinib and NMTi3 treatment in-

duced a ~70% increase of radioiodide uptake in the absence of PBF over-expression, and a ~90% increase in its presence in both MCF-7 and MDA-MB-231 cells (**p<0.01; N=3), and significantly increased intracellular radioiodide retention time. Thus, disrupting Src phosphorylation of PBF by (i) targeted mutagenesis, (ii) Src kinase inhibition and (iii) myristoylation inhibition collectively reveal that radioiodide uptake into breast cells can be significantly enhanced through therapeutic approaches focussed on Src:PBF:NIS, making radioiodide treatment of breast cancer a potentially viable new strategy.

OR47-02

The epigenome landscape of prostate cancer stroma reinforces the pro-tumourigenic actions of estrogen receptor α

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Objective The cross-talk between the epithelium and stroma in the prostate is tightly regulated by the actions of steroid hormone receptors, including estrogen receptor α (ERα). These reciprocal interactions are crucial for normal prostate development and homeostasis, but are perturbed in prostate cancer. It is often assumed that the aberrant signals from cancer cells only induce transient changes in the adjacent tumour stroma, but there is increasing evidence that the alterations are more enduring. Yet, how these changes are encoded at the molecular level is unknown.

We hypothesised that tumour stroma acquires epigenetic modifications that fundamentally alter the balance of steroid hormone action and confer tumourigenicity. Therefore, the objective of this study was to establish the first complete DNA methylation profile of tumour stroma and determine the functional consequences of epigenome changes.

Methods Primary cultures of non-malignant prostate fibroblasts (NPFs) and cancer-associated fibroblasts (CAFs) were established from matched benign and malignant tissue from 17 men with localised prostate cancer. In vivo tissue recombination assays were used to verify that CAFs induced BPH-1 prostate epithelial cells to form tumours, but NPFs did not. We used whole genome bisulphite sequencing (WGBS) to compile the first complete epigenome map of CAFs and NPFs covering 95% of all CpG sites. SNP arrays were used to assess genomic aberrations, while RNAseq and Affymetrix arrays were used to compare mRNA abundance. To investigate the downstream functional effects of ERα signalling, in vitro migration assays were performed with CAFs, NPFs and the HMC-1 mast cell line.

Results Our data revealed that NPFs and CAFs have remarkably different epigenome profiles characterised by locus-specific rather than global changes in DNA methylation. CAFs exhibited more than 7500 differentially methylated regions compared to NPFs. In contrast, no recurrent genomic aberrations were detected in CAFs, emphasising the importance of epigenome changes in reinforcing their pro-tumorigenic phenotype. Many differentially methylated regions occurred at known regulatory loci and were associated with differentially expressed genes measured using RNAseq. The methylation and gene expression changes were highly consistent across patients when validated using an independent cohort of patient-matched NPFs and CAFs. The ESR1 gene, encoding ERα, was a prominent example of a differentially methylated and differentially expressed gene. The promoter of ESR1 was hypomethylated in CAFs and this was associated with increased expression in CAFs compared to NPFs. Accordingly, immunohistochemistry with patient tissue specimens showed that there was a significant increase in the ratio of ERa staining within tumour stroma. Furthermore, the increased expression of ERα in CAFs was correlated with the enrichment of an estrogen-regulated gene signature. The most highly over-expressed gene downstream of ERα in this signature was the potent chemokine CXCL12. Functional assays showed that CXCL12 secreted by CAFs recruited CXCR4+ mast cells in migration assays. The mast cells in turn secreted pro-tumourigenic cytokines in response to estrogen, forming a pro-tumourigenic loop in the tumour microenvironment.

Conclusion Changes in DNA methylation are highly consistent between patients and are an underlying mechanism for the functional differences between NPFs and CAFs. Epigenetically-regulated genes, such as ESR1, also have functional roles in the progression of prostate cancer. Collectively, these data demonstrate the tumour microenvironment exhibits enduring epigenome differences in key genes that may be targetable across multiple patients.

OR47-03

The dual inhibition of RNA Pol I transcription and PIM kinase as a new therapeutic approach to treat advanced prostate cancer

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Objective The MYC oncogene is frequently over-expressed in prostate cancer (PC). Upregulation of ribosome biogenesis and function is characteristic of MYC-driven tumors. Additionally, PIM kinases activate MYC signaling and mRNA translation in PC and cooperate with MYC to accelerate tumorigenesis. Here, we investigate the efficacy of a single and dual approach targeting ribosome biogenesis and function to treat PC.

Methods The inhibition of ribosomal RNA (rRNA) synthesis with CX-5461, a potent, selective and orally bioavailable inhibitor of RNA polymerase I (Pol I) transcription has been successfully exploited therapeutically, but only in models of hematological malignancy. CX-5461 and CX-6258, a pan-PIM kinase inhibitor, were tested alone and in combination in PC cell lines, in Hi-MYC and PTEN-deficient mouse models and in patient derived xenografts (PDX) of metastatic tissue obtained from a castration-resistant PC patient.

Results CX-5461 inhibited anchorage-independent growth and induced cell cycle arrest in PC cell lines at nanomolar concentrations. Oral administration of 50 mg/kg CX-5461 induced p53 expression and activity and reduced proliferation (Ki-67) and invasion (loss of ductal actin) in Hi-MYC tumors, but not in PTEN null (low MYC) tumors. While 100 mg/kg CX-6258 showed limited effect alone, its combination with CX-5461 further suppressed proliferation and dramatically reduced large invasive lesions in both models. This rational combination strategy significantly inhibited proliferation andinduced cell death in PDX of PC.

Conclusion Our results demonstrate preclinical efficacy of targeting the ribosome at multiple levels and provide a new approach for the treatment of PC.

OR47-04

Transcriptome profiling of single prostate cancer cells in the castrate setting

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Objective The standard of care for men with metastatic prostate cancer is medical or surgical castration. Virtually all patients respond but resistance is inevitable, leading to a lethal form of the disease referred to as castration-resistant prostate cancer (CRPC). Using patient-derived xenografts (PDX) of localised castrate-sensitive tumours, we have identified a rare sub-population of 'castration-tolerant' prostate cancer cells that survive following castration. Importantly, these castration-tolerant cells actively repopulate tumours upon testosterone re-administration, raising the prospect that progression to CRPC may be delayed or even prevented by targeting these cells. The aim of this study was to molecularly characterise castrate-tolerant prostate cancer cells and identify novel targeting strategies to eliminate them. Our approach combined PDX technology and genomics to address the long-standing question of why castration fails to eradicate a rare subset of prostate cancer cells.
Methods To study the genomic features of castrate-tolerant cells, we enriched for prostate cancer cells from PDXs and subjected them to single cell isolation and RNA seq. In the absence of a definitive cell–surface antigen for prostate cancer, we have developed a panel of 16 fluorescent surface-markers to segregate and significantly enrich for luminal prostate cancer using FACS, facilitating the purification and enrichment of rare tumor cells from PDX grafts. Our target population was processed using the Fluidigm C1 platform to capture and sequence single luminal cells. We efficiently captured and sequenced > 50 cells from pre- (intact luminal) and post-castration (castrate luminal) prostate cancer PDXs. Sequencing of isolated single cells and pooled populations was performed using the Illumina HiSeq in rapid mode with 50 bp fragment sequencing chemistry (3Million reads/cell).
Results Multidimensional scaling analysis showed that pooled populations of intact and castrate-tolerant cells clustered separately from each other, and from either of the single cell populations. Our data indicated that the response to castration is not uniform in all cells, and there is different degrees of heterogeneity within intact and castrate groups. Within the single cell groups, intact luminal and castrate-tolerant luminal cells clustered independently and a unique gene set was identified. We identified distinct changes in energy metabolism, including suppression of ATP production, that aid cell survival. We also identified alterations in steroid metabolism and nuclear receptorsignallingleading to activation of pathways identified after clinical specimens following ADT (Rajan et al., European Urology, 2014, PMID: 24054872) and in CRPC (Taylor et al., Cancer Cell, 2010, PMID: 20579941).
Conclusion This is the first study to report of gene expression in single human prostate cells and revealed a novel gene profile prior to and following androgen deprivation. We identified altered key adaptive responses to androgen withdrawal, and our data suggest that further and/oralternativehormone suppression may be effective in targeting castration-tolerant prostate cancer cells. We propose that these cells underpin the clinical progression to CRPC, and thus the approaches used to identify new therapeutic strategies could inform the design of potentiallyground breakingpre-clinical trials to improve the management of prostate cancer.

OR48-01

Oral hypoglycemic drugs in the intervention of aging, report from drosophila melanogaster

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Aim Aging is an irreversible process that accompanies many progressively metabolic disorders such as insulin resistance, hyperlipidemia, and obesity. Recently, metformin, a biguanide drug which is commonly used to treat type-2 diabetes, has been shown to extend lifespan in C. elegans, mice, rats, and even humans in some clinical reports, which arose quite a lot attention in exploring the new applications in traditional oral hypoglycemic drugs.
Methods Here we use drosophila melanogaster, a classical model in aging studies, to testify whether clinically widely used hypoglycemic agents have the pro-lifespan effects. Firstly, we profiled the levels of series genes related to glucose metabolisms in different ages of flies (1w/3w/6w), which mimicked the natural aging process of flies. Then we did systematic pharmacological studies evaluating the anti-aging properties of clinical hypoglycemic drugs that may target those pathways. Age-matched Drosophila flies were fed with six common anti-diabetic drugs in two different doses separately (metformin: 1/10 g/L; glimepiride 1/10 mg/L; sitagliptin 10/100mg/L; acarbose 0.1/1 g/L; repaglinide 1/10 mg/L; pioglitazone 10/100mg/L). After 3 weeks' feeding, flies were challenged with medium containing oxidative-stress (5% H2O2), a common test that always reflected the whole lifespan of flies.
Results We found that as with aging, genes related to insulin pathway such as *dilp2, dilp3, dilp5, tor, thor, s6k, InR* and genes regulated glucose such as *Akh* decreased a lot ($t<0.05$), which was a strong evidence of glucose disorders in the aged flies. The oxidative-stress experiments showed that only pioglitazone (10/100mg/L) and sitagliptin(10 mg/L) had extended lifespan when compared to flies feed with blank food medium without drugs($t<0.05$).
Conclusions In summary, fly models bear intriguing similarities to the pathophysiology of aging of humans especially in glucose metabolism, and clinically hypoglycemic drugs can provide new insights into intervention of aging.

OR48-02

Oral hypoglycemic drugs in the intervention of drosophila melanogasters' aging

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Aim Aging is an irreversible process that accompanies many progressively metabolic disorders such as insulin resistance, hyperlipidemia, and obesity. Recently, metformin, a biguanide drug which is commonly used to treat type-2 diabetes, has been shown to extend lifespan in C. elegans, mice, rats, and even humans in some clinical reports, which arose quite a lot attention in exploring the new applications in traditional oral hypoglycemic drugs.
Methods Here we use drosophila melanogaster, a classical model in aging studies, to testify whether clinically widely used hypoglycemic agents have the pro-lifespan effects. Firstly, we profiled the levels of series genes related to glucose metabolisms in different ages of flies (1w/3w/6w), which mimicked the natural aging process of flies. We extracted both the RNA of flies' body and head, and got the cDNA accordingly. Real-time PCR was performed subsequently and genes' quantification was done using the internal control gene RP49. Then we did systematic pharmacological studies evaluating the anti-aging properties of clinical hypoglycemic drugs that may target those pathways. Age-matched Drosophila flies were fed with six common anti-diabetic drugs in two different doses separately (metformin: 1/10 g/L; glimepiride 1/10 mg/L; si-

tagliptin 10/100mg/L; acarbose 0.1/1 g/L; repaglinide 1/10 mg/L; pioglitazone 10/100mg/L), which we referred to high and low does. Male and female flies were selected at the day 3 after they were born. Each vial contained 30 flies separately. After 3 weeks' feeding, flies were challenged with medium containing oxidative-stress (5% H2O2), a common test that always reflected the whole lifespan of flies. The number of dead flies were recorded every 12 hours.

Results We found that as with aging, genes related to insulin pathway such as dilp2, dilp3, dilp5, tor, thor, s6k, InR and genes regulated glucose such as Akh decreased a lot ($t<0.05$), which was a strong evidence of glucose disorders in the aged flies. The oxidative-stress experiments showed that pioglitazone (10/100mg/L) and sitagliptin(10 mg/L) had extended both female and male flies' lifespan, when compared to flies feed with blank food medium without drugs($t<0.05$). 1 g/L metformin and 1 mg/L repaglinide extended only the male flies' lifespan ($t<0.01$), while there were no obvious changes in female flies or other does or kinds drugs.

Conclusions: In summary, fly models bear intriguing similarities to the pathophysiology of aging of humans especially in glucose metabolism, and clinically hypoglycemic drugs can provide new insights into intervention of aging.

OR48-03

Xanamem: a novel 11beta-HSD1 inhibitor with potential to provide durable symptomatic and disease modifying benefits in Alzheimer's disease

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Objective Hypothalamic-pituitary-adrenal (HPA) axis dysregulation is implicated in Alzheimer's disease (AD) with cortisol mediating and maintaining synaptic compromise. 11beta-HSD1 regenerates cortisol and amplifies glucocorticoid signalling in key brain regions, notably hippocampus. In aged mice, 11beta-HSD1 inhibition protects against cognitive dysfunction and in Tg2576 mice reduces amyloid plaque deposition. 11beta-HSD1 is thus a therapeutic target for the treatment of patients with AD. We sought to design potent, brain penetrant 11beta-HSD1 inhibitors as potential medicines for the treatment of AD. Here, we report the discovery of Xanamem, a selective 11beta-HSD1 inhibitor, and its effects in humans.

Methods Medicinal chemistry and extensive in vitro and in vivo profiling of compounds was carried out to identify a candidate molecule. Xanamem was selected and Phase 1 SAD, MAD and single-dose fed-fasted studies were performed to determine the safety, pharmacokinetics and pharmacodynamic effects of Xanamem administration. Pharmacodynamics were monitored by measurement of adrenal steroids in serum, ACTH in plasma and steroid metabolite ratios in urine. A separate study in four healthy volunteers was also conducted to determine concentrations of Xanamem in CSF.

Results During preclinical optimization a series of 3,3-disubstituted-(8-aza-bicyclo[3.2.1]oct-8-yl)-[5-(1H-pyrazol-4-yl)-thiophen-3-yl]-methanones were identified as potent and selective 11beta-HSD1 inhibitors. Brain penetration and optimized pharmacokinetic parameters were used as key drivers for lead selection and Xanamem was identified as a candidate molecule for clinical development. In Phase 1 studies in humans, Xanamem was well tolerated with no major safety issues noted at any dose. Following multiple doses of Xanamem, plasma levels were approximately dose proportional and the terminal half-life ranged from 10-14 h. ACTH but not plasma cortisol was activated at doses of 10mg and above indicating substantial inhibition of extra-adrenal regeneration of cortisol by 11beta-HSD1. Following multiple doses of Xanamem, the adrenal steroids 4-androstenedioneand DHEA-sulphate were elevated, but increases were independent of dose and in line with increases in ACTH. No dose- dependent changes were observed for testosterone. The urinary steroid metabolite ratio (THFs/THE) was reduced maximally at doses of 10mg and above, indicating substantial inhibition of enzyme in the liver. Concentrations of Xanamem in the CSF were 8 to 12 % of total plasma levels, confirming that Xanamem reaches the brain. The levels of Xanamem in the CSF at Cmax were substantiallyhigher than the cellular IC50 for Xanamem. The results provide the basis for a 12-week double-blind, placebo-controlled RCT Phase 2 XanADu study (n=200) that has commenced to assess the efficacy of using XanamemTM in mild Alzheimer's with ADCOMS and ADAS-Cogv14 as co-primary outcomes.

Conclusion Xanamem is a potent 11beta-HSD1 inhibitor being developed for the symptomatic treatment of mild AD. Phase 1 studies demonstrate Xanamem is safe and well tolerated, gives high pharmacodynamic inhibition and is brain penetrant. A Phase 2 study has commenced.

OR48-04

Is exposure to famine in different life stages associated with phenotype of obesity: Results from REACTION study

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Objective We aim to illustrate that (1) whether metabolically healthy but obese" (MHO) actually exists (2) is exposure to famine is associated with an increased risk of overweight or obese in later life (3) association between phenotype of obesity and different life stages when exposed to famine.

Methods Our data of 20179 adults were from a cross-sectional REACTION study in 2011. Among them, 16383 participants were included in the famine exposure analysis. In 2014,5850 adults underwent a 3-year follow up study.

Results Firstly, a substantial fraction of individuals who are metabolically healthy but overweight or obese at baseline are no longer metabolically healthy at 3-year follow-up. Compared with metabolically healthy normal weight, metabolically healthy but overweight or obese are at higher risk of metabolically abnormal overweight or obese (OR 10.3, 95%CI 8.4~12.7), the association remains significant after adjusting for potential confounders. Secondly, exposure to famine during the fetal period and puberty period were associated with a higher risk of metabolically abnormal overweight or obese (OR 1.5, 95%CI 1.2~1.8), (OR 3.4, 95%CI 2.8~4.1) respectively. Thirdly, living in areas with high economic status in adulthood is further associated with an increased risk of metabolically abnormaloverweight or obese. Finally, men are protected from becoming metabolically abnormal.

Conclusion In conclusion, the results of this study suggest that although metabolically healthy but overweight or obese individuals may present benign conditions in short run, they are prone to become metabolically abnormal, thereby predisposing to obesity related complications. Without proper control and effective measures, this obesity phenotype may develop detrimental outcomes. Therefore, it is imperative to draw more attention and take proper measures to monitor and control this obesity phenotype. Meanwhile, exposure to famine during the fetal period and puberty period may increase risk of metabolically abnormal overweight or obese. Thus, it is important to improve fetal nutrition and control BMI in adulthood, thereby preventing metabolic derangements and obesity.

Poster

September 1, 2016

Setup Time: September 1, 2016 09:00-10:00
Poster Discussion Time: September 1, 2016 13:00-14:00
Poster Removal Time: September 1, 2016 17:00-17:30

PT01-01-01

Association of Occupational & Prediabetes Status with Obesity in middle aged Women

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Bharati vidyapeeth Medical college pune

PT01-01-02

The value of urine red blood cell morphology in the development of diabetic nephropathy

Linan Liu*, Hong Zhang, Minghua Zhang, Suli Wang, Chen Cheng

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PT01-01-03

25- Hydroxyvitamin D status and it's relation to some cardiovascular risk factors in Egyptian female patients with type 2 diabetes

Zeinab Hassan, Dina Abaza Abaza, Mohamed Saed, Inass Hassan*

Al Azhar faculty of Medicine

PT01-01-04

The benefits of a low-carbohydrate diet for patients with impaired glucose tolerance at breakfast

Qian Xu, Minxiu Yao

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PT01-01-05

Gut microbiota via short-chain fatty acids promote antimicrobial peptide CRAMP expression and protect against autoimmune diabetes

Jia Sun, Julien Diana

Jiangnan University

PT01-01-06

Lipoprotein associated phospholipase A2: A surrogate marker of coronary artery disease in diabetic patients

Saswati Das

Maulana azad medical college

PT01-01-07

Low Testosterone Predicts Premature Death and All Site Cancer in Chinese Men with Type 2 Diabetes

Kitty Cheung, Eric Lau, Wing Yee So, Ronald Ma, Risa Ozaki, Alice Kong, Francis Chow, Juliana Chan, Andrea Luk

Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Prince of Wales Hospital

PT01-01-08

Clinical Characteristics and Outcomes of the Oldest Old people with Type 2 Diabetes – Thailand's perspective

Yotsapon Thewjitcharoen, Sirinate Krittiyawong, Ekgaluck Wanothayaroj, Somboon Vongterapak, Tawee Anuntakulnatee, Worawit Kittipooom, Soontaree Nakasatien, Thep Himathongkam

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PT01-01-09

Factor Analysis of the length of stay for diabetes by the first page of medical records

Dongjin Huang, Xie Lingzhu, Zheng Yangcun, Qiu Yang

Guangdong Shantou Central Hospital

PT01-01-10

Beliefs and practices of diabetic patients in Vhembe district of Limpopo province

Hilda Shilubane*, Lizzy Netshikweta, T Ralineba

University of Venda

PT01-01-11

Erythropoietin treatment reverses the cognitive defects and hippocampus histological changes induced by diabetes mellitus in mice

Amer Al Ansari[1], Ebrahim Rajab[2], Manal Othman[1], Muhammad AlNaisar[1], Ahmmed Almubarak[1]

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2. RCSI / Medical University of Bahrain

PT01-01-12

The Prevalence Of Dyslipidemia Among Cambodian With Diabetes Mellitus Type 2 (135 Cases at Preah Ket Mealea Hospital from January-December 2015)

Pagnavuth CHHANG

Preah Ket Mealea Hospital

PT01-01-13

Most of the Bangladeshi adult patients with type 2 diabetes fails to achieve or maintain target glycemic control.

Shahjada Selim[*], F Pathan, ZA Latif, M Saifuddin, N Karim, H Lona

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PT01-01-14

Gastroenteropathy and its Covariates in Type 2 Diabetes Mellitus

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PT01-01-15

Evaluation of a chinese diabetes education seminar

Shannon Lin

Diabetes NSW

PT01-01-16

Glucose intolerance present in over half the patients with Tuberculosis in North India

Abraham Alex Kodiatte, Jubbin Jagan Jacob[*], Mary John

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PT01-01-17

The Relationship Between Neutrophil-to-Lymphocyte Ratio and Diabetic Peripheral Neuropathy in Type 2 Diabetes Mellitus

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PT01-01-18

Anti Diabetic Effects of Cinnamon Extract in Albino Rats with Effects on the Serum Insulin Levels

Baljinder Singh[1*], Rupali Gupta[2]

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2. Sukh Amrit Foundation

PT01-01-19

Geniposide acutely stimulates insulin secretion in pancreatic β-cells by regulating GLP-1 receptor/cAMP signaling and ion channels

Yaqin Ding[1], Xiangqin Zhong[1], Jingying Gao[1], Tao Bai[1,2], Hui Wang[1], Lele Ren[1], Yangyan Guo[1], Yunfeng Liu[1,2], Jing Yang[1,2], Yi Zhang[1]

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PT01-01-20

Nitrate-nitrite-nitrosamines exposure and the risk of type 1 diabetes: A systematic review of current data

Zahra Bahadoran[1], Parvin Mirmiran[1*], Asghar Ghasemi[2], Fereidoun Azizi[3], Farzad Hadaegh[4]

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PT01-01-21

A study of the influence of diabetic neuropathy on plantar pressure

xiaofen Lian, fan Zhang, yali Dai, lingchuan Han, donghui Lu, yuan Lin, qian Xie, ningbo Zhang, peixian Wu

Peking University Shenzhen Hospital

PT01-01-22

IGFBP2 Ameliorates Vascular Insulin Resistance and Contributes to Vasodilation More than Vasoconstriction

Zhuo Li, Chenglin Sun, Fei Li, You Lv, Weiying Guo, Xiaokun Gang, Guixia Wang

Endocrinology and Metabolism Department, The First Hospital of Jilin University

PT01-01-23

Efficacy of Vitamin D2 on Diabetic Peripheral Neuropathy :A Multicenter Random Double Blind Trial

Xiaoxia Shi[1], Dexue Liu[1], Yueyue Zheng[1], Wei Guo[1], Na Xu[2], Ruige Li[3]

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PT01-01-24

Comparison of insulin resistance and beta cell dysfunction between the young and the elderly in normal glucose tolerance and pre-diabetes population: Results from REACTION study

Gang Chen[1], Lidan Shi[1], Wei Lin[1], Jumping Wen[1], Guang Ning[2]

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PT01-01-25

Is beta-cell aging involve in the pathogenesis of diabetes?

Gang Chen, Junping Wen, Ting Xue

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PT01-01-26

Clinical features of elderly patients with type 2 diabetes mellitus in Japan

Satsuki Kawasaki[1*], Hiroe Shibata[1], Haruo Misawa[1], Yasushi Tamura[1], Tetsumasa Kamei[1], Shozo Kito[1], Yasuo Terauchi[2]

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PT01-01-27

Microbial flora in diabetic foot ulcer

Kulbarshin Akyshbayeva*, Aizhan Musaeva, Asel Anuarbek, Rinat Karazhanov, Yultuz Kasimova

Asfendiyarov named Kazakh National Medical University

PT01-01-28

Risk factors for diabetic foot ulcer development in patient from Almaty City Hospital №4

Riza Esergeneva*, Aizhan Musaeva, Asel Anuarbek, Yultuz Kasimova, Rinat Karazhanov

Asfendiyarov named Kazakh National Medical University

PT01-01-29

Insulin resistance is an independent risk factor for silent lacunar infarction

JIN HO PARK

Seoul National University Hospital

PT01-01-30

APPL1 affects on glucose uptake induced by mechanical stretch in C2C12 myotubes

Tsugumichi Saito, Ryo Shibusawa, Yoko Shimoda, Yuko Tagaya, Aya Osaki, Eijiro Yamada, Shuichi Okada, Masanobu Yamada*

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PT01-01-31

Polymorphism of the Renalase gene in Pregnancy Induced Diabetes

Sadia Fatima, Hajira Zafar, Saroosh Madhani, Noman Rehmani, Muhammad Saad Ahmad, Amna Rabbani, Tayyab Shabbir

Aga Khan University

PT01-01-32

Rationale and design of BEYOND VII (glargine starting dose): A Phase IV randomized trial comparing initiation of basal insulin at doses of 0.3 U/kg and 0.2 U/kg in overweight and obese Chinese people with type 2 diabetes mellitus

Linong Ji

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PT01-01-33

increased serumγ-glutamyl transpeptidase are associated with higher risk of Impaired glucose regulation and diabetes mellitus

Nan Zhao, Yanhe Cai, Hongtao Yin, Donghu Zhen, fang Yang, Xulei Tang

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PT01-01-34

Sorbitol inhibits intestinal glucose absorption, increases muscle glucose uptake and decreases blood glucose in normal and type 2 diabetic rats

Md. Shahidul Islam*, Chika Ifeanyi Chukwuma

University of KwaZulu-Natal

PT01-01-35

Brain metabolite changes on magnetic resonances spectroscopy in children with poorly controlled type 1 diabetes mellitus.

Akinci Akinci*, Saraç Kaya, Sığırcı Ahmet, Dündar Ismail

Inonu University

PT01-01-36

Clinical Characteristics and Renal Structure in Diabetic Patients with Normoalbuminuria

Fangqiu Zheng, Feifei Zhang, hongling Han, Mingcai Qiu

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PT01-01-37

The survey of the foot and eye care status in type II diabetic patients based ofthe theory of Planned Behavior

Seyyd mansour Kashfi*, ali khani jeihooni, niloufar eskandarzadeh

shiraz university of medical sciences

PT01-01-38

Frequency, Precipitating Factor and Outcome Of Diabetic Ketoacidosis In Type 1 Diabetes At Tertiary Care Hospital

Muhammad Imran Hasan Khan, Junaid Mushtaq Cheema*

Ameer ud din Medical College/postgraduate medical Institute, Lahore

PT01-01-39

One-year cohort study about changes in fasting blood sugar and incidence of diabetes mellitus after liver transplantation

Seyed Jalil Massoumi[1,2,3], Zohreh Mazloom[1,2], Abbas Rezaianzadeh[4], Saman Nikeghbalian[5,6], Seyed Ali Malek-Hosseini[5,6], Heshmatollah Salahi[5,6]

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6. Transplant Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

PT01-01-40

The effect of soy nut on serum total antioxidant, endothelial function and cardiovascular risk factors in patients with type 2 diabetes

Hajieh Shahbazian[1,1], Alireza Sedaghat[1,1], Afshin Rezazadeh[1,1], Fatemeh Haidari[2,2], Seyed Mahmoud Latifi[1,1], Armaghan Moravej Aleali[1,1]

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PT01-01-41

Real world evaluation of Glycemic control and Weight loss among Obese Chinese Type 2 Diabetes (T2DM) subjects treated with GLP-1 Agonists (GLP-1 RAs)

Elaine Yun Ning Cheung, Grace Kam, CS Hung, Flora Ho, Ivy Ng, Man Wo Tsang

United Christian Hospital

PT01-01-42

Association between Toll-Like Receptor 4 and Occurrence of Type 2 Diabetes Mellitus Susceptible to Pulmonary Tuberculosis in Northeast China

yuze li[1,2], dianzhong li[2], jinfeng zhang[1], shurui liu[1], haijun chen[3], kun wu[1]

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PT01-01-43

Incidence of prediabetes and type 2 diabetes amongst people aged over 20 years in Ahvaz: A 5 Year Perspective Study (2009-2014)

Hajieh Shahbazian[1,1], Majid Karandish[2,2], Seyed Mahmoud Latifi[1,1]

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PT01-01-44

Differential Efficacy of Methylcobalamin and Alpha-lipoic Acid Treatment on Negative and Positive Symptoms of (Type 2) Diabetic Peripheral Neuropathy

Yajuan Han, Min Wang, Jie Shen, Zhen Zhang, Min Zhao, Jing Huang, Youming Chen, Zhi Chen, Yulan Hu, Yubing Wang

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PT01-01-45

Insulin degludec/insulin aspart (IDegAsp) suppresses insulin index, hypoglycemia, and PAID score in type 2 diabetes mellitus: A small prospective study.

Shinichiro Koga, Satono Morita, Yuko RN, Erika Murayama, Kazunaga RN

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PT01-01-46

Islet Transplantation for Prevention of Hypoglycaemic Unawareness in Overweight Type 1 Diabetes

Cheuk Wah Ho[1*], Melena Bellin[2], James Harmon Jr[2], Bernhard Hering[2]

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PT01-01-47

The PLC/PKC/Ras/MEK/Kv channel pathway is involved in uncarboxylated osteocalcin-regulated insulin secretion in rats

Jingying Gao[1,2,3], Tao Bai[1,2,4], Lele Ren[1], Yaqin Ding[1], Xiangqin Zhong[1], Hui Wang[1], Yangyan Guo[1], Yunfeng Liu[4], Jing Yang[4], Yi Zhang[1,2]

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PT01-01-48

The changes in miR-130b levels in human serum and the correlation with the severity of diabetic nephropathy

Chuan Lv, Yue-hong Zhou, Qiu-yue Wang

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PT01-01-49

Decreased Cardiometabolic Risk after Roux-en-Y Gastric Bypass Surgery in Chinese Diabetic Patients with Mild Obesity: a 18-month follow up

Xue Zhao[1], Wenyan Duan[2], Xiaokun Gang[1], Chenglin Sun[1], Zhuo Li[1], Yujia Liu[1], Xianchao Xiao[1], Gang Wang[1], Guixia Wang[1]

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PT01-01-50

The Impact of Gestational Diabetes Mellitus on Neonatal Lipid Metabolism and Growth

Qian Ren, Yuhang Ma, Su Chen, Yufan Wang

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PT01-01-51

IGF-II Restores Rapamycin-induced Suppression of β -cell Differentiation and Expansion of Adult Pancreas Stem Cells

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PT01-01-52

Application of Telemedicine in the Management of Type 2 Diabetes Mellitus

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PT01-01-53

Identification and characterization of adult-onset autoimmune diabetes using a new 3 Screen ICA(TM) ELISA

Zhida Wang[1], Liang Guo[2], Jun Guan[3], Shu Chen[2], Jadwiga Furmaniak[2], Bernard Rees Smith[2], Liming Chen[1*]

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PT01-01-54

Association between sleep pattern and glycemic control in patients with type 2 diabetes

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PT01-01-55

3 Screen: a sensitive and specific ELISA for the combined measurement of autoantibodies to GAD65, to IA-2 and to ZnT8

Michael Powell[1*], Marie Amoroso[1], Rebecca Coles[1], Lorraine Carr[1], Monika Chlebowska[1], Jadwiga Furmaniak[1], Marlon Scholz[2], Peter Achenbach[2], Anette-Gabriele Ziegler[2], Ezio Bonifacio[3], Bernard Rees Smith[1]

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PT01-01-56

DEPTOR polymorphisms influence late complications in type 2 diabetes patients

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PT01-01-57

Association analysis and changes of serum levels of CTRP12 in patients with obesity and newly diagnosed type 2 diabetes

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PT01-01-58

Oral sodium nitrite administration improves glucose tolerance, lipid profile, and glucose-stimulated insulin secretion from pancreatic isolated islets in obese type 2 diabetic rats

Asghar Ghasemi[1*], Sevda Gheibi[2], Homeira Zardooz[2], Sajad Jeddi[1], Fatemeh Bakhtiarzadeh[1]

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PT01-01-59

General practitioners' knowledge and clinical practice in management of people with type 2 diabetes in Iran; the impact of continuous medical education programs

Rokhsareh Aghili[1], Mojtaba Malek[1], Hamidreza Baradaran[1], AliAsghar Peyvandi[2], Ameneh Ebrahim Valojerdi[1], Mohammad Ebrahim Khamseh[1*]

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PT01-01-60

Biphasic Insulin Aspart 30 vs. NPH plus Regular Human Insulin in Type 2 Diabetic Patients; A Cost-Effectiveness Study

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PT01-01-61

The Advantages of Insulin therapy Compared to Oral Glucose Lowering Drugs in type 2 diabetes: A Cost-effectiveness Analysis

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PT01-01-62

Disturbed Sleep in type 2 Diabetes Mellitus independent of chronic complications, Pain, and Nocturia

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PT01-01-63

Association of Eating Behaviors and Demographic Profiles of Filipino Adults with Type 2 Diabetes Mellitus seen in a Tertiary Hospital

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PT01-01-64

DPP-4 Inhibitors Treatment for Type 1 Diabetes Mellitus calls for more clinical trials

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PT01-01-65

Successful diagnosis and treatment of a patient with refractory insulin allergy

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PT01-01-66

The impact of the DPP4 inhibitor saxagliptin on the body weight of patients with type 2 diabetes:a clinical observation

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PT01-01-67

Cinnamic Aldehyde promotes the migration of human fibroblasts under Hyperglycaemic condition via NRF2 pathways

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PT01-01-68

Cinnamic Aldehyde promotes the migration of human fibroblasts under Hyperglycaemic condition by activating NRF2 pathways

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PT01-01-69

Assiociation Between Pioglitazone Therapy and Bladder Cancer Risk in Patients with Diabets Mellitus:A Systematic Review and Updated Meta-Analysis

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PT01-01-71

Improved Glycemic Control and Weight Loss with Once Weekly Dulaglutide versus Placebo, Both Added to Titrated Daily Insulin Glargine, in Type 2 Diabetes Patients (AWARD-9)

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PT01-01-72

Alpha-Lipoic acid alleviats diabetic cardiomyopathy in diabetic rats

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PT01-01-73

AD-MSCs alleviate hyperglycemia through promoting hepatic glycolysis in type 2 diabetic rats

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PT01-01-74

Prenatal and postnatal exposure to severer famine and higher diabetes risk in adulthood

Ningjian Wang[1], Jing Cheng[1], Bing Han[1], Qin Li[1], Yi Chen[1], Chunfang Zhu[1], Yingchao Chen[1], Boren Jiang[1], Michael Jensen[2], Yingli Lu[1]

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PT01-01-76

Utility of hypertriglyceridemic-waist phenotype for predicting incident type 2 diabetes: the Isfahan Diabetes Prevention Study

Mohsen Janghorbani

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PT01-01-77

The source of circulating selenoprotein S and its association with type 2 diabetes mellitus and atherosclerosis: a preliminary study

Shanshan Yu[1], Lili Men[1], Jialing Wu[1], Liwei Huang[1], Qian Xing[1], Junjie Yao[1], Yongbo Wang[1], Guirong Song[2], Huishu Guo[1], Guohua Sun[1], Yuhong Zhang[3], Hua Li[2], Jianling Du*[1]

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PT01-01-78

Dietary nitrate and nitrite intakes and the risk of type 2 diabetes: A 6-year follow-up in Tehran Lipid and Glucose Study

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PT01-01-79

The Effects of Glycine on Renal Nrf2 Translocation in Diabetic Rats

Ziwei Wang, Junqing Zhang, Dan Zhao, Jingjing Li, Lei Chen, Hong Zhang, Xiaohui Guo

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PT01-01-80

Protective Effect of Activated PPARβ/δ on Lipotoxic Apoptosis in Type 2 Diabetic Rat Pancreatic β Cells via GPR40

Juan Li, Shishi Xu, Guangju Zhou, Nanwei Tong

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PT01-01-81

Efficacy of bromocriptine-QR in type 2 diabetes: a systematic review and meta-analysis

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PT01-01-82

Effects of intensive glucose lowering in treatment of type 2 diabetes mellitus on cardiovascular outcomes: A meta-analysis of data from 58,160 patients in 13 randomized controlled trials

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PT01-01-83

Acute phase proteins and diabetes microvascular complications

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PT01-01-84

Dry eye and its correlation to diabetes microvascular complications in people with type 2 diabetes mellitus

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PT01-01-85

Dry eye disease in type 2 diabetes mellitus; comparison of the tear osmolarity test with other common diagnostic tests: a diagnostic accuracy study using STARD standard

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PT01-01-86

Liraglutide treatment in a real-life setting: A retrospective review in a specialized diabetes center from Thailand

Areeya Malidaeng, Soontaree Nakasatien, Sirinate Krittiyawong, Ekgaluck Wanothayaroj, Yotsapon Thewjitcharoen, Thep Himathongkam

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PT01-01-87

Long Non-coding RNA ENSMUST00000147869 Protects Mesangial Cells from Proliferation and Fibrosis Induced by Diabetic Nephropathy

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PT01-01-88

A novel long non-coding RNA CYP4B1-PS1-001 regulates proliferation and fibrosis in diabetic nephropathy

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PT01-01-89

The effects of LRP16 inhibition on adiponectin functions and insulin resistance

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PT01-01-90

Exendin-4 upregulates adiponectin level via Sirt1/Foxo-1 signaling pathway in adipocytes

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PT01-01-91

miRNAs in Urine Extracellular Vesicles as Predictors of Early-Stage Diabetic Kidney Disease

Yijie Jia, Meiping Guan, Zongji Zheng, Qian Zhang, Chuan Tang, Wenwei Xu, Zhizhou Xiao, Ling Wang, Yaoming Xue

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PT02-01-01

Subacute thyroiditis: the pattern of TSH changes within the first 6 months after a short-term corticotherapy

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PT02-01-02

Typical Grave's ophthalmopathy in Primary Hypothyroidism

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PT02-01-03

Status of Serum Nitrite/Nitrate in the Patients with Medullary Thyroid Carcinoma

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PT02-01-04

HYPOTHYROIDISM IN CHILDREN- DENTO-MAXILLARY IMPLACATIONS

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PT02-01-05

Thyroid function and metabolic syndrome, the population-based Tehran Thyroid Study

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PT02-01-06

Thyrotoxic hypokalemic periodic paralysis in a Chinese man following injection of methylprednisolone and review of the literature

Xiao Zhu, Jie Shen, Tong Zhang, Chenzhong Li, Heng Wan

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PT02-01-07

Anti-GAD antibodies may not predict the occurrence of diabetes in patients with non-diabetic Graves' disease: A long-term follow-up study

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PT02-01-08

Frequency, various clinical presentations and treatment indications of Subclinical Hypothyroidism

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PT02-01-09

Number and Size of Metastatic Lymph Nodes as Risk Stratification for Recurrence in Filipinos with Papillary Thyroid Cancer with Nodal Metastases

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PT02-01-10

Shift work elevating serum TSH and thyroid hormone levels in nurses

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PT02-01-11

Comparison of therapeutic effects of Apelin, T4 or in combination of both on body weight in the PTU-induced hypothyroid rats

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PT02-01-12

Thyroid hormone deficiency during fetal life decreases myocardial tolerance to ischemia reperfusion injury in aged rats: role of nitric oxide

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PT02-01-13

Endoplasmic Reticulum Stress might Play a Pivotal Role in Lipid Metabolic Disorders Detected in a Novel Subclinical Hypothyroidism Mouse Model

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PT02-01-14

The Expression and Significance of DAPK Related miR-124 miR-506 in Organization and Peripheral Venous Blood from Benign and Malignant Thyroid Nodules

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PT02-01-15

Clinical outcomes and predictors of treatment failure following radioiodine therapy in Graves' thyrotoxicosis

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PT02-01-16

Protein disulfide isomerase A3 is a non-classical autoantigen in autoimmune thyroiditis

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PT02-01-17

Low Serum Vitamin D Is Associated with Anti-Thyroid-Globulin Antibody in Female Individuals

Xinling Wang, Zynat Jazyra, Yanying Guo, Osiman Reziwan, Tuhuti Aihemaitjan, Hongli Zhao, Abdunaimu Munira, Huili Wang, Jin Xiaoping, Xing Shuqing

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PT02-01-18

Dietary nitrite exposure is associated with the risk of thyroid cancer: Meta-analysis of cohort studies

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PT02-01-19

General practitioner's knowledge toward thyroid disorders during pregnancy in Iran

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PT02-01-20

Diagnostic value in differentiating malignant thyroid nodules: comparison between the Thyroid Imaging Reporting and Data System and the 2015 American Thyroid Association Management Guidelines

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PT02-01-21

Prevalence of Thyroid Disorder and Associated Risk Factors with Different Glycemic Status Among Northern Chinese Adults

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PT02-01-22

Study on the expression of Gcm2 in secondary hyperparathyroidism rats

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PT02-01-23

Changes of subtests of Wechsler Memory Scale and cognitive function in subjects with subclinical hypothyroidism following treatment with levothyroxine

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PT02-01-24

Relationship between chronic kidney disease and subclinical hypothyroidism: a case-control and accumulated evidence from the real world

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PT02-01-25

Depressive symptoms in patients with subclinical hypothyroidism – the effect of treatment with levothyroxine: a double-blind randomized clinical trial

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PT02-01-26

Increase in CD14++CD16+ Intermediate Monocytes in Subclinical Hypothyroidism

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PT02-01-27

Changes of the serum thyroid hormone levels among migrants and non-migrants on new diagonis patients with type 2 diabetes in south-to-north water diversion area

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PT02-01-28

The Effects of LDOC1 on biological behaviour of papillary thyroid cancer cells TPC-1

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PT02-01-29

Cytokine levels in tears correlate with disease activity and the outcome of orbital radiotherapy in thyroid associated ophthalmopathy

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PT02-01-30

LDOC1 promotes apoptosis of papillary thyroid carcinoma cells TPC-1 by regulating NF-κB activity

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PT02-01-31

Efficacy and safety of intravenous glucocorticoids for thyroid-associated ophthalmopathy: a systematic review and meta-analysis

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PT02-01-32

The improvement effect of astragalus on Hypothyroid ocurrence of rats treated with radioiodine-131

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PT02-01-33

The effect of Insulin resistance on Thyroid nodule formation in women with subclinical hypothyroidism, living in Iodine-deficient region of Georgia

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PT02-01-34

Reporting quality and characteristics of systematic reviews of hyperthyroidism

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PT02-01-35

Low dose of bisphenol A enhance the susceptibility of thyroid carcinoma stimulated by DHPN and iodine excess in F344 rats

Jing Zhang[1], Xiaochen Zhang[2], Yanan Li[3], Zhenzhen Zhou[4], Chuanlong Wu[1], Zhiyan Liu[5], Lanxiang Hao[1,6], Shanshan Fan[1], Fang Jiang[1], Yan Xie[1], Ling Jiang[1]

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PT03-01-01

Prevalence of Metabolic Syndrome among Iranian People Referring to Heart Center

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PT03-01-02

Long term consequence of breastfeeding on maternal obesity in middle-aged and elderly Chinese women

Lin Diaozhu, Qi Yiqin, Wang Chuan, Huang Chulin, Li Feng, Yang Chuan, Ren Meng, Yan Li, Sun Kan

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PT03-01-03

A link between obesity and microangiopathy is realistic or fictitious? Results from REACTION study

Wei Lin[1], Gang Chen[1], Junping Wen[1], Jixing Liang[1], Guang Ning[2]

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PT03-01-04

Possible weight-loss mechanism(s) of action of aqueous and methanol extracts of Vernonia amygdalina Del. leaves

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PT03-01-05

Neck Circumstance — a new predicting measurement of BMC

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PT03-01-06

Association of Microalbuminuria with Metabolic Syndrome among Aged Population

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PT03-01-07

Association of Serum Gamma Glutamyl Transferase with the Parameters of Metabolic Syndrome

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PT03-01-08

Association between Thyroid function and Body-Mass Index: A 10 year follow-up

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PT03-01-09

Body Mass Index, Fat Distribution and Menarcheal Age in Iranian Adolescent Girls

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PT03-01-10

Peripheral invariant natural killer T cell deficiency in metabolically obese but normal weight versus metabolically healthy but obese individuals

Xiaoli Wang, Xiangyun Chang, Sun Kan

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PT03-01-11

Alteration of FXR Phosphorylation and Sumoylation in Liver in the development of Adult Catch-up Growth

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PT03-01-12

Pycnogenol inhibits hepatic lipid accumulation in Apolipoprotein E deficient mice

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PT03-01-13

P62/SQSTM1: a multifunctional hub for obesity

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PT03-01-14

THE EFFECT OF CALORIC RESTRICTION ON BODY COMPOSITION IN OBESE PATIENTS USING THE PHASE ANGLE MEASUREMENT.

Carolina Ivet Marín Aragón, Lorena del Rocío Ibarra Reynoso, Itzel López Aguilar, Mauricio Sánchez Barajas, Juan Manuel Malacara*

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PT03-01-15

Impact of weight change on endothelial function, intima media thickness of carotid arteries and cognitive function in Georgian obese and overweight hypertensive subjects

Ketevan Chagunava

New Hospitals

PT03-01-16

The effect of vibration training on AKT signaling pathway in aorta of obesity rat

Chang liu, Xiaoshi Feng

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PT03-01-17

Effects of vibration training on insulin resistance in adipose tissue of obese rats

Chang liu, Xinyao Jiang

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PT03-01-18

Inhibition of GPR120 expression in macrophages by LPS/TLR4/NF-kappaB signaling pathway

Yufeng Zhao, Di Chen, Rong Xie, Yingguang Liu, Xingli Su

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PT03-01-19

Pex11a deficiency impairs energy expeniture and contributes to obesity

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PT03-01-20

Energy expenditure, physical activity and maximal oxygen uptake in adults with Prader–Willi syndrome

Harry Hirsch[1], Itai Gross[2], Naama Constantini[3], Shachar Nice[3], Yehuda Pollak[4], Larry Genstil[1], Talia Eldar-Geva[5,6], Varda Gross-Tsur[1,5]

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PT03-01-21

Magnesium Status and Its Association with Overweight and Obese Adolescents and Children of Chinese Population

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PT03-01-22

Adenosine 2A Receptor Protects against Obesity-associated NAFLD

YULI CAI[1,2,4], JUAN ZHENG[1], XIN GUO[2], HONGGUI LI[2], YA PEI[2], Rachel Botchlett[2], Shih-Lung Woo[2], Mengyang Liu[2], Guang Chen[2], Lulu Chen[1], Yuqin Huo[3], Chaodong Wu[2]

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4. Renmin hospital of Wuhan University

PT03-01-23

Neck Fat Thickness Is Associated with Metabolic Syndrome and Its Components

Haoyu Wang, Yaxin Lai, Yumeng Yan, Xun Gong, Tianxiao Pang, Tong Zhao, Yibing Zhang, Weiping Teng, Zhongyan Shan

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PT03-01-24

Circulating Zinc-a2-Glycoprotein Level Decreased in Polycystic Ovarian Syndrome Women and improved by Exenatide or Metformin Treatment

Siyuan Zheng, Ying Zhang

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PT03-01-25

I148M VARIANT OF PNPLA3 INCREASES THE SUSCEPTIBILITY TO NON-ALCOHOLIC FATTY LIVER DISEASE CAUSED BY OBESITY AND METABOLIC DISORDERS

Mingfeng Xia, Yan Ling, Hua Bian, Huan-Dong Lin, Hong-Mei Yan, Xin-Xia Chang, Lin-Shan Zhang, Xin Gao

Department of Endocrinology and Metabolism, Zhongshan Hospital, Fudan University

PT03-01-26

Assessment of liver fat content using quantitative ultrasonography to evaluate risks for metabolic diseases

Mingfeng Xia, Hua Bian, Hongmei Yan, Huandong Lin, Xinxia Chang, Xiaoming Li, Hui Ma, Wanyuan He, Naiqing Zhao, Pu Xia, Xin Gao

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PT03-01-27

The effect of thyroid function changes in euthyroid subjects on anthropometric indices; the Tehran Thyroid Study (TTS)

Behrang Motamed, Anita Eftekharzadeh, Farhad Hosseinpanah*, Maryam Tohidi, Mitra Hasheminia, Fereidoun Azizi

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PT03-01-28

The association of glucose hemostasis and insulin resistance with FTO gene expression in omental and subcutaneous adipose tissues among morbid obese subjects

Maryam Zarkesh[1], Emad Yuzbashian[2], Golaleh Asghari[2], Mehdi Hedayati[1], Parvin Mirmiran[2], Alireza Khalaj[3]

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PT04-01-01

When Hyperinsulinemia is not an Insulinoma : A Case and Review of Nesidioblastosis

Roselyn Mateo

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PT04-01-02

CYCLICAL GRAVES DISEASE IN A HIV PATIENT CO-INFECTED

WITH HEPATITIS C

Cherng Jye Seow

Tan Tock Seng Hospital

PT04-01-03

One case of a patient with hypercalcemia associated with hypopituitarism and post-partum thyrotoxicosis

Luyang Yang, Yunfeng Liu, Jing Yang

First Hospital of Shanxi Medical University

PT04-01-04

Cyclical cushing's syndrome masquerading as polycystic ovarian syndrome: a case report

Emily Ho*, Lih Ming Loh

Singapore General Hospital

PT04-01-05

A Case of Thyroid Hormone Resistance and Review of Treatment Strategies and Complications

Seng Kiong Tan, Cherng Jye Seow*, Alvin WK Tan

Tan Tock Seng Hospital

PT04-01-06

Spinal metastasis in childhood-onset craniopharyngioma – Case report, review of the literature and experiences in the German childhood-onset craniopharyngioma registry

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PT04-01-07

Elevated testosterone and 17-hydroxyprogesterone in a patient with ovarian virilizing tumor

Subhash Yadav, David D Chandy, Manoj Jain*

Sanjay Gandhi Post Graduate Institute of Medical Sciences

PT04-01-08

Microcephalic (Majewski) osteodysplastic primordial dwarfism type II with hyperandrogenism

Zareen Kiran*, Saad Farooq, Saira Furqan, Owais Rashid

Aga Khan University Hospital

PT04-01-09

Coexistence of papillary and follicular carcinoma of thyroid. Rare existence of thyroid collision tumor

Owais Rashid*, Haq Naeemul, Hameedulah Atiya, Kiran Zareen, Islam Najmul

Aga Khan University Hospital

PT04-01-10

Primary Adrenal Non Hodgkins Lymphoma: a rare occurrence

Nanik Ram*, Imran Ul Haq

The Aga Khan University Hospital

PT04-01-11

A case report of Prader-Willi syndrome and observation of the therapeutic efficacy of exenatide

Baoping fan, yongxiang sun, lili li, xialian li

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PT04-01-12

Primary hyperparathyroidism to whom applied cinacalcet HCl

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PT04-01-13

Combination of Klinefelter Syndrome and Acromegaly: A Rare Case Report

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PT04-01-14

Persistent arthralgia,hypercalcemia,and extensive osteoporosis as the initial symptoms of hyperthyroidism:a case report

Jingfang Liu, Xulei Tang, Jianguo Cheng, Liting Wang, Xiaomei Yang, Yan Wang

The First Hospital of Lanzhou University, Lanzhou,Gansu

PT04-01-15

Is there a link between primary hyperparathyroidism and hyperthyroidism? A systematic report of 4 cases.

Linxi Zhang[1,2,3], Jie Li[4], Chuanfu Dai[5], Haibin Wang[2], Weijun Gu[2], Yiming Mu[2*]

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3. Endocrine Unit, Massachusetts General Hospital
4. Department of Pathology, Chinese PLA General Hospital
5. Department of Otolaryngology Head and Neck Surgery, Chinese PLA General Hospital

PT04-01-16

A rare case of Gitelman syndrome with insulin resistance

jing yu, jing li, zhenxian du, xiaoli wang, qiuyue wang, zhongyan shan

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PT04-01-17

Acute Intermittent Porphyria Associated with Hyperthyroidism——A Case Report and Literature Review

Heyuan Wang[1], Bing Wu[2], Ying Gao[1], Yujia Liu[1], Xue Zhao[1], Zhonghua Sun[1], Shugang Xi[1], Guixia Wang[1]

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PT05-01-01

Longtime napping is associated with cardiovascular risk estimation according to Framingham risk score in postmenopausal women

Kan Sun, Feng Li, Diaozhu Lin, Yiqin Qi, Yan Li, Li Yan, Meng Ren

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PT05-01-02

Retrospective study of Metabolic Syndrome related to Cardiovascular Events and Diabetes Mellitus type 2 (138 Cases at Medicine department of Preah Ket Mealea Hospital from January-December 2015)

Pagnavuth CHHANG

Preah Ket Mealea Hospital

PT05-01-03

Cranberry extract improves the lipid profile, but not other metabolic risk parameters in overweight and obese women with metabolic syndrome

Mohammad Hassan Eftekhari*, Mansoure Alaei, Sharooz Khosropanah, Zahra Sohrabi

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PT05-01-04

The effects of incretin on artery lesions in a model of atherosclerosis in apolipoprotein E-deficient mice

Ruoran Chen[1], Jianmei Wang[2,2], Yu Wang[1], Chenghui Yan[1], Linlang Liang[1]

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2. CNPC Central Hospital

PT05-01-05

Uric acid induces endothelial dysfunction by activating HMGB1/RAGE signaling pathway

Ximei Duan[1], Wei Cai[2], Ying Liu[1], Jiao Yu[1], Lingyan Zhu[1], Shan Jiang[1], Jianying Liu[1], Jixiong Xu*[1]

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2. Medical College of Nanchang University

PT05-01-06

Association between prenatal exposure to Chinese famine and hypertension based on hypertension susceptibility genes in China She population

Gang Chen, Fengye Zhu, Junping Wen

Fujian Provincial Hospital

PT05-01-07

Genetics of S474X polymorphism correlates with serum triglycerides and HDL-cholesterol levels

Akhtar Ali*, Masroor Ellahi Babar, Tanveer Hussain, Rashid Saif

Virtual University of Pakistan

PT05-01-09

Exenatide activates adiponectin and its following pathway to reduce the apoptosis of the cardiomyocyte which induced by glucolipotoxicity

qinan wu, xiaotian lei, xiaguang gan, weiling leng, wuquan deng, bing chen, ziwen liang

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PT05-01-10

The effects of Klotho protein on ox-LDL-induced oxidative stress in human umbilical vein endothelial cells

chang liu, yan-sheng yao

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PT05-01-11

Free Fatty Acids Mediates Human Umbilical Vein Endothelial Cells Inflammation through Toll-Like Receptor-4

ling chen

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PT05-01-12

Factors associated with pre-hypertension among Tehranian adults: A novel application of structural equation models

Reza Taherian, Sara Jalali-Farahani, Mehrdad Karimi, Parisa Amiri*, Emad Maghsoodi, Parvin Mirmiran, Fereidoun Azizi

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PT05-01-13

The effect of a healthy lifestyle intervention on the risk of metabolic syndrome in children considering parental charactristics: Findings of a thirteen year follow-up

Parisa Amiri, Hasti Masihay Akbar, Leila Cheraghi, Mehrdad Karimi, Sara Jalali-Farahani, Fereidoun Azizi*

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PT05-01-14

A Case Series of Lipid Disorders Manifestation among Patients with Human Immunodeficiency Virus due to Highly Active Antiretroviral Therapy at the Care Support Treatment Clinic of Sanglah Hospital, Bali

Muhammad Faisal Putro Utomo[1*], Anindia Reina Yolanda[1], Petrus Kanisius Yogi Hariyanto[1], Nur Rizky Amaliah[1], I Made Susila Utama[2]

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PT06-01-01

Is microagiopathy an independent risk factor of vertebral fracture? Results from REACTION study

Gang Chen[1], Junping Wen[1], Kaka Tang[1], Guang Ning[2]

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2. Rujin Hospital

PT06-01-02

Exposure to the Chinese famine in early life and the risk of osteoporosis in adulthood: Results from REACTION study

Gang Chen[1], Jixing Liang[1], Liyao Zong[1], Junping Wen[1], Guang Ning[2]

1. Fujian Provincial Hospital
2. Ruijin Hospital

PT06-01-03

Application of educational program based Health Belief Model about osteoporosis and BMD in women

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PT06-01-04

Selective Targeting of the Mineralocorticoid Receptor in Cardiovascular Disease

Morag Young

Hudson Institute of Medical Research

PT06-01-05

Positive Association Between Serum Levels of Bone Resorption Marker CTX and HbA1c in Women With Normal Glucose Tolerance

yan xuan

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PT06-01-07

Assessment the relationship between osteoporosis with tooth loss and dry mouth in women with osteoporosis

Yasin Jari mourjan, Ali Khani Jeihouni*

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PT06-01-08

A novel mutation in the SLCO2A1 gene in a Chinese family with primary hypertrophic osteoarthropathy

Ping Jin, Qin Zhang, Zhaohui Mo, Yanhong Xie, Changsheng Dong

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PT07-01-01

Morphopathol gical Oral-Dental Syndrome In Patients With Acromegaly – Dental Implications

Razvan Circo, Cristina Gosu, Eduard Circo*

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PT07-01-03

Clinical investigation of the hormonal profile in patients with hypopituitarism

Xiaokun Gang, Zhuo Li, Lin Sun, Yujia Liu, Chenglin Sun, Fei Li, Xianchao Xiao, Guixia Wang

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PT07-01-04

The Prevalence of Pituitary Adenomas: A Retrospective single centre Study in Saudi community based hospital

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PT07-01-05

Analysis of the correlation between lipotoxicity and pituitary-thyroid axis hormone levels in men and male rats

Jianmei Yang[1,2,3], Ling Gao[2,3,4], Xu Zhang[1,2,3], Chunxiao Yu[1,2,3], Yongfeng Song[1,2,3], Guimei Li[5], Jiajun Zhao[1,2,3]

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PT07-01-06

The effect of hemorrhagic shock to hypothalamus-pituitary-thyroid axis in Wistar rat

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PT07-01-07

Comparison of efficacy between the serum cortisol and 24 hour urine free cortisol in combined dexamethasone suppression test in the diagnosis of Cushing syndrome

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PT07-01-08

Novel Genes in Pituitary-related Pathways Are Likely Engaged in Pituitary Stalk Interruption Syndrome: A Whole Exome Sequencing Study of 24 Typical Chinese Patients

Chengzhi Wang, Qinghua Guo, Lingling Guo, Baiyu Han, Anping Wang, Baoan Wang, Yiming Mu

Chinese PLA Gerneral Hospital

PT08-01-01

Analysis of Clinical Features and Outcomes of Congenital Adrenal Hyperplasia with Adrenal Adenoma

Yulin Gu, Weijun Gu, Jingtao Dou, Zhaohui Lv, Jianming Ba, Yiming Mu

Chinese People's Liberation Army General Hospital

PT08-01-02

Potential effects of gender on screening for aldosteronoma

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PT08-01-03

Investigation of clinical importance of assessement of dehydroepiandrosterone sulfate (DHEAS) in Lithuania (2014)

Aiste Galkine[2*], Julija Mazeikaite[1], Mazvydas Uzkurnys[1], Sarune Tribusauskaite[1], Ilona Banisauskaite[1], Tomas Kurakovas[1], Vaidotas Urbanavicius[2], Rasa Verkauskiene[1], Valentinas Matulevicius[1]

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PT08-01-04

Mifepristone Treatment a Patient with Glucocorticoid Hyperreative Syndrome

Yunfeng Liu[1], Yi Zhang[2], Linxin Xu[1], Chenyu Xiang[1], Jing Yang[1*]

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PT08-01-05

Mifepristone successful treatment of primary adrenal ACTH-independent Cushings syndrome in a Chinese elderly patient

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PT08-01-06

Reassessment of the Cosyntropin Stimulation Test in the Confirmatory Diagnosis and Subtype Classification of Primary Aldosteronism

Hironobu Umakoshi, Mitsuhide Naruse*

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PT09-01-01

Duodenal Glucagon-like peptide-1 (GLP)-1 Trigger a Gut–Brain–Liver Axis to Regulate Hepatic Insulin Signaling and Glucose Production

Lei Yuan, Ling Li, Gangyi Yang

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PT09-01-02

Restoration of Molecular, behavioral and biochemical changes in aging rat brain on treatment with 17beta estardiol--a promising anti-aging agent.

Pardeep Kumar*, Najma Baquer

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PT09-01-03

Nuchal skinfold thickness: a novel parameter for assessment of body composition in childhood craniopharyngioma

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PT09-01-04

History before diagnosis in childhood craniopharyngioma: Associations with initial presentation and long-term prognosis

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PT09-01-05

Hydrocephalus and hypothalamic involvement in pediatric patients with craniopharyngioma or cysts of Rathke's pouch: Impact on long-term prognosis

Anna Daubenbüchel[1,2], Anika Hoffmann[1], Ursel Gebhardt[1], Monika Warmuth-Metz[3], Anthe S. Sterkenburg[1,2], Hermann L. Müller[1]

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PT09-01-06

Nonalcoholic fatty liver disease and fatigue in long-term survivors of childhood-onset craniopharyngioma

Anika Hoffmann[1], Klaus Bootsveld[2], Ursel Gebhardt[1], Anna M.M. Daubenbüchel[1,3], Anthe S. Sterkenburg[1,3], Hermann L. Müller[1*]

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PT10-01-01

Evaluation of the effect of extra-amniotic normal saline infusion alone or in combination with dexamethasone for the induction of labor

Kashanian Maryam*, Salvasadat Naghghash

Iran University of Medical Sciences

PT10-01-02

Lipid profile and its association with insulin resistance in Polycystic Ovary women 18-45 years old

Homeira Rashidi

Health Research Institute

PT10-01-03

The relationship of serum 25-dihydroxy vitamin D3 concentrations with metabolic parameters in non-obese women with polycystic ovary syndrome

Homeira Rashidi, mehri tolabi, mahin nazafian, Seyed Mahmoud Latifi

Health Research Institute

PT10-01-04

Metforming-induced AMPK activation inhibits KiSS1 receptor gene expression in GT1-7 cells

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PT10-01-05

Information on Early menopause: Is the internet the place to search?

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2. Monash Centre for Health Research and Implementation-MCHRI
3. Monash University
4. Hudson Institute

PT10-01-06

Association between idiopathic hirsutism and metabolic syndrome (Tehran Lipid and Glucose Study)

Samira Behboudi-Gandevani[1*], Fahimeh Ramezani Tehrani[1], Fereidoun Azizi[1,3]

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PT11-01-01

Correlation of serum Vitamin D level with mortality in patients with sepsis

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PT11-01-02

Vitamin D status in infants during the first 9 months of age and its effect on growth and other biochemical markers: A Prospective Cohort Study

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PT11-01-03

VITAMIN D DEFICIENCY – A POSSIBLE INVOLVEMENT IN MAJOR VASCULAR ACCIDENTS

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Ovidius University of Constanta

PT11-01-04

Vitamin D status is negatively correlated with insulin resistance in Chinese type 2 diabetes

Jie Zhang[1,2], Jianhong Ye[2], Gang Guo[2], Zhenhao Lan[3], Xing Li[4], Zhiming Pan[2], Zongji Zheng[1], Fangtao Luo[2], Luping Lin[2], Zhihua Lin[2], Yaoming Xue[1]

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PT11-01-05

Clinical Characteristics of Adult-onset Non-surgical Hypoparathyroidism : A Retrospective Analysis of 200 Cases

Tingting Quan, Yuepeng Li, Ou Wang, Yan Jiang, Weibo Xiang, Mei Li, Xunwu Meng, Xiaoping Xing

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PT12-01-01

The effects of soy isoflavones on metabolic status of patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial

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3. Department of Gynecology and Obstetrics, School of Medicine, Arak University of Medical Sciences, Arak, Iran
4. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Kashan University of Medical Sciences, Kashan, I.R. Iran

PT12-01-02

A comparison between the effects of metformin and N-acetyl cysteine (NAC) on some metabolic and endocrine characteristics of women with polycystic ovary syndrome

Maryam Rahimi, Maryam Kashanian

Department of Gynecology and Obstetrics, School of Medicine, Iran University of Medical Sciences,

PT12-01-03

Detection of undeclared androgens in sport supplements sold on the Australian market

Alison Heather

University of Otago

PT12-01-04

Identification of Genetic Pathology for Patients with 46, XY Disorders of Sex Development by using Targeted Gene Capture with Second-Generation Sequencing

Zhaoxiang Liu, Jiangfeng Mao, Xueyan Wu, Min Nie, Xi Wang, Junjie Zheng

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PT12-01-05

Roles of Circulating WNT-Signaling Proteins and WNT-Inhibitors of Southern Chinese Women with PCOS

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PT13-01-01

Role of homeobox transcription factor PROX1 in follicular thyroid cancer metastasis

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PT13-01-02

Role of renin-angiotensin-aldosterone system in adrenal incidentalomas

Xueqiong Li[1,2], Kang Chen[1], Shuangshuang Wang[1], Jinjing Wang[1,3], Juming Lu[1], Jingtao Dou[1], Zhaohui Lü[1], Weijun Gu[1], Nan Jin[1], Li Zang[1], Yiming Mu[1]

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PT13-01-03

RET proto oncogene germline mutations in Iranian patients with Medullary Thyroid Carcinoma

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PT13-01-04

Association between plasma pevels of Vaspin, RBP4 and Medullary Thyroid Carcinoma

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PT13-01-05

Association between plasma levels of Ceruloplasmin and Adiponectin with Medullary Thyroid Carcinoma

Razavi Fatemeh[1], Shady Fathi[1], sara sheikholeslami[2], Marjan Zarif Yeganeh[2], Laleh Hoghooghi Rad[2], Hoda Golab Ghadaksaz[2], Mehdi Hedayati[2*], Naji Tahereh[3]

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PT14-01-01

Diurnal Rhythm of Follicle-Stimulating Hormone Is Associated With Nonalcoholic Fatty Liver Disease in Chinese Elderly Population

Xiaoming Li, Gang Chen

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PT14-01-02

A novel FSHbeta mutation in a male patient presented with infertility and isolated FSH deficiency

Junjie ZHENG, Jiangfeng MAO, Zhaojiang LIU, Mingxuan CUI, Xi WANG, Shuyu XIONG, Min NIE, Xueyan WU

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PT14-01-03

Gonadotropin-induced Spermatogenesis in Congenital Hypogonadotropic Hypogonadism Patients with Cryptorchidism

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PT14-01-04

Alterations of androgen receptor-regulated enhancer RNAs (eRNAs) contribute to enzalutamide resistance in castration-resistant prostate cancer

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PT15-01-01

Maternal circulating PlGF levels in relation to fetal insulin sensitivity and beta-cell function indices in infants born small-for-gestational-age

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PT15-01-02

Maternal circulating PlGF levels in relation to leptin and adi-

ponectin concentrations in infants born small-for-gestational-age

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PT15-01-03

Analysis of the clinical and molecular characteristics of a child with achondroplasia

Jingfang Liu, Xulei Tang, Jianguo Cheng, Liting Wang, Xiaomei Yang, Yan Wang

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PT15-01-04

The natural history of euthyroid Hashimoto thyroiditis in children and adolescents

Feneli Karachaliou[1], Maria Kafetzi[2], Dimitris Thomas[1], Elpis Vlachopapathopoulou[1], Irini Kaloumenou[1], Antonia Kapella[1], Aspasia Fotinou[2], Stefanos Michalakos[1]

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PT16-01-01

Clinical Spectrum of Disorders of Sexual Differentiation

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PT16-01-02

New method of treatment of a thyroid gland.

Yulia Chukova

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PT16-01-03

Effects of body weight gain during early postnatal period on pancreatic and gastric peptides

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PT17-01-01

Two sisters with nonclassic congenital adrenal hyperplasia due to a compound heterozygous mutation of CYP21A2 gene

Corina Neamtu, Camelia Procopiuc, Andra Andra Caragheorgheopol, C upea

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PT17-01-02

LAMP3 reprograms lipid metabolism in hepatocellular carcinoma cells

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PT18-01-01

Incidence of adrenal insufficiency and its relation to mortality in patients with septic shock

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PT18-01-02

Diagnosic value of standard posture test in adrenal incidentalomas

Shuangshuang Wang, Xueqiong Li, Kang Chen, Weijun Gu, Jingtao Dou, Guoqing Yang, Nan Jin, Jin Du, Li Zang, Qinghua Guo, Jianming Ba, Zhaohui Lv, Yiming Mu

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PT19-01-01

Effects of Fibronectin / Integrin β Signaling on Short-term HFD Induced Hepatic Steatosis and its Underlying Mechanism

Fei-fei Zhang[1], Xue-jiao Zhang[2], Chun-jiong Wang[2], Liu Yao[2], Ding Ai[2], Fang-qiu Zheng[1]

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PT20-01-01

Conventional radiotherapy versus radiosurgery in acromegaly treatment

Cristina Mariana Valeria Ghervan

University of Medicine and Pharmacy Cluj-Napoca

September 2, 2016

Setup Time: September 2, 2016 09:00-10:00
Poster Discussion Time: September 2, 2016 13:00-14:00
Poster Removal Time: September 2, 2016 17:00-17:30

PT01-02-01

The coordinated roles of miR-26a and miR-30c in regulating TGFβ1-induced EMT in diabetic kidney disease

Zongji Zheng[1], Meiping Guan[1], Yijie Jia[1], Dan Wang[1], Ruoyu Pang[1], Fuping Lv[1], Zhizhou Xiao[1], Ling Wang[1], Hongbin Zhang[2], Yaoming Xue[1]

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PT01-02-02

A comparison of tissue versus swab culturing of infected diabetic foot wounds

Ying Huang, Ying Cao, Mengchen Zou, Xiangrong Luo, Ya Jiang, Yaoming Xue, Fang Gao

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PT01-02-03

Effect of Exenatide after Short-time Intensive Insulin Therapy on Maintenance of 2-year Drug-free

Xiulin Shi[1], Mingzhu Lin[1], Ning Chen[1], Weijuan Su[1], Huijie Zhang[1], Changqin Liu[1], Haiqu Song[1], Liying Wang[1], Wei Liu[1], Shuyu Yang[1,2], Xiaoying Li[1,2,3], Zhibin Li[1], Xuejun Li[1,4]

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PT01-02-04

The Effect and Molecular Mechanism of Forkhead Transcription Factor O1 on High Glucose-Induced Mitophagy of Mice Podocyte Cells

Guijun Qin, Wen Li, Qingzhu Wang, Mengmeng Du, Lina Wu, Xiaojun Ma

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PT01-02-05

Exendin-4 ameliorates inflammation and renal interstitial fibrosis by blocking the NF-κB and TGF-β1/Smad3 signalling pathways in a model of unilateral ureteral obstruction

Mengling Cheng, ying Le, Junyu Xue, Zongji Zheng, Qian Zhang, Meiping Guan, Yaoming Xue

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PT01-02-06

Rosiglitazone attenuates TGFβ1-induced EMT directly through the miR-22/PPAR-γ /ERK1/2 pathways

Zongji Zheng, Meiping Guan, Yijie Jia, Wenqi Li, Dan Wang, Ruoyu Pang, Fuping Lv, Ling Wang, Yaoming Xue

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PT01-02-07

The effect and mechanism of human umbilical cord-derived mesenchymal stem cells on type 2 diabetic rats

Jieqing Gao[1,2], Zongyan Xie[1], Yiming Mu[1], Haojie Hao[1], Ming Xie[1], Yu Cheng[1], Qi Zhang[1]

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PT01-02-08

Electronic Documentation of Lifestyle Counseling in Primary Care is Associated with Lower Risk of Cardiovascular Events in Patients with Diabetes

Huabing Zhang[1,2,3], Naoshi Hosomura[2,3], Maria Shubina[3], Donald C. Simonson[2,3], Marcia A. Testa[4], Alexander Turchin[2,3,5*]

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PT01-02-09

Nonalcoholic Fatty Liver Disease Is Associated with Left Ventricular Systolic Dysfunction in Patients with Type 2 Diabetes

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PT01-02-10

Elevated serum free triiodothyronine (FT3) level is an independent risk factor for insulin resistance in patients with type 2 diabetes

Bingjie Zhang, Shanmei Shen, Tian Tian, Jiayi Liu, Xiao Ye, Hong Huang, Ping Li, Wenhuan Feng, Yan Bi, Dalong Zhu

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PT01-02-11

Short-Term Effects of Information Integration Glucose Management in Patients with Diabetes Mellitus Who Underwent Orthopedic Surgery

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PT01-02-12

Methylcobalamin on diabetic peripheral neuropathy treatment assessment

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PT01-02-13

SIRT1 and FOXO1 SNPs Genetic Susceptibility to type 2 Diabetic Nephropathy in Chinese Han population

yanyan zhao[1], qingzhu wang[1], huimiao liu[2], feng guo[1], yingni zhou[1], yuanyuan zhang[1], yunhui qu[1], guijun qin[1]

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PT01-02-14

Glucagon-like peptide-1 receptor agonist improve renal injury through its anti-inflammatory action with down-regulating HMGBl expression in a rat model of diabetes

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PT01-02-15

The safety and effect of statins augmentation for patients with diabetes mellitus: a meta-analysis and systematic review

Wanjia Xing, Zhaoshun Jiang, Zongjing Zhang, Wei Qu

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PT01-02-16

Serum Levels of Nesfatin-1 are Increased in Gestational Diabetes Mellitus

Jiahui Lu, Ying Zhang

The Third Affiliated Hospital of Guangzhou Medical University

PT01-02-17

Exendin-4 attenuates interstitial fibrosis partly via restoring the balance of intrarenal renin-angiotensin system and inhibiting Ang II-mediated TGF-β1/Smad3 signaling pathway in unilateral ureteral obstruction mice

Ying Le, Zong-Ji Zheng, Jun-Yu Xue, Meng-Ling Cheng, Mei-Ping Guan, Yao-Ming Xue

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PT01-02-18

The activation of ERK pathway in hippocampus by Pioglitazone to improve ability of learning and memory in T2DM rats

Fei Gao, Li Zang, Qian ZHang, GuangLei Tian, HaiBin Wang, YiMing Mu

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PT01-02-19

The glucagon-like peptide-1 analogue liraglutide promotes autophagy through the modulation of 5′-AMP-activated protein kinase in INS-1 β-cells under high glucose conditions

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PT01-02-20

Effect of individualized physical activity treatment on drug na?ve type 2 diabetic patients

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PT01-02-21

Gene Polymorphisms in the RANKL/RANK/OPG Pathway are Associated with Type 2 Diabetes Mellitus in Southern Han Chinese Women

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PT01-02-22

The effects of aspirin versus intensive glucose management on the incidence of cardiovascular events in diabetic patients at very high risk or secondary prevention of CVD: a meta-analysis and adjusted indirect Comparisons

Shishi Xu, Yuwei Zhang, Juan Li, Nanwei Tong

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PT01-02-23

A combination of Latent Autoimmune Diabetes,thyroiditis and Stiff person syndrome associated with GAD-65 antibody

Ping Li[1], Lin-lang Liang[1], Ruo-ran Chen[1], Jing-hua Zhang[2], Cheng Xia[2]

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PT01-02-24

Autophagy Inhibition Exacerbated the insulin secretion and insulin content of the pancreaticβcells during the 4 hour□H□ high glucose-infusion in mice

Dien Yan[1,2], Yingsheng Zhou[2], Liming Xiao[1], Jianping Guo[1]

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PT01-02-25

Yang- warming method in the treatment of diabetic peripheral neuropathy: An updated systematic review and meta-analysis

Tianshu Gao, Sharad Panthi, Xirun Jing

Liaoning University of Traditional Chinese Medicine

PT01-02-26

CHANGE IN DNA METHYLATION STATUS AND REPEAT ELEMENT EXPRESSION IN DAIBETIC RAT BRAIN

Somnath Mukherjee*, K.C Upadhyaya, Deepak Sharma

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PT01-02-27

HYPOGLYCEMIC AND AMELIORATIVE EFFECT OF FRACTION OF FICUS EXASPERATA ON THE PATHOPHYSIOLOGICAL COMPLICATIONS OF TYPE 1 DIABETES MELLITUS IN ALBINO RATS.

Gloria Otito Izu*, Akindele Oluwatosin Adeyi

University of Ibadan

PT01-02-28

Metformin therapy and risk of breast and gynecology cancer in patients with type 2 diabetes mellitus: a meta-analysis

Hanjiao Qin

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PT01-02-29

Berberine for the treatment of type 2 diabetes: a meta-analysis

Lili Chen[1], Renming Hu[1], Chao Liu[2]

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PT01-02-30

The role of autophagy in chronic inflammation inducing the damage of islet cell

Linlei Wang, Hongwei Jiang, Jie Wang

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PT01-02-31

COMPARISON OF TWO PROTOCOLS IN MANAGEMENT OF GLUCOCORTICOID-INDUCED HYPERGLYCEMIA AMONGST HOSPITALIZED PATIENTS

Om Lakhani*, Surender Kumar, Mitali Desai

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PT01-02-32

A registry of acromegaly patients in Taiwan to evaluate the health outcome of acromegaly with special emphasis of early diagnosis

Fen-Yu Tseng[1], Tien-Shang Huang[1], Jen-Der Lin[2], Rue-Tsuan Liu[3], Wayne Huey-Herng Sheu[4], Tien-Chun Chang[1]

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4. Department of Internal Medicine, Taichung Veterans General Hospital

PT01-02-33

GLP1 agonist treatment in patients with type 1 diabetes mellitus: effects on weight and glycaemic control in an Emirati population

Raya A Almazrouei, Fatima M Alkaabi, Nader Lessan, Maha T Barakat

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PT01-02-34

Awareness about Diabetes Mellitus amongst Diabetics in a secondary care hospital in Bangladesh

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PT01-02-35

IL-22 Exerts Both Cytotoxic and Proliferative Effects in Pancreatic β cells Depending on the Inflammatory Context Via IL-22R-STAT-3 Pathway

Ruxing Zhao, Li Qing, Lingshu Wang, Tianyi He, Yu Wang, Lei Sun, Li Chen

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PT01-02-36

Blood pressure and risk for cardiovascular diseases and mortality in patients with type 2 Diabetes in a long-term Middle Eastern cohort: Tehran lipid and glucose study(TLGS)

Sadjad Riyahi-Alam[1], Nasrin Mansournia[2], Arash Derakhshan[1], Mohammad Ali Mansournia[3], Fereidoun Azizi[1], Farzad Hadaegh[1*]

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PT01-02-37

A STUDY OF THE DISEASE CHARACTERISTICS AND COMPLICATIONS IN FIBROCALCULOUS PANCREATIC DIABETES FROM EASTERN INDIA

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PT01-02-38

A randomized controlled trial to investigate the impact of sleep education program on glycemic control in Hong Kong Chinese type 2 diabetic patients with short sleep duration: An interim analysis at 6 months of intervention

Alice Pik Shan Kong, Kai Chow Choi, Chenzhao Ding, Jihui Zhang, Andrea On Yan Luk, Ronald Ching Wan Ma, Wing Yee So, Kitty Kit Ting Cheung, Yun Kwok Wing, Francis Chun Chung Chow, Juliana Chung Ngor Chan

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PT01-02-39

Georgian Union of Diabetes and Endocrine Associations- 28 Years Supporting People with Diabetes

Ramaz Kurashvili[1,1,1], Elena Shelestova[1,1,1], Liana Tsutskiridze[1,1,1], Mzia Dundua[1,1,1], Givi Kurashvili[1,1,1], Simon Gabrichidze[2,2,2], Ketevan Gordeladze[3,3,3], Marina Shakhvadze[4,4,4]

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3. Red Cross, Georgia
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PT01-02-40

Pregnancy Outcomes and Complication Rate Twelve-Years Post-Partum in Women with Type 1 Diabetes

Natalia Asatiani[1,1], Ramaz Kurashvili[1,1*], Elena Shelestova[1,1], Mzia Dundua[1,1], Liana Tsutskiridze[1,1], Moshe Hod[2,2]

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PT01-02-42

Prevalence of Risk Factors of Type 2 Diabetes and predicting the Probability of Type 2 Diabetes in Georgia

Nikoloz Dzmanashvili[1], Liana Tsutskiridze[2], Ramaz Kurashvili[2], Elena Shelestova[2]

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PT01-02-43

Organization of Diabetic Foot Service - Project "Diabetic Foot Care Improvement"

Elena Shelestova[1,1], Natia Amilakhvari[2,2], Simon Gabrichidze[2,2], Ramaz Kurashvili[1,1], Liana Tsutskiridze[1,1]

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PT01-02-44

Education of People with Diabetes and Healthcare Providers - Joint Affords of Eastern–European Diabetes Associations

Liana Tsutskiridze[1,1,1], Ramaz Kurashvili[1,1,1], Elena Shelestova[1,1,1], Mzia Dundua[1,1,1], Elvira Gudtova[2,2,2*], Lyudmila Petrenko[2,2,2], Natalya Vlasenko[3,3,3], Nilufar Ibragimova[4,4,4]

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3. International Diabetes Association of the Ukraine, Kiev, United Kingdomraine
4. UMID-Uzbekistan, Uzbekistan

PT01-02-45

Displaced Persons from Abkhazia and South Ossetia – Insight in the Health Status

Dalila Khorava[1,1], Ketevan Kvaratskhelia[1,1], Shota Chanturia[1,1], Liana Tsutskiridze[2,2], Elena Shelestova[2,2]

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PT01-02-46

Utility of hypertriglyceridemic-waist phenotype for predicting incident type 2 diabetes: the Isfahan Diabetes Prevention Study

Mohsen Janghorbani

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PT01-02-47

Efficacy of Itopride in Treatment of Diabetic Gastroparesis

Iryna Kostitska

Ivano-Frankivsk National Medical University

PT01-02-48

Different Combination of Glucose Tolerance and Blood Pressure Status and Incident Diabetes, Hypertension and Chronic Kidney Disease

Azra Ramezankhani[1], Arash Derakhshani[1], Banafsheh Arshi[1], Fereidoun Azizi[2], Farzad Hadaegh[1*]

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PT01-02-49

Project Diabetes Prevention and Care Improvement Realized by the Welfare Foundation Georgia in Collaboration with Georgian Union of Diabetes and Endocrine Associations

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PT01-02-50

Surveillance system for diabetes mellitus in Tbilisi, Georgia – results and evaluation

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PT01-02-51

Diabetes Prevention in Rural Georgia – Project carried out by the Georgian Red Cross Society and Georgian Union of Diabetes and Endocrine Associations

Ketevan Mindeli[1,1], Keti Gordeladze[1,1*], Shorena Tsiklauri[1,1], Nino Osepaishvili[1,1], Ramaz Kurashvili[2,2], Elena Shelestova[2,2], Liana Tsutskiridze [2,2], Tinatin Akhobadze[2,2], Natalya Asatiani[2,2]

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2. Georgian Union of Diabetes and Endocrine Associations/GUDEAS, Tbilisi, Georgia

PT01-02-52

Prevalence of risk-factors for Diabetes 2 and other Non-Communicable Diseases are high among school-children in Tbilisi, Georgia 2015

Nana Mebonia[1,1], Rusudan Kvanchakhadze[1,1], Saba Zhizhilashvili[2,2], Dali Trapaidze[1,1], Nino Kasradze[2,2]

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PT01-02-53

Transcriptional Factor MafB mediates high glucose diet-induced hepatic steatosis

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PT01-02-54

Lineage conversion of mouse fibroblasts to pancreatic α-cells

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PT01-02-55

Association between diabetes and depression amongst adults in Shanghai Changzeng hospital. A Case-control study

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PT01-02-56

Evaluation of diabetic patients' education about diabetes mellitus in Shanghai Changzheng Hospital China

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PT01-02-57

Transplantation of betatrophin-expressing adipose-derived mesenchymal stem cells induces β-cell proliferation in diabetic mice

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PT01-02-58

Vitamin D level and diabetic neuropathy in Type 2 diabetes

Mustafa Boz, Cuneyt Muderrisoglu, Fusun Erdenen, Hayri Polat, Esma Altunoglu, Feray Akbas

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PT01-02-59

Six-month results of diabetes prevention program in a regional hospital of south Taiwan

Ying-Chuen Lai*, Yi-Shan Li, Ying-Huei Chen, Wei-Yi Hsu

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PT01-02-60

Effect of kolaviron, a biflavonoid complex from Garcinia kola seeds, on the antioxidant, hormonal and spermatogenic indices of diabetic male rats

Oluwatosin Adaramoye, Semiu Lawal

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PT01-02-61

The role of the high-sensitivity C-reactive protein, a marker of inflammation and Resistive Index in diabetic nephropathy

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PT01-02-62

Alpha-lipoic acid cytoprotective therapy in type 2 diabetes patients

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VSMU named after N.N.Burdenko

PT01-02-63

Association between Uncontrolled Glycosylated Hemoglobin and Elderly Status with Diabetic Retinopathy (DR) Types among Balinese in Sanglah General Hospital, Bali Province

Ni Kadek Vani Apriyanti[1*], Muhammad Faisal Putro Utomo[1], I Gusti Ayu Ariningrat[1], Devina Martina Bumi[1], Desak Made Wihandani[2], Anak Agung Mas Putrawati Triningrat[3]

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PT01-02-64

Camel milk has beneficial effect on diabetes mellitus: A Systematic Review

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PT01-02-65

Correlation between Arterial Hypertension with Severity of Diabetic Retinopathy among Balinese in Sanglah General Hospital

I Gusti Ayu Ariningrat[1*], Ni Kadek Vani Apriyanti[1], Muhammad Faisal Putro Utomo Utomo[1], Devina Martina Bumi[1], Desak Made Wihandani[2], Anak Agung Mas Putrawati Triningrat[3]

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PT01-02-67

African tea leaf (Vernonia amygdalina) exract decreased of blood glucose levels; an experimental study using dibetic mice (Mus musculus)

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PT01-02-68

Molecular Signatures of Calpain 10 Isoforms Sequences,Envisage Functional Similarity and Therapeutic Potential.

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PT01-02-69

Title: A Study of Diabetes Prevalence and Associated Risk Factors in the rural area of Madhya Pradesh-India

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Peoples college of Medical sciences and Research

PT01-02-70

The effect of Metformin Monotherapy on plasma concentration of resistin, leptin, IL-6, IL-2, TNF-a in newly diagnosed patients with DM2.

Alina Urbanovych

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PT01-02-71

Feature mitochondrial cytopathology in experimental diabetes

Oksana Pivovarova[1*], Oleg Loskutov[1], Ekaterina Rozova[2], Boris Mankovsky[1]

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PT01-02-73

Hypoglycaemia amongst inpatients

Kerri Rosettenstein[1], Yuk Fun Chan[2*], Barbara Depczynski[2], Karlie Foster[2], Christopher White[2]

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2. Prince of Wales Hospital

PT01-02-74

Fibrocalculous pancreatic diabetes: Insulin Resistance, Cardiac Autonomic dysfunction & Peridontal Disease

Pradip Mukhopadhyay, Beatrice Anne, Sujoy Ghosh, Subhankar Chowdhury

Institute of Post Graduate Medical Education & Research

PT01-02-75

Excorine insufficiency in Fibrocalculous pancreatic diabetes compared to type 1 & type 2 diabetes

Kaushik Pandit, Beatrice Anne, Sujoy Ghosh, Pradip Mukhopadhyay, subhankar Chowdhury

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PT01-02-76

Short-term effect of fenofibrate on diabetes progress: A systematic review meta-analysis of randomized controlled trials

Yumeng Luo, Yuan Sun, Yong Zeng, Huijuan Zhu, Hui Pan, Naishi Li, Yu Jiang

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PT01-02-77

Dietary L-arginine intakes and the risk of metabolic syndrome: A 6-year follow-up in Tehran Lipid and Glucose Study

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PT01-02-78

Dietary patterns and the incidence of insulin resistance: A prospective approach in Tehran Lipid and Glucose Study

Parvin Mirmiran[1], zahra Bahadoran[1], Tayebeh Doostvandi[2], Hasan Mozzafari-Khosravi[2], Maryam Tohidi[3], Fereidoun Azizi[4*]

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PT01-02-79

Reduced risk of hypoglycaemia with insulin degludec vs. insulin glargine U100 in Chinese insulin-na?ve patients with T2D

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PT01-02-80

The effect of combined treatment with SGLT2 inhibitors and GLP1 agonists on weight and glycaemic control: analysis of data on 1688 patients with type 2 diabetes

Wafic Wafa

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PT01-02-81

High risk of sleep apnoea among Emirati patients with diabetes and obesity

Sama Hassan, Adam Buckley, Tameem Al Tameemi, Nader Lessan*, Maha Barakat

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PT01-02-82

A study of diabetes in the highlands

Nick Crabb

Watermeadow

PT01-02-83

HYPOGLYCEMIC AND AMELIORATIVE EFFECTS OF GAMMA-SITOSTEROL OBTAINED FROM FICUS EXASPERATA ON THE PATHOPHYSIOLOGICAL COMPLICATIONS OF TYPE 1 DIABETES MELLITUS IN ALBINO RATS.

Akindele Adeyi, Gloria Izu

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PT01-02-84

Relationship of Vitamin D with Clinical Parameters of Diabetes among Newly Diagnosed Pakistani Subjects.

Tasnim Farasat, Saima Sharif*, Farkhanda Manzoor, Maroof Amjad, Shagufta Naz

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PT01-02-85

Lifestyle parameters and gestational diabetes risk

Polina Popova[1,2*], Alexandra Tkachuk[1], Alexandra Dronova[1], Andrey Gerasimov[1], Yana Bolotko[1], Ksenia Demidova[2], Elena Grineva[1,2]

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PT01-02-86

The Prevalence of Gestational Diabetes Mellitus in Iranian women, a comparison between the old and the new criteria

Mahtab Niroomand*, Jamileh Afsar, Farhad Hosseinpanah, Maryam Afrakhteh, Sara Serahati

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PT01-02-87

Diabetes Knowledge, Attitude and Practice (KAP) Study among Iranian Patients: A Cross Sectional Study

Mahtab Niroomand[1], Seyedeh Najmeh Ghasemi[1], Hamidreza Karimi-Sari[2*], Sara Kazempour-Ardebili[1], Parisa Amiri[1], Mohammad Hossein Khosravi[2]

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PT01-02-88

Diabetes Knowledge, Attitude and Practice (KAP) Study among Iranian Internist: A Cross Sectional Study

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PT01-02-89

The effect of metformin on expression of insulin receptor in liver and skeletal muscle in a new model of type 2 diabetic rats

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PT01-02-90

Histopathology of pancreas and liver in diabetic rats

Dewi Ratna Sari*, Rimbun , Tri Hartini Yuliawati

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PT02-02-01

Treatment Of Severe Graves' Ophthalmopathy With A Parenteral And Oral Ppar-Γ Antagonist And Cyclooxigenase-2 Inhibitor (Sodium Diclofenac)

Janete Pereira de Moura, Lidia Y Mimura, Walter Bloise

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PT02-02-02

Iron Store Deficit During the First Trimester Pregnancy Might Predict the Occurrence of Hypothyroxinemia and Overt Hypothyroidism in the Second Trimester Pregnancy: A Prospective Study in Chinese Pregnant Women

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PT02-02-03

Nine-year follow-up for women with subclinical hypothyroidism in pregnancy

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PT02-02-04

The Expression and Significance of DAPK Related miR-124、miR-506 in Organization and Peripheral Venous Blood from Benign and Malignant Thyroid Nodules

qi zhang, Feng Wei, Cheng Chi

Baotou Medical School First Affiliated Hospital

PT02-02-05

Activation of the Nrf2-Keap 1 antioxidative defense in short term iodide excess in the thyroid in rats

Qi duan, Xiaomei Yao, Iruni Roshanie Abeysekera

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PT02-02-06

Study on risk factors of papillary thyroid microcarcinoma and papillary thyroid carcinomas of 1-2cm recurrence

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PT02-02-07

Transoral endoscopic thyroidectomy vestibular approach: a case report

Michelle Cornel, Ruby Go

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PT02-02-08

Clinicopathological characteristics and molecular mechanism of Chinese anaplastic thyroid cancer

Meiqi Ni[1], Tingting Liu[1], Xiaoguang Shi[1], Enhua Wang[2], Yahong Luo[3], Xianghong Yang[4], Jianling Du[5], Zhongyan Shan[1], Weiping Teng[1]

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PT02-02-09

Serum Fibroblast Growth Factor 19 is Decreased in Patients with Overt Hypothyroidism and Subclinical Hypothyroidism

Yaxin Lai, Haoyu Wang, Xinghai Xia, Cheng Han, Zhaojun Wang, Chenling Fan, Hong Wang, Hongmei Zhang, Shuangning Ding, Weiping Teng, Zhongyan Shan

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PT02-02-10

Soft tissue invasion of papillary thyroid carcinoma

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PT02-02-11

Comparative study on iodine metabolism of iodine rich Chinese herbal medicine and iodine excess in rats with PTU induced goiter

Tianshu Gao, Qu Zheng, Xirun Jing, Sharad Panthi

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PT02-02-12

Effect of iodine-rich Herbs on the oxidative stress and TH17 cells differentiation in iodine-deficiency NOD.H-2h4 mice

Tianshu Gao, Jinqiao Qu, Xirun Jing, Sharad Panthi

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PT02-02-13

Mean Peak Systolic Velocity of the Superior Thyroid Artery is Correlated with Radioactive Iodine Uptake in Untreated Thyrotoxicosis

Lili Chen[1], Xiaolong Zhao[1], Hongying Ye[1], Yong Wang[2], Huiqing Zhu[3], Linuo Zhou[1], Yiming Li[1], Renming Hu[1], Hong Liu[1]

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PT02-02-14

Evaluated diagnostic efficiency of ultrasound features on malignant thyroid nodules in Chinese patients

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PT02-02-15

Is it cost- effective to set reference values for TSH during pregnancy?

Fidel J Enciso Izquierdo[1], Jesús María Lavado García[2], Jose Luis Bote Mohedano[2], Juan Parra Barona[3,3], María José Amaya García[1]

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PT02-02-16

The Assessment of Circulating Proteins in the Patients with Medullary Thyroid Cancer: Can It Be Utilized as a Panel for Early Diagnosis?

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PT02-02-17

Can Serum Level of Myostatin be considered as an Informative Factor for Cachexia Prevention in Patients with Medullary Thyroid Cancer?

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PT02-02-18

Triiodothyronine-Predominant Graves' Disease in Pregnancy

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PT02-02-19

Epidemiological study of thyroiditis with encephalopathy in Beijing community

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PT02-02-20

INDETERMINATE THYROID NODULES (THY3) AND THE RISK OF MALIGNANCY IN UAE RESIDENTS- THE ROLE OF ULTRASOUND RISK STRATIFIATION

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PT02-02-21

The impact of guideline on managements of thyroid nodule patients undergoing surgery

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PT02-02-22

Correlation study about body mass index and the risk of papillary thyroid carcinoma in male patients

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PT02-02-23

A cross-sectional retrospective study to identify indicators for initiating thyroid hormone replacement therapy in patients with subclinical hypothyroidism

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PT02-02-24

Low CD26 expression in Hashimoto's thyroiditis

Yalei Liu[1], Nan Yu[1], Ran You[2], Yang Zhang[1], Yan Gong[2], Chenxue Qu[2], Youyuan Huang[1], Hong Zhang[1], Guizhi Lu[1], Ying Gao[1], Yanming Gao[1], Xiaohui Guo[1]

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PT02-02-25

Hyperthyroidism and Acute Hepatitis A infection, the Role of Lithium and Plasmapharesis in the Management of Hyperthyroidism: A Case Report

Erva Magbanua, Rebecca Lim-Alba*

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PT02-02-26

Thyroid hormone resistance syndrome caused by heterozygous A317T mutation in thyroid hormone receptor β gene

Qinghua Guo[1,2], Baoan Wang[1], Chengzhi Wang[1], Min Wang[1], Zhaohui Lv[1], Yiming Mu[1]

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PT02-02-27

Evaluation of thyroid gland by the ultrasonographic screening for 4 years in human dry dock

Mutsuo Beniko[1*], Hiroyuki Ikawa[1], Takayuki Mori[1], Yasuo Mashio[2]

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PT02-02-28

TSH inhibits SERCA2a and the PKA/PLN pathway in rat cardi-

omyocytes

Jiajia Dong, Limin Tian

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PT02-02-29

Psychometric Evaluation of Turkish Versions of ThyDQoL, ThySRQ and ThyTSQ Questionnaires in Adequately Treated Hypothyroid Patients

Aysegul Atmaca*, Leman Tomak, Feyzi Gokosmanoglu, Ugur Avci, Ozan Pazvantoglu

Ondokuz Mayis University School of Medicine

PT02-02-30

Whether billewicz scoring method precisely predicts thyroid dysfunction in pregnant women? A population based cohort study.

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PT02-02-31

Taxonomic Profile of Gastroenterological Pathology in Patients with Autoimmune Thyroiditis at the Stage of Subclinical Hypothyroidism

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PT02-02-32

The prevalence and the role of BRAFV600E mutation in patients with papillary thyroid carcinoma in Greece, a former iodine deficient country

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PT02-02-34

The expression of neonatal Fc receptor in thyrocytes of Hashimoto's thyroiditis

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PT02-02-35

A Chinese woman with fifty-year-hyperthyroidism with coexistence of a novel TSHR gene and TBG gene mutations

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PT03-02-01

Carbohydrate intake is associated with higher apelin gene expression in visceral and subcutaneous adipose tissues

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PT03-02-02

The responses of anabolic, catabolic and appetite hormone on resistance exercise of various intensities

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Sahmyook University

PT03-02-04

Effect of long-term oral administration of sodium nitrate on obesity indices in female rats

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PT03-02-05

Adipose-specific deletion of Kif5b exacerbates high-fat-diet induced obesity and insulin resistance

Ju Cui[1], Jing Pang[1], Ya-Jun Lin[1], Huan Gong[1], Ping Jiang[1], Zai Wang[2], Zhen-He Wang[3], Yun-Xuan Li[3], Jin Li[1], Jian Li[1], Jian-Ping Cai[1], Jian-Dong Huang[4], Tie-Mei Zhang[1]

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PT03-02-06

Lessons from long–term effects of meal replacements as a weight loss strategy in Thai obese people: A 3-year follow-up study after "BeMo Fat FighterTM" weight loss program.

Haruethai Jaita[1,2], Panita Chaturawit[1,3], Phawinpon Chotwanvirat[2], Ekgaluck Wanothayaroj[3], Yotsapon Thewjitcharoen[3], Thep Himathongkam[3]

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PT03-02-07

FTO gene polymorphisms, dietary patterns and the risk of obesity in Tehranian adults

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PT03-02-08

Fibroblast Growth Factor 21 Associated with Obesity, Insulin Resistance, and Adipokines in Chinese Children and Teenagers: from the BCAMS Study

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PT03-02-09

Challenging sixty-two years of misinformation: the hCG+diet protocol for obesity treatment

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PT03-02-10

Effect of sleep extension on body weight, insulin levels and inflammation markers, under energy restriction in adolescents with obesity.

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PT03-02-11

Utility of DEXA and CT body fat analysis and endocrine correlates in profiling and therapy of type 2 diabetes in Asian Indians

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7. DISHA DOSTI Program
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PT03-02-12

Trend of obesity in 10 years of follow-up among Tehranian children and adolescent: Tehran Lipid and Glucose Study (TLGS)

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PT03-02-13

Accuracy of body composition for identifying cardiovascular risk factors in Tehranian population: Tehran lipid and Glucose Study

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PT03-02-14

Different obesity phenotypes and cardiovascular risks: Tehran Lipid and Glucose study (TLGS)

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PT03-02-15

Abdominal obesity phenotypes and risk of Type 2 Diabetes over 12 years of follow-up: The Tehran Lipid and Glucose Study

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PT03-02-16

Risk of all-cause mortality in abdominal obesity phenotypes: Tehran Lipid and Glucose Study

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PT03-02-17

Insulin increases the expression of the genes associated with glycoprotein 130 signaling in human skeletal muscle

and this effect is reversed by free fatty acids

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PT03-02-18

Subcutaneous adipose tissue circadian genes NR1D2 and DBP expression is associated with obesity, insulin action and increases after weight loss in humans

Monika Karczewska-Kupczewska[1,2*], Natalia Matulewicz[2], Magdalena Stefanowicz[2], Agnieszka Nikolajuk[1], Radoslaw Majewski[1], Remigiusz Filarski[1], Marek Straczkowski[1,2]

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PT03-02-19

Incidence of obesity and its predictors in children and adolescents in 10 years of follow up: Tehran Lipid and glucose Study (TLGS)

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PT03-02-20

Comparative analysis of local CDC and IOTF criteria for detecting cardiovascular risk factors in Tehranian children

Maryam Barzain, Sara Serahati, Farhad Hosseinpanah[*], Sorena Keihani, Majid Valizadeh, Fereidoun Azizi

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PT03-02-21

Incorporation of anthropometric measures into the Framingham risk score for prediction of CHD: Tehran Lipid and Glucose Study

Maryam Barzain, Golaleh Asghari, Farhad Hosseinpanah[*], Majid Valizadeh, Fereidoun Azizi

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PT03-02-22

p53-upregulated-modulator-of-apoptosis (PUMA) deficiency affects food intake, adipocyte size and leptin levels in diet-induced obesity.

Esteban Gurzov, Sara Litwak, Kim Loh, Evan Pappas, Jibran Wali, Helen Thomas

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PT03-02-23

Effect of Roux-en Y gastric bypass operation on glycemic control in type 2 diabetic patients

Fatih Sumer[1], Ibrahim Sahin[2], Sedat Cetin[2], Lale Gonenir Erbay[3], Aygun Guven[2], Asim Onur[1], Cuneyt Kayaalp[1]

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PT03-02-24

The effects of Ramadan fasting on energy expenditure in healthy non-obese individuals

Ilham Saadane[1], John Speakman JR[1], Catherine Hambly[1], Nicholas Finer[3], Nader Lessan[1], Maha Barakat[1]

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PT03-02-25

The Effect of Excessive Body Mass on The Footprint of Children Aged 8 – 10 Years.

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PT03-02-26

Long-term glucose metabolism, insulin resistance and adipokines changes in the morbildy obese individuals after laporascopic adjustable gastric banding surgery

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PT03-02-27

A new idea for weight loss in morbidly obese toddlers (A case report)

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PT03-02-28

Hypertriglyceridemic Waist Phenotype and Cancer

Maryam Zarif Yeganeh[1,2], Farhad Hosseinpanah[2*], Mitra Atifeh[2], Sara Serahati[2], Golaleh Asghari[3], Jaleh Tahmasebi[4], Parvin Mirmiran[3], Fereidoun Azizi[4]

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PT04-02-01

Extensive polyostotic fibrous dysplasia of right lower limb: a case report and literature review

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PT04-02-02

Recurrent diabetic muscle infarction: a rare complication of advanced diabetes mellitus

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PT04-02-03

Optic Disc Swelling Due to Diabetic Papillopathy as an Ocular Complication of Type 2 DIabetes Mellitus : a Case Study

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PT04-02-04

An Unusual Case of Hyponatremia from Primary Hypothyroidism secondary to Metastatic Lung Adenocarcinoma to the Thyroid: A Review of Incidence and Complications

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PT04-02-05

Unusual association of Parathyroid Adenoma and Metastatic Mediastinal Atypical Carcinoid.

Zareen Kiran*, Asma Ahmed, Saira Fatima, Faizan Malik, Owais Rashid, Saulat Fatimi, Mubasher Ikram

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PT04-02-06

A RARE CAUSE OF OSTEOPOROSIS: LYSINURIC PROTEIN INTOLERANCE

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PT04-02-07

A rare advers effect of insulin analogues: allergic skin reaction

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PT04-02-08

A Compelling Case of Thyroid Cancer: SETTLE or synovial sarcoma?

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PT04-02-09

A rare presentation of Schmidt syndrome: starting simultaneously with hypothyroidism and Adrenal insufficiency

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PT04-02-10

Clinical analysis of 195 cases of renal tubular acidosis

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PT04-02-11

A rare complication of imatinib altered metabolic homeostasis - A case report

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PT04-02-12

Importance of investigation of secondary causes in diabetic patients with unregulated glycemia despite intensive antidiabetic therapy: a case report

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PT04-02-13

A CASE REPORT OF LADA PRESENTING WITH DIABETIC KETOACIDOSIS AT OLDER AGE

Seyid Ahmet Ay*, Kamil Ba?k?y, ?brahim ?etinda?l?, Ferhat Deniz, Aynur Y?ld?r?m, Arif Yonem

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PT04-02-14

A steadi increase of chromogranin A without the evidence of a neuroendocrine tumor

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PT04-02-15

Insulin Glargine Dosing every 16 Hours for a Complicated Type I Diabetic Case

Amal Khan, Khaled Alswat*

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PT04-02-16

An AIP-positive R304X man with genetically and histologically distinct synchronous GH-secreting adenomas

Nisa Sheriff[1,2*], Mark McCabe[1,3], Raha Madadi Ghahan[4], Sunita MC De Sousa[1,5], Tanya Thomson[1], Jesper Maag[3], Mark Winder[6], Richard Harvey[7], Peter Earls[4], Ann I McCormack[1,2]

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PT04-02-17

Dual development of acute onset type 1 diabetes and Hashimoto thyroiditis: A case of autoimmune polyglandular syndrome type 3 variant with typical HLA haplotype.

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PT05-02-01

Impact of metabolic syndrome on long term prognosis and recurrence of acute ischemic stroke

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PT05-02-02

Risk Factors for coronary heart disease incidence as estimated using the Survival Tree analysis

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PT05-02-03

Incidence and Risk of Dyslipidemia in Middle-aged and Elderly Population: A Three-year Follow-up Study

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PT05-02-04

Dietary patterns, CCND2 gene variation and the risk of metabolic syndrome: Gene-diet interaction analysis in Tehranian population

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PT05-02-05

Dietary aromatic amino acids and increased risk of hypertension: Tehran Lipid and Glucose Study

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PT05-02-06

The effect of dietary advanced glycation end-products consumption on lipid profile

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PT05-02-07

The short- and long-term effects of a community-based multidisciplinary lifestyle intervention on metabolic syndrome and its components in an Eastern-Mediterranean adolescent population: Findings of a decade follow-up

Parisa Amiri, Sara Jalali-Farahani, Hasti Masihay Akbar, Leila Cheraghi, Davood Khalili, Amirabbas Momenan, Parvin Mirmiran, Arash Ghanbarian, Mehdi Hedayati, Fereidoun Azizi

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PT05-02-08

Association of telomere length in adults with birthweight and early catch up growth: data from "the New Delhi Birth Cohort (NDBC)

Mohamad Tarik[1], Ramakrishnan Lakshmy[1], Sikha Sinha[2], Harshpal S. Sachdev[2], Nikhil Tandon[3], Ambuj Roy[4], Santosh Bhargava[5], Bhaskar Singh[5], NDBC [1,2,5]

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PT05-02-09

Dietary Approaches to Stop Hypertension is associated with incident chronic kidney disease in patients with high blood pressure

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PT05-02-10

Association of birthweight with cellular senescence in adults: data from New Delhi Birth Cohort

Ramakrishnan Lakshmy[1], Mohamad Tarik[1], Sikha Sinha[2], Harshpal S. Sachdev[2], Nikhil Tandon[3], Ambuj Roy[4], Bhaskar Singh[5], Santosh Bhargava[5], NDBC [1,2,5]

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PT05-02-11

Efficacy and safety of glucagon-like peptide-1 receptor agonists in non-alcoholic fatty liver disease: A systematic review and meta-analysis

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PT05-02-12

Higher branched chain amino acid intake is associated with higher incidence of hypertension: Tehran Lipid and Glucose Study

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PT05-02-13

Risk factors for ischemic stroke; a 12 year follow-up of participants in the Tehran Lipid and Glucose Study

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PT05-02-14

Astragaloside IV attenuates lipid accumulation via AMPK activation in HepG2 cells

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PT06-02-01

Screening and identification of a novel hTERT-interacting protein

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PT06-02-02

Radionuclide Parathyroid Imaging to Assist in Diagnosis of Parathyroid Crisis in 1 Case and Literature Review

Qingyao Zuo, Fang Yang, Zhixin Wang, Xue Zhan, Nan Bai, Baoyue Liu, Wei Deng

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PT06-02-03

Resveratrol prevents osteoporosis via up-regulating the FoxO1 transcriptional activity

Yanling Feng, Xiaotong Jiang, Fangfang Ma, Jie Han, Xulei Tang

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PT06-02-04

Selenium levels in postmenopausal osteopenic females

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PT06-02-05

Bone Mineral and related Endocrine disorders in Adult Patients of E-Beta Thalassemia

Sujoy Ghosh, Paramita Chowdhury, Rana Bhattacharjee, Pradip Mukhopadhyay, Satinath Mukhopadhyay, Maitrayee Bhattacharya, Subhankar Chowdhury

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PT06-02-06

Profile of bone health in postmenopausal Asian Indian women: Community based Bone Mineral Density [BMD] and radiographic Vertebral Fracture Assessment [VFA].

Akshaya Hegde[1], Rajeshwari A[4], Owais Haqq[9], Ashwini KJ[2], Vibha Ashish Rao[5], Marimuttu B[9], Geetha Rao[9], Uma Dayashanker[2], Chandraprabha s[5], Pushpa Ravikumar[3], Kamala T[6], Reshma Harsha[9], Lakshmi Reddy[6], Sumati M[4], Babitha Thyagaraj[8], Muralidhara CS[8], Vasanthi Nath[7], Tejaswini Deepak[6], Sharda A[4], Srikanta S[9]

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PT06-02-07

Drug Induced Fanconis Syndrome and Metabolic Bone Dis-

ease (Hypophosphatemic Osteomalacia) due to Nucleotide Reverse Transcriptase Inhibitors: Need for Increased awareness and Prospective Surveillance

Vibha Ashish Rao[1], Owais Haqq[8], Akshaya Hegde[9], Ashwini Kj[10], Marimuthu B[9], Rajeshwari Ashok[5], Geetha Rao[10], Usha Rangaraj[9], Mahalakshmi H[2], Kamala T[7], Vasanthi Nath[3], Lakshmi Reddy[6], Reshma Harsha[8], Babitha Devi T[2], Chandrika Km[6], Chandraprabha S[10], Sumathi M[5], Tejeswini D[6], Sharda A[5], Srikanta S[10]

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PT06-02-08

Tumor resection versus medical therapy on bone mineral density in tumor induced osteomalacia patients

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PT07-02-01

Clinical Characteristics in 128 Hospitalized Patients with the Syndrome of Inappropriate Antidiuretic

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PT07-02-02

Clinical characteristic analysis of 114 cases of pituitary stalk interruption syndrome

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PT07-02-03

Exercise improves the success rate of fertility and secondary sex characteristics in idiopathic hypogonadotropic hypogonadism after hormone replacement therapy

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PT07-02-04

Misdiagnosis analysis to 96 cases with pituitary stalk interruption syndrome

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PT07-02-05

The Beneficial effect of vasopression on the patients with hypernatremia post operation of space-occupying lesions in the sellar area

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PT07-02-06

Octreotide normalize hypercalcemia in patient with an acromegaly.

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PT07-02-07

Spectrum of water and electrolyte imbalance after sellar, suprasellar and parasellar surgery

Zareen Kiran*, Aisha Sheikh, Sehrish Nizar, Safia Awan, Owais Rashid, Najmul Islam

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PT07-02-08

The regulatory effect and mechanism of leukemia related protein 16 (LRP16) on estrogen-induced pituitary prolactinoma in C57BL mice

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PT08-02-01

Evaluation of the 1mg dexamethasone suppression test in the diagnosis of the subclinical Cushing's syndrome in patient with Adrenal Incidentaloma

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PT08-02-02

Evaluation of plasma aldosterone-to-active-renin ratio in combination with aldosterone concenration in the diagnosis of aldosteronma

Jie Zhu, Nan Jin, Li Zang, Weijun Gu, Guoqing Yang, Lijuan Yang, Qing-

hua Guo, Xianling Wang, Zhaohui Lv, Jianming Ba, Jingtao Dou, Yiming Mu

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PT08-02-03

Effect of sex on the use of ARR for the screening of aldosterone

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PT08-02-04

Higher screening aldosterone to renin ratio in primary aldosteronism patients with diabetes mellitus

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PT08-02-05

Long Non-coding RNA Plays a Role in Aldosterone-producing Adenoma through PCP4

Jiachao Chen, Jing Cheng, Yu Luo, Fei Leng, Fang Li, Gulibositan Aji, Chen Chen, Zhiqiang Lu*

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PT08-02-06

Addisons disease and pregnancy: Severe intrapartum hypotension due to cerebellar tonsillar herniation, but not Addisonian crisis.

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6. Shanthi Hospital and Research Center
7. DISHA DOSTI Program
8. Surana Preventive Diabetology Center
9. Jnana Sanjeevini Diabetes Hospital and Medical Center

PT09-02-01

Obsessive-Compulsive Disorder in general hospital OGTT outpatients:prevalence, correlates and comorbidity in Lanzhou, China

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PT09-02-03

A case-series study to explore the efficacy of short-term preoperative octreotide in treating TSH-secreting pituitary adenomas

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PT09-02-04

Synchronous activation of gonadotropin-reeleasing hormone (GnRH) gene transcription and secretion by pulsatile kisspeptin stimulation

Kyungjin Kim, Han Kyoung Choe, Jeongah Kim, Doyeon Kim

Daegu Gyeongbuk Institute of Science and Technology (DGIST) and Korea Brain Research Institute (KBRI

PT09-02-05

Synchronous activation of gonadotropin-reeleasing hormone (GnRH) gene transcription and secretion by pulsatile kisspeptin stimulation

Kyungjin Kim, Han Kyoung Choe, Jeongah Kim, Doyeon Kim

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PT10-02-01

Differential DNA methylation patterns of polycystic ovarian syndrome in whole blood of Chinese women

Shuxia Li[1,1,1], Dongyi Zhu[2], Hongmei Duan[3*], Dorte Glintborg[4], Marianne Andersen[4], Mads Thomassen[1], Torben Kruse[1], Qihua Tan[1,5]

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PT10-02-02

Liraglutide activates the phosphorylation of PI3K/ Akt / FoxO1 pathway in ovaries of polycystic ovary syndrome

Haiyan Yang, Xinhong Lu, Zhenxing Huang, Ruyin Tan, Li Li, Xinghuan Liang, Yingfen Qin, Zuojie Luo

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PT10-02-03

Serum levels of fibronectin in obese and non-obese women with polycystic ovary syndrome.

Liliya Mogylnytska

Khmelnytsky regional hospital

PT10-02-04

Silent coronary artery disease and ovarian reserve status: a longitudinal study

Seyed Ali Montazeri, Fereidoun Azizi, Fahimeh Ramezani Tehrani*

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PT10-02-05

Effect of intramuscular administration of dexamethasone on the duration of labor

Kashanian Maryam*, Fattaneh Mokhtari

Iran University of Medical Sciences

PT10-02-06

Occult Breast Cancer: biology, diagnosis, potential treatment

Richard Santen

University of Virginia

PT11-02-01

Vitamin D and osteocalcin independently involve in glucose metabolism in type 2 diabetics: a cross-sectional study

Junlei Su[1], Bei Xu[1], Mingxin Xu[1], Jie Hao[1], Zhiyin Zhang[1], Ni Zhong[1], Ran Cui[1], Tienan Feng[2], Feng Li[1], Ge Zhang[3], Hui Sheng[1], Shen Qu[1]

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PT11-02-02

Primary hyperparathyroidism in children and adolescents

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PT11-02-03

STATUS OF VITAMIN D IN PATIENTS DIAGNOSED WITH DEPRESSION

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PT11-02-04

Increased Calcium Fractional Absorption from Synthetic Stable Amorphous Calcium Carbonate

Nachum Vaisman

Sourasky Medical Center

PT11-02-05

Clinical development of Amorphous Calcium Carbonate. New treatment concept for hypocalcemia associated hypoparathyroidism

Amorphical Amorphical

Amorphical

PT12-02-01

Changes in the reproductive Function of males by a daily exposure to the endocrine disruptor 3-methylcholanthrene.

Eric Rhon-Calderon*, Rocío Alejandra Galarza, Santiago Condemi, Alicia Graciela Faletti

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PT12-02-02

Assessment of oxidative stress in rat's brain by exposure of BPA

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PT12-02-03

Influence of Hubble Bubble Smoking on Glycemic Profile and Gluco-regulatory Hormones in Egyptian Healthy Subjects

Fahmy Amara[1*], Magdy Helmy Megalaa[1], Noha Gaber Amin[1], Mohamed Abdel Raauf[2], Mohamed Fahmy Amara[1]

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PT12-02-04

Bisphenol A promotes adiposity and inflammation in a non-monotonic dose- response way in five-week old male and female C57BL/6J mice fed a low-calorie diet

Minglan Yang, Maopei Chen, Jiqiu Wang, Min Xu, Jichao Sun, Lin Ding, Xiaofei Lv, Qinyun Ma, Yufang Bi, Ruixin Liu, Jie Hong, Guang Ning

Shanghai Rui-Jin Hospital, Shanghai Jiao-Tong University School of Medicine

PT12-02-05

Management of Hyponatraemia in Acute Hospital Admissions: Effect on Length of stay, Readmission and Mortality

Aditi Sharma*, Parizad Avari, Jasmeet Singh, Monica Anyasodor, Julia E Ostberg, Senan Devendra

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PT13-02-01

Plasma level of Omentin in patients with Medullary Thyroid Carcinoma

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PT13-02-02

Association between plasma Calcitonin level, mir323-a expression, and RET mutation in Medullary Thyroid Carcinoma

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PT13-02-03

Parathyroid Surgery – indications and outcome at a tertiary care hospital in a developing country

Hamdan Pasha, Moghira Siddiqui*

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PT13-02-04

Co-Culture of Human Peripheral Blood Lymphocytes from Patients with Polycystic Ovary Syndrome (PCOS) with Ovarian Tumor Cell Lines (SKOV3, A2780): Study of Their In-Vitro Immunological Interactions and Comparison to Healthy Women

Mehri Hajiaghayi[1], Fatemeh Rezayat[1], Nazanin Ghasemi[1], Mehrnaz Mesdaghi[1], Nariman Mossafa[1], Fahimeh Ramezani Tehrani[1]

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PT13-02-05

Expression of p27Kip1 and β-catenin in multiple endocrine neoplasia type 1 related parathyroid tumors

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PT14-02-01

Alterations of androgen receptor-regulated enhancer RNAs (eRNAs) contribute to enzalutamide resistance

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2. Mayo Clinic College of Medicine, Rochester, MN

PT14-02-02

Improvement of sexual function in POEMS syndrome after combination therapy of Lenalidomide and dexamethasone

Hongbo Yang, Xufei Huang, Qianqian Cai, Chen Wang, Xinxin Cao, Daobin Zhou, Jian Li

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PT14-02-03

Effects of phytosterol on the sexual behavior and testis function in the male Japanese quail

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PT14-02-04

The influence of the testosterone replacement therapy on the glycemic prandial control and oxidative status at the religious men with type 2 diabetes mellitus

Alexander Ametov, Ludmila Kamynina, Olga Rozhdestvenskaia

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PT15-02-01

Psychosocial profile, glycemic control and wellbeing in poverty associated type 1 diabetes mellitus adolescents in India

OWAIS HAQQ[1,6], Sanjana Malhotra[1,3,9], Rajiv K[1,2,3], Sunitha B[1,4,5], Muralidhar Krishna[1,9,7], Kamala T[1,2,3], Vasanthi Nath[1,3,2], Vibha Rao[1,8,7], Reshma Harsha[1,4,6], Akshaya Hegde[1,4,5], Mari Muthu[1,5,4], Owais Haqq[1,5,6], Ashwini KJ[1,2,3], Babitha Rani[3,5,7], Sharda A[4,8,7], Tejeswini Deepak[5,2,4], Chandrika KM[4,7,3], Chandraprabha P[3,7,8], Geetha Rao[7,3,5], S Srikanta[3,1,2]

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PT15-02-02

Poverty associated childhood diabetes in India: Complications, comorbidities and challenges

VIBHA ASHISH RAO[1], AKSHAYA HEGDE[9], ASHWINI KJ[9], OWAIS HAQQ[7], MARIMUTHU B[7], RAJESHWARI ASHOK[1], NANDINI JAYARAM[1], GEETHA RAO[7], UMA DAYASHANKHAR[3], USHA RANGARAJ[9], VASANTHALAKSHMI H K[9], KAMALA T[6], VASANTHI NATH[8], RESHMA HARSHA[8], CHANDRIKA KM[5], RAJEEV K[7], MURALIDHARA KRISHNA[7], TEJESWINI DEEPAK[5], SHARDA A[3], SRIKANTA S[9]

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PT15-02-03

Adipokine status of newborns borned from mothers with obesity and overweight

Veronika Prilutskaya*, Angelika Solntseva, Aleksei Sapotnickii, Elena Dashkevich

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PT15-02-04

Suboptimal cortisol response to ACTH stimulation test in Non-Classical Congenital Adrenal Hyperplasia (NCCAH)

Feneli Karachaliou[1*], Maria Kafetzi[2], Antonia Psina[2], Elpis Vlachopapathopoulou[1], Sofia Leka[1], Maria Drakopoulou[3], Antonia Kapella[1], Aspasia

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PT16-02-01

Caffeine intake antagonizes salt sensitive hypertension through improvement of renal sodium handling

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PT16-02-02

Diagnosis and Management of Ovotesticular Disorders of Sex Development (DSD)

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PT16-02-03

Risk Factors for Incidence of Cardiovascular Diseases and All-Cause Mortality in a Middle Eastern Population over a Decade Follow-up: Tehran Lipid and Glucose Study

Mahsa Sardarinia

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PT17-02-01

Thyroid Stimulating Hormone Increases Hepatic Gluconeogenesis via CRTC2

Yujie Li[1,2,3], Laicheng Wang[3], Lingyan Zhou[1], Yongfeng Song[1,2,2], Shizhan Ma[1,2,3], Chunxiao Yu[1,2,3], Jiajun Zhao[1,2,3], Chao Xu[1,2,3], Ling Gao[3]

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PT17-02-02

Anti-androgenic effects of phytosterol enriched refined extract of Brassica campestris L. pollen on benign prostatic hyperplasia (BPH) rat model

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PT18-02-01

Management of adrenal pheochromocytoma rupture by transcatheter arterial embolization: Case report

Naoki Edo[1], Takahiro Yamamoto[2], Hiroki Koyasu[3], Satoshi Takahashi[1], Yamato Mashimo[1], Masaki Kimura[3], Koji Morita[1], Koji Saito[4], Hiroshi Kondo[2], Yuko Sasajima[4], Fukuo Kondo[4], Hiroko Okinaga[1], Toshio Isikawa[1]

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PT18-02-02

Performance of plasma free metanephrines in the diagnosis of Pheochromocytomas and Paragangliomas

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PT19-02-01

Thyroid hormone suppresses hepatocarcinogenesis via DAPK2 and SQSTM1 dependent selective autophagy

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September 3, 2016

Setup Time: September 3, 2016 09:00-10:00
Poster Discussion Time: September 3, 2016 13:00-14:00
Poster Removal Time: September 3, 2016 17:00-17:30

PT01-03-01

Community Diabetes Care Physician Manpower Development: Experiences from India's largest Regional Center

ASHWINI K J, Akshaya Hegde, Vibha Ashish Rao, Marimuttu B, Rajesshwari A, Owais Haqq, Nandini jayaram, Chitra MDC, Murali M, Chandrika Km, Lakshmi Reddy, Vasanthi Nath, Reshma Harsha, Babitha Thyagaraj, Sumathi M, kamala T, Chandraprabha S, Tejaswini Deepak, Sharada A, Srikanta S

SCIENCE FOR HEALTH

PT01-03-02

Observational study of the incidence of hypoglycaemia among insulin-treated patients with diabetes in Singapore

Yong Mong Bee[1*], Ngiap Chuan Tan [2], Rinkoo Dalan [3], Arvind Gadekar [4], Eric Yin-Hao Khoo [5,6], Shweta Uppal [7], Su-Yen Goh [1]

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PT01-03-03

Ramadan with hot and long light days - the main principles of the safety at the patients with type 2 diabetes mellitus

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PT01-03-04

Focused Point Prevalence Survey at?a Specialist Clinic in Kathmandu, Nepal – Identifying Level of Clinical Inertia.?

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Norvic International Hospital

PT01-03-05

Glycemic control in established Type 2 diabetes mellitus at tertiary care centre

Dina Shrestha

Norvic International Hospital

PT01-03-07

Validation of FINDRISC Questionnaire as a Screening Tool for Diabetes and Pre-Diabetes in the Outpatient Department of Medicine of St. Lukes Medical Center-Quezon City: A Cross-Sectional Study

Annabel Mata[1*], Armin Masbang[2], Katherine Rose Acosta Acosta[2], Dianne Shari Cabrera[2], Dianne Katherine Joy Closa[2], Mel Valerie Cruz[2], Jhobeleen De Leon[2], Ma. Marylaine Dujunco[2], June Hayrelle Gorriceta[2], Rowena Inocencio[2], Rosella Lacsamana[2], Sheila Marie Reyes[2], Rachell Ann Siute[2], Jose Maria Angbengco[2], Reynaldo Rosales[1]

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PT01-03-08

The Curret status of blood glucose control and related factors of type 2 diabetes in Anshan

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PT01-03-09

PREDICTORS OF INSULIN RESISTANCE: SEX MATTERS.

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PT01-03-10

Does Diabetes Influence Clinical Outcomes and Mortality in Mechanically-ventilated Critically Ill Patients?

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PT01-03-11

Sphingosine-1-phosphate (S1P) stimulates insulin secretion via S1PR2/KV channel pathway in Rat Islets

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PT01-03-12

Intraplatelet Cations and Ultra-structural Changes in Platelets from Qatari and Asian Indian Type 2 Diabetics

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PT01-03-13

Diabetes Management and Thyroid Function Influences on Pregnancy and Birth outcomes

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PT01-03-14

Metabolic control in patients with type 1 or type 2 diabetes mellitus associated with depression

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PT01-03-15

Establish prediction model for type 2 diabetes by combining with obesity,MS and WBC

Jingjing Tian, Chi Zhang, Ying Liu

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PT01-03-16

An Audit of In-Patient Management of Diabetic Ketoacidosis: Is treatment-induced hypoglycaemia a mere bystander or byproduct?

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PT01-03-17

The association of the PAX4 gene R192H polymorphisms in Chinese Han type 2 diabetes

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PT01-03-18

Fasting plasma glucose change and incident type2 diabetes mellitus in Iranian men and women: a 6 years follow-up study

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PT01-03-19

Study on the Association between Medication Adherence Combined with Self-management Behaviors and Glycemic Control among Patients with Diabetes in Community

Xuxi Zhang[1], Kaige Sun[1], Shiyan Wu[1], Shuaishuai Yang[1], Sijia Liu[2], Weilan Jian[2], Chunxin Shao[2], Xinying Sun[1*]

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PT01-03-20

Association between soluble CD14 and cytokeratin 18 suggest role of gut barrier dysfunction in liver injury in type 2 diabetes mellitus

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PT01-03-21

A novel approach to determine potential predictors of diabetes among pre-diabetic women: a population-based cohort study

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PT01-03-22

Incorporating clinical consequences to screen for pre-diabetes: a cost sensitive cut-off for fasting plasma glucose

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PT01-03-23

IRS-2 partially compensates for the defects of insulin signaling pathway in IRS-1 deficient mice mediated by miR-33

Chen-Yi Tang[1], Xiao-Fei Man[1], Yue Guo[1], Hao-Neng Tang[1], Jun Tang[1], Ci-La Zhou[1], Shu-Wen Tan[1], Min Wang[2], Hou-De Zhou[1]

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PT01-03-24

Mandatory need of screening for mental health disorders in Diabetes Clinics: Potential for improved diabetes and health outcomes

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PT01-03-25

Risk of development of diabetes mellitus in hepatitis C patients : a systematic review and meta-analysis

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PT01-03-26

ASSESSMENT OF CIRCULATING ENDOTHELIUM-DERIVED MICROVESICLES (EMV) IN TYPE 2 DIABETIC PATIENTS: EFFECTS OF LIRAGLUTIDE AND GLICLAZIDE TREATMENT

Maria Pompea Antonia Baldassarre, Pamela Di Tomo, Paola Lanuti, Fabrizio Febo, Assunta Pandolfi, Agostino Consoli, Gloria Formoso

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PT01-03-27

Diabetic ketoacidosis in type 2 diabetic patients, a hospital based study Characteristics & differences, type 1 vs type 2

Muhammad Rashid, Aisha Sheikh, Abdus Salam, Unaib Rabbani, Zareen Kiran, Najmul Islam

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PT01-03-28

Does HDL-C have a U-shape relationship with diabetes mellitus? An analysis from a cohort study

Nan Zhang, Xiang Hu, Tianshu Zeng, Jiaoyue Zhang, Jie Min, Shenghua Tian, Miaomiao Peng, Limin Wan, Qiulan Huang, Jingqi Zhou, Lulu Chen

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PT01-03-29

Bromocriptine: An orphan grossly underutilized and neglected diabetes medication with cardiovascular benefits?

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PT01-03-30

Places of worship as fertile locations for community diabetes awareness and screening: "One day at the gates of a temple":

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PT01-03-31

Prevalence and control of high blood pressure among Iranian patients with type 2 diabetes: The National Survey of Risk Factors for Non-communicable Diseases

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PT01-03-32

Changing pattern of lipid lowering and antihypertensive medication use and control among type 2 diabetes patients in a decade follow up: Tehran Lipid and Glucose Study

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PT01-03-33

GLP-1R agonists ameliorate peripheral nerve dysfunction and inflammation via p38MAPK/NF-kB signaling pathways in streptozotocin-induced diabetic rats

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PT01-03-34

Personality types and glycaemic parameters in type 2 diabetic patients

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PT01-03-36

Assessment of erectile dysfunction and associated psychological distress in Chinese men with type 2 diabetes mellitus

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PT01-03-37

Effects of Bariatric Surgery on Glucose Control, Weight Reduction and Disease Remission among Patients with Type 2 Diabetes Mellitus: Systematic Review and Meta-Analysis

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PT01-03-38

Carriers of positive hepatitis B viral surface antibody is associated with lower risk of metabolic syndrome

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PT01-03-39

Effects of pre-diabetes mellitus alone or plus hypertension on cardiovascular diseases: Tehran Lipid and Glucose Study

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PT01-03-40

Lower level of serum bilirubin is associated with incidence of metabolic syndrome during five years of follow-up

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PT01-03-41

Relationship between Home Blood Pressure Variability and Renal Clearance of Uric Acid in Patients with Diabetic Nephropathy

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PT01-03-42

Management of Overweight and Obese Inpatients with Type 2 Diabetes Mellitus —Shift of Therapeutic Target from Blood Glucose Normalization to Bodyweight Control

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PT01-03-43

Outcome of diabetic inpatient admissions in a Nigerian tertiary hospital

Bolanle Okunowo*, Ifedayo Odeniyi, Sandra Iwuala, Olufemi Fasanmade, Augustine Ohwovoriole

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PT01-03-44

CLINICAL CHARACTERISTICS OF LATENT AUTOIMMUNE DIABETES IN ADULTS

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PT01-03-45

SILENCING ANGIOTENSIN II TYPE 1 RECEPTOR TO EXPLORE THE INFLUENCE AND MECHANISM OF IRBESARTAN ON APOPTOSIS INDUCED BY STZ IN NIT-1 CELLS

Liwen Mo, Decheng Lu, Xinghuan Liang, Li Li, Jingwei Cai, Zuojie Luo

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PT01-03-46

Stastical analysis of CSII in perioperative type 2 diabetes

AIRONG CHEN, YAO MEN

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PT01-03-47

Effect of dipeptidyl peptidase-4 inhibitor sitagliptin on blood glucose and β-cell function of type 2 diabetes patients in different diabetes duration.

XIUPING BAI

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PT01-03-48

The profile of blood glucose, islet area, and muscle insulin receptor expression in rat models of type 2 diabetes mellitus

Rimbun Rimbun, Dewi Ratna Sari, Tri Hartini Yuliawati, Harjanto JM, Ari Gunawan

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PT01-03-49

Frequency Of Obstructive Sleep Apnea In Patients With Diabetes Mellitus

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PT01-03-50

Relationship of self-monitoring of blood glucose with glycemic control among patients attending a tertiary care hospital

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PT01-03-51

Diabetes mellitus- one disease, many names

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PT01-03-52

DKA in type 2 diabetics: Precipitating factors and changing patterns in mortality in a tertiary care hospital in Pakistan.

Owais Rashid, Aisha Sheikh, Saad Farooq, Hashaam Arshad, Najmul Islam

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PT01-03-53

Screening and diagnosis of type 2 diabetes with glycated haemoglobin (HbA1c) in adult Nigerians.

Mansur Aliyu RAMALAN

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PT01-03-54

Cardiometabolic mortality rate across countries is more dependent on the prevalence of diabetes in men than on this prevalence in women: An ecological study

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PT01-03-55

Risk of diabetic foot syndrome in patients during implementation of new national protocol in diabetes management

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PT01-03-56

EFFECT OF METFORMIN THERAPY ON CIRCULATING SFRP5 LEVELS IN PATIENTS WITH TYPE 2 DIABETES

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PT01-03-57

Awareness and Dietary Habits About Salt Consumption in Type 2 Diabetic Patients

Aysegul Atmaca

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PT01-03-58

A new approach to metabolic syndrome components using Latent Class Analysis (LCA): Dysglycemia apart from other components

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PT01-03-59

The number needed to treat for intensive statin therapy in diabetic men and women according to 2013 ACC/AHA guideline

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PT01-03-60

Gastric Bypass vs Medical/Lifestyle Care for Type 2 Diabetes in South Asians with BMI 25-40 kg/m2: the COSMID Randomized Trial

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PT01-03-61

DETERMINANTS OF INHERITANCE OF DIABETES MELLITUS AMONG NIGERIANS

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PT01-03-62

Effect of CYP2C9 and OCT polymorphisms on metformin and sulphonylureas therapy in mexican diabetic patients

María Guadalupe Ortiz-Lopez[1*], Katy Sanchez-Pozos[2], Joel Jaimes-Santoyo[1], Carolina Rivera-Santiago[2], Bárbara Itzel Pe?a-Espinoza[4], María de los ángeles Granados-Silvestre[1], Marta Menjivar[2,4,4]

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PT01-03-63

R230C of ABCA1 is associated with metabolic syndrome in Mexican Maya children

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PT01-03-64

Clinical utility of coronary artery calcium [CAC] scores as good markers of preclinical atherosclerosis and need for aggressive therapy in diabetes

VIBHA ASHISH RAO[1], Akshaya Hegde[8], ASHWINI K J[1], MARIMUTHU B[8], OWAIS HAQQ[8], RAJESHWARI ASHOK[4], BabithaDevi T[10], Geetha Rao[2], Nandini Jayaram[8], Reshma Harsha[4], Vasanthi Nath[2], Kamala T[7], Chandraprabha S[1], Pushpa Ravikumar[6], Lakshmi Reddy[10], Sumathi M[5], Chandrika KM[1], Tejeswini D[5], Sharda A[7], Srikanta S[1]

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PT01-03-65

Type 2 Diabetes and coexistent Cardiovascular disease: Profile and trends of renal dysfunction and medication dosing

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PT01-03-66

Antidiabetic Effect and Mechanism of BDDE

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PT01-03-67

The Evaluation for the Pilot Chinese Gestational Diabetes Group Education Program (Oct 2015 – April 2016)

Shannon Lin

Diabetes NSW

PT01-03-68

Toll like receptors 2 and 9 (TLR2 & TLR9) gene polymorphism in type 2 diabetic patients with diabetic foot

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PT01-03-69

Identification of plasma vascular endothelia-cadherin as a biomarker for coronary artery disease in Type 2 diabetes mellitus patients

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PT01-03-70

Pressure Pain Perception Research in Diabetes Patients

Xiaoqiang Hu, quanmin Li, Lin Li, Wenjun Li, Xia Li

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PT01-03-71

Study of the diagnostic efficacy of current perception threshold and different common scales for diabetic peripheral neuropathy

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PT01-03-72

Angiotensin -regulated miR-375 targets Mapkap1 gene in MIN6 cells

Lin Cheng, Mingtong Xu, Yan Wan, Xiaofang Pan, Xiaoyun Chen, Xiaoyun Wang, Meng Ren, Yan Li, Li Yan

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PT01-03-73

Association of osteoprotegerin with impaired glucose regulation and microalbuminuria

Niu Yixin, Yang Zhen, Li Xiaoyong, Zhang Weiwei, Zhang Hongmei, Zhu Lingfei, Qin Li, Su Qing

Association of osteoprotegerin with impaired glucose regulation and microalbuminuria

PT01-03-74

Plasma osteoprotegerin levels are inversely associated with nonalcoholic fatty liver disease in patients with type 2 diabetes: A case-control study in China.

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PT01-03-75

Association of plasma osteoprotegerin levels with the severity of lower extremity arterial disease in patients with type 2 diabetes

Niu Yixin, Zhang Weiwei, Yang Zhen, Li Xiaoyong, Zhang Hongmei, Fang Wenjun, Qin Li, Qing Su

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PT01-03-76

DPP-4 Inhibitors Reduce the Level of IL-6 and TNF-α in Association with Decreased CD26 Positive T Lymphocytes and TLR4 Positive Monocytes

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PT01-03-77

The comparision of different screening methods in diagnosing diabetic peripheral neuropathy by receriver operating characteristic curve

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PT01-03-78

Rapid diagnosis of bacterial pathogens based on 16S rRNA Next-Generation Sequencing: A comparison of bacterial composition in diabetic foot wounds and contralateral intact skin.

Ying Huang, Ying Cao, Mengchen Zou, Xiangrong Luo, Ya Jiang, Yaoming Xue, Fang Gao

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PT01-03-79

Analysis of Biomechanical characteristics to 303 patients with type 2 diabetes

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PT01-03-80

Dipeptidyl peptidase-4 inhibitor impact the expression of Bcl-2 and Bax through γamino acid bwtyric acid in pancreas islet

YING DONG, QIANG LI

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PT01-03-81

Effects of GLP-1 on the expression of microRNAs and genes associated with pancreatitis and apoptosis

Chang Guo, Qiang Li

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PT01-03-82

The effect of GLP-1 on the content of intracellular NMN and NAD and the insulin secretion of INS-1

Dapeng Wang, Qiang Li

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PT01-03-83

The Effects of Incretin on the Expression of RBP4 in Liver of Diabetic Fatty Model Rats

Yue Yao, Qiang Li

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PT01-03-84

MicroRNA-34a contributes to the protective effects of glucagon-like peptide-1 against lipotoxicity in INS-1 cells

Minnan Wang, Qiang Li

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PT01-03-85

Association of The Dynamic Changes of Sedentary Behavior with The Outcome of Normal Glucose Tolerance after Three Years

Hui Xue, Qiang LI

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PT01-03-86

A clinical research of the change of insulin sensitivity and β-cell function in a patient with Prader-Willi syndrome and type 2 diabetes mellitus after Laparoscopic Sleeve Gastrectomy

Lili Jiang, bin yao, yanhua zhu, xubin yang, jinhua yan, wen xu

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PT01-03-87

The Effect of Caveolin-1 on the Process of Proliferation and Apoptosis and Function Regulation in Beta Cell

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PT01-03-88

Revascularization and changes of angiogenesis gene of transplantation of endothelial progenitor cells for hindlimb ischemia in diabetic rabbit model

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PT01-03-89

The effect of glucagon-like peptide-1 to reduce high and fluctuant glucose induced paotosis in INS-1 cells

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PT02-03-01

Comparison of various schemes of the reduction period of the treatment programs of ATD oral-taking of Graves, A multicenter randomized study

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PT02-03-02

Sub Clinical Hypothyroidism In Pregnant Women Visiting Antenatal Clinic Of Trivuwan University Teaching Hospital, Kathmandu: A Cross Section Study From Nepal; An Endemic Of Iodine Deficiency

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PT02-03-03

IGF-1R, CD34 and FOXP3, PPAR-γ expression in the orbital fat/connective tissue of patients with mild and severe Graves orbitopathy

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PT02-03-04

Pharmacological effects of 3-iodothyronamine (T1AM) and 3-iodothyroacetic acid (T1A) reveal a novel pathway connecting the thyroid with the histaminergic system

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PT02-03-05

Hypovitaminosis D - a Key player in Gestational Hypothyroidism??

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PT02-03-06

Circulating microRNA Predicts Insensitivity to Glucocorticoid Therapy in Graves' Ophthalmopathy

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PT02-03-07

Association of serum growth differentiation factor 15 levels and thyroid nodules in Chinese middle-aged and elderly individuals

Zhang Hongmei, Yang Zhen, Zhang Weiwei, Niu Yixin, Li Xiaoyong, Qin Li, Su Qing

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PT02-03-08

Higher serum osteoprotegerin levels in subjects with thyroid nodules

Zhang Hongmei, Yang Zhen, Zhang Weiwei, Niu Yixin, Li Xiaoyong, Qin Li, Su Qing

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PT02-03-09

Perinatal hypothyroidism modulates antioxidant defence status in the developing rat liver and heart

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PT02-03-10

A SMALL MOLECULE WHICH BLOCKS TSH RECEPTOR SIGNALING

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Icahn school of medicine at Mount Sinai

PT02-03-11

Role of Thyroglobulin in the follow up of the differentiated thyroid cancer in Albania

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PT02-03-12

Effect of fetal hypothyroidism on uterine smooth muscle contractions induced by carbachol and oxytocin in rat

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PT02-03-13

Changes in arterial structure and hemodynamic parameters of adult male rat with fetal hypothyroidism

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PT02-03-14

Chronic thyroiditis: a cross-sectional study in subjects already confirmed with the diagnosis

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PT02-03-15

The association between smoking status and thyroid function tests in Tehran Thyroid Study

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PT02-03-16

Analysis of diagnosis and treatment of Hurthle cell tumor

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PT02-03-17

Clinical manifestations and diagnostic difficulties of children and adolescents with Hashimoto thyroiditis: report and review of three cases

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PT02-03-18

The Pathognomonic Thyroid Phenotype of SBP2 Deficiency Is Replicated in a Mouse Model

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PT02-03-19

Consequences of Iodine on Extrathyronine Tissues

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PT02-03-20

Neuroendocrine tumor metastatic to preexisting thyroid nodules

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PT02-03-21

Ultrasound guided fine needle aspiration biopsy of thyroid nodule, what is the expected cost to arrive at a diagnosis of malignancy, a descriptive study.

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PT02-03-22

MiR-21 and MiR-181b in association with BRAFV600E mutation and clinicopathological features of papillary thyroid cancer

Guanghui Yang, Kui Che, Xiaolong Yu, Xu Hou, Yangang Wang, Shihua Zhao

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PT02-03-23

The role of thyroid hormone receptors in neurodevelopment and its relation to iodine intake

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PT02-03-24

Vildagliptin increased anaplastic thyroid cancer cell survival via inhibition of CD26 and activation of CD9

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PT02-03-25

The effects of hydroxychloroquine on thyroid function and anti-thyroid autoantibodies in subjects with Hashimoto's thyroiditis

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PT02-03-26

Role of Thyrotropin-Releasing Hormone (TRH) in Cold-Induced Adaptive Thermogenesis in Mouse.

Atsushi Ozawa*, Takuya Watanabe, Takuya Tomaru, Sumiyasu Ishii,

Nobuyuki Shibusawa, Shuichi Okada, Masatomo Mori, Tetsurou Satoh, Masanobu Yamada

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PT02-03-27

Effect of MiRNA-130a on the Biological Behavior of papillary thyroid carcinoma cells

Ping Wang, Zhaohai Jing, Guanghui Yang, Fei Wang, Xiaolong Yu, Shihua Zhao, Xu Hou, Mingzhao Xing, Yangang Wang

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PT02-03-28

changing trends in incidence of thyroid carcinoma

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PT02-03-29

Clinical variabiliy and translational approach in medullary thyroid carcinoma

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PT02-03-30

Plasma hsa-miR-505-5p up-regulated expression in papillary thyroid carcinoma

Xuejia Song, Xiaolong Yu, Xu Hou, Shihua Zhao, Fei Wang, Ping Wang, Yangang Wang

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PT02-03-31

The Association Between SCH And Diabetic Nephropathy Among Patients With Type 2 Diabetes Mellitus

Ping Zhang, Yan Chen, Shan Huang

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PT02-03-32

Investigation of thyroid function in Sickle cell disease subject with or without leg ulcers

Olayiwola Popoola

Achievers University

PT02-03-33

Increased all-cause mortality, hospital admission rate and cardiovascular morbidity in hospitalised hyperthyroid patients–a nested case-control study

Barbara Torlinska, Jayne Franklyn, Jamie Coleman, Kristien Boelaert

University of Birmingham

PT02-03-34

Who moved my thyroid?--a cohort study with a surgical option of Prognostic evaluation on papillary thyroid carcinoma

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PT02-03-35

Metformin Inhibits the Proliferation of Thyroid Cancer Stem Cells by Up-regulating Tumor Suppressor miRNAs

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PT03-03-01

The association between total antioxidant capacity and apelin gene expression in adipose tissue among morbid obese and non-obese subjects

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PT03-03-02

Association of FTO and apelin gene expression with dietary glycemic index and glycemic load among morbid obese and non-obese subjects

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PT03-03-03

The association of dietary linoleic, linolenic, oleic, and arachidonic acid intakes with apelin and FTO gene expression

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PT03-03-04

Attitudes of physicians towards patients with excess weight in Turkey

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PT03-03-05

The association of dietary food group intakes with apelin and FTO gene expression

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PT03-03-06

Dietary Approaches to Stop Hypertension is associated with incident chronic kidney disease in adults with abdominal obesity

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PT03-03-07

Disorders in the sexual maturation, ovulation and oocyte quality in female offspring caused by maternal overweight

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PT03-03-08

Effects of metformin on weight management, insulin resistance and lipid profile in overweight and obese patients

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PT03-03-09

Alterations in the sexual maturation, spermatogenesis and spermatozoa quality in male offspring caused by maternal overweight

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PT03-03-10

The changes of thyroid hormones within normal range in metabolically healthy obesity

chi zhang, qing liao, ying liu

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PT03-03-11

The obesity paradox in patients with recurrent coronary heart disease: data from the Tehran lipid and Glucose Study

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PT03-03-12

Relationship between blood visfatin level and fatty liver in metabolic syndrome patients

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PT03-03-13

Efficacy of a 12-week Yoga-based lifestyle intervention on components of metabolic syndrome, adipocytokines & lipid peroxidation

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PT03-03-14

Relationship between non-alcoholic fatty liver disease, metabolic syndrome and insulin resistance: A cross-sectional study

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PT03-03-16

LONG-TERM EFFECTS OF ROUX-EN-Y GASTRIC BYPASS SURGERY (GBP) ON QUALITY OF LIFE (QOL) OF SEVERELY OBESE BRAZILIAN PATIENTS

Alline Beleigoli, Roberta Rodrigues, Marco Tulio Diniz, Alexandre Savassi-Rocha, Lucas Freitas, Victor Van Eijk, Nicholas Magario, Alexandre Can?ado, Maria de Fatima Diniz

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PT03-03-17

Serum vitamin D levels and muscle strength in morbid obese patients.

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PT03-03-18

Pregestational Body Mass Index is related with Free β-hCG, fast glucose, lipid profile levels and eating habits on pregnant Mexican women

Karen Benitez, Ana Gabriela Martínez, Vicente Beltrán-Campos, Herlinda Aguilar-Zavala*

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PT03-03-19

Long-term outcomes on eating behavior, physical activity and alcohol consumption after bariatric surgery and relation to quality of life: a follow-up study of Brazilian severely obese patients

Alline Beleigoli, Roberta Rodrigues, Nicholas Magario, Alexandre Can?ado, Victor Van Eijk, Lucas Freitas, Marco Tulio Diniz, Alexandre Savassi-Rocha, Maria de Fatima Diniz

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PT03-03-20

Nutritional pre-operative management of obese patients scheduled for bariatric surgery.

Diego Mastino[1*], Giovanni Fantola[2], Roberto Moroni[2], Valentino Cabras[2], Efisio Cossu[1], Marco Giorgio Baroni[3], Stefano Pintus[2]

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PT03-03-21

Long-term comorbidities outcomes of Roux-en-Y gastric bypass

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PT03-03-22

Metabolic syndrome and loss skeletal muscle

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PT03-03-23

Factors associated with weight loss within an online weight management community

Alline Beleigoli, Tiago Cunha, Paulo Bicalho, Ana Paula Silva, Wagner Meira Jr, Antonio Ribeiro, Gisele Pappa

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PT03-03-24

Itinerary to Health Complications through Common Inflammatory Factors in Obesity and Diabetes

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PT03-03-25

Association of Serum Levels of Adropin and Irisin with Overweight/Obesity and Related Metabolic Characteristics

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PT03-03-26

Calf circumference, insulin resistance and non-alcohol fatty liver disease among middle-aged and elderly Chinese individuals

Zhang Weiwei, Yang Zhen, Niu Yixin, Li Xiaoyong, Zhang Hongmei, Qin Li, Su Qing

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PT03-03-27

Apelin INHIBITS INSULIN SECRETION IN PANCREATIC BETA CELLS BY ACTIVATION OF PI3K-PDE3B pathway

Lin Guo, Qiang Li

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PT03-03-28

The effect of short-term very low calorie diet on glucose and lipid metabolism in patients with metabolic syndrome

Guofang Chen, Yaofu Fan, Hongjie Di, Xiaoduo Xiang, Jie Chen, Chao Liu

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PT04-03-01

Spindle Epithelial Tumor with Thymus-Like Differentiation (SETTLE) of the Thyroid: A Case Report

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PT04-03-02

Severe Hypoinsulinemic Hypoglycaemia in Beckwith-Wiedemann Syndrome (BWS): Potential Mechanisms and Therapeutic Implications

RAJESHWARI ASHOK, Vibha Rao, Owais Haqq, Reshma Harsha, Mari Muthu, Babitha Rani, Muralidhar Krishna, Chandraprabha P, Akshaya Hegde, Geetha Rao, Usha Rangarajan, Chandrika KM, Vasanthi Nath, Uma Dayashankar, Sharda A, Sunitha B, Tejeswini Deepak, Nandhini Jayaram, Bina naik, Srikanta S

ENDOCRINE AND DIABETES CENTER

PT04-03-03

Two cases of anorexia nervosa-induced amenorrhea in twins treated by GnRH pump

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PT04-03-06

Five-year follow-up findings from a case of hyperparathyroidism crisis secondary to bone fracture surgery

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PT04-03-07

Genetic diagnosis and treatment of a Chinese ketosis-prone MODY 3 family with depression

Jun Tang, Chenyi Tang, Fang Wang, Xiaofei Man, Yue Guo, Haoneng Tang, Cila Zhou, Shuwen Tan, Shiping Liu, houde Zhou

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PT04-03-08

Novel anti-cancer drug associated with dysglycaemia: Nivolumab-induced autoimmune diabetes

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PT04-03-09

Too much sugar and salt: Hyperglycaemic Hyperosmolar State precipitated by Nephrogenic Diabetes Insipidus

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PT04-03-10

Carney Complex [CC]: Unique and desperate [endocrine and non-endocrine] diagnostic - therapeutic challenges and biologic mystery.

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5. Sparsh Mulispeciality Hospital
6. Shanthi Hospital and Research Center
7. DISHA DOSTI Programme
8. Surana Preventive Diabetology
9. Jnana Sanjeevini Diabetes Hospital and Medical Center

PT04-03-11

Thyroid gland metastasis from nonsmall cell lung cancer: an unusual site of metastatis and rapid progression

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PT04-03-12

Prolonged hyperkalemia after unilateral adrenalectomy in patient with adrenal cosecretion adenoma

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PT04-03-13

Life-threatening hypocalcemia in a osteoporotic patient treated with denosumab

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PT04-03-14

Acquired post partum severe (but reversible) renal tubular dysfunction with periodic paralysis (hypokalemia, hypophosphatemia) and nephrogenic diabetes insipidus

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PT04-03-15

Primary aldosteronism – Not just about potassium and blood pressure

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PT04-03-16

Primary aldosteronism: a case report

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PT05-03-01

Oxidized low-density lipoprotein-induced cell membrane damage in bone marrow stem cells is independent of ROS formation

Xin Li[1,2], Yuqi Cui[2], Tao Tan[3], Chandrakala A Narasimhulu[4], Yuan Xiao[2], Jia Zhang[2], Hong Hao[2], Lingjuan Liu[2], Jianjie Ma[3], Catherine M Verfaillie[5], Sampath Parthasarathy[4], Hua Zhu[3], Zhenguo Liu[2]

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PT05-03-02

3-Year Follow-Up Study On Epidemic Characteristics Of Dyslipidemia In The Elderly Population In Guiyang City

ying zhang, miao zhang

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PT05-03-03

Contralateral suppression of basal aldosterone levels is rare in lateralized cases of primary aldosteronism during adrenal venous sampling

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PT05-03-04

Serine intake and risk of incident hypertension: Tehran Lipid and Glucose Study

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PT05-03-05

Associations of GCKR rs780094 and rs126036 polymorphisms with plasma lipid levels: A systematic review and meta-analysis

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PT05-03-06

The Positive Association of Branched-Chain Amino Acids and Metabolic Dyslipidemia in Chinese Han population

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PT05-03-07

Divergent pathway of Lipid profile components for cardiovascular disease and all-cause mortality event: Results of over a decade follow-up among Iran population.

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PT05-03-08

The Role Of Adrenocorticotropic Hormone Stimulation In Primary Aldosteronism: A Tale Of Two Hospitals

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PT05-03-09

Prevalence of Metabolic Syndrome among Adult Filipino Patients with Thyroid Disease in an Outpatient Clinic in Cebu City from 2004 - 2015

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Cebu Doctors University Hospital

PT05-03-10

Ranolazine improves insulin resistance in non-diabetic patients with coronary heart disease. A pilot study

Giuseppe Caminiti, Rosalba Massaro, Chiara Fossati, Maurizio Volterrani

S.Raffaele IRCCS Rome

PT05-03-11

A Study of Lipid Profile and carotid intima–media thickness as marker of early atherosclerosis in children with parental history of premature ischemic heart disease

PUNEETH K PAI

Mysore mediclal college and research institute

PT05-03-12

Resting heart rate and the risk for metabolic syndrome

Limor Friedensohn-Zuck[1,2*], Yael Bar-Zeev[2], Adam Dalal[2]

1. Ichilov
2. Israeli Defence forces medical corps

PT05-03-13

Impaired lung function is associated with non-alcoholic fatty liver disease independently of metabolic syndrome features in Chinese people

Qin Li, Yang Zhen, Zhang Weiwei, Li Xiaoyong, Niu Yixin, Zhu Lingfei, Su Qing

Department of Endocrinology, Xinhua Hospital, Shanghai Jiaotong University School of Medicine

PT05-03-14

Application of ROC curve predict MS neck circumference cut points

Lichao Zhao, Qiang Li

Second Affiliated Hospital of Harbin Medical University

PT06-03-01

Psychometric properties of a developed questionnaire to assess knowledge, attitude and practice (KAP) regarding vitamin D

Parisa Amiri, Hoda Sadrosadat, Mehrdad Karimi, Golaleh Asghari, Atieh Amouzegar, Parvin Mirmiran, Fereidoun Azizi*

Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences

PT06-03-02

Insulin-like growth factor-1 promotes osteogenic differentiation and collagen I alpha 2 synthesis via induction of mRNA-binding protein LARP6 expression

Yue Guo, Tang Chen-Yi, Man Xiao-Fei, Tang Hao-Neng, Zhou Hou-De

Institute of Metabolism and Endocrinology, National Clinical Research Center for Metabolic Disease, The Second Xiang-Ya Hospital of Central South University

PT06-03-03

Bone mineral density and metabolic bone indices in Asian Indian postmenopausal women with and without diabetes

RAJESHWARI ASHOK[1,2,3], Akshya Hegde[2,1,3], Aswini KJ[3,9,8], Owais Haqq[9,1,6], Vibha ashish Rao[3,1,2], Marimuttu B[8,1,2], geetha Rao[9,1,3], Uma Dayashanker[3,1,2], Pushpa Ravikumar[9,8,6], Chandraprabha S[3,1,2], Babitha Thyagaraj[3,4,2], Vasanthi Nath[7,1,2], Reshma Harsha[9], Muralidahara CS[8], Rajeev k[7], Chitra MD[9], Kamala t[6], Tejaswini Deepak[5], Sharada A[4], Srikanta S[9]

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2. Samatvam: Science And Research For Human Welfare Trust
3. Science for Health
4. Samatvam Endocrinology Diabetes Center
5. Sparsh Multispeciality Hospital
6. Shanthi Hospital and Research Center
7. DISHA DOSTI Program
8. Surana Preventive Diabetology Center
9. Jnana Sanjeevini Diabetes Hospital and Medical Center

PT06-03-04

ACE inhibitors and the risk of fractures:a meta-analysis of observational studies

yanzhen cheng[1], zhenzi huang[1], li yang[1], shitao rao[2]

1. Zhujiang Hospital, South Medical University
2. Hongkong Chinese University

PT06-03-05

Positive association between HbA1c and hip bone mineral density in males with type 2 diabetes mellitus

Junlei Su[1], Mingxin Xu[1], Zhiyin Zhang[1], Ni Zhong[1], Ran Cui[1], Feng Li[1], Ge Zhang[2], Hui Sheng[1], Sheng Qu[1]

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2. Institute for Advancing Translational Medicine in Bone &Joint Diseases, School of Chinese Medicine, Hong Kong Baptist University, Hong Kong SAR, China

PT06-03-06

Metabolic syndrome and osteoporotic fracture: a population-based study in China

Qin Li, Yang Zhen, Zhang Weiwei, Li Xiaoyong, Zhu Lingfei, Zhang Hongmei, Niu Yixin, Su Qing

Department of Endocrinology, Xinhua Hospital, Shanghai Jiaotong University School of Medicine

PT06-03-07

MicroRNA-17-92 cluster regulates osteoclast differentiation and function

xiao ji

Department of Endocrinology, West China Hospital, Sichuan University

PT07-03-01

Aberrancies in circulating levels of Th1, Th2 and Th17 associated chemokines in hyperprolactinemia patients

Jeanette Wahlberg[1], Lea Ewerman[1], Eva Landberg[2], Maria C Jenmalm[3], Bertil Ekman[1], Jan Ernerudh[3]

1. Department of Endocrinology and Department of Medical and Health Sciences, Linkping University, Linkping, Sweden
2. Department of Clinical Chemistry and Department of Clinical and Experimental Medicine,

Linkping University, Linkping, Sweden
3. Department of Clinical and Experimental Medicine, Division of Inflammation Medicine, Linkping University, Linkping, Sweden.

PT07-03-02

Fall in TSH by ≥80% is associated with development of ipilimumab-induced hypophysitis

Nisa Sheriff[1,2*], Sunita MC De Sousa[1,3], Alexander M Menzies[4], Venessa HM Tsang[5], Georgina V Long[4], Katherine T Tonks[2]

1. Garvan Institute of Medical Research, Sydney, Australia
2. Department of Endocrinology, St Vincent's Hospital, Sydney, Australia
3. Endocrine & Metabolic Unit, Royal Adelaide Hospital, Adelaide, Australia
4. Melanoma Institute Australia, Sydney, Australia
5. Department of Endocrinology, Royal North Shore Hospital, Sydney, Australia

PT07-03-03

PP4C restrains dopamine D2 receptor expression via NF-κB signaling pathway in rat pituitary MMQ cells

Na Yi, Bin Lu

Huashan Hospital

PT07-03-04

The influence of serum Phenylalanine and Tyrosin level on Prolactin concentration in adult patients with phenylketonuria.

Peter Reismann[1*], Eszter Juhász[1], Erika Kiss[2], Erika Simonova[2], Attila Patócs[3], Károly Rácz[1]

1. 2nd Department of Medicine, Semmelweis University, Budapest, H-1088, Szentkirályi street 46.,Hungary
2. st Department of Pediatrics, Semmelweis University, Budapest, H-1083, Bókay J. street 53, Hungary
3. Hungarian Academy of Sciences and Semmelweis University "Lendület" Hereditary Endocrine Tumors Research Group, Budapest, H-1088, Szentkirályi Street 46. Hungary

PT07-03-05

Rituximab was used to treat recurrent IgG4-related hypophysitis with ophthalmopathy as the initial presentation: a case report and literature review

qian zhang[1,4], weijun gu[1], jian zhu[2], jie li[3], yiming mu[1]

1. Department of Endocrinology, the Chinese PLA General Hospital
2. Department of Rheumatology, the Chinese PLA General Hospital
3. Department of Pathology, the Chinese PLA General Hospital
4. Department of Endocrinology, the Chinese PLA Army General Hospital

PT07-03-06

The impact of body mass index in interpreting testing of the hypothalamic-pituitary-adrenal axis function: low-dose vs high-dose Cosyntropin stimulation

Christine Yedinak, Maria Fleseriu

Oregon Health & Sciences University, 3181 SW Sam Jackson Park Rd, Portland. Or. 97239. U.S.A

PT07-03-07

six cases misdiagnosed as lymphocytic hypophysitis and literature review

Qian Wei, li Zang, Guoqing Yang

Department of Endocrinology, the PLA General Hospital

PT08-03-01

Long term effects of Cushing's cardiomyopathy on ventricular systolic function: A Case Study

Simon Edeghere[*], Tabinda Dugal

Royal Cornwall Hospital, Truro United Kingdom

PT08-03-02

Reduced temperature and the chemical chaperone 4-phenylbutyrate enhance stability of 21-OHD mutations

Yiqing Chen[1], Kerstin Schaefer[1], Maria Gasteiger[1], Angela Taylor[3], Wiebke Arlt[3], Nils Krone[4], Soeren Gersting[2], Nicole Reisch[1*]

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3. School of Clinical & Experimental Medicine, Institute of Metabolism and Systems Research, University of Birmingham, IBR Tower, Rm 225, B15 2TT, Birmingham
4. Academic Unit of Child Health, Department of Oncology and Metabolism, University of Sheffield, Western Bank,S10 2TH, Sheffield

PT08-03-03

Role of Cortisol/ACTH Ratio in Subclinical Cushing's Syndrome Screening in Patients with Adrenal Incidentaloma

Jingtao Dou

Department of Endocrinology, Chinese PLA General Hospital, Beijing, 100853, China

PT08-03-04

Effect of estimated glomerular filtration rate on aldosterone to renin ratio in the screening of primary aldosteronism

Xiaomu Li, Yan Ling, Zhiqiang Lu, Xin Gao

Zhongshan Hospital, Fudan University

PT08-03-05

The correlation between serum uric acid and early renal damage in patients with primary aldosteronism

Yajuan Deng, Shaoling Zhang, Li Yan, Juying Tang, Lifang Mai

Sun Yat-sen Memorial Hospital, Sun Yat-sen University

PT08-03-06

Using FF Index to Evaluate Early Postoperative HPA Axis Deficiency of pituitary adenomas

Lin Wang, Qiang Li

The Second Affiliated Hospital of Harbin Medical University

PT09-03-01

The clinical feature and prognosis analysis to the patients with hypernatremia after space-occupying lesions surgery in the sellar area

Xintong liu[1], MIn Wang[1], Tao Zhou[1], Qinghua Guo[1,2], Yimming Mu[1]

1. PLA general hospital, 100853
2. Hainan Branch of PLA general hospital, 572000

PT09-03-02

Effect of fasting on the central arm of the hypothalamus-pituitary-thyroid axis in female rats; focus on the thyrotropin-releasing hormone degrading ectoenzyme

Jean-Louis Charli*, Ivan Lazcano, Lorraine Jaimes-Hoy, Patricia Joseph-Bravo

Universidad Nacional Autonoma de Mexico

PT09-03-03

Revealing the morphological plasticity of tuberoinfundibular dopaminergic neurons using an in vivo viral-mediated cell filling technique

Siew Hoong Yip[1], David Grattan[1], Brian Hyland[2], Stephen Bunn[1]

1. Department of Anatomy, University of Otago
2. Department of Physiology, University of Otago

PT09-03-04

Diagnosis of primary autoimmune hypophysitis in a single monocentric experience

Sabrina Chiloiro[1], Tommaso Tartaglione[2], Flavia Angelini[3], Antonio Bianchi[1], Vincenzo Arena[4], Antonella Giampietro[1], Marilda Mormando[1], Serena Piacentini[1], Chiara Bima[1], Maria Elena Bracaccia[1], Maria Carmela Sciandra[2], Maria Elena Laino[2], Laura De Marinis[1]

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4. Department of Pathology, Catholic University School of Medicine, Largo Agostino Gemelli, 8, 00168, Rome, Italy

PT09-03-05

Fusiform Dilatation of the Internal Carotid Artery in Childhood-onset Craniopharyngioma – Multicentre Study on Incidence and Long-term Outcome

Hermann L [1], Monika Warmuth-Metz[2], Kristin Lohle[1], Julia Reichel[1], Anna M. Daubenbüchel[1,3], Anthe S. Sterkenburg[1,3], Hermann L. Müller[1*]

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2. Dep. of Neuroradiology, University Hospital Würzburg, Germany
3. University of Groningen, UMCG, Groningen, The Netherlands

PT09-03-06

Severe Hyponatremia in a Previously undiagnosed case of Sheehans Syndrome associated with Extrapontine Demyelonosis: A Case Report

Claire Berbano, Theresa Marie Faller*, Reginald MD

Worldciti Medical center

PT10-03-01

Menstrual Cycle Irregularity and metabolic Disorders, a population based prospective study

Marzieh Rostami Dovom[1], Fahimeh Ramezani Tehrani[1*], Ferydoun Azizi[2]

1. Reproductive Endocrinology Research Center, Endocrine Sciences Research Institute, Shahid Beheshti Medical Sciences University
2. Endocrinology Sciences Research Institute

PT10-03-02

Prenatal exposure to androgen excess affects sexual function of women with polycystic ovary syndrome in adulthood

Mahsa Noroozzadeh[1], Fahimeh Ramezani Tehrani[1*], Fereidoun Azizi[2]

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2. Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

PT10-03-03

The Relationship between Serum Total Testosterone and Sexual Function among Post-menopausal Women

Soheila Nazarpour[1], Masoumeh Simbar[2,3*], Fahimeh Ramezani Tehrani[3], Maryam Tohidi[4], Hamid Alavi Majd[5]

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5. Department of Biostatistics, School of Paramedicine, Shahid Beheshti University of Medical Sciences and Health Services, Tehran, Iran

PT10-03-05

The study of TNF-α cytokine production ,expression of CD8 marker and proliferation of peripheral blood lymphocyte of multiparous women compared with nulliparous women by Co-culture with MDA-231 and MCF-7 breast tumor cell lines

Nazanin Ghasemi[1], Mehri Hajiaghayi[1], Fatemeh Rezayat[1], Mehrnaz Mesdaghi[1], Fahimeh Ramezani Tehrani[2], Nariman Mosaffa[1]

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PT11-03-01

Parathyroid Carcinoma: A Case Series of 20 Patients.

Begum Bahcecioglu, Nafiye Helvaci, Selcuk Dagdelen, Volkan Kaynaroglu, Belkis Erbas, Cenk Sokmensuer, Miyase Bayraktar, Tomris Erbas*

Hacettepe University Medical School

PT11-03-02

Patient-reported outcomes in primary hyperparathyroidism showing mild hypercalcemia without classical symptoms: a systematic review of the literature

Takahiro Okamoto*, Yusaku Yoshida

Department of Surgery II, Tokyo Womens Medical University

PT11-03-03

Poor Nutrition Status of Vitamin D: A Survey from Area with the Lowest Sunshine in China

Pianpian Fan[1], Qin Wang[1], Chunyan Lu[1], Yong Xu[2], Hongyi Cao[3], Xiaohua Xie[4], Xueyan Wu[5], Yan Chen[1], Ting Liu[1], Yanhong Guo[1], Jing Li[1], Decai Chen[1]

1. West China Hospital of Sichuan University
2. The Affiliated Hospital of Southwest Medical University
3. Chengdu Fifth People's Hospital
4. First people's Hospital of Liangshan
5. Guangyuan Central Hospital

PT11-03-04

Parathyroid Function Index: A New Diagnostic Index of Primary Hyperparathyroidism

Yanhong Guo[2], Qin Wan[1], Chunyan Lu[1], Pianpian Fan[1], Jin Li[1], Ximing Luo[1], Decai Chen[1]

1. Endocrinology Department of West China Hospital, Sichuan University
2. Hospital of Chengdu Office of People's Government of Tibetan autonomous Region

PT12-03-01

Effects of environmental estrogen bisphenol A on the characteristics thyroid cancer cell lines

yong-hong zhang[1], ling jiang[2], feng wei[1]

1. Inner Mongolia University of Technology, Department of Endocrinology, First Affiliated Hospital, Mongolian-baotou
2. Qilu Hospital of Shandong University

PT12-03-02

The expression and the diagnostic value of microRNA-3146 in patients with acute gouty arthritis

Bin Wang, Kui Che, JingWei Chi, Yuhang Zhao, Xiaolong Yu, Xu Hou, Yangang Wang

Department of Endocrinology, the Affiliated Hospital of Qingdao University, China

PT12-03-03

Negative allosteric modulation of the endocrine disruptor p,p'DDT on the hCG/LH receptor activity

Mathilde Munier[1,2,3*], Claire Briet[3,4], Louis Gourdin[2,3], Daniel Henrion[1,2], Marie Chabbert[1,2], Régis Coutant[3,5], Eric Reiter[6], Patrice Rodien[3,4], Mohammed Akli Ayoub[6]

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6. INRA 85 – CNRS7247; University of Tours

PT13-03-01

6 cases of Paraganglioma in Taipai Tzuchi Hospital

Ya Hui Hu[1], Chia-Hui Chang[1], Yao-Chou Tsai[2*], Che-Hsiung Wu[3], Vin-Cent Wu[4], Hui-Fang Chang[5]

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5. Division of Endocrinology and Metabolism, Department of Internal Medicine, Hsinchu Mackay Memorial Hospital

PT13-03-02

Challenges in Implementing Pre-emptive Medicine in Japan: Case Series of Inherited Tumor Syndromes Predisposing to Pheochromocytoma and Paraganglioma

Katsutoshi Takahashi[1,2], Megumi Fujita[1], Kazuhiro Yoshiuchi[3], Masaomi Nangaku[1]

1. Department of Nephrology and Endocrinology, University of Tokyo Hospital, Tokyo 113-8655, Japan
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3. Department of Psychosomatic Medicine, University of Tokyo Hospital, Tokyo 113-8655, Japan

PT13-03-03

Proteasome inhibitor MG132 causes apoptosis in thyroid cancer cell lines partially through regulating FOXO3a

Wei Qiang, Wei Liu, Bingyin Shi, Peng Hou

Department of Endocrinology, the First Affiliated Hospital of Xi'an Jiaotong University School of Medicine

PT14-03-01

Case Report of 3 the characteristics of diabetes in patients with Klinefelter's syndrome

Fang Zou, Xiaoyang Lai

the Second Affiliated Hospital of Nanchang Medical University

PT14-03-02

Development of a male contraceptive from traditional medicinal plants

Pratap Mali

University of Rajasthan,Jaipur

PT14-03-03

Immunohistochemical Evaluation of Androgen receptors and Ki-67 expression in the Testes of STZ-Nicotinamide-Induced Diabetic Rats under HAART: Role of Hypoxia hemerocallidea

Ismail Olasile Onanuga[1*], AI Jegede[1], O Ugochukwu[1], O Ogedengbe[1], AI Peter[1], ECS Naidu[1], OO Azu[1]

1. University of KwaZulu-Natal, South Africa.
2. Kampala International University, Tanzania.

PT15-03-01

Thyroid dysfunction, celiac disease, economic impoverishment and childhood diabetes in India

ASHWINI K J[1], Owais Haqq[9], Akshya Hegade[1], Vibha Ashish Rao[3], Rajeshwari A[4], Marimuttu B[8], Usha Rangaraj[9], Geetha Ra0[9], vasanthalakshmi HK[7], Kavitha M[9], Babitha Thyagaraj[3], Muralidhara CS[8], Chandraprabha S[3],

Reshma Harsha[9], Sunitha Vidhyanand[5], Vasanthi Nath[6], Kamala T[6], Tejaswini Deepak[5], Sharada A[4], Srikanta S[9]

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4. Endocrinology Diabetes Center
5. Sparsh Multispeciality Hospital
6. Shanthi Hospital and Research Center
7. DISHA DOSTI Program
8. Surana Preventive Diabetology Center
9. Jnana Sanjeevini Diabetes Hospital and Medical Center

PT15-03-02

Hypergonadotrophic hypogonadism in 2 siblings with DIDMOAD syndrome and its associations

Vibha Ashish Rao[1], Akshya Hegde[10], Ashwini Kj[2], Owais Haqq[3], Rajeshwari Ashok[3], Marimuthu B[8], Geetha Rao[9], Nandini Jayaram[5], Uma Dayashankhar[2], Reshma Harsha[8], Babithadevi T[8], Chandrika Km[1], Kamala T[6], Sumathi K[1], Lakshmi Reddy[5], Chandraprabha S[1], Vasanthi Nath[2], Tejeswini D[5], Sharda A[3], Srikanta S[10]

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8. DISHA DOSTI Program
9. Surana Preventive Diabetology Center
10. Jnana Sanjeevini Diabetes Hospital and Medical Center

PT15-03-03

Analysis of Clinical Characteristics and Etiology in Young Patients with Hyperuricemia

Chenzhong Li[1], Qian Zhang[2], Yaoming Xue[2], jie Shen[1]

1. Department of Endocrinology and Metabolism, the Third Affiliated Hospital of Southern Medical University
2. Department of Endocrinology and Metabolism, Nanfang Hospital of Southern Medical University

PT16-03-01

Maternal and fetal α- and γ-tocopherols, retinol and carotene concentrations in pregnancies with gestational diabetes mellitus

Qinwen Du[1], Emile Levy[2], Anne Monique Nuyt[3], William Fraser[4], Zhong-Cheng LUO[1]

1. Ministry of Education-Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital
2. Departments of Obstetrics and Gynecology, Sainte- Justine Hospital Research Center, University of Montreal
3. Departments of Obstetrics and Gynecology, Nutrition University of Montreal
4. Department of Obstetrics and Gynecology, University of Sherbrooke

PT16-03-02

Cortisol and Betamethasone activate a different yet overlapping set of glucocorticoid receptor-regulated target genes during mammalian lung development

Bennet KL Seow[1], Annie RA McDougall[3], Megan J Wallace[2,3], Timothy J Cole[1]

1. Department of Biochemistry and Molecular Biology
2. Department of Obstetrics and Gynaecology, Monash University, Melbourne and
3. The Ritchie Centre, Hudson InstituteResearch, Melbourne, Australia

PT16-03-03

The relationship between serum ferritin and nonalcoholic fatty liver disease

Yan Ye, Haoming Tian

Department of Endocrinology and Metabolism, West China Hospital, Sichuan University

PT17-03-02

Epidemiology of Glucocorticoid induced Diabetes in Hematological Disorders in a tertiary care centre in India

Krishna Shankar Gopal Sankar*, Nilanjan Sengupta, Prantar Chakrabarti, Soumik Goswami, Pranab Kumar Sahana, Arjun Baidya

Nilratan Sircar Medical College

PT18-03-01

SDHC Immunohistochemistry in Pheochromocytoma and Paraganglioma: A Novel Tool to Detect Germline SDHx mutation

Chuan Shi, Zhengpei Zeng, Zhiyong Liang, Dachun Zhao, Anli Tong, Lin Lu, Shi Chen, Hanzhong Li, Qi Miao, Wenling Zhu

Peking Union Medical College Hospital, Beijing, P.R. China

PT19-03-01

Relationship between iodide excess and hypothyroidism

Gargi Naha, Xiaomei Yao

Department of Physiology and Pathophysiology, School of Basic Medicine, Tianjin Medical University, Tianjin 300070, China

FONDATION IPSEN

2016 Endocrine regulations Prize

John W. Funder

Steroid Receptor Biology Laboratory,
Prince Henry´s Institute
Victoria, Australia

Since 1967, John Funder has worked primarily in the area of adrenal steroids and hypertension, from basic studies on mineralocorticoid receptors to clinical guidelines for the management of Primary Aldosteronism. In the process he has supervised 40 PhD students, authored almost 600 peer-reviewed papers with an h-index of 75 and given over 200 invited international presentations. He served on the Council of the ISE from 1988-1996, was Presiding Councillor from 1996-2000, and Honorary President from 2004-2010. In 2002, he was the first non-North American to be elected to the Council of the Endocrine Society (USA); in 2008, he received the Novartis Prize of the Council for High Blood Pressure Research; in 2013, the Endocrine Society Robert H. Williams Award for Distinguished Leadership in Endocrinology; and in 2014, the International Society of Hypertension Tigerstedt Lifetime Achievement Award. In active retirement, he continues to write and lecture, peer-reviews over 200 manuscripts per year, and lives on a small vineyard 50 km from the centre of Melbourne.

Primary Aldosteronism: Past, Present and Future

Classically, Primary Aldosteronism (PA) was thought (and taught) to be a rare (< 1%) and relatively benign form of hypertension; now we know neither to be the case. Currently, PA is considered to represent 5-10% of hypertension, with a much higher risk profile than age-, sex and blood pressure-matched essential hypertension. In the immediate future the focus in PA is likely to be in two broad areas. The first is on what is exciting (eg further studies on somatic mutations causing aldosterone producing adenomas; familial hyperaldosteronism, especially FH-II; potential drivers of bilateral adrenal hyperplasia). The second is what is potentially tractable in the medium-term (eg standardization of assays for aldosterone, renin and angiotensin; harmonisation of the diversity of confirmatory tests into a single safe and acceptable procedure; lateralization by methods other than adrenal venous sampling). In addition there are two longer term, intersecting questions for PA that need to be addressed: the first is its prevalence and the second its management as a public health issue. There is both historic and recent evidence pointing to a prevalence of relatively autonomous aldosterone over-secretion being causative in ~30% of hypertensives, and very recent data suggesting that the figure may be ~60% ; such studies need to be repeated, extended and refined. Secondly, even at a prevalence of 10%, fewer than 1% of patients in any jurisdiction are ever screened, let along diagnosed and appropriately treated. Primum non nocere: but low-dose mineralocorticoid receptor antagonists (MRAs) are safe (and efficacious) in essential hypertension, specific in resistant hypertension and 'low renin' hypertension, and game-changing in PA. Given the higher risk profile of PA, the fact that >99% of PA will remain occult, and that no jurisdiction has the will or resources to screen, diagnose and treat the population as a whole, consideration should be given to including a low-dose MRA in first-line therapy in all patients with hypertension.

Award lecture

SEPTEMBER 1st, 2016

4:15 - 5:00 pm

China National Convention Center

Plenary Hall - 4/F

(ICE 17th meeting, Beijing, China)

Chair:	**Ian Robinson** *(President of the Jury)*
4:15 - 4:20 pm	**Yves Christen** *(President of Fondation IPSEN)* Introduction to the Endocrine Regulation Prize
4:20 - 4:25 pm	**Ian Robinson** *(The Francis Crick Institute, London, UK)* Introduction to the Laureate
4:25 - 5:00 pm	**John W. Funder** *(Prince Henry´s Institut, Victoria, Australia)* Primary Aldosteronism: Past, Present and Future

PREVIOUS LAUREATES

2002 **Wylie Vale** *(Salk Institute for Biological Studies, La Jolla, USA)*
2003 **Robert Lefkowitz** *(Duke University, Durham, USA)*
2004 **Pierre Chambon** *(IGBMC, Université Louis Pasteur, Strasbourg, France)*
2005 **Tomas Hökfelt** *(Karolinska Institute, Stockholm-Sweden)*
2006 **Roger Cone** *(Oregon Health and Science University, Portland, USA)*
2007 **William Crowley** *(Harvard Medical School, MGH, Boston, USA)*
2008 **Ronald Evans** *(Salk Institute for Biological Studies, La Jolla, USA)*
2009 **Gilbert Vassart** *(Université Libre de Bruxelles, Bruxelles, Belgium)*
2010 **Shlomo Melmed** *(Cedars-Sinai Medical Center, Los Angeles, USA)*
2011 **Paolo Sassone-Corsi** *(University of California, Irvine, USA)*
2012 **Jeffrey M. Friedman** *(The Rockefeller University, New York, USA)*
2013 **Bert W. O'Malley** *(Baylor College of Medicine, Houston, USA)*
2014 **Maria I. New** *(Mount Sinai School of Medicine, New York, USA)*
2015 **C. Ronald Kahn** *(Harvard University, Boston, USA)*

JURY

Iain Robinson *(National Institute for Medical Research, London, UK)* **President**
Xavier Bertagna *(Hôpital Cochin, Paris, France)*
Felipe Casanueva *(Universidad de Santiago de Compostela, Santiago de Compostela, Spain)*
Michael Conn *(Texas Tech University Health Sciences Center, Lubbock, USA)*
Ezio Ghigo *(Ospedale Molinette, Turin, Italy)*
Ilpo Huhtaniemi *(Imperial College Faculty of Medicine, London, UK)*
Gérard Karsenty *(Columbia University, New York, USA)*
Paul Kelly *(Faculté de Médecine Necker Enfants Malades, Paris, France)*
Stafford Lightman *(University of Bristol, Bristol, UK)*
Günter Stalla *(Max Planck Institute of Psychiatry, Munich, Germany)*
Phyllis M. Wise *(University of Illinois at Urbana-Champaign, Champaign, USA)*

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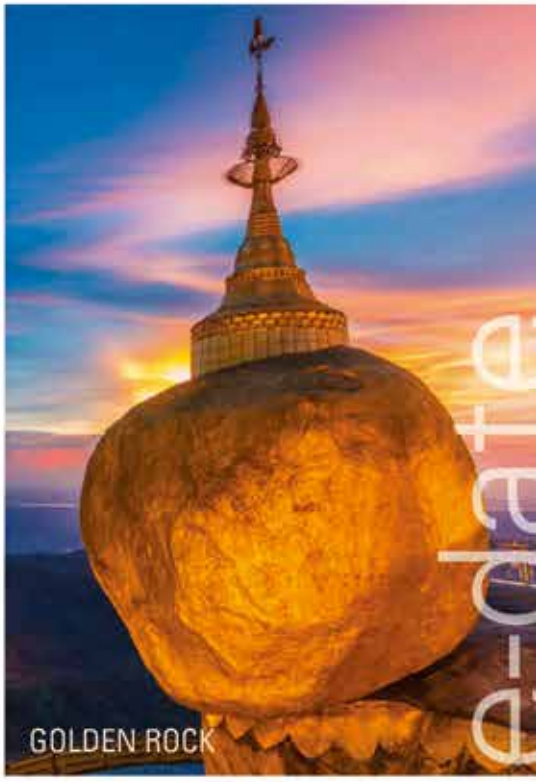
AFES 09-12 NOVEMBER 2017

MYANMAR

19th ASEAN Federation of Endocrine Societies Congress

THE BIENNIAL SCIENTIFIC MEETING OF THE ASEAN FEDERATION OF ENDOCRINOLOGY SOCIETIES



save-the-date

NOVEMBER 09-12, 2017
YANGON, MYANMAR

Synergy among ASEAN

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ICE•CSE 2016

BEIJING, CHINA

31 AUGUST - 4 SEPTEMBER 2016 | CHINA NATIONAL CONVENTION CENTRE, BEIJING, CHINA

1ST JOINT GLOBAL SYMPOSIUM ON: OBESITY

The first of a regular series of collaborative sessions organised by the International Society of Endocrinology (ISE), European Society of Endocrinology (ESE) and Endocrine Society (ES), featuring National, Regional and International thought leaders focusing on prominent global endocrine issues. In this symposium, focusing on Obesity, we will hear from world experts in the field who will present their cutting edge research and discuss the question: ***"You might think you know, but why do we actually have an Obesity pandemic?***

Session Chaired by:
Henry Kronenberg, President, ES
AJ van der Lely, President ESE
Paul Stewart, Secretary-Treasurer, ISE

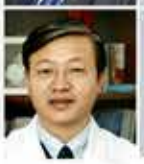


YOU MIGHT THINK YOU KNOW, BUT WHY DO WE ACTUALLY HAVE AN OBESITY PANDEMIC?

THURSDAY, 1 SEPTEMBER 2016 - 10:15 -11:45AM - AUDITORIUM

HOMEOSTATIC AND NON-HOMEOSTATIC CONTROL OF WEIGHT WHICH WINS?
Amy Rothberg, Endocrine Society, USA

EPIGENETIC FACTS IN THE GENESIS AND COMPLICATIONS OF OBESITY EPIDEMICS
Felipe Casanueva, European Society of Endocrinology, SPAIN



OBESITY, DIABETES AND HYPERTENSION IN CHINA
Yiming MU, Chinese Society of Endocrinology, CHINA

A COLLABORATIVE SESSION BROUGHT TO YOU BY:

ENDOCRINE SOCIETY

European Society of Endocrinology

ISE international society of endocrinology

CSE

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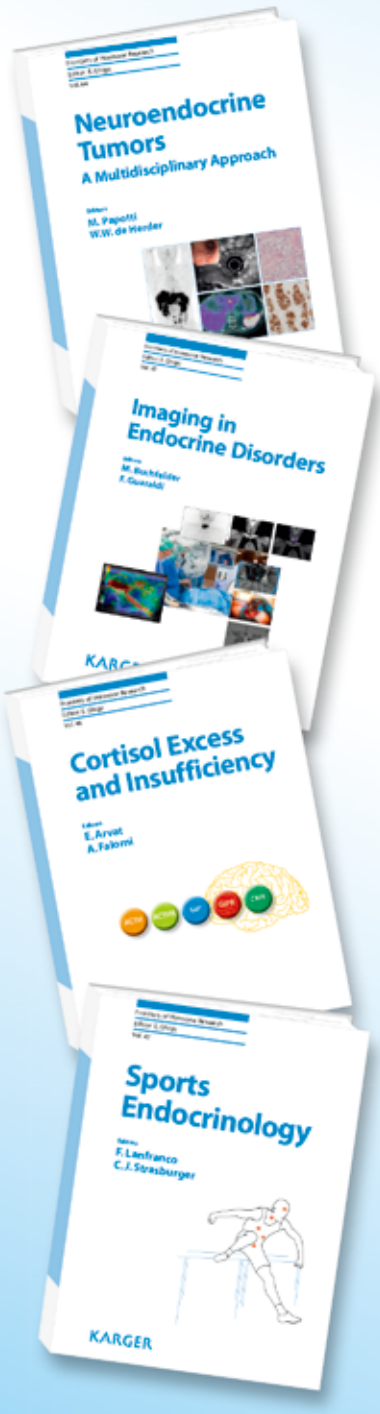

NET – from contemporary clinical management to controversies and new frontiers

Neuroendocrine Tumors: A Multidisciplinary Approach
Editors: M. Papotti (Turin); W.W. de Herder (Rotterdam)
X + 270 p., 51 fig., 26 in color, 27 tab., 2015
Special price: CHF 140.00 / EUR 131.00 / USD 165.00
(hard cover or online)
ISBN 978–3–318–02772–3

A concise and well-illustrated reference book

Imaging in Endocrine Disorders
Editors: M. Buchfelder (Erlangen); F. Guaraldi (Turin)
VIII + 156 p., 33 fig., 5 in color, 9 tab., 2016
Special price: CHF 117.00 / EUR 109.00 / USD 138.00
(hard cover or online)
ISBN 978–3–318–02737–2

Top experts on the challenge of hyper- and hypocortisolism management

Cortisol Excess and Insufficiency
Editors: E. Arvat (Turin); A. Falorni (Perugia)
VIII + 216 p., 16 fig., 5 in color, 20 tab., 2016
Special price: CHF 127.00 / EUR 119.00 / USD 150.00
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ISBN 978–3–318–05839–0

Guidance through the complex interaction between physical activity and the endocrine system

Sports Endocrinology
Editors: F. Lanfranco (Turin); C. Strasburger (Berlin)
VIII + 172 p., 5 fig., 5 in color, 13 tab., 2016
Special price: CHF 104.00 / EUR 98.00 / USD 122.00
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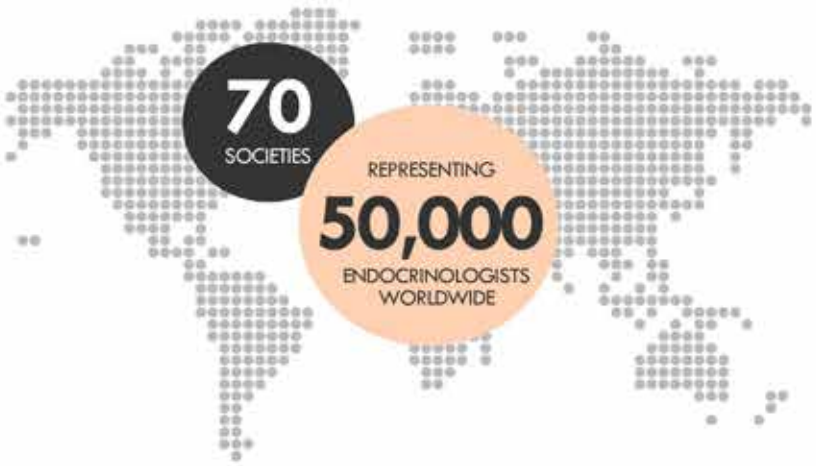
FUCEN

INTERNATIONAL SOCIETY OF ENDOCRINOLOGY

PROMOTING INTERNATIONAL COOPERATION AND SCIENTIFIC EXCHANGE IN ENDOCRINOLOGY

The International Society of Endocrinology (ISE) is a global federation made up of 70 Endocrinology Societies representing over **50,000 endocrinologists** from around the world.



We are governed by an Executive Committee comprising 12 leading endocrinologists elected from around the world.

Our Member Societies have a global voice, each with a representative on our General Council, comprising the Presidents of each society.

GLOBAL REGIONAL NATIONAL

Our flagship meeting, the **International Congress of Endocrinology (ICE)** is the most widely attended medical conference of its field. The rich, diverse and colourful content of the event coupled with its global perspective make it a congress not to be missed by academics, clinicians, researchers and industry partners from across the globe. Every two years we partner with one of our Member Society meetings in rotation around the world.

ICE/CSE 2016
Beijing, CHINA 31 Aug-4 Sep

ICE 2018
Cape Town, SOUTH AFRICA 1-4 Dec

ICE 2020
Buenos Aires, ARGENTINA 9-13 Oct

We award

100,000

dollars in fellowship support grants to allow young researchers to present their research to a global audience and learn best practice from their peers.

We bring international content to local meetings and facilitate cross-cultural educational intiatives in underepresented areas.

We build partnerships at global, regional and national level to promote international cooperation and scientific exchange.

www.isendo.org ⊕ headoffice@isendo.org ⊕ @isendo

PLAN TO ATTEND

THE 18TH INTERNATIONAL CONGRESS OF ENDOCRINOLOGY

Cape Town and the **Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA)** will host the **18th International Congress of Endocrinology on 1-4 December 2018.**

Cape Town, with its natural beauty, diversity and world-class facilities will provide the perfect venue to welcome endocrinologists and physicians from around the world to the first ICE in Africa.

ICE 2018

18th International Congress of Endocrinology

53rd SEMDSA Congress

1 - 4 December 2018 - Cape Town - South Africa

www.ice2018.org

IOF Regionals Singapore'16

www.iofbonehealth.org/singapore-2016

6th Asia-Pacific Osteoporosis Meeting

SUNTEC SINGAPORE CONVENTION AND EXHIBITION CENTRE
SINGAPORE • NOVEMBER 4-6, 2016

第六届亚太骨质疏松大会议程

2016年11月4-6日
新加坡新达城国际会议展览中心

超过40场的大型讲座以及与专家近距离互动的单元

骨骼与癌症
糖皮质激素引起骨质疏松症
绝经前骨质疏松症
肥胖与骨骼
骨微结构评估
骨折后运动
肾功能衰竭骨质疏松症管理
短暂药物停用法、接续性疗法与综合疗法
营养与骨质疏松症
少肌症
骨骼与糖尿病
骨折后管理
继发性骨折预防
新型疗法
高龄骨科医学

会前课程

骨质疏松核心课程:
2016年11月2-3日

骨骼测量仪器工作原理
透视学、辐射安全与质量保证
骨骼健康临床评价
使用骨密度用于骨质疏松症诊断
骨折风险评估
骨质疏松症预防与治疗：非药理
使用**DXA**监测骨质疏松症治疗
使用**DXA**设备做椎体骨折评估 (VFA)
DXA 扫描解读与报告

	价格单位：美元	
第六届亚太骨质疏松大会报名	提前报名价格	一般报名价格
中国代表	425	500
专职医疗人员	300	375
学生/研究员	200	250
仅参加骨质疏松症核心课程	195	265
套票（核心课程 + IOF亚太骨质疏松大会）	**495**	**665**

International Osteoporosis Foundation
国际骨质疏松基金会

中文日程

Chinese Sessions

大会组织机构

大会主席

母义明

顾问委员会

陈家伦	陈家伟	方佩华	高　妍	葛家璞	郭晓蕙	李光伟
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邱明才	项坤三	曾正陪				

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母义明*

副主席

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大会组织委员会

主 席

赵家军*

副主席

洪天配	王卫庆	吕朝晖

成 员

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秘书处

贾　玲	李晨嫣	孙　静	徐　焰	谷伟军

* 为中华医学会内分泌学分会常委

大会综合信息

基本信息

会议时间：2016 年 8 月 31 日 –9 月 4 日
报到时间：2016 年 8 月 31 日　　09:00–18:30
会议地点：北京国家会议中心
报到地点：北京国家会议中心一层大堂（北京市朝阳区天辰东路 7 号）

主 会 场：北京国家会议中心四层大会堂
试 片 室：三层 308
秘 书 处：三层 308
展　　厅：北京国家会议中心 E1–E2 馆

会议注册及资料领取

报到地点：北京国家会议中心一层大堂（北京市朝阳区天辰东路 7 号）
请在报到地点领取注册流程卡，按照流程进行会议注册及领取资料。

学　　分

所有参加会议的注册代表可获得国家级医学继续教育学分，学分为电子学分。项目编号：2016–03–06–272（国）。参会代表请于会议结束后一个月后登录中华医学会官网（www.cma.org.cn），点击“继续教育”栏目，查找已发布项目，选择年度，输入姓名即可查询并打印电子学分证书。

胸　　牌

所有参会人员进入会场、展厅和参加会议社会活动时都必须佩带胸牌，胸牌遗失补打收费 100 美元。

胸牌颜色		人员类型
	蓝　色	正式参会代表
	红　色	VIP
	黄　色	工作人员
	绿　色	展商代表

展览开放时间及地点

厂家报到时间：8 月 31 日　09:00–17:00
报到地点：北京国家会议中心 E1–E2 馆笔克展览服务台
厂商进行现场注册报到，领取工作证及会议的有关资料。
布 展 时 间：8 月 30 日　　08:30–17:30
　　8 月 31 日　　08:30–17:30
展览开放时间：9 月 1–3 日　　09:00–16:30
撤 展 时 间：9 月 3 日　　17:00–21:00

用餐地点及时间

午　餐：

9 月 1–2 日　12:00–12:30 北京国家会议中心一层、三层卫星会会场外及 B1 五号馆

9 月 3 日　12:00–12:30 北京国家会议中心 B1 五号馆

晚　餐：

大会不提供晚餐，请自行解决

大会 PPT 学术视频回顾区

地　　点：北京国家会议中心三层平台

友情支持：礼来苏州制药有限公司

大会活动

展览开幕式

时　间：9 月 1 日　09:00–09:30

地　点：北京国家会议中心 E1–E2 序厅

中青年英文演讲比赛

时　间：9 月 1 日　16:10–18:15

地　点：北京国家会议中心三层 311A、311B

大会开幕式

时　间：8 月 31 日　18:00–18:30

地　点：北京国家会议中心四层大会堂

中华医学会内分泌学分会全委会及常委会

时　间：8 月 31 日　20:30–21:30

地　点：307 会议室

中华医学会内分泌学分会全体学组成员会议

时　间：8 月 31 日　16:30–17:30

地　点：307 会议室

大会闭幕式

时　间：9 月 4 日　10:40–11:00

地　点：北京国家会议中心一层多功能 AB

班车时刻表

大会在亚运村宾馆、汇园酒店公寓贵宾楼、五洲大酒店、西藏大厦、民族园智选假日酒店、名人国际大酒店、元辰鑫国际大酒设有班车

8 月 31 日	17:00–17:30 由各个酒店发往北京国家会议中心
	18:30 由北京国家会议中心发往各个酒店
9 月 1 日	07:00–08:00 由各个酒店发往北京国家会议中心
9 月 2–4 日	07:30–08:00 由各个酒店发往北京国家会议中心
9 月 1–3 日	18:00 由北京国家会议中心发往各个酒店
9 月 4 日	会议结束后由北京国家会议中心发往各个酒店

试片室地点及开放时间

地　　点：北京国家会议中心三层 308

开放时间：8 月 31 日　10:00–17:30

9 月 1 日　08:00–17:30

9 月 2 日　08:00–17:30

9 月 3 日　08:00–17:30

9 月 4 日　08:00–11:30

发言人须知

1. 发言人须在报到时再次确认报告时间、熟悉会议厅位置。
2. 须在议程开始前 10 分钟前向该次学术单元的主持人报到。
3. 参加中青年英文演讲比赛和优秀论文发言专场的讲者请准备英文幻灯，其他会议发言者可准备中文幻灯。
4. 为保证大会顺利进行，本次大会采用幻灯片自动传输播放系统，请准备好 CDROM 或 U 盘，并在报告前至少 1 天将您的报告文件预交到大会试片室并提交到系统，会场不允许使用自己的计算机。
5. 所有发言者必须严格遵守会议时间安排，屏幕上有倒计时提示，到时间后幻灯将自动停止放映，结束演讲。

主持人须知

1. 会议主持人必须在 2016 年 8 月 31 日到大会试片室（秘书处）报到，确认您所主持的会议时间和会议厅位置。
2. 会议主持人必须提前 15 分钟到场，了解会议安排有无变动、演讲人有无缺席、幻灯设备及其它会议设备运行是否良好。
3. 所有会议时间段安排十分紧凑，主持者必须严格控制时间，一定不能超时。
4. 主持人要组织合适的针对主题的讨论，控制会场的秩序。遇特殊情况及时通知会场工作人员，向大会秘书处和学术委员会报告。

壁报展示须知

请向壁报工作台负责壁报的工作人员要胶带和壁报号码，将制作好的壁报于 9 月 1 日 10:00 前张贴在北京国家会议 E1 馆 CSE 壁报展区。

会议有关规定

★ 大会拥有会议所有内容的版权，未经允许严禁拍摄会议演讲幻灯、视频演示或展示的图片，尤其是严禁拍摄 ICE 英文会场的 PPT，不听劝阻，后果自负。

★ 严禁在会议中心会场内外散发或摆放未经大会组委会允许的任何学术或产品资料。

★ 会议期间进入会场及展厅必须佩带胸牌，没有佩带胸牌者，门卫将拒绝您进入会场。

★ 吸烟者必须在专设的吸烟区吸烟，会场及展览大厅内严禁吸烟。

★ 请自觉将矿泉水瓶、餐盒、会议资料带出会场，保持会场的整洁。

★ 会议期间请将手机置静音或关机状态，保持会场的安静。

中华医学会内分泌学分会官方微信公众平台

进一步提高年会服务水平，中华医学会内分泌学分会已开通了微信公众号服务平台。中华医学会内分泌学分会的官方认证微信号为：CMACSE，微信名称为中华医学会内分泌学分会。用微信扫描右侧二维码，关注官方微信号，获取大会最新动态信息，查询学术日程和学分信息，收看大会精彩幻灯讲座视频。

获大会资助参会的边远地区医生名单

姓名	单位
吴胜利	新疆克拉玛依市人民医院
陈　蓉	新疆哈密地区中心医院
阿卜杜合力力·沙吾尔	新疆墨玉县人民医院
艾热提·麦麦提	新疆墨玉县人民医院
张惠萍	昌吉州人民医院
谢　倩	四川省乐山市人民医院
何劲松	四川省达州市中心医院
王　艳	德阳市人民医院
袁　宁	南充市中心医院
蔡芸莹	云南省第一人民医院
李梦洁	云南中医学院
王云枝	包头医学院第一附属医院
迟　程	内蒙古科技大学包头医学院第一附属医院
张晓丽	包头市蒙医中医医院
才布登道日吉	内蒙古阿拉善特戈熙甲状腺蒙医专科医院
马丽华	兰州大学第一医院
车红霞	甘肃省第三人民医院
王晓敏	白银市第一人民医院
陈爱荣	兰州大学第二医院
焦　翔	西安交通大学医学院第一附属医院
高志飞	榆林市第一医院
杨海燕	广西医科大学第一附属医院
何笑云	桂林医学院附属医院
张姣娇	广西医科大学第一附属医院
张　冰	广西医科大学第一附属医院
饶卫平	解放军第四十四医院
张　颖	贵州医科大学
王晓丽	石河子大学医学院第一附属医院
颜迪恩	吉安市中心人民医院
王　颖	阳泉市第一人民医院
谷丽娟	江西省丰城市人民医院
方向南	赣南医学院第一附属医院
仁春梅	西藏自治区人民医院

2016-09-01

Function Hall A

12:00–12:45 诺和诺德卫星会 — 主持人：洪天配

	12:00-12:45	二型糖尿病合并腹型肥胖的综合管理	彭永德　上海市第一人民医院

13:00–15:00 专题 1：降糖药物心血管结局研究 — 主持人：潘长玉　翻译：于淼

CS-117	13:00-13:40	思维模式转变的驱动力—LEADER 研究对 2 型糖尿病管理的影响	纪立农　北京大学人民医院
CS-118	13:40-15:00	透过结果，解析本质—LEADER 研究的机制解析及临床意义	Jens J. Holst　哥本哈根大学健康科学院

Auditorium

13:00–14:30 专题 2：糖尿病综合管理 1 — 主持人：母义明，陈璐璐

CS-119	13:00-13:30	探讨 2 型糖尿病合并肥胖 / 超重患者的临床管理规范	邹大进　第二军医大学附属长海医院
CS-120	13:30-14:00	短期胰岛素强化序贯艾塞那肽治疗对新诊断 2 型糖尿病 2 年血糖缓解率的影响	李学军　厦门市第一医院
CS-121	14:00-14:30	DPP-4 抑制剂中国人群新证——SUNSHINE 研究结果解读	王卫庆　上海交通大学医学院附属瑞金医院

14:30–16:00 专题 2：糖尿病综合管理 2 — 主持人：赵家军，王卫庆

CS-122	14:30-15:00	创新机制：肾脏在 2 型糖尿病血糖调控中的作用	杨文英　中日友好医院
CS-123	15:00-15:30	SGLT-2 抑制剂临床循证与实践	李玉秀　北京协和医院
CS-124	15:30-16:00	聚焦 SGLT2- 抑制剂与肾脏安全性	李　航　北京协和医院

Room 309A

12:00–12:45 甘李卫星会 — 主持人：邢小平 杨涛

	12:00-12:05	主席致辞	邢小平　北京协和医院 杨　涛　南京医科大学第一附属医院
	12:05-12:20	甘李药业产品海外注册进展汇报	吴见青　甘李药业研发部
	12:20-12:35	同类胰岛素类似物药效学比较研究	马建华　南京市第一医院
	12:35-12:45	会议总结	邢小平　杨　涛

Room 309B

12:00–12:45 默沙东卫星会 — 主持人：宁光，赵家军

	12:00-12:20	从指南到临床看 DPP-4 抑制剂的疗效和安全性	陈璐璐　华中科技大学同济医学院附属协和医院
	12:20-12:40	从中国 2 型糖尿病患者达标所面临的挑战看西格列汀固定复方制剂的临床应用前景	王卫庆　上海交通大学医学院附属瑞金医院

Room 310

12:00–12:45 赛诺菲来得时卫星会　　主持人：翁建平

	12:00-12:05	开场致辞	翁建平　中山大学附属第三医院
	12:05-12:15	承诺 改善 希翼——从质量改善探寻糖尿病防控出路	翁建平　中山大学附属第三医院
	12:15-12:40	千里之行，始于足下——糖尿病管理的质量改善	李启富　重庆医科大学附属第一医院
	12:40-12:45	讨论总结	

12:50–13:35 赛诺菲亚莫利卫星会　　主持人：陈璐璐

	12:50-12:55	开场致词	陈璐璐　华中科技大学同济医学院附属协和医院
	12:55-13:25	磺脲类药物安全性的综合评价	窦京涛　解放军总医院
	13:25-13:30	讨论	
	13:30-13:35	总结	陈璐璐　华中科技大学同济医学院附属协和医院

Room 311A

07:30–08:15 美敦力“全权由我”早餐卫星会　　主持人：母义明

	07:30-08:15	全院血糖管理的实战经验分享	姬秋和　第四军医大学西京医院

12:00–12:45 东宝卫星会　　主持人：纪立农

	12:00-12:45	胰岛素注射技术现状及新进展	郭晓蕙　北京大学第一医院

16:15–18:15 中青年英文演讲比赛（会场一）　　主持人：毕宇芳，吕朝晖

Y-01	16:15-16:23	The microRNAs in the pathogenesis of metabolic memory	廖云飞　华中科技大学同济医学院附属协和医院
Y-02	16:23-16:31	Ablation of TSH receptor delays atherosclerosis development by reducing macrophage inflammation	杨重博　山东省立医院
Y-03	16:31-16:39	Systematic safety evaluation of encapsulated xenogeneic islets transplantation	李　珅　大连市中心医院
Y-04	16:39-16:47	1 case report of type B insulin-resistance syndrome and reviews of the literatures	白金运　山东大学齐鲁医院
Y-05	16:47-16:55	Role of AVPR2/3 receptors in ACTH secreting tumors and potential therapeutic implications	王　熠　复旦大学附属华山医院
Y-06	16:55-17:03	Identification of a novel mutation in pseudohypoparathyroidism type Ia in a Chinese family	唐雨晨　浙江大学医学院附属邵逸夫医院
Y-07	17:03-17:11	The Role of MicroRNAs and Target Genes in the Protective Effects of Glucagon-like peptide-1 on Preserving Pancreatic β-cells in high-fat diet induced mice	孙懿琼　哈尔滨医科大学附属第二医院
Y-08	17:11-17:19	Optimization of the diabetic rat mesenchymal stem cell differentiation by 3D culture in Pluronic F-127 hydrogel	范丽君　南方医科大学第三附属医院
Y-09	17:19-17:27	Study on glucose metabolism in patients with Klinefelter's syndrome	彭　璐　解放军总医院

Y-10	17:27-17:35	Ablation of Lgr4 enhances energy adaptation in skeletal muscle via activation of Ampk/Sirt1/Pgc1 α pathway	孙英凯	上海交通大学医学院附属瑞金医院
Y-11	17:35-17:43	Identification of differential circulating LncRNAs as novel metabolic biomarkers in obese patients	阮玉婷	南方医科大学珠江医院
Y-12	17:43-17:51	Plasma glucose and hemoglobin A1c for the detection of diabetes in Chinese adults: analysis of a nationwide survey	徐　瑜	上海交通大学医学院附属瑞金医院
	17:51-18:15	讨论		

Room 311B

07:30–08:15 诺和诺德早餐卫星会　　主持人：潘长玉

	07:30-08:15	餐后新论——重视日常危害 提升博弈策略	李全民	中国人民解放军火箭军总医院

12:00–12:45 默克卫星会

	12:00-12:05	开场致辞		
	12:05-12:25	相得“胰”彰，全程获益	母义明	中国人民解放军总医院
	12:25-12:45	关注病理核心，实施精确治疗	郭立新	卫生部北京医院

16:15–18:15 中青年英文演讲比赛（会场二）　　主持人：李静，刘超

Y-13	16:15-16:23	Effects of L-Thyroxine Replacement Therapy on Serum Lipid Profiles in Patients with Mild Subclinical Hypothyroidism: An Open-Label, Randomized, Controlled Trial	赵　萌	山东省立医院
Y-14	16:23-16:31	Identification of a novel function of adipocyte plasma membrane-associated protein (APMAP) in gestational diabetes mellitus by proteomic analysis of omental adipose tissue	马宇航	上海市第一人民医院
Y-15	16:31-16:39	miR-21-3p、1297-3p mediates PTEN expression in nodular thyroid disease through tissues and blood	迟　程	包头医学院第一附属医院
Y-16	16:39-16:47	Liraglutide enhance the insulin signaling on lipogenesis in subcutaneous adipose tissue of db/db mice	邵一珉	北京大学第一医院
Y-17	16:47-16:55	Analysis of Clinical Features and Outcomes of Congenital Adrenal Hyperplasia with Adenomatoid Adrenal Gland	顾钰琳	解放军总医院
Y-18	16:55-17:03	Association between reproductive factors and hyperuricemia in people aged over 50 years: a population-based study	李梦娇	华中科技大学同济医学院附属协和医院
Y-19	17:03-17:11	30 years of experience：The clinical features of 73 cases with ectopic ACTH syndrome in a single center	杜函泽	北京协和医院
Y-20	17:11-17:19	M2 macrophage infusion ameliorates obesity and insulin resistance by remodeling inflammatory homeostasis in obese mice	张　琪	解放军总医院
Y-21	17:19-17:27	GABA ameliorates hepatic steatosis and improves insulin sensitivity through Sirt1 pathway	姜冬冬	复旦大学附属华山医院

Y-22	17:27-17:35	Nonalcoholic fatty liver disease is associated with low-grade albuminuria in Chinese adults	林　琳　上海交通大学医学院附属瑞金医院
Y-23	17:35-17:43	The Effect of Thyrotropin on Proatherosclerotic Factors via the activation of Akt	焉雨濛　中国医科大学附属第一医院
Y-24	17:43-17:51	Circulating periostin in relation to insulin resistance and nonalcoholic fatty liver disease among overweight and obese subjects	张伟伟　上海交通大学医学院附属新华医院
	17:51-18:15	讨论	

Room 306

12:00–12:45 礼来卫星会　　主持人：高鑫，严励

	12:00-12:05	开场致辞	高鑫、严励
	12:05-12:25	糖尿病治疗的东西方差异	窦京涛　解放军总医院
	12:25-12:45	CLASSIFY 研究最新介绍 ——糖尿病临床问题的解析	杨文英　中日友好医院

Room 307

12:00–12:45 拜耳卫星会　　主持人：潘长玉

	12:00-12:05	会议主席致词	潘长玉　中国人民解放军总医院
	12:05-12:25	审视不同时代心血管结局相关研究所带来的启示	杨文英　中日友好医院
	12:25-12:45	东西方差异之量体裁衣式 2 型糖尿病管理	朱大龙　南京市鼓楼医院

2016-09-02

Function Hall A

09:00–10:40 糖尿病与精准医学　　主持人：陈丽，张俊清

CS-001	09:00-09:20	糖尿病领域的精准医学研究概况	纪立农　北京大学人民医院
CS-002	09:20-09:40	新生儿糖尿病的诊疗新进展	肖新华　北京协和医院
CS-003	09:40-10:00	糖尿病的表观遗传	李小英　复旦大学附属中山医院
CS-004	10:00-10:20	单基因糖尿病：从基础到临床	刘　铭　天津医科大学总医院
	10:20-10:40	讨论	

10:40–11:45 口头发言　　主持人：洪天配

COR-01	10:40-10:48	二甲双胍通过促进 eNOS 复偶联和抑制 NADPH 氧化酶改善波动性高糖所致的内皮功能障碍	柯　静　北京大学第三医院
COR-02	10:48-10:56	自体骨髓干细胞移植联合长球囊血管成形术治疗糖尿病足下肢血管病变的临床研究	孙铭良　山东省立医院

COR-03	10:56-11:04	阿卡波糖通过调控糖尿病大鼠小肠 miRNA 改善糖代谢的机制研究	张　茜	北京协和医院
COR-04	11:04-11:12	父代心理应激对子代糖代谢的影响及机制研究	焦　阳	上海交通大学医学院附属瑞金医院
COR-05	11:12-11:20	下丘脑背内侧核神经肽的表达缺失通过促进 PI3k/Akt/GSK-3 β 的磷酸化改善肥胖导致的胰岛素抵抗	秦　迁	郑州大学第一附属医院
COR-06	11:20-11:28	2 型糖尿病患者及尿白蛋白正常的 2 型糖尿病患者肾功能降低的危险因素研究 ——回顾性队列研究	胡　萍	北京大学人民医院
	11:28-11:45	讨论		

12:00–12:45 诺和诺德卫星会　　主持人：王卫庆

	12:00-12:45	中国 T2DM 的血糖管理决策——透过现象看本质	郭晓蕙	北京大学第一医院

14:00–15:50 糖尿病与肿瘤　　主持人：李玉秀，毕宇芳

CS-005	14:00-14:20	糖尿病与肿瘤相关性	毕宇芳	上海交通大学医学院附属瑞金医院
CS-006	14:20-14:40	传统降糖药物与肿瘤之间的关系	周翔海	北京大学人民医院
CS-007	14:40-15:10	新型降糖药物与肿瘤之间的关系	洪天配	北京大学第三医院
CS-008	15:10-15:30	二甲双胍抗肿瘤作用的相关研究证据	彭永德	上海市第一人民医院
	15:30-15:50	讨论		

15:50–17:15 口头发言　　主持人：杨刚毅，杨静

COR-07	15:50-15:58	叉头状转录因子 O1 通过抑制足细胞上皮间质转分化保护糖尿病肾病小鼠肾脏损伤	秦贵军	郑州大学第一附属医院
COR-08	15:58-16:06	脂肪间充质干细胞通过促进肝脏糖酵解改善 2 型糖尿病大鼠血糖	谢　敏	解放军总医院
COR-09	16:06-16:14	SIRT1 介导的 p53 乙酰化在高糖诱导的 SH-SY5Y 神经细胞凋亡中的作用及机制	皮林华	中南大学湘雅医院
COR-10	16:14-16:22	PPAR β / δ 激动剂通过 GPR40 改善 2 型糖尿病 GK 大鼠胰岛 β 细胞脂毒性凋亡的研究	李　娟	四川大学华西医院
COR-11	16:22-16:30	M2 型巨噬细胞介导 α 细胞经 EMT 转变为 β 细胞的研究	程　愈	解放军总医院
COR-12	16:30-16:38	胰岛 β 细胞特异敲除 GABA B1R 小鼠的糖代谢异常	刘　瑞	复旦大学附属华山医院
COR-13	16:38-16:46	即使 UACR 与 eGFR 在正常范围内的变异或低水平的异常已可能是糖尿病周围神经病变相关的危险信号	严孙杰	福建医科大学附属第一医院
COR-14	16:46-16:54	利格列汀以非葡萄糖依赖性的方式增加抗氧化功能以改善糖尿病小鼠的肾脏肥大和蛋白尿	Zhihong Yang	Joslin Diabetes Center, Boston, United States
	16:54-17:15	讨论		

Function Hall BC

09:00–10:00 会见教授：如何早期鉴别甲状腺结节的良恶性　　主持人：单忠艳，刘超

CS-009	09:00-09:30	循环 RNA 在甲状腺乳头状癌中的诊断作用	肖海鹏	中山大学附属第一医院

CS-010	09:30-10:00	甲状腺细针穿刺细胞基因学检测在鉴别甲状腺结节良恶性中作用	武晓泓　江苏省人民医院

10:00–11:00 大会报告　　**主持人：高妍**

CPL-01	10:00-11:00	甲状腺癌的惰性生物学特征	滕卫平　中国医科大学内分泌研究所

11:00–11:45 口头发言　　**主持人：江霞**

COR-15	11:00-11:08	妊娠期亚临床甲减妇女产后 9 年的甲功转归	岳　瑶　中国医科大学附属第一医院
COR-16	11:08-11:16	左甲状腺替代治疗对亚临床甲状腺功能减退患者非酒精性脂肪性肝病的影响	刘　璐　山东省立医院
COR-17	11:16-11:24	中国人群恶性甲状腺结节超声诊断效力的分析	李如强　上海交通大学医学院附属新华医院
COR-18	11:24-11:32	S1PR1 阻滞剂 FTY720 在自身免疫性甲状腺炎中的作用及机制研究	韩　成　中国医科大学附属第一医院
	11:32-11:45	讨论	

14:00–15:40 妊娠甲状腺疾病专题　　**主持人：连小兰，何兰杰**

CS-011	14:00-14:20	再谈妊娠期甲状腺疾病的诊断标准	单忠艳　中国医科大学附属第一医院
CS-012	14:20-14:40	妊娠期和产后甲减患者 L-T4 的应用	何兰杰　宁夏医科大学附属医院
CS-013	14:40-15:00	妊娠期抗甲状腺药物的选择	连小兰　北京协和医院
CS-014	15:00-15:20	妊娠期 TPOAb 阳性的危害和治疗	李　静　中国医科大学附属第一医院
	15:20-15:40	讨论	

15:50–17:15 口头发言　　**主持人：李静，闫朝丽**

COR-19	15:50-15:58	亚临床甲状腺机能减退症妇女体外受精结局的研究	蔡芸莹　云南省第一人民医院
COR-20	15:58-16:06	妊娠 4-8 周轻度甲状腺功能减退对妊娠并发症的影响	李　妍　中国医科大学附属第一医院
COR-21	16:06-16:14	Graves 病 CD4+T 淋巴细胞中 miR-4443 作用机制研究	綦一澄　上海交通大学医学院附属瑞金医院
COR-22	16:14-16:22	短程泼尼松治疗中重度亚急性甲状腺炎—— 一项前瞻，随机，对照，单盲研究	段　炼　第三军医大学新桥医院
COR-23	16:22-16:30	重组人 II 型肿瘤坏死因子受体 - 抗体融合蛋白治疗甲状腺相关性眼病的临床研究	崔　岱　南京医科大学第一附属医院
COR-24	16:30-16:38	microRNA-20b 在甲状腺乳头癌中的表达及其作用机制	洪澍彬　中山大学附属第一医院
COR-25	16:38-16:46	环磷酰胺联合骁悉序贯治疗激素复发性甲状腺相关性眼病 20 例疗效分析	王欢欢　郑州大学第一附属医院
COR-26	16:46-16:54	妊娠妇女孕早期的铁缺乏可能预示其孕中期低甲状腺素血症和临床甲状腺功能减退症的发生	滕晓春　中国医科大学附属第一医院
COR-27	16:54-17:02	不同体质指数人群正常范围内血清甲状腺激素的变化及其意义	张　弛　湖南省人民医院
	17:02-17:15	讨论	

Auditorium

09:00–10:00 大会报告　　主持人：母义明

CPL-02	09:00-10:00	面壁十年图破壁—降糖治疗与心血管疾病的关系	李光伟　阜外心血管病医院

12:00–12:45 勃林格卫星会　　主持人：洪天配　王卫庆

	12:00-12:05	开场致辞	洪天配　北京大学第三医院 王卫庆　上海交通大学医学院附属瑞金医院
	12:05-12:25	从 AACE ACE 指南看利格列汀的全程守护轻松管控	陈璐璐　华中科技大学同济医学院附属协和医院
	12:25-12:45	独特创新——从作用机制与代谢排泄看利格列汀的临床价值	赵志刚　北京天坛医院

16:00–18:15 肾上腺专题　　主持人：王卫庆，张波

CS-015	16:00-16:20	肾上腺疾病年度进展	王卫庆　上海交通大学医学院附属瑞金医院
CS-016	16:20-16:40	嗜铬细胞瘤临床诊治共识解读	童安莉　北京协和医院
CS-017	16:40-17:00	嗜铬细胞瘤临床诊治经验分享	苏颋为　上海交通大学医学院附属瑞金医院
CS-018	17:00-17:20	中国原醛专家共识解读	蒋怡然　上海交通大学医学院附属瑞金医院
CS-019	17:20-17:40	血浆肾素和醛固酮测定进展	李启富　重庆医科大学附属第一医院
	17:40-18:15	讨论	

Room 307

09:00–10:00 大会报告　　主持人：高鑫

CPL-03	09:00-10:00	脂肪酸转运与胰岛素抵抗	陈璐璐　华中科技大学同济医学院附属协和医院

12:00–12:45 天麦生物卫星会　　主持人：宁光

	12:00-12:05	开场致辞	宁　光　上海交通大学医学院附属瑞金医院
	12:05-12:40	口服胰岛素胶囊 FDA II 期 B 临床试验结果	Dr.Miriam Kidron　OraMed(以色列)
	12:40-12:50	口服胰岛素动物实验结果	伊秀林　天津药物研究院
	12:50-13:00	总结，散会	宁　光　上海交通大学医学院附属瑞金医院

14:00–15:00 脂肪性肝病与代谢专题　　主持人：汤旭磊，王桂侠

CS-020	14:00-14:20	非酒精性脂肪性肝病年度进展报告	高　鑫　复旦大学附属中山医院
CS-021	14:20-14:40	核受体在肝脏脂肪沉积中的作用及机制研究	陆　炎　复旦大学附属中山医院
	14:40-15:00	讨论	

15:00–16:00 辩论 NAFLD 是否应当干预?　　主持人：陈兵，常向云

CS-022	15:00-15:20	NAFLD 应当干预	何兰杰　宁夏医科大学附属医院
CS-023	15:20-15:40	非酒精性脂肪性肝病—约束还是纵容?	刘　超　江苏省中西医结合医院
	15:40-16:00	讨论	

16:00–18:15 口头发言　　主持人：刘建英

COR-28	16:00-16:08	采用 PDCA 循环引导的全程运动干预模式对 2 型糖尿病患者相关代谢指标影响的研究	马丽华　兰州大学第一医院
COR-29	16:08-16:16	丁酸梭菌对于高脂膳食诱导的肥胖和结肠免疫紊乱的调节作用	孙　嘉　江南大学

COR-30	16:16-16:24	LAMP3 在肝脏脂代谢中的调控作用及机制研究	廖晓玉	第三军医大学新桥医院
COR-31	16:24-16:32	Orexin A 及其受体 1 干预 Hep3B 人肝癌细胞葡萄糖摄取和有氧代谢及其分子机制的研究	刘媛媛	中国医科大学附属第一医院
COR-32	16:32-16:40	胰腺衍生因子 PANDER 与代谢综合征组份聚集相关	阳池娇	中山大学附属第一医院
COR-33	16:40-16:48	Meta 分析：中国人群中非酒精性脂肪性肝病与维生素 D 水平负相关	张　冰	广西医科大学第一附属医院
COR-34	16:48-16:56	硒暴露与非酒精性脂肪肝病发病的关联性研究	杨　震	上海交通大学医学院附属新华医院
COR-35	16:56-17:04	儿童期和胎儿期经历饥荒与成年非酒精性脂肪性肝病的相关性研究	王宁荐	上海交通大学医学院附属第九人民医院
COR-36	17:04-17:12	小檗碱预防肝脏脂肪沉积向脂肪性肝炎和纤维化发展的机制研究	姚霜霜	上海交通大学医学院附属瑞金医院
	17:12-18:15	讨论		

Room 309A

16:15–18:15 水和电解质代谢专题　　**主持人：李强，吕雪梅**

CS-024	16:15-16:35	低钠血症的诊断和治疗	王桂侠	吉林大学第一医院
CS-025	16:35-16:55	低钾血症的诊断思路	龚玉萍	萍乡市人民医院
CS-026	16:55-17:15	Gitelman 综合征与 Bartter 综合征诊治进展	童南伟	四川大学华西医院
CS-027	17:15-17:35	药物相关电解质紊乱	金　楠	解放军总医院
CS-028	17:35-17:55	不适当抗利尿激素分泌综合征	李艳波	哈尔滨医科大学附属第一医院
	17:55-18:15	讨论		

Room 309B

09:00–10:00 大会报告　　**主持人：潘长玉**

CPL-04	09:00-10:00	肾上腺疾病精准医学	宁　光	上海市内分泌代谢病研究所

12:00–12:45 诺华卫星会——新“瑞”绽放，精彩全程　　**主持人：宁光，赵家军**

	12:00-12:05	开场致辞		
	12:05-12:25	宜合瑞（二甲双胍 / 维格列汀单片复方制剂）在 2 型糖尿病管理中的应用	彭永德	上海市第一人民医院
	12:25-12:45	佳维乐——循证证据指导下的全程治疗伙伴	曾龙驿	中山大学附属第三医院

12:50–13:35 诺华卫星会——热点争鸣 全“心”出发　　**主持人：母义明，朱大龙**

	12:50-12:55	开场致辞		
	12:55-13:15	DPP-4 抑制剂的“心”选择——全面、平稳、安全	陈璐璐	华中科技大学同济医学院附属协和医院
	13:15-13:35	肾素 - 血管紧张素系统与代谢疾病	严晓伟	北京协和医院

16:00–18:15 性腺疾病专场　　**主持人：秦贵军，窦京涛**

CS-029	16:00-16:20	性发育异常疾病年度进展报告	秦贵军	郑州大学第一附属医院
CS-030	16:20-16:40	男性肥胖相关性腺功能减退症	窦京涛	解放军总医院
CS-031	16:40-17:00	小阴茎的诊治进展	伍学焱	北京协和医院

CS-032	17:00-17:20	肠道菌群是多囊卵巢综合征的致病因素吗?	刘　伟　上海交通大学医学院附属仁济医院
CS-033	17:20-17:40	女性多毛的病因探讨	李芳萍　中山大学孙逸仙纪念医院
CS-034	17:40-18:00	IHH 致病基因解析	孙首悦　上海交通大学医学院附属瑞金医院

Room 310

09:00–10:00 大会报告　　主持人：陈家伟

CPL-05	09:00-10:00	库欣综合征研究新发现	王卫庆　上海交通大学医学院附属瑞金医院

12:00–12:45 医云卫星会　　主持人：纪立农，朱大龙

	12:00-12:20	互联网慢病管理的困境与出路	母义明　中国人民解放军总医院
	12:20-12:40	医云健康在慢病管理中的探索	李启富　重庆医科大学附属第一医院

16:00–18:15 下丘脑 – 垂体疾病专场　　主持人：童南伟，钟历勇

CS-035	16:00-16:20	下丘脑垂体年度进展	谷伟军　解放军总医院
CS-036	16:20-16:40	中国 Cushing 病规范化诊治	童南伟　四川大学华西医院
CS-037	16:40-17:00	中枢性尿崩症的诊断和治疗	朱慧娟　北京协和医院
CS-038	17:00-17:20	自身免疫性垂体炎的再认识	吕朝晖　解放军总医院
CS-039	17:20-17:40	垂体泌乳素瘤与妊娠	张俊清　北京大学第一医院
CS-040	17:40-18:00	生长激素瘤的诊治进展	姚　斌　中山大学附属第三医院
	18:00-18:15	讨论	

Room 311A

09:00–10:00 大会报告　　主持人：曾正陪

CPL-06	09:00-10:00	FSH 与胆固醇	赵家军　山东省立医院

12:00–12:45 东宝卫星会　　主持人：朱大龙

	12:00-12:20	互联网形式下糖尿病宣教与患者管理新模式	陈　蓉　通化东宝药业股份有限公司
	12:20-12:40	基于人文关怀的优质医疗服务与糖尿病特殊患者管理	王　砚　云南省第一人民医院

16:00–18:15 骨代谢专场　　主持人：孟迅吾，邢小平

CS-041	16:00-16:20	骨质疏松症的现状和防治策略	夏维波　北京协和医院
CS-042	16:20-16:40	骨对糖代谢的调控作用	刘建民　上海交通大学医学院附属瑞金医院
CS-043	16:40-17:00	同位素骨显像在代谢性骨病诊断与鉴别诊断中的价值	陈德才　四川华西医院
CS-044	17:00-17:20	低磷血症的诊治	巴建明　解放军总医院
CS-045	17:20-17:40	欧美甲状旁腺功能减退症新指南简介	邢小平　北京协和医院
CS-046	17:40-18:00	肾科医生视角——肾衰甲旁亢治疗策略	张　凌　北京中日友好医院
	18:00-18:15	讨论	

Room 311B

09:00–10:00 大会报告　　主持人：严励

CPL-07	09:00-10:00	GLP-1 受体激动剂的血管保护效应及其机制	洪天配　北京大学第三医院

12:00–12:45 默克卫星会　　主持人：单忠艳

	12:00-12:45	导升明——糖尿病视网膜病变（DR）管理新视角	张新媛　北京同仁医院

16:00–18:15 肥胖专题及口头发言　　主持人：严励，周翔海

CS-047	16:00-16:20	肥胖学组年度进展报告	陈　兵　第三军医大学西南医院
CS-048	16:20-16:40	肥胖——胰岛功能盛极至衰的起点	杨　涛　南京医科大学第一附属医院
CS-049	16:40-17:00	肥胖糖尿病治疗的新策略：代谢手术	包玉倩　上海市第六人民医院
CS-050	17:00-17:20	限食减重改善胰岛素储备功能的效果与机制	周迎生　首都医科大学附属北京安贞医院
CS-051	17:20-17:40	甲状腺功能与肥胖	徐明彤　中山大学孙逸仙纪念医院
COR-37	17:40-17:48	Prkar2b 缺失通过上调 creb 及 p38 磷酸化水平激活白色脂肪组织产热	苏　静　复旦大学附属华山医院
COR-38	17:48-17:56	代谢正常肥胖转归糖尿病风险的前瞻性队列研究	刘　丹　泸州医学院
COR-39	17:56-18:04	二甲双胍对高脂饮食诱导肥胖小鼠肠道菌群、短链脂肪酸及 GLP-1 的影响	李　岱　重庆医科大学附属第一医院
	18:04-18:15	讨论	

2016-09-03

Function Hall A

09:00–10:20 特殊人群的血糖管理　　主持人：李强，向光大

CS-052	09:00-09:20	高血糖人群的妊娠前准备	童南伟　四川大学华西医院
CS-053	09:20-09:40	妊娠合并糖尿病的血糖管理	刘彦君　中国人民解放军第三 0 六医院
CS-054	09:40-10:00	儿童青少年糖尿病患者的血糖管理	吴　迪　首都医科大学附属北京儿童医院
CS-055	10:00-10:20	高龄老年糖尿病患者的血糖管理	郭立新　卫生部北京医院

10:20–11:45 口头发言　　主持人：杜建玲，张力辉

COR-40	10:20-10:28	妊娠期糖尿病与妊娠期甲状腺功能状态的相关性分析	邱　情　南方医科大学第三附属医院
COR-41	10:28-10:36	腹腔镜下代谢手术治疗肥胖的 2 型糖尿病患者近期疗效观察	杨　郁　大连医科大学附属第一医院
COR-42	10:36-10:44	SGLT-2 抑制剂达格列净通过抑制 NLRP3 炎症小体活化减轻了糖尿病 ApoE-/- 鼠动脉粥样硬化斑块形成	梁自文　第三军医大学西南医院
COR-43	10:44-10:52	Notch 信号通路在二甲双胍调节 HepG2 人肝癌细胞生物学特性中的作用探讨	邱　谦　中南大学湘雅二医院
COR-44	10:52-11:00	1 例先天性全身脂肪萎缩性糖尿病家系的临床和基因诊治	黄爱洁　南京医科大学第一附属医院
COR-45	11:00-11:08	皮下注射利拉鲁肽通过调节 Akt/GSK-3 β 信号通路改善甲基乙二醛诱导的拟阿尔海默病样病变	齐利琴　福建医科大学附属协和医院

COR-46	11:08-11:16	胰岛素治疗对 2 型糖尿病胰岛 α 细胞功能的影响	朱海英	沈阳军区总医院
COR-47	11:16-11:24	长期不完全睡眠剥夺对大鼠糖代谢的影响及机制研究	林来祥	天津医科大学代谢病医院
COR-48	11:24-11:32	小檗碱通过 Plac8/ C/EBP β /PRDM16 通路诱导内脏白色脂肪组织棕色化改善 2 型糖尿病地鼠脂诱性胰岛素抵抗的研究	刘栩晗	大连市中心医院
	11:32-11:45	讨论		

14:00–16:00 优秀论文汇报 主持人：包玉倩，李艳波

EA-01	14:00-14:10	Sodium intake regulates glucose homeostasis through the PPAR δ /adiponectin-mediated SGLT2 pathway	赵　宇	第三军医大学大坪医院
EA-02	14:10-14:20	NRF2 activation by antioxidant antidiabetic agents accelerates tumor metastasis	王　慧	第三军医大学新桥医院
EA-03	14:20-14:30	Altered peripheral B-lymphocyte subsets in Type 1 diabetes and latent autoimmune diabetes in adults	邓　超	中南大学湘雅二医院
EA-04	14:30-14:40	Efficacy and safety of liraglutide versus sitagliptin, both in combination with metformin, in Chinese patients with type 2 diabetes: a 26-week, open-label, randomised, active comparator clinical trial	臧　丽	解放军总医院
EA-05	14:40-14:50	Diabetes and risk of arterial stiffness: a mendelian randomization analysis	徐　敏	上海交通大学医学院附属瑞金医院
EA-06	14:50-15:00	Ameliorating endothelial mitochondrial dysfunction restores coronary function via transient receptor potential vanilloid 1-mediated protein kinase A/uncoupling protein 2 pathway	熊诗强	第三军医大学大坪医院
EA-07	15:00-15:10	GLP-1 receptor agonist promotes brown remodelling in mouse white adipose tissue through SIRT1	徐　芬	广东中山大学附属第三医院
EA-08	15:10-15:20	Impaired pancreatic beta cell compensatory function is the main cause of type 2 diabetes in individuals with high genetic risk: a 9 year prospective cohort study in the Chinese population	严　婧	上海第六人民医院
EA-09	15:20-15:30	Prolactin-stimulated survivin induction is required for beta cell mass expansion during pregnancy in mice	武晓泓	江苏省人民医院
EA-10	15:30-15:40	Characterization of relatively malignant form of osteopetrosis Ca used by a novel mutation in the PLEKHM1 gene	薄　涛	山东省立医院
EA-11	15:40-15:50	The urinei odine to creatinine as an optimal index of iodine during pregnancy in an iodine adequate area in China	李晨嫣	中国医科大学附属第一医院
EA-12	15:50-16:00	Cardiovascular risk in early onset type 2 diabetes	高蕾丽	北京大学人民医院

16:00–17:15 性腺专题 主持人：汪耀，刘礼斌

CS-056	16:00-16:20	男性乳腺发育治疗	徐　勇	西南医科大学附属医院
CS-057	16:20-16:40	血糖与勃起功能障碍	向光大	广州军区武汉总医院
CS-058	16:40-17:00	肥胖对男性性腺功能的影响	管庆波	山东大学附属省立医院
	17:00-17:15	讨论		

Function Hall B

14:00–16:40 高尿酸血症和痛风专题　　主持人：赵家军，朱筠

CS-059	14:00-14:30	痛风研究十年	邹和建　复旦大学附属华山医院
CS-060	14:30-15:00	自发高尿酸血症动物模型的构建及应用研究	李长贵　青岛大学附属医院
CS-061	15:00-15:30	ACR/EULAR 痛风分类标准的解读	伍沪生　北京积水潭医院
CS-062	15:30-16:10	高尿酸血症与肾脏疾病：现状及展望	陈香美　中国人民解放军总医院
CS-063	16:10-16:40	高尿酸血症与心血管疾病的研究进展	张抒扬　北京协和医院

16:40–17:30 辩论：痛风石的处理内科治疗还是外科治疗好　　主持人：焦凯，李长贵

CS-064	16:40-17:30	辩论：痛风石的处理内科治疗还是外科治疗好	陈海冰　上海市第六人民医院
CS-065	16:40-17:30	辩论：痛风石的处理内科治疗还是外科治疗好	成志锋　哈尔滨医科大学附属第四医院

Function Hall C

14:00–15:40 转化医学专场　　主持人：彭永德，肖海鹏

CS-066	14:00-14:20	肠道：代谢性疾病防治新视角	彭永德　上海市第一人民医院
CS-067	14:20-14:40	谱系重编程：胰岛 β 细胞再生的新策略	洪天配　北京大学第三医院
CS-068	14:40-15:00	体脂分布与糖尿病	李小英　复旦大学附属中山医院
CS-069	15:00-15:20	胰岛细胞功能和容量的在体评估和调控	王　琛　上海市第六人民医院
CS-125	15:20-15:40	推进分级诊疗环境下地市级医院内分泌代谢科建设体会 `	苏晓清　萍乡市人民医院

15:40–17:40 甲状腺炎专题　　主持人：汤旭磊，秦贵军

CS-070	15:40-16:00	桥本甲亢的诊断与鉴别	李玉姝　中国医科大学附属第一医院
CS-071	16:00-16:20	迁延不愈的亚急性甲状腺炎的处理	吕朝晖　解放军总医院
CS-072	16:20-16:40	对 AITD 分型的再认识	高　莹　北京大学第一医院
CS-073	16:40-17:00	亚临床甲减的干预治疗	赵家军　山东省立医院
CS-074	17:00-17:20	自身免疫性甲状腺病的并发和伴发疾病	石勇铨　第二军医大学附属长征医院
	17:20-17:40	讨论	

Function Hall BC

09:00–11:00 甲状腺领域年度进展及病例讨论：不同类型甲亢的治疗　　主持人：白耀，连小兰

CS-075	09:00-09:20	甲状腺临床研究的年度进展	刘　超　江苏省中西医结合医院
CS-076	09:20-09:40	Graves 免疫学研究进展	王　曙　上海交通大学医学院附属瑞金医院
CS-077	09:40-10:00	亚临床甲亢的诊治	童南伟　四川大学华西医院
CS-078	10:00-10:20	Graves 眼病的诊治进展	沈　洁　南方医科大学第三附属医院
CS-079	10:20-11:00	^{131}I 治疗甲亢的优势	邢家骝　解放军第 307 医院

11:00–11:45 口头发言　　主持人：周翔海

COR-49	11:00-11:08	B-rafV600E 介导基因 H3K27 甲基化沉默促进甲状腺癌发生发展的机制研究	曲以平	西安交通大学医学院第一附属医院
COR-50	11:08-11:16	诱导 Balb/c 小鼠对 Graves 病新生口服耐受的研究	焦　翔	西安交通大学医学院第一附属医院
COR-51	11:16-11:24	妊娠早期甲状腺毒症对下一代发育水平的影响	徐樱溪	中国医科大学附属第一医院
COR-52	11:24-11:32	巨噬细胞在甲状腺滤泡癌和甲状腺腺瘤中的密度差异及其机制研究	黄凤姣	上海交通大学医学院附属瑞金医院
	11:32-11:45	讨论		

Auditorium

09:00–10:00 大会报告　　主持人：滕卫平

CPL-08	09:00-10:00	妊娠期甲状腺疾病诊治的热点问题	单忠艳	中国医科大学附属第一医院

14:00–15:40 肾上腺专题　　主持人：吕朝晖，张力辉

CS-080	14:00-14:20	肾上腺库欣的内科治疗进展	周薇薇	上海交通大学医学院附属瑞金医院
CS-081	14:20-14:40	肾上腺手术在治疗皮质醇增多症中的进展	孙福康	上海交通大学医学院附属瑞金医院
CS-082	14:40-15:00	肾上腺肿瘤的腹腔镜手术治疗	祝　宇	上海交通大学医学院附属瑞金医院
CS-083	15:00-15:20	病例报告：一例家族性原发性醛固酮增多症 III 型的诊治	童安莉	北京协和医院
CS-084	15:20-15:40	病例报告：双侧肾上腺腺瘤的库欣综合征	谷伟军	解放军总医院

15:40–16:15 会见教授：疑难肾上腺疾病诊治经验　　主持人：秦映芬

CS-085	15:40-16:15	疑难肾上腺疾病的诊治经验	王卫庆	上海交通大学医学院附属瑞金医院

16:15–17:15 口头发言　　主持人：叶山东

COR-53	16:15-16:23	鞘磷脂代谢通路 SphK1-S1P 异常激活促进肾上腺皮质癌发生发展	徐云泽	上海交通大学医学院附属瑞金医院
COR-54	16:23-16:31	即时尿钾 / 尿肌酐比值在低钾血症病因研究中可能是 24 小时尿钾的替代性指标	林春妹	中国医科大学附属第一医院
COR-55	16:31-16:39	肾上腺髓性脂肪瘤 36 例临床分析	单　帅	郑州大学第一附属医院
COR-56	16:39-16:47	地塞米松抑制试验在原发色素结节性肾上腺皮质病诊断中的作用	陈　适	北京协和医院
COR-57	16:47-16:55	先天性低促性腺激素性性腺功能减退症男性患者生精治疗：GnRH 泵优于双促	茅江峰	北京协和医院
COR-58	16:55-17:03	性腺功能异常的病因构成及疾病谱变迁趋势	崔　佳	解放军总医院
	17:03-17:15	讨论		

Room 307

15:00–17:20 糖尿病口头发言　　主持人：谢忠建，张巧

COR-59	15:00-15:08	miR-192 调控高糖培养大鼠肾小球系膜细胞中 MCP-1 表达的作用机制研究	陈芬琴	中国医科大学附属第一医院

COR-60	15:08-15:16	Ccrn4l 介导糖尿病肾病近端肾小管损伤的机制	郭诗哲	复旦大学附属华山医院
COR-61	15:16-15:24	胰岛素泵治疗对冠脉搭桥术后 2 型糖尿病患者血糖控制及住院天数的影响	冯新星	中国医学科学院阜外医院
COR-62	15:24-15:32	糖尿病前期人群十年转归及与性别相关的危险因素分析	宋晓敏	同济大学附属杨浦医院
COR-63	15:32-15:40	非酒精性脂肪肝人群发生糖代谢异常风险的前瞻性研究 – 上海长风研究	林寰东	复旦大学附属中山医院
COR-64	15:40-15:48	GLP-1 受体激动剂通过激活 cAMP/PKA/CREB 信号通络对 AGEs 诱导的星形胶质细胞炎症损伤的保护作用	宝　轶	第二军医大学附属长征医院
COR-65	15:48-15:56	胰岛细胞瘤中微小 RNA-144/ 451 通过靶向 PTEN / Akt 信号通路促进细胞增殖的研究	姜秀丽	上海交通大学医学院附属瑞金医院
COR-66	15:56-16:04	胰岛 β 细胞特异性 INS1 驱动基因过表达和敲除小鼠模型的构建和表征	程玉龙	上海交通大学医学院附属瑞金医院
COR-67	16:04-16:12	miR-375 靶向调控 Mapkap1 在血管紧张素 II 影响胰岛 β 细胞中的作用及机制	程　琳	中山大学孙逸仙纪念医院
COR-68	16:12-16:20	EPC 移植治疗糖尿病兔下肢缺血的血管重建和血管生成相关基因的表达	于　萍	哈尔滨医科大学附属第二医院
COR-69	16:20-16:28	应用血清胰岛素与 C 肽指标预测使用外源性胰岛素的 2 型糖尿病患者 IAA 阳性的最佳临界值探讨	郭　蓉	四川大学华西医院内分泌科
COR-70	16:28-16:36	糖尿病足创面感染病原菌分布特点及耐药性 15 年变迁	黄　莺	南方医科大学南方医院
COR-71	16:36-16:44	贝前列素钠联合阿司匹林对 2 型糖尿病大血管病变的作用及安全性研究	林　娴	中山大学孙逸仙纪念医院
	16:44-17:20	讨论		

17:20–18:15 骨代谢口头发言　　主持人 : 苏恒

COR-72	17:20-17:28	SERPINF1 基因新突变导致五个 VI 型成骨不全症的家系研究	王建一	北京协和医院
COR-73	17:28-17:36	200 例成年起病的非手术性甲状旁腺功能减退症临床分析	全婷婷	北京协和医院
COR-74	17:36-17:44	肝脏脂肪含量、肝酶与骨代谢及其标志物的关系研究	夏明锋	复旦大学附属中山医院
COR-75	17:44-17:52	甲状旁腺激素和成纤维生长因子 23 对于表皮角质形成细胞 25 羟维生素 D-1 α 羟化酶和 24 羟化酶的调节	吴汶霖	中南大学湘雅二医院
COR-76	17:52-18:00	50 岁以上男性体重指数、体质成分、骨密度的变化特征及其相关性分析	裴　育	解放军总医院
	18:00-18:15	讨论		

Room 309B

09:00–10:00 大会报告　　主持人 : 李秀钧

CPL-09	09:00-10:00	罕见病例在认识糖尿病中的重要作用	贾伟平	上海市第六人民医院

16:15–18:15 性腺疾病专场　　主持人：赵志刚，苏青

CS-086	16:15-16:35	垂体柄中断综合征患者下丘脑 - 垂体 - 性腺轴功能重建	全会标　海南省人民医院
CS-087	16:35-16:55	非经典 21 羟化酶缺陷症的识别和处理	卢　琳　北京协和医院
CS-088	16:55-17:15	性发育异常的基因诊断	李小英　复旦大学附属中山医院
CS-089	17:15-17:35	性早熟诊治指南解读	巩纯秀　北京儿童医院
CS-090	17:35-17:55	分泌雄性激素肿瘤	杜　锦　解放军总医院
CS-091	17:55-18:15	染色体与性反转	乔　洁　上海交通大学医学院附属第九人民医院

Room 310

09:00–10:00 性腺疾病专场　　主持人：汤旭磊

CS-092	09:00-09:20	双促与 GnRH 泵治疗的疗效	茅江峰　北京协和医院
CS-093	09:20-09:40	闭经的诊断思路	李江源　解放军总医院
CS-094	09:40-10:00	抗甲状腺抗体与女性妊娠	高洪伟　北京大学第三医院

16:15–17:35 下丘脑 – 垂体疾病专场　　主持人：张俊清，谷伟军

CS-095	16:15-16:35	基于共表达受体治疗策略的功能性垂体瘤治疗进展	钟历勇　北京天坛医院
CS-096	16:35-16:55	垂体瘤术后功能评估与替代治疗	谷　卫　浙江大学医学院附属第二医院
CS-097	16:55-17:15	国际先天性低促性腺激素性性腺功能减退症诊治共识解读	窦京涛　解放军总医院
CS-098	17:15-17:35	动态增强核磁技术参数在 ACTH 依赖性库欣综合征诊断中的价值	郭清华　解放军总医院

17:35–18:23 口头发言　　主持人：吕朝晖

COR-77	17:35-17:43	运用全基因组外显子测序技术进行垂体柄中断综合征的致病基因研究：一项针对 24 例典型患者的研究	王成芷　解放军总医院
COR-78	17:43-17:51	失血性休克对 Wistar 大鼠下丘脑 - 垂体 - 甲状腺轴的影响	李　莹　中国医科大学附属第一医院
COR-79	17:51-17:59	颅咽管瘤神经内分泌功能分级与腺垂体生长激素储备功能评价和重建	梁　丹　首都医科大学附属北京天坛医院
COR-80	17:59-18:07	青少年促皮质素依赖性库欣综合征的定位诊断特点	陈　适　北京协和医院
COR-81	18:07-18:15	114 例垂体柄中断综合征临床分析	韩白玉　解放军总医院
COR-82	18:15-18:23	评价垂体柄中断综合征垂体柄形态变化对垂体前叶功能影响	蒋怡然　上海交通大学医学院附属瑞金医院

Room 311A

09:00–10:00 大会报告　　主持人：陆召麟

CPL-10	09:00-10:00	下丘脑 - 垂体疾病诊断中存在的问题	母义明　中国人民解放军总医院

16:15–18:15 骨代谢专场　　主持人：刘建民，巴建明

CS-106	16:15-16:35	抗骨质疏松药物的研究进展	金小岚　成都军区总医院
CS-107	16:35-16:55	放射科医生视角 - 代谢性骨病影像学诊断	余　卫　北京协和医院
CS-108	16:55-17:15	男性骨质疏松症的诊治	裴　育　解放军总医院
CS-109	17:15-17:35	脂肪和骨骼之间的信号交流及其在骨质疏松中的病理作用	余希杰　四川大学华西医院
CS-110	17:35-17:55	迟发性佝偻病	焦　凯　第四军医大学唐都医院
CS-111	17:55-18:15	原发性骨质疏松症干预的疗效监测与评估	朱　梅　天津医科大学总医院

Room 311B

09:00–10:00 热点辩论：甲状腺癌过度诊断和治疗了吗?　　主持人：赵家军

CS-099	09:00-09:30	正方观点：甲状腺癌没有过度诊断和治疗	曲　伸　同济大学附属第十人民医院
CS-100	09:30-10:00	反方观点：甲状腺癌过度诊断和治疗了	关海霞　中国医科大学附属第一医院

16:15–18:15 脂代谢专题　　主持人：杨涛，曲伸

CS-101	16:15-16:35	2015—2016 年度血脂调控研究进展	陈璐璐　华中科技大学同济医学院附属协和医院
CS-102	16:35-16:55	脂代谢紊乱，我们应该关注什么?	曲　伸　同济大学附属第十人民医院
CS-103	16:55-17:15	国内外血脂指南评析	杨　静　山西医科大学第一医院
CS-104	17:15-17:35	脂代谢在肿瘤发生中的作用与靶向治疗新启示	王桂侠　吉林大学第一医院
CS-105	17:35-17:55	糖尿病合并高胆固醇血症伴蛋白尿的他汀治疗	刘建英　南昌大学第一附属医院
	17:55-18:15	讨论	

2016-09-04

Function Hall AB

09:00–10:40 中国之声　　主持人：滕卫平，宁光

CS-112	09:00-09:20	REACTION 研究	毕宇芳　上海交通大学医学院附属瑞金医院
CS-113	09:20-09:40	Compass 研究及其对临床工作的启示	纪立农　北京大学人民医院
CS-114	09:40-10:00	妊娠早期甲状腺功能干预（SHEP）研究	单忠艳　中国医科大学附属第一医院
CS-115	10:00-10:20	牛磺酸在高血压前期患者降低血压和改善血管功能的随机、双盲和安慰剂对照研究	祝之明　第三军医大学大坪医院
CS-116	10:20-10:40	SMART 研究报告	母义明　中国人民解放军总医院

10:40–11:00 大会闭幕式　　主持人：吕朝晖

	10:40-10:50	颁奖	
	10:50-11:00	致闭幕词	赵家军　山东省立医院

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CPL-01

甲状腺癌的惰性生物学特征

滕卫平

中国医科大学内分泌研究所

滕卫平，现任中国医科大学内分泌研究所所长，教授，博士研究生导师，国务院特殊津贴专家。曾任中华医学会内分泌学分会第六届、第七届副主任委员，第八届侯任主任委员，第九届主任委员，第十届后任主任委员。亚大地区甲状腺学会副主席、美国甲状腺学会会员，美国内分泌学会会员。1976 年毕业中国医科大学医疗系。1988–1990 年留学英国剑桥大学，1994–1995 年留学加拿大多伦多大学。研究方向甲状腺疾病，曾在甲状腺疾病流行病学、碘过量与甲状腺疾病、Graves 病的遗传易感基因、自身免疫甲状腺疾病、妊娠与甲状腺疾病等方面在国内外核心杂志发表学术论文 300 余篇，其代表性论著发表在国际著名的《新英格兰医学杂志》。2007 年荣获国家科技进步二等奖一项。他所在的中国医科大学附属第一医院内分泌代谢病科 2007 年晋升为教育部国家级重点学科；他领导的辽宁省内分泌疾病重点实验室 2010 年通过国家科技部评审，晋升为国家重点实验室培育基地。

2015 年以来国际学术界聚焦甲状腺癌。首先美国《新英格兰医学杂志》发表专栏文章介绍韩国的甲状腺癌“海啸”；美国 ATA 颁布修改后的《甲状腺结节和分化型甲状腺癌的诊治指南》；美国《临床医生癌症杂志》(IF=115) 报告中国的甲状腺癌的高发病率;《美国医学杂志》(JAMA) 提出修改非侵袭型的变异性 PTC 的名称，摒弃癌症的名称。

近三十年来，世界各地的甲状腺癌的发病率增加 2-4 倍。多数专家认为过度诊断的基础是甲状腺癌的惰性生物学特性。① 尸检的结果显示，隐匿性甲状腺癌的检出率 10-36%。这些癌症缺乏临床症状，可以伴随人类安度一生；② 4—5 项 2 万例以上样本的随访研究证实：经手术治疗的甲状腺癌，十年特异生存率 98% 以上，十年复发率 6-7%；甲状腺全切和叶切除的术式的生存率和复发率没有区别；③ 日本库马医院对未手术的 1,245 例甲状腺微小癌的随访 75 个月，无死亡，无远隔转移，仅有 1.5% 发生颈部淋巴结转移；④ Roti 分析手术的甲状腺微小癌 9,379 例，复发率 0.3%，远隔转移率 0.27%，特异死亡率 0.34%。⑤ 最近报告福冈核泄漏地区 30 万 6-18 岁儿童接受甲癌的 B 超筛查，经手术证实的甲状腺癌发病率高达 137/10 万，远远超过日本成人的 B 超筛查结果 (5-10/10 万)。结果提示成人的甲状腺癌可能发生在儿童，绝大多数可以隐藏在体内，相安无事地度过一生。

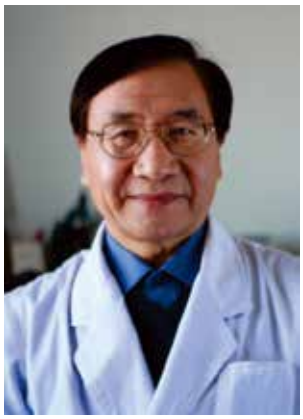
新近颁布的 ATA《2015 甲状腺结节和分化型甲状腺癌诊治指南》根据甲状腺癌的惰性生物特征提出了规范谨慎的诊治新策略。例如 ①是否应当开展甲状腺癌的筛查？② <1.0 cm 甲状腺癌的处理原则；③ 1.0—4.0cm 甲状腺癌的手术切除范围；④ 中央淋巴结切除的指证；⑤放射碘治疗的指证和剂量等。《美国医学杂志》(JAMA) 提出的甲状腺癌新亚型 NIFTP 将被编入第 4 版《WHO 内分泌肿瘤分类》，10-20% 的甲状腺癌将免于手术治疗。

CPL-02

面壁十年图破壁——降糖治疗与心血管疾病的关系

李光伟

阜外心血管病医院



李光伟，男，72岁，主任医师，教授，博士生导师，现任医科院阜外心血管病医院内分泌心血管病中心主任，卫生部中日友好医院内分泌首席专家。重点科研领域为糖尿病防治及胰岛素抵抗。他主持的大庆糖尿病研究20年及23随访研究报告‘六年强化生活方式干预预防糖尿病的效果可在干预结束后持续14年之久’并首次报告‘六年生活方式干预可降低心血管病死亡和全因死亡’，论文于2008和2014发表于国际著名医学柳叶刀系列杂志多年来中国的大庆糖尿病研究与其后的美国、芬兰的同类研究同被称为世界糖尿病一级预防的里程碑。曾任七、八两届中华医学会内分泌分会副主任委员。现兼任老年医学研究会内分泌代谢分会主任委员。卫生部心血管防治研究中心专家组成员、卫生部临床医生科普项目专家委员会委员。国家药监局新药评审委员，国家科技奖、中华医学科技奖评审委员，国家继续医学教育项目评审委员，中央保健会诊专家，北京医学会医疗事故鉴定专家，中华内分泌代谢杂志副主编及中华内科杂志等多家医学杂志编委。

2008年之前多项研究发现降糖对大血管病变有益处，无论是二甲双胍、磺脲类还是胰岛素。但是总有人顽固地坚持这些结果并非在‘试验期间’发生，是推测的‘代谢记忆’的后果。人们的梦想是在有限的几年试验期间看到‘货真价实’的结果。于是近10年来开展了几项大型《追梦》临床试验。也许是天意，这些《追梦》实验遭到接二连三的失利：DVANCE、ACCORD到VADT的研究结果均未能显示降糖心血管获益、出乎意料有研究甚至报告严格降糖组死亡率增加。这些研究无一例外的是入选的都是老年人群。研究者分析认为是这些已经有严重动脉粥样硬化，长期高血压和心梗病史的人群坏了他们的大事 --- 这些老人经受不起低血糖的考验，而传统治疗中不能不选入的胰岛素和刺激胰岛素分泌的药物几乎无一不诱发低血糖。降糖药的希望之路在何方？可能在于不诱发低血糖的新药。于是研究者们把目光投向—DPP4抑制剂，开始了新一轮《希望》之旅。不料，SAVOR、EXAMINE和TECOS三个超大型研究又无一显示新的治疗在降低心血管事件方面较安慰剂有任何优势，有的研究又意外地出现了心衰风险的增加。真是‘屋漏便遇连天雨，船破屡遭大风天’，以至于研究者们无奈地说他们得到了‘中性’的结果，因为人们已经厌倦‘阴性’！当然这些参加者为5，000人甚至超过15，000人的试验还是在老年人群进行的，因为只有‘银髮’才能造就足够的死亡或心梗的‘硬’终点可供统计之用。滑铁卢都发生在‘银髮’的海洋，我们不能逃离吗？回答是也许不能。因为‘黑髮’的海洋中不会在短暂的3~5年研究期间出现那么多‘硬’终点。在这里长出足够数量的硬终点需要20年或更久。没有谁（无论企业和政府）愿意出资做这种费力又前途渺茫的消耗性试验。近来，常有一个声音不厌其烦地提醒说，现在的’循证医学’在寻找降血糖治疗是否能降低死亡和心血管事件方面可能有一个‘盲区’。

国外已经有人发问‘我们还需要更多这种中性试验吗？’。我们是否也该问自己：还要在‘银髮海洋中’遨游多久？‘银髮陷阱’中的证据能够指导在‘普遍’人群的医疗实践吗？人们已经隐约地感觉到那些在老年试验中被宣判为阴性或中性的药物，即使在年轻人中使用也不遭人正眼相看。这些结果甚至耗尽了DCCT和UKPDS‘好的代谢记忆’带给我们的正能量。

‘十年面壁突破壁’，2015-2016年ADA送来了爆炸新闻 --- 新型降糖药SGLT2抑制剂和GLP1受体激动剂在短短的数年研究期间都在高危人群显著降低心血管病风险。这一振奋人心的数据让心脏病专家兴奋溢于言表，评论说：‘心血管获益强度前所未有！SGLT2抑制剂是个心血管药物伴对DM有益作用’。不过，说老实话，它也没能解决血糖降低多少、降到多低最有益的问题。因为这两类新药都不仅能降低血糖、还能显著减轻体重、降低血压、改善血脂紊乱。也许正是其多重作用机制带来降低心血管风险‘突破性’的良好结局。

世界上没有完美的研究，‘去粗取精、去伪存真’是永远需要的。中国几千年的文明提醒我们‘凡事有度，过犹不及’。我们的降血糖治疗也要遵循这些古训，不去追求那些我们做不到的东西，尽管看上去它也许很诱人。

CPL-03

脂肪酸转运与胰岛素抵抗

陈璐璐

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陈璐璐，华中科技大学同济医学院协和医院内分泌科主任，医学博士，教授、主任医师，博士研究生导师；

中华医学会内分泌学分会副主任委员；中华医学会内分泌学分会血脂学组组长；中国医师协会内分泌代谢医师分会常务委员；中国女医师协会糖尿病学会副主任委员：湖北省糖尿病学会主任委员；湖北省医学会常务委员；湖北省女医师协会副会长；中国胰岛素分泌研究组组长《Jof Diabetes》、《Nature Review Endocrinology》、JCEM、柳叶刀内分泌糖尿病分册中文版、《中华内分泌代谢杂志》、中国糖尿病杂志、《华中科技大学学报医学外文版》、《临床内科杂志》等编委。

脂质异位沉积，即脂肪沉积于心脏、肝脏、骨骼肌等非脂肪器官中，是引起代谢性疾病尤其是胰岛素抵抗的重要原因。因此，脂质异位沉积是引起胰岛素抵抗的重要原因。目前研究发现，异位脂质沉积引起胰岛素抵抗的主要机制是甘油二酯（DAG）沉积通过一系列效应阻断了 PI3K 信号通路的激活及葡萄糖转运蛋白（GLUT4）的转位，从而导致组织对葡萄糖的摄取减少，出现胰岛素抵抗。目前，已有研究部分阐述了脂质转运过程及其影响因素，然而，关于脂质转运的具体机制及其干预靶点仍未明了。现有研究发现血管内皮生长因子家族（VEGF 家族）中 VEGF-B 在介导脂质跨内皮转运中起着重要的作用。本课题组在前期研究中发现，追赶生长动物在无过多能量摄入的条件下，出现了内脏器官脂肪的堆积及胰岛素抵抗。那么该过程中引起内脏脂肪堆积的具体机制是什么呢？本课题组通过体内外实验研究发现，追赶生长大鼠骨骼肌内 VEGF-B 表达量明显增加，其下游的脂肪酸转运蛋白（FATP3，4）也明显增加，该结果阐明了追赶生长动物模型中脂质溢出的重要机制，同时为治疗营养变迁所致胰岛素抵抗及糖尿病的治疗提供了新的靶点。

CPL-04

肾上腺疾病精准医学

宁光

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宁光，教授，中国工程院院士、中国医师协会内分泌代谢科医师分会会长、中华医学会内分泌学分会前任主任委员和《中华内分泌代谢杂志》总编辑，是国家杰出青年科学基金获得者、教育部长江学者特聘教授、973项目首席科学家、国际内分泌学会执委会委员。

宁光教授长期从事内分泌代谢病临床与科研工作，尤其在内分泌肿瘤与糖尿病诊治及研究领域成果丰硕。在Science、JAMA、NatCellBiol、JACC、NatGenet等SCI杂志发表论文250余篇，获国家科技进步二等奖3项（2项排名第一，1项第二）及上海市科技进步一等奖3项（排名第一）。宁光教授获评2014年度中国医师奖、吴阶平医药创新奖、美国内分泌医师协会International Endocrinologist Award及以色列糖尿病学会与以色列卫生部共同授予的Lifetime Awardin Diabetes，并带领瑞金内分泌代谢学科成为国家重点学科、国家代谢性疾病临床医学研究中心、基金委创新群体、国家卫计委临床重点专科及《中国最佳专科声誉排行榜》连续五年排名第一，为推动我国内分泌代谢病事业的发展及提升国际地位做出了积极贡献。

肾上腺疾病是一组非常重要的内分泌疾病，包括一系列发病机制、激素分泌以及临床表现差异较大的疾病。传统功能测定价值有限，定位诊断困难，而且发病机制不清。我们首先建立血尿间羟肾上腺素测定等多项诊断新技术，以及双侧岩下窦静脉采血等三项分段采血技术，实现肾上腺肿瘤早期精准诊断。进一步针对恶性嗜铬细胞瘤不能早期诊断的临床困境，发现ERBB-2蛋白检测可作为嗜铬细胞瘤转移风险的重要评估指标。库欣综合征患者病死率高，针对导致库欣综合征的肾上腺库欣腺瘤，我们通过外显子组测序发现PRKACA基因L205R热点突变与肾上腺皮质腺瘤发生密切相关，提出肾上腺库欣腺瘤分为PKA激活型和PKA非激活型，实现肾上腺库欣的精准诊断，并为精准治疗奠定基础。先天性肾上腺皮质增生症（CAH）是最为常见的遗传疾病之一，包括9种酶缺陷导致的临床亚型，临床表型复杂多样，非经典型诊断困难，我们建立了基因诊断与激素质谱测定panel，实现CAH的精准诊断。

CPL-05

库欣综合征研究新发现

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库欣综合征是一种复杂疑难的内分泌疾病，往往合并多种并发症（糖脂代谢异常、高血压、心脏病和感染），致残和致死率较高。如何准确诊断和治疗并有效控制疾病活动状态，是内分泌临床医生所共同面临的挑战。首先，ACTH 依赖性库欣综合征的病因诊断仍然是临床上的诊断难点。内分泌激素和相关动态试验并不能完全区分库欣病和异位 ACTH 综合征，而影像学检查用于病因诊断的价值也有限。在 ACTH 依赖性库欣综合征尤其是临床生化和影像学结果矛盾患者中常规开展双侧岩下窦静脉采血，并引入泌乳素进行校正有利于提高病因诊断的准确性。对无条件开展双侧岩下窦静脉采血的医院可选择去氨加压素试验进行部分替代。其次，加深对 ACTH 非依赖性库欣综合征以及特殊类型如原发性双侧大结节样肾上腺增生和原发性色素性结节性肾上腺病认识有利于早期诊断和选择正确的手术方案。全外显子测序发现 69.2% 肾上腺皮质腺瘤存在 PRKACA 基因 L205R 热点突变，L205R 突变引起蛋白活性增加和磷酸化催化能力增强，通过底物磷酸化促进了肿瘤的发生和类固醇的生成。基础研究显示 ARMC5 基因的突变与原发性双侧大结节样肾上腺增生的发生密切相关，为诊断和治疗提供了新思路。鉴于 Carney 综合征约有一半有家族性聚集倾向，对明确诊断 PPNAD 患者除需详细询问家族史和体格检查外，还需评价是否存在患 Carney 综合征可能性和进行基因检测。再者，相当一部份库欣病患者无法通过垂体手术或放射治疗获得缓解，对仍处于疾病活动状态或者 ACTH 肿瘤定位不明患者应用药物控制高激素水平有助于改善并发症和提高生存率。目前可选用药物治疗方案包括垂体靶向药物、肾上腺酶抑制剂及糖皮质激素受体抑制剂三大类。尤其是新型生长抑素类似物帕瑞肽是近年来库欣病治疗热点。最后，通过分别探讨异位 ACTH 综合征发病机制、大剂量地塞米松抑制试验不被抑制与糖皮质激素抵抗等为库欣综合征今后诊治提供新方向。

CPL-06

FSH 与胆固醇

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赵家军，1983 年毕业于泰山医学院，1994 年毕业于上海第二医科大学（现上海交通大学）获内分泌代谢病专业博士学位。现山东省立医院内分泌科主任医师、山东大学教授，博士生导师，泰山学者，山东省临床医学研究院内分泌代谢研究所所长。中华医学会内分泌分会侯任主任委员，山东省糖尿病分会主任委员。全国优秀科技工作者；卫生部突出贡献中青年专家；全国卫生先进工作者；享受国务院政府特殊津贴；山东省突出贡献中青年专家；山东省“十大名医”；指导博士研究生 60 余名，博士后 7 名。主持科技部“十一五”国家科技支撑计划、973 子课题、国家自然科学基金等科研项目 20 余项。获国家科技进步二等奖 1 项，山东省科学技术最高奖，山东省自然科学一等奖 1 项，山东省科技进步一等奖 4 项。省部级二等奖 4 项。在国内外专业杂志发表论文 300 余篇，其中 130 余篇被 SCI 收录，总影响因子 500。

研究方向：内分泌与脂代谢的交互作用与影响

目的　绝经是导致中老年女性发生血脂紊乱的重要危险因素，但其内在的病理生理学机制目前尚未阐明。传统理论大多将其归因于雌激素的缺乏，然而，早期围绝经期女性仅有血清卵泡刺激素（follicle-stimulating hormone，FSH）水平升高，雌激素水平尚在正常参考值范围内，其血清胆固醇水平明显高于生育期女性，这一临床现象难以用传统理论完善解释。本研究旨在探究 FSH 对胆固醇代谢的调节作用及其内在机制。

方法　采用前瞻性队列研究，对来自山东省宁阳县的 3,047 名研究对象的 3 年随访资料进行分析。采用 Logistic 回归模型评估基线 FSH 水平与高脂血症发病风险的相关性。

结果　单因素 Logistic 回归分析显示，高 TC 血症的发病率随基线 FSH 水平的升高而逐渐升高；校正雌二醇、孕酮及黄体生成素后，基线 FSH 水平与高 TC 血症的发病风险仍然呈剂量依赖关系：与基线 FSH 水平最低组（<39.67 mIU/mL）相比，第二（39.67-62.99 mIU/mL）、三（63.00-81.78 mIU/mL）、四组（>81.78 mIU/mL）高 TC 血症的发病风险依次为最低组的 1.6 倍（P=0.003）、1.9 倍（P<0.001）、2.0 倍（P<0.001）。

CPL-07

GLP-1 受体激动剂的血管保护效应及其机制

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洪天配，教授，主任医师，博士生导师。1991 年毕业于北京大学医学部，获医学博士学位。现任北京大学第三医院内分泌科主任兼检验科主任。担任中华医学会内分泌学分会副主任委员兼糖尿病学组组长、中国医师协会内分泌代谢科医师分会副会长、北京内分泌学会前任主任委员等。担任中华内分泌代谢杂志、中国糖尿病杂志、中国医学前沿杂志副主编、JCEM 中文版等期刊的副主编，Clin Diabetes Endocrinol、中华糖尿病杂志、中华医学杂志等多个期刊的编委，JCEM、Diabetes ObesMetab 等多个 SCI 期刊的审稿专家。牵头制订中华人民共和国卫生行业标准《糖尿病筛查和诊断》。主要研究方向是糖尿病基础与临床研究、干细胞分化研究。先后负责过国家级和省部级科研课题 20 余项，包括国家自然科学基金 6 项、国家 973 计划项目 2 项、国家 863 计划项目 1 项等。在国内核心期刊上发表论文 200 余篇，在 Trends Endocrinol-Metab、Diabetologia、Diabetes ObesMetab、Endocrinology、Am J Physiol Endocrinol Metab等 SCI 期刊发表论文 40 余篇。

心血管疾病在 2 型糖尿病患者中的发生风险为非糖尿病患者的 2-4 倍，是糖尿病患者致死和致残的最主要原因。胰高糖素样肽 1（GLP-1）受体激动剂是近年来新上市的抗糖尿病药物，不但降糖效果良好，而且可避免低血糖风险增加和保护胰岛 β 细胞功能。此外，还具有减轻体重、改善血脂异常、降低血压、改善血管内皮功能等方面的作用，提示其可能具有心血管保护作用方面的益处。因此，GLP-1 受体激动剂在国内外 2 型糖尿病治疗指南中的地位越来越高。2007 年，Nissen 和 Wolski 发表的一项 meta 分析显示，罗格列酮与心肌梗死风险增加显著相关。2008 年，美国食品和药品监督管理局（FDA）发布了新型降糖药物上市监管指南，该指南要求所有新型降糖药上市均需要进行心血管安全性评估。2016 年 6 月 13 日，利拉鲁肽心血管结局研究（LEADER）的结果在今年美国糖尿病学会（ADA）科学年会上进行了公布。LEADER 研究结果显示，在伴有心血管疾病病史或心血管危险因素的 2 型糖尿病患者中，利拉鲁肽治疗不仅不增加主要心血管不良事件（MACE，即非致死性心肌梗死、非致死性卒中及心血管死亡的复合终点）的发生风险，反而可降低 MACE 和微血管事件的发生风险，提示利拉鲁肽具有大血管和微血管保护效应。本讲座除了介绍 GLP-1 受体激动剂改善心血管代谢危险因素外，将着重讨论 GLP-1 受体激动剂对血管的直接保护效应及其作用机制。

CPL-08

妊娠期甲状腺疾病诊治的热点问题

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单忠艳，教授，MD,PhD. 毕业于中国医科大学，曾在美国斯坦福大学医学院做博士后研究。现任中国医科大学附属第一医院内分泌科主任，中华医学会内分泌学分会副主任委员，甲状腺学组组长，中国内分泌代谢病医师协会常委。辽宁省糖尿病学分会前任主任委员，辽宁省医学会内分泌学分会后任主任委员。主要研究方向，甲状腺疾病，特别是妊娠期甲状腺疾病。

最近几年，国内外关于妊娠期甲状腺疾病诊治的临床证据不断增多，对原有诊治方案甚至指南提出了质疑，形成了该研究领域的一些热点问题。

1. 妊娠早期血清 TSH 上限切点值是 2.5mIU/L 还是妊娠特异参考范围上限？ 美国甲状腺学会和其他国外指南均建议妊娠早期 TSH 上限切点值为 2.5mIU/L。在我国没有获得本国妊娠妇女调查数据之前，我们采用了国外的诊断标准。但是，近年来自本研究组和我国其他研究的结果表明，如果采用 2.5mIU/L 作为妊娠早期甲减的诊断标准，我国妊娠早期亚临床甲减的患病率高达 27.8%，而且按照上述标准诊断的亚临床甲减，在妊娠中期和晚期仍为亚临床甲减的符合率仅为 30% 和 20% 左右。

2. 妊娠期评估甲状腺功能采用 TT4 还是 FT4？ 妊娠期由于甲状腺素结合球蛋白（TBG）水平增加，使得结合型 T4 水平升高，TT4 水平随之升高。但是，需要注意的是，TT4 水平在妊娠后逐渐升高，直到妊娠 16 周才达到平稳的水平，约是非妊娠时的 1.5 倍，并持续到分娩。所以，在妊娠早期，采用 1.5 倍的基础 TT4 水平诊断妊娠早期甲减是不合适的。在妊娠情况下由于 TBG 水平升高，可能影响 FT4 的测定值。但是根据我们对同一人群进行的前瞻性观察，应用电化学发光法测得的 FT4 与 ICP-MS 测得的 FT4 有很好的一致性，提示可以采用 FT4 作为妊娠期甲减和单纯低甲状腺素血症的诊断指标。FT4 应采用试剂特异和妊娠期特异的参考范围。

3. 妊娠妇女 TPOAb 阴性，TSH>2.5 mIU/L 是否治疗？ 根据美国 ATA 指南，上述妊娠妇女可以不治疗。中华医学会内分泌学分会指南建议可以治疗也可以不治疗。目前的研究证据支持妊娠妇女 TPOAb 阴性，TSH> 妊娠期特异参考范围上限的亚临床甲减患者给予 L-T4 治疗。对于 TPOAb 阴性，TSH>2.5 mIU/L 但是低于妊娠期特异参考范围上限的妊娠妇女是否治疗，应该个体化选择。从诊断上来说这些妊娠妇女不能诊断甲减或亚临床甲减。但是本研究组的研究显示当妊娠早期妇女TPOAb阴性，TSH>2.5mIU/L 但是低于妊娠特异参考范围上限，就可使流产发生风险增加，随着 TSH 升高流产发生风险进一步提高，如果加上 TPOAb 阳性，流产的发生风险更高。所以，鉴于 L-T4 在妊娠妇女应用的安全性，既往有流产史的妊娠妇女，虽然 TPOAb 阴性，TSH>2.5mIU/L，建议给予治疗。

4. 其他热点问题：诸如妊娠期低甲状腺素血症发生的原因？是否对母胎有不良影响？是否需要治疗？如何治疗？妊娠期妇女碘营养的评估？碘充足地区妊娠妇女如何补碘？上述问题我将在报告中详细报告。

CPL-09

罕见病例在认识糖尿病中的重要作用

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贾伟平，女，医学博士，主任医师、教授、博士生导师、973首席科学家。现任上海交通大学附属第六人民医院院长、上海市糖尿病临床医学中心主任、上海市糖尿病重点实验室主任和上海市糖尿病研究所所长，兼任中华医学会糖尿病学会主任委员、中华医学会内科分会副主任委员。近年来，主持973、国家自然基金重点项目等各类重大科研项目20项；在国内外杂志发表论文400余篇，其中以第一或通讯作者发表SCI收录论文200余篇，包括BMJ、Lancet Diabetes Endocrinology、Diabetes、Journalof Hepatology等。担任中华内科杂志主编、Journalof DiabetesInvestigation副主编、中华医学杂志副总编辑、中华糖尿病杂志副主编，Lancet Diabetes Endocrinology、Diabetes等期刊编委。享受国务院特殊津贴。获国家、教育部、上海市等各级科技进步奖20项，其中第一完成人10项。入选“领军人才”、“优秀学科带头人”等人才培养计划，2006获卫生部有突出贡献中青年专家称号、2007年获得上海市劳动模范称号、2008年被评为上海市三八红旗手标兵、2009年被评为全国三八红旗手、2010年获得全国先进工作者称号、2011年获上海市科技精英、2012年获全国优秀科技工作者、2015年获吴杨奖。

糖尿病是一种由胰岛素分泌不足和/或作用缺陷导致的以临床高血糖为主要特征并全身代谢异常的疾病。临床上可分为1型糖尿病、2型糖尿病、妊娠期糖尿病及特殊类型糖尿病，尽管不同类型糖尿病发病机制不尽相同，但遗传因素均在其中发挥至关重要的作用。其中，特殊类型糖尿病约占糖尿病患者的3%，发病原因多为基因突变所致。尽管特殊类型糖尿病所占比例不高，但其表型特征强烈，危害严重，且多能代代相传，因此，明确不同特殊类型糖尿病的遗传突变，不仅有利于临床分子筛查、明确诊断、指导治疗，还可由此进行深入的疾病机制研究，为充分认识疾病奠定重要基础。以线粒体突变糖尿病为例，该疾病早在1962年就有相关家系报道，临床特点起病早，有母系遗传家族史，除糖尿病以外，常伴有轻至中度神经性耳聋以及其他神经系统受损表现，直至1992年，van den Ouweland等人正式定位线粒体tRNA Leu(UUR)基因3243位核苷酸A-G突变为该疾病最主要致病突变，随后的功能学研究发现线粒体基因上的突变直接导致ATP合成障碍，能量来源不足及ROS生成过多，最终启动细胞凋亡而致病。因而在治疗方面，针对ß细胞功能缺陷的特点，主张以胰岛素治疗为主，辅以磺脲类药物，但避免使用双胍类药物。目前，线粒体突变糖尿病在临床上以简易的分子生物学技术即可检出，已成为首个进入常规临床基因诊断的一种糖尿病亚型。另外，由于导致特殊类型糖尿病的致病基因与2型糖尿病诸多易感基因可能存在重叠，故从罕见病例及家系出发，定位致病基因，还可为探讨2型糖尿病遗传易感性提供新的线索。以青少年发病的成人型糖尿病（MODY）为例，目前，全世界已明确了13种MODY亚型，均可通过基因突变筛查而明确诊断并指导后续治疗。有趣的是，研究者们发现导致MODY发生的基因亦可能是2型糖尿病的易感基因，如MODY5的致病基因HNF1ß，MODY9的致病基因PAX4，均被证实是中国人2型糖尿病的易感基因之一。

综上，对罕见的特殊类型糖尿病的致病基因定位及机制研究不仅对临床诊疗具有重要价值，还为我们了解复杂型糖尿病的发病机制提供了新的线索和契机。

CPL-10

下丘脑 - 垂体疾病诊断中存在的问题

母义明

中国人民解放军总医院

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下丘脑 - 垂体 - 靶腺轴是内分泌调节的主要结构和生理基础。下丘脑和垂体疾病的发病率在成人内分泌领域疾病中约占第四位。由于其结构和调节功能的复杂性、疾病表现的多样性和非特异性并存，以及相对在治疗前难以获得病理结果，使得临床上治疗的难度明显增加。功能亢进性疾病通过比较典型的临床表现、化验检查和影像学检查诊断并不困难。但功能减退性的局部占位或破坏性疾病的诊断难度很大，尤其鞍上病变活检标本难以获得，再加上我们目前的激素刺激功能试验不完善，造成临床最终治疗的盲目性和潜在的副作用明显增加。本报告重点介绍临床少见的下丘脑和垂体疾病的诊断思路、难点和治疗中存在的问题。内容包括功能减退性疾病，如 IgG4 相关下丘脑垂体炎、淋巴细胞性下丘脑垂体炎和生殖细胞瘤之间的鉴别和治疗方法，以及存在的问题。

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专题发言

CS-001

糖尿病领域的精准医学研究概况

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纪立农，主任医师，教授，现任北京大学人民医院内分泌科主任，北京大学糖尿病中心共同主任，北京大学衰老研究中心副主任，博士生导师；

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世界糖尿病同盟（GDA）督导委员会成员

摘要暂缺

CS-002

新生儿糖尿病的诊疗新进展

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肖新华，医学博士主任医师教授博士生导师。中国医学科学院糖尿病研究中心秘书长，中国老年保健协会糖尿病专业委员会侯任主委，中国糖尿病防治康复促进会（中国糖防会）副会长，中华医学会糖尿病学分会常委兼糖尿病营养学组组长，中华中医药学会糖尿病分会常委，中央保健会诊专家。参与多部学术专著的编写，为《糖尿病现代治疗学》副主编，以第一或通讯作者发表论文及综述 200 余篇，其中发表在 PNAS,DiabetesCare 和 Metabolism 等在内的 Sci 文章 40 余篇．主持申请多项国家级科研课题。现任《Diabetes Researchand Clinical Practice》中文版副主编、«Diabetes Metabolism Researchandreviewer»、《Chinese Medical Journal》英文版编委以及《中华糖尿病杂志》、《内科急危重杂志》和《国际糖尿病》等杂志编委。同时任国家科技奖评审专家，国家自然基金评审专家，北京市科学技术奖励评审专家，教育部博士点基金评审专家，中华医学科技奖评审专家。主要研究方向是糖尿病的发病机制及早期防治，特殊糖尿病的分子遗传学研究。

新生儿糖尿病（NDM）是一种少见的特殊类型糖尿病糖尿病，分为暂时性新生儿糖尿病（TNDM）和永久性新生儿糖尿病（PNDM）两种临床类型。过去 NDM 一直被误诊为 1 型糖尿病，终生给予胰岛素治疗。新近 NDM 的分子遗传学研究取得了突破性进展，其特殊基因突变类型正逐渐得以鉴定明确，迄今至少已经发现 12 种与胰岛素分泌和胰腺发育异常有关的 NDM 致病基因，包括染色体 6q24 异常、KCNJ11、ABCC8 基因突变、以及胰岛素启动因子 1（IPF1）、葡萄糖激酶（GCK）、胰岛素基

因（INS）、真核生物翻译起始因子 2 激酶 3（EIF2AK3）、葡萄糖转运蛋白 2（GLUT2）、肝细胞核因子 1（HNF1β）、GLIS 家族锌指 3 基因（GLIS3）、PTF1A 和 FOXP3 等基因异常。其中，染色体 6q24 异常和 KCNJ11 基因杂合子激活突变分别被确认为 TNDM 和 PNDM 的主要致病基因。

当前，有关 NDM 的基础和临床研究基本上均来自欧美国家，亚洲人群中仅有来自日本和韩国的少数病例研究报道。在中国，这一特殊类型的糖尿病尚未引起足够重视，大部分 NDM 患者仍被诊断为 1 型糖尿病，终身给予胰岛素治疗，某些突变基因如 KCNJ11 或 ABCC8 基因杂合子激活突变导致的 NDM 患者，胰岛素治疗并不是其最佳选择，口服降糖药物可以更好地控制血糖并改善其相应临床症状，提高患者的生活质量和临床预后。因此，对中国 NDM 患者开展基因诊断和临床转换治疗研究具有重要的临床意义。而且积极开展这类少见单基因异常导致的 NDM 的研究也有助于我们深入阐明 2 型糖尿病中潜在的特殊类型糖尿病的相关致病基因，并进一步了解正常胰腺发育和胰岛功能异常的病理生理学机制。

CS-003

糖尿病的表观遗传

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李小英，男，博士生导师。复旦大学附属中山医院内分泌科主任，主任医师、教授；上海市优秀学科带头人。兼中华医学会糖尿病学分会常委，上海市糖尿病学会候任主委。《Journal of Diabetes》杂志副主编，《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中国糖尿病杂志》编委。1983 年毕业于衡阳医学院，获学士学位；1987 年毕业于第三军医大学，获硕士学位；1996 年毕业于上海第二医科大学，获博士学位。1998–2003 年先后在美国 Baylor 医学院、加拿大 McGill 大学和 UBC 大学做博士后研究。主要从事代谢性疾病发病机制和性发育障碍临床研究。在 Cell Metabolism，JCI，Diabetes,Gastroenterology,Gut,JCEM,Development，Journal of Hepatology,Cancer Research 等杂志发表论文 88 篇，撰写专著 3 部。

当前，中国 2 型糖尿病发病率呈“爆炸式”增长，其原因固然与人群的遗传易感性密切相关。但是生活方式改变、营养失衡和行为改变等环境因素在 2 型糖尿病发生发展过程中的作用可能更为关键。也就是说，2 型糖尿病的发生发展是环境因素与遗传因素相互作用的结果。

当今社会，随着经济水平的发展，生活方式的转型，焦虑、紧张、抑郁等心理压力与应激日益频繁，已严重危害人类健康。大量人群流行病学研究表明，心理应激（Psychological stress）与多个疾病的发生发展密切相关，如神经退行性疾病、心血管疾病、肿瘤、2 型糖尿病等。此外，近年来的研究表明，母亲的心理应激，尤其是妊娠期间的应激，可促进子代肥胖和 2 型糖尿病的发生。但父亲应激，能否影响或调控子代的糖代谢情况，目前尚无文献报道。鉴于此，双方课题组通力协作，以 C57BL/6 小鼠为动物模型，系统的探讨了这一跨代遗传现象及背后的分子机制。研究人员将 8 周龄雄性小鼠置于 50 毫升离心管中 (Restraint stress)，每天 2 小时，持续 2 周 (Stress 组)。对照组小鼠 (Control 组) 在此期间，自由进食与活动。2 周后，将两组小鼠分别与正常雌鼠交配，进而获得子代小鼠 (F1)。进而，课题组详细观察了两组小鼠 (Control-F1、Stress-F1) 的糖代谢表型，并发现：Stress-F1 小鼠表现为血糖升高，丙酮酸耐量实验表明肝脏糖异生和肝糖输出能力增强，而葡萄糖和胰岛素耐量实验表明胰岛素敏感性并未改变。在基因表达层面，Stress-F1 小鼠肝脏 PEPCK 的蛋白水平显著增加，但 mRNA 无明显改变，提示 PEPCK 的表达可能受到转录后水平的调节。由此，课题组通过 MicroRNA 表达谱芯片，筛选出调节 PEPCK 表达的一个 MicroRNA: miRNA-466b-3p 的表达在 Stress-F1 小鼠肝脏中显著下调。在此基础上，课题组发现父亲应激后，血清糖皮质激素水平显著升高，引起精子 miRNA-466b-3p 启动子区域甲基化程度的增加，并遗传至子代小鼠，导致其肝脏中 miR-466b-3p 的表达下调，引起 PEPCK 蛋白表达的增加，从而引发子代小鼠糖异生增加，血糖升高。

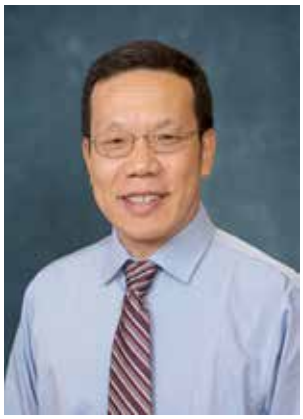
本研究首次发现，父亲的心理应激，通过表观遗传等机制，调控子代的糖代谢状况。有趣的是，近年来，父亲至子代的跨代遗传调控作用 (Intergeneration)，已在多个动物模型上被发现。例如，给予父亲高脂、低蛋白等饮食处理后，可影响子代胰岛、肝脏中糖脂代谢相关基因的表达，进而影响子代小鼠的糖脂代谢稳态。因此，本研究进一步证实了环境因素介导的跨代遗传调控作用。而这些结果，将为日后人群层面相关疾病的研究提供有益的线索和理论基础。

CS-004

单基因糖尿病：从基础到临床

刘铭

天津医科大学总医院



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Medicine 杂志编委，Molecular

Aspectsof Medicine 客座编委，

Diabetes, JCEM, Obesity,AJP，Endocrinology 等 15 家 SCI 杂志特约审稿专家。

美国国立健康研究院 (NIH)、美国宾西法尼亚大学糖尿病中心研究基金、英国 DiabetesUK 基金会和中国国家自然科学基金评审专家。

主持美国健康研究院 (NIH,RO1) 等国际课题 5 项，国家自然科学基金 3 项，共同主持 NIHRO1 课题 2 项 (Co-PI)

在PNAS, JCI, Diabetes, Molecular Aspects of Medicine, JBC, JCS等杂志发表SCI论文44篇，总影响因子超过 280。

单基因突变所致的特殊类型糖尿病占所有类型糖尿病的 1-5%，在 35 岁前发病的糖尿病患者中，单基因糖尿病比例超过 15%，研究表明，小于 20 岁的单基因糖尿病患者中，有 94% 被误诊为 1 型或 2 型糖尿病，其中 76% 被错误治疗。至今为止，超过 30 个基因突变已被证实可导致新生儿糖尿病 (Neonatal diabetes mellitus, NDM) 或青少年发病的成年型糖尿病(maturity-onset diabetes of the young，MODY)，这两种最常见的单基因糖尿病。本讲座将在总体概括导致单基因糖尿病致病基因和临床特征的基础上，重点介绍由胰岛素基因突变所致糖尿病的临床特征和发病机制，同时也将与参会同仁分享我们在这一领域的最新研究结果和将来可能用于该类型糖尿病靶向治疗策略。

CS-005

糖尿病与肿瘤相关性

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毕宇芳，上海交通大学医学院附属瑞金医院内分泌代谢科，主任医师、博士生导师，上海市内分泌代谢病研究所副所长。兼任中华医学会内分泌学分会委员与青年委员会副主任委员，主要致力于 2 型糖尿病的临床诊治与早期防控研究，在 JAMA、JACC、DiabetesCare、JCEM 等 SCI 收录杂志发表论文 60 余篇。作为第一责任人分别承担国家自然科学优秀青年基金与国际合作基金。

近年来，许多流行病学研究结果表明：糖尿病与部分恶性肿瘤的发病显著相关，相关研究无论在糖尿病学领域还是肿瘤学领域都受到高度关注。糖尿病状态为何会导致恶性肿瘤风险增加？是否受到糖尿病病程、服用糖尿病药物的种类和剂量、血糖控制水平等影响？对于这些问题，研究结果并不一致。基于这些尚待明确的问题，中国 2 型糖尿病患者肿瘤发生风险的流行病学研究 (Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal study，REACTION 研究) 希望能够通过长期随访加以阐明，目前该研究已完成基线调查。基线调查结果初步显示，糖尿病人群的恶性肿瘤患病率明显高于糖代谢正常人

群。其中男性糖尿病人群患病率显著高于糖代谢正常人群的恶性肿瘤分别为：结直肠癌、肺癌、膀胱癌、肾癌、前列腺癌等；女性糖尿病人群患病率显著高于糖代谢正常人群的恶性肿瘤分别为：乳腺癌、子宫内膜癌、结直肠癌、卵巢癌、肾癌等。糖尿病病史、糖尿病病程、血糖水平与恶性肿瘤的患病风险存在相关性。研究目前随访进展中，期待进一步深入阐述糖尿病与恶性肿瘤的相关性。

CS-006

传统降糖药物与肿瘤之间的关系

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现任第十届中华医学会内分泌学分会委员；第八届北京医学会内分泌学分会委员、学术秘书；中国女医师协会糖尿病专业委员会委员；中华医学会糖尿病学分会流行病学学组成员；《中国糖尿病杂志》编委；Diabetes research and clinical practice 杂志编辑及中文版副主编。北京市继续医学教育委员会第四届学科组专家。

主要研究领域为糖尿病及其并发症流行病学。2009–2010 年于芬兰赫尔辛基大学公共卫生系进行糖尿病流行病学博士后研究期间，对欧洲 DECODE 数据分析，研究糖尿病与肿瘤死亡风险之间的关系，研究结果发表在 Diabetologia 杂志。参与多项国家级及省、市级科研课题。在国际和国内专业期刊发表学术论文 40 余篇。

降糖药物可能改变肿瘤的发病风险。在传统的降糖药物中，二甲双胍通过 AMPK 依赖和非依赖的机制可能降低肿瘤的发生风险，而外源性胰岛素及胰岛素促泌剂磺脲类药物可能通过激活胰岛素样生长因子— 1 点受体而产生促进肿瘤生长的作用。

随着流行病学研究证据的积累，降糖药物与肿瘤之间关系的研究已经发展为能够对多个研究进行 Meta 分析，但是，由于大多数的研究为观察性研究，难以避免混杂因素的影响，随机对照的临床试验的样本量则相对较小，不能达到有效的统计学效力。由于研究机构、观察人群、参照治疗、混杂因素调整的不同，Meta 分析的结果往往具有较高的异质性，降糖药物和肿瘤之间的相关性也可能与肿瘤的部位有关，这些因素都导致各个研究结果的不一致。

目前较为一致的结果是二甲双胍的使用和肿瘤的发病风险降低相关，在一项对观察性研究进行的 Meta 分析中，与未使用二甲双胍的糖尿病患者相比，使用二甲双胍的糖尿病患者肿瘤的发病风险降低 40%，在对结肠直肠癌和肝细胞癌发生风险进行的 Meta 分析中，二甲双胍使用者的发病风险较非使用者降低。

脲类药物与肿瘤发生风险的关系之间的研究结果不一致。在一项对观察性研究进行的 Meta 分析中，磺脲类药物与肿瘤发生风险不相关；而在对不同部位肿瘤发生风险的 Meta 分析中，与非磺脲类药物治疗相比，磺脲类药物的使用与肝细胞癌和胰腺癌发生风险增高相关。

在观察性研究中，胰岛素与肿瘤发生风险的 Meta 分析存在很强的异质性，去除人数最少的研究后，异质性减小，结果显示使用胰岛素者的肿瘤发生风险较从未使用过胰岛素者增加了 23%。在新诊断的糖尿病患者中，使用胰岛素者胰腺癌发生风险增高，但不除外反向的因果关系。按肿瘤部位进行分析显示，胰岛素的使用可能与肝细胞癌发生风险增高相关。

两个 Meta 分析显示，吡格列酮的治疗与膀胱癌的发生风险增高相关。

由于现有的研究以观察性研究为主，对降糖药物和肿瘤之间的关系作出肯定的结论尚需要更多的证据的积累。

CS-007

新型降糖药物与肿瘤之间的关系

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洪天配，教授，主任医师，博士生导师。1991 年毕业于北京大学医学部，获医学博士学位。现任北京大学第三医院内分泌科主任兼检验科主任。担任中华医学会内分泌学分会副主任委员兼糖尿病学组组长、中国医师协会内分泌代谢科医师分会副会长、北京内分泌学会前任主任委员等。担任中华内分泌代谢杂志、中国糖尿病杂志、中国医学前沿杂志副主编、JCEM 中文版等期刊的副主编，ClinDiabetes Endocrinol、中华糖尿病杂志、中华医学杂志等多个期刊的编委，JCEM、Diabetes ObesMetab 等多个 SCI 期刊的审稿专家。牵头制订中华人民共和国卫生行业标准《糖尿病筛查和诊断》。主要研究方向是糖尿病基础与临床研究、干细胞分化研究。先后负责过国家级和省部级科研课题 20 余项，包括国家自然科学基金 6 项、国家 973 计划项目 2 项、国家 863 计划项目 1 项等。在国内核心期刊上发表论文 200 余篇，在 TrendsEndocrinolMetab、Diabetologia、Diabetes ObesMetab、Endocrinology、Am J Physiol Endocrinol Metab 等 SCI 期刊发表论文 40 余篇

近年来，胰高糖素样肽 1（GLP-1）受体激动剂、二肽基肽酶 4（DPP-4）抑制剂、钠 - 葡萄糖协同转运蛋白 2（SGLT-2）抑制剂等新型降糖药物先后被批准上市。对于新型降糖药物而言，除需要证实具有明确的疗效外，其安全性也越来越受到重视。2007 年，Nissen 和 Wolski 发表的一项 meta 分析显示，罗格列酮与心肌梗死风险增加显著相关，与心血管死亡风险增加的相关性在统计学上处于临界状态。2008 年，美国食品和药品监督管理局（FDA）发布了新型降糖药物上市监管指南，该指南要求所有新型降糖药上市均需要进行心血管安全性评估。此外，新型降糖药与肿瘤发生风险的相关性近年来也受到了广泛关注。本专题将从基础研究结果、队列研究数据、药品注册临床试验数据的 meta 分析、大型心血管终点临床试验数据等多个层面，对新型降糖药物与肿瘤之间的关系进行讨论。

CS-008

二甲双胍抗肿瘤作用的相关研究证据

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《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中华器官移植杂志》、《中国糖尿病杂志》、《中国临床保健杂志》及《上海医学》杂志编委，《Journalof Diabetesandits Complications》、《Metabolism》、《Chinese Journalof Medicine》、《Diabetology& Metabolic Syndrome》、《国际内分泌代谢杂志》及《上海交通大学学报（医学版）》等杂志特邀审稿人

2004 年获上海市杰出回国留学人员专项资金资助，已在国、内外发表学术论文 240 篇（SCI40 篇），参编专著或教材 12 部。2012 年获上海市医学科技二等奖，2014 获中华医学科技三等奖、华夏医学科技三等奖。2014 年获上海市第一人民医院院长奖。

100 多年前，Maynard 教授就提出糖尿病与肿瘤的关系，引起科学家们对糖尿病和肿瘤这两大疾病领域相关性的思考，当时是因为统计方法存在问题和材料不足，难以得出两种疾病是否具有显著相关性的结论。2010 年由内分泌和肿瘤两大领域发布的糖尿病与肿瘤的共识报告总结了糖尿病与肿瘤存在诸多共同风险因素，如年龄，肥胖，饮食，吸烟和饮酒等；2013 年回顾分析显示糖尿病患病时间越长，肿瘤患病风险越高；2015 年一项大型的系统评价，与非糖尿病患者相比，2 型糖尿病增加乳腺癌，结直肠癌，肝内胆管癌，子宫内膜癌等发生风险。而对 UKPDS，ACCORD，VADT 等多项研究 meta 分析显示，强化降糖并不能降低肿瘤的发生风险和死亡率。

2005 年，Evans 等首次报道二甲双胍可以降低糖尿病患者恶性肿瘤的发生率，其后 11 年间，越来越多的研究者关注二甲双胍对恶性肿瘤的抑制作用，多项流行病学调查显示糖尿病患者服用二甲双胍与恶性肿瘤发生和预后存在密切关系，2012 年，一项筛选了 401 项研究，入选 17 项研究，各部位肿瘤共 37,632 多患者的 meta 分析显示，二甲双胍降低总体肿瘤风险 39%，结直肠癌风险 36%，胰腺癌风险 62%，2013 年美国一项关于降糖药与肝细胞癌风险的 meta 分析显示，二甲双胍显著降低肝细胞癌的风险，2014 年台湾一项 6 年的随访研究显示，二甲双胍降低肿瘤风险与其剂量呈正相关。

目前推测其抑制肿瘤存在这直接途径和间接途径这双重作用的机制，直接机制是二甲双胍从多个水平上进行调节，从而抑制 mTORC1。1. 二甲双胍激活 AMPK，AMPK 激活抑癌基因 TSC2，从而抑制 mTORC1 的激活剂 RHEB.2. 二甲双胍通过降低胰岛素的水平和 AMPK 依赖的 IRS-1 的磷酸化，来降低 IGF-1 下游信号，从而抑制 AKT 和 mTORC1 信号。3. 二甲双胍可以不依赖 AMPK 抑制 mTORC1。间接机制主要是通过二甲双胍降低血糖和血中的胰岛素水平，从而降低胰岛素介导的肿瘤细胞生长和进展；另外二甲双胍的抗炎作用也能降低肿瘤风险。另外其他机制研究发现，二甲双胍还可以通过抑制细胞有丝分裂和增殖，降低氧自由基，DNA 损伤和基因突变，作用于 miRNA 降低细胞癌变的发生率，抑制肿瘤干细胞生长等。

目前对二甲双胍抑制肿瘤的研究大多为回顾性病例分析和 meta 分析，回顾性研究选择对象时难以完全平衡年龄，肥胖，吸烟等混杂因素的影响，仅有少量前瞻性的小样本研究探索二甲双胍的恶性肿瘤抑制作用，未来尚需要前瞻性，多中心和随机队列研究来进一步探讨和证实其作用。

CS-009

循环 RNA 在甲状腺乳头状癌中的诊断作用

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目前对于甲状腺乳头状癌与良性结节的鉴别缺乏可靠和有效的标志物，近年来研究显示循环血 RNA 可能可以作为诊断甲状腺乳头状癌 (PTC) 无创分子标记物，与 FNA 和超声协同诊断作用。循环血中甲状腺特异性 mRNA，例如促甲状腺激素受体 mRNA，甲状腺球蛋白 mRNA 和钠 / 碘同向转运 mRNA 是甲状腺癌的诊断和预后标记，但在多个研究中显示利用定量 RNA 分析这些分子具有可变性和不一致，因而限制其临床应用。

既往研究发现血清 microRNA(miRNA) 可能成为多种肿瘤的诊断和预后的分子标志物。我们的研究通过检测 PTC、甲状腺良性结节和正常对照者血清中 miRNA 表达。研究发现血清 let-7e、miR-151-5p 和 miR-222 在 PTC 中表达明显升高，并发现这三个 miRNA 具有较高的诊断特异性和灵敏度；血清 miR-151-5p 和 miR-222 在 PTC 患者术后表达显著下降，可能可以作为预后及复发的预测因子；miR-151-5p 和 miR-222 在组织和血清中表达一致。我们的研究结果提示血清 miRNA 可能可以作为诊断甲状腺乳头状癌的新的无创性分子标记物。

lncRNA(lncRNA) 与多种肿瘤的发生、发展密切相关，报道证明外周血中存在与肿瘤相关的 lncRNA。我们在通过芯片及 qRT-PCR 方法发现与结节性甲状腺肿患者和正常对照者相比，PTC 患者血浆中的 AK026079、uc001tdk.2 和 NR_003503 表达水平均显著升高，这 3 个 lncRNA 可能可作为诊断 PTC 的无创性分子标志物。通过体外实验发现 uc001tdk.2 和 NR_003503 可能参与了 PTC 细胞的迁移、侵袭过程。

此外，环状 RNA(circRNA) 是一类新近发现的内源性非编码 RNA，是 RNA 领域的最新研究热点。研究发现，circRNA 在人体细胞中广泛表达，在转录后水平具有调控基因表达的重要功能。circRNA 被证实在可以大量分泌到外周血中，这使得循环血 circRNA 的筛查可能可以为 PTC 早期诊断生物标记物。循环血 RNA 为 PTC 诊断开辟了新的视角，然而 , 循环 RNA 分子样品制备的标准化及质量评估是目前迫切需要的解决的问题，这也是循环 RNA 应用于临床实践最关键的步骤。

CS-010

甲状腺细针穿刺细胞基因学检测在鉴别甲状腺结节良恶性中作用

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甲状腺细针穿刺细胞病理学检查是术前甲状腺结节评估的金标准，其诊断的敏感性为 65%-98%，特异性为 72%-100%。根据 Bethesda 分类系统，其中细胞学检查不能确定的结节占 25%-30%。2015 年版的 ATA 指南建议针对这部分病人可以进行分子标记物检测。目前，甲状腺结节细针穿刺细胞基因学检测包括：基因突变和重排检测、基因表达分类谱。

基因突变和重排的检测包括 BRAF V600E、N-ras、H-ras、K-ras 基因突变，RET/PTC1、RET/PTC2、RET/PTC3、PAX8/PPAR γ 基因重排。BRAF V600E 突变导致 BRAF 激酶持续激活，并使丝裂原活化蛋白激酶（MAPK）下游传导分子高表达，从而导致细胞过度增殖、分化，最终导致甲状腺细胞的恶性转化。Ras 基因突变多见于甲状腺滤泡癌（FTC），占 FTC 的 40%-50%，占甲状腺乳头状癌（PTC）的 10%-20%。RET 原癌基因的突变在 PTC 中主要表现为基因重排，RET/PTC 重排在 PTC 中约占 10%-20%。PAX8/PPAR γ 重排在 FTC 中约占 30%-35%。荟萃分析显示：BRAF V600E 基因突变对于可疑恶性的甲状腺结节，敏感性为 61.9%，特异性为 99.7%。为了提高其敏感度，临床采用多个标记物联合检测，设计了分子标记物面板。Asuragen（Austin，TX）miRinform 甲状腺面板包括了上述基因突变、重排及其他重排融合基因。对于滤泡性肿瘤和可疑滤泡性肿瘤（FN/SFN 结节），其敏感性为 57%-75%，特异性为 97%-100%。ThyroSeq v2 是第二代的基因检测面板，其基于单个碱基的插入与缺失以及基因重排融合。一项单中心研究显示，检测 143 例滤泡性肿瘤标本，其敏感性为 90%，特异性为 93%。

其他基于 mRNA 标记物和 microRNAs 标记物，用于 FNAB 不确定的甲状腺肿瘤的分子诊断也不断涌现。Veracyte 开发的 Afirma GEC 通过评价 FNAB 标本中 167 个基因的表达以鉴别结节的良恶性。在前瞻性多中心研究中，GEC 对于甲状腺滤泡性肿瘤的诊断，具有较高的敏感性（92%）和阴性预测值为 94%。其阴性的结果将恶性的风险从 24% 降至 5%。因此，GEC 检测

结果阴性多用于甲状腺癌的排除诊断，避免外科手术治疗。

CS-011

再谈妊娠期甲状腺疾病的诊断标准

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单忠艳，教授，MD,PhD. 毕业于中国医科大学，曾在美国斯坦福大学医学院做博士后研究。现任中国医科大学附属第一医院内分泌科主任，中华医学会内分泌学分会副主任委员，甲状腺学组组长，中国内分泌代谢病医师协会常委。辽宁省糖尿病学分会前任主任委员，辽宁省医学会内分泌学分会后任主任委员。主要研究方向，甲状腺疾病，特别是妊娠期甲状腺疾病。

妊娠期甲状腺功能异常同普通人群一样，是以甲状腺性为主，所以血清 TSH 仍然是评估甲状腺功能最敏感的指标，而 T4 是诊断甲减的指标，T3 或 T4 是诊断甲亢的指标。对于妊娠期 TSH 诊断的切点值，一直存在争议。

美国甲状腺学会和其他国外指南均建议 TSH 上限切点值妊娠早期为 2.5mIU/L，妊娠中晚期为 3.0 mIU/L。在我国没有获得本国妊娠妇女调查数据之前，我们采用了国外的诊断标准。但是，近年来自本研究组和我国其他研究的结果表明，如果采用 2.5mIU/L 作为妊娠早期甲减的诊断标准，我国妊娠早期亚临床甲减的患病率高达 27.8%，而且按照上述标准诊断的亚临床甲减，在妊娠中期和晚期 TSH 仍超过 3.0mIU/L 符合率仅为 30% 和 20%。我们的研究还发现妊娠小于 7 周的妇女，TSH 上限切点值可以采用普通人群的参考范围上限。与非妊娠期参考范围相比，由于 hCG 的作用，妊娠期 TSH 下限降低 0.1-0.2，有少数妊娠妇女 TSH 可能降低至不能检测到的水平（< 0.01mIU/L），TSH 降低程度与 hCG 水平相关，TSH 与 hCG 浓度呈负相关。妊娠早期 TSH 降低，中期和晚期逐渐升高，但是仍低于非妊娠妇女。所以应该采用妊娠期特异 TSH 参考范围诊断妊娠期甲状腺疾病。

妊娠期由于甲状腺素结合球蛋白（TBG）水平增加，使得结合型T4水平升高，TT4水平随之升高。但是，需要注意的是，TT4 水平在妊娠后逐渐升高，直到妊娠 16 周才达到平稳的水平，约是非妊娠时的 1.5 倍，并持续到分娩。所以，在妊娠早期，采用基础 TT4 水平的 1.5 倍诊断妊娠早期甲减是不合适的。FT4 仅占 TT4 的 0.03%。当结合型 T4 增多和有波动时，例如妊娠，FT4 的测定更为困难。使用 LC/MS/MS) 检测的 FT4 与传统的平衡透析法测得的 FT4 相似，根据我们对同一人群进行的前瞻性观察，应用电化学免疫发光法测得的 FT4 与 ICP-MS 测得的 FT4 有很好的一致性，提示可以采用目前医院广泛应用的免疫化学发光发测得的 FT4 作为妊娠期甲减和单纯低甲状腺素血症的诊断指标。但是 FT4 应采用试剂特异和妊娠期特异的参考范围。

CS-012

妊娠期和产后甲减患者 L-T4 的应用

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妊娠期及产后甲状腺疾病的发生率不断增加，其对妊娠、产后的影响正得到越来越多的重视，同时对于妊娠期及产后甲状腺疾病的认识也在逐步深入。

L-T4 是妊娠妇女或准备妊娠的妇女甲状腺激素替代治疗首选制剂，左甲状腺素对妊娠和哺乳均安全，目前无致畸大量进入乳汁的证据。胎儿发育尤其是脑发育主要依赖母体充足的 T4 水平，而不是 T3 水平。

治疗目标

一旦确诊，应及时、足量补充外源性左甲状腺素，保证妊娠早期母体对胎儿的甲状腺激素的供应，满足胎儿第一个脑快速发育期对甲状腺激素的需要。现有资料表明，妊娠早期的 TSH 2.5 mlU ／ L 可以作为补充左甲状腺素纠正甲减的目标值，但由于 hCG 的影响，妊娠早期 TSH 受抑制处于偏低水平，左甲状腺素剂量的调整需根据 FT4 和 TSH 确定。血清 FT4 保持在非妊娠成人正常范围的上限；血清 TT4 维持在非妊娠成人正常值的 1.5 倍水平。

治疗时机

时间越早越好，最好妊娠开始即达到血清 TSH<2.5 mlU ／ L 的标准。

治疗剂量

通常左甲状腺素剂量较非妊娠需要量增加 30% ~ 50%。有研究表明：对于妊娠期间首次诊断甲状腺功能减退症的患者，建议：TSH 水平＜ 4.2 mIU/L 的亚临床甲减者 1.20 μg/kg/ 天；TSH 水平＜ 4.2~10mIU/L 的亚临床甲减者 1.42 μg/kg/ 天；临床甲减者 2.33 μg/kg/ 天。妊娠前确诊甲减妇女，如果在左甲状腺素治疗中，孕前应当调整左甲状腺素剂量，使 TSH 控制在 2.5 mlU ／ L 以下。

剂量调整的依据

妊娠期间，如果左甲状腺素剂量稳定，建议每 6 ~ 8 周测定一次 TSH。如果调整左甲状腺素剂量，每 4 ~ 6 周测定一次。妊娠早期还未充分治疗的母亲需要每 2 周测定一次。

CS-013

妊娠期抗甲状腺药物的选择

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甲状腺功能亢进症（甲亢）好发于育龄期妇女。甲亢妇女受孕几率下降，但仍会出现甲亢妇

女受孕或是一些妇女在妊娠期发生甲亢的情况。妊娠期甲亢的治疗、特别是抗甲状腺药物的选择是一个重要的临床问题。

抗甲状腺药物专指抑制甲状腺过氧化物酶活性减少甲状腺激素合成的药物。目前国内使用的甲巯咪唑和丙硫氧嘧啶。二者都能有效的控制甲亢，但都有不同程度的不良事件发生的风险，如粒细胞减少或缺乏、肝功能异常、ANCA 相关性血管炎等。同时，二者都有一定的致畸性，特别是甲巯咪唑还有一定的导致胚胎发育不良的风险。因此，妊娠期合理的选择抗甲状腺药物是非常重要的。目前国内外妊娠期甲亢诊治指南推荐妊娠不同阶段选择不同的药物。具体妊娠早期选择丙硫氧嘧啶，妊娠中晚期选择甲巯咪唑。同时监测药物不良反应和疗效。推荐在妊娠期间选择最小的有效治疗剂量。总之，妊娠期甲亢的治疗要根据病人的情况，根据所处妊娠阶段合理的选择药物，以期实现使用最安全最有效的治疗药物

CS-014

妊娠期 TPOAb 阳性的危害和治疗

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李静，女，1999 年毕业于中国医科大学，获医学博士学位。现任中国医科大学附属第一医院内分泌科教授、主任医师、博士生导师。并任第九届中华医学会内分泌学分会青年委员会副主任委员、辽宁省医学会内分泌学分会常委、辽宁省第四批特聘教授、中国甲状腺学组成员。主要研究方向为甲状腺疾病与自身免疫，承担国家自然科学基金面上项目 2 项及部省级课题 4 项，已发表学术论文 40 余篇。目前是《中华内分泌代谢杂志》及《中国实用内科杂志》等多家杂志编委、审稿专家以及国家自然科学基金初审专家。

当妊娠期妇女血清甲状腺过氧化物酶抗体（TPOAb）滴度超过试剂盒提供的参考值上限时即可诊断为甲状腺自身抗体阳性。但也有研究认为其在妊娠期的诊断界值还有待于进一步确定，以免导致过度诊断。单纯甲状腺自身抗体阳性不伴有血清 TSH 升高和 FT4 降低，也称为甲功正常的甲状腺自身抗体阳性。已有不少研究发现孕期 TPOAb 阳性与母体血 TSH 增高、尤其是妊娠晚期甲状腺功能或储备功能不足相关。而且虽然研究结果不完全一致，多数研究以及荟萃分析均显示 TPOAb 阳性患者流产风险明显增加，但补充 L-T4 后流产的发生率仅减少约 50%，提示甲状腺自身抗体相关流产风险的增加并不仅与甲状腺功能不足有关，尚有其它机制参与。此外，TPOAb 阳性孕妇发生妊娠期高血压、糖尿病、羊水过多、早产、产后甲状腺炎的风险也明显增高。其中产后甲状腺炎不仅可引起患者甲功波动，还与产后抑郁的发生明显相关。而且TPOAb阳性孕妇的后代智力和运动发育还可能有一定程度受损。因此，对妊娠期 TPOAb 可能带来的危害应给予关注，对其可能的相关机制值得进行深入研究。尽管目前缺乏针对甲状腺自身免疫本身的治疗手段，仍应积极对拟妊娠者筛查血 TPOAb，尤其对超重或肥胖者、弓形虫感染患者和受到全氟烷酸、铅等环境内分泌干扰物暴露者进行筛查，并给予适当手段（如硒制剂、一些中草药等）进行干预治疗，可能减少妊娠后母体及后代的不良结局发生。有研究发现对妊娠期妇女，如仅采用对高危病例筛查血 TPOAb，将会有约三分之一患者被漏诊。对于甲功正常的 TPOAb 阳性孕妇应实行甲功监测，每 4-6 周检查一次；如发现 TSH 升高超过妊娠期特异参考范围，应该及时给予 L-T4 治疗。在分娩后应继续监测甲功，评估有无产后甲状腺炎的发生。

CS-015

肾上腺年度进展报告

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王卫庆，教授，主任医师，博士生导师。上海交通大学医学院附属瑞金医院内分泌科主任。第六届全国优秀科技工作者，中国女医师协会五洲女子科技奖。享受国务院特殊津贴。上海市领军人才、上海市优秀学科带头人、上海市“十佳”医生。现任中华医学会内分泌学分会副主任委员，中国医师协会内分泌代谢科医师分会总干事，上海市医学会内分泌学会主任委员、上海康复学会糖尿病分会副主任委员，《JournalofDiabetes》杂志副主编。目前承担科技部国际科技合作专项，国家自然基金重点课题、十一五攻关计划等多项课题。发表 SCI 论文 100 篇（JAMA 及 Science 通讯作者等）。三次获国家科技进步二等奖，第一完成者获上海科技进步一等奖、上海医学科技奖一等奖、上海医学科技推广将及中华医学科技奖三等奖等。

肾上腺疾病主要包括原发性醛固酮增多症、库欣综合征、嗜铬细胞瘤及肾上腺皮质癌。近年，肾上腺疾病诊断、治疗及基础研究又有了新的进展。

原发性醛固酮增多症：首次报道中国难治性高血压人群中原醛症患病率为 7.1%。发现座位比卧位生理盐水试验诊断原醛症敏感性更高。ACTH 兴奋试验对原醛症分型诊断有一定价值。不同研究报道原醛症中存在 KCNJ5、ATP1A1、ATP2B3、CACNA1D、CTNNB1 等通道基因突变。MicroRNA 与原醛症的发生、发展相关。治疗上醛固酮合成酶抑制剂有望通过减少醛固酮合成来治疗原醛症。

库欣综合征：帕瑞肽、维甲酸、米非司酮、美替拉酮等药物治疗库欣综合征疗效评估。库欣综合征不同类型影响术后肾上腺功能恢复。瑞金医院首次报道 65.5% 肾上腺库欣腺瘤存在 L205R 基因突变。华山医院研究报道 62% 垂体库欣瘤存在 USP8 基因突变。国外研究发现大结节样肾上腺增生患者存在 ARMC5 基因突变。

肾上腺皮质癌：miRNA 和循环肿瘤细胞可以作为肾上腺皮质癌的早期诊断和预后预测的标志物，米托坦是治疗皮质癌一线推荐药物。肾上腺皮质癌预后不佳，复发率高，皮质醇分泌是影响预后的独立危险因素。肾上腺皮质癌分子分型对于治疗选择有指导意义，肾上腺分化指数（ADS）与皮质癌分泌功能，Wnt 通路基因突变呈正相关（$P < 0.01$）。

嗜铬细胞瘤：甲氧酪胺诊断恶性嗜铬细胞瘤具有一定意义。依维莫司和舒尼替尼治疗恶性嗜铬细胞瘤需进一步的临床研究。利用全外显子测序技术，发现 ATRX 基因突变与嗜铬细胞瘤 / 副神经节瘤端粒延长替代和临床侵袭行为相关。瑞金医院研究发现 ERBB-2 高表达患者非转移生存率降低，ERBB-2 高表达是嗜铬细胞瘤患者转移的独立危险因素。

CS-016

嗜铬细胞瘤临床诊治共识解读

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童安莉，北京协和医院内分泌科副教授、副主任医师、硕士研究生导师。2002 年毕业于中国协和医科大学，获内分泌专业博士学位，2009–2010 年在美国国立卫生研究院做访问学者。长期从事内分泌专业临床医疗工作，具有较丰富的临床经验，科研方向为内分泌性高血压和肾上腺疾病，在国内外医学杂志发表第一或通讯作者论文 20 余篇。承担人事部、教育部及中华医学会等多项课题，担任中华医学会内分泌学分会肾上腺学组副组长。

为规范嗜铬细胞瘤和副神经节瘤 (PPGL) 的临床诊疗，中华医学会内分泌学分会肾上腺学组讨论制定了嗜铬细胞瘤的临床诊治共识。共识主要参考国际指南及结合国内的研究和实践而制定，涵盖了 PPGL 的定义和流行病学特征、病因、临床表现、生化及影像学检查、治疗、长期随诊、PPGL 中的特殊问题等多个方面。

PPGL 是一种少见的内分泌疾病，国内尚缺乏其发病率或患病率的数据。50% 的 PPGL 的发生与致病基因的突变有关，目前已知有 17 个致病基因，其中 35% ~ 40% 为胚系突变，15 ~ 25% 为体系突变。不同基因突变的患者在 PPGL 的肿瘤部位、良恶性、儿茶酚胺分泌及复发倾向上均明显不同，因此，推荐对所有 PPGL 患者均进行基因检测，明确其致病基因，以便对患者的临床情况进行预测，并有利于手术后对患者随访和对其家系成员进行筛查。诊断 PPGL 的生化检验首选测定血游离或尿甲氧基肾上腺素和甲氧基去甲肾上腺素浓度，其次为血或尿儿茶酚胺浓度和 VMA。影像学检查建议首选腹盆增强 CT，MRI 可做为 CT 检查的补充。不同的功能显像方法各有优缺点，需要根据患者的临床来决定选用。建议对有转移的恶性 PPGL 患者用 ^{131}I-MIBG 显像来评价 ^{131}I-MIBG 治疗的可能性，用生长抑素受体显像来筛查副神经节瘤病灶及多发或转移病灶，^{18}F-FDG-PET/CT 为恶性和 (或)SDHB 相关的 PPGL 的首选定位转移灶的手段。确诊 PPGL 后应尽早手术切除肿瘤，术前必须进行充分的药物准备，以避免麻醉和术中、术后出现血压大幅度波动而危及患者生命。用 α - 受体阻滞剂做术前准备，准备时间存在个体差异，一般至少为 2 ~ 4 周。手术后需对患者进行终身随访，建议每年至少复查 1 次以评估肿瘤有无复发或转移；而对有基因突变的 PPGL 患者应 3 ~ 6 个月随访 1 次。

本共识针对PPGL的诊断和治疗进行了全面讨论，有助于临床医生对疾病进行正确处理。因为PPGL临床上个体差异很大，治疗和随访要遵循个体化原则。

CS-017

嗜铬细胞瘤临床诊治经验分享

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长期从事垂体－肾上腺疾病的临床以及基础研究

目的：探讨在嗜铬细胞瘤患者中的儿茶酚胺心肌病；

病人：54 岁女性，“阵发性头晕、头痛、多汗伴血压升高三个月”就诊。诊断为左肾上腺嗜铬细胞瘤。检查过程中出现胸痛，胸闷，心肌蛋白水平升高，心电图提示广泛 ST-T 变化，并呈现动态改变，急诊冠脉造影提示不存在器质性冠状动脉病变。经过手术前准备，患者全麻下左侧肾上腺嗜铬细胞瘤摘除术。手术后患者血压回复正常。

结果：患者诊断为左肾上腺嗜铬细胞瘤，儿茶酚胺心肌病。

结论：嗜铬细胞瘤患者的儿茶酚胺心肌病可以表现为类似急性冠脉综合症的经过，及时给予 α 受体阻滞剂可以改善患者临床表现，必要时冠脉造影可以明确诊断。

CS-018

中国原醛专家共识解读

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蒋怡然，上海交通大学医学院附属瑞金医院内分泌代谢科，博士，主治医师。主要专长及研究方向：肾上腺疾病研究，尤其是原发性醛固酮增多症的临床诊治和分子生物学研究。作为项目主要完成者参与中国难治性高血压人群中原醛症的流行病学调查及全基因组关联分析研究，在国内首次报道难治性高血压人群中原醛患病率为 7.1%（J Hypertens）；用 ACTH 兴奋试验区分单侧原醛症及双侧原醛症，为原醛症进一步治疗提供依据（J Clin Endocrinol Metab）。以第一负责人承担国家自然基金“miR-375 及其靶基因 MTDH 在醛固酮瘤中的表达及机制研究”；上海市优秀青年教师科研专项基金“原发性醛固酮增多症的异位受体表达”，上海卫生局项目“原发性醛固酮增多症的基因组关联分析”，上海市自然基金“MicroRNA 在原发性醛固酮增多症中的发病机制研究”等多项课题。

过去几十年，原醛症一直被认为是少见病，在高血压人群中患病率小于 1%，随着诊断技术提高，其患病率可达 10%。国内相关研究报道较少，2010 年由中华医学会内分泌分会牵头在全国 11 个省 19 个中心对 1656 例难治性高血压患者进行了原醛症的筛查，首次报道其患病率为 7.1%。为规范原发性醛固酮增多症的诊断和治疗，中华医学会内分泌学分会肾上腺学组经讨论，完成了专家共识的初稿。随机 ARR 作为原醛症最常用筛查指标，已被广泛应用于临床，特别在门诊开展随机 ARR 测定，可以在很大程度上提高该病检出率。所有 ARR 阳性患者须选择口服高钠负荷试验、生理盐水试验、氟氢可的松抑制试验或卡托普利试验中任何一项确诊或排除原醛。这 4 项试验各有其优缺点，临床医生可根据患者基本情况进行选择。原醛症分型诊断一直是临床上难点，影像学检查往往不能发现小腺瘤，双侧肾上腺静脉采血（AVS）被认为是分型诊断的“金标准”。在治疗方面，醛固酮腺瘤或单侧肾上腺增生患者行肾上腺切除可以取得较满意的治疗效果，但对于那些不愿意手术或存在手术禁忌证的患者可以选择药物治疗。而特醛症及糖皮质激素可抑制性原醛症首选药物治疗。

CS-019

血浆肾素和醛固酮测定进展

李启富

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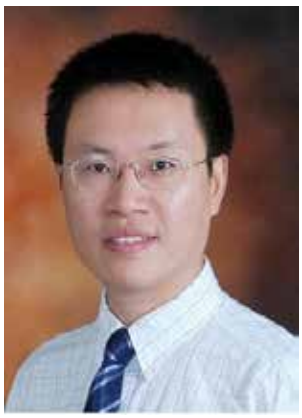

李启富、博士，教授 / 主任医师，博士生导师，现任重庆医科大学附一院内分泌科主任、重庆市糖尿病中心主任、中华医学会糖尿病分会常委、中华医师协会内分泌代谢病分会常委、重庆市卫生局内分泌科质量控制中心副主任。获国家自然科学基金、教育部博士点基金等共 20 余项；获得中华医学奖 1 项、重庆市科技成果奖 2 项。2013 年获“重庆市有突出贡献中青年专家”称号。发表论文百余篇（DiabetesCare、JCEM、Endocrinology 等杂志发表 SCI20 余篇）。主编专著 2 部，参编 5 部。研究兴趣：内分泌高血压及糖尿病并发症。

原发性醛固酮增多症（Primary Aldosterism，PA），简称原醛症，是指肾上腺皮质病变导致自主性醛同酮分泌增多及肾素-血管紧张素系统受抑制，临床表现为高血压伴(或不伴)低血钾，实验室检查常有血浆醛固酮增高和肾素降低。尽管原醛症的病因和发病机制比较明确，诊断措施和治疗有效，但目前国内外的现状是：绝大部分患者仍然未被发现和正确治疗。

原醛症的诊断包括筛查、确诊和分型三部分。筛查采用立位 2 小时血浆醛固酮浓度（PAC）/ 肾素活性（PRA）比值，或醛固酮浓度（PAC）/ 肾素浓度（DRC）比值。国内外比值的最佳筛查切点尚未完全统一。一般推荐立位 PAC/PRA 比值最佳切点为 30 $ngdl^{-1}/ngml^{-1}h^{-1}$。我们的资料显示中国人立位 PAC/DRC 比值 43 $pg\cdot ml^{-1}/\mu IU\cdot ml^{-1}$ 是原醛症初筛的最佳切点。值得重视的是，血浆醛固酮、肾素测定会受到一些降压药物、血钾水平、钠摄入量等因素的严重影响，筛查前需根据患者情况做足够长时间的准备。此外，肾素和醛固酮的测定方法、样本的处理条件等因素均影响测定结果。

目前国内原醛症的发现率低、误诊率高，其原因包括：对原醛症的认识和重视不够；诊断流程较复杂；血浆醛固酮 / 肾素测定开展不广泛；血浆醛固酮 / 肾素测定标准不统一；等等。

针对我国原醛症的诊治现状，应及早做好以下工作：强化筛查的重要性；广泛开展血浆醛固酮 / 肾素测定；促进血浆醛固酮 / 肾素测定方法标准化；积累中国人原醛症筛查、确诊、分型方面的资料。

CS-020

非酒精性脂肪性肝病年度进展报告

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高鑫，复旦大学附属中山医院内分泌科主任、博士生导师，副院长
复旦大学慢性代谢疾病研究所所长
中华内分泌学会常委员
中国医师学会内分泌代谢分会副会长
中华内分泌学分会《中西医结合学组》组长
中华内分泌学分会《肝病与代谢学组》前任组长
上海内分泌分会前任主任委员。
上海药学会药物治疗专委会主任委员
中华内分泌代谢杂志编委、中国糖尿病杂志编委、国际内分泌代谢杂志编委
复旦大学学报（医学版）编委、上海医学编委、《临床》杂志编委、柳叶刀糖尿病内分泌子刊中文版编委
承担和参加国家十．五、十．一五课题、国家“973”课题、自然科学基金项目、上海市科委重大课题、重点课题
近年开展肥胖、非酒精性脂肪性肝病与代谢紊乱的临床和发病机制研究，在国内首次报道了 1H 磁共振波谱分析方法用于肝脏脂肪定量的研究，首次建立超声肝脏脂肪定量方法并逐渐在国内推广应用。获得上海卫生科技二等奖和上海卫生科技推广奖。

非酒精性脂肪性肝病（NAFLD）是目前患病率迅速上升的慢性疾病，在西方承认的患病率高达 17-46%，在肥胖和糖尿病人群中 NAFLD 患病率高达 60-80%。我国人口中 NAFLD 还缺乏全国性大样本资料，已有几项不同地区的研究报道，在 40 岁以上人群的患病率约达到在 30%。NAFLD 的流行与代谢综合征及其各个成分的流行相似，这也增加了成人和儿童进展多中慢性代谢疾病的风险和不良结局。肝脏脂肪的过量沉积不仅增加了代谢相关疾病的风险，而且加速加重的肝病的进展。

针对 NAFLD 与多种代谢疾病、尤其与糖尿病为共患疾病，二者并存加重代谢紊乱和不良肝病结局，今年首次由欧洲肝脏研究协会（EASL）、欧洲糖尿病研究协会（EASD）和欧洲肥胖研究协会（EASO）共同制定了非酒精性脂肪肝的诊断、治疗及随访指南。该联合和指南的制定成为本年度 NAFLD 领域最重要的进展。

该指南将 2 型糖尿病伴随 NAFLD 的患者确定进展性肝纤维化的高危人群，因此推荐所有脂肪肝的患者都应筛查代谢综合征 (MetS) 的各个组分，对肥胖或代谢综合征（MetS）患者，通过肝酶和 / 或超声筛查 NAFLD 应成为常规检查的一部分。建议在高风险人群 (年龄 >50 岁，T2DM，MetS) 中筛查进展性疾病 (如，非酒精性脂肪型肝炎伴肝纤维化) (A2)。无论何时只要 NAFLD 被怀疑为第一诊断或做为伴发疾病，都应评估肝脂肪变性的的程度、伴发代谢紊乱常情况和密切随访，因为 NAFLD 预测将来发生糖尿病、心血管事件及高血压。目前尚没有诊断非酒精性脂肪性肝炎（NASH）的无创检查方法，对 NASH 和进展性肝纤维化的高风险人群推荐肝活检进行病理诊断，并建议至少在 5 年随访后进行包括再次肝活检的检测。

NAFLD 不仅与肝脏胰岛素抵抗密切相关，而且还与肌肉和脂肪组织胰岛素抵抗密切相关，与谢综合征各个组分密切相关，且独立于 BMI 外，对每一位代谢综合征都应该评估 NAFLD 的风险，反之，存在 NAFLD 患者中也应该评估代谢综合症的所有组分。

建议对怀疑 NAFLD 的患者应该检测以下项目进行综合评估。

NAFLD 患者的综合性评估项目

	变量
基本项目	1. 酒精摄入量：<20g / 日（女性），30g/ 日（男性）
	2. 糖尿病、高血压及心血管疾病的个人及家族史
	3. BMI，腰围，体重的变化
	4. 乙型肝炎 / 丙型肝炎
	5. 脂肪肝相关药物使用史
	6. 肝酶（天冬氨酸和丙氨酸转氨酶（γ- 谷氨酰转肽酶））
	7. 空腹血糖，糖化血红蛋白 A1c，OGTT，（空腹胰岛素［HOMA-IR］）
	8. 全血红细胞计数
	9. 血清总胆固醇、高密度脂蛋白胆固醇，甘油三酯，尿酸
	10. 超声检查（如果怀疑肝酶升高）
扩展项目	1. 铁蛋白和转铁蛋白饱和度
	2. 检查腹部和甲状腺疾病、多囊卵巢综合征
	3. 筛查罕见的肝脏疾病（威尔逊，自身免疫性疾病，α 1 抗胰蛋白 酶缺乏）

CS-021

核受体在肝脏脂肪沉积中的作用及机制研究

陆炎

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陆炎博士，复旦大学研究员，主要从事肝脏糖脂代谢的病理生理机制研究。截至目前，主持国家自然科学基金 2 项、上海市卫生局基金 1 项、上海市教委‘晨光计划’1 项，并以主要参与人身份完成国家自然科学基金重大项目，在研科技部 973 子课题和基金委中加合作等项目。工作期间，以第一作者 / 共同第一作者在 Cell Metabolism、JCI、GUT、Diabetes 等杂志发表 SCI 论文 8 篇，单篇最高影响因子 17.56，累计影响因子 93.92。相关研究成果多次在中华医学会全国内分泌学术年会、中华医学会全国糖尿病学术年会、上海市内分泌－糖尿病东方论坛上做口头发言或专题报告。上述研究结果还获得了本领域著名专家的高度评价和推荐。其中，发表在 GUT 上的研究论文荣登杂志当期封面 (Coverpaper)；发表在 JCI 上的研究论文，荣获 Cell-Metabolism 杂志的专题评述 (Preview)。

近年来，随着我国经济水平的提高，生活方式和饮食结构的改变，非酒精性脂肪肝病 (NAFLD) 等慢性代谢性疾病已成为一个重要的公共卫生问题。多个大型人群流行病学的研究结果表明：在我国部分地区，成人 NAFLD 的患病率已达到 15%，且成持续升高态势。NAFLD 除了本身所造成的健康和心理问题外，其伴随的多种相关疾病如 2 型糖尿病、心脑血管疾病、肝纤维化和肝硬化等，也严重威胁人类身心健康和生活质量，大大增加了家庭和社会的经济负担。

NAFLD 的实质是肝细胞内甘油三酯的过量沉积。有研究表明：代谢性核受体主要包括胆汁酸受体 (FXR)、肝 X 受体 (LXR)、过氧化物酶体增殖物激活受体 (PPARs) 等，在 NAFLD 的发生发展中起着重要的调控作用。本研究则以 FXR、PPARa 等代谢性核受体为切入点，借助基因敲除、过表达和干扰表达等研究手段，通过一系列分子和细胞生物学方法，在人群、动物、细胞和分子机制等层面，系统地探讨了代谢性核受体在肝脏乃至全身脂代谢稳态中的调控作用。

CS-022

NAFLD 应当干预

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何兰杰，教授、主任医师，硕士研究生导师。

现任中华医学会内分泌分会第九届委员会委员、中国医师协会内分泌代谢科医师分会常委、宁夏医学会内分泌学分会主任委员。

摘要暂缺

CS-023

非酒精性脂肪性肝病—约束还是纵容?

刘超

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刘超，中国中医科学院江苏分院，江苏省中医药研究院（南京中医药大学附属中西医结合医院）内分泌科，主任医师，2 级教授，博士生导师、癭病证治国家重点实验室主任。

荣誉称号：

江苏省“333 工程”和“江苏省六大人才高峰”培养对象、“江苏省医学重点人才”、“江苏省医学领军人才”、江苏省有突出贡献的中青年专家。

学术任职：

国际甲状腺大会（ITC）学术委员会理事、亚洲和大洋洲甲状腺学会（AOTA）委员，AOTA 学术委员会主席、世界中医药学会联合会内分泌专业委员会副会长、中国中医药研究促进会内分泌分会副主任委员、中华医学会内分泌学分会常委、中华医学会内分泌学分会肝病与代谢学组组长、中华医学会内分泌学分会中西医结合学组副组长、中华医学会内分泌学分会中青年委员会主任委员、中国医师学会中西医结合学分会糖尿病专业委员会副主任委员、中国医师协会中西医结合医师分会内分泌代谢病学专家委员会副主任委员、中华医学会江苏内分泌学分会名誉（前任）主任委员、江苏省中西医结合学会内分泌专业委员会主任委员、江苏省糖尿病学分会副主任委员、江苏省中西医结合学会常务理事、江苏省健康产业协会副会长。

杂志编委：

现任《Hormone Metabolism Research》、《Journal of Diabetes》、《Nature Review Endocrinology》（中文版）、《Thyroid》（中文版）、《Journal of Clinical Endcrinology and Metabolism》（中文版）编委，《药品评价》副主编，《中国实用内科杂志》常务编委，《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中国糖尿病杂志》等杂志编委。

论文和成果：

目前承担国家和省级基金项目十项。发表论文 1000 余篇，SCI 引录论文 48 篇，主编和参编学术专著 38 部，获专利 3 项。

非酒精性脂肪性肝病（NFALD）如同糖尿病一般，具有暴发和加重趋势。本病是一种遗传 - 环境 - 代谢应激相关性疾病，肝细胞内脂肪过度沉积为其病理学改变的主要特征，它是当前引起慢性肝脏疾病的首要原因。目前，大约 15%-46% 的成人存在非酒精性单纯性脂肪肝，其中，多数患者仅表现为肝脏脂肪变性，部分伴有炎症反应甚至纤维化，严重者会发生肝细胞癌。更为重要的是，NAFLD 还被认为是代谢综合征的一个组成成分，亚太地区的调查发现，NAFLD 是 2 型糖尿病和冠心病的高危因素，需要给予高度重视。

和其他代谢性疾病一样，NAFLD 的治疗主要包括生活方式的调整、药物以及必要时的减重手术等综合措施。但是，迄今为止，临床上还缺乏公认有效的药物治疗措施，各大权威指南依然强调生活方式干预作为首要治疗举措，但并不推荐调脂、降糖或减重类药物用于 NAFLD 患者，减重手术亦不是本病的适应症。

如果仅仅把药物和手术算作 NAFLD 的治疗方法的话，那么，可以说，NAFLD 不需要治疗。

然而，生活方式改变，尤其是运动疗法和医学营养治疗却是防治 NAFLD 不可或缺的措施，并可适当食用一些特殊食品、食物添加剂或饮料，以达到最好的防治效果。这些举措，皆属于自然疗法的范畴。

营养疗法

营养治疗主要考虑限食疗法，包括热卡限制或组份限食等，即通过减少热量摄入和 / 或调整饮食结构达到治疗 NAFLD 的目的，因其简便易行且疗效确切被各大权威组织推荐为本病治疗的基础。患者可以选择持续限食或隔日限食的方法，以标准体重计算出每日需要总热量的基础上减少 500-1000kcal/d可以有效治疗NAFLD。研究发现低碳水化合物饮食（40%–45%总能量），并减少饮食中的饱和脂肪酸，增加不饱和脂肪酸以及膳食纤维，可以有效改善 NAFLD 患者病情。

咖啡

虽然咖啡是否可以阻止 NAFLD 的发病还存在争议，但是最新的 Meta 分析显示经常饮用咖啡可以有效地降低 NAFLD 患者肝脏纤维化的风险。

运动疗法

有氧运动可以有效控制体重、减少内脏脂肪含量，从而治疗 NAFLD。建议患者选择中等量有氧运动，每周 4 次以上，累计锻炼时间至少 150 min。近年来的研究发现抗阻运动同样对 NAFLD 患者有治疗作用，是有氧运动一种补充。

针灸疗法

研究表明，针灸具有调脂、改善胰岛素抵抗的功效，其治疗 NAFLD 亦取得了满意的疗效。临床一般取穴丰隆、足三里、太冲、肝俞、三阴交等，根据患者的情况采取不同手法及方式，或补或泻，或针或灸，或采用其他穴位刺激法。

中药疗法

经过多年的临床实践，中药治疗 NAFLD 已经积累了非常丰富的经验，一些限食模拟剂，如桑椹、虎杖等具有确切的疗效，而五味子、黄连等在调脂和防治 NAFLD 中的作用亦被逐渐认可。

总之，自然疗法运用各种自然的手段如健康的生活方式等来增强机体对某种疾病的自愈能力，从而达到防治疾病的目的，在 NAFLD 的预防和治疗中发挥了重要的作用。临床上，针对运动、营养和中医中药治疗的研究逐步深入，但这些措施尚缺乏公认而可行的规范，今后尚需更多的探索。

CS-024

低钠血症的诊断和治疗

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王桂侠，博士。主任医师，教授，博士研究生导师，吉林大学引进人才，现任吉林大学白求恩第一医院内分泌代谢科主任，曾在美国 Minnesota 大学担任副教授，同时获得美国行医执照证书。现任中华医学会内分泌分会委员，血脂组副组长、吉林省医学会内分泌分会主任委员等多项学术兼职。承担国家自然科学基金，国家卫计委项目、教育部博士点基金，中华医学会基金等多项国家级及省部级科研课题，参与美国国家科研基金课题。在国内外杂志上共发表学术论文 70 余篇，SCI37 篇。

低钠血症定义为血清钠 <135 mmol/L，是临床上最常见的体液和电解质失衡性疾病。按血钠水平下降程度分为轻、中、重度。在明确低钠血症诊断前，应该排除假性低钠血症。根据病理生理与病因，低钠血症分为等渗 / 高渗性低钠血症，低渗性低钠血症。明确低钠的病因是有效治疗的前提。

主要参与水、钠调节的激素作用与调节机制包括：抗利尿激素，肾素 - 血管紧张素 - 醛固酮系统，利钠肽系统。根据细胞外容量的变化情况：1）细胞外容量下降时，可能存在经肾脏（肾病、利尿剂、脑耗盐综合征）或肾外（消化道、皮肤）丢失钠离子；2）细胞外容量正常时，应考虑各种原因导致的 ADH 分泌不适当升高，或 ADH 的抗利尿作用不适当增强，肾上腺功能减退，甲状腺功能减退，心肾功能下降有关；3）细胞外容量增加时，多见于心功能衰竭、肝硬化、肾病综合征等低有效血容量。

低钠血症治疗原则：基于病情的全面评估，分清缓急；密切监测，权衡利弊，控制补钠速度。 优先治疗严重低钠血症：要高度重视需要紧急治疗的低钠血症 (不论是何病因)。此时更应考虑及时干预治疗以抢救生命。在患者病情稳定前，进行干预治疗比找到病因更重要。治疗时避免补钠速度过快及矫枉过正：过度纠正低钠血症可引起渗透性脱髓鞘综合征 (ODS)，ODS 会对大脑造成持续性永久性的损害。慢性非严重低钠血症：积极查找病因。

以下述病例为例：

21 岁女性，因间断腹痛、恶心、呕吐、停止排气排便 2 年，加重伴抽搐 5 天入院。既往史：甲亢病史 2 月余，口服甲巯咪唑 10mg 2/ 日；入院时查体：脉搏 102 次 / 分，血压 142/82mmHg，意识不清，轻度贫血貌，球结膜轻度水肿，眼球略突出，瞳孔等大等圆，直径约 3mm，甲状腺 I 度肿大，质地柔软，全身浅表淋巴结未触及肿大。听诊双肺呼吸音粗，未；心界不大，心率 102 次 / 分，节律规整，各瓣膜听诊区未闻及额外心音及杂音。腹部平坦，未见胃型、肠型及蠕动波，腹软，肝肋下未触及，无移动性浊音，肠鸣音 3 次 / 分，病理反射征未引出，双下肢无水肿。电解质：Na113mmol/l，CL82.6mmol/l，K3.76mmol/l,Ca2.0CO2CP18.7mmol/l,9。血常规：RBC3.36x1010-12/L,HB91g/L,MCV78.9fL, 肝功、肾功正常，血淀粉酶正常。全腹部多排 CT：胆囊炎不除外，盆腔少许积液，结肠弥漫可疑改变。

腹痛、恶心及呕吐原因是什么？另外除了呕吐，有否其他原因导致低钠血症？我们该如何展开诊疗？

CS-025

低钾血症的诊断思路

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龚玉萍，萍乡市人民医院内分泌科副主任医师，从事内分泌专业 14 年，担任中华医学会内分泌学会性腺组委员，中国医疗保健国际交流促进会糖尿病分会委员，萍乡市医学会内分泌分会常委，曾发现国内第一例 DAX-1 基因突变病例，有多篇论文发表在国内外知名医学杂志，并承担省级、市级科研课题多项，擅长于性腺疾病、糖尿病、甲状腺、垂体、肾上腺等内分泌疾病的诊治

主要内容

一、体内钾代谢

二、低血钾的概述

三、低钾血症诊断思路及常见低血钾的疾病特点

四、病例分析

主要内容

一、体内钾代谢

概述

钾是人体生命活动中必须的矿物质之一，正常人血清钾浓度 3.5~5.5(5.0)mEq/L, 其中 98% 在细胞内，仅 2% 在胞外，我们测定的血钾指胞外钾浓度。

钾平衡调节：细胞内外转移

二、低血钾的概述

★ 严重低钾血症的界定和特点

低钾血症：血清钾 < 3.5mmol/L

轻度低钾血症：血清钾 3.5~3.0 mmol/L，症状甚少

中度低钾血症：血清钾 3.0~2.5 mmol/L，多有症状

严重低钾血症：血清钾 < 2.5 mmol/L，出现严重症状。

致死性低钾血症：血清钾 <1mmol/L，随时具有生命危险

患者症状出现严重程度及预后取决于缺钾的数量、速度和机体所处的状态。

★低血钾的临床表现

1. 神经肌肉系统；2. 平滑肌；3. 中枢神经系统；4. 心脏；5. 肾功能损害

★根据病因对低血钾进行鉴别

★钾向细胞内转移

1. 胰岛素和 / 或葡萄糖；2. 碱中毒；3. 低钾性周期性麻痹；4. 甲状腺机能亢症；5. 钡中毒；6. 细胞摄钾过多；7. 急性应激状态；8. 反复输入冷存红细胞；9. 某些药物：肾上腺素、麻黄碱类药物、支气管扩张剂、茶碱、咖啡因、维拉帕米中毒等，均促使 K+ 向胞内转移而发生低血钾症。

三、低钾血症诊断思路及常见低血钾的疾病特点

★肾脏排钾过多

定义：

血钾 < 3.5mmol/L，尿钾 > 25mmol/d

血钾 < 3.0mmol/L，尿钾 > 20mmol/d

★低钾血症鉴别诊断

★肾脏排钾过多

血压正常或偏低：?

1. 利尿剂：噻嗪类，速尿。渗透性利尿剂（甘露醇、葡萄糖）。吲达帕胺（寿比山）；2. 肾小管酸中毒（Ⅰ型和Ⅱ型），棉酚中毒；3. 范可尼 (Fanconi) 综合征；4. 巴特 (Bartter) 综合征；5. 低钾伴缺镁 , 高钙血症伴低血钾，DKA 治疗中；6. 其他：动脉硬化?

★肾小管酸中毒

肾小管分泌 H^+和 / 或重吸收 $HCO3^-$障碍，尿液酸化功能失常，发生慢性酸中毒及盐类调节失常，出现各种症状。

分类

肾小管酸中毒的特点

Liddle 综合征

肾素瘤

★低钾血症的诊断思路

★低钾血症原因的鉴别诊断思路

四、病例分析

病例 1：病例摘要

病例 2：病例摘要。低钾血症的治疗、经典的静脉补钾不宜原则、补钾注意点。

CS-026

Gitelman 综合征与 Bartter 综合征诊治进展

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童南伟，四川大学华西医院内分泌代谢科教授、博士生导师、科主任。现任中华医学会内分泌学分会常委，中国医师协会内分泌代谢科医师分会常委。国家卫计委合理用药专家委员会内分泌与代谢药物专业组专家。四川省医学会内分泌暨糖尿病专委会前任及候任主委。四川省医师协会内分泌代谢科医师专科分会会长。四川省糖尿病防治协会副会长。

Gentleman综合征（GS）与Bartter综合征（BS）常以低钾血症和继发性醛固酮增多症为表现，虽然通过电解质紊乱不同可以区别，但是绝大部分不能区别，因此确诊常常需要基因诊断。东方人 GS 不少见，只是不典型被误诊为 BS，实际上成人的 BG 及其罕见。本报告仅限于成人 GS 与 BS 相关诊断的讨论。

CS-027

药物相关电解质紊乱

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主要研究方向：肾上腺与性腺疾病的临床与基础研究。

电解质紊乱是临床常见疾病，其表现从无症状到危及生命多种多样。常见的电解质紊乱包括了血钠、血钾、血钙、血磷及血镁的代谢紊乱，在社区、住院，特别是危重症患者中均有较高的发病率。

导致电解质紊乱的常见病因包括：摄入不足、胃肠道丢失、肾脏丢失、体内内环境的紊乱（酸中毒或碱中毒）以及药物等等，其中常常又以药物性影响最为常见。多种利尿剂使得肾脏钠排出增多，导致低钠血症；抗抑郁药物、抗精神病药物、抗癫痫药物及抗肿瘤药物影响 ADH 分泌，均导致低钠血症。而锂剂、膦甲酸、两性霉素 B 等药物可能导致肾性尿崩症，从而升高血钠。螺内酯、氰化物、氟化物等多种毒物可以影响肾脏对钾的排泄，造成高钾血症；低钾血症的最常见原因是排钾利尿剂和胰岛素的使用。此外，较为常见的还包括钙、磷和镁的代谢紊乱。多种螯合剂如 EDTA、柠檬酸可直接螯合钙离子造成低钙血症；双膦酸盐类药物强烈抑制破骨活性，苯妥英钠等药物造成维生素 D 缺乏，最终均导致低钙血症。相反，过量维生素 D、维生素 A、锂剂、噻嗪类利尿剂可以升高血钙。临床上常用的利尿剂、抑酸剂亦会影响镁的代谢及血镁水平。

电解质的代谢稳态易被多种药物影响，早期可能缺乏特异性症状，使用相关药物期间做好监测，及时干预，可取得较好的临床预后。

CS-028

不适当抗利尿激素分泌综合征

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李艳波，哈尔滨医科大学附属第一医院内分泌一病房主任，教授。研究生导师。黑龙江省首位内分泌专业博士、博士后。

学术兼职：中华医学会内分泌学分会委员；中华医学会内分泌学分会肝病与代谢学组副组长；中国老年医学学会内分泌代谢分会委员；中国女医师协会内分泌与代谢病分会委员；黑龙江省医学会骨质疏松与骨矿盐疾病分会侯任主任委员；黑龙江省医学会内分泌学分会副主任委员；中华医学科技奖评审委员会委员；中华医学杂志英文版审稿专家；中华内分泌代谢杂志编委会编委；中国糖尿病杂志审稿专家。

在国内外核心期刊发表论文（包括 SCI 收录文章）50 余篇；主持国家级、省级课题 10 余项；获省级成果奖 6 项；参编著作 6 部。

抗利尿激素分泌失调综合征 (Syndrome of inappropriate antidiuretic hormone secretion，SIADH) 指由于内源性抗利尿激素 (ADH，即精氨酸加压素 AVP) 分泌异常增多或其活性作用超常所导致的以水潴留、尿钠不适当增多和体液低渗为主要生化异常的一组临床综合征。SIADH 病因繁杂，起病和发展常隐袭、缺乏特征性临床表现，误诊和漏诊率高，处理棘手，常因恶性原发病和诊疗上的延误而预后不良。

低钠血症及其相关症状是 SIADH 的主要临床表现和查找病因的起点。也是住院病人中最常见的水电解质代谢异常。SIADH 的常见病因为恶性肿瘤、呼吸系统和神经系统疾病、炎症、药物和外科手术。部分原因不明者称之为特发性 SIADH。

临床症状的出现及其轻重与水潴留和低钠血症的程度和发生速度有关。SIADH 的诊断依据：①血清钠降低（常低于 130mmol/L）；②尿钠浓度增高（常超过 30mmol/L）；③血浆渗透压降低 (常低于 270mOsm/L)；④尿渗透压 >100mOsm/kgH2O，甚至超过血浆渗透压；⑤无临床可测的低血压或低血容量，无应用利尿药史，甲状腺和肾上腺功能正常；⑥血浆 AVP 不适当增高，对 SIADH 的诊断有重要意义；⑦水负荷后 4h 排负荷率 <90%，尿渗透压不能降至 100mOsm/kgH2O 以下；⑧扩容治疗不能纠正血浆低渗透压，但限水后血浆渗透压改善。

低钠血症与低渗血症的病因多种多样，主要与如下疾病鉴别。①肾失钠所致低钠血症：特别是肾上腺皮质功能减退症、失盐性肾病、醛固酮减少症、Fanconi 综合征、利尿药治疗等。②胃肠消化液丧失：如腹泻、呕吐，及胃肠、胆道、胰腺造瘘或胃肠减压等。③甲状腺功能减退症。④顽固性心力衰竭、晚期肝硬化伴腹水或肾病综合征等。⑤精神性烦渴。⑥脑性盐耗综合征 (CSWS)。

SIADH 的预后取决于基础疾病。由药物、肺部感染、中枢神经系统可逆性疾病所致者，常为一过性，预后良好。由恶性肿瘤如肺癌、胰腺癌等所致者，预后较差。

CS-029

性发育异常疾病年度进展报告

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秦贵军，主任医师，教授，博士生导师。现任郑州大学第一附属医院内分泌科主任，河南省内分泌及代谢性疾病诊疗中心主任，兼任中华医学会内分泌学分会常委，性腺病学组组长；河南省糖尿病学会主任委员。

性发育异常疾病（Disorders of sex development, DSD）是一类染色体、性腺、外生殖器表现不一致的疾病。近些年，DSD 研究领域发展迅速，不仅有多个指南、专家共识发布或更新，更有众多包括发病机制、干预措施在内的热点研究成果发表在国内外杂志上。现就该领域近一年时间内主要研究进展回顾和总结，希望对临床医生提高 DSD 诊治水平有所裨益。

国际 DSD 研究领域最新进展

1、高促性腺激素性腺功能减退症：Belli 等探索了 Klinefelter 综合症患者雄激素合成不足的机制，通过评估 hCG 兴奋试验前后睾酮合成通路上各个类固醇激素的水平，发现克氏症患者低睾酮血症主要与 17β - 羟类固醇脱氢酶活性受损有关；Baetens 等发现 NR5A1（SF-1）突变既可导致 46,XY DSD，也可是 46,XX 性反转及真两性畸形的发病机制，提示 NR5A1 基因在性腺发育过程中发挥着非常重要的作用。

2、低促性腺激素性腺功能减退：Goncalves 等发现 FGFR1 基因 8 号外显子可变剪接所致的两个基因亚型 FGFR1 Ⅲ b、Ⅲ C 缺陷均可导致 IHH 发生，为 IHH 患者 FGFR1 基因筛查提供新的视角。

3、CAH 诊断：de Carvalho 等对 480 例巴西 21-OHD 患者基因型与表型进行关联分析，为由基因型预测表型的严重程度提供数据支持，该研究显示巴西 21-OHD 患者最常见突变位点为 p.V281L (26.6%)，IVS2-13A/C>G (21.1%) 及 p.I172N (7.5%)。

4、CAH 治疗：21-OHD 患者需要长期糖皮质激素（GC）替代治疗，既往认为过多 GC 替代可增加骨质疏松及骨折风险，而 Ceccato 等研究发现 21-OHD 患者 BMD 的降低与 GC 替代剂量无关；Noppe 等发现检测头发中 17- 羟孕酮及雄烯二酮水平可较好监测 CAH 治疗。

国内 DSD 研究领域最新进展

1、解放军 301 医院母义明、窦京涛教授团队对 7 个中国 Kallmann 综合症家系进行已知致病基因筛查，其中 5 个家系筛得突变；该团队还发现 IHH 男性患者与健康男性相比，ACTH 水平高、皮质醇水平低，而非酒精性脂肪肝是 ACTH 水平的独立相关因素。

2、郑州大学第一附属医院秦贵军教授团队研究发现糖尿病可导致大鼠雄激素水平、睾丸重量与体重比值降低、生精功能受损，而补充 Vit D 可在一定程度上改善糖尿病大鼠睾丸功能。

3、瑞金医院性腺小组牵头的全国多中心临床研究发现每天口服补充 40mg 锌元素进一步促进接受双促治疗的男性 IHH 患者精子生成的作用有限；该小组在国内首次明确报道 2 例 3β - 羟类固醇脱氢酶缺陷症患者，并从临床表型到分子机制对该疾病进行详尽剖析。

4、协和医院伍学焱教授团队比较 GnRH 脉冲治疗和双促性腺激素治疗男性 IHH 患者的疗效，结果显示接受脉冲治疗患者的精子生成起始时间要早于接受双促治疗患者。

5、新华医院顾学范教授团队对 230 例 21-OHD 患者进行基因型及表型关联分析，结果显示 89.6% 患者关联良好，该研究显示中国 21-OHD 患者最常见突变位点为 c.292-13A/C>G (I2G) (35%)、p.I173N (14.3%)、p.R357W (5.9%) 及 p.Q319* (4.6%)。

CS-030

男性肥胖相关性腺功能减退症

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窦京涛，医学博士，主任医师、教授，博士研究生导师；现为解放军总医院内分泌科副主任，解放军医学院教学指导委员会委员。

现兼任中华医学会糖尿病学分会常委；北京医学会糖尿病学分会副主任委员；全军医学科学技术委员会内分泌学专业常委；中国高血压联盟理事；曾任中华医学会内分泌学分会性腺学组组长。

现任中华内分泌代谢杂志、中华糖尿病杂志、解放军医学杂志、中国实用内科杂志、中国糖尿病杂志、中华老年多器官疾病杂志等多个杂志编委。

2015 年中国疾控中心研究数据显示：我国成人超重比例达 27.1%，肥胖比例达 5.2%，青少年肥胖患病率达 2.6%。肥胖是胰岛素抵抗、高血压、2 型糖尿病、睡眠呼吸暂停等多种心血管疾病危险因素的核心。已有研究显示，男性肥胖患者常伴有睾酮水平降低，促性腺激素水平轻度降低或保持正常水平，称为男性肥胖相关性腺功能减退症（Male Obesity associated Secondary Hypogonadism，MOSH）。其发病机制为肥胖患者体内有大量的脂肪组织，而芳香化酶主要在脂肪组织中表达，在体内芳香化酶可以使睾酮转变成雌二醇，导致睾酮减少和雌二醇水平增加，过高浓度的雌二醇负反馈抑制下丘脑 GnRH 分泌和垂体 FSH 和 LH 的分泌，导致睾丸产生的雄激素减少。MOSH 的发生率和肥胖的严重程度相关。在 BMI≥30kg/m^2 的人群中，性腺功能减退症的发生率为 40-50%。遗憾的是，临床上对于 MOSH 尚缺乏足够的重视。该病临床上主要表现为睾酮减退的一系列症状，包括：勃起功能障碍、性欲减退、乏力、记忆力降低、情绪低落、骨量减少 / 骨质疏松以及腹部脂肪增多等。诊断要点包括：（1）男性 BMI > 30 kg/m^2；（2）有性腺功能减退症的症状，包括性腺功能异常、男性乳房发育、阵发潮热、乏力、情绪低落等；（3）在性激素结合球蛋白正常的情况下，重复测定两次，血总睾酮水平均小于 8nmol/L；（4）促性腺激素 FSH 和 LH 水平降低或正常；（5）除外其他导致性腺功能减退症的系统性疾病。治疗方面，目前研究显示减轻体重是最佳方案，无论通过低热卡的饮食控制，还是通过胃肠道减肥手术，只要体重有明显降低，患者的促性腺激素水平会升高，睾酮水平也会随之升高。此外，芳香化酶抑制剂通过阻断外周组织中睾酮向雌二醇的转化，肥胖患者应用药物后，雌二醇水平降低，雌二醇对下丘脑 GnRH 分泌的负反馈抑制作用减少，导致垂体分泌 FSH 和 LH 增多，进而促进睾丸产生更多的雄激素和精子。对有生育要求者，还可考虑行 HCG/HMG 序贯治疗或 GnRH 泵治疗。应用外源性睾酮可能会在体内芳香化酶作用下转化为更多的雌二醇而加重对下丘脑 - 垂体 - 性腺轴的抑制，故不推荐采用睾酮替代治疗。

CS-031

小阴茎的诊治进展

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伍学焱，医学博士，中国医学科学院北京协和医学院教授、博士研究生导师，北京协和医院内分泌科主任医师、垂体－性腺学组负责人。致力于生殖内分泌学领域研究，涉猎范围从性分化、青春发育异常到不孕不育。现任中华内分泌学会性腺学组副组长、北京男科学分会副主委、中国老年保健协会抗衰老协会后任主委、中国医师协会青春期专业委员会副主任委员、CFDA 食品安全风险交流专家组成员等。担任多家杂志的编委和审稿专家。曾参与 10 余部医学专著如《协和内分泌与代谢学》的撰写。发表论著近 100 篇、SCI 论文多篇。

阴茎的大小和长度，随阴茎是否充血状态而有很大差异。医学上所指的阴茎的长度，通常指其非充血、松弛状态下伸长的长度。测量方法是用硬直尺从阴茎背侧根部抵向耻骨联合，同时扶正阴茎，测量耻骨联合到阴茎龟头顶端的长度。青春发育前的小阴茎是指阴茎伸长绝对值小于 2.5 厘米，或比同龄、同种族儿童短 2.5SD。但是阴茎的结构往往正常。

需要提醒的是，小阴茎要和隐匿性阴茎加以鉴别。隐匿性阴茎是指由于耻骨前皮下脂肪丰富，附着于阴茎体的阴茎皮肤相对不足，使本来正常的阴茎埋藏于皮下脂肪中，从外表看来，阴茎显得明显短小。若用手推开阴茎周围的脂肪组织，即可显露正常大小的阴茎外形。长期、严重的隐匿性阴茎，也会影响阴茎发育，最终导致阴茎短小。

男性胎儿阴茎在母体怀孕 8-12 周时形成，此后阴茎增长主要靠雄激素的作用。若雄激素不足或作用障碍，阴茎增长都会受阻。常见的导致雄激素不能合成的疾病包括卡尔曼综合征、垂体前叶功能减退症、克兰菲尔特综合征等。常见的导致雄激素作用障碍的疾病包括部分性雄激素抵抗和 5a 还原酶缺陷症等。

若确诊是小阴茎，首先尽可能明确病因，以便对因治疗。常用的治疗方法包括睾酮或双氢睾酮或促性腺激素治疗。在治疗过程中既要观察其有效性，同时应严密注意是否出现性早熟征象，如胡须生长、变声和骨龄增长过快等不良反应。

CS-032

肠道菌群是多囊卵巢综合征的致病因素吗?

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上海市疾控中心内分泌专家组成员
中华内分泌代谢杂志编委
中华糖尿病杂志编委
上海交通大学学报（医学版）编委
以第一责任人获国家自然科学基金资助 5 项，以第一作者或通讯作者在国内外核心期刊发表学术论文 120 余篇（其中 SCI 文章 20 篇）。

多囊卵巢综合征（Polycystic Ovary Syndrome，PCOS）育龄妇女常见的生殖内分泌代谢疾病，发病率为 5-10%，临床常表现为月经异常、不孕、高雄激素征、卵巢多囊样表现等，可伴有肥胖、胰岛素抵抗、血脂异常等代谢异常，是 2 型糖尿病、心脑血管疾病和子宫内膜癌发病的高危人群。众所周知，多囊卵巢综合征（PCOS）的两大核心病理机制是高雄激素血症和高胰岛素血症。所以一直以来，PCOS 的临床干预主要是围绕着降雄和胰岛素增敏进行。近年来，随着炎症和肠道在代谢性疾病中的作用逐渐被大家认识接受，二者与 PCOS 的研究也日益兴起。

肠道菌群是个动态变化的系统，受饮食结构等多种因素影响。因其在调节人体正常生理代谢方面具有不可替代的作用，一旦肠道菌群结构改变或失调，则可能引起机体代谢紊乱。目前越来越多的研究表明，肠道菌群可能与肥胖及 2 型糖尿病等代谢性疾病的发生发展密切相关。以肠道菌群为切入点来探索代谢性疾病的发病机制已成为国际上的研究新热点。肠道负责了我们身体 80% 的免疫功能，健康的小肠粘膜是紧密连接的，只允许某些营养物质进入血液，而把很多毒素、大分子、微生物拒之门外。肠道细菌群落失调会提高肠粘膜渗透性，而小肠渗透力增加（俗称“漏肠”）会导致肠内发炎和肠道绒毛的破坏，进而影响了肠道壁细胞间的紧密连接，导致脂多糖从革兰阴性菌进入体循环的进程加快，进而引起了身体抗原 - 抗体反应，引起免

疫系统激活和慢性炎症。免疫系统激活妨碍了胰岛素受体的功能，提升了血清中的胰岛素水平，从而导致卵巢产生更多的雄激素并干扰了正常卵泡的发育。由此，肠道菌群失调导致 PCOS 的理论可以解释该综合征的三种症状—稀发排卵 / 月经失调、高雄（痤疮、多毛）和卵巢多囊表现。我们及国外的研究均提示 PCOS 患者存在肠促胰素轴活动的缺陷，而更重要的是，以肠道菌群为靶标的治疗策略（饮食运动，代谢手术，调节肠道菌群的药物，菌群移植）在 PCOS 患者中的获益，均提供了有利的证据提示肠道菌群是 PCOS 重要的致病因素，但是否是唯一的因素还需更多的临床和基础研究的证据。

CS-033

女性多毛的病因探讨

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李芳萍，中山大学孙逸仙纪念医院内分泌科主任医师、医学博士、硕士生导师。兼任中华医学会内分泌学分会性腺组组员，中华医学会男科学分会生殖内分泌学组组员，广东省糖尿病学会委员，广东省慢性病预防学会委员。近年在性腺疾病方面开展的主要工作为：从女性高雄激素血症中筛查非经典型 21 羟化酶缺陷症；男性 2 型糖尿病患者勃起功能障碍发生机制的探讨、迟发性性腺功能减退症与代谢综合征的研究，男性低促性腺激素低下性性功能减退症的生精治疗。

多毛症（hirsutism）是指女性雄激素敏感部位出现毛发过多，在育龄女性中的发生率约 10%。多毛症的评估主要根据改良 Ferriman-Gallwey 评分法，它将 9 个雄激素敏感部位的毛发生长分别评 0-4 分。雄激素增多是多毛症的基础，但是雄激素水平和毛发生长的数量之间仅中度相关，且有明显的种族差异。特发性多毛症仅表现为多毛，常有多毛家族史，原因是外周组织特别是毛囊、皮脂腺的雄激素代谢异常，5α 还原酶活性增强，使 T 转化为活性更强的 DHT 增多，而出现多毛。多囊卵巢综合征（PCOS）是多毛症中最常见的病因，约占 90%，其诊断时需排除先天性肾上腺皮质增生（CAH）、Cushing 综合征、分泌雄激素的肿瘤等其他高雄激素的病因。CAH 极易误诊为 PCOS，约占多毛症病因的 10%。基础 17- 羟孕酮测定是筛查 CAH 的基本手段，必要时可行快速 ACTH 兴奋试验及基因诊断确诊非经典 CAH。多毛症中，分泌雄激素的肿瘤患者不多见，但如血雄激素水平升高特别明显，要警惕卵巢或肾上腺分泌雄激素的肿瘤。使用雄激素或具有雄激素作用的药物可引起多毛。应激时下丘脑的促肾上腺释放激素增多，刺激ACTH分泌增加，导致雄激素增加而引起多毛。绝经后因FSH、LH水平升高，刺激卵巢间质产生雄激素引起多毛。妊娠期大量的人绒毛膜促性腺激素可刺激卵巢门细胞产生雄激素，引起多毛。

CS-034

IHH 致病基因解析

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孙首悦，副主任医师，硕士生导师。1998 年毕业于上海第二医科大学，2006 年获比利时布鲁塞尔自由大学硕士学位，现为上海交通大学医学院附属瑞金医院内分泌科副主任医师。中国医师协会青春期医学专业委员会内分泌学组委员、中华医学会内分泌学分会性腺组委员、上海市医学会内分泌分会性腺学组秘书、上海市医学会内分泌分会垂体学组委员、中华内分泌代谢杂志第七届编辑委员会通讯编委。主要从事低促性腺激素性性腺功能减退、垂体功能减退、先天性肾上腺皮质增生症等性腺发育异常疾病。参与新型 GnRH 脉冲泵研发并获得专利，国内率先

开展新型 GnRH 脉冲泵的临床应用治疗低促性腺激素性腺功能减退症、中枢性闭经、非肥胖多囊卵巢综合征。承担国家自然科学基金青年基金一项，中华医学会课题一项，上海市市级医院新兴前沿技术联合攻关项目主要完成人，获实用新型专利一项。

特发性低促性素性腺功能减退症（IHH）是一种复杂的寡基因疾病，可为散发性（约 70%）和家族性（约 30%），遗传方式呈多样化，如家族性 IHH 可呈常染色体显性遗传、常染色体隐性遗传、X 染色体连锁隐性遗传。在 GnRH 神经元的分化、迁移、释放、作用过程中所涉及到的任何基因突变都有可能导致 IHH 的发生。目前为止发现的 IHH 致病基因有 30 余种，其中卡尔曼综合征（KS）常见的致病基因有 KAL1、FEZF1、SOX10、TSHZ1、HESX1、TUBB3，嗅觉正常的 IHH（nIHH）常见的有 GNRH1/GNRHR、LEP/LEPR、KISS1/KISS1R、TACR3/TAC3、NROB1 和 PCSK1，两者均有的致病基因有 FGF8/FGFR1、PROK2/PROKR2、CHD7、HS6ST1、NELF、WDR11、SEMA3A、AXL、SOX2、FGF17、IL17RD、DUSP6、SRY4、FLRT3。尽管过去二十多年里发现了多个致病基因，有近 60% 的 IHH 患者仍找不到基因突变。

以往认为 IHH 是一种单基因遗传病，近年来更倾向于其通过寡基因模式致病。Sykiotis 等人检测了 397 位 IHH 患者和 179 位正常对照者的 8 个常见致病基因，在 22% 的患者中发现了基因突变，其中 11.3% 为寡基因性突变，而对照者寡基因突变率为 0（$P<0.05$）。由于致病基因众多，很难对每一个 IHH 患者进行全基因的筛查。Barbosa 等人研究了 151 位检测出基因突变的 IHH 患者的基因型与表型的对应关系，发现一些临床特征与基因型高度相关，故认为可以根据患者的临床症状有针对性地选择相应的致病基因进行筛查。但其他致病基因与临床表型是否存在相关性仍有待大规模研究，而且考虑到 IHH 的寡基因致病性，仅筛查某几个基因可能会遗漏其他罕见致病基因，故其临床应用比较有限。

CS-035

下丘脑垂体年度进展

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谷伟军，毕业于解放军军医学院，获内分泌代谢专业医学博士。现为解放军总医院内分泌科副主任医师、副教授、硕士生导师。长期从事于垂体、性腺、肾上腺、糖尿病等内分泌代谢疾病的临床工作。目前以第一作者发表论文 30 余篇，承担北京市自然科学基金、中华医学会课题、国际交流基金等课题。现为中国医师协会内分泌代谢科医师分会青年副主任委员，北京医学会糖尿病学会青年委员，《国际糖尿病杂志》青年编委，《药品评价》编委，《中华内分泌代谢杂志》通讯编委。

在过去的一年中，国际上以及国内垂体疾病研究领域进展迅速。关于垂体疾病发病机制以及诊断和治疗研究的文献大量发表。经过筛选，现将部分对临床有更多借鉴意义的重点期刊的经典文献简单汇总，供临床医生参考。

一、库欣病（CD）。2016 年 3 月，中华医学杂志颁布中国库欣病诊治专家共识，对库欣病诊断及治疗更趋规范。一项多国家、多中心的回顾性队列研究探讨了术后缓解率 ≥10 年库欣病（CD）患者的预后情况，该研究显示与健康人群相比，术后缓解率 ≥10 年的 CD 患者仍存在较高病死率，尤其是易患心血管疾病；治疗方案越复杂说明疾病越难以控制，生存期也就越短。在库欣病致病基因研究方面，一项研究对 10 例垂体 ACTH 瘤进行外显子测序，并研究 USP8 基因功能，结果显示 USP8 基因突变通过激活 EGF 受体信号导致库欣病。另一项研究也显示 USP8 基因突变状态可预测 CD 患者对药物治疗的敏感性。对于 CD 和异位 ACTH 综合征鉴别诊断，国内外研究较多，这些研究分别探讨了大剂量地塞米松抑制试验（HDDST）、DDAVP 刺激试验、岩下窦静脉取血（IPSS）、改良岩下窦静脉取血（PRL 校正）、CD 鉴别诊断中的应用，对临床工作有很大指导意义。二、垂体 GH 瘤。对 GH 瘤研究主要集中在基因测序（包括一代、二代测序、拷贝数变异）探讨致病机制方面。国内学者研究发现 STAT3 上调可以诱导 GH 过多分泌。三、垂体 PRL 瘤。中华医学会妇产科学分会内分泌学组颁布高泌乳素血症诊治专家共识，该共识发表于 2016 年第 3 期中华妇产科杂志。垂体 PRL 瘤临床研究较多见。国内学者总结了 107 例治疗前成年男性 PRL 瘤患者的病例资料，对成年男性 PRL 瘤垂体功能减退模式进行探讨，结果显示男性 PRL 瘤患者生长激素轴和性腺轴减退发生率

最高，对于大腺瘤（≥1cm）患者，瘤体直径增大和高泌乳素血症并不明显增加垂体功能减退的发生率，但是可作为临床上判断垂体功能减退程度的参考指标。PRL 分泌大腺瘤通常指瘤体在 10-40mm 之间，瘤体直径 ≥40mm 者较为少见，≥60mm 者更是罕见，国外研究总结了 18 例（男 16 例、女 2 例）瘤体直径 ≥60mm、PRL ＞ 1000ng/ml 患者临床特征、治疗方案及随访情况，结果显示大腺瘤往往具有侵袭性，但是对药物治疗反应良好；对多数患者，长期大剂量卡麦角林联合垂体手术是治疗关键，可以获得临床和生化缓解。四、其他方面。垂体柄中断综合征（PSIS）致病机制尚不清楚，法国学者首次报道一例表现为新生儿低血糖症、胆汁淤积，生化检查 TSH、GH、ACTH 缺乏，垂体 MRI 提示垂体柄缺如，外显子测序结果提示 CDON 基因突变，该研究首次报道 CDON 基因突变致 PSIS。淋巴细胞瘤垂体炎诊断较为困难，症状、体征缺乏特异性，国外学者对其血清 HLA 标记物进行筛选，结果显示 HLA DQ8、DR53 有助于淋巴细胞瘤垂体炎与其他鞍区病变的鉴别诊断。

国内垂体疾病研究存在问题：一、缺少多中心、大样本、前瞻性研究。即使所谓少见或者罕见性腺疾病，在我国的患病就诊人数与国外相比也非常可观，目前国内垂体疾病的研究和报道几乎都是以单中心为主，以回顾性总结分析为主，前瞻性研究更能够科学回答临床问题，对临床诊疗有更好地借鉴意义；二、缺少多学科协作诊治的习惯。国内垂体疾病患者往往首诊于神经外科、肿瘤科、妇科、男科等，各个专业组对这些疾病的认知程度不一，容易造成误诊和漏诊，缺乏术前内分泌功能评估及术后功能评估（术后复查未引起充分重视；低复查率导致低替代率）。因此，我们的研究趋势及努力方向：一、垂体学组协调组建多中心疑难病协作中心；二、组织开展多中心前瞻性临床研究；三、多科室合作，尤其与神经外科，关注患者术前评估、术后长期随访及替代治疗是否充分、合理；四、在互联网医疗时代，依托大数据医疗平台，建立垂体疾病慢病管理体系，有助于纵向观察疾病演变及治疗效果。

CS-036

中国 Cushing 病规范化诊治

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童南伟，四川大学华西医院内分泌代谢科教授、博士生导师、科主任。现任中华医学会内分泌学分会常委，中国医师协会内分泌代谢科医师分会常委。国家卫计委合理用药专家委员会内分泌与代谢药物专业组专家。四川省医学会内分泌暨糖尿病专委会前任及候任主委。四川省医师协会内分泌代谢科医师专科分会会长。四川省糖尿病防治协会副会长。

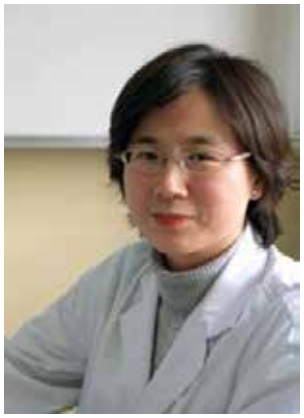
Cushing 综合征（CS）的诊断不难，CS 的病因诊断有时困难。其中 Cushing 病（CD）虽然在 CS 占绝大多数，但 CD 与异源行 ACTH 综合征的鉴别有时困难。CD 术后的复发机会多，治疗棘手。本报告重点介绍最新发布的国际国内有关 CD 的指南，以规范其治疗。

CS-037

中枢性尿崩症的诊断和治疗

朱慧娟

北京协和医院



朱惠娟，副主任医师，硕士生导师。1995 年起至今于北京协和医院内分泌科工作，长期从事内分泌疾病的临床诊治和基础研究，特别是下丘脑－垂体疾病、儿童生长发育临床诊治。主持国家自然科学基金课题面上项目等课题，在 JCEM 等专业期刊发表论著。现任中国垂体瘤协作组委员兼秘书，中国医师协会内分泌代谢医师分会青委会副主任委员，中国医师协会青春期医学专业委员会副主任委员，北京医学会内分泌学分会青委会副主委，北京医师协会内分泌学分会干事长

尿崩症（diabetes insipidus），是肾脏不能保留水分而造成的尿液排出过多，临床上主要表现为排出大量低渗透压、低比重的尿和烦渴、多饮。根据病变部位不同可分为由于抗利尿激素 (antidiuretic hormone，ADH) 分泌和释放不足导致的中枢性尿崩症（central diabetes insipidus，CDI），和 ADH 对肾小管作用障碍导致的肾性尿崩症。

【病因】任何导致 ADH 合成、分泌与释放受损的情况都可导致 CDI。具体病因如下：（一）下丘脑 - 垂体区的占位性病变或浸润性病变：包括（1）各种良性或恶性肿瘤性病变，如颅咽管瘤、生殖细胞瘤、脑膜瘤、胶质瘤、星形细胞瘤等；也可见于肺或乳腺等转移癌、淋巴瘤、白血病等。（2）肉芽肿性、感染性或自身免疫相关疾病：如结节病、组织细胞增多症、脑炎或脑膜炎（结核性、真菌性）、淋巴细胞性垂体炎等。（3）血管性或其他病变，如希恩综合征、动脉瘤、动脉粥样硬化等。以上是 CDI 最需注意的病因，约占 CDI 的三分之一，部分患者可合并不同程度的垂体前叶功能低减的表现。（二）头部外伤；（三）医源性：涉及下丘脑区的手术几乎都并发不同程度的 CDI。多数患者发生一过性暂时性尿崩，多在 2-3 天内消失，术后尿崩症状持续 3 周以上不减轻者，可能成为永久性尿崩症。（四）特发性：经仔细检查后排除了各种颅内病变和全身性疾病后才能谨慎考虑，目前发现该类患者视上核和室旁核神经元及循环血中存在室旁核抗体，可能与该病发生相关。通常儿童期起病，合并垂体前叶功能减退者少见。（五）遗传缺陷相关：如 Wolfram 综合征或称 DIDMOAD 综合征，是一种常染色体隐性遗传疾病，临床症群包括尿崩症、糖尿病、视神经萎缩和耳聋，常为家族性，患者自幼多尿，可能由于渗透压感受器缺陷所致。

【临床表现】（一）低渗性多尿：CDI 是一种以低渗性多尿为特征的临床综合征，可发生于任何年龄，但青年人多见，男女之比为 2：1。烦渴、多饮、日夜尿量相仿；部分患者出现脱水、皮肤干燥、心悸、汗液及唾液减少。（二）原发病的表现：如颅脑外伤或手术所致的头痛、视力减退及其它中枢神经系统受损所致的症状和定位体征。肿瘤所致的 CDI 多因肿瘤压迫下丘脑、垂体所致，亦有头痛、视野缺损或原发肿瘤的临床表现

【实验室检查】（一）血、尿渗透压：患者血渗透压正常或稍高（血渗透压正常值为 290~310mOsm/L），尿渗透压多低于 300mOsm/kgH2O（尿渗透压正常值为 600~800mOsm/ kgH2O），严重者低于 60~70mOsm/kgH2O。（二）禁水加压素试验：（三）其他检查：腺垂体功能检查、视力、视野、蝶鞍 X 线平片、头颅 CT 和鞍区 MRI 等，以进一步寻找 CDI 病因，必要时可考虑行相关基因检测。（四）部分患者需要行组织活检进行病理诊断，以明确病因决定下一步的治疗方案。

【治疗】（一）病因治疗：针对各种不同的病因积极治疗有关疾病，如手术治疗、放射治疗、免疫抑制治疗。（二）药物治疗：抗利尿激素替代治疗，部分患者还需要垂体前叶相关激素的替代治疗。

CS-038

自身免疫性垂体炎的再认识

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1998 年毕业于解放军军医进修学院获博士学位，师从于潘长玉教授一直致力于糖尿病和内分泌疾病的临床工作。

2004.11–2006.6 美国南伊利诺伊大学医学院访问学者。

中华医学会内分泌学分会委员、《中华内分泌代谢杂志》编委。

自身免疫性垂体炎是一种由于自身免疫功能紊乱引起的垂体炎症性疾病，根据病因可分为原发性和继发性垂体炎。原发性垂体炎主要包括淋巴细胞性垂体炎、肉芽肿性垂体炎、黄瘤病性垂体炎、IgG4 相关性垂体炎和混合型垂体炎。继发性垂体炎指有明确病因的垂体炎，包括继发于鞍上疾病和因免疫调节药物引起的垂体炎。

原发性垂体炎中以淋巴细胞性垂体炎最为常见，以女性多见，妊娠期或产后发生者约占 40%；MRI 可见垂体弥漫性增大，特征表现为病变沿下丘脑基底部向下丘脑扩展呈“舌状”改变；增强扫描示病变均匀强化，垂体柄增粗，向上压迫视交叉，如有后叶受累表现为垂体后叶高信号消失。典型病理改变为大量炎性细胞包括淋巴细胞、浆细胞以及散在的嗜酸性粒细胞浸润，部分神经垂体受累，残存的垂体前叶细胞结构仍能保持正常，随着病程的进展可发生不同程度纤维化、坏死等。

IgG4 相关性垂体炎是一种罕见的原发性垂体炎，2004 年首次报道，2007 年第一例病理学诊断。主要表现为垂体功能减退和尿崩症，影像学显示为鞍区肿物或垂体柄增粗；组织学检查可见大量淋巴、浆细胞浸润，极易误诊为垂体非特异性炎症。IgG4 相关性垂体炎与其他类型垂体炎的主要区别在于其血清 IgG4 浓度升高，垂体组织活检可发现 IgG4 阳性浆细胞。2011 年 Leporati 等提出的诊断标准包括：1.垂体组织中单核细胞浸润，淋巴细胞和浆细胞富集，每高倍镜视野IgG4 阳性浆细胞≥10 个；2. 垂体 MRI 显示鞍区肿物和 / 或垂体柄增粗；3. 其他受累器官活检可见 IgG4 阳性浆细胞；4. 血清 IgG4 浓度 >140 mg/dl；5. 激素治疗后垂体肿块迅速缩小，症状改善。当满足标准 1 或标准 2 和 3 或同时满足 2、4、5 时即可诊断。

尽管部分典型病例可以通过临床特点、影像学改变和实验室检查获得确诊，然而，相当一部分病例在缺乏病理学证据时常常难以明确诊断甚至误诊而误治。因此，对于不必手术治疗的鞍区病变尤其是高度怀疑垂体炎时，活检是既能获得病理诊断又尽可能减少手术风险的最佳措施。

CS-039

垂体泌乳素瘤与妊娠

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1983.08–1989.07 北京医科大学医学系，获医学学士学位

1997.08–2000.12 北京大学医学部，获医学博士学位

2003.09–2005.09 美国哈佛大学 Joslin 糖尿病中心，博士后

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专业特长和研究方向：

1989 年起在北京大学第一医院内分泌科工作至今，长期从事内分泌疾病诊治的临床和科研工作，具有丰富的临床经验，擅长糖尿病及其并发症、代谢综合症、甲状腺疾病和肾上腺疾病的诊断和治疗。主要研究方向为胰岛素信号传导、胰岛素抵抗、糖尿病及其血管并发症的发病机制。曾参与并负责多项国际国内多中心临床试验，获得多个研究基金资助，主持多项国家及省部级科研课题。

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中华医学会内分泌学分会委员兼副秘书长，中国医师协会内分泌代谢病学分会委员兼副总干事，北京医学会糖尿病学分会副主任委员，北京医师协会内分泌代谢学分会常务理事，中华预防医学会糖尿病防控专业委员会常委，中国老年保健医学研究会老年内分泌与代谢病分会委员。《中国糖尿病杂志》、《中国医学前沿杂志（电子版）》、《国际糖尿病》等杂志编委。

垂体泌乳素瘤是最常见的垂体分泌肿瘤，占垂体肿瘤的 40%，男 / 女比例为 1：4，女性泌乳素瘤中微腺瘤 / 大腺瘤的比率约为 3:1。

高泌乳素血症可以抑制促性腺激素释放激素和黄体生成激素的分泌，抑制卵巢孕酮和雌激素的产生和分泌，因此，溢乳、闭经是泌乳素瘤的主要症状，也是引起女性不孕的重要原因。另外，怀孕过程中雌激素对垂体泌乳素细胞具有刺激作用，使细胞增生和数量增加，文献统计，1.6%—4.5% 的微腺瘤患者和 15.6%—35.7% 的大腺瘤患者怀孕期间肿瘤体积明显增长。而大腺瘤患者孕前接受过外科或者放射治疗，孕期肿瘤增长的几率下降到 4.3%。因此，应加强对垂体泌乳毒瘤患者妊娠前和妊娠期的管理。

对于微腺瘤患者，手术和溴隐亭治疗都可以帮助患者恢复月经和顺利怀孕。且怀孕期间肿瘤显著增长的几率较低，可以在确认怀孕后停用溴隐亭。但孕期需注意观察是否有新发的头痛症状及视力改变，定期做视野检查。若出现上述症状或视野改变，需立即复查垂体核磁，若发现肿瘤明显增长可以恢复服用溴隐亭。

对于大腺瘤患者，应先采用外科手术等治疗措施使肿瘤体积缩小后再考虑怀孕。对已经怀孕的大腺瘤患者，需要根据患者情况采取以下治疗方案：1）确认怀孕后停用溴隐亭，但需密切观察视力视野情况。2）肿瘤较大者怀孕期间可持续服用溴隐亭控制肿瘤生长。3）若溴隐亭控制肿瘤效果不佳可在妊娠后期采用经鼻手术切除肿瘤。4）怀孕期间肿瘤持续生长，妊娠后期若胎儿条件允许可提前生产，生产后行手术治疗切除肿瘤。

溴隐亭在孕前和孕期服用是相对安全的，目前还没有证据表明溴隐亭能增加胎儿畸形和流产的危险，但还需要更长时期和更多病例的观察来评估其安全性和副作用，原则上在肿瘤稳定的前提下应尽量减少胎儿对药物的暴露时间。

CS-040

生长激素瘤的诊治进展

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广东省内分泌学会副主任委员

广东省骨质疏松学会常务委员

中华内分泌代谢杂志编委

肢端肥大症的最主要原因为垂体生长激素腺瘤。GH 腺瘤的形成是由一系列影响生长激素细胞的发育、营养状态及激素分泌的因子所调控，基因的改变导致了染色体的不稳定性、表观异常的改变及变异，从而导致 GH 腺瘤的发生 。肢端肥大症的患病情况为 60 人 / 百万人群。该病起病隐匿，患者常在症状出现 7-10 年后才得到确诊，有些患者直到出现严重的糖尿病、高血压、心脑血管病等并发症才意识到需要就诊，就诊不及时，就诊率低；患者和医生对该病缺乏足够认识，未能及时就诊或及早发现该病。该病临床表现多样，不推荐应用随机 GH 水平来诊断肢端肥大症。患者 IGF-1 水平升高或模棱两可时，推荐应用口服糖耐量试验来确诊GH是否受到抑制(GH<1ug/L)。在生物学确诊肢端肥大症后，推荐应用垂体MRI进行肿瘤的定位诊断，如患者存在禁忌可选用 CT 检查。 如患者垂体 MRI 未显示肿瘤时，需考虑进行 GHRH 检测，并且行胸部或腹部 CT 以了解是否存在垂体外 GH 分泌性肿瘤。 极少数肢大患者是由于单基因缺陷导致，如多发性内分泌腺瘤 1 型 MEN,McCune Albright 综合征和 Carney 综合征等，需要进一步对相关并发疾病进行筛查和诊断。 所有肢端肥大症患者需进行共病症的评估，包括高血压、糖尿病、心血管疾病、骨关节炎、睡眠呼吸暂停等。 这些共病症需要给予长期的监控及严格的管理。管理目标：建议 IGF-1 需达到年龄相匹配的正常水平，这样的生物学目标可提示肢端肥大症得到控制，采用 GH<1.0ug/L 作为治疗目标，该目标与肢端肥大症是否得到控制相关，全程的管理监测中。

CS-041

骨质疏松症的现状和防治策略

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夏维波，医学博士，现任中国医学科学院北京协和医院内分泌科常务副主任、教授、主任医师、博士研究生导师。兼任中华医学会骨质疏松和骨矿盐疾病分会主任委员；中华医学会理事；卫生部合理用药专家委员会内分泌代谢组副组长；北京市糖尿病防治协会副理事长。曾于 2000 年至 2001 年在日本东京大学做访问学者。主要从事内分泌和代谢疾病的临床和研究工作。对内分泌和代谢性疾病诸如糖尿病、甲状腺疾病、垂体疾病、肾上腺疾病和代谢性骨病均具有丰富的诊疗经验。目前专注于代谢性骨病的基础和临床研究，承担多项国家级科研课题。发表科研论文 150 余篇，其中在 Am J HumGenet、J Bone and MinerRes、OsteoporosisInt，Bone、Calcified TissueInt 等杂志上发表论文 50 余篇。现担任 Journalof Boneand Mineral Research，Current Osteoporosis Reports 等国内外多个医学杂志的编委，及《中华骨质疏松和骨矿盐疾病杂志》副主编和编辑部主任。

骨质疏松症的患病率正在迅猛增加，骨质疏松症及其骨折所带来的危害也愈加严重。因此需要加强对骨质疏松症的防治，保障“健康中国”的顺利实施。

一、骨质疏松症伴随人口老龄化如约而至

我国自 2000 年已进入老龄化社会，65 岁以上的老龄人口至 2014 年达到 13755 万人，占总人口的 10.1%。到 2050 年，我国老龄人口将达到总人口数的三分之一。根据世界卫生组织（WHO）的估计，50 岁以上的妇女中约有 30% 罹患此病。骨质疏松症将会成为我国所面临的重要公共健康问题。

1. 骨质疏松症的患病率：骨质疏松症是一种“静悄悄的”流行病，2009 公布的亚洲骨质疏松流行病学、花费和负担白皮书显示中国骨质疏松症的患病人数达 6940 万，骨量减少的人口近 2 亿。

2. 骨质疏松性骨折的流行病学特征：骨质疏松性骨折的常见部位是脊椎、髋部和前臂远端。北京等地区 50 岁以上妇女脊椎骨折的患病率为 15%，相当于每 7 名 50 岁以上妇女中就有一位发生过脊椎骨折。近年来，我国髋部骨折的发生率也有明显上升趋势。据统计预测中国大陆地区 2030 年骨质疏松性骨折年发生 436 万例次，至 2050 年达 599 万例次，相应的医疗支出达 178 亿美元和 254 亿美元。骨质疏松性骨折的危害很大，导致病残率和死亡率增加。。

二、我国骨质疏松症的防治策略

骨质疏松症防治的关键在于将防治的重心下移和关口前移，做到“上医治未病”。

1. 骨质疏松症及骨质疏松骨折高危人群的筛查和识别：首先要重视骨质疏松症及其骨折高危因素的筛查。可采用 IOF 1 分

钟自测、OSTA 和 FRAX 等。如指示为高风险则推荐骨密度测定，还推荐对绝经后妇女和 50 岁以上的男性开展骨质疏松症的筛查。

2. 骨质疏松性骨折人群的全程管理和再骨折的防治：2012 年国际骨质疏松日主题定为“止于第一次——让你的第一次骨折成为最后一次”，以期引起临床医生及民众对于患者发生初次骨折的重视。目前国际社会推荐的骨折患者联络服务（FLS）是防治再发骨折的有效管理方式，此种多科协作模式值得在我国推广和普及。

3. 骨质疏松症综合防治模式的探索和推广：骨质疏松的防治被描述为“金字塔”样模式。模式的第一步是基本措施即生活方式干预，包括摄入充足的钙和维生素 D、适当的体力活动和预防摔倒；模式的第二步是寻找和治疗引起骨质疏松的继发因素；第三步是药物干预提高骨密度和降低骨折危险性。

4. 合理防治骨质疏松症药物的选择：防治骨质疏松症的药物包括骨吸收抑制剂、骨形成促进剂和具有多重作用的药物。

5. 骨质疏松症列入慢病管理、分级诊疗的势在必行：在不同医疗机构之间开展社区管理、分级诊疗，才能抓牢我国骨质疏松症防治的瓶颈，全面有效地防控骨质疏松症及其骨折。

CS-042

骨对糖代谢的调控作用

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刘建民，1966 年 5 月，上海交通大学医学院附属瑞金医院内分泌代谢科副主任，主任医师，教授，博导、上海市内分泌代谢病临床医学中心副主任

工作经历：

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学会任职：

2011 ~ ：中华医学会上海分会骨质疏松委员会名誉主任委员

2008 ~ 2011：中华医学会上海分会骨质疏松委员会主任委员

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杂志编委会任职：

2015 ~ :《中华内分泌代谢杂志》副主编，编辑部主任

2013 ~ :《Journalof Boneand Mineral Research》编委

2008 ~ :《Journalof Diabetes》副主编

2008 ~ :《中华骨质疏松和骨矿盐研究杂志》编委

骨骼是一内分泌器官，对全身能量代谢其中一定的调控作用。骨钙素是由成骨细胞合成分泌的骨基质含量最丰富的非胶原蛋白，其主要以两种形式存在于血循环中，即羧化骨钙素及非羧化骨钙素。近年来动物研究显示非羧化骨钙素可作为一种激素对能量代谢发挥重要的调节作用，包括作用于胰腺促进胰岛 b 细胞增殖及胰岛素分泌，作用于脂肪细胞促进脂联素分泌改善胰岛素敏感性，以及通过提高胰高血糖素肽 -1 表达间接促进胰岛素分泌等作用。人群横断面研究和荟萃分析显示血糖水平随血清骨钙素浓度升高而降低，而队列研究及病例对照研究结果尚并不足以支持低血清骨钙素与糖尿病发生相关。除骨钙素外，基线血钙水平似乎对糖尿病的发生也有一定的预报价值。本课题组的人群研究发现破骨细胞活性与正常人的 HbA1c 正相关，并

可带动骨钙素水平升高，而且这一变化可持续到糖尿病前期患者。据此，我们提出在糖尿病的发生过程中，可能存在着一个骨骼代偿 / 衰竭模型，即在出现糖代谢紊乱的早期（血糖和 HbA1c 在正常范围内的升高），人体很可能以牺牲骨骼为代价增强骨吸收，促进骨钙素形成，以维持正常糖代谢。骨骼对糖代谢的这些保护性变化在糖尿病前期达到最大效应。当糖代谢紊乱进一步发展，一旦骨骼代偿衰竭，骨转换减慢，则发展成糖尿病。进一步的 4 年随访也支持了这一假说。当然对这一假设还需要大量临床研究，尤其是前瞻性研究的证实。

CS-043

同位素骨显像在代谢性骨病诊断与鉴别诊断中的价值

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主要担任的职务有：中华医学会骨质疏松和骨矿盐疾病分会常务委员，四川省医学会骨质疏松专委会主任委员，成都医学会骨质疏松专科分会主任委员

承担多项国际合作课题、科技部十一五科技支撑计划项目分课题、国家 863 计划项目子项目、四川省科技厅科技支撑计划项目、中华医学会骨质疏松症专项基金项目、中国循证医学中心项目，负责国家药监局临床药物研究课题七项。作为主研人参研国家自然科学基金项目三项，完成国家、省级科研课题九项，获四川省科技进步三等奖一项，获得我国国家发明专利一项及欧共体发明专利一项。在国内外核心学术期刊以第一 / 通信作者发表科研论著六十余篇，并副主编专著《骨质疏松性骨折的临床诊断与治疗》，副主译《骨质疏松营养学》，参编专著十余部。

背景　低骨量类疾病的鉴别诊断一直是临床上的难点，虽然全身核素骨显像可以定性反映这类骨病的代谢情况，但受到主观经验判断的限制。因此，利用不同代谢性骨病代谢特点不一致的特性，本研究以骨质疏松症（primary osteoporosis, OP）、原发性甲状旁腺功能亢进症（primary hyperparathyroidism, PHPT）、骨软化症（osteomalacia, OM）作为低骨量类疾病的代表，旨在探究全身核素骨显像定量分析在代谢性骨病鉴别诊断中的作用。

对象和方法　本研究于 2015-08 至 2016-03 共纳入就诊于四川大学华西医院内分泌代谢科的代谢性骨病患者 129 名，包括 OP 患者 85 例、PHPT 患者 29 例及 OM 患者 15 例。对所有患者行全身核素骨显像检查，在对应的前后位图像上圈画感兴趣区（region of interest, ROI），包括松质骨优势区：腰 1- 腰 4 后位、股骨颈前位，和皮质骨优势区：颅骨、肱骨中段、股骨中段及胫骨中段前后位，并记录各感兴趣区的放射性核素计数均值（average radionuclide counts, ARC）。以大腿内侧软组织前位 ROI 的 ARC 作为协变量，将三种疾病各 ROI 的 ARC 行协方差分析。

结果　OP 组、PHPT 组和 OM 组在松质骨优势区 ARC 差异具有统计学意义，具体为腰 1- 腰 4 后位（ARC 分别为 22.1 ± 8.3，27.5 ± 10.4，34.6 ± 14.0; $p<0.05$）、股骨颈前位（ARC 分别为 13.1 ± 6.1，19.3 ± 9.6，33.0 ± 35.2; $p<0.05$），即 OM ＞ PHPT ＞ OP；而三组在皮质骨优势区的 ARC 值具体为股骨中段前位（9.0 ± 4.1，13.8 ± 7.4，8.7 ± 6.5）、股骨中段后位（6.6 ± 2.9，8.0 ± 3.1，5.9 ± 4.2），即 PHPT ＞ OM（$p<0.05$），PHPT ＞ OP（$p<0.05$），OP 组和 OM 组间差异无统计学意义。这三组在其它皮质骨优势区 ARC 值差异无统计学意义。

结论　在松质骨优势区，骨软化症患者 ARC 值明显高于原发性骨质疏松症和原发性甲状旁腺功能亢进症。而在皮质骨优势区，原发性甲状旁腺功能亢进症患者 ARC 值明显高于骨质疏松症和骨软化症。提示全身核素骨显像定量分析为这三种疾病的鉴别诊断提供了新思路。

CS-044

低磷血症的诊治

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磷是人体必需元素，含磷化合物在细胞组成、能量代谢、维持酸碱平衡及骨骼发育和骨矿化中均起着关键作用。正常成人血磷正常值 : 0.83 ~ 1.45 mmol/L (儿童：1.29 ~ 1.94 mmol/L)；低磷血症定义为血清磷 ≤0.8mmol/L；血清磷 ＜ 0.3 ~ 0.5mmol/L 为重度低磷血症。血清磷水平受甲状旁腺激素，维生素 D 及称为“排磷激素”的系列肽类物质，如 FGF23 的调控，使其维持在一个较为狭窄的范围。

引起低磷血症的原因多种多样，主要原因包括：一、肠道吸收减少：如营养不良、脂肪泻、慢性腹泻及吸收不良综合征及服用铝镁抗酸剂等。二、磷转移入细胞内：1、糖尿病酮症酸中毒；2、呼吸性和代谢性碱中毒；3、细胞增殖过快：如白血病等。三、综合性原因：包括严重烧伤、急慢性酒精中毒及长期应用无磷透析液或肾移植术后患者。四、经肾脏丢失：1、维生素 D 缺乏；2、肾小管疾病：肾小管酸中毒、范尼可综合征、累及肾小管的全身性疾病；3、甲状旁腺功能亢进症；4、低磷骨软化症：包括某些遗传性低磷性软骨病、肿瘤相关性低磷骨软化症 (TIO) 及特发性高尿钙等；5、某些药物如阿德福韦酯，静脉补铁等亦可导致继发性低磷血症。

肾脏是维持正常磷平衡的重要脏器。正常情况下，90%磷经肾小球滤过，其中 85% ~ 95%在近端肾小管重吸收。肾脏磷的丢失是慢性低磷血症的重要原因，肾小管上皮的钠 - 磷共转运蛋白 II (NPT- Ⅱ) 负责肠道磷的吸收。而肾脏排磷调节的关键因素如FGF23，FGF23 水平增加可以促进肾小管对磷的排泄,导致低血磷、高尿磷, 进而引起骨骼矿化障碍和骨质软化性改变。

轻、中度低磷血症多无明显临床症状，严重的低磷血症可出现肌无力，反射低下，惊厥或昏迷，呼吸衰竭等，并可能与多脏器功能障碍有关。长期慢性低磷血症可以导致骨矿化障碍，是骨软化症的重要原因。

与 FGF23 异常有关的疾病包括遗传性和肿瘤性骨软化症，如 X 连锁低磷骨软化症 (XLH)；常染色体显性 (ADHR) 和隐性 (ARHR) 遗传低磷骨软化症及肿瘤性骨软化症 (Tumor-induced osteomalacia，TIO)。

综上所述，应加强对临床上慢性低磷血症的认识，某些低磷血症如由糖尿病酮症酸中毒及原发性甲旁亢等引起者，在原发病纠正后血磷多可很快恢复正常。肾脏磷丢失增加是慢性低磷血症及由此引起的骨软化症的主要原因；某些遗传性疾病 XLH、ADHR 及 TIO 是慢性低磷血症及低磷骨软化症的重要原因，其中 TIO 为可治愈性疾病，因此要特别关注。TIO 患者如能发现肿瘤，手术切除肿瘤后血磷多可恢复正常，多数患者可彻底治愈。无法手术切除者或XLH、ADHR 等可使用药物治疗，如补充中性磷合剂及维生素 D 等。

CS-045

欧美甲状旁腺功能减退症新指南简介

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甲状旁腺功能减退症（甲旁减）由于甲状旁腺素（PTH）合成或分泌不足而导致血钙降低、血磷升高。如靶器官（骨骼、肾脏等）对 PTH 反应降低或作用抵抗，则导致假性甲状旁腺功能减退症（假性甲旁减）。近期，欧洲内分泌学会及首届国际甲旁减诊治会议就甲旁减诊治相关要点分别在《欧洲内分泌学杂志 European Journal of Endocrinology》（2015 年 8 月）和《临床内分泌代谢杂志 Journal of Clinical Endocrinology and Metabolism》（2016 年 6 月）上发布最新指南。

诊断方面，当甲状旁腺功能正常时，血钙降低会刺激甲状旁腺分泌数倍于正常范围的 PTH；若血钙水平已经明显降低，但 PTH 仍不恰当的波动于正常范围内，则需考虑诊断甲旁减。需要注意的是，低镁血症会导致 PTH 分泌障碍且导致 PTH 在靶组织的作用受损，因此诊断甲旁减时需除外低镁血症。

甲旁减治疗其实是在寻找一个平衡，即在改善临床症状的基础上，血钙水平控制于正常低限，同时不引起尿钙水平升高，降低泌尿系结石风险。甲旁减患者有低钙血症临床表现和（或）血总钙水平低于 2.0mmol/l（8mg/dl）、游离钙水平低于 1.0mmol/，即可启动治疗。指南推荐以活性维生素 D 和钙剂作为起始治疗；如难以获得，可考虑使用普通维生素 D，根据患者临床表现及血钙范围调整药物剂量。如出现高钙尿症，建议减少药物剂量、适当低钠饮食和（或）加用噻嗪类利尿剂；如出现血磷、血钙磷乘积升高，建议进行饮食控制和（或）调整钙剂、维生素 D 类似物用量；对于低镁血症患者，建议考虑加用升高血镁的治疗。不推荐常规使用 PTH 或 PTH 类似物替代治疗。

药物治疗后，推荐每 3-6 个月进行常规监测血钙或游离钙、血磷、肌酐 (eGFR) 及临床表现；如处于药物调整期，建议每周或每两周监测生化指标。治疗期间需定期监测 24h 尿钙、肌酐清除率等，如出现泌尿系结石症状或肌酐开始上升，需进一步行泌尿系影像学检查。同时，建议每年进行甲旁减相关并发症筛查，如头颅 CT、眼科晶状体筛查等。

另外，假性甲旁减治疗重点在于纠正低钙血症、维持 PTH 于正常范围内，并且在不导致高血钙的情况下尽可能维持 PTH 于正常范围内，以减少骨病和三发性甲旁亢风险。

CS-046

肾科医生视角 - 肾衰甲旁亢治疗策略

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摘要暂缺

CS-047

肥胖学组年度进展报告

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肥胖患病率逐年增加。以 BMI 为标准，国民超重肥胖率为 41.22%；以体脂为标准，肥胖率增至 56.93%；以腰围为标准，肥胖率高达 54.1%。我国 BMI>28 的肥胖人群现已突破 1 亿，肥胖率已突破 10%；城市成年人体重超重者已经突破 40%；中国现在有 4600 万成人肥胖，3 亿人超重，18 岁以下超重人群已达 1.2 亿；到 2030 年预计我国会有 8 亿超重或肥胖患者。肥胖罹患 2 型糖尿病、冠心病 、高血压及癌症等危害极大疾病的风险大大增加，已成为危害人类健康和加重经济负担的社会问题。AHA 在 Circulation 杂志上发文认为不同种族人群中肥胖和心血管病风险识别方法中，BMI 是常用的方式，但不是最理想的方式，尤其对于亚洲人群缺乏敏感性，对于黑人，太平洋诸岛等种族也不理想；而腰围联合 BMI 相对较好，Framingham 风险指数可能是目前评估肥胖及其心血管风险较为理想的方法；同时指出影像学及其他无创检查技术并不作为肥胖的常规筛查及心血管风险评估。本年度欧洲发表了肥胖领域中的较为全面的“欧洲成人肥胖管理指南”。而对于儿童肥胖问题也有学者给予了关注，EASD 有学者研究发现，成长环境不佳增加童年时期超重 / 肥胖风险。来自中国和美国的调查的数据显示，童年早期超重增加青春期超重风险。ACOG 推出的“妊娠期肥胖的管理”进一步将肥胖管理前推到妊娠期。本年度美国“肥胖的药物管理：美国内分泌学会临床实践指南”和“2016ACCE 肥胖临床指南”对现阶段肥胖具体管理办法有了较好的概括。包括中国学者在内的“减肥手术的胃中心假说”、“肥胖的迷走神经阻断术疗法”和“肥胖基因 FTO”等研究，也成为本年度肥胖研究的亮点。

CS-048

肥胖—胰岛功能盛极至衰的起点

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研究计划 1 项，发表 SCI 文章 50 多篇。

2 型糖尿病的自然病程不仅仅是平均血糖水平逐年升高、抗糖尿病治疗强度越来越大的过程，更是胰岛功能由盛至衰的病理过程。从肥胖伴高胰岛素血症的糖代谢代偿期到糖耐量受损的失代偿期，然后进入临床糖尿病期，胰岛功能衰竭的进程并没有停止，直至发展到必须外源性胰岛素替代治疗，其中交织着胰岛损伤因素和胰岛再生因素相互博弈，但最终难以纠转胰岛功能衰竭的趋势，其中胰岛损伤因素的不断加强，是了解糖尿病进展的关键。

糖尿病确诊只是标志疾病发展已达到诊断标准，并不能完全体现过程。糖尿病致病机制尚不完全阐明，但致血糖增高直接原因是胰岛 β 细胞功能障碍，随病程发展，胰岛素功能可持续缓慢下降。目前临床治疗糖尿病的药物，可减轻胰岛负担、或替代缺失的胰岛功能。如何在诊断之初使患者残存的胰岛功能不再丧失或减缓衰竭就至关重要。尤其在早期肥胖伴高胰岛素血症时期，了解胰岛功能代偿的状态以及维持高功能代偿的机制，对于糖尿病早期保护胰岛保护提供干预靶点。

模拟生理状态下胰岛素分泌的模式，使患者血糖水平达到良好的控制，是最理想的治疗方法，但在不了解胰岛功能所处状态而单纯以降低血糖为目标的治疗方式，并不一定适用于所有初诊 2 型糖尿病患者，从长期来看也是弊大于利。因此，根据初诊时患者胰岛功能状态，制定相应治疗方案而尽可能去保护胰岛功能尤为重要。对于初诊时还存在较高胰岛素水平或严重胰岛素抵抗的患者，不适合胰岛素治疗。对于初诊时胰岛素分泌水平较低患者，不适合选择口服降糖药，而最好采用完全的胰岛素替代治疗。

CS-049

肥胖糖尿病治疗的新策略：代谢手术

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包玉倩，主任医师、博士生导师、上海市领军人才、优秀学科带头人，现任上海交通大学附属第六人民医院内分泌代谢科主任、上海市糖尿病临床医学中心常务副主任、中华预防医学会糖尿病预防与控制专业委员会副主任委员、中华医学会内分泌学分会委员、上海市医学会糖尿病专科分会主任委员。主要从事肥胖、糖尿病及代谢综合征的临床研究，迄今共获得国家科技进步奖、中华医学科技奖、上海市科技进步奖等奖励 14 项。

糖尿病管理的内容包括健康教育、营养治疗、运动、药物、血糖监测。然而，即便采取上述综合措施，仍有部分患者的病情不能得到有效控制。代谢手术的临床应用已有超过 50 年的历史，尽管国内起步较晚，但近年发展迅速。来自国内外的证据表明，代谢手术不仅对于肥胖、糖尿病本身具有传统内科治疗无法企及的疗效，还对多种肥胖及糖尿病的合并症、并发症如代谢综合征、睡眠呼吸暂停综合征、糖尿病肾病等具有良好的改善和缓解作用，有力地证实了代谢手术的临床价值及治疗地位。今年 5 月 24 日美国糖尿病学会官方杂志 Diabetes Care 在线发表了“代谢手术作为 2 型糖尿病治疗方案：国际糖尿病组织联合声明”，这是全球首次由多个国际糖尿病组织共同推荐将代谢手术纳入 2 型糖尿病临床治疗路径。

代谢手术的治疗机制复杂，主要有：①前肠假说：由于消化道路径的改变，减少了食物对十二指肠及近端空场上皮细胞的刺激，抑制了产生促进胰岛素抵抗的信号；②后肠假说：加速食糜进入末端回肠，刺激 L 细胞分泌 GLP-1 和 PYY，从而抑制食欲、减少胃肠蠕动，进而降低血糖。③其他，包括肠道菌群变化，胆汁酸分泌改变等。

2011 年 2 月上海市糖尿病临床医学中心组建了以内分泌代谢科与普外科为核心的“代谢手术治疗协作团队”，形成了分工明确、协作互补、井然有序的工作规范，取得了显著成效，被国际同行誉为“上海模式”。至今完成手术 350 余例，体重指数最大为 61kg/m^2。其中袖状胃成形术占比 21%，胃转流术 79%，2 型糖尿病的完全缓解率为 76.5%，达到国际先进水平。术后营养相关并发症明显低于国际同行。进一步分析发现，术前血清 C 肽水平大于 2 ng/ml 对术后完全缓解具有较好预测价值，糖尿病病程短、腹内脂肪聚集程度高的患者手术获益更大。此外，术前中心型肥胖，以及 RYGB 术后减重较多的患者肺功能改善更显著，RYGB 术后腹内脂肪的减少对改善患者的动脉弹性有积极作用。

尽管代谢手术为伴肥胖的 2 型糖尿病患者带来理想的疗效，但其潜在风险不容忽视。代谢手术堪比系统工程，需要多学科的通力合作。

CS-050

限食减重改善胰岛素储备功能的效果与机制

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目的　轻度或中度限食能否逆转肥胖损伤胰岛 β 细胞功能及其机制尚不明确。本研究探索中度限食、减重改善胰岛素储备及分泌功能的效果与机制。

方法　高脂（HF）喂养 DIO C57BL/6 小鼠经过 3 周限食干预，分别为正常热量（HF → NC group）、40% 正常热量（HF → NC CR group）。通过腹腔葡萄糖耐量实验（IPGTT）、离体胰岛葡萄糖刺激分泌胰岛素实验（glucose-stimulated insulin secretion，GSIS）反映胰岛素分泌功能。免疫组化、电镜方法观察形态学变化，蛋白电泳分析信号传导通路特点。

结果　40% 正常热量 (HF → NC CR group) 干预的 DIO 小鼠，体重恢复正常，葡萄糖耐量异常、第一时相胰岛素分泌减低及胰岛素敏感性下降均逆转至正常。胰岛缩小至正常直径。此外，胰岛 β 细胞自噬（autophagy）能力提高，而 AMPK 磷酸化水平没有改变。相比之下，转为正常热量（HF → NC group）干预后，只有葡萄糖耐量异常恢复，其他指标有所改善但没有逆转至正常。

结论　中度限食可以逆转肥胖小鼠体重、胰岛素抵抗、葡萄糖耐量异常。胰岛 β 细胞内储备的胰岛素恢复正常及细胞自噬能力提升是胰岛素分泌功能逆转的直接原因。

CS-051

甲状腺功能与肥胖

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甲状腺功能与肥胖、体重调节存在重要的关联。人群研究提示甲状腺功能除与基础甲状腺

疾病相关外，也与肥胖有一定相关。甲状腺正常的肥胖者存在下丘脑 - 垂体 - 甲状腺轴的激活，表现为血清促甲状腺素水平和甲状腺激素水平的升高。甲状腺功能与肥胖的多种参数，如体重、体重指数、腰围、臀围、腰臀比和体脂百分比呈一定的相关关系。另一方面，当体重有较大的起伏时甲状腺功能也随之产生变化。目前的研究显示下丘脑 - 垂体 - 甲状腺轴与脂肪组织存在交联。脂肪细胞可表达促甲状腺素受体，促甲状腺素在脂肪细胞的生长分化中起作用。此外，促甲状腺素与多种脂肪因子的分泌有关，由此进一步调节能量代谢，进而影响体重。对甲状腺激素在体重管理中的应用也有不少的学者进行了探讨。

CS-052

高血糖人群的妊娠前准备

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童南伟，四川大学华西医院内分泌代谢科教授、博士生导师、科主任。现任中华医学会内分泌学分会常委，中国医师协会内分泌代谢科医师分会常委。国家卫计委合理用药专家委员会内分泌与代谢药物专业组专家。四川省医学会内分泌暨糖尿病专委会前任及候任主委。四川省医师协会内分泌代谢科医师专科分会会长。四川省糖尿病防治协会副会长。

妊娠对女性及其后代来说都极为重要，尤其我国第二胎政策放开，妊前高血糖人群会渐增加。对男性来说，高血糖对女性妊娠有何影响？妊前准备高血糖以外的代谢异常怎么纠正？也许这些问题都是社会关注，医务人员必须面对的问题。本报告将对这些话题展开讨论。

CS-053

妊娠合并糖尿病的血糖管理

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刘彦君，博士，主任医师，306 医院内分泌科主任，全军糖尿病诊治中心中心副主任。博士后工作站导师、硕士生导师。兼任全军内分泌学会常委、中国医师协会内分泌专业委员会委员、北京市中西医结合糖尿病分会副主任委员、北京市内分泌学会常委、北京市糖尿病防治协会副理事长、北京市健康科普专家。承担国家自然科学基金、北京市首都特色医学研究重点项目等科研课题。获得军队科技进步二等奖 2 项，军队科技进步三等奖 2 项，军队医疗成果三等奖 5 项，北京市科技进步三等奖 1 项，在国内外杂志和学术会议发表论文 100 余篇，主编科普书籍 2 部，参编科普书籍 3 部。专业特色为糖尿病及其并发症诊治、特别是糖尿病足及妊娠期糖尿病的诊治，内分泌疾病诊治等。

妊娠期孕妇高血糖的状况包括 2 种情况，妊娠糖尿病 (gestational diabetes mellitus, GDM) 及糖尿病合并妊娠。GDM 指的是妊娠期首次发生或首次发现的不同程度的糖耐量异常。不包括妊娠前已存在的糖尿病。妊娠前已经确诊糖尿病的孕妇是糖尿病合并妊娠。

妊娠期糖尿病导致母儿孕、产期不良妊娠结局及产后远期代谢异常几率增多，严重影响了母亲及其后代的健康。常见的母

婴近期并发症包括：孕妇自然流产、早产、羊水过多、妊娠期高血压以及子痫前期、剖宫产，巨大儿、新生儿低血糖以及呼吸窘迫综合症等。糖尿病合并妊娠孕妇除上述情况多发外，患糖尿病酮症以及酮症酸中毒（DKA）的风险明显增加，后代先天畸形、围产儿死亡率也明显增加。并发妊娠糖尿病的女性之后发展为糖尿病的风险是增加的。GDM 患者后代未来发生糖代谢异常、超重或肥胖、脂代谢紊乱、高血压等疾病、女性后代孕期发生 GDM 的风险增加。

妊娠期糖尿病的治疗有其特殊性。

一、糖尿病妇女的孕前准备：

1. 糖尿病妇女应计划妊娠，在糖尿病未得到满意控制之前应采取避孕措施。应告知已妊娠的糖尿病妇女在妊娠期间强化血糖控制的重要性以及高血糖可能对母婴带来的危险。

2. 筛查糖尿病的并发症、合并症，对糖尿病肾脏病变、神经病变、视网膜病变、以及心血管病变、高血压、脂代谢紊乱、抑郁、甲状腺疾病进行评估和治疗。由糖尿病医师和妇产科医师评估是否适于妊娠。

3. 根据患者病情调整治疗方案，包括停用口服降糖药物，改用胰岛素控制血糖；将控制高血压的 ACEI 和 ARB 改为甲基多巴或钙拮抗剂，严格将血压控制在 130/80mmHg 以下；停用他汀类及贝特类调脂药物。

4. 严格控制血糖，加强血糖监测。餐前血糖控制在 3.9 ～ 6.5mmol/L（70 ～ 117mg/dl），餐后血糖在 8.5mmol/L（<153.0mg/dl）以下，HbA1c 控制在 7.0% 以下（用胰岛素治疗者），在避免低血糖的情况下尽量控制在 6.5% 以下。

5. 加强糖尿病教育；戒烟。

二、孕期血糖控制目标：

（一）糖尿病合并妊娠的血糖控制目标：

在不发生低血糖的情况下，

餐前、睡眠及夜间血糖 60–99 mg/dL (3.3–5.4 mmol/L)

餐后峰值血糖 100–129mg/dL (5.4–7.1 mmol/L)

Hb A1C <6.0%

（二）GDM 的血糖控制目标：

餐前血糖 ≤95mg/dL (5.3mmol/L),

餐后 1 小时血糖 ≤140mg/dL (7.8 mmol/L)

餐后 2 小时血糖 ≤120mg/dL (6.7 mmol/L)

三、生活方式管理是妊娠期糖尿病管理的基础

（一）饮食管理

妊娠期间的饮食控制标准：既能保证孕妇和胎儿能量需要，又能维持血糖在正常范围而且不发生饥饿性酮症。尽可能选择低生糖指数的碳水化合物。对使用胰岛素者，要根据胰岛素的剂型和剂量来选择碳水化合物的种类和数量。应实行少量多餐制，每日分 5 ～ 6 餐。

尿酮体阳性时，应检查血糖（因孕妇肾糖阈下降，尿糖不能准确反映孕妇血糖水平），如血糖正常，考虑饥饿性酮症，及时增加食物摄入，必要时在监测血糖的情况下静脉输入适量葡萄糖。若出现酮症酸中毒，按酮症酸中毒治疗原则处理。

（二）运动管理

运动增加葡萄糖消耗，增加胰岛素敏感性，对于 GDM 血糖管理十分重要。每日 30 分钟轻中度强度的运动，如散步或适当的快走，对于没有运动禁忌症的 GDM 孕妇是有益的。有先兆流产、妊高症、严重的糖尿病并发症、血糖过高、发热，或医生评估不适宜运动的孕妇，均不建议运动。

四、药物治疗

近 80% 的 GDM 患者通过生活方式的管理可以将血糖控制在理想范围，仅 20% 左右的 GDM 患者生活方式管理血糖不能达标，需要合并药物治疗。孕妇应避免使用口服降糖药，通过饮食治疗血糖控制不能达标时，使用胰岛素治疗。

人胰岛素优于动物胰岛素。临床证据显示速效胰岛素类似物赖脯胰岛素和门冬胰岛素以及长效胰岛素类似物地特胰岛素在妊娠期使用是安全有效的。为了吸收一致性，注射部位应选择腹部和臀部。

空腹血糖升高时，可选用中效胰岛素 (NPH)，或地特胰岛素，餐后血糖升高，选用短效胰岛素或速效胰岛素类似物。后者优势在于更有效地降低餐后血糖，而低血糖发生率更低，餐食给药更加方便。胰岛素用量应根据血糖监测结果，个体化调整，直至达标。

随着孕期的增加，胎盘增大，胎儿体重增加，母体能量需求增大，使得胰岛素的需要量不断增加，因此，孕妇需要持续进行血糖监测，不断调整胰岛素用量。

分娩时和产后加强血糖监测，保持良好的血糖控制。择期剖宫产或临产后应停用皮下注射的胰岛素，需要胰岛素的患者，改为静脉给药。每 2 小时监测血糖，维持血糖在 4.4-6.7mmol/l，血糖升高时注意测尿酮体，并根据血糖水平调整静脉胰岛素用

量。

糖尿病合并妊娠者在分娩后胰岛素的需要量会明显减少，应注意血糖监测，适时减少胰岛素的用量，避免低血糖。哺乳期血糖控制范围与孕期相同。妊娠糖尿病使用胰岛素者多数在分娩后可以停用胰岛素，继续监测血糖。停药后血糖不能达标的患者，应在哺乳期继续胰岛素治疗。

五、血糖监测是有效控制血糖的保障

有条件的医院应对糖尿病合并妊娠及 GDM 患者进行动态血糖监测，以明确患者血糖波动规律，发现未检测到的高血糖和低血糖，给予针对性的诊疗。

患者需进行自我血糖监测，每日测定空腹和餐后血糖 4 ~ 6 次。对于血糖波动大、控制不理想的患者，应监测三餐前后及睡前、必要时包括夜间血糖，或进行动态血糖监测，以便调整治疗方案。

CS-054

儿童青少年糖尿病患者的血糖管理

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吴迪，主任医师，医学博士，副教授，硕士研究生导师，首都医科大学附属北京儿童医院内分泌遗传代谢科副主任。现任中国医师协会青春期委员会副主任委员及青年学组副组长、中华医学会糖尿病学分会委员、中华医学会儿科内分泌遗传代谢学组委员、中国医师协会内分泌遗传代谢科青年委员、北京医学会儿科内分泌遗传代谢学组委员兼秘书、北京医学会内分泌分会青年委员、北京药理学会临床药理专业委员会青年委员。中华糖尿病杂志通讯编委，中华临床医师杂志审稿专家。

长期在临床一线工作。承担及参与多项科研基金。近 5 年核心期刊发表文章 20 余篇，SCI2 篇。参编书籍十余部。2014 年赴美国纽约 Morgan Stanleychildren’shospital 进修。主要研究方向为儿童糖尿病、DSD 体格发育、Silver Russell 综合征等。

儿童青少年 1 型糖尿病在世界范围内明显增长。北京儿童医院采用住院登记调查方法发现，1995 年 -2010 年北京地区儿童 1 型糖尿病发病率呈逐年增高趋势，平均年增长率为 4.36%。增长速度赶超欧美等高发病率国家，尤其小于 5 岁的小幼儿增长速度最快。这意味着儿童 1 型糖尿病将有更长带病生存期，预示着并发症诊治更为严峻。儿童青少年 1 型糖尿病血糖管理亟需重视。

关于儿童青少年 1 型糖尿病血糖管理总体情况不容乐观，只有少部分患儿达到管理目标，即 HbA1C ＜ 7.5%，即使在发达国家亦如此。血糖控制水平受到胰岛素治疗、血糖监测、生活方式、社会心理因素及糖尿病教育等多方面影响。现代科学技术的发展，带来治疗手段不断更新。如血糖监测、CGMS、新型智能胰岛素泵，以及多种新型胰岛素制剂。但是无论新诊断糖尿病的 DKA 发生率还是糖尿病总体血糖控制、并发症的发生率，都不令人满意。

自从 DCCT 证明强化治疗能减少糖尿病长期并发症之后，通过强化治疗降低血糖、减少或延缓并发症已被全世界推广。由于 DCCT 对于胰岛素治疗作用有明确要求，使很多人误认为胰岛素的作用远远大于包括糖尿病教育在内的糖尿病治疗的其他方面。现在很多人存在一个错误的理念，即强化治疗等同于 MDI 或 CSII，而很少有人注意到糖尿病教育所起到的作用。在糖尿病强化治疗中究竟哪一环节最重要？是胰岛素治疗还是糖尿病教育和支持？笔者认为在自律性差的患者身上仅仅将胰岛素的治疗方法复杂化是达不到预期目的，而加强糖尿病教育、改善患者行为及心理支持等方面的治疗反而能促进血糖控制。开启私人订制模式、制定个体化治疗方案，才能有助于血糖管理。糖尿病治疗的成功并不简单地是医疗技术的改进，也不是患者自己单方面或者医疗提供者的问题，而是涉及医、患、政策等的综合和持久的问题。

CS-055

高龄老年糖尿病患者的血糖管理

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国家卫生和计划生育委员会慢病咨询专家委员会委员、中央保健会诊专家、中华医学会糖尿病学分会副主任委员、北京医学会糖尿病学分会主任委员、北京医师协会内分泌分会副会长、中国医师协会内分泌代谢科分会常委兼副总干事．糖尿病教育委员会主任委员、中国药品安全合作联盟专家委员会副主任委员。

《中华内分泌代谢杂志》、《中国糖尿病杂志》、《中华保健医学杂志》、《中华国际医学论坛》、《中华临床营养杂志》编委 / 常务编委；《糖尿病研究与临床实践．中文版》副主编、《中华糖尿病杂志》副总编。

老年糖尿病包括原患有糖尿病随年龄增加进入老年阶段和进入老年后新发现糖尿病的两类人群。2013 的资料显示，我国 65 岁及以上人口 12714 万人，占总人口的 9.4%。有研究显示我国 ≥60 岁人群糖尿病患病率为 20.4%，而高龄老年人群中此比例可能会进一步升高。无论从患者的预后角度还是对整个社会经济负担方面考虑，老年糖尿病的管理的成败是管理糖尿病的关键要素之一。

高龄老年糖尿病控制的首要目标依然是预防微血管及大血管并发症。年龄增加本身也增加了糖尿病的预防和治疗的难度。伴随着年龄的增大，高龄老年糖尿病患者普遍出现记忆力下降、认知功能降低、抑郁状态、视力和体力下降等问题；骨关节病变、视力下降、外周血管病变以及神经病变也使得患者难以进行有效的体育活动；合并多种其他疾病使糖尿病的自我监测和治疗变得更加困难。

老年人同时罹患多种疾病，服用药物种类多，药物本身以及药物相互作用都可能增加不良反应的风险，使老年糖尿病患者的病情更加复杂而难以达到糖化血红蛋白目标。年龄超过 80 岁的糖尿病患者，有 2/3 的急诊入院患者是无意中服用降糖药物过量引起。老年人群具有其自身的特殊性。虽然同属老年人，但是这部分人群应个体化对待。即使年龄相同的患者，从临床特征、社会心理身体状况、各个系统的功能、认知行为以及经济状况都存在着巨大差异。

低血糖是所有的 2 型糖尿病患者治疗达标的障碍，对老年患者尤其如此。然而在老年患者中，这种致命的危害往往缺乏症状而直接导致功能损害。如前所述，年龄已经被证实是严重低血糖的独立危险因素。在很多老年患者易发生无症状低血糖，增加了发生严重低血糖的风险。

老年糖尿病患者的血糖管理应更加注重人性化与个体化。目前尚没有指南非常明确地界定老年人糖化血红蛋白控制的靶目标值，原则是在尽可能避免低血糖的情况下达到血糖的合理控制，目标是最大化地给患者带来获益而将额外的风险降至最低。防范低血糖，尤其是无症状性低血糖是高龄老年糖尿病患者的第一要务。另外，针对老年患者专门设计的临床实验较少，呼吁临床医生能设计出更多更好的针对老年糖尿病患者的临床试验，为临床诊疗带来更加科学客观的循证医学证据。

CS-056

男性乳腺发育治疗

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男性乳腺发育症 (GYN)，又称男性乳腺增生症，是指男性乳腺组织异常增生、发育。一般是由于雄性激素与雌激素作用比例失调、睾酮分泌减少或作用不足和 (或) 雌激素产生过多所致。

GYN 可发生于任何年龄，临床上根据病因不同分为生理性、病理性。其治疗应根据其不同病因、病史长短、有无伴随症状、乳腺大小等作出合理选择。由于大多数生理性男性乳腺发育可自发性消退，多数并不需要治疗。但是，对临床上伴有乳腺疼痛或触痛，较大的乳腺发育持续存在且影响患者的形体美容和心理者，则需要给予临床干预。常用的方法有药物治疗、手术治疗和停用有关的药物。

药物治疗：(1) 选择性雌激素受体拮抗剂 ：口服他莫昔芬 (三苯氧胺)，20mg/d，连续 3 个月，80% 的男性乳房发育部分消退，60% 的患者完全消退。(2) 雄激素治疗：庚烷酸双氢睾酮 200mg，每 3 ~ 4 周肌注 1 次。对雄激素缺乏者可以减轻乳腺发育，但在雄激素水平正常的患者中常因雄激素在体内转化为雌激素反而加重乳腺发育并不推荐。(3) 芳香化酶抑制剂：包括睾酮内酯和达曲唑等：安全、有效。外科手术治疗：目前认为，当 GYN 病程较长，内科治疗难以奏效时，需给予手术治疗。主要指征：①乳腺直径 >4 cm，持续 24 个月不消退者；②有症状者；③可疑恶性变者；④药物治疗无效者；⑤影响美观或患者恐惧癌症要求手术者。大体可以分为 3 种，即脂肪抽吸术、开放式切除术以及脂肪抽吸联合开放式切除术。

CS-057

血糖与勃起功能障碍

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向光大，广州军区武汉总医院内分泌科主任，教授，主任医师，医学博士，博士生导师。2010–2011 年在美国德克萨斯大学访问学者。入选湖北省医学领军人才，全军科技拔尖人才，获中国医师奖。担任中华医学会内分泌学分会委员，中华医学会性腺组副组长，解放军内分泌专业副主任委员，中国微循环学会糖尿病与微循环专业副主任委员，广州军区内分泌专业主任委员、湖北省医学会内分泌专业副主任委员，湖北省医学会内科学副主任委员，武汉医学会内分泌专业副主任委员。同时担任《DiabetesMetabolismResearchandReview》、《中华糖尿病杂志》、《中国糖尿病杂志》和《临床内科杂志》编委。先后发表学术论文 300 多篇，其中以第一作

者在《Diabetes》、《Diabetes Care》、《Diabetologia》、《JClin Endocrinol Metab》、《EuropeanJ of Endocrinology》等刊物上发表 SCI 学术论文 30 多篇。以第一完成人获得湖北省科技进步一等奖 2 项，军队医疗成果二等奖 3 项。主编《临床甲状腺病学》（人民卫生出版社）

一、勃起功能障碍（ED）定义

患者阴茎不能获得或维持充分的硬度以完成满意的性交。

二、流行病学数据

马萨诸塞州男性增龄研究显示 ED 在年龄 40-70 岁男性中常见，随年龄增大患病率增加；我国研究显示 2003 年 ED 在中国的患病率已达 26.1%，其中 40 岁及以上年龄段为 40.2%，且诊断率及正规治疗率较低。

三、ED 的分类及常见原因

ED 分为心理性、器质性和混合性三类，目前认为器质性占 60% 以上。器质性 ED 最常见的病因是动脉粥样硬化，与动脉粥样硬化相关的高血压、心脏病及其危险因素包括糖尿病、高脂血症、吸烟等。

四、糖尿病性勃起功能障碍的发病机制

糖尿病通过多种途径导致性欲减退，勃起和射精障碍，主要致病机制包括：性激素异常、海绵体结构和功能改变，血管内皮功能紊乱、神经病变。

五、糖尿病与 ED 关系

糖尿病是器质性 ED 最常见的原因，糖尿病患者 ED 风险显著增加；ED 可能是糖尿病的早期标志及糖尿病神经病变的第一临床表现。

六、糖尿病 ED 的治疗

在生活方式的改变（包括减重、戒烟、运动等）的基础上循序渐进采取“三线治疗”策略

一线治疗：心理治疗、真空泵装置及促勃起药物。

（1）、5 型磷酸二酯酶抑制剂（PED5）抑制剂：万艾可、艾力达、希爱力

（2）、雄性激素：睾酮

（3）、血管扩张剂：育亨宾、酚妥拉明

（4）、中枢活性药：曲唑酮、阿朴吗啡、百忧解

（5）、抗氧化剂：维生素 C、维生素 E、α - 硫辛酸

二线治疗：阴茎海绵体内或尿道内局部注射血管活性药物（罂粟碱、前列地尔、酚妥拉明）。

三线治疗：阴茎假体植入手术或静脉手术。

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肥胖对男性性腺功能的影响

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中国医师协会内分泌代谢科医师分会委员

中华医学会内分泌学分会性腺学组委员
中华医学会糖尿病学分会糖尿病神经并发症学组委员
中国微循环学会糖尿病与微循环专业委员会委员
中国老年保健医学研究会老年内分泌与代谢病分会常务委员
中国糖尿病防治康复促进会常务理事
山东大学学报(医学版)编委会委员
《中华临床医师杂志(电子版)》特约编辑
主要研究方向：垂体－肾上腺、性腺疾病；糖尿病及其并发症的基础和临床；放射性 ^{131} 碘治疗甲状腺疾病。
主持国家自然基金 3 项，中国中医药局基金、中华医学会国际交流基金各 1 项，山东省自然基金、卫生厅课题、中医药局课题等多项。获卫生部三等奖 1 项，山东科技进步奖、山东医学科技奖、院级科技进步奖等多项。发表论文 100 余篇，SCI 收录 27 篇，其中第一作者或通讯作者发表 17 篇。主编、副主编专业书籍 4 部，参编 8 部

目前肥胖在全球广泛流行，WHO 报告，2014 年 18 岁及以上的成年人中有超过 19 亿人超重，其中 6 亿人肥胖。脂毒性是肥胖主要的致病机制。近来肥胖及脂毒性对男性性腺及生殖功能影响也引起广泛的关注。肥胖对男性性腺的影响主要有三个方面：生殖内分泌异常、精液参数异常及勃起功能障碍。

肥胖男性患者常伴有血清睾酮(T)水平下降，流行病学调查显示，肥胖与血清 T 水平下降密切相关，体重指数越高，T 水平越低。随着年龄增加血清 T 水平较瘦体型者下降更显著；动物研究显示，非酒精性脂肪性肝病大鼠睾丸组织的类固醇合成急性调节蛋白(StAR)、P45 胆固醇侧链裂解酶(P450scc)、P45017α 羟化酶(P45017α)、17β 羟基固醇脱氢酶(17β-HSD)的表达水平下降，提示肥胖可降低 T 合成关键蛋白和酶的表达。T 低下可导致性功能障碍和生殖能力下降，增加心血管疾病的风险和全因死亡的风险。由于肥胖患者体内大量的白脂肪组织致使芳香化酶的活性增加，T 转化为雌激素引起雌激素升高而 T 水平进一步下降，促性腺激素、抑制素 B 浓度降低，引起下丘脑 - 垂体 - 性腺 (HPG) 生殖轴的功能障碍，加重勃起功能障碍，影响精子的生成。

研究发现肥胖患者男性精子总数、精子浓度和精子形态出现异常变化。对 483 例不育男性患者研究发现，BMI 越大射精量越少，BMI ≥35 kg/m2 者的精子总数低于 BMI 正常者。肥胖患者随肝脏脂肪含量的增加，精子密度、精子数和精子活性下降趋势越明显。动物实验发现，正常体重小鼠精子超活化能力要大于肥胖鼠的 3 倍，而肥胖小鼠精子活力比正常鼠低 20%。

然而目前关于脂毒性对男性性腺及功能影响的的作用机制的研究还很少，对肥胖引起的精液异常和男性生殖方面的干预性研究还不多，因此深入研究脂毒性对男性生殖健康的影响，探索有效的治疗方案包括生活方式的改变、药物治疗以及手术治疗，具有极其重要的临床价值和社会意义。

CS-059

痛风研究十年

邹和建

复旦大学附属华山医院

邹和建，复旦大学附属华山医院风湿科教授、主任医师、博士研究生导师。复旦大学风湿、免疫、过敏性疾病研究中心主任、复旦大学附属华山医院分子与转化医学研究所所长；国际硬皮病临床与研究协作网(InSCAR)副主席；上海医学会风湿病学分会前任主任委员、上海医师协会风湿免疫科医师分会副会长、海峡两岸医药卫生交流协会风湿免疫病分会痛风学组主委。《药物不良反应杂志》副总编辑。曾任中华医学会风湿病学分会第七、第八届委员会副主任委员、中国医师协会风湿免疫科医师分会第一、第二届委员会副会长。近 5 年承担国家自然科学基金、211 学科新增长点基金、上海市科委重大、重点项目、卫生部科研项目、973 项目子课题、上海市优秀学术带头人计划共 10 余项。近 5 年来发表第一作者或通讯作者 SCI 论文 30 余篇。主编、副主编学术专著 9 部。HLA-B*5801 基因检测技术获国家专利发明授权，并获得上海市 2016 年度发明金奖。主要从事痛风基础与临床研究。2011 年入选上海市领军人才，上海

市优秀学术带头人；2012 年获“宝钢优秀教师”奖。

随着对痛风、高尿酸血症的重视度不断上升，其研究已经成为国内研究的热点。风湿科、内分泌代谢科、肾病科、中医科均有相关专家学者开展基础和临床研究。尽管目前总体上看国内学者发表的高分值 SCI 论文不多，但是无论中基础研究、转化医学研究研究还是临床研究都取得了一定进展。

遗传因素在痛风和高尿酸血症发病中的作用一直是研究的热点，近十年来，在尿酸代谢相关基因的 SNP 研究方面有较多论文发表，着重比较了中国人群与西方人群遗传学上的差异。师咏勇、李长贵教授发表的痛风相关 GWAS 研究是国内首个该领域的大规模研究。王久存、邹和建教授则从 CNV 及表观遗传学方面开展相关的研究。周京国教授课题组也在遗传学研究方面做了大量工作。为了阐明痛风发病机制，以 NLRP3 为代表通路的研究正在不断继续，从固有免疫的巨噬细胞到获得性免疫在痛风发病中的作用，正在深入进行；为了更好地验证高尿酸血症的危害以及制定干预策略，大型队列研究正在进行中，并且已经取得阶段性成果；为了进一步规范高尿酸血症和痛风的治疗，多个学科制定了相应的专家共识或治疗指南，尽管存在分歧，或者缺乏充分的循证医学证据，但是通过共识、指南颁布后引发的讨论，使同行学者看到了研究中存在的问题，为今后联合攻关指明了方向。

CS-060

自发高尿酸血症动物模型的构建及应用研究

李长贵

青岛大学附属医院

李长贵，医学博士，教授，博士研究生导师，博士后指导导师，科技部重点研发计划首席科学家，科技部 973 计划前期研究专项首席科学家，中华医学会内分泌学会高尿酸学组执行组长，海峡两岸医药卫生交流协会风湿免疫病学专业委员会高级顾问兼痛风学组副组长，中华医学会山东省糖尿病学会副主任委员。山东省泰山学者，山东省痛风病临床医学中心主任，山东省代谢性疾病重点实验室主任，青岛大学代谢病研究院院长，青岛大学附属医院代谢病科主任，《Goutand Hyperuricemia》杂志主编，《中华内分泌代谢杂志》编委。主要从事原发性高尿酸血症和痛风的基础及临床研究。作为课题负责人，在痛风病研究方向先后承担了科技部重点研发计划 1 项（首席），科技部 973 计划前期研究专项 1 项（首席），国家自然科学基金重点国际合作项目 1 项（负责人），国家自然科学基金面上项目 4 项（负责人）。获教育部科技进步二等奖 1 项（首位），山东省科技创新成果一等奖 1 项（首位），山东省科技进步二等奖 2 项（首位），山东省自然科学三等奖 1 项（首位）。近 5 年来第一或通信作者 SCI 收录杂志论著 40 余篇，其中 1 篇发表于 Nature Communication 杂志，累及影响因子近 120 分。

原发性高尿酸血症目前已成为继糖尿病之后又一常见代谢性疾病，患病率已达 13.3%。高尿酸血症可直接导致关节、肾脏的损伤，但高尿酸血症与糖代谢、脂代谢及心脑血管疾病间的因果关系不清。

高尿酸血症动物模型是研究高尿酸血症危害及新药开发的必经之路，然而传统的高尿酸酸血症动物模型构建方法存在明显的缺陷，表现为血尿酸水平介于 200-300 之间，达不到人类高尿酸血症的诊断标准；血尿酸水平不稳定，波动幅度大；操作繁琐。为此我们采用 TALEN 技术，成功构建了 C57BL/6J 背景的尿酸氧化酶基因敲除小鼠模型，该模型小鼠自发高尿酸血症，血尿酸介于 400-600umol/L, 血尿酸水平稳定，小鼠可长期存活。初步研究的结果显示，长期高尿酸血症通过诱发胰岛素抵抗和损伤胰岛细胞功能，直接导致糖代谢紊乱；长期高尿酸血症可导致脂代谢紊乱；长期高尿酸血症可导致高血压；长期高尿酸血症可损伤内皮依赖性血管舒张功能；高尿酸血症持续 6 周即开始出现肾脏结构异常，表现为鲍曼囊扩张，轻度肾间质纤维化，炎性细胞浸润；自发高尿酸血症动物模型对临床常用降尿酸药物非布司他、别嘌呤醇和苯 溴马隆具有良好的反应性。该研究结果显示，该自发高尿酸血症动物模型，是研究高尿酸血症危害和新药开发的良好模型。

CS-061

ACR/EULAR 痛风分类标准的解读

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1982 年毕业于广州中山医科大学医疗系，在积水潭医院风湿免疫科长期从事医教研工作。公开发表 50 余篇专业文章，参加 10 余部专著的撰写，主编《痛风与晶体性关节病》，副主编《实用痛风病学》。

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本次发言就《2015 年美国风湿病学会 / 欧洲抗风湿联盟痛风分类标准》分四方面进行阐述

1. 新分类标准的产生背景

现存的多个痛风分类及诊断标准对慢性痛风性关节炎诊断效力不足，与其他关节炎鉴别有限，缺乏先进的影像学手段，如超声、双能 CT。

为新药的临床验证，满足临床研究的和基础研究的需要，有必要产生新的分类标准。

2. 新分类标准的解读

1. 适用标准：明确了适用人群为至少有 1 次关节炎发作

2. 确定标准：在曾有症状的关节、滑囊、痛风石证实存在尿酸钠晶体。此时即可确诊，无需进入以下的分类标准。

3. 分类标准：

1. 临床项目：4 个条目

2. 实验室项目：2 个条目

3. 影像学项目：2 个条目

各条目赋予不同的权重和积分，总分之和为 23 分，评分 ≥8 分时可诊断痛风。

1. 新分类标准的产生

第一阶段：明确分类标准所需要考虑的因素，首先请临床专家列出痛风与其他风湿病鉴别的项目；利用横断面诊断研究对上述项目进行验证；对痛风影像学方法进行系统文献回顾。

第二阶段：补充临床经验，对第一阶段所获得的数据，确定最优的用于鉴别痛风及其他风湿病的项目，并对这些项目赋予权重，形成初稿。

第三阶段：将所得到的项目及权重评分简化为整数字，纳入分类标准中，并利用横断面诊断研究对最终分类标准进行验证。

2. 新分类标准的评价

纳入了最新的影像学证据，以证实尿酸钠晶体的存在为金标准，为评分系统设立权重，给各项核心条目赋分。同时适用于急性期和慢性期痛风的诊断。

完整版的分类标准（包含影像学的 MSU 结果）

敏感性 0.92 特异性 0.89

临床版的分类标准（仅有临床参数）

敏感性 0.85 特异性 0.78

新分类标准的特异性、敏感性均高于现存的其它分类诊断标准，具有较高的诊断效力。

CS-062

高尿酸血症与肾脏疾病：现状及展望

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陈香美，中国工程院院士，中国人民解放军总医院主任医师、教授、博士生导师，全军肾脏病研究所所长，肾脏疾病国家重点实验室主任。国家慢性肾病临床医学研究中心主任，国家肾脏疾病质量控制中心主任，中华医学会常务理事，中华肾脏病学会第七、八届主任委员，中国中西医结合学会会长、中国医师协会肾脏内科医师分会会长。

在过去的几十年里，高尿酸血症（Hyperuricemia，HUA）患病率逐年升高，逐渐成为了全球常见的疾病之一。我国根据地域不同人群 HUA 患病率在 8.4%-21.8%，以南方和沿海经济发达地区患病率居高。保守估计我国 HUA 患者人数已达 1.2 亿。已成为继高血压、高血脂、高血糖之后的临床“第四高”。

传统观念的高尿酸血症相关肾损害包括三种类型：（1）严重高尿酸血症和（或）高尿酸尿症阻塞肾小管导致急性肾损伤；（2）多年反复引起痛风的严重高尿酸血症导致慢性高尿酸血症性肾病（痛风肾病）；（3）高尿酸尿症导致泌尿系结石。认为不引起痛风的轻到中等程度血尿酸增高不具有致病作用，因此在临床上高尿酸血症通常被认为是肾衰竭的标志，而不是慢性肾脏疾病（Chronic kidney disease，CKD）进展的危险因素。

新近的研究显示，HUA 的病理意义远远超过了痛风和尿酸盐结石的范畴。除了一小部分高尿酸血症患者发生痛风（2% 左右），HUA 是急性肾损伤、慢性肾病、心血管疾病、2 型糖尿病等疾病发生的独立危险因素。随着尿酸增高，慢性肾病（CKD）患病率显著增加。HUA 患者尿毒症的发生危险分别增加 4 倍（男性）和 9 倍（女性）。透析患者中高尿酸血症与病人全因死亡率和心血管疾病密切相关。

高尿酸血症的肾脏毒性作用表现为肾血管收缩、球内高压以及肾小管间质损伤，最终导致肾小球硬化。目前认为 RAS 及环氧合酶 2(COX-2) 系统的激活、内皮细胞功能异常以及尿酸对血管平滑肌细胞 (VSMC) 和内皮细胞的直接作用在高尿酸血症所致肾脏损伤中起着重要作用。

目前高尿酸血症导致肾损伤的研究瓶颈在于：没有预测 HUA 导致肾脏靶器官损伤的风险因子；临床 HUA 诊断指标单一，缺乏遗传学指标参与，何时干预 HUA 能够保护肾脏损伤，缺乏诊断标准和治疗时机。目前，作为精准医疗关键技术—高通量组学检测技术已趋成熟，我国组学技术水平已居国际领先地位。因此，整合基因组、表观遗传组、蛋白质组、代谢组等信息建立多组学功能扰动网络，通过病例对照研究和前瞻性队列研究，寻找高尿酸血症出现肾脏器官损伤预警标志物；建立基于多组学特征的 HUA 分子分型标准，建立 HUA 精准治疗特征组学谱，制定个体化诊疗方案是未来研究的方向。新近发现的肾脏尿酸转运蛋白 URAT1、MRP4、OAT1、OAT3 等，有可能成为将来药物研制的新靶点。

CS-063

高尿酸血症与心血管疾病的研究进展

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张抒扬，教授，博士后，主任医师。北京协和医院副院长兼中国医学科院北京协和医学院副院校长，北京协和医院药理研究中心主任，转化医学研究中心副主任。

临床上擅长内科及心血管系统常见病、疑难杂症及危重病症的诊断与处理，尤其擅长多重危险因素的综合管理与冠心病的介入诊断与治疗。因临床效果好，深受患者信赖。

研究方向：致力于冠心病、以及各种疾病引起的血管损害的基础与临床研究，积极领衔与参与国家级与省部级研究项目（涉及早发冠心病，冠脉扩张症、血管炎对心血管损害，肠道微生物与冠心病关系等问题相关研究），牵头十三五精准医学研究规划罕见病队列研究。此外，八十年代起参与多项国际多中心药物临床试验，目前牵头和参与多项国内多中心药物临床研究项目。

社会兼职：中华医学会常务理事，中华医学会内科学分会副主任委员、中华医学会临床药学分会副主任委员、北京医学会临床药学分会主任委员、中华医学会心血管病分会委员、中国高血压联盟常务理事等多项专业学会职务，多年来担任《中华内科杂志》、《中华心血管病杂志等》十余种杂志编委。是国家卫生计生委公益性行业专项基金首席专家，国家十三五精准医学研究发展规划中罕见病队列研究的首席专家。

流行病学资料显示我国高尿酸血症患病率逐渐升高，目前已经超过 10%，已经成为危害中国居民健康的另一常见疾病。目前多个学会已经出台相应的专家共识以提高大家对高尿酸血症的认识及治疗的规范性。

18 个前瞻性队列研究 Meta 分析显示血尿酸每升高 1mg/dl，高血压发病风险增加 13%。动物研究表明药物诱导尿酸升高的同时血压也随之升高，而使用降尿酸药物后血压也随尿酸下降。此外发表在 JAMA 杂志上的随机双盲交叉组研究表明对于合并高尿酸血症的高血压患者，在不使用降压药的情况下，单纯降低尿酸后其血压水平可以明显下降。这些证据提示高尿酸与高血压之间存在因果关系。Dehghand 等对 4,536 例基线非糖尿病患者长达 10.1 年的随访发现，高尿酸血症是糖尿病发生的一个强大而独立的危险因素，11 个前瞻性队列研究 Meta 分析显示血尿酸每升高 1mg/dl，高血压发病风险增加 17%。美国第三次全国健康和营养调查（1988-1994）研究显示随着血尿酸（SUA）升高，代谢综合征发生率明显增加，其机制可能与尿酸可以通过抑制胰岛素信号通路传导而诱发胰岛素抵抗有关。

一个纳入 26 个研究共 402，997 例患者的荟萃分析显示高尿酸血症与冠心病及其死亡相关，是冠心病的独立危险因素。而尿酸降低后可以有效改善冠心病患者的心绞痛症状，进一步研究表明尿酸水平与冠状动脉血流相关。同时高尿酸血症不仅增加心力衰竭的发病风险，还增加心力衰竭患者的心血管及全因死亡的风险。在脑卒中方面的研究也表明，尿酸的水平的与卒中的严重程度呈正相关关系。

别嘌呤醇作为降低尿酸一线用药，可能存在心脏保护作用。早期研究表明其具有改善内皮功能，左心室肥厚，动脉坚硬度及颈动脉内膜中层厚度的作用。2015 年发表的两个大型病例对照研究证实别嘌呤醇具有降低心肌梗死的风险，且使用时间越长获益越大。但新近两个随机对照研究结论并不一致，113 例 CKD 患者随机接受别嘌呤醇 100mg/d 或安慰剂，2 年随访结果表明，别嘌呤醇在降低尿酸、改善肾功能的同时，有效的降低心血管事件。然而，253 例 CHF 随机接受别嘌呤醇 600mg/d 或安慰剂，随访 24 周后发现，与安慰剂相比，别嘌呤醇并不能改善 CHF 患者心功能。

总之，高尿酸血症与高血压、糖尿病、代谢综合征密切相关，同时也是心血管疾病的独立危险因素，尿酸有望成为未来心血管疾病的干预靶点。

CS-064

辩论：痛风石的处理内科治疗还是外科治疗好

陈海冰

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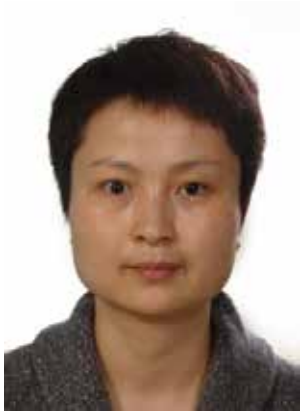

陈海冰，女，博士，主任医师，上海交通大学博士生导师。现任上海市第六人民医院内分泌科行政副主任，中华医学会上海分会内分泌学会委员，是中华医学会内分泌学会高尿酸血症学组委员，海协会痛风学组常务委员，是“教育部新世纪人才计划”“浦江人才计划”“上海交通大学晨星学者奖励A类计划”获得者。近年来主要聚焦在痛风/高尿酸血症、糖尿病慢性并发症糖尿病肾病的基础及临床诊治。近年来作为课题负责人承担的科研项目主要有：主持国家自然科学基金面上项目两项、欧洲糖尿病基金会资助项目一项、参与973重大专项1项。获华夏医学科技奖一等奖（第3完成人），教育部科技进步奖二等奖一项（第四完成人），中华医学科技奖三等奖（第3完成人），明治乳业生命科学奖（第一完成人），上海市卫生系统“银蛇奖”提名奖。以第一作者和通讯作者发表SCI收录期刊20篇，累计IF80.138。

摘要暂无

CS-065

辩论：痛风石的处理内科治疗还是外科治疗好

成志锋

哈尔滨医科大学附属第四医院

成志锋，中华医学会内分泌专业委员会高尿酸血症组委员，海峡两岸医药交流协会风湿免疫病分会痛风学组常务委员，中国慢性病基金促进会管理委员会委员，中国老年保健医学研究会老年骨质疏松分会委员，中国医师协会创伤外科医师分会创面治疗医师专业委员会委员，国际血管联盟中国糖尿病足学会，黑龙江省分会副主任委员，中华医学会内分泌学分会第六届青年委员会青年委员，中国微循环学会糖尿病与微循环专业委员会常务委员，黑龙江省医学会高尿酸血症与痛风专业委员会主任委员，黑龙江省内分泌专业委员会副主任委员，黑龙江省糖尿病专业委员会副主任委员，黑龙江省医师协会内分泌代谢科专业委员会副主任委员，黑龙江省骨质疏松专业委员会副主任委员，发表SCI论文10余篇，国家级论文30余篇，撰写胰岛素泵规范应用教程1部。承担国家级（973计划前期研究专项子课题）、省级、市级课题20余项。获省科学技术三等奖二项、省中医管理局中医药科学技术进步一等奖一项、黑龙江省医疗新技术一等奖一项、黑龙江省医疗新技术二等奖二项。多次被评为黑龙江省先进女职工，校优秀教师，院优秀教师，院十佳教师。

痛风石是由于尿酸盐多次在关节、软组织等处沉积，使单核细胞、组织细胞、白细胞聚集在受损关节处产生的慢性异物样反应。大多在痛风病史10年以上出现。痛风石形成的典型部位在耳廓，也常见于足趾、手指、腕、踝、肘等关节。有研究表明在人体正常温度下，尿酸盐在体内的溶解度随着身体温度的升高而增大，因此痛风石易在皮肤温度较低的外周关节形成。少数患者在机体的隐匿部位，如脊柱、肩胛骨、肋骨，也可形成痛风石，对少见部位痛风石的确诊，对于提高痛风的诊断率和治疗效果是有重要意义的。痛风石数量多、体积大会破坏关节、影响肢体的正常功能，甚至出现强直等严重后果。治疗：1) 碱化尿液：碱化尿液有利于尿酸盐的溶解和排泄，尤其对于预防尿酸性肾结石和痛风性肾病具有重要意义。这包括多吃碱性食物

和合理应用碱性药物，但这一点常常不被人们所重视。(2) 降尿酸药物的治疗 : 降尿酸药物治疗是有指征的，一般认为，降尿酸药在下列情况下应用：每年发作 2-3 次以上的急性痛风性关节炎，有痛风石、肾损害表现，或经饮食控制血尿酸仍显著升高者。(3) 手术疗法 : 如果痛风石不大，不影响脏器功能，不必手术治疗，因为手术切除痛风石并不能根治本病，只有在下列情况下才手术治疗：痛风石影响关节功能或压迫神经；切除因尿酸盐侵蚀的坏死指 (趾) 或矫正畸形的关节；切除巨大的痛风石以减轻肾脏负担。手术宜在血尿酸正常后进行，为防止手术诱发急性痛风性关节炎，最好在术前、术后一周内服用非甾类抗炎药。

CS-066

肠道：代谢性疾病防治的新视角

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中华医学会内分泌学会常委兼基础学组组长、上海市医学会内分泌分会侯任主任委员兼基础学组组长、中华糖尿病协会副会长、上海市康复医学工程研究会常务理事、上海市糖尿病康复协会名誉主任委员、中国医师协会内分泌代谢科医师分会委员

《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中华器官移植杂志》、《中国糖尿病杂志》、《中国临床保健杂志》及《上海医学》杂志编委，《Journal of Diabetesandits Complications》、《Metabolism》、《Chinese Journalof Medicine》、《Diabetology& Metabolic Syndrome》、《国际内分泌代谢杂志》及《上海交通大学学报 (医学版)》等杂志特邀审稿人

2004 年获上海市杰出回国留学人员专项资金资助，已在国、内外发表学术论文 240 篇 (SCI40 篇)，参编专著或教材 12 部。2012 年获上海市医学科技二等奖，2014 获中华医学科技三等奖、华夏医学科技三等奖。2014 年获上海市第一人民医院院长奖

近年来研究显示肠道菌群的结构失衡，破坏肠屏障，导致机体慢性低度炎症状态，从而成为糖尿病等多种代谢性疾病发生的诱因。胃肠道是人体最大最复杂的内分泌器官，分泌超过 40 种激素。肠道激素是脑 - 肠 - 外周组织轴的信使。多种胃肠道激素参与糖脂代谢，调节食欲、食物分解与吸收、控制能量代谢及储存。肠道除作为体内最大的内分泌器官外，同时是体内细菌定植的主要场所，肠道定植的细菌数量巨大，具有多样化、复杂性和动态性的特点。人体肠道中存在着除人体自身以外的第二套基因组，即肠道菌群基因组。胃肠道微生态对人体非常重要，肠道菌群与宿主处于共生的状态，肠道菌群对宿主发挥增强肠道屏障功能、参与营养吸收及代谢、延缓衰老、和抗肿瘤作用。

通过一套以肠道菌群为靶点的糖尿病营养治疗方案，系统评估以肠道菌群为靶点的糖尿病营养治疗方案的疗效与可行性。研究患者肠道菌群得到改善后，糖尿病及其并发症是否可以得到缓解，并进一步论证肠道菌群在 2 型糖尿病发生发展中的地位和作用。进一步研究有害的肠道菌群作为糖尿病发病原因的可能性。

分析干预过程中肠道菌群结构、宿主代谢和炎症指标的特征性变化规律，探讨肠道菌群结构与 2 型糖尿病的关系；研究治疗过程中，肠道菌群功能基因及代谢路径与宿主糖脂代谢状况的关系，探讨肠道菌群参与宿主膳食代谢的机制，肠道菌群机构参与调控胃肠肽、脑肠肽、肠道通透性和脑 - 肠 - 胰岛轴生物学作用。

肠道菌群结构失调在糖尿病和代谢综合征等慢性炎症性疾病的发生、发展中具有十分重要的作用。肠道是 2 型糖尿病发病八重奏的重要一环，肠道激素、肠道菌群和肠道结构均参与糖脂代谢的诸多环节，肠道激素失衡能导致体重调节紊乱以及营养代谢异常。基于肠道的糖尿病治疗策略必将对防治糖尿病带来更多科学、有效的新方法。

CS-067

谱系重编程：胰岛 β 细胞再生的新策略

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洪天配，教授，主任医师，博士生导师。1991 年毕业于北京大学医学部，获医学博士学位。现任北京大学第三医院内分泌科主任兼检验科主任。担任中华医学会内分泌学分会副主任委员兼糖尿病学组组长、中国医师协会内分泌代谢科医师分会副会长、北京内分泌学会前任主任委员等。担任中华内分泌代谢杂志、中国糖尿病杂志、中国医学前沿杂志副主编、JCEM 中文版等期刊的副主编，Clin Diabetes Endocrinol、中华糖尿病杂志、中华医学杂志等多个期刊的编委，JCEM、DiabetesObes Metab 等多个 SCI 期刊的审稿专家。牵头制订中华人民共和国卫生行业标准《糖尿病筛查和诊断》。主要研究方向是糖尿病基础与临床研究、干细胞分化研究。先后负责过国家级和省部级科研课题 20 余项，包括国家自然科学基金 6 项、国家 973 计划项目 2 项、国家 863 计划项目 1 项等。在国内核心期刊上发表论文 200 余篇，在 TrendsEndocrinol Metab、Diabetologia、DiabetesObesMetab、Endocrinology、Am J Physiol Endocrinol Metab 等 SCI 期刊发表论文 40 余篇。

胰岛 β 细胞再生是重建胰岛功能的重要策略。目前 β 细胞再生的方案主要有三种：(1)将多潜能干细胞(包括胚胎干细胞和诱导性多潜能干细胞)或各种类型成体干细胞(如间充质干细胞、肝脏前体细胞等)在体外诱导分化为胰岛素产生细胞后进行移植，补充胰岛细胞数量；(2)促进成体干细胞(如胰腺干细胞等)在体内直接转分化为胰岛细胞，恢复 β 细胞总量；(3)将终末分化细胞(如成纤维细胞等)在体内或体外直接转化为 β 细胞。研究显示，胰腺本身具有较高的可塑性。胰腺导管细胞、腺泡细胞、胰腺内分泌其他类型细胞均可转化为 β 细胞，且 β 细胞也具有自我增殖、去分化和再分化的潜能。与胰岛有共同发育路径的肠道内分泌 K 和 L 细胞、肠道内分泌前体细胞、成熟肝细胞、肝前体细胞等在一定条件下可转化为胰岛 β 细胞。甚至与胰岛起源相距较远的中胚层来源的肌细胞、外胚层来源的成纤维细胞和神经细胞等也可以跨胚层直接转化为胰岛细胞。这些不同谱系之间的细胞类型转化称为谱系重编程。

谱系重编程在体内和体外均可完成。体外重编程易于基因操作和细胞表型鉴定，并可用于药物筛选。体内重编程可避免免疫排斥，而且体内微环境有助于重编程细胞的进一步成熟。然而，在临床应用前必须考虑其脱靶效应和潜在的副作用。诱导谱系重编程主要有如下几种策略。细胞表型受复杂的、网络状的转录因子的调控，因此通过过表达胰岛发育相关的重要转录因子或 β 细胞成熟特异性的因子，敲除或抑制原有细胞的转录因子均可将原有细胞转化为胰岛 β 细胞。另外，转录因子和表观遗传修饰的相互作用对于维持细胞表型至关重要。因此，通过调控表观遗传(如组蛋白去乙酰化、DNA 甲基化、miRNA 等)也有助于细胞类型的相互转化。值得注意的是，小分子物质近年来也被用来调控谱系重编程。小分子化合物价格低廉、容易合成、重编程的过程容易掌控、批间差异小、能够大规模操作，因此可能是谱系重编程未来的一个重要发展方向。

CS-068

体脂分布与糖尿病

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李小英，男，博士生导师。复旦大学附属中山医院内分泌科主任，主任医师、教授；上海市优秀学科带头人。兼中华医学会糖尿病学分会常委，上海市糖尿病学会候任主委。《JournalofDiabetes》杂志副主编，《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中国糖尿病杂志》编委。1983年毕业于衡阳医学院，获学士学位；1987年毕业于第三军医大学，获硕士学位；1996年毕业于上海第二医科大学，获博士学位。1998–2003年先后在美国Baylor医学院、加拿大McGill大学和UBC大学做博士后研究。主要从事代谢性疾病发病机制和性发育障碍临床研究。在 Cell Metabolism，JCI，Diabetes,Gastroenterology,Gut,JCEM,Development，Journalof Hepatology,Cancer Research 等杂志发表论文88篇，撰写专著3部。

肥胖是糖尿病发生的一个十分重要的危险因素。这些年，随着肥胖发病率增加，糖尿病的发病率显著增加。然而，皮下脂肪、内脏脂肪、肝内脂肪与糖尿病的关系十分复杂。我们通过对社区人群观察，发现全身性肥胖患者的2型糖尿病患病风险是非全身性肥胖患者的2.11倍（95%CI:1.85 – 2.40）。进一步校正腰围以后，风险程度降低明显，为1.43（95%CI:1.24 – 1.66）。校正脂肪肝患病情况，结果和校正腰围相似，风险程度降低更为明显，为1.21（95%CI:1.05 – 1.40）。进一步发现，中心性肥胖患者的2型糖尿病患病风险是非中心性肥胖患者的2.37倍（95%CI:2.10 – 2.67）。进一步校正BMI以后，风险程度略下降，为2.05（95%CI:1.79 – 2.35）。校正脂肪肝患病情况，风险程度降低较为明显，为1.41（95%CI:1.24 – 1.62）。脂肪肝患者的2型糖尿病患病风险是非脂肪肝患者的3.89倍（95%CI:3.46 – 4.37）。 进一步校正BMI或腰围以后，风险程度未见明显下降，分别为3.66（95%CI:3.23 – 4.15），3.36（95%CI:2.95 – 3.82）。

按照全身体脂含量分层，发现随着体脂含量增加，空腹血糖上升不明显（P for trend = 0.30），而餐后2小时血糖呈现显著的上升趋势（P for trend = 0.02）。随着皮下脂肪面积的增加，空腹血糖（P for trend = 0.08）和餐后2小时血糖（P for trend = 0.60）均未呈现明显的上升或是下降趋势。然而，随着内脏脂肪面积的增加，空腹血糖和餐后2小时血糖均呈现明显的上升趋势 (P both ≤ 0.001)。随着肝脏脂肪含量增加，空腹血糖和餐后2小时血糖均呈现明显的上升趋势（P for trend < 0.001）。总之，内脏脂肪面积和肝脏脂肪含量和血糖、胰岛素抵抗密切相关。而皮下脂肪和血糖、胰岛素抵抗的相关性并不显著。

CS-069

胰岛细胞功能和容量的在体评估和调控

王琛

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王琛，医学博士，教授，上海交通大学医学院博士生导师。现任上海交通大学糖尿病研究所副所长，上海市糖尿病重点实验室副主任。中华医学会内分泌分会基础转化组委员、中华医学会糖尿病分会再生学组副组长、中国胰岛素分泌小组副组长、中华医学会上海糖尿病分会委员。

从事内分泌代谢专业的医疗、科研及教学工作。研究方向：糖尿病细胞治疗，β 细胞功能及糖尿病发病的基础和临床等方面研究。在国内外刊物上发表相关科学论文多篇，其中SCI收录30余篇。主持并参与多项科研基金项目，曾获国家科技成果奖，以及2016年中国胰岛素分泌小组研究成就奖。

胰岛素抵抗和胰岛 β 细胞功能障碍和 / 或容量减少是 2 型糖尿病发病的重要病理生理机制。其中，胰岛 β 细胞功能障碍和 / 或容量减少，导致胰岛素分泌不能满足机体需求是糖尿病发病的核心环节，是糖尿病发生和发展的重要因素。研究显示，2 型糖尿病患者在确诊时 β 细胞总量就减少达 50% 。胰岛 β 细胞数量 / 容量在疾病的演变过程中何时开始减少，随着疾病的进程如何发展，目前还远远不清。众所周知，糖尿病是终身性疾病，一旦出现糖代谢紊乱将难以逆转。因而迫切需要在出现血糖紊乱前，通过活体定量胰岛 β 细胞数量 / 容量，在其开始减少时就对疾病进行预警，从而达到挽救胰岛 β 细胞、阻止和逆转胰岛 β 细胞数量 / 容量的减少、阻断糖尿病的发生和发展的目的。测定胰岛细胞功能的方法包括细胞水平和整体水平的检测。细胞水平有细胞灌流，静态培养测定细胞对刺激物的胰岛素分泌反应；整体水平包括静脉葡萄糖耐量，高葡萄糖钳夹技术等，其中高葡萄糖钳夹技术是测定胰岛细胞功能的金指标。然而，目前还没有敏感性和特异性高、在整体水平上测定细胞数量 / 容积的方法。以往相关数据是通过尸体胰腺组织的组织学分析得到，由于死后组织的自溶等影响，因此也缺乏有关各种糖尿病发生发展过程中胰岛细胞数量 / 容积的数据资料。上海交通大学附属第六人民医院内分泌代谢科、上海市糖尿病研究所针对胰岛 β 细胞容量及其调控作用方面进行了探讨，研究结果将为大家做一介绍。

CS-070

桥本甲亢的诊断与鉴别

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李玉姝，中国医科大学附属第一医院内分泌科教授、主任医师、博士研究生导师，辽宁省特聘教授。现任亚大地区甲状腺学会会员、中华医学会骨质疏松和骨矿盐疾病分会青年委员、辽宁省医学会骨质疏松与骨矿盐疾病分会副主任委员、辽宁省中西医结合学会内分泌专业委员会副主任委员。先后两次留学日本京都大学医学部。主持和参加多项国家自然科学基金课题、国家“十五”科技攻关课题、863 计划项目等国家级课题。在国际及国内核心期刊发表论文 50 余篇。参与研究的成果获得国家科技进步二等奖、辽宁省科技进步一等奖、二等奖等多个奖项。

桥本甲亢（Hashitoxicosis）的概念由梅奥诊所的 Fatourechi V 等于 1971 年首次提出，指出患者具有 Graves 病甲状腺功能亢进的临床特征和桥本病（HT）的病理表型，是一种病理诊断：甲状腺组织内可见大量淋巴细胞、浆细胞、生发中心、嗜酸性变的 Hürther 细胞等 HT 的表现；并存局部滤泡细胞乳头状、高柱状增生等 Graves 病的表现。临床表现上最初的甲状腺功能亢进阶段几乎和 Graves 病无法区分，包括甲状腺放射性碘吸收率增加和促甲状腺素受体抗体的存在，同时存在高水平的甲状腺过氧化物酶抗体和 / 或甲状腺球蛋白抗体。然而，一般甲状腺功能亢进的症状相对较轻、且甲状功能亢进阶段比较短暂，突眼和胫前粘液水肿亦少见。桥本甲亢患者对抗甲状腺药物反应敏感，治疗过程中易出现甲状腺功能减退，多经过 3 - 24 个月会演变成永久性甲状腺功能减退。因此治疗时抗甲状腺药物宜小剂量起始，甲功检测宜频繁，药物调整宜及时。桥本甲亢应注意与桥本一过性甲状腺毒症相鉴别，后者也称为无痛性甲状腺炎或发生于产后一年内的产后甲状腺炎，甲状腺毒症为甲状腺滤泡细胞的炎症破坏所至，甲状腺吸碘率降低，核素扫描为低摄取，甲状腺过氧化物酶抗体和 / 或甲状腺球蛋白抗体阳性，甲状腺毒症阶段短暂，随后进入甲状腺功能减退阶段，然后甲功恢复正常，也有部分患者遗留永久甲减，甲状腺毒症阶段应避免给予抗甲药物。

CS-071

迁延不愈的亚急性甲状腺炎的处理

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1998 年毕业于解放军军医进修学院获博士学位，师从于潘长玉教授一直致力于糖尿病和内分泌疾病的临床工作。

2004.11－2006.6 美国南伊利诺伊大学医学院访问学者。

中华医学会内分泌学分会委员、《中华内分泌代谢杂志》编委。

亚急性甲状腺炎（subacute thyroiditis），又称为亚急性肉芽肿性甲状腺炎、巨细胞甲状腺炎、移行性甲状腺炎及 De Quervain 甲状腺炎等。本病呈自限性，女性更多见，是最常见的甲状腺疼痛疾病，多由甲状腺的病毒感染引起。亚急性甲状腺炎的发病率约为 4.9/10 万 / 年，占甲状腺疾病的 0.5%~6.2%。

亚急性甲状腺炎发病时可出现上呼吸道感染前驱症状及体征，体温可呈现不同程度增高，一般发病 3~4 天达峰。此外，常伴有甲状腺区疼痛性结节，疼痛表现为游走性疼痛或放射痛。甲状腺肿大常为弥漫性、不对称性，以一叶为著。实验室检查可见血沉早期增快、甲状腺功能与碘摄取率双向分离、早期可见白细胞增高。就病理表现而言，早期典型细胞学涂片可见多核巨细胞、片状上皮样细胞及不同程度炎性细胞，晚期则往往见不到典型表现。

亚急性甲状腺炎的治疗可分为一般治疗、特殊治疗以及针对甲亢及甲减的治疗。一般治疗强调加强日常护理、注意休息及避免劳累。就亚急性甲状腺炎而言，治疗目的决定了治疗方案的选择，早期治疗以减轻炎症及缓解疼痛为目的。解热镇痛药及糖皮质激素均可有效缓解症状及体征，但不影响疾病自然进程。前者适用于轻症患者，疗程一般 2-4 周左右；后者适用于疼痛剧烈、体温持续显著升高、水杨酸或其他非甾体类消炎药治疗无效者，可迅速缓解疼痛，减轻甲状腺毒症症状，一般在症状控制后 1~2 周后可根据症状、体征及血沉变化情况逐渐减量，总疗程为 6~8 周以上，应用时不可频繁改变剂量、过快减量、过早停药及长期使用。约 10-20% 的亚急性甲状腺炎经过正规治疗后仍可复发，对于糖皮质激素治疗期间停药或减量过程中出现反复者即迁延不愈者，仍可使用糖皮质激素并获得较好效果。研究发现复发组与治愈组的临床特点和实验室检查没有显著差异，尽管两组激素起始剂量没有差异，但复发组减量更快、维持时间更短。此外，有研究显示中药也可有效缓解迁延不愈亚急性甲状腺炎患者的症状及体征，减少复发率，避免长期使用激素的副作用。针对迁延不愈的亚甲炎患者，需要强调的是在逐渐减少激素用量时应联合小剂量非甾体类消炎药，避免或缓解减药过程中患者的不适感及担心复发所导致的焦虑感；同时，还应根据患者的病情特点灵活调整给药时间，以便更好地对症治疗并缓解症状。

CS-072

对 AITD 分型的再认识

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高莹，医学博士，北京大学第一医院内分泌科工作，主任医师，教授，博士研究生导师，中华医学会内分泌学分会青年委员会委员，甲状腺学组及基础内分泌学组成员，北京医学会内分泌学分会青年委员会副主任委员。研究方向为自身免疫甲状腺疾病。多次获得国家及北京市自然基金资助，已发表中英文论文 50 余篇，曾获得“华夏内分泌大会青年研究者奖”，”北京大学黄廷芳 / 信和青年杰出学者奖“，参与的研究项目获得中华医学科技奖三等奖及教育部高等学校科学研究优秀成果奖（科学技术）自然科学奖一等奖，并入选了北京大学医学部“青年学

者”奖励计划，北京市“科技新星”及教育部“新世纪优秀人才支持计划”。

自身免疫性甲状腺疾病（AITD）是一类器官特异性自身免疫性疾病，包括 Graves 病、桥本甲状腺炎（HT）等。IgG4 相关性疾病（IgG4-RD）是一组以密集的淋巴细胞、浆细胞浸润，IgG4 阳性浆细胞比例明显升高，席轮状纤维化及部分病人血清 IgG4 水平升高为特点的慢性纤维炎性疾病。基于一部分 HT 患者具有与 IgG4-RD 极为相似的病理学特征，如弥漫性淋巴细胞、浆细胞浸润以及间质纤维化，2009 年 Li 等依据甲状腺组织病理切片中 IgG4 及 IgG 免疫组化染色结果将 HT 分为 IgG4 阳性及 IgG4 阴性 HT 两组。近年来上述分类方法得到多个研究组的证实。文献报道 IgG4 阳性 HT 的发生率约为 12.6%-42.4%。IgG4 阳性 HT 患者具有以下临床特征：男性比例更高；接受手术时年龄更轻；患病时间短；接受 L-T4 治疗量更大，更常表现为亚临床甲减；合并甲状腺乳头状癌（PTC）的发生率明显高于 IgG4 阴性 HT 患者，且合并 PTC 的预后比 IgG4 阴性 HT 合并者更差；而 IgG4 阳性 HT 患者血清 TgAb 和 TPOAb 水平高于 IgG4 阴性 HT 患者。因此该种分类方法可能有助于识别临床进展快的 HT 患者。

在 IgG4-RD 中，以血清 IgG4 水平 135mg/dL 作为分组依据，对诊断 IgG4-RD 有一定的帮助。在 AITD 中，近来研究者报道，以同样的血清 IgG4 标准作为分类指标，发现 IgG4 水平高于 135mg/dL 的 HT 组患者年龄更大，超声更容易发现增大的低回声区及纤维化征象，需要 L-T4 治疗的剂量也更大，即应用血清 IgG4 水平作为分组标准可能可以发现一部分病情进展较快、破坏性更强的 HT 类型，但这类 HT 是否与 IgG4 阳性 HT 相关仍有待进一步研究。此外，文献报道在大约 6.4% 的 Graves 病患者血清中也能够检测到异常升高的 IgG4 水平，同单纯的 Graves 病患者相比，合并 Graves 眼病的患者血清 IgG4 水平更高。但在 Graves 病患者术后的病理切片中，研究者发现仅 0.74% 的患者具有弥漫的淋巴细胞浸润，且并未发现显著的纤维化及闭塞性静脉炎等 IgG4-RD 或 IgG4 阳性甲状腺炎的组织病理学特点。

综上，IgG4 阳性 HT 及血清 IgG4 水平升高的 AITD 的临床意义仍有待进一步研究。

CS-073

亚临床甲减的干预治疗

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赵家军，1983 年毕业于泰山医学院，1994 年毕业于上海第二医科大学（现上海交通大学）获内分泌代谢病专业博士学位。现山东省立医院内分泌科主任医师、山东大学教授，博士生导师，泰山学者，山东省临床医学研究院内分泌代谢研究所所长。中华医学会内分泌分会候任主任委员，山东省糖尿病分会主任委员。全国优秀科技工作者；卫生部突出贡献中青年专家；全国卫生先进工作者；享受国务院政府特殊津贴；山东省突出贡献中青年专家；山东省“十大名医”；指导博士研究生 60 余名，博士后 7 名。主持科技部“十一五”国家科技支撑计划、973 子课题、国家自然科学基金等科研项目 20 余项。获国家科技进步二等奖 1 项，山东省科学技术最高奖，山东省自然科学一等奖 1 项，山东省科技进步一等奖 4 项。省部级二等奖 4 项。在国内外专业杂志发表论文 300 余篇，其中 130 余篇被 SCI 收录，总影响因子 500。

研究方向：内分泌与脂代谢的交互作用与影响

目的　亚临床甲状腺功能减退（简称亚甲减）在成年人中患病率持续增长，是导致血脂异常、非酒精性脂肪肝（non-alcoholic fatty liver disease，NAFLD）等代谢性疾病的重要危险因素。根据成人甲状腺功能减退症诊治指南，重度亚甲减（TSH ≥10 mIU/L）推荐给予左 - 甲状腺素替代治疗，而对于轻度亚甲减（TSH <10 mIU/L）是否需要治疗，目前尚存在争议。既往虽然有临床研究探索左 - 甲状腺素替代治疗能否改善轻度亚甲减患者的血脂谱，但是其样本量较小且研究结论不一致。而左 - 甲状腺素对亚甲减患者的 NAFLD 是否具有改善作用，目前尚无研究。本研究旨在探讨左 - 甲状腺素替代治疗对亚甲减患者的血脂谱及 NAFLD 的作用。

方法　本研究为一项开放性、随机、对照临床试验。经过两次甲功检测，共有 388 名亚甲减患者纳入研究。重度亚甲减患

者全部给予左 - 甲状腺素替代治疗；轻度亚甲减患者按照 1.5:1（干预组：对照组）的比例随机分配，干预组给予治疗，对照组不予治疗。研究的主要终点为血清总胆固醇（total cholesterol，TC）水平的变化；在治疗前不同 TSH 或 TC 水平的轻度亚甲减患者中对 TC 的变化进行亚组分析；对 NAFLD 的患病率变化进行事后分析。（临床试验注册号：NCT01848171）

结果 重度亚甲减患者治疗后血清 TC 下降 0.47 mmol/L；轻度亚甲减患者干预组 TC 下降 0.41 mmol/L（p<0.001），对照组 TC 下降 0.17 mmol/L（p=0.019），干预组较对照组下降更明显（p=0.012）。血清低密度脂蛋白胆固醇的变化趋势与 TC 一致。亚组分析结果显示，将研究人群按照治疗前 TSH 水平分层，所有给予左 - 甲状腺素替代治疗的患者 TC 均明显下降（所有 p<0.001）；而按照治疗前 TC 水平分层，所有给予治疗的患者亦均可获益。对 NAFLD 患病率的变化进行事后分析显示，重度亚甲减患者给予治疗后，NAFLD 的患病率由 48.5% 下降到 24.2%（p =0.041）；轻度亚甲减患者治疗后 NAFLD 患病率虽然无明显变化，但对于合并血脂异常的轻度亚甲减患者，给予治疗后 NAFLD 患病率明显下降（p =0.035）。

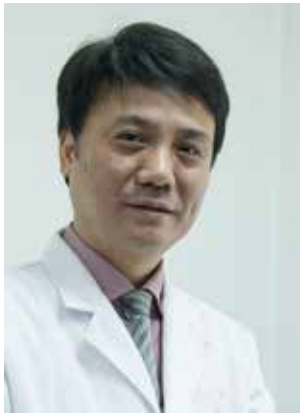
结论 左 - 甲状腺素替代治疗对亚甲减患者的血脂谱及 NAFLD 具有改善作用。在今后的研究中，我们将进一步观察左 - 甲状腺素替代治疗对心血管疾病发生及死亡的影响。

CS-074

自身免疫性甲状腺病的并发和伴发疾病

石勇铨

第二军医大学附属长征医院



石勇铨，医学博士，第二军医大学附属长征医院内分泌科主任，第二军医大学甲亢眼病诊治中心主任，主任医师，教授，博导。现任中华医学会糖尿病分会委员，中国医师协会内分泌学分会委员、胰腺病分会委员，中国老年保健医学研究会骨质疏松分会常委、老年内分泌学分会委员，上海市医学会内分泌学会副主任委员，上海市糖尿病康复协会主任委员，上海市中西医结合学会糖尿病学会常委，解放军医学会内分泌学会常委，《中国内科年鉴》内分泌专业主编。从事内分泌代谢病基础和临床研究工作 20 余年，获得国家级和省部级基金资助项目共 20 项，发表文章 100 余篇，主编和参编专著 10 余部。

自身免疫性甲状腺病 (autoimmune thyroid disease, AITD) 是由于自身免疫紊乱导致的甲状腺器官特异性疾病，包括 Graves’ 病（GD），慢性淋巴细胞性甲状腺炎，萎缩性甲状腺炎（AT），桥本甲状腺炎（HT），产后甲状腺炎（PPT）等。由于其发生机制是遗传因素、环境、内在因素共同作用导致的自身免疫监控缺陷，所以疾病常常累及甲状腺外的组织器官或伴有一些其他自身免疫疾病，且影响妊娠妇女健康和妊娠结局，肿瘤发生率亦显著升高。

常见的并发和伴发疾病主要有：甲亢眼病，GO 人群患病率 0.1% -0.3%，甲亢患者中发病率 20%，中青年多见，常与 Graves 病的发生相关。肾病综合征，甲状腺功能减低及抗体阳性人群易合并肾病综合征，研究表明甲状腺抗原介导的免疫复合物（TG-Ab、TPo-Ab）在肾脏沉积可引起肾损伤。AITD 相关糖皮质激素敏感性脑病，AITD 相关糖皮质激素敏感性脑病又称桥本脑病，平均发病年龄 44 岁，女性多见，男女比例 1：3.6-5.0。肌肉骨骼系统疾病，甲亢患者易发生骨骼系统病变，妊娠及生长发育异常，甲状腺功能及甲状腺抗体与妊娠及胎儿的生长发育密切相关；其他自身免疫性疾病，AITD 可以合并其他自身免疫疾病，包括乳糜泻、白癜风、A 型自身免疫性胃炎、风湿性关节炎、自身免疫性肝炎、干燥综合征、1 型糖尿病、系统性红斑狼疮、爱迪生病、结节病、原发性性腺机能减退、硬皮病、原发性甲状旁腺功能减退、重症肌无力、斑秃等。肿瘤的发生率升高，甲状腺乳头状癌及甲状腺外癌如子宫、乳腺、血液系统、直肠、肾脏、卵巢等器官恶性肿瘤发生率显著升高。

CS-075

甲状腺领域年度进展

刘超

江苏省中西医结合医院

刘超，中国中医科学院江苏分院，江苏省中医药研究院（南京中医药大学附属中西医结合医院）内分泌科，主任医师，2级教授，博士生导师、癭病证治国家重点实验室主任。

荣誉称号：

江苏省“333工程”和“江苏省六大人才高峰”培养对象、“江苏省医学重点人才”、“江苏省医学领军人才”、江苏省有突出贡献的中青年专家。

学术任职：

国际甲状腺大会（ITC）学术委员会理事、亚洲和大洋洲甲状腺学会（AOTA）委员，AOTA学术委员会主席、世界中医药学会联合会内分泌专业委员会副会长、中国中医药研究促进会内分泌分会副主任委员、中华医学会内分泌学分会常委、中华医学会内分泌学分会肝病与代谢学组组长、中华医学会内分泌学分会中西医结合学组副组长、中华医学会内分泌学分会中青年委员会主任委员、中国医师学会中西医结合学分会糖尿病专业委员会副主任委员、中国医师协会中西医结合医师分会内分泌代谢病学专家委员会副主任委员、中华医学会江苏内分泌学分会名誉（前任）主任委员、江苏省中西医结合学会内分泌专业委员会主任委员、江苏省糖尿病学分会副主任委员、江苏省中西医结合学会常务理事、江苏省健康产业协会副会长。

杂志编委：

现任《Hormone Metabolism Research》、《Journal of Diabetes》、《Nature Review Endocrinology》（中文版）、《Thyroid》（中文版）、《Journal of Clinical Endcrinology and Metabolism》（中文版）编委，《药品评价》副主编，《中国实用内科杂志》常务编委，《中华内分泌代谢杂志》、《中华糖尿病杂志》、《中国糖尿病杂志》等杂志编委。

论文和成果：

目前承担国家和省级基金项目十项。发表论文1000余篇，SCI引录论文48篇，主编和参编学术专著38部，获专利3项。

受多种因素的影响，甲状腺疾病已成为较为常见的临床疾病，其相关的基础与临床研究在过去几年之内增加极为显著。作者通过pubmed检索2015年7月1日至今的临床研究相关文献，以“thyroid”、“thyroid nodule”、“thyroid cancer”、“thyroid carcinoma”、“Graves’ disease”、“autoimmune thyroid diseases”、“Hashimoto’s thyroiditis”、“hypothyroidism”为关键词，并通过对杂志和文章质量进行筛选，以总结过去一年以来甲状腺领域较为重要、对临床具有指导意义的进展。

过去一年多里，多个国际国内学会和组织颁布了甲状腺相关的指南或专家共识。国际上出现了较多有影响力的指南，如美国甲状腺学会（ATA）颁布了《成人甲状腺结节与分化型甲状腺癌指南》、《儿童甲状腺结节和分化型甲状腺癌的管理指南》、《甲状腺髓样癌的管理指南（修订版）》、《淋巴结复发性/持续性的分化型甲状腺癌处理共识声明：手术治疗及主动监控利弊论述》、《甲状腺癌术前影像学声明》；美国临床内分泌医师学会（AACE）也推出了《甲状腺结节的诊断和管理指南》、《甲状腺功能异常病例发现的立场声明》；美国国家综合癌症网络（NCCN）也推出了《甲状腺癌指南》；欧洲甲状腺协会（ETA）和欧洲Graves眼病工作组（EUGOGO）联合推出了《Graves眼病的管理指南》，前者还推出了《内源性亚临床甲亢的诊断和治疗指南》；美国头颈学会（AHNS）推出了《甲状腺与甲状旁腺手术喉部检查的共识声明》、《分化型甲状腺癌局部外放射治疗的声明》。国内的中国抗癌协会甲状腺癌专业委员会（CATO）也推出了《甲状腺微小乳头状癌诊断与治疗专家共识》，中国临床肿瘤学会（CSCO）则推出《复发转移性分化型甲状腺癌诊治共识》，中国医师协会外科医师分会则推出了《甲状腺手术中甲状旁腺保护专家共识》。这些指南和专家共识的推出为临床医师在进行临床决策时提供了更多依据和指导。

尽管较有影响力的临床研究不多，但针对Graves病的一些新研究更多探讨了手术、同位素和高碘等治疗方式对Graves病和甲状腺相关性眼病的影响。自身免疫性甲状腺疾病（AITD）的发病机制依然值得关注，不少研究探讨了胚胎细胞微嵌合、IgG4相关性疾病、B细胞激活因子及其受体、调节性T细胞、氧化应激、维生素D和硒等与AITD之间的联系。同时，有部分高质量的研究关注了自身免疫性糖尿病和2型糖尿病与甲状腺疾病之间的相关性。当然，数量最多的文献仍是关注于甲状腺结节与肿瘤。从韩国乃至国际到国内的甲状腺结节和肿瘤的患病率“海啸”已经令人震惊。从良恶性甲状腺结节的临床特征、

超声对甲状腺结节的价值，到传统分子标志物的新认识、新分子标志物的诊断价值，从传统的 Bethesda 病理类型到新的病理亚型，从术前颈部淋巴结转移的早期发现到其对预后的影响，从髓样癌的分子标志物到其淋巴结转移的临床应对，从手术范围对甲状腺癌预后的影响到不同类型多激酶抑制剂的临床疗效，从桥本甲状腺炎对甲状腺肿瘤的合并存在到其对淋巴结转移的影响，各个领域和方向都有些诸多的临床进展。

CS-076

Graves 免疫学研究进展

王曙

上海交通大学医学院附属瑞金医院

王曙，上海交通大学医学院附属瑞金医院内分泌科主任医师，博士生导师。从事内分泌及代谢性疾病临床和研究工作 20 余年，长期致力于甲状腺疾病的研究。目前担任中华医学会内分泌学分会甲状腺学组委员；亚洲 & 大洋洲甲状腺协会（AOTA）会员；中华内分泌代谢杂志编委；内科理论与实践杂志编委，中国研究型医院学会甲状腺疾病专业委员会委员。

Graves’ 病的发病机制尚未完全阐明。环境因素、遗传易感性及免疫因素等多因素共同参与致病的器官特异性自身免疫性疾病。上世纪 60 年代长效甲状腺刺激因子（LATS）首次发现以来，目前较明确的是 Graves’ 病的病因是机体产生了针对甲状腺上皮细胞表面 TSH 受体抗体（TRAb）。诸多研究致力于探索 TRAb 产生机制以揭示 Graves’ 病的具体发病机制。机体免疫反应的第一道防线是固有免疫。外源性抗原（细菌、病毒及环境干扰物等）导致甲状腺细胞损伤，使得甲状腺自身抗原释放，此时固有免疫细胞如树突状细胞（DC）、巨噬细胞等激活并分泌大量的细胞因子，进一步激活 T/B 细胞，从而开启适应性免疫。研究显示 Graves’ 病患者的外周单核白细胞中，浆细胞样的 DC 细胞亚群比例增加。$CD4^+$T 淋巴细胞是 Graves’ 病免疫紊乱的重要参与者，Naive $CD4^+$T 细胞可分化为 Th1、Th2、Th17、Treg、Th22 以及 Th19 等多个亚群。在 GD 早期，以 Th1 介导的细胞免疫为主，Th1 细胞激活后可产生和分泌 IFN-γ，而后期以 Th2 细胞介导的体液免疫为主，产生 TRAb 释放入血。研究提示 Th17 及 Th22 也可能参与了 Graves’ 病的发病。在甲状腺局部可见以 $CD4^+$T 淋巴细胞为主的多种淋巴细胞的浸润，使得 TRAb 持续产生。而 IFN-α/IFN-γ 等细胞因子可直接作用于甲状腺细胞表面，促进 MHC-Ⅱ类分子的表达，IFN-γ 可促进甲状腺细胞分泌 CXCL9、CXCL10、CXCL11 等趋化因子放大免疫反应。越来越多的证据显示甲状腺细胞有可能直接参与 TRAb 的产生。Graves’ 病患者机体免疫耐受的丢失是近年来研究者关注的重点。研究显示，携带 TSHR 易感基因患者的胸腺 TSHR 表达水平明显下调，从而针对自身抗原 TSHR 的自反应 T 细胞发生中枢免疫逃逸。进一步研究提示在 IFN-α 的作用下携带 TSHR 易感基因的人群更易发生 Graves’ 病。胸腺免疫耐受障碍为 Graves’ 病发病机制的研究提供了新的视角。

CS-077

亚临床甲亢的诊治

童南伟

四川大学华西医院

童南伟，四川大学华西医院内分泌代谢科教授、博士生导师、科主任。现任中华医学会内分泌学分会常委，中国医师协会内分泌代谢科医师分会常委。国家卫计委合理用药专家委员会内分泌与代谢药物专业组专家。四川省医学会内分泌暨糖尿病专委会前任及候任主委。四川省医师协会内分泌代谢科医师专科分会会长。四川省糖尿病防治协会副会长。

欧洲甲状腺学会（ETA）发布了最新的内源性亚临床甲亢的指南，美国内分泌医师协会（AACE）也颁布了发现甲状腺功能异常人群的声明。两者是否观点相同？中国医生如何面对这些问题？本报告希望回答这些也许大家有兴趣的问题。

CS-078

Graves 眼病的诊治进展

沈洁

南方医科大学第三附属医院

沈洁，现任南方医科大学第三附属医院副院长、内分泌代谢科科室主任，主任医师，教授，博士生导师。广东省医学会内分泌分会副主任委员、广东药学会内分泌代谢用药专业委员会常务副主任委员，亚太区甲状腺协作组成员、中华医学会内分泌代谢分会甲状腺学组委员，中华医学科技奖评委、中华医学会“糖尿病教育单位认证项目评审”专家;《Thyroid》中文版等多部期刊编委。从事本专业临床、教研工作近 30 年，主持省级各类科研课题项目 10 余项，发表论文 120 余篇，获得省级科技进步奖 2 项，获得军队医疗成果奖 1 项。

Graves 眼病 (Graves ophthalmopathy GO) 是常见的眼眶疾病，在国内外成年人眼眶疾病中发病率均为第一位，通常认为它是一种与甲状腺疾病相关的器官特异性的自身免疫性疾病。但目前认为眼眶成纤维细胞可能是主要的效应细胞，其表面高表达 TSHR 和 IGF-1R 等自身抗原，自身抗体与之结合可引起脂肪合成、透明质酸形成、趋化因子产生等改变。既往研究表明患者病程可分为症状快速进展的活动期和症状缓慢消退的稳定期，进一步的研究发现在活动期进行免疫抑制、球后放射等治疗效果较好，稳定期则效果差，因此在临床上正确判断疾病的严重性和活动性是决定患者是否需要治疗的两项重要指标。目前较常用的是临床活动评分 (CAS)，但存在主观性，缺乏量化的不足。MRI 是继 CT 之后又一项新的影像诊断技术，可以较好的反映眼眶组织的水肿和炎症状态等病理信息，本团队既往研究提示眼外肌信号强度比值、眼外肌增大比值、球内侧脂肪厚度等均与疾病活动度相关，是判断疾病活动性的可靠的量化指标。既往国内外对于疾病活动期的判定主要集中在眼外肌病变上，但近年来球后脂肪增生也成为研究热点。其次血清和泪液相关细胞因子也有助于判断疾病的活动性。大量的基础研究中证实，血清 Th1、Th2、Th17 型细胞因子在一定程度可能作为 TAO 活动性判断指标，细胞因子表达的强弱可能决定着 TAO 的发展方向。目前采取的治疗方案主要有激素冲击治疗、球后放疗、手术治疗、免疫抑制治疗等。2016 年 ETA 联合 EUGOGO 发布 GO 病管理指南，其中指出对于活动性中重度患者首选大剂量静脉激素治疗，其中大部分患者推荐中等剂量（累积剂量 4.5g）的甲基泼尼松龙周脉冲治疗。对于静脉激素

治疗不敏感患者可联合眶内放射治疗或联合免疫抑制剂治疗。本团队率先在国内开展直线加速器治疗甲亢恶性突眼，球后放射治疗有效率高达 76.23%。近年来细胞因子活性抑制剂 , 如 TNF-α 阻滞剂英夫利昔单抗及 IL-1 受体阻滞剂 ; 阻断 T 淋巴细胞共刺激信号因子 , 如细胞毒性 T 淋巴细胞相关抗原 4-Ig;B 淋巴细胞缺失因子 , 如抗 CD20 单克隆抗体利妥昔单抗 (Rituximab); 阻断 TSHR 或 IGF1-R, 如生长抑素类似物奥曲肽、SOM230；PPA R γ 拮抗剂（抑制眶内脂肪分化的作用），如双酚丙烷二环氧丙醚和 GW9662 等新型靶向治疗策略对于治疗 TAO 带来新的希望，但仍需行多中心随机对照的治疗试验研究证实其效力。

CS-079

^{131}I 治疗甲亢的优势

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目的　交流 40 多年用 ^{131}I 治疗难治性重度甲亢的经验，讨论 ^{131}I 在治疗甲亢中的地位。

方法　根据拟定的诊断和疗效判定标准，按照“综合、个体化和尽早用 ^{131}I 治疗”的原则，不用 ATD 预治疗，只用 ^{131}I 治疗难治性重度甲亢病人并做 1 年 ~ 23 年 (平均 4.2 ± 3.3 年) 随访，判定 ^{131}I 治疗的安全性和远期疗效。

结果　1.1975 年 ~ 2014 年，用 ^{131}I 治疗难治性重度甲亢 791 例，随访 615 例 (随访率 77.8%)，根据病情特点分为 7 组：①单纯甲状腺激素 (TH) > 正常上限 3 倍 58 例；②甲亢合并心脏病 196 例；③甲亢合并肝功重度异常 39 例；④甲亢合并大甲状腺肿 116 例；⑤甲亢合并巨大甲状腺肿 128 例；⑥甲亢合并重度血细胞减少 45 例；⑦甲亢合并 PTU 小血管炎肾炎、慢性肾功不全、控制不好的 DM 等 33 例。治愈 519 例 (含甲减 297 例)，总治愈率 84.4%，甲减发生率 48.3%。2. 同期用 ^{131}I 治疗甲亢 13 896 例 (含难治性重度甲亢 791 例)，没有 1 例在 ^{131}I 治疗后出现甲亢症状明显加重现象。观察了 39 例在 ^{131}I 治疗后血中 TH 水平，结果：+3d TH 水平开始下降 ($P > 0.05$)，+5d TT3、TT4、FT3、FT4 分别下降 24.6%、10.54%、23.15%、12.91% ($P < 0.01$)。如果在 ^{131}I 治疗前后短期加用碳酸锂，TH 下降变化更明显。3. 甲亢心脏功能和结构病变，及时用 ^{131}I 治疗后，都可以恢复正常。4.^{131}I 的治疗活度和疗效密切相关，大至 200 μ Ci ~ 300 μ Ci/g 甲状腺、1 次总活度达到 2 960MBq (80mCi) 是安全的。5.^{131}I治疗后重度黄疸在 3 ~ 4 个月内消失，甲功恢复正常。6.^{131}I治疗重度甲亢同时合并巨大甲状腺肿 (含胸骨后甲状腺肿)、房颤等多器官损害时，有独特的优势，可以安全地代替手术治疗。7. 本组 31 名病人生育了 33 名健康婴儿。8.2016 年美国发表了我们的 2 篇论著，结论分别为：①不用 ATD 预治疗，用 ^{131}I 治疗重度甲亢合并重度黄疸安全有效，应尽早用 ^{131}I 治疗这样的病人 (Endocr Pract. 2016Feb;22(2): 173-9)；②不用 ATD 预治疗，只用 ^{131}I 治疗难治性重度甲亢安全有效，对这些病人应优先用 ^{131}I 治疗 (Exp Biol Med.2016 Feb;241 (3): 290)。这是国外首次发表这样的论著。

结论　^{131}I 治疗难治性重度甲亢有不可替代的优势地位，是唯一可能挽救某些病人生命的治疗措施。

CS-080

肾上腺库欣的内科治疗进展

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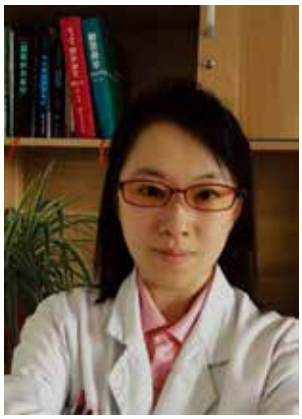

周薇薇，上海市内分泌代谢病临床医学中心，上海交通大学医学院附属瑞金医院内分泌代谢科，主治医师，医学博士。主要从事垂体及肾上腺疾病的临床和基础研究，参与编撰《临床内分泌学》、《糖尿病学》等多本书籍，获得专利一项。目前承担持国家自然科学基金、中华医学会等多项课题。

肾上腺库欣综合征由肾上腺肿瘤或者增生自主分泌皮质醇过多所引起，称为 ACTH 非依赖性库欣综合征。以肾上腺皮质腺瘤多见（占库欣综合征 10-20%），其次为肾上腺皮质癌，而原发性双侧大结节样肾上腺增生和原发性色素沉着结节性肾上腺皮质病罕见。肾上腺库欣综合征的首选治疗方式为手术治疗，但在临床中对合并严重并发症无法接受手术或通过手术不能获得治愈的患者，往往需要药物治疗来控制高皮质醇血症。近来用于降低高皮质醇血症的药物靶点主要分为三类，通过抑制肾上腺糖皮质激素的合成和分泌、阻断外周糖皮质激素的效应和控制下丘脑 - 垂体的 ACTH 合成和分泌来发挥作用。与肾上腺库欣综合征相关的内科治疗包括以肾上腺为靶点的药物和以外周靶器官糖皮质激素受体为靶点的药物。前者通过抑制肾上腺类固醇激素合成酶来达到抑制皮质醇合成和分泌的目的，代表药物包括酮康唑、美吡酮、米托坦、依托咪酯等；后者在受体水平拮抗糖皮质激素的作用，通过阻断皮质醇外周作用来缓解高皮质醇血症的临床表现，代表药物为米非司酮。以肾上腺为靶点的药物大多有效，或是干扰细胞色素 P450 酶的活性，或是破坏肾上腺组织来达到改善高皮质醇血症的作用。药物治疗作为二线治疗，是肾上腺库欣综合征内科治疗必不可少的治疗手段。随着对肾上腺库欣综合征发病机制的深入研究，为内科药物治疗提供了更多潜在有效的药物靶点和科学证据。

CS-081

肾上腺手术在治疗皮质醇增多症中的进展

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孙福康，上海交通大学医学院附属瑞金医院泌尿外科主任医师，硕士生导师，上海市泌尿外科前列腺学组委员，上海市泌尿外科质量控制组成员，上海市癌症学会委员，加拿大 CAUJ 杂志和英国 International Journal of Experimental Pathology 杂志的外审专家。美国霍普金斯大学附属医院泌尿外科进修。擅长肾上腺疾病的微创治疗包括普通腹腔镜和机器人辅助腹腔镜手术，对各类巨大、疑难和危重的肾上腺疾病的外科治疗积累了较多的经验。在肾上腺外科疾病的基础研究方面取得了令人瞩目的成绩。在前列腺炎的基础和临床综合治疗方面，以及前列腺癌术前判断和手术以及综合治疗都积累了丰富的经验。近年来在国际和中华系列等杂志发表论文 40 余篇；以主要负责人承担国家自然基金项目 1 项，上海市科委研究研项目 2 项，上海市教委项目 1 项；参与完成的科研项目曾获得国家科学技术进步二等奖、教育部科技进步一等奖、中华医学科技奖三等奖和上海市医学科技进步一等奖、三等奖等。

目的：提高皮质醇增多症的治疗水平。

方法：总结 90 例皮质醇增多症的临床资料以及随访情况。90 例患者均有库欣综合征的临床表现，内分泌检查提示高皮质

醇状态。71 例患者影像学检查发现肾上腺肿块 , 其中左侧 32 例 , 右侧 34 例 ; 双侧肾上腺肿块 5 例。19 例患者显示双侧肾上腺结节样增生。

结果：90 例患者均行肾上腺手术，其中 60 例行肾上腺肿块切除加同侧肾上腺部分切除；6 例行肾上腺肿块切除加同侧肾上腺全切除；4 例行同时行双侧肾上腺全切除术，6 例行先后双侧肾上腺全切除术；11 例行单侧肾上腺全切除术；3 例行先后双侧肾上腺次全切除。病理显示 6 例原发性色素性皮质结节状肾上腺皮质增生（PPNAD)；5 例大结节样肾上腺皮质增生 (AIMAH)；57 例肾上腺皮质腺瘤；5 例肾上腺皮质癌；17 例肾上腺皮质结节样增生 , 其中 7 例考虑异位 ACTH 综合征所致。

结论 : 肾上腺皮质腺瘤切除术效果最好，库欣症状改善最显著。迁延难愈的库欣病，单侧肾上腺全切除，在短期内能缓解代谢症状。分时分侧行肾上腺全切除术，对治疗 AIMAH 和 PPNAD 更安全、稳定；根据异位 ACT H 综合征患者症状和病程，可同时行双侧肾上腺全切除或单侧肾上腺全切除。

CS-082

肾上腺肿瘤的腹腔镜手术治疗

祝宇

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研究方向：肾上腺外科、泌尿系肿瘤和前列腺疾病。

近 5 年来，在国内核心期刊共发表第一作者和通讯作者论文 37 篇，SCI 收录论文 16 篇。目前主持在研国家自然科学基金面上项目 1 项，上海市科委医学引导项目 1 项。

目前腹腔镜手术已成为治疗肾上腺疾病的金标准。腹腔镜肾上腺手术的手术径路主要包括：经腹腔入路的腹腔镜肾上腺手术和经后腹腔入路的腹腔镜肾上腺手术，两种手术径路的优劣难分伯仲，目前尚无统一认识。从手术器械与设备的角度分类，腹腔镜肾上腺手术包括：传统腹腔镜肾上腺手术和达芬奇机器人辅助腹腔镜肾上腺手术。本文主要以手术视频，介绍后腹腔镜肾上腺全切术、后腹腔镜肾上腺肿瘤切除术；经腹腹腔镜（包括机器人辅助腹腔镜肾上腺手术）库兴大结节增生肾上腺切除术、腹主动脉旁副节细胞瘤切除术、下腔静脉旁巨大肾上腺嗜铬细胞瘤切除术、大于 10cm 以上的肾上腺肿瘤切除术；复发性肾上腺肿瘤切除术（原发性醛固酮增多症肾上腺腺瘤术后复发、库欣综合征肾上腺腺瘤术后复发、肾上腺皮质癌术后复发）的手术要点，以及上述疾病围手术期的注意事项，以期提高腹腔镜肾上腺手术治疗的安全性。

CS-083

病例报告：一例家族性原发性醛固酮增多症 III 型的诊治

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童安莉，北京协和医院内分泌科副教授、副主任医师、硕士研究生导师。2002 年毕业于中国协和医科大学，获内分泌专业博士学位，2009–2010 年在美国国立卫生研究院做访问学者。长期从事内分泌专业临床医疗工作，具有较丰富的临床经验，科研方向为内分泌性高血压和肾上腺疾病，在国内外医学杂志发表第一或通讯作者论文 20 余篇。承担人事部、教育部及中华医学会等多项课题，担任中华医学会内分泌学分会肾上腺学组副组长。

目的　家族性醛固酮增多症（Familial hyperaldosteronism，FH）非常少见，其中，FH-III 型尤为罕见，迄今共报道 10 个家系。这些 FH-III 患者具有典型的原醛症的临床表现和生化改变，但不伴其他肾上腺激素的分泌异常。现报道一例同时患有原醛症和库欣综合征的 FH-III 病例的临床诊治。

方法　分析患者的临床特征，进行 KCNJ5 等基因的扩增测序。

结果　患者 2 岁时出现严重高血压（120-140/80-90 mmHg）和低血钾（2.0 mmol/L），检查发现患者存在高醛固酮水平和低血浆肾素活性，用螺内酯和氯化钾治疗，患者血压血钾控制良好。20 岁时，患者出现体重增加、脸圆和皮肤紫纹；血压 160-180/95-130mmHg，血钾 3.0 mmol/L; 血醛固酮 46.4 ng/dl, 血浆肾素活性 0.01 ng/ml/h; UFC 1611.5 μg/24h，大剂量地塞米松抑制试验不抑制，ACTH<5 pg/ml；其他肾上腺激素水平正常；增强 CT 示双肾上腺明显增粗。行左侧肾上腺切除，病理提示弥漫性肾上腺皮质增生。术后患者库欣症状明显缓解，血压较前下降。患者外周血及肾上腺组织均存在 KCNJ5 p. Glu145Gln 突变，肾上腺组织 β -catenin和P53 免疫染色阴性。该增生的肾上腺高表达CYP11B2，而CYP11B1、CYP17A1 和STAR表达相对较低。钙通道阻断剂能显著抑制体外培养的肾上腺细胞的醛固酮和皮质醇分泌以及 CYP11B1、CYP11B2、CYP17A1 和 STAR 表达。

结论　首次报道同时患有原醛症和库欣综合征的 FH-III 病例。患者肾上腺明显增生可能导致了皮质醇分泌增多；该肾上腺的皮质醇与醛固酮分泌均由电压门控的 Ca^{2+} 通道的介导。

CS-084

病例报告：双侧肾上腺腺瘤的库欣综合征

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BAA 最早由 CHAPELL1963 年首次报道。双侧腺瘤可能性有三种：双侧皮质腺瘤、单侧功能瘤对侧无功能瘤、单侧功能瘤而对侧有分泌功能（如醛固酮瘤、嗜铬细胞瘤、雄激素瘤）。非 ACTH 依赖的肾上腺皮质腺瘤中单侧腺瘤占近 90%，而双侧少见。目前报道有 30 余例，主要

依靠血生化和肾上腺 CT 检查。影像学可以部分鉴别诊断，如 PPNAD、AIMAH, 但难以鉴别哪侧肿瘤具有分泌功能。131I-6β碘代甲基 -19- 去甲胆固醇（NP-59）显像有助于功能测占位的诊断，但目前国内尚无该种显像剂，静脉分段取血（AVS）在对于功能定位上具有重要意义。现报道 1 例患者。患者女性，31 岁；2 年前发现体重增加、颜面部皮肤发红、脸变圆，皮肤易出淤斑；1 月前诊断“高血压”，血压最高 190/100mmHg，口服硝苯地平缓释片 40mg 2/ 日，血压控制 140-150/90-100mmHg。双肾上腺增强CT示：双肾上腺多发占位，腺瘤可能。为进一步就诊入住我院。查体：满月脸，向心性肥胖，皮肤菲薄，毳毛增多，散在痤疮，可见瘀斑，宽大紫纹。双下肢轻度水肿，双足趾甲部分脱落。入院检查：UFC 明显升高，ACTH-F 节律紊乱，大、小地塞米松试验均未被抑制，CT 示双侧肾上腺占位，垂体 MRI 未见明显异常。诊断考虑非 ACTH 依赖性皮质醇增多症，双侧肾上腺占位。进一步行双侧肾上腺静脉分段取血，结果提示皮质醇左侧肾上腺 / 下腔静脉远端比值为 16.00，皮质醇右侧肾上腺 / 下腔静脉远端比值为 8.29；F/ALD 左右侧比值为 1.23（<2.3），提示可能为双侧功能腺瘤。腹腔镜下行左侧肾上腺腺瘤切除术，术后评估大小剂量地塞米松抑制试验仍未被抑制，目前出院随访，建议 3 月后切除右侧肾上腺占位。

CS-085

疑难肾上腺疾病的诊治经验

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肾上腺是人体相当重要的内分泌器官，主要分为肾上腺皮质及随着。肾上腺皮质从外往里可分为球状带、束状带和网状带三部分，分泌盐皮质激素、糖皮质激素和性激素，如激素分泌异常可导致原发性醛固酮增多症、库欣综合征及下先天性肾上腺皮质增生；而髓质位于肾上腺的中央部，分泌肾上腺素及去甲肾上腺素，可导致嗜铬细胞瘤。疑难肾上腺疾病的诊断一直是临床上的难点，在很大程度上影响了治疗方案的选择，特别对于双侧肾上腺占位患者的诊断及治疗给临床上带来了极大的困扰，瑞金医院内分泌代谢病科累积了一定的临床病例，包括双侧肾上腺淋巴瘤，ACTH 非依赖性大结节样肾上腺增生，ACTH 非依赖性小结节样肾上腺增生，双侧肾上腺嗜铬细胞瘤，特发性醛固酮增多症，先天性肾上腺皮质增生，肾上腺结核等，我们将从不同角度对这些疾病进行分析及探讨，为进一步诊断及治疗提供依据。

CS-086

垂体柄中断综合征患者下丘脑 - 垂体 - 性腺轴功能重建

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海南省医师协会内分泌代谢科分会常委兼总干事
第一作者或者通信作者发表学术论文 30 余篇，其中 SCI 收录 4 篇。中国糖尿病杂志编委、中国热带医学杂志编委，参编专著 3 部，主持、参与多项海南省重点科技计划项目课题、省自然科学基金课题

垂体柄中断综合征（Pituitary Stalk Interruption Syndrome, PSIS）是指垂体柄纤细或缺如导致下丘脑分泌的促激素释放激素不能通过垂体柄运送到垂体所致的一系列主要表现为垂体前叶功能不全的临床症候群。PSIS 是内分泌系统的罕见疾病，国外及国内分别于 1987 年及 2005 年才首次报道。

PSIS 在影像学 (MRI) 上表现为垂体柄缺如，垂体后叶正常高信号消失，而在下视丘脑部位（第 3 脑室漏斗窝区域）出现高信号（即垂体后叶异位）。近年来随着 MRI 的广泛应用，病案报告陆续增多。

PSIS 患者多为男性，出生时难产的发生率高。目前 PSIS 的确切病因尚未明确，先天发育异常可能是 PSIS 的主要原因。患者就诊的主要原因是生长发育缓慢和第二性征不发育、垂体前叶功能减退症。多数就诊患者为青少年，智力基本正常，骨龄落后。

PSIS 垂体后叶功能正常。PSIS 患者垂体后叶高信号消失，但存在异位的神经垂体，下丘脑分泌的抗利尿激素可能通过移位的神经垂体束运输并储存在某部位，MRI 提示的异位高信号即为异位的神经垂体，第 3 脑室漏斗窝区域（视交叉下）是最常见的异位部位 , 后者能接受渗透压、血压等调节发挥生理作用 , 临床上无中枢性尿崩症症状。

鉴别诊断：

PSIS VS 特发性低促性腺激素性性腺功能减退症（IHH）VS 单纯垂体性侏儒

（1）PSlS 异常胎位（主要为臀位生产）比例高达 61.1%-88.9%，IHH 仅 5.4%；（2）两疾病下部量大于上部量，但 IHH 比 PSIS 有较高的身高，PSIS 指间距小于身高；（3）骨龄检测，PSIS 较 IHH 骨龄落后更显著；（4）PSIS 常合并多种垂体前叶激素缺乏，而 IHH 以促性腺激素和生长激素缺乏为主；（5）垂体 MRI 是鉴别两疾病的有效方法：PSIS 表现为垂体柄中断合并垂体后叶异位，而大部分 IHH 患者仅垂体体积变小。

下丘脑 - 垂体 - 性腺轴功能评估：促性腺激素释放激素（GnRH）兴奋试验（戈那瑞林 100 ug）测定注射前 15、30 min 及注射后 30、60 和 120min 血 LH 和 FSH 水平。

PSIS 性腺功能低下的治疗主要包括以下几方面：（1）靶腺激素替代治疗。（2）垂体促性腺激素治疗（双促）：女性患者先用 HMG 促进卵泡生成，后用 HCG 促排卵治疗。（3）GnRH 脉冲泵治疗：模仿生理脉冲式释放，是治疗低促性腺激素性性腺功能减退最合理的方法，前提是垂体储备功能良好，GnRH 可兴奋。

CS-087

非经典 21 羟化酶缺陷症的识别和处理

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研究方向为库欣综合征、先天性肾上腺皮质增生症的临床诊治和发病机制的研究。参与《马丁代尔药典》的“糖皮质激素”章节的编译工作、《内分泌内科学》和《系统性疾病与心脏》相关章节的编写。参与中华医学会内分泌学分会《库欣综合征专家共识》和中国垂体瘤协作组《垂体 ACTH 腺瘤诊治的专家共识》的编写工作，多次在中华医学会内分泌年会上进行相关研究内容的口头发言。

先天性肾上腺皮质增生症是由于编码肾上腺皮质激素合成酶的基因突变引起的一类疾病，因酶的缺陷导致肾上腺皮质激素合成不足和前体物质堆积而导致患儿性分化异常和肾上腺皮质功能减退。21- 羟化酶缺陷症（21 hydroxylase deficiency，21-OHD）是先天性肾上腺皮质增生症中最常见的类型，约占 90-95%，它也是最常见的的一组常染色体隐性遗传性疾病之一。

因为 21 羟化酶功能受损引起体内前体产物如雄激素的堆积导致患者出现性早熟和骨骺过早闭合，终身高矮，对于女性患者还可引起青春期不发育、原发闭经或者不孕症。此外，因酶缺陷会引起不同程度的肾上腺皮质功能减退的表现。按照 21 羟化酶受损的程度该病可以分为失盐型（酶活性 <1%）、单纯男性化型（酶活性 1-2%）和非经典型（酶活性 20-50%）。目前关于此病的研究还提示 21OHD 基因携带者也会出现症状和生化的异常。在女性高雄激素血症的患者中，21OHD 并不是主要原因，约占 3.3%。早期诊断21OHD，尤其是临床症状不典型的非经典型21OHD，对改善患者的生活质量，尤其是生育状况有着重要意义。

而从临床角度来讲，非经典型 21OHD 通常与其他引起高雄激素血症的疾病如多囊卵巢综合征临床表现难以鉴别，睾酮、孕酮水平两者之间往往有很大交叉，因此 17 羟孕酮的检测对非经典型 21OHD 的诊断具有重要价值，此外，如果能进行 ACTH 兴奋实验、中剂量地塞米松抑制试验都具有很重要的价值。早期能够识别非经典型 21 羟化酶缺陷症，并给予相应的糖皮质激素治疗，对改善非经典型 21OHD 患者的生育具有重要意义。

CS-088

性发育异常的基因诊断

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性别可以分为社会性别、表型性别、内分泌性别、性腺性别和染色体性别五个层次。正常人在以上五个层次上，保持完全一致，一旦其中任何一个层次上性别出现差异，即表现为性分化异常。我们知道，性分化有两个法则，一是染色体决定性腺分化；二是内分泌，或者说激素决定生殖器分化。长久以来，人们知道，Y 染色体有一种或一组基因决定睾丸分化，称为睾丸决定因子。1990 年，从 46XX 男性性反转病人，克隆了 SRY 基因。SRY 基因只有一个外显子，编码 204 个氨基酸，24kD 大小，具有转录因子活性，DNA 结合域序列为 A/TAACAAT/A。绝大部分 46XY 女性性反转病人，都为该部分基因突变。原始性腺始基只有一个，46XY 核型，由于携带有 SRY 基因，性腺分化为睾丸；而 46XX 核型，由于缺少 SRY 基因，性腺分化为卵巢。

睾丸组织有三种重要细胞，Sertoli 细胞、Leydig 细胞和生精细胞；卵巢也有三种细胞，鞘膜细胞、颗粒细胞和卵母细胞。Sertoli 细胞表达抗苗勒氏管激素（AMH），促使苗勒氏管调亡，退化。Sertoli 细胞还产生抑制素素（inhibin）和激活素（activin），负反馈调节垂体的 FSH 分泌。Leydig 细胞主要合成睾酮，产生的雄激素对中肾管的发育起重要促进作用。卵巢中的鞘膜细胞主要合成孕激素和雌二醇前体，颗粒细胞为主要合成雌激素的部位，颗粒细胞也产生抑制素和激活素，调节垂体 FSH 的分泌。雌激素在性腺分化的作用并不重要，但在青春期女性外阴发育和第二性征发育上，起重要作用。

外生殖器始基只有一套，在雄激素作用下分化为阴茎、阴囊，在缺乏雄激素的作用下，分化为阴蒂、大小阴唇。睾酮与双氢睾酮的作用有所差别。总之，Y 染色体上的 SRY 基因决定睾丸分化，雄激素和 AMH 决定内生殖器分化，双氢睾酮在外生殖器分化中起重要作用。

性发育异常（DSD）可以分为染色体异常，主要包括 45XO 的 Turner 综合症，47XXY 的 Klinefelter 综合症。46XYDSD，为男性假两性畸形，主要包括先天性肾上腺增生、17b- 羟类固醇脱氢酶缺陷、雄激素不敏感综合症、还有 5a- 还原酶缺陷症等。46XXDSD，为女性假两性畸形，主要包括先天性肾上腺增生、芳香化酶缺陷等。

总之，Y 染色体上的 SRY 基因决定性腺分化，内分泌，或激素决定内、外生殖器分化。部分 17a —羟化酶缺陷症患者，可以表现为不典型的高血压、低血钾和性幼稚，与基因突变类型密切相关。部分非典型 21 羟化酶缺陷症患者表现为 PCOS，需要鉴别。男性假两性畸形患者，出现青春期男性化表现，伴乳房发育，首先要考虑 17b-HSD，同时要与 5a- 还原酶缺陷症和部分雄激素不敏感综合症鉴别。

CS-089

性早熟诊治指南解读

巩纯秀

北京儿童医院

巩纯秀，首都医科大学附属北京儿童医院内分泌遗传代谢中心，教授、主任医师，教授。中华医学会儿科内分泌遗传代谢学组副组长，中华医学会糖尿病学分会 1 型糖尿病学组副组长中国医师协会内分泌代谢学委员。青春期医学副主委和内分泌学组副组长。从事小儿内分泌遗传代谢性疾病临床、教学及研究工作 20 余年。研究以儿科内分泌为主要研究方向，其中又以糖脂代谢和儿童生长和性腺疾病为主。且主要为转化医学研究。 糖尿病领域，进行多次流行病学调查并持续监测发病率至今 32 年；2000 年后进一步推进研究及临床转化，在卫生部、北京科委、北京卫生局的糖尿病管理系列研究支持下，首次研究并推荐了合理的儿童 T2DM 筛查方案；近年来研究特殊类型和新生儿糖尿病精准医疗和随访，并率先使用 APP 管理儿童 DM。开展多中心调查儿童暴发型 1 型糖尿病、DKA 起病的发生率和儿童糖尿病控制的地区差异及儿童糖尿病血糖波动和氧化应激的相关性及胰岛素治疗起始剂量对氧化应激影响的 RCT 研究。主笔儿童糖尿病酮症酸中毒和胰岛素治疗指南。国内外多次演讲中国儿童糖尿病的研究和治疗。内分泌、糖尿病及性腺系列论文发表 200 余篇，包括顶级期刊 JCEM 和 Pediatric Diabetes 上的 SCI20 篇。糖尿病教育著作 1 部。

获奖

1. 参与完成的项目“重组人生长激素系列产品研制与产业化”获得国家科学技术进步奖二等奖第 6 完成人获奖号 2015-J-235-2-02-R06。

2. 作为课题负责人完成的项目“儿童糖尿病流行及并发症诊疗和血糖控制系列研究”获得妇幼健康会第一届的科技成果奖三等奖获奖号 2015-A-C16-01。

3.“转型期成人慢性病防治项目”获得中华预防医学奖二等奖第 4 名（证书号 20090108-2-G1004）

中枢性性早熟 (central precocious puberty，CPP) 是指由于下丘脑．垂体．性腺轴 (hypothalamie—pituitary—gonadal axis，HPGA) 功能提前启动而导致女孩 8 岁前，男孩 9 岁前出现内外生殖器官快速发育及第二性征呈现的一种常见儿科内分泌疾病。目前国内外普遍应用促性腺激素释放激素类似物 (gonadotropin．releasing hormone analogs，GnRHa) 治疗 CPP。但是在临床诊疗中仍有不少医师存在误解和不规范之处。为规范儿童 CPP 的诊疗，中华医学会儿科学分会内分泌遗传代谢学组对 GnRHa 的临床应用存在较多颇具争议的问题，组织进行讨论并达成共识来指导儿科内分泌医师对 CPP 诊疗。

CS-090

分泌雄激素的肿瘤

杜锦

解放军总医院

杜锦，临床博士
解放军总医院内分泌科副主任医师
中华医学会糖尿病分会肥胖学组委员
中华医学会内分泌分会肥胖学组委员

主要研究方向是糖尿病及其慢性并发症的防治，对甲状腺、肾上腺、性腺疾病亦多有研究女性出现不同程度的男性化体征，如多毛、声音变粗、喉结、阴蒂肥大等，化验检查提示睾酮水平升高，常见于卵巢和肾上腺性疾病。

分泌雄激素的肾上腺皮质肿瘤 (androgen-producing adrenocortical tumor), 亦称男性化肾上腺皮质肿瘤 , 是指能够产生过量的雄激素使患者出现不同程度男性化表现的肾上腺皮质肿瘤。该肿瘤主要发生于女性 , 表现为性发育异常或不同程度的男性化，男性则多发生于童年时期 , 并以性早熟及骨龄提前为特征 ; 青春期前女性表现为性发育异常 , 成年女性则表现为不同程度的男性化。在该类肿瘤中 , 恶性肿瘤远多于良性。在临床上分泌雄激素的肾上腺皮质肿瘤极少见 , 而单纯分泌雄激素的良性肾上腺皮质肿瘤更为罕见 , 国内外文献报道仅占肾上腺肿瘤的 0.13% ~ 2. 60%，多为个案报道。解放军总医院内分泌科近 18 年来共收治 1 494 例肾上腺肿瘤病例 , 其中单纯分泌雄激素的肾上腺皮质肿瘤仅有 2 例,约占总数的 0. 13%。文献报道 75% 的男性化肾上腺皮质肿瘤为恶性。而恶性肾上腺皮质肿瘤预后极差,生存率低。

分泌雄激素的肾上腺皮质肿瘤患者血清睾酮水平通常明显升高 , 促性腺激素水平没有被抑制。血 DHEAS 及尿 17- 酮类固醇明显增加 , 且不能被地塞米松抑制 , 呈自主性分泌而不依赖于 ACTH。由于 CYP21 及 CYP11 的活性正常或降低 , 患者的醛固酮、皮质醇及其尿代谢产物 17- 羟皮质类固醇水平降低。因此只有约 1/4 的男性化肾上腺皮质肿瘤同时伴有库欣综合症 , 且其中大部分病例经病理证实为肾上腺皮质腺癌。

分泌雄激素的卵巢肿瘤也极为少见，仅占卵巢肿瘤 0．38% 。最常见类型有卵巢支持一间质细胞肿瘤、脂质细胞瘤，前者好发于生育年龄妇女，后者好发于绝经前后妇女，少见的还有颗粒细胞瘤、泡膜细胞瘤，罕见的有卵巢内膜腺癌 。此类肿瘤一般较小，直径 ≤5 cm，多为单侧 (双侧 ≤3)、实性。临床上若出现月经紊乱及逐渐加重的男性化症状，血清 T 显著升高，并排除肾上腺疾病时应考虑为分泌高雄激素卵巢肿瘤。由于该类卵巢肿瘤较小，即使影像学检查 (超声、CT、核磁共振) 未提示卵巢肿瘤，也不能轻易排除。DEX 抑制试验常用于鉴别肿瘤与非肿瘤来源的高雄激素血症；性激素测定、ACTH 兴奋试验、促性腺激素释放激素激动剂 (GnRH-a) 抑制试验等用于确定病变部位。如果无法明确肿瘤来源时，可通过股静脉插管取卵巢及肾上腺静脉血样，测定性激素浓度梯度来判断肿瘤部位。切除病变卵巢。通过定期阴道超声检查，动态观察卵巢，如出现卵巢不对称性改变，局部血流丰富，往往提示该侧卵巢存在肿瘤。

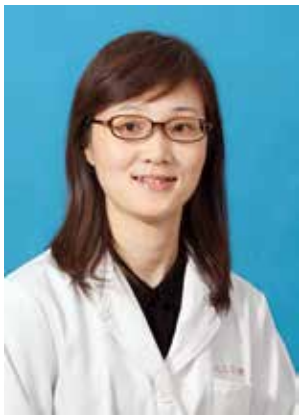
临床明确女性男性化源于卵巢肿瘤，应手术治疗。术后肿瘤分化不良者，应辅助放化疗并长期随访。由于肿瘤具有分泌 T 的特征，术后定期检测 T 水平可监测肿瘤的复发与发展

CS-091

染色体与性反转

乔洁

上海交通大学医学院附属第九人民医院



乔洁，上海交通大学医学院附属第九人民医院内分泌科主任医师，博士生导师。兼任上海市医学会糖尿病分会委员，上海市医学会内分泌分会基础学组成员，美国内分泌学会（Endocrine Society）成员。长期从事内分泌疾病的临床工作和基础研究，在糖尿病、甲状腺疾病和性腺疾病的诊疗中积累了一定的临床经验，发表 SCI 论文 20 余篇，是中华内分泌代谢杂志的通讯编委。以项目负责人承担国家自然基金 3 项，上海市自然基金 1 项。

对于性别分化和性别决定的认识经历了漫长的历史过程，直到 1991 年，研究者通过转基因技术发现 Y 染色体的 SRY 基因的转入，可使 XX 的小鼠出现性反转，明确 SRY 基因即“睾丸决定因子”。既往认为，哺乳动物的性别二态性是由睾丸的双重分泌功能，即 Sertoli 细胞分泌的 AMH 和 Leydig 细胞分泌的睾酮所决定；而不是由卵巢决定。早期的胚胎的性腺原基，具有双向分化潜能，除非有男性化激素因子的干预，否则将自发发育为女性。然而，近年的研究发现，在性发育的过程中，还有许多未能明晰的调控环节，而且可能存在所谓的“卵巢决定因子”或“抗睾丸因子”。根据 2006 年欧洲儿科内分泌协会和 Lawson Wilkins 儿科内分泌协会的共识，目前性发育异常疾病的分类方案中，将 XX 男性或 XX 性反转定义为 46，XX 睾丸性 DSD（46,XX testicular DSD）；而将 XY 性反转定义为 46，XY 完全性性腺退化（46,XY complete gonadal dysgenesis）。

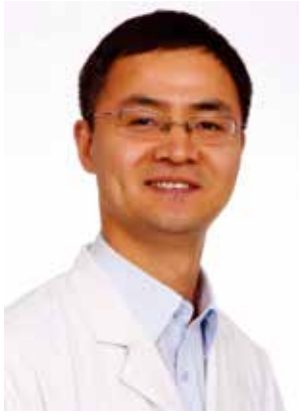
SRY 蛋白是一种转录因子，可启动下游的 SOX9 基因，而 SRY 基因的表达又依赖于 SF-1，WT-1 和 GATA4 等转录因子的共同作用。在动物模型中发现，Xp21 的 DAX-1 基因和 1p35 的 WNT4 基因重复，可导致原始性腺向卵巢方向分化；目前认为 SOX9 和 FGF9 是“促雄”基因；而 WNT4 和 RSPO-1 是“促雌”基因。临床上观察到仅有 10-15% 完全性性腺退化（Swyer 综合症）的患者由 SRY 基因突变导致。在其余的候选基因 DAX-1, SF-1, WNT4, SOX3, LHX9 和 FOG-2 中，发现 SF-1 基因的杂合突变是 46，XY DSD 中睾丸性腺退化较为常见的病因，且常不伴有肾上腺皮质功能减退。对于性反转疾病的临床病例和动物模型研究进一步拓展了人们对于性别分化和性别决定过程的认识。

CS-092

双促与 GnRH 泵治疗的疗效

茅江峰

北京协和医院



茅江峰，博士，北京协和医院内分泌科副主任医师，硕士生导师。2012 年在美国哈佛大学医学院附属医院访问 3 个月，2013 年在新疆医科大学附一院援疆工作 1 年。擅长矮小、青春发育异常和垂体疾病的诊治。以第一或通讯作者，发表英文 SCI 文章 12 篇，中文核心期刊论文 40 余篇，主持完成国家自然科学基金 1 项。目前为中华医学会内分泌学分会性腺学组委员，是《中华内分泌代谢杂志》通讯编委，是《中华医学杂志》等期刊的审稿专家。

目的　比较促性腺激素释放激素（Gonadotropin Releasing Hormone, GnRH）脉冲式皮下输注和绒促性素 / 尿促性素（Human Chorionic Gonadotropin/Human Menopausal Gonadotropin, HCG/HMG）联合肌注治疗男性特发性低促性腺激素性性腺功能减退症（Idiopathic hypogonadotropic hypogonadism，IHH）生精疗效。

方法 这项回顾性研究纳入 2010 年 5 月至 2014 年 10 月在北京协和医院内分泌科门诊就诊的男性 IHH 患者 92 例。患者自愿选择一种治疗方案，并据此将 92 例 IHH 患者分成两组：GnRH 脉冲式治疗组（GnRH 组，n=40）；HCG/HMG 联合治疗组（HCG/HMG 组，n=52）。观察 GnRH 组在治疗第 1 周和每月的 LH 及 FSH 水平；每月随诊观察两组患者血总睾酮（serum total testosterone, TT）水平、睾丸体积（testicular volume, TV）和精子生成率的变化情况。并比较 GnRH 组和 HCG/HMG 组在治疗过程中 TT 水平、TV 和精子生成率的差异。

结果 所有患者均治疗 3 个月以上。GnRH 组和 HCG/HMG 组随访中位时间分别为 8.2（3.0-18.4）个月和 9.2（3.0-18.6）个月，P=0.413。GnRH 组治疗 1 周时，LH（0.5 ± 0.6 vs. 3.4 ± 2.4 IU/L，P<0.01）和 FSH（1.3 ± 1.1 vs. 5.8 ± 3.8 IU/L，P<0.01）水平较治疗前显著升高。GnRH 组治疗 2 个月时与治疗前比较，TT（1.0 ± 1.0 vs. 8.2 ± 7.3 nmol/L，P<0.01）水平显著升高，TV（2.3 ± 1.5 vs. 6.0 ± 2.5mL，P=0.001）显著增大。GnRH 组患者末次随诊 TT 水平（7.4 ± 5.2）nmol/L 和 TV（8.1 ± 4.0）mL 分别较治疗前 TT 水平（1.0 ± 1.0）nmol/L 和 TV（2.3 ± 1.5）mL 显著升高和增大，均 P ＜ 0.01。HCG/HMG 组末次随诊 TT 水平（14.4 ± 8.0）nmol/L 和 TV（7.6 ± 4.2）mL 分别较治疗前 TT 水平（0.8 ± 0.6）nmol/L 和 TV（2.3 ± 2.1）mL 显著升高和增大，均 P ＜ 0.01。GnRH 组和 HCG/HMG 组分别有 20 人（20/40，50.0%）和 15 人（15/52，28.8%）生成精子，P=0.038。精子初现时间方面，GnRH 组（6.5 ± 3.1）月短于 HCG/HMG 组（10.8 ± 3.7）月，P=0.001。精子初现时，GnRH 组和 HCG/HMG 组的 TT 水平分别为（9.0 ± 5.1）nmol/L 和（14.8 ± 8.8）nmol/L，P=0.034。

结论 GnRH 脉冲式皮下输注治疗男性 IHH 比 HCG/HMG 联合肌注更早产生精子。

CS-093

闭经的诊断思路

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《生殖医学杂志》副主编

闭经可分为原发性闭经和继发性闭经，前者是指年龄 15 岁或乳房发育后 5 年仍无初潮；后者定义为原有规律月经，连续停经超过 3 个月或月经稀少超过 6 个月。

原发性闭经的原因

1 生殖道发育异常：处女膜闭锁，苗勒管发育不全，睾丸女性化；

2 卵巢发育不全：特纳综合征，单纯性性腺发育不全，17a- 羟化酶缺乏症；

3 垂体病变：颅咽管瘤，垂体柄中断综合征，垂体性侏儒；

4 下丘脑病变：生殖细胞瘤，IHH；

继发性闭经的原因

1 子宫病变：Asherman 综合征 (反复刮宫引起粘连闭锁)；

2 卵巢病变 : PCOS，卵巢肿瘤，自身免疫性卵巢炎，盆腔放疗，化疗；

3 垂体病变：垂体炎，垂体占位病变，席汉综合征，高泌乳素血症，感染；

4 下丘脑病变：营养不良，高强度运动，情感应激，颅内感染，颅内肿瘤，颅脑创伤；

5 其他疾病：原发性甲减，慢性全身性疾病；

6 药物：抗抑郁药，抗精神病药，抗组胺药，毒品；

7 生理性：哺乳，妊娠，避孕药，绝经（卵巢早衰）。

诊断检查

1 病史：个人史：饮食习惯，多饮多尿，运动，体重变化，药物，慢性疾病，放化疗史，精神应激史；家族史：初潮年龄，遗传疾病；

2 体检：身高，体重，甲状腺肿，乳房大小，溢乳，多毛，痤疮，躯体畸形；

3 辅助检查：性激素 6 项，妊娠试验，甲状腺功能，ACTH，F，DHEA，17-OHP，染色体核型分析。

4 影像学检查：盆腔超声，下丘脑 - 垂体 MRI，肾上腺 CT；

5 黄体酮试验（非必须）：甲羟孕酮 10mg/d X 10d，口服，有撤退出血提示雌激素水平适当。

原发性闭经的诊断思路证：阴道闭锁不是真正的闭经，而是月经不能从阴道排出，患者往往有周期性小腹坠胀疼痛，影响学检查可以发现病变。睾丸女性化患者的表型为女性，无子宫输卵管，阴毛缺如，血清 LH 和 TT 水平升高，染色体核型 46，XY。Turner 综合征患者卵巢不发育，身材矮，多发躯体畸形，血清 LH 和（或）FSH 水平升高，E 水平显著降低，经典型患者的染色体核型 45,X。颅咽管瘤多见于青少年，表现为肿瘤压迫症状，尿崩症和（或）垂体前叶功能减退，下丘脑 - 垂体 MRI 可以明确诊断。生殖细胞瘤亦以青少年多见，发生在松果体区的生殖细胞瘤以脑积水，颅压高，颅神经麻痹为主要表现；鞍区或鞍上生殖细胞瘤常常表现尿崩症，视神经压迫和垂体前叶功能减退。MRI 可以发现肿瘤，部分患者在脑脊液中可检出瘤细胞和（或）hCG 水平升高。

继发性闭经的诊断思路：PCOS 是育龄期妇女最常见的闭经原因，以多毛和痤疮等雄激素增多症状或高雄激素血症以及闭经不排卵为主要表现，往往有肥胖和黑棘皮病，超声检查可见多囊卵巢。随着 MRI 检查的普及，垂体炎的检出增多，影像学上表现为垂体柄增粗和垂体增大，症状主要为尿崩症和垂体前叶功能减退。营养不良，高强度运动和情感应激都可以通过抑制 GnRH 的脉冲分泌而引起月经紊乱或闭经，称为功能性下丘脑闭经。

CS-094

抗甲状腺抗体与女性妊娠

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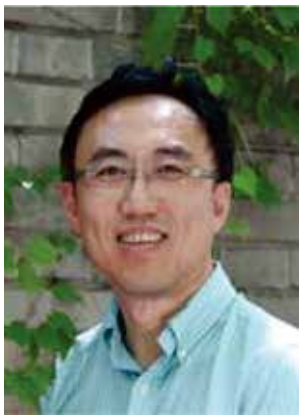

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甲状腺自身抗体与不良妊娠结局是目前相关临床研究的热点之一，研究结论将影响临床实践。1990 年，Stagnaro-Green 首次报道了甲状腺自身抗体与妊娠结局的关系。552 例妊娠妇女在妊娠早期筛查甲状腺自身抗体，其中 19.6% 为自身抗体阳性。自身抗体阳性的女性，其流产率为 17%，显著高于对照组的 8.4%。此后，一系列类似研究陆续报道，多数研究结果表明，甲状腺自身抗体是流产的危险因素。目前，甲状腺自身抗体导致自然妊娠流产率升高已经被大多数学者所接收。流产率升高的可能原因包括以下几个方面：（1）年龄因素：甲状腺自身抗体阳性者年龄偏大，故此流产率高；（2）免疫异常：甲状腺自身抗体阳性者可伴随其它免疫疾病或免疫紊乱；（3）抗体的直接作用：甲状腺自身抗体对胚胎有不良影响。已经有研究在羊水中检测到甲状腺自身抗体；（4）甲状腺功能低下：自身抗体阳性者在妊娠过程中容易出现轻度的甲减。虽然甲状腺自身抗体可能与不良妊娠结果有关，但是相关的干预研究罕见报道，因此目前尚没有公认的有效干预方法。左旋甲状腺素干预仅有一个小样本 RCT 研究显示了疗效，尚无更多的研究证实。

甲状腺自身抗体增加自然妊娠流产率，理论上甲状腺自身抗体对 IVF-ET 的妊娠结局也应存在一定的影响。实际上，确实有一些研究发，甲功正常但甲状腺自身抗体养性的不孕症患者，IVF/ICSI 妊娠的流产率显著升高。然而，仍有些研究结果并未证实甲状腺自身抗体阳性增加 IVF/ICSI 妊娠流产率。对上述相关研究结果进行正确解读非常必要，但并不容易。这些研究多为回顾性研究，研究的样本数均较小，流产事件数在 1-10 之间，存在严重的抽样误差，因此需要大样本前瞻性研究来明确甲状腺自身抗体是否增加 IVF/ICSI 妊娠流产率。我院进行了大样本的前瞻性研究，初步研究结果显示，甲状腺 TPO 抗体阳性但甲功正常的不孕症患者，借助 IVF/ICSI 技术成功妊娠后，早期流产率与甲状腺自身抗体阴性组相比并无显著升高。我们的研究结果提示，TPO 抗体不增加 IVF/ICSI 妊娠流产率，因此，对自身抗体阳性但甲功正常的不孕症女性进行左旋甲状腺素干预可能是不必要的。

CS-095

基于共表达受体治疗策略的功能性垂体瘤治疗进展

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钟历勇，教授、主任医师、博士研究生导师、医学博士。现任首都医科大学附属北京天坛医院内分泌科主任、首都医科大学内分泌与代谢学系副主任、中华医学会内分泌学分会委员、中华医学会内分泌学分会下丘脑—垂体学组副组长、中国医师协会内分泌代谢专科医师分会委员、北京医学会内分泌学分会常务委员、北京医师协会内分泌专科医师分会常务理事、北京医学会糖尿病学分会委员、国家卫计委脑卒中防治工程委员会中青年委员（内分泌代谢学组）、兼任中华内分泌代谢杂志编委、中国卒中杂志编委、中国医师进修杂志编委、中国医药科学杂志编委、同时还兼任中华糖尿病杂志、中华神经外科杂志、中国细胞生物学学报、Exp.Clin. Endocrin.&Diab. 等杂志审稿人以及《MIMS 内分泌与代谢疾病用药指南》编辑顾问。

发表 SCI 与核心刊物收录第一作者与责任作者学术论文 90 余篇，参加编写专著 15 部，主持或参与的国家级、省部级或校级课题 10 余项。长期从事临床医学本科生教育以及内分泌与代谢病研究生教育工作。从事临床工作近 30 年，擅长下丘脑—垂体—靶腺（肾上腺、甲状腺、性腺）疾病、糖尿病及其慢性并发症诸如糖尿病神经病变、糖尿病肾脏病变及糖尿病伴缺血性卒中的综合诊治；对甲状腺疾病、痛风、肥胖病、高脂血症、多囊卵巢综合症、骨质疏松症和继发性高血压病等有独特的诊治经验。

垂体腺瘤 (Pituitary Adenoma) 是由垂体前叶三种上皮细胞形成的良性肿瘤，约占颅内肿瘤的 10% — 20%，发病率仅次于胶质瘤和脑膜瘤。垂体腺瘤按分泌激素与否可分为功能性 / 分泌性腺瘤（Functioning Pituitary Adenoma）和无功能性腺瘤（Non-functioning Pituitary Adenoma），而功能性腺瘤又可以分为单激素腺瘤和多激素腺瘤（混合腺瘤）。功能性垂体腺瘤通过免疫组化病理诊断的方法，按其免疫组化阳性（激素分泌活性）可以分为生长激素（GH）瘤、泌乳素（PRL）瘤、促肾上腺皮质激素（ACTH）瘤、促甲状腺激素（TSH）瘤、促性腺激素（GnH）瘤、混合瘤等，其中最常见的 PRL 瘤占垂体腺瘤的 50%-55%，GH 瘤占 20%-23%，ACTH 瘤占 5%-8%，TSH 瘤、GnH 瘤非常罕见，而无功能腺瘤则占 20%-25%。

垂体腺瘤的治疗方法主要有神经外科手术、放射治疗和药物治疗三种。但除垂体泌乳素瘤外，多数类型的垂体腺瘤均宜首选神经外科手术治疗，辅以药物治疗与放射治疗。近年来基于垂体共用受体治疗策略的功能性垂体腺瘤的药物治疗正日趋成熟抑或有待规范。

基于免疫组化、基因芯片等实验技术研究发现，各型垂体腺瘤上均存在类似的受体亚家族，如垂体 GH 瘤、垂体 ACTH 瘤与垂体 TSH 瘤上均有生长抑素受体 1-5 亚型（SSTR1 — 5）与多巴胺受体的表达，相应配体药物（如生长抑素类似物与溴隐亭 / 卡麦角林）被实验性应用于临床治疗当中，基于共表达受体策略的药物治疗逐渐显露头角。 大约 70-80% 的 ACTH 瘤 D2 受体呈阳性，中长效非麦角类多巴胺受体激动剂—卡麦角林（Carbegoline）可以使其 ACTH 分泌下降。垂体 GH 瘤细胞亦存在 D2 受体和 SSTR2、SSTR5 受体表达，可以依靠 2 种及以上药物联合应用抑制垂体 GH 瘤自主性分泌 GH，如使用溴隐亭 / 卡麦角林联合奥曲肽（Octreotide）或者另一种新型的生长抑素类似物选择性 SSTR5 激动剂帕瑞肽（Pasireotide）。业已证明，生长抑素类似物奥曲肽对于 SSTR2 和 SSTR5 均有结合力，对于 SSTR2 结合力更好；目前认为帕瑞肽（Pasireotide）是广谱 SSTA，对 SSTR1 — 3、SSTR5 均有结合力，且对 SSTR5 的结合力和功能活性分别为奥曲肽的 40 倍和 158 倍。

TSH 瘤主要表达 SSTR2 和 SSTR5 受体，奥曲肽对于垂体 TSH 瘤自主分泌的抑制作用有效率大于 90%，长期规律应用奥曲肽对于 TSH 瘤的临床、生化治愈率可以接近于 73-78%，可缩小瘤体的作用在约 1/3 的病例中发现，特别是针对大腺瘤，作用更为显著，如果经济条件允许，长期应用奥曲肽对于不能手术或术后复发的 THS 瘤患者，亦不失为一个选择。SSTR5 在 ACTH 瘤（库欣病）和 PRL 瘤上均有表达，理论上选择性 SSTR5 激动剂帕瑞肽对于此两种肿瘤的治疗应具有较好的临床前景。为期 12 个月的 3 期帕瑞肽治疗库欣病的临床研究已显示帕瑞肽可显著降低库欣病患者皮质醇水平，支持帕瑞肽作为潜在的治疗垂体 ACTH 瘤的垂体靶向治疗药物，有关帕瑞肽和奥曲肽治疗垂体 GH（肢端肥大症）的优效性头对头研究已显示帕瑞肽 LAR 的疗效优于奥曲肽 LAR。

CS-096

垂体瘤术后功能评估与替代治疗

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近年来有兴趣于糖尿病、代谢综合征等慢病的长程临床管理、参与了十一五支撑计划代谢综合征的生活方式干预子课题研究。参与了十三五国家精准医学糖尿病项目研究。参与了难治性高血压原醛症的多中心筛查、参与了垂体瘤术生长激素缺乏症的多中心研究。

近年来发表相关 SCI 论文数篇，分别获浙江省科技进步三等奖一项，浙江省卫生厅科技进步二等奖一项。

目前垂体瘤术后致的垂体功能不全占所有垂体功能不全的患者一半。所以对垂体瘤术前、术中、术后的管理非常重要。多学科合作共同管理垂体瘤术后的内分泌功能紊乱已成为一种趋势。内分泌科在垂体瘤管理中承担了重要的责任。

垂体瘤术后患者多半是因为肿瘤压迫或手术损伤所致。其影响的内分泌功能往往是生长激素 - 促性腺激素 - 促甲状腺素 - 促肾上腺皮质激素。临床表现以垂体前、后叶内分泌激素缺乏、内分泌功能性肿瘤复发为主要表现。诊断依赖于内分泌基础激素测定、及功能试验。治疗与干预主要是替代以提高生活质量与生存寿命。

在垂体瘤患者管理中最重要的是制定相应临床路径，术前规范评估包括内分泌功能评估、肿瘤大小评估、肿瘤涉及范围评估，术后也分为早期评做、晚期评估与长期随访，并要与神经外科建议密切良好的合作是每个垂体瘤患者顺利渡过手术期和术后管理的重要因素。

CS-097

国际先天性低促性腺激素性性腺功能减退症诊治共识解读

窦京涛

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窦京涛，医学博士，主任医师、教授，博士研究生导师；现为解放军总医院内分泌科副主任，解放军医学院教学指导委员会委员。

现兼任中华医学会糖尿病学分会常委；北京医学会糖尿病学分会副主任委员；全军医学科学技术委员会内分泌学专业常委；中国高血压联盟理事；曾任中华医学会内分泌学分会性腺学组组长。

现任中华内分泌代谢杂志、中华糖尿病杂志、解放军医学杂志、中国实用内科杂志、中国糖尿病杂志、中华老年多器官疾病杂志等多个杂志编委。

先天性低促性腺激素性性腺功能减退症 (CHH) 是一种罕见病，但日益被内分泌科医生认识并重视，由于其发病机制、诊断和治疗复杂，中华内分泌学会性腺学组于 2015 年 7 月推出了主要基于我国人群研究的《特发性低促性腺激素性性腺功能减退症专家共识》，同期，欧洲学会关于《欧洲共识：先天性低促性腺激素性性腺功能减退症的发病机制、诊断和治疗》也正式刊登，现对欧洲的共识进行解读，旨在抛砖引玉，为临床医生提供

更好的理论依据，以指导临床诊疗。

欧洲共识在阐述 GnRH 神经系统生物学、青春期和生殖生理的基础上，主要从 CHH 临床表现、遗传学特征、诊断和治疗方面进行详述，以期改善患者的发育和、生殖和疾病管理。CHH 是由调控生殖轴的主要激素促性腺激素释放激素（GnRH）合成、分泌或作用缺陷导致的。CHH 患者中约 50% 伴有嗅觉的减退或缺失，称为 Kallamam 综合征，这一疾病被认为是由于胚胎期 GnRH 合成神经元迁移不完整引起。CHH 的表现具有临床和遗传异质性，其临床特征在新生儿和儿童期男性患儿主要表现为隐睾和小阴茎，女性患儿无明显表现，但二者双亲可能伴有 CHH；在青春期 CHH 患儿由于 HPG 无法激活，其最典型的表现为青春期发育延迟，即男性患儿到 14 岁无明显睾丸体积增大（<4cm），女性患儿至 13 岁仍无乳腺发育，这一期患儿最容易出现性心理发育障碍，也较难与体质性青春期发育延迟相鉴别；若在青春期仍未及时诊治，在成年期则主要表现为不育和骨质疏松。在遗传方面 CHH 被归为经典的单基因病，其既有散发病例，也有家族性发病。目前已被证实的遗传模式包括 X 连锁隐性遗传、常染色体显性 / 隐性遗传。在 Kallmann 综合征 /CHH 患者中已鉴定出超过 25 种突变基因，但值得注意的是这些突变基因所能鉴定出的病例仍不到 10%。目前大样本队列研究数据表明超过 20% 的 CHH 是一种寡基因病，这一遗传模式的提出有助于研究基因型与表型的相关性。在诊断方面，详细地评估是至关重要的，包括生长（尤其关注骨骺闭合时间）、性发育（男性有无隐睾、阴毛和阴茎 tanner 分期、睾丸体积，女性乳腺发育情况和初潮年龄等）和嗅觉、视神经发育、外耳形状和听力、皮肤和毛发颜色、牙齿数目等。为了排除垂体瘤或功能性原因导致的其他疾病，生化评估和影响学检查是十分必要的，包括出提垂体前叶激素及其相应靶器官激素水平（LH、FSH、雌激素、睾酮、TSH、游离 T4、GH、IGF-1、ACTH、皮质醇）、内分泌功能试验（GnRH/HCG 兴奋试验、血清抑制素 B、AMH、INSL3）、男性精子情况、肝肾功能、铁负荷、骨龄、骨密度、肾脏超声、颅脑核磁共振等。此外，基因检查对于诊断和预后判别也是有重要意义的。在治疗方面，对于不同年龄段的 CHH 患者其关注重点和治疗目标是有所差异的，对于新生儿和儿童期的患者主要关注其睾丸缺失和阴茎发育情况，通常建议隐睾患儿在 6 个月之前可以通过促性腺激素和睾酮治疗，必要时应于 1 岁内行睾丸固定术；对于青春期患儿主要是促进第二性征发育、维持正常生长和骨发育及生殖功能评估，治疗以性激素替代治疗为主，是否采用促性腺激素治疗仍存在争议；对于成年患者主要是维持第二性征并尽量改善生育功能，治疗方案包括性激素替代治疗、HCG 或联合 FSH、GnRH 泵治疗方案。最后，本共识还提出了应关注如何减少长期治疗所带来的副作用。

总之，本共识针对 CHH 的诊治进行了全方位的阐述，对于诊治过程中可能遇到的问题提供一定的理论指导，有助于临床医生作出及时、恰当的临床处理，以期患者获得更佳的临床预后。

CS-098

动态增强核磁技术参数在 ACTH 依赖性库欣综合征诊断中的价值

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研究方向：糖尿病；垂体和肾上腺疾病等

中华医学会内分泌分会垂体组委员和中华医学会内分泌学会血脂组委员，三亚市内分泌学会副主委;《国际糖尿病》青年编委，美国内分泌学会会员，国家自然科学基金委员会评审专家；

主持国自然金面上项目 2 项、海南省自然基金、国际合作课题、科技创新等多项课题，参与多项国家、院级以及国际合作及国家科技支撑计划课题科技创新课题等多项发表学术论文 40 余篇，多篇被 SCI 或 Medline 收录，参编和参译多本书籍获军队和总医院医疗成果二等奖两项

库欣综合征是由于肾上腺皮质长期分泌过量皮质醇而造成的一系列临床症候群。可表现为向心性肥胖、紫纹、痤疮、多毛、月经紊乱 (女性)、高血压、血糖代谢紊乱、性功能低下等。1932 年由美国神经外科医生 Harvey Cushing 首次描述了这一类临床症候群。

由垂体分泌促肾上腺皮质激素 (ACTH) 过多导致皮质醇增多者，称之为库欣病 (cushing’s disease)，该病 70% ~80%是由垂体 ACTH 腺瘤造成的；由垂体外肿瘤组织异位分泌 ACTH 造成的皮质醇增多考虑异位 ACTH 综合征。两者均属于 ACTH 依赖性库欣综合征。

ACTH 依赖性库欣综合征的临床表现多样，难以根治，容易复发，目前仍是困扰人类健康的一大难题。尽管其发病率不高，但高皮质醇血症的后果非常严重。心、脑血管并发症，严重感染和电解质紊乱都有可能威胁生命；儿童生长发育迟缓、严重骨质疏松可以致残；成年患者在疾病未愈时几乎丧失生育能力。因此，及时正确诊断定位，采取有效治疗手段至关重要。

由于类癌起病缓慢，临床表现和库欣并非常类似，同时正常人有 10% 存在无功能瘤，加之库欣病 40% 患者影像学检查可能是阴性，因此 ACTH 依赖性库欣综合征的诊断和鉴别诊断是难点。

目前 ACTH 依赖性库欣综合征的诊断分三步进行，首先需要通过临床表现和血尿皮质醇测定以及小剂量地塞米松抑制试验等明确存在内源性皮质醇分泌过多的状态；其次需要测定血中 ACTH 水平明确是否 ACTH 依赖性库欣综合征；最后需要定位诊断，也是最难的一步。目前常用的用于定位的手段有血浆 ACTH 水平测定、大剂量地塞米松抑制试验、CRH 兴奋试验、去氨加压素兴奋试验、双侧岩下窦静脉取血 (BIPSS) 等，但检测的敏感性和特异性都有待进一步提高。目前认为，BIPPS 是鉴别库欣病和异位 ACTH 综合征最有价值的诊断性试验，其敏感性、特异性和准确性都达到了 85% ~ 90%。但作为又创检查，有发生严重的并发症如静脉血栓、肺栓塞、颅神经麻痹、脑干血管受损等的可能，另外依赖于有操作经验的介入科医生。

影像学检查对 ACTH 依赖性库欣综合征的病因鉴别及肿瘤定位是必不可少的。蝶鞍 MRI 检查为首选。MRI 薄层加强化的发现率仅 50% ~60%。采用动态强化技术能提高垂体微腺瘤的检出率。目前 MRI 诊断直径大于 3 mm 的垂体微腺瘤的准确性在 75% ~ 95%。但是ACTH增高的库欣患者垂体的微小占位并不一定是垂体库欣瘤，有可能是异位ACTH合并垂体无功能瘤，如何鉴别是非常棘手的问题，诊断不明确，治疗策略将发相径庭。

我们采用动态增强的核磁技术，通过计算核磁瘤体的的各种参数，为 ACTH 依赖性库欣的鉴别提供了更多的手段和依据。

CS-099

甲状腺癌过度诊断和治疗了吗 正方观点

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中华医学会内分泌学会全国委员，脂代谢学组副组长、《中华内分泌代谢杂志》编委、中国医师协会内分泌学会全国委员、中华医学会上海市内分泌学会副主任委员，肥胖学组组长。

近三年团队承担各类基金 30 余项，发表 SCI 文章 60 余篇，主、参编专著 10 余部。第一完成人获教育部自然科学二等奖，上海市医学科技三等奖及自然科学三等奖奖各一项，团队承担国家自然基金 19 项。

主要专业方向为年轻糖尿病的鉴别诊断、肥胖与代谢紊乱、甲状腺疾病等内分泌代谢疾病。

甲状腺癌的诊断治疗目前处于一种比较困惑和混乱的状态，虽然有指南可依，但仍存在着执行困难和理解偏差的问题。甲状腺癌发病率的升高是现实，但甲状腺癌增加的幅度受多种主观和客观因素的影响，甲状腺癌的发病 20 年间从 5 倍到 15 倍的增长使人惊恐，但相对长的生存率和较低的死亡数目又让我们对现在的治疗产生更多的怀疑，甲状腺癌的发生、发展及转移预后究竟与哪些因素相关也是迷雾重重，需要更多的基础、临床与转化医学证据。

目前存在的问题与焦点在于：

1、在正常人群中是否要进行甲状腺 B 超的检查和筛查。指南已经不推荐，但我们仍然在坚持。

2、甲状腺结节的鉴别诊断问题，对于结节性质的认识，影像学的价值，内分泌激素检查及同位素检查的时机、价值及判断问题，尚没有达到共识，执行的也不统一。

3、甲状腺细针穿刺是术前的常规步骤，但现在由于条件和技术的限制，仍没有得到广泛的普及和正确的理解，甚至还存在误区。

4、甲状腺手术的选择，如淋巴结转移、切除范围，清甲治疗等，基本形成共识，但仍存变数。

5、甲状腺预后的判断，目前的证据有限，分子生物学检测和基因突变检测提供了有效的手段，但在种族，性别及肿瘤类型中的鉴别诊断各有不同，需要更多的临床和询证医学证据。

综上所述，甲状腺癌的增多与基因、环境、生活方式、精神压力、风云变幻等均有一定的关系，但现代诊疗技术的发展及对健康的重视和不恰当的过度体检和舆论导向都是导致甲状腺癌井喷式增长的原因，我们需要更理性的分析甲状腺癌的病理基础、诊疗手段和制定合理的治疗原则。今后的研究重点可能要着眼于干预甲状腺癌发生的病理机制，寻求“静息癌”与“侵袭癌”的临床特点与分子生物学标志物，不同细胞类型甲状腺癌发生、发展的临床规律及治疗方案。推广正确的甲状腺结节的干预常识与推广甲状腺细针穿刺和发现新的分子生物学标志物可能是预防甲状腺过度诊疗的有效途径。

CS-100

甲状腺癌过度诊断和治疗了吗？反方观点

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关海霞，女，医学博士。中国医科大学附属第一医院内分泌科教授、主任医师、博士生导师。2006 年 11 月 –2007 年 12 月美国约翰霍普金斯大学医学院访问学者。中华医学会内分泌学分会青年委员、核医学分会治疗组副组长；中国抗癌协会甲状腺癌专业委员会委员、青委会副主委；辽宁省内分泌学会委员；美国内分泌学会、美国甲状腺学会会员。先后承担国家自然科学基金课题、教育部留学归国人员启动基金等课题。在美国临床内分泌代谢杂志、癌症杂志、英国临床内分泌杂志等国内外知名学术期刊发表论文。参与编写我国《甲状腺结节和分化型甲状腺癌诊治指南》和《碘 –131 治疗格雷夫斯甲亢指南》。主译《解读甲状腺癌》一书。曾获霍英东教育基金会第十二届高等院校青年教师奖三等奖。

摘要暂无

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2015-2016 年度血脂调控研究进展

陈璐璐

华中科技大学同济医学院附属协和医院

陈璐璐，华中科技大学同济医学院协和医院内分泌科主任，医学博士，教授、主任医师，博士研究生导师；

中华医学会内分泌学分会副主任委员；中华医学会内分泌学分会血脂学组组长；中国医师协会内分泌代谢医师分会常务委员；中国女医师协会糖尿病学会副主任委员；湖北省糖尿病学会主任委员；湖北省医学会常务委员；湖北省女医师协会副会长；中国胰岛素分泌研究组组长

《Jof Diabetes》、《Nature Review Endocrinology》、JCEM、柳叶刀内分泌糖尿病分册中文版、《中华内分泌代谢杂志》、中国糖尿病杂志、《华中科技大学学报医学外文版》、《临床内科杂志》等编委。

2015–2016 年度血脂调控的研究进展为临床血脂异常的防治策略提供了新的思路及依据。

既往临床实践中，血脂检查常规使用空腹样本。2016 年欧洲动脉粥样硬化协会、欧洲临床化学和实验医学联合会（EAS/EFLM）的共识中提出常规血脂检测不需要空腹，并给出了非空腹血脂的异常值范围；美国心脏协会（AHA）心血管风险评估指南专家组主席 Steven L. Driver 在 JACC 杂志上也提出了临床医生应该如何在空腹及非空腹血脂样本中进行抉择的八大意见。

美国临床内分泌医师协会和美国内分泌学会（（AACE/ACE）发布了 2016 年的 2 型糖尿病综合管理共识，根据危险分层提出了 2 型糖尿病患者血脂控制的具体目标值。2016 年美国糖尿病学会（ADA）指南给出了 2 型糖尿病患者血脂管理的启动时机、干预强度及他汀类药物的使用风险；分别强调了儿童、青少年及老年糖尿病患者的血脂控制目标。

药物治疗方面，他汀类仍是降脂治疗的排头兵，HOPE-3 研究提示在无心血管疾病的中危人群中应用他汀类药物亦可获益，进一步为该药物适用人群的扩大提供了相关数据支持。2016 年美国心脏病学学会（ACC）年会上发布了动脉粥样硬化性心血管疾病（ASCVD）风险管理中降低 LDL-c 的非他汀类降脂药物治疗的专家共识，提出了治疗方案的适用人群、用药时机及药物选择方案。近一年来，非他汀类降脂药物的相关临床研究亦获得了各自的进展。

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脂代谢紊乱，我们应该关注什么？

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近三年团队承担各类基金 30 余项，发表 SCI 文章 60 余篇，主、参编专著 10 余部。第一完成人获教育部自然科学二等奖，上海市医学科技三等奖及自然科学三等奖奖各一项，团队承担国家自然基金 19 项。

主要专业方向为年轻糖尿病的鉴别诊断、肥胖与代谢紊乱、甲状腺疾病等内分泌代谢疾病。

糖脂代谢紊乱被公认为是心脑血管疾病，肝肾功能异常的双重杀手，也是肥胖和非酒精性脂肪肝的帮凶。长期以来，我们在控制糖脂代谢异常中却顾此失彼，结果迥异。如高胆固醇血症引起冠心病已成共识，但冠心病患者却有 50% 的胆固醇水平正常，降脂治疗被认为是减少斑块，预防动脉硬化的关键因素，在发生过缺血性心脑血管疾病患者，即使血脂正常，如果伴有动脉粥样硬化和糖尿病肾病，临床上也多采用他汀类进行二级预防，降脂目标一降再降，甚至提出了越低越好的概念，但仍存非议。近年来的循证医学研究也在不断更新我们的理念，如美国营养学会取消了限制食物中胆固醇摄入的规定，对于严重的高脂血症，我们的降脂目标也有所放松，而且对于降脂药物对于血糖调节的影响和糖尿病视网膜病变的影响，现在也有争议。低脂血症和低胆固醇血症对人类的长期影响现在也逐渐引起关注。

我们现在对血脂的认识和干预还仅仅局限在降低血中的甘油三脂、LDL- 水平和总胆固醇水平，还没有上升到病因治疗和个体化治疗的高度，高脂血症的原因和类型不同，其发病的机制也有不同，治疗的措施也不同，如高甘油三脂血症与饮食，肝脏本身代谢的能力，胃肠道的分解能力都密切相关，高胆固醇血症与家族遗传，酶活性甚至内分泌激素水平都有关系，混合性的高脂血症更各有所异，而高脂血症造成的危害却不单纯和血脂水平呈正比，如脂肪肝的严重程度除了和高脂血症相关，与胰岛素抵抗和炎症也不无干系，动脉粥样硬化除了胆固醇的沉积，与血管内皮功能，吞噬细胞功能和炎症等也有关联，因此，在临床中治疗高脂血症，对病因的关注尤为重要，而对 HDL 的调控更为重要，针对 acLDL 和 oxLDL 的治疗可能收效更强，增加胆固醇的逆转录功能（RCT）和 HDL 的水平和功能可能是临床上较为有效的治疗目标。

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国内外血脂指南评析

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社会任职：中华医学会内分泌专业委员会常委；中国医师协会内分泌分会常委；中华医学会糖尿病专业委员会委员；中华医学会山西分会内分泌专业委员会主任委员；中华医学会山西分会糖尿病专业委员会副主任委员；中华预防医学会山西分会糖尿病专业委员会主任委员；山西省糖尿病防治办公室常务副主任。

1997 年我国首次出版血脂异常防治建议，是国内第一部专门针对血脂异常制定的防治指导方针。我国现行指南为 2007 年中国成人血脂异常防治指南。2014 年又另行发布中国胆固醇教育计划血脂异常防治专家建议，对 2007 年指南起到补充更新作用。2016 年 1 月，中国成人血脂异常防治指南（修订版）定稿，将从血脂检测与分型、血脂流行病学与风险评估、血脂异常治疗原则与靶目标（值）确定、血脂异常干预治疗等方面对指南进行系统全面修订。而近 30 年来，美国和欧洲等有关医学会也多次出版和更新脂代谢异常的管理指南，目的是采用最新的研究证据，为血脂异常的防治工作提供更加详细合理的指导。专题讲座将从血脂异常的定义、筛查、监测、风险评估、治疗目标（值）、治疗方案（包括他汀类降脂药物用药强度和）等角度，总结对比国内外不同医学组织发布的现行的血脂异常管理指南的异同。除上述国内指南和专家建议外，我们所解析的现行国外指南包括：2002 NHLBI 成人高胆固醇的检测、评估与治疗（成人治疗专家组 III），2013 美国心脏协会和美国心脏病学会 (AHA/ACC) 颁布的成人血脂治疗与降低心血管风险指南，2015 年美国全国血脂协会（NLA）颁布的血脂异常管理指南，2011 欧洲心脏病学会和欧洲动脉粥样硬化学会颁布的血脂异常管理指南，2016ESC 临床实践中心血管疾病的预防指南和 2013 年国际动脉粥样硬化学会（IAS ）立场报告：全球血脂异常诊治建议。这些指南和建议其基本指导思想和策略比较一致，但在具体细节制定上存在较大差异，反映出各国在脂代谢异常方面的不同的疾病特点和医疗政策的差异。我们本次解析的目的在于通过探讨这些指南的异同来为我国相关领域提供参考，使国内的脂代谢异常的防治既能保持与世界同步，也能结合我国的具体情况。

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脂代谢在肿瘤发生中的作用与靶向治疗新启示

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王桂侠，博士。主任医师，教授，博士研究生导师，吉林大学引进人才，现任吉林大学白求恩第一医院内分泌代谢科主任，曾在美国 Minnesota 大学担任副教授，同时获得美国行医执照证书。现任中华医学会内分泌分会委员，血脂组副组长、吉林省医学会内分泌分会主任委员等多项学术兼职。承担国家自然科学基金，国家卫计委项目、教育部博士点基金，中华医学会基金等多项国家级及省部级科研课题，参与美国国家科研基金课题。在国内外杂志上共发表学术论文 70 余篇，SCI37 篇。

随着对癌症研究的不断深入，很多研究者把目光集中到了肿瘤的代谢变化上。从分解代谢向合成代谢转变，作为肿瘤发生发展过程中的重要特点，成为了备受关注的新靶点。包括前列

腺癌在内，肿瘤的代谢主要有以下三个特点：第一，肿瘤细胞可以在有氧条件下，通过糖酵解途径消耗大量葡萄糖，产生大量乳酸（“有氧糖酵解”）。第二，肿瘤细胞存在高效的能量消耗，驱动更多的蛋白质和活性 DNA 的合成。最后，癌细胞的第三个重要的特点，即启动脂肪酸从头合成途径，致脂肪酸合成大量增加。

前列腺癌细胞依赖持续的脂肪酸从头合成提供大量脂质，用于膜结构的生成、能量的供给、并参与很多重要促肿瘤信号传导通路，以维持肿瘤细胞存活和旺盛的生长，并产生药物抵抗。脂肪酸经从头合成途径合成的异常增加，甚至在肿瘤的早期阶段就可以发现，与肿瘤进展快、预后差和生存期短密切相关。

脂肪酸合成酶（FASN）是最终催化脂肪酸合成的关键酶，在脂肪酸合成中起着至关重要的核心作用。FASN 在包括前列腺癌在内的诸多肿瘤中表现出促肿瘤特性，前列癌的生存和发展过程中扮演至关重要的角色。对于 FASN 的调控存在于转录、翻译以及翻译后修饰等一系列过程中。应该指出的是，在调节 FASN 表达的过程中，这些调控会同时存在，互相协同，在肿瘤细胞中，抑制生理状态下脂质合成的调节方式，持久保持FASN的高表达和高活性。而实际上，FASN的调控机制仍不十分清楚，对于 FASN 的调控机制的研究仍有待进一步的深入。

p300，也被称为 EP300 (E1A binding protein p300) 是十分重要的转录共激活因子之一，参与众多基因是转录调控，在肿瘤的发生发展过程中有着十分重要的作用。p300 在前列腺癌中的也有着重要的促肿瘤特性。

本课题组基于对p300 的染色质免疫沉淀 - 测序的分析及预试验结果，发现 p300 结合于 FASN 启动子，启动组蛋白乙酰化，转录激活FASN的表达。通过体内、外试验，进一步研究p300 对FASN调控的分子机制，及其对脂肪酸合成和肿瘤增殖的影响。并深入探讨 FASN 抑制剂与 p300 抑制剂或去乙酰化酶抑制剂的联合应用对前列腺癌的治疗效果及应用前景。本研究有助于分析转录共激活因子与 DNA 之间的相互作用，及组蛋白乙酰化对基因转录的影响；有助于更深入了解前列腺癌中脂肪酸合成的调控机制；更有助于确立前列腺癌的新的治疗靶点，以更科学合理的联合药物治疗，为前列腺癌治疗提供新的思路。

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糖尿病合并高胆固醇血症伴蛋白尿的他汀治疗

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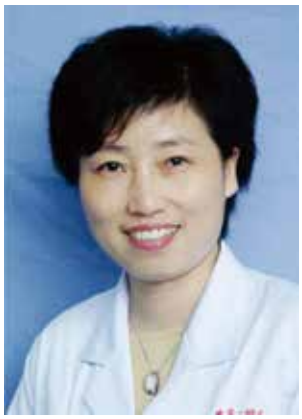

刘建英、教授、主任医师，硕导。现任南昌大学第一附属医院内科教研室主任、内分泌科科主任；兼任中华医学会内分泌学分会第十届委员会委员、脂代谢学组副组长；中华医学会糖尿病学分会第五～七届委员会委员、1 型糖尿病学组组员；中国医师协会内分泌代谢科医师分会常委；江西省内分泌学会候任主委；江西省中西医结合内分泌专业委员会副主任委员；兼任《中华糖尿病杂志》、《糖尿病临床》、《药物评价》等杂志编委。现主持国家自然科学基金 1 项、省科技厅项目 3 项，发表学术论文 40 余篇，获江西省科技进步奖一项。目前正在进行 2 型糖尿病及其并发症的研究。

糖尿病可引起多种血管并发症，严重时危及生命，糖尿病肾病可进一步增加心血管疾病的风险。研究表明，糖尿病性肾病及其心血管疾病风险的增加与血脂异常有着密切的联系：一方面，糖尿病性肾病自身可加速血脂紊乱；另一方面，血脂异常又促进糖尿病性肾病的发生发展，促进动脉粥样硬化的形成，从而为心血管事件的发生提供了有利条件。

众所周知，他汀类药物是心血管疾病一级预防和二级预防的基石，越来越多的研究表明，他汀类药物不仅可以稳定血管斑块，还可减轻肾脏蛋白尿的排泄，对肾脏起着一定的保护作用；其作用机制很可能是通过抑制 Rho 激酶的作用，减少肾脏内的氧化应激、巨噬细胞的浸润、细胞外基质的过度生产，一定程度上抑制糖尿病性肾病的发生发展。

关于糖尿病性肾病他汀药物的使用，各国指南不尽相同。我国 2014 年糖尿病性肾病防治共识中明确指出血脂的干预治疗切点与其治疗目标。而 2015 年 ADA 糖尿病指南中提出他汀的使用不是根据血脂的特点来启动，而是根据心血管风险状态；该指南还提出控制脂质能预防动脉粥样硬化病，延缓 DKD 的发展，只有他汀能降低心血管事件的发生。虽然各大指南对他汀的使用建议有所差别，但这些足以说明他汀在糖尿病，尤其是糖尿病性肾病合并高血清胆固醇和（或）高血清低密度脂蛋白的人群中应用的肯定地位，当然，他汀类药物在不同时期糖尿病性肾病中应用的获益，仍需要大量研究实践来探索和证实。

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抗骨质疏松药物的研究进展

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金小岚，1986 年 8 月—1989 年 8 月第三军医大学攻读硕士研究生，获医学硕士学位；
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内分泌科攻读博士研究生，获医学博士学位；
1995 年 8 月至今成都军区总医院内分泌科任副主任医师、主任医师、教授、科主任和副院长等职。兼任中华医学会骨质疏松和骨矿盐疾病分会副主任委员、中华医学会内分泌学分会骨代谢学组委员、四川省医学会骨质疏松专业委员会第三、四、五届主任委员、中国人民解放军内分泌专业委员会委员、成都军区血液、内分泌和肾脏病专委会主任委员、中国医院协会医疗质量管理专业委员会委员、中华医药科技奖评审委员会委员、四川省医药科技成果评审专家、中华骨质疏松和骨矿盐疾病杂志副总编、四川医学杂志编委、西南国防医药杂志编委。
发表论著 100 余篇，参编专著 9 部，译著 1 部。
获奖情况曾获国家卫生部医药科技进步一等奖，一项；
中国人民解放军医药科技进步二等奖，一项；
中国人民解放军医药科技进步三等奖，两项抗骨质疏松药物使用的现状和存在的缺陷

目前在临床上应用的抗骨质疏松药物（抑制骨吸收，促进骨形成）在增加骨量、减少跌倒、降低骨折风险和提高患者生活质量方面，发挥了重要作用。但限于对骨生物学认识水平的局限，这些药物的开发多数是以“寻宝”的方式意外发现（如，双膦酸盐），故在开发初期对其作用机制、不良反应等的认识是不足的，它们在长期的临床应用中也显现出一些缺陷：过度抑制骨转换，增加不典型性骨折、ONJ 的风险；受共患疾病的限制（药物相互作用，肾功能等）；用药方式和治疗的长期性导致依从性差；对长期用药安全性的担忧等。

骨生物学研究的进展和药物开发的潜在靶点

近些年来，随着骨细胞生物学研究的深入，尤其是对骨再建（remodeling) 和骨塑建（modeling) 及其参与细胞间相互作用机制认识的深入，发现了一些新的信号通路（如，受体、通路和酶等），为有针对性地抗骨质疏松药物的开发提供了潜在的靶点，使得新药的开发呈现出加速、蓬勃的景象：denosumab(靶点：Rank-Rankl-OPG),Cathepsin K 抑制剂（odanacatib,ODN),abaloparatide(a PTH-related peptid analog), 针对 Wnt signaling 的天然抑制子 Dkk-1 的拮抗剂和骨硬化蛋白的抗体（Romosozumab) 的开发，使更多的促骨形成的药物在不久的将来可望进入临床。还有一些正在进行临床前研究的药物有 actinin A 拮抗剂、β -arrestin analogs、calcilytics 等，还有在日本已经上市的活性维生素 D 类似物（ED-71），不仅显示出良好的疗效，还有独特的作用机制。

抗骨质疏松新药的特点及今后药物开发的方向

这些新开发的抗骨质疏松药物有如下特点：在作用机制方面，针对性强，靶点清楚，促进骨再建中破骨细胞与成骨细胞的“解偶联”，如 Cathepsin K 抑制剂（odanacatib), 在抑制破骨细胞活性的同时并不明显抑制成骨细胞活性；针对体内天然存在的影响成骨的 Wnt 途径的抑制子，骨硬化蛋白(sclerosin) 和 Dkk-1, 开发抑制剂或抗体；促进成骨；促进骨微塑建(minimodeling), 如 ED-71，促进骨形成。由于靶点清楚，有利于对骨再建的操控，不仅疗效明显提高，用药的灵活性也增加，避免对骨再建的过度抑制，降低不良反应的发生。给药方式的方便和投药间隔时间的延长提高的患者的依从性。

理想的抗骨质疏松药物应具有如下特性：1. 在多个骨骼部位均有抗骨折的效力（如脊椎、髋部和非脊椎部位）；2，对骨骼和骨外均有较好的安全范围；3. 给药方式简便和投药间隔时间长，提高依从性；4. 较少药物的相互作用；5. 价格较便宜。

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放射科医生视角 - 代谢性骨病影像学诊断

余卫

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余卫，1984 年 9 月毕业于中国医科大学医疗系。其后至今在中国协和医科大学北京协和医院放射科工作。于 1991 年获中国协和医科大学医学博士学位。1993 年 1 月 –1995 年 5 月在美国加州旧金山医学院并获博士后证书。1997 年 –1998 年由美国加州大学旧金山医学院邀请，任加洲大学旧金山医学院放射科客座副教授。1999 年晋升为教授，2002 年获准为博士生导师。现为世界卫生组织（WHO）骨质疏松特别专题组委员；美国国际骨放射学会委员；中华放射学杂志编委；中华医学会骨质疏松和骨矿盐疾病学会副主任委员；北京骨质疏松和骨矿盐疾病学会副主任委员。曾任北京 2008 年奥运会综合诊所放射科主任、中华放射学会中青年委员；中华放射学会北京分会秘书、中华医学会骨质疏松和骨矿盐疾病学会常委、秘书长。曾分别获 1998 年国家卫生部科技进步一等奖和 2003 年国家科学技术进步二等奖。

摘要暂无

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男性骨质疏松症的诊治

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裴育，解放军总医院内分泌科副主任医师，医学博士，毕业于中国医学科学院北京协和医院内分泌代谢病专业，研究方向为骨质疏松症的发病机制及综合防治。

现任中华医学会骨质疏松和骨矿盐疾病分会青年委员、中国毒理学会临床毒理专业委员会委员、北京医学会骨质疏松和骨矿盐疾病分会委员，《中华骨质疏松和骨矿盐疾病杂志》、《中国计划生育学杂志》、《药物不良反应杂志》编委。

承担全军十一五课题、国家自然科学基金青年学者项目、首都医学科研基金课题等，第一作者及通讯作者发表论文 30 余篇，SCI 引文 7 篇。获 2006 及 2008 年度军队医疗成果三等奖。

老年男性的骨质疏松性骨折往往滞后于绝经后妇女 10 年，其发生率（约为 10-25%）也仅为绝经后妇女的一半，但其髋部骨折的致死率、致残率以及骨折后再发骨折的风险均明显高于女性。因此，应重视男性骨质疏松症的防治。

男性骨质疏松症的病因及发病机制不如绝经后骨质疏松症那样清晰，性腺激素本身就直接影响着男女骨骼生物学及形态上的不同，随着增龄雌激素、雄激素以及性激素结合蛋白的变化等均影响了男性骨质疏松症的发生。

骨质疏松症是一种骨强度下降导致骨折风险增加为特征的代谢性骨病，骨强度即包括骨质又包括骨量，尽管 DEXA 骨密度测定还不能很好地显示骨质的变化，目前男性骨质疏松症的诊断仍沿用了绝经后妇女骨质疏松症的标准。

充足的钙剂（至少 1000mg/ 日元素钙）和维生素 D（至少 800IU/ 日）补充以及防摔无疑是男女骨质疏松症患者的基础防治措施，药物治疗方面除女性激素外，其他抗骨质疏松药物，如双膦酸盐、denosumab、特立帕肽、雷奈酸锶（限于某些国家）等均可应用于男性骨质疏松症人群。

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脂肪和骨骼之间的信号交流及其在骨质疏松中的病理作用

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1999 年获华西医科大学（四川大学华西临床医学院）医学博士学位；1999 年至 2001 年在北京大学第三临床医学院博士后；2001 年至 2007 年在美国印第安纳大学医学院历任博士后，副研究员，助理教授；2008 年至 2009 年在美国缅因州人类基因与健康研究所任科学家（Scientist，faculty），并担任博士研究生导师，同时兼任美国缅因大学助理教授 /Jackson Laboratory 科学家；2010 年以第一层次引进人才及四川省海外高层次留学归国人才身份回华西医院工作。

担任四川省第九届卫生厅学术技术带头人、四川省骨质疏松专委会副主任委员、四川省人才研究会理事、专家委员会副主任委员。同时担任英文杂志 Orthopaedic Surgery、Chinese Journal of Biology、Journal of Endocrine Disorders、RNA&DISEASE、World Journalof Orthopedics、中国修复重建外科杂志、中华骨质疏松与骨矿盐杂志等七种杂志编委。

已在国际、国内学术期刊发表论文 70 余篇，发表论文总影响因子超过 180，论文已被引用超过 2000 次，多次应邀到国际学术会议作大会发言。2016 年获得美国癌症研究学会（AACR）论文最高引用奖励、2014 年获得美国国家专利局授权专利一项、2010 年获得中华医学会骨科分会赵以甦骨科基础研究奖、2005 年获得美国骨矿物研究协会年度杰出青年奖、2002 年获得 SunValley 国际骨矿物研究协会年度杰出青年奖。近 5 年获得包括 4 项国家自然科学基金面上项目的多项基金资助，总研究经费 800 余万元。已经培养博士后及研究生 10 余人。

脂质代谢紊乱和骨质疏松症是中老年人群中最常见的两类疾病。近年的研究表明两类疾病间可能存在内在的相关性，证据表明在长期使用糖皮质激素所诱发的骨质疏松症的患者中，其骨髓腔内脂肪组织的含量显著增加；与此同时，骨质疏松症的患者应用他汀类药物治疗后，其骨密度增加、骨折风险显著降低。脂肪细胞和成骨细胞起源于共同的祖细胞 - 间充质干细胞 (mesenchymal stem cells，MSCs), Runx2 和 osterix 介导 MSCs 向成骨细胞分化，而 PPARγ2 介导 MSCs 向脂肪细胞分化。抑制 PPARγ 将促进 MSCs 的成骨分化而上调 PPARγ 将抑制 MSCs 的成骨分化，提示成骨分化和成脂分化为负相关。另一方面，PPARγ 在骨髓中的表达随年龄的增加而上调，这可能为增龄导致骨量减少及骨髓脂肪沉积直接病理机制。PPARγ 信号的激活还通过 PGC-1beta 和 RANKL 而促进破骨细胞的生成和骨吸收。这些证据说明 PPARγ 信号可能在骨质疏松的发生发展过程中发挥重要病理作用。

在脂肪调节骨代谢的调节方面，腹部脂肪沉积引起炎症反应所释放的炎症因子如 TNF-α, IL-6 等将上调破骨细胞形成和功能而下调成骨细胞功能、骨重建（remodeling）的偶联失衡；我们的研究提示基因敲除这些炎症因子可以逆转高脂肪饮食导致的骨量丢失。另外，脂肪细胞分泌的瘦素通过中枢系统和交感神经系统反馈至骨，促进破骨细胞对骨的吸收、抑制成骨细胞介导的骨形成而负调控骨重建，最近研究还表明瘦素可能通过血循环直接作用于成骨细胞和破骨细胞而对骨重建发挥外周调控作用；而脂肪细胞分泌的脂联素则发挥相反作用。

在骨对脂代谢的调节方面，成骨细胞产生的骨钙素以低羧化骨钙素 (undercarboxylated-osteocalcin，ucOCN) 的形式释放入血，通过血液循环达到多种组织器官调节能量代谢，作用于胰岛 β 细胞，促进胰岛素的产生和分泌。胰岛素是脂肪细胞功能活动的关键调控激素，一方面可促进脂肪细胞对葡萄糖的摄取并抑制脂肪的降解，另一方面可促进脂肪细胞的分化并调节脂肪对机体能量需求的应答。同时，低羧化骨钙素还直接作用于脂肪细胞，促进脂肪细胞分泌脂联素，增加其对胰岛素的敏感性，脂肪细胞分泌的瘦素通过交感神经系统反馈至骨，负向调控骨钙素的活化。

基于脂代谢和骨代谢的密切关系，它们之间的重要信号分子如 PPARγ、瘦素、脂联素、炎症因子和骨钙素等可能成为治疗骨质疏松症的新靶点。

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迟发性佝偻病

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承担国家自然基金 2 项，陕西省科技攻关课题 2 项。发表论文 50 余篇。

营养不良性佝偻病是由于维生素 D 缺乏 / 钙摄入不足导致的生长板软骨细胞分化和矿化障碍以及类骨质矿化障碍。对儿童 / 青少年的生长发育影响很大，严重者可以出现反复骨折或低钙性心肌病导致致死性心衰。该病婴幼儿期多发且日益受到家长重视，但对于是否存在晚发曾有争议而且家长和医生尤其是内分泌医生认识不够，导致孩童多在发生骨折或肢体明显畸形时才得以明确诊断。1977 年 Ellis 在伯明翰调查 13 岁男孩 , 发现 78% 亚裔儿童血 25 (OH) D3 接近佝偻病水平。1981 年英国的 Rewitt 对晚发性佝偻病发表了肯定性的报告。但至今没有明确的定义，一般指 3 岁以后到 19 岁。

发病率：IOM 指出，以 25(OH)D 低于 20 ng/ml-30 ng/ml 为标准欧美国家大约 20%-100% 儿童和成人维生素 D 不足或缺乏。在中国目前尚缺乏权威性的流调结果，从已发表的文献看晚发佝偻病的发病率大致在 10%-15%。尽管本病患病率较高 , 但由于其临床表现与婴儿佝偻病不同 , 其症状无特异性 , 故易漏诊或误诊。

晚发性常发生于生长发育较快的儿童 (5-15 岁), 可能与(1)生长发育迅速。(2) VitD 及钙摄入不足。(3)儿童户外活动少 , 日光照射不足有关。由于当今孩童学习压力增大，户外活动明显减少；或户外活动穿着防紫外线服装等导致近年来晚发性佝偻病发病明显增多。

诊断：依靠维生素 D/ 钙摄入不足的病史。体格检查 : 有无骨骼畸形等。实验室检查：低血钙，低血磷，低尿钙，低 25(OH)D；高 PTH，高 ALP，高尿磷。X 光片。明确诊断。

佝偻病和骨软化的主要临床表现 :

(1)低钙性癫痫、强直性痉挛;(2)威胁生命的低钙性心肌病; (3)骨痛或肌无力;(4)肢体或骨盆畸形; (5)生长迟缓; (6)发育延迟;(7)牙齿发育不良 / 畸形(8) 低钙性心肌病导致的致死性心衰。(9) 骨盆狭小导致生育时母婴死亡 .

2016 年全球预防佝偻病的维生素 D 和钙推荐剂量：

维生素 D 水平：基于 (25OHD) 水平：>50 nmol/L，充足；30–50 nmol/L，不足；<30 nmol/L，缺乏。这一推荐水平远低于 2011 年 ENDO 等推荐的美国水平。

元素钙摄入量：>500 mg/d，充足；300–500 mg/d，不足；<300 mg/d 缺乏。

1–18 岁儿童和青少年 , IOM 推荐钙摄入 700–1300 mg/d；维生素 D 补充至少 600 IU/d (15ug)。

佝偻病治疗：维生素 D 推荐剂量至少 2000 IU/d (50u g)，不同年龄、不同国家推荐剂量不一。D2/D3 效果一样，推荐口服；元素钙 500 mg/d。

希望对晚发性佝偻病能够引起内分泌医生、家长、国家的足够重视，呼吁在食品中添加维生素 D 和钙。

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原发性骨质疏松症干预的疗效监测与评估

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2005 年 5 月至 2008 年 11 月在美国 University of Rochester Medical Center,Department of Orthopedics,Center for Musculoskeletal Research 做博士后研究工作。

2014 年 9 月至 2014 年 11 月在英国 Vascular&Inflammatory Diseases Research Unit,Division of Cardiovascular&Diabetes Medicine,Ninewells Hospital&Medical School,University of Dundee 做访问学者。

现任中华医学会内分泌学分会常委、中华医学会骨质疏松和骨矿盐疾病分会常委、天津市医学会内分泌学分会副主任委员、天津市医学会骨质疏松和骨矿盐疾病分会副主任委员、美国内分泌学会会员。

担任《中华骨质疏松和骨矿盐疾病杂志》编委，JBMR 中文版编委。目前已发表学术论文七十余篇，参编学术专著五部。

随着时间的推移和学术进步以及临床经验的不断积累，骨质疏松的疗效检测和评估引起越来越多的关注。为此骨松学会在廖二元教授的主持下，经过大家的充分讨论和酝酿，形成了《原发性骨质疏松症干预的疗效检测与评估专家意见》，希望对骨质疏松症的防治工作有进一步推动作用。

由于骨质疏松症是一个静悄悄的骨流失过程，骨折风险的降低在个体不易监测，而且部分患者临床症状不明显，无法直观地观察治疗效果，通常抗骨质疏松药物治疗需要较长时间才可以显著降低临床或影像学骨折的发生率，骨质疏松患者不依从治疗的情况非常普遍。所以良好依从性是确保疗效的前提。

监测和随访的目的和意义：1. 保证药物按时正确服用；2. 保证足够的钙和维生素 D 的摄入；3. 解决患者的不良反应及患者对不良反应的恐惧；4. 确保无减少预期疗效的联合治疗或其它治疗药物；从而最大程度地降低骨折发生风险。

疗效评价的综合建议：有效：符合以下情况之一；治疗期间无新发骨折；骨密度升高；骨转换被抑制（抑制骨吸收药）

无效：符合以下情况之一；治疗期间发生二次以上新发骨折；一次新发骨折 + 骨转换（P1NP，CTX) 未被抑制（变化 <25%）；一次新发骨折 + BMD 明显下降 (腰椎 BMD 下降 ≥5%；股骨 BMD 下降 ≥4%)。

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REACTION 研究

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毕宇芳，上海交通大学医学院附属瑞金医院内分泌代谢科，主任医师、博士生导师，上海市内分泌代谢病研究所副所长。兼任中华医学会内分泌学分会委员与青年委员会副主任委员，主要致力于 2 型糖尿病的临床诊治与早期防控研究，在 JAMA、JACC、DiabetesCare、JCEM 等 SCI 收录杂志发表论文 60 余篇。作为第一责任人分别承担国家自然科学优秀青年基金与国际合作基金。

中国 2 型糖尿病患者恶性肿瘤发生风险的流行病学研究 (Risk Evaluation of cAncers in Chi-

nese diabeTic Individuals: a lONgitudinal study，REACTION Study) 是在 40 岁以上中国社区人群中开展的一项前瞻性队列研究，通过对糖尿病相关代谢指标、并发症、心血管事件发生及恶性肿瘤发生情况进行调查，从而探究糖尿病与恶性肿瘤发生风险的相关性，提出了对中国不同地区人群代谢状况的评估及诊断切点，分析糖尿病患者及糖耐量异常人群胰岛素抵抗与 β 细胞功能的相关性，同时也揭示糖代谢异常人群骨质疏松、肾脏损伤、甲状腺结节等疾病的流行现状及相关危险因素。该大型队列研究为肥胖、糖尿病等代谢性疾病的高危因素、发病机制、早期诊断、并发症管理、与恶性肿瘤发生风险相关性等诸多重要问题的研究提供了一个资源丰富的探索平台。研究基线结果初步显示，糖尿病人群的恶性肿瘤患病率明显高于糖代谢正常人群。糖尿病病史、糖尿病病程、血糖水平与恶性肿瘤的患病风险存在相关性。研究目前随访进展中，期待进一步深入阐述糖尿病与恶性肿瘤的相关性。

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Compass 研究及其对临床工作的启示

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中华医学会糖尿病学会前任主任委员、国际糖尿病联盟（IDF）副主席、北京市糖尿病学专业委员会名誉主任委员、亚洲分子糖尿病学会理事、中国医师学会循证医学委员会常务委员、北京市内分泌学会理事。

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摘要暂缺

CS-114

妊娠早期甲状腺功能干预（SHEP）研究

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摘要暂缺

CS-115

牛磺酸在高血压前期患者降低血压和改善血管功能的随机、双盲和安慰剂对照研究

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目的 高血压是脑卒中、心力衰竭以及肾功能不全的独立危险因素，高血压前期是血压从正常到升高的关键过渡期。牛磺酸（Taurine）在高血压大鼠动物模型证实有降低血压作用，但有关牛磺酸对高血压人群的临床研究甚少。我们前期研究发现 TRPC3 在高血压发病中发挥重要作用，CBS 和 CSE 是硫化氢（H2S）合成的关键酶。因此，是否长期小剂量的 taurine 干预能够通过促进 H2S 合成，抑制 TRPC3，进而对高血压前期人群有降压并改善血管功能的作用尚未见报道。

方法 本研究为前瞻性、随机双盲、安慰剂对照的临床研究。从 2012 年 12 月到 2014 年 12 月期间，在重庆市高血压研究所招募高血压前期志愿者。经体格检查和实验室筛查入选高血压前期 120 名为研究对象，随机分为安慰剂组（1.6 克 / 天）和 taurine 组（1.6 克 / 天）干预 12 周，并于第 4、8、12 周随访及检测相关指标，包括诊室血压和 24h 动态血压，血管功能等相关指标。机制研究包括对 $TRPC3^{-/-}$ 小鼠的主动脉和肠系膜动脉、健康志愿者的肠系膜动脉以及 SHR 大鼠的主动脉进行免疫印迹、免疫荧光、血管舒张反应以及细胞内钙浓度测定。

结果 两组患者在基线时各项指标无统计学差异。（1）在 12 周干预终点时，49 例 taurine 组和 48 例安慰剂组的高血压前期志愿者完成研究，完成率均大于 80%；（2）与安慰剂相比较，taurine 干预能显著降低高血压前期志愿者的诊室血压及 24 小时动态血压；（3）Taurine 能显著改善内皮依赖（FMD）及非依赖的血管舒张功能（NMD）；（4）Taurine 干预能明显增加血浆 taurine 及 H2S 的水平，且 taurine 干预组的血压下降值与血浆 taurine 和 H2S 水平呈显著的正相关；（5）Taurine 干预在人肠系膜动脉（离体实验）以及饮 taurine 水的 SHR 大鼠主动脉（在体实验）增加 H2S 合成关键酶 CSE 和 CBS 的表达，抑制血管平滑肌 TRPC3 蛋白表达；（6）离体研究证实 H2S 的供体 NaHS 能抑制人肠系膜动脉苯肾上腺素介导的钙内流及血管收缩反应；分离 $TRPC3^{-/-}$ 小鼠肠系膜动脉，发现 NaHS 能抑制 WT 小鼠的肠系膜动脉 PE 介导的钙内流，而这种作用在 $TRPC3^{-/-}$ 小鼠中减弱。

结论 牛磺酸干预能降低高血压前期人群的血压并改善血管功能，机制是通过促进 CSE / CBS 的表达并抑制 TRPC3 介导的钙内流。

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SMART 研究报告

母义明

中国人民解放军总医院

母义明，解放军总医院内分泌科主任，主任医师、教授，博士生导师。清华大学医学院教授，博士生导师和南开大学学院教授，博士生导师。现任中华医学会内分泌学分会主任委员，解放军医学会内分泌专业委员会主任委员，中国医师协会内分泌代谢分会副会长，北京市医学会糖尿病学分会前任主任委员，《中华内分泌代谢杂志》、《中国医学前沿杂志》和《实用内科杂志》副主编、《药品评价杂志》主编、《中华内科杂志》和《中华糖尿病杂志》等杂志编委。《J Clin Endocrinol Metab》中文版主编、《Nat Rev Endocrinol》和《Lancet Diabet Endicrinol》中文版副主编。在 SCI 期刊发表论文 150 余篇，国内核心期刊发表论文 200 余篇。承担国家重大科技研究项目 3 项和国家自然科学基金 4 项，2008 年获得全军杰出青年基金。2012 年被中华医学会授予杰出贡献奖。

既往数据已经表明，DPP-4 抑制剂的疗效与 AGI 相似，但其 GI 耐受性更佳，因此这种治疗选择对于 T2DM 患者也更具吸引力。但是，至今从未有临床试验比较沙格列汀与 AGI 相比的疗效和安全性。

SMART 研究是一项为期 24 周、多中心、随机化、平行组、开放性、活性对照、IV 期临床研究，该研究旨在评估二甲双胍单药治疗控制不佳的 2 型糖尿病 (T2DM) 患者接受沙格列汀联合二甲双胍治疗与阿卡波糖联合二甲双胍治疗相比的疗效、安全性和耐受性的为期 24 周、多中心、随机化、平行组、开放性、活性对照、IV 期临床研究。

该研究于 2014 年启动，共有来自 35 个研究中心的 488 例患者参加该研究，符合方案的患者随机分为沙格列汀（5mg/ 次，1 次 / 天，n=238）联合二甲双胍和阿卡波糖（100mg/ 次，3 次 / 天，n=243）联合二甲双胍治疗。12 周的研究结果显示，沙格列汀联合二甲双胍降低 HbA1c（分别为 -0.79% versus -0.61%, p=0.0355）和空腹血糖（分别为 -1.06 mmol/L versus -0.63 mmol/L, p=0.0086）。24 周的研究结果显示，沙格列汀联合二甲双胍非劣于阿卡波糖联合二甲双胍，降低 HbA1c 分别为 -0.82% 和 -0.78%, p=0.6236，并且两组空腹血糖（分别为 -0.99mmol/L 和 -1.01mmol/L, p=0.8915）和餐后 2 小时血糖（分别为 -0.77 mmol/L versus -1.07 mmol/L, p=0.2248）的变化无统计学差异。此外，沙格列汀组发生胃肠道不良反应的患者显著低于阿卡波糖组，分别为 5.5% 和 24.5%，P< 0.0001。两组低血糖的发生率相似，沙格列汀组为 1.2%，阿卡波糖组为 1.6%，两组均无严重低血糖病例发生。该研究提供证据证实中国 2 型糖尿病患者接受沙格列汀与阿卡波糖相比的疗效和安全性，为临床医生在二甲双胍单药治疗无效，选择二线治疗时提供更多临床证据。

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思维模式转变的驱动力 -LEADER 研究对 2 型糖尿病管理的影响

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兼任中国医师协会内分泌代谢医师分会副会长、中华医学会糖尿病学会前任主任委员、国际糖尿病联盟（IDF）副主席、北京市糖尿病学专业委员会名誉主任委员、亚洲分子糖尿病学会理事、中国医师学会循证医学委员会常务委员、北京市内分泌学会理事、国际糖尿病联盟亚洲西太平洋地区（IDF）糖尿病政策组成员、国际自我血糖监测（SMBG）研究组督导委员会成员、世界糖尿病同盟（GDA）督导委员会成员。

严格的血糖控制是否能够减少糖尿病患者的心血管风险一直存在争议，FDA 于 2008 年制定了评估降糖药物的心血管安全性的行业标准，要求企业应当确保新型降糖药物不会导致心血管风险的明显升高。因此，2008 年后面世的新型降糖药物均陆续开展了心血管结局研究（CVOT），以证实降糖药物的心血管安全性。2016 年 6 月，评估 GLP-1 受体激动剂利拉鲁肽的 CVOT 研究——LEADER 研究结果公布，显示 GLP-1 受体激动剂利拉鲁肽能够显著降低 2 型糖尿病患者主要心血管不良事件风险。本讲座将纵览降糖药物的 CVOT，并着重介绍 LEADER 研究的研究设计，基线数据和研究结果，并围绕 LEADER 研究的临床意义展开讨论。

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透过结果，解析本质—LEADER 研究的机制解析及临床意义

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2010– 至今　哥本哈根大学健康科学院，诺和诺德基础代谢研究基金中心研究总监
2005– 至今　哥本哈根大学健康科学院糖尿病与肥胖研究中心主席
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1999– 至今　医学院课程委员会成员
1983–1991　哥本哈根大学医学院临床前研究 ("studienævn") 委员会主席
Endocrinology(内分泌学),J Clin Endocrinol Metab(临床内分泌代谢杂志),Diabetes(糖尿病),J Diabetes invest(糖尿病研究杂志) 编委。

利拉鲁肽的心血管结局研究 LEADER 在今年 ADA 上公布了结果，它是目前唯一一个获得证实可以带来心血管获益的肠促胰素类降糖药物。虽然目前学界对利拉鲁肽心血管获益的机制尚不十分明确，但由于利拉鲁肽可以明确的降低血糖，减轻患者体重，还可以带来血压和血脂的改善，因此这种心血管获益很可能是来自于这种综合的疗效。另外，很多研究也发现，利拉鲁肽可以直接或间接的作用与心脏和血管内皮，还可以延缓动脉粥样硬化的进展，这些也可能参与到其心血管获益的作用中。虽然，我们目前无法明确的了解利拉鲁肽心血管获益的确切机制，但是 LEADER 研究证实了利拉鲁肽显著降低 MACE 风险达 13%，降低心血管死亡风险达 22% 及全因死亡风险下降 15% 是确实可信的，这一定会给糖尿病患者带来福音，使他们在降糖的同时获得更全面的获益。

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探讨 2 型糖尿病合并肥胖 / 超重患者的临床管理规范

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肥胖是导致 2 型糖尿病发生的重要因素，二者常合并存在。中国 2 型糖尿病患者的超重和肥胖的比例高达六成，其中中心性肥胖比例也非常高，对这部分人群应加以关注。

因此，《探讨 2 型糖尿病合并肥胖超重患者的临床管理规范》针对 2 型糖尿病合并肥胖 / 超重人群，探讨和制定科学、规范、具有可操作性的临床管理规范，以期规范临床管理环节、提

高血糖达标率及体重控制率、降低心血管疾病风险、改善患者生活质量。主要内容包括：多学科诊疗团队的组建、高危肥胖个体的筛查、患者的确认、登记患者基本信息、完善辅助检查、患者评估和分级、制定干预方案、实施干预措施。本规范通过对以上八关键步骤的系统化和规范化，以期作为指导临床医生诊断和治疗的 2 型糖尿病合并肥胖 / 超重患者的参考。

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短期胰岛素强化序贯艾塞那肽治疗对新诊断 2 型糖尿病 2 年血糖缓解率的影响

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承担国家自然科学基金课题和省市级科研课题 10 余项。

发表学术论文 50 余篇，其中 SCI 收录 20 篇，出版专著 5 部。

目的：新诊断初治 2 型糖尿病患者经短期胰岛素强化治疗虽可诱导血糖长期缓解，但大多数患者在 1-2 年内将再次面临高血糖。艾塞那肽具有多重胰岛 β 细胞保护作用，短期胰岛素序贯艾塞那肽治疗是否能诱导更高的血糖缓解，目前尚无相关报道。因此，该随机平行对照试验旨在探讨短期胰岛素强化后序贯艾塞那肽治疗对新诊断 2 型糖尿病患者 2 年血糖缓解率的影响。

方法：157 例新诊断 2 型糖尿病患者在 2012 年 10 月 -2014 年 10 月经厦门大学附属第一医院筛选，其中 129 例被随机分到短期胰岛素强化组（对照组，n=63 例）及艾塞那肽序贯治疗组（试验组，n=66 例）。两组患者首先均给予胰岛素泵持续皮下胰岛素输注治疗，血糖达标并强化 2 周后停用，对照组仅单纯饮食、运动治疗，而艾塞那肽组则在饮食和运动治疗的基础上给予序贯艾塞那肽治疗 12 周停用。治疗前后、1 年及 2 年时检测血糖、血脂及胰岛素，计算稳态模型 β 细胞功能指数 (HOMA-β) 和胰岛素抵抗指数 (HOMA-IR)。主要终点为 2 年血糖缓解率。该研究已在 ClinicalTrials 和 www.chictr.org.cn 注册，注册号：NCT01776788 和 ChiCTR-IPR-15006298。

结果：短期胰岛素强化治疗后 1 和 2 年，艾塞那肽序贯组分别有 47 例和 37 例患者仍保持血糖处于缓解状态，血糖缓解率分别为 68.2 ± 5.7% 和 53.0 ± 6.1%，而胰岛素强化组分别仅 25 例和 22 例患者血糖保持缓解，血糖缓解率分别为 36.5 ± 6.1% 和 31.8 ± 5.9 %，艾塞那肽序贯组血糖缓解率明显高于胰岛素强化组，有统计学意义（log-rank tests: p-values<0.001）。然而，进一步研究分析显示，血糖缓解率的差异主要来源于治疗的前 12 周，后续随访差异无明显统计学意义。在 12 周时，与胰岛素强化组相比，艾塞那肽序贯组腰围、低密度脂蛋白和糖化血红蛋白明显降低，有统计学意义，但在随访 1 年和 2 年时，差异消失。矫正混在因素后，艾塞那肽治疗和高的基线胰岛功能与高血糖复发低风险相关，而糖尿病阳性家族史与复发高风险明显相关。

结论：短期胰岛素序贯艾塞那肽治疗对血糖缓解率的影响主要发生在艾塞那肽治疗的 12 周，但在停止治疗后，这种优势将逐渐消失。

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DPP-4 抑制剂中国人群新证——SUNSHINE 研究结果解读

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第六届全国优秀科技工作者，中国女医师协会五洲女子科技奖。享受国务院特殊津贴。上海市领军人才、上海市优秀学科带头人、上海市“十佳”医生。现任中华医学会内分泌学分会副主任委员，中国医师协会内分泌代谢科医师分会总干事，上海市医学会内分泌学会主任委员、上海康复学会糖尿病分会副主任委员，《Journal of Diabetes》杂志副主编。目前承担科技部国际科技合作专项，国家自然基金重点课题、十一五攻关计划等多项课题。发表 SCI 论文 100 篇 (JAMA 及 Science 通讯作者等)。三次获国家科技进步二等奖，第一完成者获上海科技进步一等奖、上海医学科技奖一等奖、上海医学科技推广将及中华医学科技奖三等奖等。

新型降糖药物 DPP-4 抑制剂由于其降糖疗效和良好安全性，在临床上应用越来越广泛，并被多项国际权威指南推荐使用，地位得到快速提升。为了在更大规模的人群中进一步探索 DPP-4 抑制剂沙格列汀对中国患者的疗效与安全性，SUNSHINE 研究随之而生。该研究由宁光院士牵头，国内 92 家中心参与，是一项为期 24 周、单臂、多中心、队列研究，旨在评估在单用饮食运动或者稳定二甲双胍剂量治疗血糖控制不佳的中国 2 型糖尿病患者中，沙格列汀 5 mg 每天一次治疗的疗效和安全性。研究结果证实，沙格列汀降低 HbA1c 达 1.61%，且低血糖风险小，整体安全性良好，是临床上 2 型糖尿病患者单药和联合治疗的理想选择之一。

CS-122

创新机制：肾脏在 2 型糖尿病血糖调控中的作用

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杨文英，主任医师、教授、博士生及博士后导师。中日友好医院内分泌代谢病中心主任、中日友好医院大内科教研室主任、曾任大内科主任，医院学术委员会主任、曾任中华医学会糖尿病分会主任委员、亚洲糖尿病学会副主席、曾任卫生部慢病咨询委员会委员，糖尿病组副组长、曾任《中华糖尿病杂志》主编、现任荣誉主编。

2012 获得北京市科技进步一等奖、中华医学会科技进步二等奖、2012 年度全国卫生系统先进个人、2013 年获首届亚洲糖尿病学会（AASD）糖尿病流行病学奖、2015 年中华医学会糖尿病分会科学贡献奖。近几年已发表在国内、外核心期刊论文 450 多篇。包括：NEJM、The Lancet diabetes& endocrinology、BMJ、Circulation、European Heart of Journal、Diabetes Care 等。

近年来，超重肥胖和糖尿病的患病率快速上升，血糖、血压和血脂达标欠佳、低血糖风险及体重等心血管危险因素管理面临巨大挑战，目前大部分降糖药物是基于依赖胰岛素的降糖机制，降糖疗效随着 β 细胞功能减退而难以持久，部分药物还存在体重增加、低血糖等副作用。随着对病因认识的逐步加深，糖尿病的管理已由“以血糖为中心”逐步发展为“多病因的、综合管理”模式转变。而作为“八重奏”靶点之一的肾脏却没有得到足够的重视，实际上肾脏在糖代谢调节乃至能量稳态调节中扮演重要角色，肾脏每日滤过和重吸收 180g 葡萄糖，其中 90% 葡萄糖重吸收由钠 - 葡萄糖协同转运蛋白 2(SGLT2) 负责。肾脏葡萄糖最大重吸收量取决于肾糖阈，而 2 型糖尿病患者的肾糖阈比正常人约升高 15%，导致

葡萄糖重吸收和再循环增加，加重高血糖的状态。SGLT-2 抑制剂可以降低肾糖阈，使多余糖分随尿排出体外，达到显著而长期的降糖效果，SGLT2 抑制剂可以通过排除体内多余葡萄糖，恢复糖代谢平衡，并显著持续地减轻体重，轻度降低血压等优势，实现对 T2DM 的多重获益，与当前综合管理理念不谋而合，值得研究者和临床工作者的关注和期待。

CS-123

SGLT-2 抑制剂临床循证与实践

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李玉秀，中国医学科学院糖尿病研究中心副秘书长，中华医学会内分泌学会第十届委员会常务委员，中华内分泌学会肝病与代谢学组、糖尿病学组委员，国家医师资格考试临床类试题开发委员会委员、内分泌组长，中华内分泌代谢杂志、中华老年多器官疾病杂志、英国医学中文版等杂志编委。

达格列净是一种强效、高选择性的 SGLT-2 抑制剂，通过促进多余葡萄糖排出降低血糖。在国内外一些列研究中均观察到在降低血糖的同时，还可以降低体重和血压。在亚洲人群中同样完成了达格列净的有效性和安全性研究，在此研究中采用多中心、平行、双盲对照试验，纳入 393 例未经治疗血糖控制不佳（10.5%≤HbA1c≤7.0%）的亚洲 T2DM 患者。纳入患者随机进行安慰剂或达格列净 5mg/10mg 治疗，观察治疗 24 周后的 HbA1c、FPG、2hPPG、体重等指标的变化，旨在评估达格列净的疗效和安全性。该研究纳入的患者中 89% 为中国糖尿病患者，为首个评估 SGLT-2 抑制剂在中国人群中疗效和安全性的临床实践研究。中国人群的亚组分析显示，治疗 24 周时达格列净 10mg 显著降低 HbA1c 达 1.16%，降低 FPG 达 1.82mmol/l，降低 2hPPG 达 3mmol/l，HbA1c 达标率达到 52.5%，体重减少 2.33kg，并具有良好的安全性和耐受性。研究结果表明，达格列净在中国人群中降糖疗效显著的同时并带来额外的获益——减轻体重，作为第一个即将在中国上市的 SGLT2 抑制剂值得瞩目和期待，将为 2 型糖尿病患者的治疗带来新希望。

CS-124

聚焦 SGLT2 抑制剂与肾脏安全性

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1993 年毕业于北京医科大学，毕业后一直在北京协和医院内科工作，任住院医师，住院总医师；2000 年毕业于中国协和医科大学，获医学博士学位，继续在北京协和医院肾内科工作，先后任肾内科主治医师，副主任医师，主任医师，教授；2002 — 2003 作为访问学者于英国伦敦大学学院皇家自由医院肾内科学习工作；2003 年底至今一直担任北京协和医院肾内科副主任；2005 年被中国协和医科大学聘为硕士研究生导师；2012 起任北京医师协会肾脏病分会副会长，北京内科医师协会常务理事，2014 年起任北京协和医院内科学系副主任。

主要从事各种原发和继发性肾脏病的临床诊治工作。擅长难治性肾病综合征，IgA 肾病，狼疮性肾炎，高血压肾损害和糖尿病肾病等疾病的治疗。

科研方面，主要从事肾脏脂质代谢和肾脏病理方面的研究。

2000 年以来以第一作者或通讯作者在国外和国内核心刊物上发表论文共 50 余篇，其中论

著 30 余篇。

SGLT-2 抑制剂可以降低肾糖阈，使多余糖分随尿排出体外，达到显著而长期的降糖效果。但 SGLT-2 抑制剂的作用机制也引起了临床医生对肾脏安全性的关注：是否会带来肾功能损害？是否会引发不可控制的泌尿系统感染？循证研究显示：在肾功能方面，SGLT-2 抑制剂对血肌酐、尿素氮等常规指标无影响，长期使用 eGFR 变化保持稳定，另有证据提示 SGLT-2 抑制剂对肾脏存在潜在保护作用，如降低血尿酸水平，通过调节管球反馈平衡延缓早期肾病进展，长期使用可以改善尿白蛋白的转归等。虽然 SGLT-2 抑制相比安慰剂增加了尿路感染和生殖器感染的发生率，但这些不良反应多为轻、中度，且常规治疗后即可恢复。相信随着研究的深入开展，更多的可靠数据将能为 SGLT2 抑制剂肾脏安全性新的佐证。

CS-125

在分级诊疗大环境下推进市级内分泌代谢科建设体会

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苏晓清，主任医师，教授，硕士研究生导师，萍乡市人民医院院长，江西省医学会理事，江西省内分泌学会常委，中国医院协会地市级医院分会委员，中国医院协会健康与疾病管理委员会宣讲员，从事内分泌专科领域的相关研究，先后在国家级和省级杂志上发表学术论文 16 篇，主持 4 项、承担及参与的 4 项省市级科研课题均通过鉴定，达到国内、国际先进水平，分获省科技进步二等奖一项，萍乡市科技进步奖一等奖一项、二等奖六项。近来领衔内分泌实验室从事糖尿病足等治疗的相关研究已获得初步成果

近年来，国家加强了对县、区医院服务能力建设，内分泌疾病诊疗水平明显提升，江西省于 2015 年试点 糖尿病分级诊疗，在这大环境下，萍乡市人民医院内分泌代谢科面对新形势，在学科建设上创新理念，推出新举措，迈开新步伐，学科不仅没受到冲击和影响，而且达到了做强做优的目标。主要措施如下：

1. 着力于人才引进；
2. 依托解放军总医院、上海瑞金医院等名院培养内分泌医务人员；
3. 依托全国本学科名师培养学科带头人；
4. 依托名校开展临床科研工作，开展研究生联合招生及培养工作；
5. 强化内涵建设，落实诊疗规范及临床路径，确保质量及安全；
6. 与眼科、心血管、肾病等专科开展糖尿病联合诊疗工作；
7. 与县区乡镇医疗机构建立上下联动的网络会诊平台；
8. 建立全院数字化血糖管理平台；
9. 建立全市糖尿病医生微信群，主导全市糖尿病分级诊疗工作。

通过上述措施，萍乡市人民医院内分泌代谢科业务量稳步上升，业务收入快速增加，近五年科室获得了江西省省市共建重点学科，获得了国家临床药物机构资格，获得省市科技成果奖 6 项。

中青年英文演讲比赛

Y-01

The microRNAs in the pathogenesis of metabolic memory

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Aim "Metabolic memory" is identified as a phenomenon that previous exposure to hyperglycemia results in the long-lasting deleterious effects on cardiovascular events. More and more researches show that epigenetics plays an important role in the pathogenesis of metabolic memory. It remains unclear whether microRNA (miRNA) dysfunctions participate in the event.

Methods In this study, the models of metabolic memory were established in endothelial cells and wistar rats. The miRNA arrays on human aortic endothelial cells were adopted to seek the miRNAs that may be involved in the metabolic memory and were verified in vivo and in vitro.

Results Sixteen miRNAs were found differentially expressed. Among these miRNAs, the expressions of miR-125b, miR-146a-5p, and miR-29a-3p were associated with persistent impaired endothelial function and altered proinflammatory gene expressions, including nuclear factor-κB (NF-κB) subunit p65. Direct inhibition of miR-125b expression or increased miR-146a-5p expression blunted NF-κB signals and improved the endothelial function. Luciferase reporter assays confirmed the biochemical relationship for miR-125b targeting on TNF-alpha-induced protein 3 and miR-146a-5p targeting on TNF receptor-associated factor 6 and IL-1 receptor-associated kinase 1 during the activation of NF-κB pathway.

Conclusion Our findings demonstrate that glucose induced changes in miR-125b and miR-146a-5p are related to the long-lasting activation of NF-κB pathway and contribute to follow-up metabolic memory.

Y-02

Ablation of TSH receptor delays atherosclerosis development by reducing macrophage inflammation

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Background and Objectives The association between TSH elevation and cardiovascular disease has long been attributed to the metabolic disparities in subclinical hypothyroidism and hypothyroidism. However, atherosclerosis is driven by chronic inflammation and whether TSH can influence the inflammation directly remains unknown. Our study aims to examine the direct effect of TSH on vascular inflammation in atherosclerosis and the mechanism underlies.

Methods An epidemiologic study (n=1110) was carried out in Ningyang, Shandong using carotid intima medium thickness (CIMT) and serum TNF-α as the indicator of atherosclerosis and inflammation, respectively, to explore their associations with TSH in the population. To study the effect of TSH on atherosclerosis, $Tshr^{-/-}$ and $Tshr^{+/+}$ mice of $Apoe^{-/-}$ background were obtained by crossing $Tshr^{+/-}$ mice with $Apoe^{-/-}$ mice, and $Tshr^{-/-}$ $Apoe^{-/-}$ mice were supplemented with 100 ppm thyroxine in the diet to maintain a thyroxine level comparable to their littermates. The size, composition and inflammation mediators of the plaques between $Tshr^{-/-}$ $Apoe^{-/-}$ and $Tshr^{+/+}$ $Apoe^{-/-}$ were compared 12, 16, or 20 weeks after the initiation of high fat diet (HFD) (2% cholesterol and 15% saturated fatty acid). The aorta and serum of macrophage-specific Tshr knockout (MKO) mice fed the HFD were further analyzed to examine the significance of the action of TSH on macrophages. The direct effect of TSH on macrophages was studied by treating macrophages with TSH in vitro, and MAPK inhibitors and Tshr siRNA were applied to elucidate the pathways involved in the action of TSH.

Results TSH levels positively correlated to serum TNF-α level and atherosclerosis in the population and TSH positively predicted CIMT in a multiple regression model controlling other traditional risk factors. Serum lipid profile and thyroid function were comparable between $Tshr^{+/+}$ $Apoe^{-/-}$ and $Tshr^{-/-}$ $Apoe^{-/-}$ mice. However, Decreased lesion size, plaque macrophages and vascular inflammatory mediators expression in the $Tshr^{-/-}$ $Apoe^{-/-}$ mice were discovered by Oil Red O stiaining, F4/80 immunohistochemistry and qPCR of the aorta, respectively, while SMA immunohistochemistry and Sirius Red revealed no significant differences in the smooth muscle cell components and collagen in plaques. Similarly, decreased inflammatory mediators in serum and vascular tissues were observed in MKO mice fed the HFD. qPCR and ELISA revealed dose-dependent induction of TNF-α and IL-6 after TSH treatment in macrophages in vitro, accompanied with IκB/NF-κB and MAPK pathways, and the response is much stronger than that in endothelial cells and smooth muscle cells. Application of ERK inhibitor (U0126), JNK inhibitor (SP600125) or TSHR siRNA was able to diminish these pro-inflammatory effects of TSH, and U0126 and SP600125 were found to work synergistically.

Conclusion Our study revealed a novel proinflammatory

effect of TSH on macrophages, which is mediated by TSHR, mediated by a TSHR/ERK&JNK/IkB/NFkB pathway, and is likely involved in the aggravation of atherosclerosis induced by TSH.

Y-03

Systematic safety evaluation of encapsulated xenogeneic islets transplantation

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Islet transplantation technology is a potential alternative therapy for type 1 diabetes, but the short supply of organ donators and the administration of immunosuppressive medications limit their use. Encapsulated islets transplantation technology can use islet cells from various sources, including allogeneic and xenogeneic islets, without any immunosuppressants. Although the material used for microcapsules is not considered intrinsically toxic, it may pose potential risks to human health, thereby raising public concern. Therefore, it is important to study the systematical toxicity of the encapsulated islet transplantation on receptors.

Aim To study the systematical toxicity of the encapsulated islet transplantation on receptors.

Materials and methods C57BL/6 mice (18-22 g) were divided into seven groups to test for acute and subacute toxicity. Two experimental groups received an intraperitoneal injection of encapsulated SD rat islets (alginate-polylysine-alginate microcapsules, APA), two experimental groups were injected with SD rat islets, two experimental groups were injected with APA microcapsules, while the control group was injected with a 0.9% NaCl aqueous solution, and the doses of all groups were 12.5 mL/kg. Mice body weight and symptoms were monitored for 14 days after the injection. At 3 and 14 days post injection, mice were sacrificed. Blood samples were collected from each mouse for chemistry test analyses, using an Automatic Biochemical Analyzer (Reflotron Plus, Roche). The major organs (heart, liver, lungs, kidneys, brain, spleen, thymus, stomach, small intestines, colorectum, and testicles or ovaries) were removed for gross and histological examinations. Statistical analyses were based on the standard deviations (SD) of 10 mice per group. Data are represented as mean ± SD. *P < 0.05 compared with that from mice in the control group by one-way ANOVA test.

Result and Discussion Encapsulated islet cells, APA microcapsules and islet cells (at the dose of 12.5 mL/kg) did not cause mortality in the exposed mice; moreover, no obvious clinical sign of toxicity was observed. C57BL/6 mice exposed to encapsulated xenogeneic islet cells, APA microcapsules and islet cells appeared healthy, and their body weight was similar to that of control mice (P > 0.05). No significant difference was found in the weight of the major organs (liver, spleen, kidney, thymus, ovary, and testis) among the experimental and control groups (both male and female, P > 0.05). Three and 14 days after exposure, all biochemical parameters of female and male mice appeared to be normal compared to the control groups. Although some of these parameters show rising trend among in the experimental than control group, these values were not statistically different (P > 0.05), nor biologically significant. Histopathological analysis was performed on the aforementioned harvested organs. We failed to observe organ damage and histopathological abnormalities in the experimental groups.

Conclusion In this study, the acute and subacute toxicity of the prepared microcapsules was systematically evaluated. No abnormalities or lesions were observed in the major organs examined. Although further examination needs to be conducted in larger animals and clinical trials, our results suggest that microcapsules may be safe for islets transplantation.

Y-04

1 case report of type B insulin-resistance syndrome and reviews of the literatures

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Background The type B insulin-resistance syndrome is characterized by the presence of anti-insulin receptor antibodies(AIRA)，which cause severe insulin resistance. It is one of a class of disease in which an autoantibody is produced against a cell surface receptor, Graves disease and myasthenia gravis are typical of these disease. However, the type B insulin-resistance syndrome is quite rare, and frequently associated with a history of other autoimmune disease such as underlying connective tissue disease. It typically presents with hyperinsulinemia, acanthosis nigricans(AN), and severe hyperglycemia that is poorly responsive to large doses of insulin but may also cause episodes of hypoglycemia if the responsible immunoglobulins stimulate rather than inhibit the signal-transducting activity of the insulin receptor. This rare autoimmune disorder has been treated with various forms of immunosuppression with mixed success.

Objective To report a rare case of diabetes mellitus caused by type B insulin-resistance syndrome. To discuss the diagnostic and therapeutic strategies of this case. And to achieve quantitative determination of anti-insulin receptor antibody in the patient's serum.

Methods 1. We make the therapeutic protocol referred to

published literature since 1975 when the type B insulin-resistance syndrome was first described. The patient was treated with an intensive combination protocol of corticosteroids(methylprednisolone) and mycophenolate mofetil aimed at control of pathogenic autoantibody production. Hematological, metabolic and endocrine parameters were monitored before and after treatment.2. Quantitative determination of anti-insulin receptor antibody in the patient's serum before and after treatment using the anti-insulin receptor antibody bioassay ELISA kit(human) bought from "USBiological".

Results A 57-year-old woman had these clinical features: severe hyperglycemia poorly responsive to large doses of insulin, hyperinsulinemia, insulin autoantibody negative, acanthosis nigricans(AN) and history of rheumatoid arthritis and Sjogen's syndrome. This case was confirmed by Quantitative determination of anti-insulin receptor antibody in the patient's serum before and after treatment. After the combination protocol of corticosteroids and mycophenolate mofetil, she gained symptom remission and her fasting blood glucose was around 7mmol/L, but postprandial blood glucose was still high.

Conclusions According to manifestation, laboratory test and quantitative determination of anti-insulin receptor antibody, this patient can be diagnosed as type B insulin-resistance syndrome. The combination protocol of corticosteroids(methylprednisolone) and mycophenolate mofetil is effective for this case.

Y-05

Role of AVPR2/3 receptors in ACTH secreting tumors and potential therapeutic implications

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Introduction Research on corticotrophin tumor receptors provided new insight for the diagnosis and treatment of ACTH-dependent Cushing's syndrome. Emerging evidence showed that ACTH releasing could be regulated by vasopressin through their receptors. There were 3 isoforms of vasopressin receptors (AVPRs). However, the role of AVPRs in ACTH secreting tumors was not conclusive. The aim of this study was to investigate the expression of AVPRs and their role in regulating ACTH secretion.

Methods We retrospectively assessed hospitalized patients in the department of Endocrinology and Neurosurgery of Huashan Hospital during the year of 2005-2011. 52 patients who were pathologically confirmed as ACTH secreting tumors were enrolled in this study. 50 patients were with pituitary corticotrophin adenomas, and the other 2 patients were ectopic ACTH syndrome. Total 12 patients with pituitary adenomas underwent bilateral petrosal sinus sampling (BIPSS) and desmopressin test. The expression of AVPR2/3 was analyzed by immunohistochemistry staining and quantified by software. The role of AVPRs regulating ACTH secretion was further studied in AtT-20 corticotrophin tumor cell line.

Results Among 50 patients with pituitary ACTH adenoma, 31 cases (62%) were AVPR2 positive, and 38 cases (76%) were AVPR3 positive. Only 5 cases (10%) of patients were both negative. 2 patients with ectopic ACTH syndrome were pathological confirmed as thymic carcinoid. Both cases were AVPR3 positive and 1 case was AVPR2 positive. In 12 patients who were underwent BIPSS, the desmopressin induced ACTH elevation ratio in central was correlated with AVPR2 staining intensity ($r=0.686$, $p=0.041$). However, both central and peripheral ACTH increasement was not associated with AVPR3 expression. QPCR showed that both AVPR2 and 3 mRNA were expressed in AtT-20 cell line. Desmopressin stimulated ACTH level increased approximately 1.8 times in AtT-20 cells. AVPR2 specific antagonist Tolvaptan could inhibit ACTH secretion in a dose dependent manner.

Conclusion Both AVPR 2 and 3 were expressed in ACTH secreting tumors. Desmopressin stimulated ACTH releasing was correlated with AVPR2 expression. The AVPR2 antagonist could inhibit ACTH secretion, which provided new therapy target for Cushing's disease.

Y-06

Identification of a novel mutation in pseudohypoparathyroidism type Ia in a Chinese family

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Context Pseudohypoparathyroidism(PHP) indicates a group of rare disorders characterized by end-organ resistance to various hormones, primarily parathyroid hormone (PTH). One of its most common type is PHP-Ia, which presents with multi-hormone resistance and typical Albright's hereditary osteodystrophy (AHO). PHP-Ia is caused by maternally inherited inactivating mutations in GNAS, while the same mutations inherited paternally usually result in pseudo-pseudohypoparathyroidism(P-PHP), which presents with AHO phenotype only. We reported a case of PHP-Ia and the genetic analysis of the family.

Subjects and Methods A 9-year-old Chinese girl presented with recurrent epileptic seizure. Biochemical and imaging

findings were consistent with PHP-Ia, including typical AHO phenotype(short statue, round face, brachydactyly and mild mental retardation), PTH resistance(hypocalcemia, hyperphosphatemia, elevated serum PTH and multiple intracranial calcification) and TSH resistance(elevated serum TSH). Mutations of the GNAS gene were investigated as well as methylation status of the GNAS locus in her family.

Results A novel mutation c.310delG(p.Glu104Lysfs*7) of the GNAS gene was found in the patient, as well as her mother . No abnormal methylation of differentially methylated regions (DMRs) in the GNAS gene was detected.

Conclusion The study further expands the spectrum of known GNAS mutations associated with PHP and lay emphasis on the genetic analysis of GNAS gene for identifying genetic abnormalities as well as making diagnosis and differentiation of various subtypes of PHP.

Y-07

The Role of MicroRNAs and Target Genes in the Protective Effects of Glucagon-like peptide-1 on Preserving Pancreatic β-cells in high-fat diet induced mice

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Objective It is confirmed that glucagon-like peptide -1 may have effects on β cells neogenesis, proliferation, and reducing β cells susceptibility to apoptosis. Besides, microRNAs participate in process of formation and growth in a variety of tissues. We hypothesized that glucagon-like peptide-1 receptor activation preserved pancreatic β-cells via regulation of microRNAs (miRNAs) and target genes.

Methods we used high-fat diet (HFD) induced C57BL/6 mice as diabetic model mice. Mice were randomly allocated to three study groups using a computer-based randomization: （1）diabetic model mice group; （2）high-dose GLP-1 treated group (30μg/kg·day); （3）low-dose GLP-1treated group (3μg/kg·day). Mice were treated with GLP-1 intraperitoneally for 13 weeks. Fasting blood glucose, postprandial blood glucose were measured using blood glucose meter. Serum insulin concentration was measured in each group using ELISA kit. ΔI30/ΔG30 、HOMA-IR index and HOMA-%β index were calculated. Pamcreatic structure was observed using light microscope and transmission electron microscopy. Pancreatic β-cell mass and proliferation were assessed by immunohistochemistry insulin and Ki-67 stain. The expression of pancreatic proliferation related microRNA（miR-7、miR-21、miR-155 and miR-221）and genes（mTOR and PTEN）, insulin secretion related microRNA（miR-9 and miR-375）and genes（OC-2 and PDK1）, pancreatic regeneration related microRNA（miR-15a, miR-16 and miR-124）and genes（Ngn3 and Foxa2）were investigated using quantitative Real-time PCR.

Results (1) 13 weeks GLP-1 treatments significantly reduced body weight and food intake in HFD induced mice ($P < 0.05$). (2) Insulin sensitivity, HOMA-IR and HOMA-% β were markedly improved in GLP-1 treated groups ($P < 0.05$). (3) Histological examination revealed that β-cell proliferation and mass were statistically increased in GLP-1 treated mice, although there was a strong tendency for increased proliferation. (4) GLP-1 significantly regulated the expression of pancreatic proliferation related microRNA（miR-7 and miR-21）and genes（mTOR and PTEN）($P < 0.05$). (5) GLP-1 significantly downregulated the expression of insulin secretion related microRNA（miR-9 and miR-375）, and in turn, upregulated the level of genes (OC-2 and PDK1)($P < 0.05$). (6) GLP-1 significantly downregulated the expression of pancreatic regeneration related microRNA（miR-15a, miR-16 and miR-124）($P < 0.05$), but did not significantly upregulated the level of genes (Ngn3 and Foxa2) ($P > 0.05$).

Conclusion GLP-1 can reduce body weight and food intake; GLP-1 was involved in preserving β-cell mass and function in HFD induced mice. MicroRNAs (miR-7, miR-21, miR-9, miR-375, miR-15a, miR-16 and miR-124) and related target genes (mTOR, OC-2, PDK1 and PTEN) contribute to the protective effects of GLP-1 on preserving pancreatic β cells.

Y-08

Optimization of the diabetic rat mesenchymal stem cell differentiation by 3D culture in Pluronic F-127 hydrogel

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There is a critical clinical need to develop therapies for non-healing diabetic foot ulcers. Topically applied mesenchymal stem cells (MSCs) provide a novel treatment to augment diabetic wound healing. A central pathological factor in nonhealing diabetic ulcers is an impaired blood supply. It was hypothesized that topically applied MSCs would improve wound healing by augmenting angiogenesis. However, delivering MSCs to wound sites while maintaining a high MSC survival rate is still a critical challenge in patients with diabetes. Using adequate cell scaffold, however, the number of cells needed for therapeutic applications can be drastically reduced. With the progress of tissue engineering, hydrogels have been widely investigated as 3D scaffolds to

mimic the natural extracellular matrix (ECM) .The role of hydrogels as scaffolds has evolved from simple cell encapsulation to the control of cell fate for growth and differentiation. Pluronic F-127 is a synthetic hydrogel, which is non-toxic, biocompatible, bioabsorbable and is FDA approved for use in humans.Here, we tested the endothelial differentiation capacity of diabetic rat adipose derived stem cells（ASCs）in the thermoreversible Pluronic F127 hydrogel scaffold in vitro. ASCs were isolated from subcutaneous adipose tissue of diabetic rats and characterized by flow cytometry. Diabetic ASCs were cultured and seeded in Pluronic F127 hydrogel（3D culture）and stem cell viability, proliferation and differentiation into endothelium were evaluated. Our results confirmed that Pluronic F-127 is a promising and non-toxic scaffold for 3D culture of diabetic ASCs, yielding high stem cell viability and proliferation. Cell growth curves by CCK-8 assay showed that there were significant differences between the 3D cultured cells and 2D cultured cells（$P<0.05$）. Moreover, after 3 weeks of endothelial differentiation in vitro, the mRNA expression of endothelial gene markers(CD31,KDR,vWF) in 3D cultured diabetic ASCs was markedly higher than the 2D-cultured cells via qPCR analysis（$P<0.05$）. To confirm the qPCR data, immunostaining was performed. Immunostaining showed CD31 antigen expressed in the cell membrane surface of differentiated diabetic ASCs. We observed more positive cells in 3D cultured cells. We also tested the ability of differentiated diabetic ASCs to take up ac-LDL. There were some positive cells uptaked ac-LDL in the 3D cultured cells but was not observed at all in the 2D cultured cells. The results of this study demonstrated that the Pluronic F127 hydrogel scaffold can enhance the endothelial differentiation of ASCs from diabetic rats through in vitro three-dimensional culture environment, which may can improve the limitations of autologous stem cell treatment for diabetic foot ulcer.

Y-09

Study on glucose metabolism in patients with Klinefelter's syndrome

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Objective To evaluate the characteristics of glucose metabolism and the possible mechanisms of glucose metabolism disorder for Klinefelter's syndrome (KS) patients complicated with diabetes mellitus (DM).

Methods This retrospective clinical research summarizes and analyzes the general condition, gonadotropic and gonadal hormone levels, lipid and glucose levels, test results after 75 g of oral glucose, and HOMA-IR for 19 KS patients, 9 and a control group with 18 DM patients.

Results（1）The incidence of DM in Klinefelter's Syndrome patients was 32.1% (9/28), while in patients with the karyotype of 47，XXY and 48，XXYY was 30.7% (8/26) and 50% (1/2), respectively;（2）Compared with simple KS patients, the age of KS patients complicated with DM was significantly older, while the testosterone (TT) level of them was significantly lower;（3）KS patients complicated with DM were much higher and heavier than the control group. Moreover, the weight difference was much bigger than that of the height;（4）A lower LDL ($p<0.05$) level can be seen when a comparison was conducted between KS patients complicated with DM and the control group;（5）the PRL level of KS patients complicated with DM was lower than that of simple KS patients as well as the control group and the decrease of PRL were all statistical; Furthermore, the decrease of the PRL level was consistent with the deficiency of the TT level.

Conclusions（1）There exists severer insulin resistance in KS patients complicated with DM, compared with simple KS patients;（2）The main factors of glucose metabolism disorder in KS patients possibly involve age, testosterone level, hyperinsulinemia, numeral abnormalities of X chromosome and autoimmune diseases.

Y-10

Ablation of Lgr4 enhances energy adaptation in skeletal muscle via activation of Ampk/Sirt1/Pgc1α pathway

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Leucine-rich repeat-containing G protein-coupled receptor 4 (Lgr4) is a newfound obese-associated gene. Previous study reveals that heterozygous mutation of Lgr4 correlates with decreased body weight in human. In our recent study, we demonstrate that Lgr4 ablation promotes browning of white adipose tissue and improves whole-body metabolic status. However little is known about its role in other metabolic tissues. Herein, we show that Lgr4 homozygous mutant (Lgr4 m/m) mice show

increased respiratory exchange ratio (RER, closer to 1.0) than wild-type mice at 12:00 AM, while decreased RER (closer to 0.75) at 12:00 PM (fasting for mice), indicating a glucose-prone versus fatty acid-prone metabolic pattern, respectively. Furthermore, Lgr4 ablation increases lipid oxidation-related gene expression while suppresses glucose transporter type 4 (Glut4) levels in skeletal muscle under fasting condition. These data suggest that Lgr4 ablation enhances the flexibility of skeletal muscle to switch energy provider from glucose to fatty acid in response to glucose depletion. We further reveal the activation of Ampk/Sirt1/Pgc1α pathway during this adaptive fuel shift due to Lgr4 ablation. This study suggests that Lgr4 might serve as an adaptive regulator between glucose and lipid metabolism in skeletal muscle and reveals a potentially new regulator for a well-established adaptive network.

Y-11

Identification of differential circulating LncRNAs as novel metabolic biomarkers in obese patients

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Objective Circulating Long non-coding RNAs (lncRNAs) have been found to be valuable biomarkers in a number of human diseases. However, lncRNAs biomarkers have yet to be identified in obesity. This study was designed to characterize circulating lncRNA expression in obese and non-obese human subjects.

Methods First, we assessed the genome-wide circulating lncRNA expression profiles in blood from 3 obese and 3 non-obese human subjects. Next, using RT-PCR we measured the expression levels of these three lncRNAs in 13 obese and 13 non-obese human subjects. Finally, we tested the circulating levels of these three lncRNAs in 9 obese human subjects who lost weight after 12 weeks of a diet-induced weight loss program.

Results We found that circulating levels of three lncRNAs (lncRNA-p5549, lncRNA-p21015 and lncRNA-p19461) were significantly decreased in obese human subjects only. The expression levels of these three lncRNAs in 13 obese and 13 non-obese human subjects were found similar differences. Moreover, the circulating levels of these three lncRNAs were negatively correlated with body mass index (BMI), waist circumference, waist to hip ratio and fasting insulin. The expression of lncRNA-p19461 was also negatively correlated significantly with homeostasis model assessment-estimated insulin resistance. We found that only the circulating level of lncRNA-p19461 signifi cantly increased after a 12 weeks of a diet-induced weight loss program.

Conclusion In summary, lncRNA-p19461 may be a potential candidate as a noninvasive metabolic biomarker of obesity.

Y-12

Plasma glucose and hemoglobin A1c for the detection of diabetes in Chinese adults: analysis of a nationwide survey

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Objective To evaluate the performance of plasma glucose (PG) and hemoglobin A1c (HbA1c) for the detection of diabetes in the general population in China.

Methods A cross-sectional analysis was conducted in a nationally representative sample of 98,658 Chinese adults aged ≥18 years who were selected using a complex, multistage, probability sampling design. Plasma glucose and HbA1c levels were measured after at least a 10-hour overnight fast among all participants. An oral glucose tolerance test (OGTT) was conducted among participants without self-reported history of diagnosed diabetes. All the analyses were weighted using coefficients derived from 2010 China Population Census and the sampling scheme of the survey to represent the total Chinese adult population aged ≥18 years.

Results An HbA1c ≥6.5% could identify 4.57% of Chinese adults as having newly-detected diabetes, followed by fasting PG (FPG) and 2-h PG at 4.52% and 3.50%, respectively. Approximately 1.95% of the total population were detected by HbA1c but not by FPG or 2-h PG. An FPG ≥7.0 mmol/l and/or HbA1c ≥6.5% identified more diabetes than an FPG ≥7.0 mmol/l and/or 2-h PG ≥11.1 mmol/l. Approximately 80% of those diagnosed by OGTT could be detected by using tests of FPG and HbA1c. The combination also identified most (85.2%) diabetes individuals defined by any of the three tests (i.e. FPG, 2-h PG, and HbA1c). The kappa statistic measuring the agreement between the combined use of FPG plus HbA1c and OGTT was 0.74 [95% confidence interval (CI): 0.73-0.75]. Levels of most cardiovascular risk factors such as body mass index, waist circumference, and cholesterol were higher in diabetes defined by FPG and HbA1c than in diabetes defined by OGTT.

Conclusions Although HbA1c ≥6.5% was recommended by the American Diabetes Association as one of the diagnostic tests for diabetes, caution should be used to avoid potential overdiagnosis when interpreting diabetes defined by elevated HbA1c alone.

Y-13

Effects of L-Thyroxine Replacement Therapy on Serum Lipid Profiles in Patients with Mild Subclinical Hypothyroidism: An Open-Label, Randomized, Controlled Trial

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Background Mild subclinical hypothyroidism (SCH) affects a large number of people and is known to be a serious risk factor for dyslipidemia. However, previous studies examining the effects of L-thyroxine on serum lipids in mild SCH have generated inconsistent results with relatively small sample sizes. Therefore, whether mild SCH patients should be treated with L-thyroxine to improve lipid profiles remains controversial. In addition, it is also unclear whether all mild SCH patients can benefit from L-thyroxine treatment regardless of basal thyrotropin or lipid levels. This study aimed to assess the effects of L-thyroxine replacement therapy on the lipid profiles of mild SCH patients.

Methods This open-label, randomized, controlled trial was performed in Ningyang County, Shandong Province, China. A total of 378 mild SCH patients with diagnoses confirmed by two thyroid function tests were randomly assigned to either the intervention group (L-thyroxine replacement therapy) or the control group (no treatment). The primary outcome was a change in serum total cholesterol (TC) concentration. Subgroup analyses were also performed in subjects with different basal thyrotropin or TC concentrations. This study is registered with ClinicalTrials.gov, number NCT01848171.

Results In all, 369 participants (210 subjects in the intervention group and 159 subjects in the control group) completed the 15-month follow-up period. The L-thyroxine replacement therapy effectively ameliorated thyroid autoimmunity in addition to improving thyroid function. Serum TC levels were decreased by 0.41 mmol/L ($p < 0.001$) in the intervention group, whereas the decline was 0.17 mmol/L ($p = 0.019$) in the control group. Reduced TC concentrations were more prominent in the intervention group than in the control group ($p = 0.012$). The changes to low-density lipoprotein cholesterol levels exhibited the same trend. Subgroup analyses were performed to assess the effects of L-thyroxine in patients with different basal thyrotropin or TC levels. When the study population was stratified according to basal thyrotropin concentration, all patients who had received L-thyroxine showed reduced TC levels (all $p < 0.001$). The treatment was similarly beneficial for all patients regardless of basal TC level. Even for subjects with TC levels less than 5.18 mmol/L, serum TC concentrations remained unchanged in the intervention group ($p = 0.936$) but increased by 0.35 mmol/L in the control group ($p = 0.004$).

Conclusion Our findings suggested that mild SCH patients could benefit from L-thyroxine treatment to improve lipid profiles regardless of basal thyrotropin or TC concentrations. Our study might provide reliable and important data for evidence-based medicine and help clinicians offer effective treatment advices to the mild SCH patients.

Y-14

Identification of a novel function of adipocyte plasma membrane-associated protein (APMAP) in gestational diabetes mellitus by proteomic analysis of omental adipose tissue

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Objective The purpose of the research is to investigate the pathogenesis of insulin resistance in gestational diabetes mellitus by proteomic analysis of omental adipose tissue.

Methods six subjects with GDM and six subjects with normal glucose tolerance (NGT; healthy controls) were enrolled in this study. The clinical and obstetric characteristics were compared between GDM and NGT subjects. We collected the omental adipose tissue from subjects during cesarean section. Label-free proteomics was used to identify differentially expressed proteins in omental adipose tissues from GDM and NGT subjects. In order to further investigate the function of adipocyte plasma membrane-associated protein (APMAP), one of the differentially expressed proteins, mature 3T3-L1 adipocytes were used to simulate omental adipocytes.

Results (1) The homeostasis model of assessment for insulin resistence index (HOMA-IR) was increased in GDM. (2) A total of 3528 proteins were identified by label-free proteomics, including 66 significantly changed proteins. (3) The inhibition of APMAP expression by RNAi impaired insulin signaling pathway and activated NFkB signaling pathyway in mature 3T3-L1 adipocytes.

Conclusions Our study revealed that the down regulation of APMAP in omental adipose tissue may play an important role in insulin resistance in the pathophysiology of GDM.

Y-15

miR-21-3p、1297-3p mediates PTEN expression in nodular thyroid disease through tissues and blood

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Objective miRNA-21、miRNA-1297 mediating PTEN express in the tissue and blood through nodular thyroid disease（goiter, thyroid adenoma, thyroid cancer），which can be a new tumor markers and targeted for diagnostic.

Method Analysed the clinical data of 93 patients who had thyroid nodules surgery in First Affiliated hospital of Baotou medical college，during the period Jan 2013 to Jan 2015，including 30cases of thyroid carcinoma,21 cases of thyroid adenoma,22 cases of nodular goiter,and 20 cases of para nodules normal control group，normal fasting peripheral venous blood in 20 cases as control group. MiRNA-21-3p、1297-3p expression by qRT-PCR in thyroid carcinoma to evaluate their involvement in the malignant progression of this tumor. The study was used statistical software SPSS 17.0, Each set of data need to be tested for normality and homogeneity of variance test, then we analyzed using single factor analysis of variance; LSD test was used to compare any two groups.

Resuts（1）The average of miRNA-21-3p，miRNA-1297-3p expression in thyroid carcinoma group、nodular goiter group、adenoma group and normal control group increased one by one in tissue and blood.（2）ROC curves about miRNA-21-3p to distinguish the thyroid cancer group and the control group yielded an AUC was 0.750(95% CI 0.635-0.865) in the tissue. miRNA-21-3p was 0.722(95% CI 0.605-0.839) in the blood. ROC curves about miRNA-1297-3p was 0.818(95% CI 0.702-0.934)in the tissue. miRNA-1297-3p was 0.754(95% CI 0.637-0.870) in the blood. Using miRNA-21-3p expression for diagnosing of thyroid cancer had a sensitivity, specificity in the tissue and blood is 77.2%、78.3% and 61.4%、78.3%. miRNA-1297-3p expression for diagnosing of thyroid cancer had a sensitivity, specificity in the tissue and blood is 87.7%、65.2% and 89.5%、56.5%.（3）There was a positive correlation of miR-21-3p、miR-1297-3p expression between plasma and tumorous tissue in PTC patients（$r = 0.523$，$P < 0.05$）（$r = 0.642$，$P < 0.05$）

Conclusions

（1）The average of miRNA-21-3p、miRNA-1297-3p expression in thyroid carcinoma group、nodular goiter group、adenoma group and normal control group increased one by one in tissue and blood.

（2）miRNA-21-3p、miR-1297-3p expression levels can be used as a reference indicator for differentiating benign and malignant thyroid nodules.

（3）The expression of miRNA-21-3p、miRNA-1297-3p had no significant related to age, gender, size of the nodule，neck lymph node enlargement,but higer expresssion about miRNA-1297-3p was related to calcification in thyroid carcinoma.

（4）Expression of miRNA-21-3p、miRNA-1297-3p in the diagnosis of thyroid carcinoma specificity and sensitivity are fair.They can help clinical diagnosis. miR-21-3p sensitivity is higher than the blood,equal in sensitivity. miR-1297-3p blood sensitivity is higer than tissue,but lower than specificity.It can help clinical diagnosis.

Y-16

Liraglutide enhance the insulin signaling on lipogenesis in subcutaneous adipose tissue of db/db mice

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Aim To examine the insulin signaling changes of subcutaneous adipose tissue (SAT) in db/db mice after liraglutide treatment.

Methods The db/db mice were divided into 2 groups: liraglutide-treated group (n=14, 8-week old, fasting glucose>10mmol/l, liraglutide 300μg/kg twice daily for 4 weeks) and control group (n=14, saline). Body weight and food intake were examined every week. Fasting plasma triglyceride and free fatty acid concentrations were tested by ELISA before and after treatment. Using Real-time PCR and Western blot, we assessed the mRNA and protein levels of lipogenetic transcription factors peroxisome proliferator-activated receptor-γ (PPARγ) and CCAAT/enhancer-binding protein-α (C/EBPα), as well as the up-stream control molecule levels, which includes the serine/threonine kinase Akt (Akt), Forkhead box protein O1 (FoxO1), P38 mitogen-activated protein kinase (p38 MAPK) and extracellular-signal-regulated kinase 1/2 (ERK1/2) in SAT. Adenosine 5'-monophosphate-activated protein kinase (AMPK) and acetyl-CoA carboxylase (ACC) were assessed too.

Results Body weight gain, food intake and blood glucose were reduced compared with control ($p<0.05$). The plasma triglyceride was reduced from 1.69±0.18 to 1.56±0.08 mmol/l ($p=0.033$) and free fatty acid (FFA) was from 491.91±29.68 to 486.78±31.41 ($p=0.673$). The mRNA and protein expressions of

PPARγ in SAT were 2.25-fold (p=0.037) and 2.62-fold (p=0.002) higher than that in control group respectively. This was associated with down regulation of FoxO1 (0.7-fold, p=0.009) induced by pAkt activation (1.10-fold, p=0.087). Besides, the p38 MAPK-ERK1/2 associated with early adipocyte differentiation were activated (1.82-fold, p=0.007) while lipogenesis inhibitor pAMPK (0.63-fold) and pACC (0.57-fold) were reduced compared with control group (p<0.01). There was no significant difference of C/EBPα between two groups.

Conclusions With liraglutide treatment, the insulin signaling of lipogenesis was activated in Akt and MAPK pathway in SAT. As a regulator of lipogenesis, GLP-1 could be an alternate pathway controlling downstream insulin signaling.

Y-17

Analysis of Clinical Features and Outcomes of Congenital Adrenal Hyperplasia with Adenomatoid Adrenal Gland

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Objective To analyze the clinical features and outcomes of congenital adrenal hyperplasia (CAH) with adenomatoid adrenal gland.

Methods Clinical data from nineteen patients clinically confirmed as CAH with adenomatoid adrenal gland, from 2008 to 2015 in PLA hospital, were retrospectively analyzed. Meanwhile, the therapeutic treatments and clinical outcomes were followed up.

Results From 2008 to 2015, there were seventy-six patients clinically confirmed as CAH in PLA General Hospital. Nineteen of them accompanied with adenomatoid adrenal gland. Of the 19 confirmed cases: 7 males and 12 females with the average age of 33.3±14.8. Nineteen confirmed cases contain 10 cases of 21-OHD(52.6%), 6 cases of 17α-OHD(31.6%), while 3 cases of 11β-OHD(15.8%). Of the 19 cases, 5 cases presented with adrenal hyperplasia with left side adenomatoid solid lesion, 2 cases presented with adrenal hyperplasia with right side adenomatoid solid lesion, 8 cases presented with double side adenomatoid solid lesion and 4 cases presented with adrenal hyperplasia with cystic or calcify changes. Nine of the 19 patients had undergone operation or fine needle biopsy, and the pathology showing 7 adenomas (21-OHD/17α-OHD 5/2) and 2 myelolipomas (21-OHD/17α-OHD 1/1). Four of them came to PLA General Hospital because of the adrenal incidentaloma. All of the confirmed patients administered glucocorticoid replacement. Eleven followed-up patients have been relieved to a certain extent. Seven of them have rechecked the CT of adrenal. After the treatment, 2 patients' adenomatoid adrenal gland decreased, 2 patients' tumors had no recurrence, 1 patient's tumor disappeared, 2 patients' adenomatoid adrenal gland were still in the same size.

Conclusion The image for adrenal of CAH with adenomatoid adrenal gland is various. It may occurs in each type of CAH presented as unilateral or bilateral, adenoma or myelolipoma. Some of the patients come into doctor because of the adrenal incidentaloma. The clinical physicians cannot narrow their thinking mode to one side or both sides of diffuse hyperplasia of adrenal about CAH.

Y-18

Association between reproductive factors and hyperuricemia in people aged over 50 years: a population-based study

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Objective It is well-known that hyperuricemia is involved in many metabolic disorders. Recently, it is reported that reproductive parameters is closely related with metabolic diseases such as diabetes. However, it is unclear whether reproductive parameters are relevant to it or not. We aimed to investigate if hyperurcemia is associated with reproductive parameters in a population-based study.

Methods 2810 women aged over 50 years and 1661 men aged over 50 years participated in this study. Reproductive parameters were obtained by standardized interviews. Blood sampling were performed after 10-12 fasting and the levels of total cholesterol(TC), triglycerides(TG), high density lipoprotein cholesterol(HDL-C), low density lipoprotein cholesterol(LDL-C), blood glucose and uric acid (UA) were determined using automatic analyzer. UA>360 μmol/L in women and UA>420 μmol/L in men are defined as hyperuricemia. Multiple logistic regression was performed to explore the OR for the risk of hyperuricemia in the individuals with different reproductive parameters after adjusting for potential confounders.

Results In this study, significant differences were observed between the group of hyperuricemia and the group of nonhyperuricemia in the age at menopause, the number of daughters in females, the number of sons in females, the number of spontaneous labor, the number of abortion, the number of artificial abortion, ever had abortion(yes/no) which OR(95%-CI) is 0.659(0.502,0.867).Additionally, we found that some reproductive factors including menopause status(yes/no) which

OR(95%CI) is 4.870(1.161,20.427), the number of abortion which OR(95%CI)is 0.886(0.810,0.969), the number of artificial abortion which OR(95%CI)is 0.897(0.821,0.980), the number of spontaneous labor which OR(95%CI)is 1.129(1.034,1.232), the number of daughters in females which OR(95%CI)is 1.458(1.169,1.817), are associated with hyperuricemia after adjusting for age, degree of culture, BMI(kg/m2), alcohol consumption(never, occasionally, often), DM(yes/no), total cholesterol (TC), triglycerides(TG), highdensity lipoprotein cholesterol(HDL-C), lowdensity lipoprotein cholesterol (LDL-C). Otherwise, no significance were observed between the group of hyperuricemia and the group of nonhyperuricemia in the number of daughters in males, the number of sons in males, the number of spontaneous abortion, the age at menarche, the age at menopause, history of ectopic pregnancy(yes/no), history of hormone replacement therapy in females (yes/no) and the weight before or after the labor ($p > 0.05$).

Conclusion Menopause status, larger number of spontaneous labor in females, larger number of daughters in females are associated with higher risk of hyperuricemia, while larger number of abortion, larger number of artificial abortion are probably protective factors of hyperuricemia.

Y-19

30 years of experience：The clinical features of 73 cases with ectopic ACTH syndrome in a single center

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Objective To investigate and discuss the diagnosis and treatment of ectopic ACTH syndrome.

Methods A retrospective study of 73 cases with ACTH-dependent Cushing syndrome reviewed from 1988 to 2016 in Peking Union Medical College Hospital.

Results 73 patients went to PUMCH with 38.6 years old average age and median 12 months duration of initial disease presentation. Most cases presented clinical and biochemical evidences of Cushing syndrome with increased serum cortisol (100%) and ACTH (96.9%). 61.4% EAS cases had obesity (BMI>24kg/m^2), and 81.7% cases had hypokalemia (2.77±0.70 mmol/L). High-dose dexamethasone suppression test (HDDST) failed to suppress UFC and 17OHCS in 80.6% cases. 21 (100%) patients showed no petrosal-to-peripheral ACTH gradient on IPSS. 64 (87.7%) patients could detect ectopic tumor by CT, MRI, octreotide or PET-CT scanning. 54 cases were definitively diagnosed as ectopic ACTH syndrome by detected ectopic tumors; 9 cases were diagnosed as ectopic ACTH by imaging examinations and 10 cases were failed to identify sources of ectopic hormone secretion, and combined 19 cases include 5 cases which were treated with bilateral orunilateral total adrenalectomy. Among 54 cases with histopathological based diagnosis, carcinoid is the most common pathology classification in EAS patients. Pulmonary and bronchia tumors were most frequently detected (44.4%, n=24), followed by thymus and mediastinum carcinoid (31.5%, n=17), pancreatic carcinoid (5.6%, n=3) and pheochromocytoma (5.6%, n=3). We identified 3 Ectopic CRH syndrome cases in our study, including perineal primitive neuroectodermal tumor, presacral teratoma and medullary thyroid carcinoma. Two of three cases had insuppressible UFC or 17OHCS after HDDST (<50%), and the other case couldsuppress UFC <80% in HDDST, however no suspicious pituitary tumor was identified by pituitary MRI scans. The ACTH staining were negative in immunohistochemistry, but CRH were positive.

Conclusions Clinical manifestations of ectopic ACTH syndrome are similar to Cushing diseases, however it is relatively difficult to localize the tumor of ectopic ACTH syndrome patients. The EAS patients had lower obesity incidence and higher hypokalemia rate than Cushing Diseases patients. Regular CT/MRI scanning could detect nearly 80% possible EAS tumor,nevertheless, for uncertain ectopic tumor patients, octreotide or PET-CT scanning have little advantage to locate suspicious tumor. Chest carcinoid tumors are the most common ectopic ACTH secreting resources in EAS patients.

Y-20

M2 macrophage infusion ameliorates obesity and insulin resistance by remodeling inflammatory homeostasis in obese mice

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Objective Obesity is characterized by progressive accumulation of inflammatory cells in adipose tissue (AT), which in turn exacerbates the onset of a series of metabolic-related diseases. Herein, we aim to investigate whether anti-inflammatory M2 macrophage infusion ameliorates obesity and insulin resistance.

Methods Bone marrow derived macrophage (BMDM) was induced in vitro with IL-4 for 36 hours to acquire an M2 mac-

rophage phenotype. A total of 5×105 cells were administered through the tail vein into the obese mice, which were fed a high-fat diet (HFD), to observe the therapeutic effect.

Results Five weeks after the injection, we found weight loss of the body weight, the fat mass, and the mass of the inguinal AT (INAT). Indirect calorimetry experiment displayed increased carbohydrate dominated substrate metabolism with increased respiratory quotient (RQ), accompanying increased O2 consumption after M2 infusion, indicating ameliorated energy consumption. Meanwhile, improved lipid metabolism in plasma with decreased cholesterol and LDL-c were observed after M2 macrophage infusion. Pathological analysis revealed that the adipocytes of the epididymal adipose tissue (EAT) and INAT were smaller, while the EAT showed significantly decreased mesenchymal structure in M2 infusion group. Further, we demonstrated that these mesenchymal cells were M1 through IF staining, and these mesenchymal matrix was fiber with Masson and Sirius staining. Later, IF and FCM found decreased M1 and qRT-PCR found significantly decreased TNF-α and MCP-1 in EAT, and FCM found decreased CCR2+CX3CR1lowLy6C+cells in blood in accordance with decreased p-NF-kB and MCP-1 in EAT by western blot, implying remodeled EAT with improved inflammation and fibrosis after M2 infusion. As inflammation affects insulin sensitivity, we next detected insulin sensitivity, ending up with increased p-AKT by Western blot in the EAT. Besides, improved intraperitoneal glucose tolerance test (IPGTT) and HOMA-IR in conjunction with improved insulin resistance. In vitro, we co-cultured M2 with the EAT of mice and human with obesity, we both found significantly increased p-AKT. To further explain how M2 infusion ameliorated AT inflammation to improve insulin sensitivity to eventually lose weight, we compared different stages of EAT after M2 infusion. We found in the early stage, EAT showed significantly increased M2 and no decrease of M1, on the contrary, in the late stage there was no significant increase of M2 instead of significantly decreased M1. Further, we found that in the early stage, EAT express more UCP1 to enforce energy metabolism and in the late stage increased p-MAPK and decreased p-Foxo1 demonstrated that M2 infusion might help to ameliorate adipocyte survival to lessen AT inflammation to sustain insulin sensitivity.

Conclusions Our study unveiled that M2 macrophage infusion can remodel AT inflammatory homeostasis to further ameliorate insulin resistance, which in turn, contributes to weight loss and metabolic improvement in obese mice, suggesting a potentially effective and healthy weight loss strategy.

Y-21
GABA ameliorates hepatic steatosis and improves insulin sensitivity through Sirt1 pathway

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Aims To investigate whether Gamma-aminobutyric acid (GABA) improves non-alcoholic fatty liver disease (NAFLD) and hepatic insulin resistance (HIR) in high-fat（HF）diet-induced mice and its mechanism.

Methods Eighteen C57BL/6 mice of 6weeks of age were randomly assigned to three groups (n=6 per group): normal chow diet (NCD), high fat diet (HFD), high fat diet plus with water containing 6mg/ml of GABA (HFD+GABA). After 12 weeks intervention, glucose tolerance and insulin sensitivity were evaluated by intraperitoneal glucose tolerance test (IPGTT) and insulin tolerance test (ITT). Then the mice were sacrificed and the liver tissues were obtained. The triglyceride (TG) levels were determined using triglyceride determination kit, genes expression of lipogenesis and fatty acid β-oxidation were detected by QT-PCR, the protein expression of Sirt1 and the key molecular of insulin signaling pathway in the liver were detected by western blot. The serum β-ydroxybutyrate was also detected using β-hydroxybutyrate colorimetric assay kit. In vitro, the HepG2 cells were transfected with Sirt1 Small interfering RNA (siRNA) to knock down Sirt1. The intracellular lipid accumulation and insulin resistance were induced by palmitate acid and the HepG2 cells were treated with GABA for 24 hours or not. Intracellular lipid levels were determined by Oil Red O staining, genes expression in lipogenesis and β-oxidation were detected by QT-PCR; the protein expression of Sirt1 and key molecular in insulin signaling pathway were detected by western blot.

Results The 12 weeks HF diet significantly increased body weight in HFD mice and induced glucose intolerance and insulin resistance; while GABA treatment prevented the HF-induced body weight gain; the glucose tolerance and insulin sensitivity also showed significant improvement in HFD+GABA mice. Hepatic TG levels in the HFD group were dramatically increased compared with the NCD group, while it was decreased in the HFD+GABA group. Besides, HF diet induced decreased expression of liver Sirt1 protein and its downstream β-oxidation related genes（pparα, cpt1α, cyp14A, cyp8A, pgc1α）, while up-regulated the expression of lipogenesis related genes（srebp-1, scd-1）. However, the protein expression of liver Sirt1 and β-oxidation genes were reversed in HFD+GABA mice, and the expression of lipogenesis genes were decreased; furthermore, the protein expression of key molecular in insulin signaling pathway were also increased (Akt, Foxo1, Gsk3-β) in HFD+GABA mice compared with those in HFD mice. In vitro, the siRNA-mediated Sirt1 knockdown didn't decrease palmitate-induced lipid droplets in

HepG2 cells compared with the control group. In agreement with this result, in Sirt1 knock down cells, the expression of lipogenesis genes, β-oxidation genes in HepG2 cells didn't change under GABA treatment.

Conclusions In summary, our findings indicated that GABA ameliorates hepatic steatosis and improves insulin resistance in the liver of HF diet-induced mice via Sirt1 signaling pathway by promoting fatty acid β-oxidation and inhibiting lipogenesis. This points that GABA could be served as a major inducer of Sirt1 in the liver tissues and be applied as a valuable new strategy for treating NAFLD, especially those with hepatic insulin resistance and type 2 diabetes.

Y-22

Nonalcoholic fatty liver disease is associated with low-grade albuminuria in Chinese adults

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Objective Nonalcoholicfatty liver disease (NAFLD) has been well established as one of the risk factors of cardiovascular disease (CVD). Low-grade albuminuria was regarded as an early predictor of atherosclerosis and CVD. However, epidemiological studies investigating the association between NAFLD and low-grade albuminuria were not available. The objective of the current study was to determine whether NAFLD is independently associated with the presence of low-grade albuminuria in Chinese middle-aged and elderly adults.

Methods A cross-sectional community-based study was performed in 10375 Chinese adultsaged 40 years or older from Jiading District, Shanghai, China, between March and August 2010. A total of 8270 participants were included in the final analysis, after excluding those with incomplete data, excessive alcohol intake, and those with more than 3 times the normal serum liver enzymes. Information was collected by using a standard questionnaire on lifestyle, medical history and the use of medications and by performing anthropometrical measurements. A first-voided early morning spot urine sample was obtained for urinary albumin and creatinine measurements. Low-grade albuminuria was defined as the highest quartile of urinary albumin-to-creatinine ratio (UACR). NAFLD was diagnosed by using ultrasonographic findings after the exclusion of alcohol abuse and other liver diseases.

Results Compared with those without NAFLD, NAFLD patients had a higher median value of UACR (5.3 mg/g vs. 4.4 mg/g, P <0.0001). The prevalence of low-grade albuminuria was significantly higher in participants with NAFLD, compared with those without NAFLD (33.6% vs. 21.3% in men and 30.4% vs. 22.8% in women, respectively). The prevalence of NAFLD was higher among participants with low-grade albuminuria, compared with those without low-grade albuminuria (37.0% vs. 26.9%, P <0.0001). In multivariate regression analysis, age, waist circumference, systolic blood pressure (SBP), estimated glomerular filtration rate (eGFR), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and NAFLD were independent determinants of UACR within the normal range. Multivariate logistic regression analysis revealed that NAFLD was significantly associated with an increased odds of low-grade albuminuria among men (odds ratio 1.50, 95% confidence interval 1.17-1.89) after adjustment for age, waist circumference, current smoking, current drinking, physical activity, lipid profiles, fasting plasma glucose and SBP. This association changed little after further adjusting for eGFR and antihypertensive drug use (odds ratio 1.47, 95% confidence interval 1.16-1.87). This association was not detected in women.

Conclusions In the present study, we found that the presence of NAFLD was significantly associated with low-grade albuminuria independent of traditional cardiovascular risk factors and other potential covariates in middle-aged and elderly Chinese men.

Y-23

The Effect of Thyrotropin on Proatherosclerotic Factors via the activation of Akt

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Objective Some studies have demonstrated the effect of TSH on endothelial cells, but the underlying mechanism remains controversial. In the present study, we want to study the effect and mechanism of TSH on some proatherosclerotic factors such as osteopontin (OPN), vascular cell adhesion molecule 1

(VCAM-1) and integrin αvβ3 in aorta tissue of Subclinical Hypothyroidism rats.

Methods In Vivo study male Wistar rats weighing 180-200g were fed normal rat chow. The rats were randomly divided into three groups: subclinical hypothyroidism (SCH,n=8), hypothyroidism (CH,n=7), and control (CON,n=8). Thyroidectomy was performed to establish a hypothyroid model for CH rat and SCH rat, while a sham operation without removing the thyroid gland was done for CON rat. Four weeks after surgery , the thyroidectomized rats of SCH were injected with L-T4 (s.c 1.0g/100g) daily, and the rats of CH and CON group received injection of physiological sodium chloride solution .Western Blot and Immunohistochemistry (IHC) were used to evaluate the expression of OPN, VCAM-1 and integrin αvβ3. Ultra-thin sections (70nm) of aorta tissue from each rat were prepared for Transmission electron microscope (TEM). In vitro study HUVECs were starved in serum-free ECM for 12h, after that treated with various concentrations of TSH(0,0.1,1,10,100 mIU/ml) for 24h, or treated with 10 mIU/ml TSH for 0,2,6,12,24,48h. Western Blot and Real-Time PCR were used to investigate the expression of OPN, VCAM-1 and integrin αvβ3 in HUVEC. HUVECs were starved in serum-free ECM for 12h before stimulation, then Ekr inhibitor PD98059 and Akt inhibitor LY294002 were given 1h before 10mIU/ml TSH stimulation for 24h.

Results Four weeks or 14 weeks after L-T4 injection, a significantly increased TSH were observed in SCH than CON, but there was no statistically significant difference in TT4 between SCH and CON group ($p<0.05$). Our results showed that, in vivo, the protein expression of these proatherosclerotic factors——OPN, VCAM-1 and integrin αvβ3 of aorta tissue in SCH and CH group was increased compared with control group ($p<0.05$). However, the effect in SCH was milder than that in CH group, there was no significant statistically difference between the two groups ($p>0.05$). In vitro, we demonstrated that different concentration gradient or different time gradient of TSH stimulation could increase the protein and mRNA expression of OPN, VCAM-1 and integrin αvβ3, and was accompanied by extracellular signal-regulated kinase 1/2 (ERK1/2) and Akt activation in HUVECs ($p<0.05$). TSH induced elevation of these proatherosclerotic factors was partially suppressed by specific Akt inhibitor ($p<0.05$) but not by specific Erk inhibitor ($p>0.05$).

Conclusions Our findings suggested that the endothelial dysfunction caused by SCH were related to increased proatherosclerotic factors induced by TSH via Akt activation.

Y-24

Circulating periostin in relation to insulin resistance and nonalcoholic fatty liver disease among overweight and obese subjects

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Objective Recent study showed periostin is a crucial contributing factor in aberrant hepatic triglyceride (TG) accumulation and in the pathogenesis of obesity-induced hepatosteatosis. However, evidence from large-scale populations about the relationship between serum periostin level and metabolic phenotypes is scarce. We sought to determine whether serum periostin associates with NAFLD, and other metabolic phenotypes.

Methods This was a cross-sectional study of 8850 Chinese adults aged 40 yr or older in the Chongming District, Shanghai, China. A questionnaire, anthropometric measurements, laboratory tests, and a hepatic ultrasonic examination were conducted. NAFLD was diagnosed by hepatic ultrasound after the exclusion of alcohol abuse and other liver diseases.

Results Among overweight and obese subjects, serum periostin levels were higher in those with NAFLD (126.75 ng/ml vs. 75.96 ng/ml, $p<0.001$); however, no difference was found in lean subjects (72.65 ng/ml vs. 58.59 ng/ml, $p=0.259$). Periostin was associated with a higher risk for NAFLD (OR 1.75 for each 1-SD increase in periostin, 95% CI 1.04-3.37, $p<0.001$) among overweight and obese subjects after controlling for potential confounders. The significant associations were not detected in lean subjects. Furthermore, periostin levels among overweight and obese subjects were correlated with waist circumference ($r=0.111$, $p=0.002$), fasting plasma insulin ($r=0.098$, $p=0.006$), homeostasis model assessment index-insulin resistance (HOMA-IR) ($r=0.154$, $p<0.001$), TG ($r=0.117$, $p=0.001$), aspartate aminotransferase (AST) ($r=0.102$, $p=0.004$) and alanine aminotransferase (ALT) ($r=0.108$, $p=0.003$).

Conclusions Elevated circulating periostin concentrations were associated with higher risk of NAFLD among overweight and obese subjects.

口头发言

COR-01

二甲双胍通过促进 eNOS 复偶联和抑制 NADPH 氧化酶改善波动性高糖所致的内皮功能障碍

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目的 观察波动性高糖(FG)对人脐静脉内皮细胞(HUVECs)氧化损伤和内皮型一氧化氮合酶(eNOS)偶联的影响，探讨二甲双胍对抗内皮细胞氧化损伤的作用及其机制。

方法 培养 HUVECs 分采用正常葡萄糖(5.6 mmol/L 葡萄糖)、持续性高糖(30 mmol/L 葡萄糖)、FG(5.6 与 30 mmol/L 葡萄糖，每 8 h 更换浓度一次)及高渗对照(5.6 mmol/L 葡萄糖 + 24.4 mmol/L 甘露醇)进行干预。内皮功能检测指标包括一氧化氮(NO)水平、活性氧簇(ROS)产生、eNOS 磷酸化水平等。评价 eNOS 偶联状态指标包括细胞内四氢生物蝶呤(BH4)和三磷酸鸟苷环化水解酶 1(GTPCH1)水平。添加二甲双胍(2 mmol/L)和(或)N- 硝基 -L 精氨酸甲酯(L-NAME)、apocynin、化合物 C 等，探讨潜在机制。

结果 ① 与正常葡萄糖相比，FG 可显著增加 ROS 产生，降低 NO 水平，引起 HUVECs 的氧化损伤。虽然 FG 组 p-eNOS 水平升高，但是 GTPCH1 和 BH4 水平却显著下降，提示 eNOS 处于脱偶联状态。② FG 可增加 NADPH 氧化酶 p47-phox 亚基的水平。添加 NADPH 氧化酶抑制剂 apocynin 和 NOS 抑制剂 L-NAME 均可抑制 FG 诱导的氧化损伤，提示 NADPH 氧化酶增加和 GTPCH1-BH4 介导的 eNOS 脱偶联参与 FG 的内皮细胞氧化损伤。③ 在 FG 损伤的 HUVECs 中，添加二甲双胍可降低 ROS 生成，增加 NO 水平，上调 GTPCH1 水平和 BH4，降低 p47-phox 水平。添加 AMPK 抑制剂化合物 C 后，可消除二甲双胍的上述效应，提示二甲双胍对抗内皮细胞氧化损伤的作用是 AMPK 通路介导的。

结论 二甲双胍激活 AMPK 通路，既可通过促进 GTPCH1 介导的 eNOS 复偶联，又可通过抑制 NADPH 氧化酶，从而改善 FG 所致的内皮细胞功能障碍。

COR-02

自体骨髓干细胞移植联合长球囊血管成形术治疗糖尿病足下肢血管病变的临床研究

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目的 观察自体骨髓干细胞移植联合长球囊血管成形术治疗糖尿病足下肢血管病变的临床疗效。

方法 选取 2008 年 7 月至 2013 年 8 月收入山东省立医院的符合标准的糖尿病足病人 40 例进行回顾性研究，将纳入研究的患者分为联合治疗组(ABMSCT 组)和单纯长球囊血管成形术治疗组(LBA 组)，比较 2 组患者的治疗效果。

结果 (1)2 组患者治疗前后皮肤温度、皮肤颜色、静息痛等主观指标均有明显改善 (P<0.05)，但实验组较对照组改善的更为明显 (P<0.05)。(2)2 组患者治疗前后踝肱指数、行走距离、经皮氧分压等客观指标均有明显改善 (P<0.05)，但实验组较对照组改善的更为明显 (P<0.05)。(3)对照组血管再狭窄或闭塞 7 例，再狭窄率为 28%；实验组血管再狭窄或闭塞 4 例，再狭窄率 16%。两组血管的再狭窄率比较有统计学差异(P<0.05)。

结论 自体骨髓干细胞移植联合长球囊血管成形术治疗糖尿病足下肢血管病变可以明显改善患者的临床症状，降低血管再狭窄率，提高临床治疗效果。

COR-03

阿卡波糖通过调控糖尿病大鼠小肠 miRNA 改善糖代谢的机制研究

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目的 糖尿病严重危害人们的健康及生存质量。阿卡波糖是一种 α 糖苷酶抑制剂，在临床上表现出很好的降糖疗效。但是，阿卡波糖在肠道吸收度很低。基于此，我们猜想阿卡波糖能在小肠起作用，改善糖代谢。本研究旨在探讨阿卡波糖是否能通过直接干预糖尿病大鼠小肠，改善血糖。

方法 SD 大鼠通过高脂饮食 / 注射 STZ 法构建糖尿病大鼠模型。72 小时后，空腹血糖高于 11.1mmol/L 的 SD 大鼠判定为糖尿病模型建立成功。将 SD 大鼠分为小剂量阿卡波糖组(30mg/kg/d)、大剂量阿卡波糖组(60mg/kg/d)、糖尿病模型组(8 只，给予等体积生理盐水)和正常对照组(8 只，给予等体积生理盐水)，均连续灌胃 8 周。每 2 周测定 SD 大鼠空腹血糖 (FBG)。7 周末进行口服糖耐量实验 (OGTT)，以观察阿卡波糖对糖尿病大鼠血糖的改善作用。取大鼠小肠组织进行 miRNA 表达谱芯片实验，并运用实时定量 RT-PCR 验证芯片结果，以期探讨阿卡波糖对糖尿病大鼠降血糖的机制。

结果 干预后，大剂量阿卡波糖组较糖尿病模型组空腹血糖(15.3 ± 6.2 vs 23.7 ± 4.9 mmol/L 治疗 8 周)和 OGTT 曲线下面积(AUC)(31.7 ± 4.7 vs 52.6 ± 6.3mmol/L,P<0.05)显著下降。大剂量阿卡波糖组小肠较糖尿病模型组有 6 个 miRNA 上调，2 个 miRNA 下调。实时定量 RT-PCR 结果显示证实的这一结果。miRNA 靶基因预测和通路分析结果揭示，阿卡波糖能通过激活 miR-10a-5p 和 miR-664 改善小肠 MAPK 通路和抑制炎症因子改善糖尿病大鼠糖代谢。

结论　阿卡波糖可能通过激活 miR-10a-5p 和 miR-664 改善小肠 MAPK 通路和抑制炎症因子改善糖尿病大鼠糖代谢。

COR-04

父代心理应激对子代糖代谢的影响及机制研究

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目的　当今社会心理应激普遍存在，大量人群流行病学研究表明，心理应激与多种疾病的发生发展密切相关。近年来的研究发现，母亲心理应激可促进子代高血糖的发生。但父亲应激是否影响子代糖代谢，目前尚不明确。本研究拟探讨父亲心理应激对子代糖代谢的调节作用及分子机制。

方法　1.8 周龄的 C57 雄鼠分为两组，应激组小鼠每天置于 50 毫升离心管中制动 2 小时，持续 2 周；对照组不予任何处理。2 周后将两组小鼠分别与正常 C57 雌鼠交配，进而获得子代小鼠。2. 分别检测两组子代小鼠的血糖和其他代谢指标，并进行葡萄糖、胰岛素、丙酮酸耐量实验。3. 检测两组子代小鼠糖异生关键酶 PEPCK、G6Pase 的表达。4. 对两组子代小鼠肝脏进行 miRNA 表达谱芯片分析，以期筛选出特异性调控肝糖异生基因的 miRNA，并验证其作用。5. 检测两组子代小鼠肝脏以及父代小鼠精子中该 miRNA 启动子区的甲基化水平。

结果　1. 与对照组子代小鼠相比，应激组子代小鼠表现为血糖升高，肝糖输出增加。2. 应激组子代小鼠肝脏 PEPCK 的蛋白水平显著增加，但 mRNA 水平没有改变，提示 PEPCK 的表达可能受到转录后水平的调节。3.miRNA 表达谱芯片结合 Q-PCR 验证，筛选出特异性调节 PEPCK 表达的 miR-466，该 miRNA 的表达在应激组子代小鼠肝脏中显著下调。4. 双荧光素酶报告基因等实验证实：miR-466 可结合在 PEPCK 基因 3’-UTR 区，抑制其蛋白表达。5. 应激组子代小鼠肝脏及父代小鼠精子中 miR-466 启动子区甲基化程度增加，从而下调其表达。

结论　上述结果表明：应激状态下，父亲精子中 miR-466 甲基化程度增强，并遗传至子代小鼠肝脏，下调该 miRNA 的表达，从而增加 PEPCK 的蛋白水平，促进子代小鼠肝糖异生和高血糖的发生。本研究首次发现，父亲的心理应激能够通过表观遗传机制调控子代糖代谢，为日后人群层面的研究提供了有益的借鉴。

COR-05

下丘脑背内侧核神经肽的表达缺失通过促进 PI3k/Akt/GSK-3β 的磷酸化改善肥胖导致的胰岛素抵抗

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目的　通过向下丘脑背内侧核注射带有荧光标记（RFP）的重组腺相关病毒（AAV）载体构建神经肽 Y（NPY）表达缺失的大鼠模型，观察外周组织是否发生胰岛素抵抗，并探究可能发生的信号通路。同时观察 NPY 低表达对 3T3-L1 脂肪细胞的葡萄糖消耗和摄取的影响，并进一步探讨 Y5 受体激动剂（S-2367）及抑制剂（L-152,804）可能参与的脂肪细胞代谢紊乱的机制。

方法　1. 以空病毒载体 (AAVshCTL) 为对照，将大鼠分为高脂饮食与常规饮食组，观察 AAVshNPY 对大鼠体重及摄食变化，同时利用糖耐量和高糖钳夹实验检测胰岛素抵抗及运用 EdU 检测 β 细胞增生情况，并检测 PI3K/Akt、GSK-3β 和 Y5 受体的蛋白表达。

2.诱导分化 3T3-L1 脂肪细胞，油红O和WB进行鉴定。以胰岛素组作为阳性对照，以 AAVshCTL 为空白对照，探讨 AAVshNPY 联合 S-2367 及 L-152,804 对 3T3-L1 细胞葡萄糖消耗和摄取的影响及可能存在的信号通路。

结果　1. 与 AAVshCTL 相比，DMH NPY 表达缺失减少摄食、减轻体重，改善胰岛素抵抗，同时促进脂肪组织的 PI3K、Akt 和 GSK-3β 磷酸化，抑制 Y5 受体表达。但没有促进胰腺 β 增生。

2. 在离体细胞中，与 AAVshCTL 和胰岛素组相比，高滴度的 NPY 的表达缺失增加了基础和胰岛素的葡萄糖消耗，抑制其摄取，同时激活 3T3-L1 脂肪细胞 PI3K 、Akt 和 GSK3β 的磷酸化，L-152,804 显著促进以上影响，S-2367 则逆转以上作用。

结论　NPY 表达缺失可以减少摄食、减轻体重，改善脂肪组织胰岛素抵抗及促进脂肪组织 PI3K 、Akt 和 GSK3β 磷酸化。但并不促进胰腺 β 细胞增生，而在 3T3-L1 细胞中，NPY 表达缺失改善外周组织的胰岛素抵抗通过上调 PI3K/Akt/GSK-3β 的磷酸化和减少 Y5 受体的表达。

COR-06

2 型糖尿病患者及尿白蛋白正常的 2 型糖尿病患者肾功能降低的危险因素研究 ——回顾性队列研究

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目的　研究 2 型糖尿病患者及基线尿白蛋白正常的 2 型糖尿病患者肾功能降低的危险因素。

方法　收集 2010 年 4 月至 12 月于北京大学人民医院住院且随访半年以上的 2 型糖尿病患者的临床资料，终点事件为肾功能降低，定义为肾小球滤过率估计值 (eGFR)<60 ml/min·1.73m^2 或血肌酐水平增高至基线水平 2 倍或 2 倍以上，

采用 Cox 风险评估模型进行肾功能降低的危险因素分析。

结果 本研究共纳入 2 型糖尿病患者 451 名，平均年龄 63 ± 14 岁，中位随访时间 3.3 年，94(20.8%) 名患者发生肾功能降低。年龄增加 (HR(95%CI)1.047(1.022,1.072))、白蛋白尿 (2.009(1.310,3.079))、肾功能轻度受损 (4.438(2.679,7.351)) 或肾小球高滤过状态 (3.700(1.504,9.106)) 及糖化血红蛋白水平升高 (1.124(1.016,1.244)) 是肾功能降低的危险因素。基线尿白蛋白正常的 2 型糖尿病患者 344 人中位随访时间 3.5 年，其中 53 人 (15.4%) 出现肾功能降低，年龄增加 (HR(95%CI) 1.087(1.048,1.128))、吸烟 (3.056(1.449,6.447))、肾功能轻度受损 (5.031(2.573,9.836)) 或肾小球高滤过状态 (4.853(1.316,17.887)) 及空腹血糖水平升高 (1.101(1.020,1.189)) 是肾功能降低的危险因素，其他危险因素包括舒张压降低。

结论 在 2 型糖尿病患者中，年龄增加、白蛋白尿、肾功能轻度受损或肾小球高滤过状态及糖化血红蛋白水平升高是肾功能降低的危险因素；在基线尿白蛋白正常的 2 型糖尿病患者中，年龄增加、吸烟、肾功能轻度受损或肾小球高滤过状态及空腹血糖水平升高和舒张压降低是肾功能降低的危险因素，应及时干预可控制的危险因素并密切监测肾功能。

COR-07

叉头状转录因子 O1 通过抑制足细胞上皮间质转分化保护糖尿病肾病小鼠肾脏损伤

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目的 肾脏靶向性注射慢病毒调节糖尿病肾病小鼠肾皮质叉头状转录因子 O1（ FoxO1 ）的表达，研究 FoxO1 对糖尿病肾病小鼠肾脏保护作用及与足细胞上皮间质转分化的关系。

方法 腹腔注射 STZ 诱导 1 型糖尿病小鼠模型，肾皮质多点注射 50μl 慢病毒，分正常组（NG 组），糖尿病（血糖 ≥16.7mmol/L ）组（DM 组），DM 小鼠注射 LV-CA-FoxO1（CA 组），DM 小鼠注射 LV-NC 组（NC 组），8 周末，检测小鼠血清肌酐、尿素氮、尿微量白蛋白、24 小时尿蛋白定量；光镜、电镜观察肾脏组织形态学损害；免疫组织化学检测 ILK、nephrin 和 PCX；RT-PCR 法检测肾皮质 FoxO1、TGF-β1 mRNA 水平；免疫印迹法检测 FoxO1、p-FoxO1、TGF-β1、Smad3、p-Smad3、ILK、nephrin 和 PCX 蛋白表达水平。

结果 与 NG 组相比，血清肌酐、尿素氮升高，尿微量白蛋白及 24 小时尿蛋白定量均升高（均 P<0.05），与 DM 组相比，CA 组以上指标均降低（均 P<0.05），HE 示 DM 组较 NG 组肾小球增大，细胞增生，基质增厚。透射及扫描电镜下示，DM 组基底膜部分增厚，足突融合 / 缺失，CA 组基底膜均匀，增厚不明显，足突排列整齐，无融合 / 缺失。与 NG 组相比，DM 组 FoxO1 mRNA 及蛋白表达无变化（均 P>0.05），p-FoxO1/FoxO1 升高（均 P<0.05），TGF-β1 mRNA 及蛋白表达升高，p-Smad3/Smad3 升高，ILK 表达增多，nephrin 和 PCX 减少（均 P<0.05）。与 DM 组相比，CA 组 FoxO1 mRNA 及蛋白表达升高，p-FoxOl/FoxO1 降低（均 P<0.05），TGF-β1 mRNA 及蛋白表达减少，p-Smad3/Smad3 减小，ILK 表达减少，nephrin 和 PCX 增多，（均 P<0.05）。免疫组化示肾小球 ILK 表达增多，nephrin 及 PCX 减少（均 P<0.05），与 DM 组相比，ILK 表达减少，nephrin 及 PCX 增多（均 P<0.05）。

结论 FoxO1 可保护糖尿病肾病肾脏，通过抑制 TGF-β1/Smad3/ILK 传导通路介导的足细胞上皮间质转分化。

COR-08

脂肪间充质干细胞通过促进肝脏糖酵解改善 2 型糖尿病大鼠血糖

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目的 观察脂肪间充质干细胞 (AD-MSCs) 的输注对 2 型糖尿病大鼠高血糖的改善情况，并初步探讨其通过肝脏糖代谢途径调控血糖的作用机制。

方法 SD 大鼠高脂喂养 8 周后腹腔单次注射小剂量链脲佐菌素 (STZ,25mg/kg) 建立 2 型糖尿病大鼠模型，通过测定血糖和 HOMA — IR 值以及 IPGTT 实验鉴定 2 型糖尿病大鼠模型建模成功。给 2 型糖尿病大鼠输注脂肪间充质干细胞后于指定时间点（0h，3h，6h，12h，24h）尾静脉取血测定血糖，同时处死大鼠留取肝脏组织标本，利用实时定量 PCR检测各组大鼠肝脏组织中糖酵解过程关键限速酶（GK，PK，PFK）的 mRNA 水平表达情况，利用 western blot 技术检测大鼠肝脏组织中 GK 和 PK 蛋白水平表达情况。

结果 将成功提取的脂肪间充质干细胞经尾静脉输注给 2 型糖尿病大鼠，大鼠血糖在短时间内明显降低；提取大鼠肝脏组织检测肝脏中糖酵解过程关键酶 mRNA 水平的表达情况，PCR 结果显示细胞输注后 3 小时糖尿病大鼠肝脏组织中 GK、PFK 都有上调的趋势，在第 6 小时 PK 被明显上调；western blot 结果显示 PK 和 GK 在脂肪间充质干细胞输注后 24 小时内被明显上调。

结论 脂肪间充质干细胞可以短时间内有效改善 2 型糖尿病大鼠高血糖 , 其调节机制可能是通过促进肝脏糖酵解过程中关键限速酶（GK，PK，PFK）表达，从而促进肝脏的糖酵解来降低血糖，那么也就初步证实了脂肪间充质干细胞短时间内的迅速降糖效应是通过调节和改善了肝脏的糖代谢。

COR-09

SIRT1 介导的 p53 乙酰化在高糖诱导的 SH-SY5Y 神经细胞凋亡中的作用及机制

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目的　探讨 SIRT1 在高糖诱导的 SH-SY5Y 细胞凋亡中的作用，并研究其机制是否涉及 p53 去乙酰化。

方法　1、SH-SY5Y 细胞用 10μmol/L RA 分化后，用不同浓度糖浓度干预不同时间，采用 Hoechst33258 染色检测细胞凋亡，选择适当的糖浓度及干预时间建立高糖损伤细胞模型；

2、建立高糖损伤模细胞型后用 Western blotting 方法检测 SIRT1、乙酰化 p53、总 p53 及凋亡蛋白 Bax、Bcl-2 的变化；SIRT1 活性试剂盒检测 SIRT1 活性。

3、为确证 SIRT1 在 SH-Y5Y 神经细胞凋亡中的作用，用 SIRT1 的激动剂白藜芦醇（20μmol/L）干预高糖损伤的 SH-SY5Y 神经细胞。培养 96h 后用 Western blotting 方法检测 SIRT1、乙酰化 p53、总 p53 及凋亡蛋白 Bax、Bcl-2 的变化；用 Hoechst 染色检测细胞凋亡。

结果　1、高糖处理 SH-SY5Y 神经细胞后细胞凋亡增加，有一定的浓度及时间依赖性，且在 75mmol/L 高糖处理 SH-SY5Y 细胞 96h 后凋亡最明显。2、与正常组比较 75mmol/L 葡萄糖处理 SH-SY5Y 神经细胞 96h 后 SIRT1 表达及活性均明显下降，乙酰化 p53 表达增加，总 p53 无明显改变，而凋亡蛋白 Bax 表达增加，Bcl-2 表达无明显改变，Bax/Bcl-2 比值增加。3、20μmol/L 白藜芦醇逆转高糖诱导的 SH-SY5Y 神经细胞凋亡，降低乙酰化 p53 表达水平，增加 Bcl-2 表达，降低 Bax 表达及 Bax/Bcl-2 比值。

结论　1、高糖导致 SH-SY5Y 神经细胞凋亡增加，其机制与 SIRT1 表达减少，乙酰化 p53 增加有关。2、SIRT1 激动剂白藜芦醇可以部分逆转高糖诱导的 SH-SY5Y 神经细胞凋亡。

COR-10

PPARβ/δ 激动剂通过 GPR40 改善 2 型糖尿病 GK 大鼠胰岛 β 细胞脂毒性凋亡的研究

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目的　探讨过氧化物酶体增殖物激活受体 β/δ（Peroxisome proliferator-activated receptor β/δ，PPARβ/δ）激动剂改善 2 型糖尿病大鼠胰岛 β 细胞脂毒性凋亡及胰岛 β 细胞功能的作用，并初步探索 G 蛋白偶联受体 40（G-protein coupled receptor 40，GPR40）在其中的作用，同时比较分析激活 PPARβ/δ 与激活 PPARγ 对 2 型糖尿病大鼠胰岛功能及脂毒性凋亡的作用是否相同。

方法　采用高脂饮食喂养自发性 2 型糖尿病大鼠（Goto-Kakizaki，GK 大鼠）建立 2 型糖尿病脂毒性凋亡模型，分别使用 PPARγ 激动剂吡格列酮、PPARβ/δ 激动剂 GW501516 干预高脂饮食喂养的 GK 大鼠，同时设置喂以标准饲料的 GK 大鼠和不给予药物干预的高脂饮食喂养的 GK 大鼠作为对照。并设置喂以标准饲料及高脂饲料的 Wistar 大鼠作为母体对照。以口服葡萄糖耐量试验联合胰岛素释放试验、腹腔胰岛素耐量试验检测胰岛 β 细胞功能及胰岛素抵抗，取血测脂代谢指标及糖化血红蛋白，取出胰腺组织采用 TUNEL 法联合胰岛素双标检测胰岛 β 细胞凋亡，免疫组化检测胰岛 β 细胞量，胰岛素 GPR40 免疫荧光双染、Western-blot 检测 GPR40 表达水平。

结果　1）GK 大鼠较 Wistar 大鼠体重轻，FBG、HbA1C 明显升高，存在明显的胰岛 β 细胞功能减低及 β 细胞凋亡、β 细胞量减低及胰岛素抵抗；2）高脂饮食进一步降低 GK 大鼠的胰岛 β 细胞功能，加重 β 细胞凋亡，进一步降低 β 细胞量，并加重胰岛素抵抗；3）GW501516 改善胰岛 β 细胞功能，抑制胰岛 β 细胞凋亡，增加 β 细胞量，且 3mg/kg.d 、6mg/kg.d 两种剂量作用相同；4）与吡咯列酮相比，GW501516 对胰岛 β 细胞凋亡及 β 细胞量的改善作用相当，而在减重方面更有优势；5）GW501516 对胰岛素抵抗无明显改善、吡咯列酮可改善胰岛素抵抗；6）GK 大鼠 GPR40 表达量降低，高脂饮食进一步降低 GPR40 表达量，GW501516、吡格列酮增加 GPR40 的表达水平，提示 GW501516 通过上调GPR40 的表达参与对胰岛 β 细胞功能、凋亡及 β 细胞量的改善作用。

结论　PPARβ/δ 激动剂 GW501516 改善 GK 大鼠胰岛 β 细胞脂毒性凋亡、增加胰岛 β 细胞量、改善胰岛 β 细胞功能，GPR40 参与上述调节作用。

COR-11

M2 型巨噬细胞介导 α 细胞经 EMT 转变为 β 细胞的研究

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目的　胰岛 β 细胞数量的缺失是糖尿病发生中心环节，原位 β 细胞再生能够针对这一中心环节有效治疗糖尿病。在白喉毒素介导极端 β 细胞损伤的条件下，α 细胞自发地向 β 细胞发生转变。然而，促发转变的机制尚不明确。近年来，越来越多的证据表明巨噬细胞在损伤后组织再生和修复过程中起到关键作用。因此，我们的研究旨在探索巨噬细胞是否参与损伤条件下 α 细胞向 β 细胞的转变。

方法　我们建立了 α 细胞谱系追踪模型小鼠，给予单次大剂量 STZ（200mg/kg）注射，注射后在相应时间点取胰腺组织行连续冰冻切片，通过免疫荧光染色观察 β 细胞的数量以及 α 细胞向 β 细胞的变迁。给予 α 细胞谱系追踪

模型小鼠氯磷酸脂质体的注射，观察 STZ 注射后 α 细胞到 β 细胞的转变。利用免疫荧光和 PCR 技术检测不同类型巨噬细胞在 STZ 注射后向胰腺的浸润。利用流式分选的方法分离 STZ 注射后浸润的 M2 型巨噬细胞，体外与仓鼠 α 细胞系 InR1-G9 细胞共培养，通过免疫荧光，Western blot，PCR 技术检测 EMT 相关指标和 β 细胞特有的标记物。

结果 STZ 注射后快速地引发 β 细胞损伤，注射后 30h，每个胰岛中 β 细胞数目不足正常对照的 1%。此后发生迅猛的 β 细胞再生。每个胰岛胰岛素阳性的细胞数目从 STZ 注射后 30h 至 36h 约增加了 11 倍。在 48h，胰岛素阳性细胞数量进一步提高，相当于正常对照的 14.1%。通过谱系追踪技术，证实 STZ 注射后 36h，α 细胞发生 EMT（Epithelial-mesenchymal Transition，上皮间质化）转变为类圆形间质细胞，失去胰高血糖素的表达，同时强烈表达胰岛素，而后发生 MET（Mesenchymal-epithelial Transition，间质上皮化），进一步转变为 β 样细胞，从而引起 β 细胞再生。而利用氯磷酸脂质体阻断 STZ 注射后巨噬细胞向胰腺的浸润，抑制了 α 细胞发生 EMT，从而 α 细胞向 β 细胞的转变受到极大的压制。STZ 注射后胰腺中 M2 型巨噬细胞的数量大幅度增加。胰腺中分离的 M2 型巨噬细胞诱发小鼠 αTC1-6 细胞发生 EMT。

结论 单次大剂量 STZ 注射诱导 β 细胞极端损伤后，M2 型巨噬细胞介导 α 细胞发生 EMT，是该模型中 α 细胞自发转变为 β 细胞的关键。我们的发现揭示了体内 α 细胞向 β 细胞转变的过程和机制，为临床上实现 α 细胞向 β 细胞转变进而实现胰岛原位再生提供线索和理论依据。

COR-12

胰岛 β 细胞特异敲除 GABA B1R 小鼠的糖代谢异常

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目的 γ-氨基丁酸（γ — aminobutyric acid，GABA）是中枢主要的神经递质之一，近些年研究证实 GABA 在外周对血糖有重要的调节作用。在胰岛，GABA 促进胰岛 β 细胞分泌胰岛素，抑制胰岛 a 细胞分泌胰高血糖素。GABA 通过结合其受体发挥作用，受体主要包括是 A 和 B 型受体。其中的 GABABR 属于 G 蛋白偶联受体超家族，是由 B1 和 B2 两个亚单位组成异二聚体。胰岛 β 细胞分泌 GABA，并表达 GABABR。全身敲除 GABABR 小鼠的糖脂代谢平衡紊乱。因此，我们希望研究 GABABR 在胰岛 β 细胞生物学功能，以及血糖平衡中的作用。我们利用 cre-loxp 技术在胰岛 b 细胞特异敲除 GABABR 的 B1 亚基，观察敲除小鼠的生物学表型。

方法 GABABR-B1-flox(+/+) 小鼠和 Mip-CreER^{Tam}(+/-) 小鼠经多代交配繁育产生 Mip-CreER^{Tam}(+/-)-GABABR-B1-flox(+/+) 小鼠，小鼠的基因组中含有 Cre 酶基因经注射 Tamoxifen（Tm）后在胰岛 β 细胞特异性中特异表达，进而敲除 B1 亚基；和 Mip-CreER^{Tam}(-/-)-GABABR-B1-flox(+/+) 小鼠的基因组中不含有 Cre 酶基因，注射玉米油的小鼠作为对照。6-8 周龄的小鼠随机分组后，分别注射 Tm 和玉米油。检测小鼠的体重，进食量，血糖，糖耐量（GTT），胰岛素耐量（ITT），评价小鼠的糖脂代谢变化；检测小鼠的胰岛素水平，糖刺激胰岛素分泌，评价小鼠胰岛 β 细胞功能。

结果 胰岛 β 细胞特异敲除 B1 小鼠，体重增加更快，伴随进食增加。随机血糖和禁食血糖没有显著差异。GTT 和 ITT 显示，敲除小鼠的糖耐受不良和胰岛素耐受不良。敲除小鼠在糖刺激时胰岛素分泌下降。

结论 以上结果提示胰岛 β 细胞的 GABA-GABABR 系统在糖刺激胰岛素分泌的过程中发挥重要作用。

COR-13

即使 UACR 与 eGFR 在正常范围内的变异或低水平的异常已可能是糖尿病周围神经病变相关的危险信号

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目的 本研究的目的在于探讨糖尿病周围神经病变（DPN）与尿白蛋白肌酐比值 (UACR) 及肾小球滤过率（eGFR）的关系，特别是 DPN 与正常及轻度异常的 UACR 和 eGFR 的关系。

方法 本研究为一项回顾性调查，共纳入 2 型糖尿病患者 1059 名，其中男性 589 名，女性 470 名。根据神经传导功能检测诊断糖尿病神经病变，其中合并 DPN 417 名，非 DPN 642 名。收集患者尿白蛋白肌酐比值、肾小球率过滤、血肌酐、尿酸、血脂、糖化血红蛋白等生化指标。肌电图测定患者正中神经、尺神经的运动神经传导速度（MCV）、感觉神经传导速度（SCV），胫神经、腓总神经的 MCV 及腓浅神经、腓肠神经的 SCV。

结果 与非 DPN 组相比，DPN 组有较高的 UACR 水平和较低的 eGFR 水平（p<0.001）。随着 UACR 的升高和 eGFR 的下降，各神经 CV 下降，DNP 的检出率升高，并且这种变化在正常或轻度异常的 UACR 和 eGFR 分组中仍然部分存在。相关分析显示，各神经的 CVU 与 ACR 呈负相关，与 eGFR 呈正相关，而在 UACR ＜ 30mg/g 和 eGFR≥60 ml/min/1.73m2 的亚组中，UACR 与 eGFR 仍与 CV 呈不同程度相关。回归分析显示，较高的 UACR 水平和较低的 eGFR水平与DPN危险比值比独立相关，OR值分别（3.666，95%CI 2.989-4.497；2.513，95%CI 2.070-3.052），而且这种关系在 UACR ＜ 30mg/g 和 eGFR≥60 ml/min/1.73m2 的人群中就已经存在（OR 分别为 2.456，95%CI 1.461-4.127；2.021，95%CI 1.276-3.203）。ROC 曲线分析，UACR、eGFR 及二者联合推断 DPN 的曲线下面积（AUC）分别为 0.749、0.662、0.731，灵敏度分别为 62.00%，47.40%，

55.30%。

结论　UACR 的上升和 eGFR 的下降是 DPN 的相关危险因素，即使 UACR 与 eGFR 在正常范围内的变异或低水平的异常已可能是 DPN 相关的危险信号；且 UACR 比 eGFR 更为敏感。单独 UACR 对 DPN 有中等提示作用，联合 eGFR 并未增加对 DPN 的提示作用。

COR-14

利格列汀以非葡萄糖依赖性的方式增加抗氧化功能以改善糖尿病小鼠的肾脏肥大和蛋白尿

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目的　研发新药以遏制糖尿病肾病（DKD）的流行十分必要。有研究表明，DPP-4 抑制剂可能通过改变活性氧类（ROS）水平而具有保护作用。本研究利用如下假说来探讨 DPP-4 抑制剂利格列汀的作用：即 DPP-4 抑制会以非葡萄糖依赖性的方式发挥抗氧化功能以改善 DKD 的疾病进程。

方法　实验选取两种小鼠模型：雄性 DBA2J 小鼠和 G6PD 缺陷小鼠。本课题组前期已证实 G6PD 缺陷小鼠可作为抗氧化功能受损的模型。糖尿病模型则通过腹腔注射链脲霉素加以诱导。小鼠随机分为 3 组：糖尿病（DM）组、糖尿病 + 利格列汀组（DM +Lina 83ppm）以及非糖尿病对照组（NDM）。小鼠给药治疗 12 周。

结果　在 DBA2J 小鼠中，DM 组和 DM+Lina 组的体重、随机血糖和空腹血糖均无差别。利格列汀改善 DM 组小鼠的蛋白尿。DKD 的早期变化是肾脏肥大。利格列汀治疗显著改善肾脏肥大（肾重 / 体重比值下降）。经过利格列汀干预治疗后，小鼠的过氧化氢酶和 MnSOD 的 mRNA 水平均有增加，提示其抗氧化作用。在 G6PD 缺陷小鼠（G6PD-DM）中，G6PD-DM 组和 G6PD-DM+Lina 组的体重和随机血糖均无差异。但在 G6PD-DM+Lina 组，经过利格列汀干预治疗后肾重 / 体重比值显著增加，小鼠尿白蛋白显著增加，提示在抗氧化功能受损伤的小鼠中，利格列汀肾脏保护作用丧失。

结论　在 DBA2J 小鼠的 DKD 模型中，利格列汀以非葡萄糖依赖性的方式增强抗氧化功能以发挥其肾脏保护作用。

COR-15

妊娠期亚临床甲减妇女产后 9 年的甲功转归

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目的　通过前瞻性流行病学调查，观察妊娠期亚临床甲减妇女产后 9 年的甲功转归情况。

方法　中国医科大学内分泌研究所在辽宁省沈阳市 10 家医疗机构的内分泌科或妇产科进行了妊娠早期妇女的甲状腺疾病的筛查，于产后 8.7 ± 0.9 年对其中的亚临床甲减妇女进行随访。获得亚临床甲减组 33 人，甲功正常组 20 人。随访指标包括血清 TSH、FT4、FT3、TPOAb、TgAb。

结果　亚甲减组共 33 人，产后 4 人（12.12%）出现临床甲减，6 人（18.18%）维持亚甲减，1 人（3.03%）出现低 T4 血症，22 人（67.67%）甲功恢复正常。其中 SCH-LT4（+）组共 15 人，产后 4 人（26.67%）出现临床甲减，3 人（20.00%）产后维持亚临床甲减，产后 8 人（53.33%）甲功恢复至正常范围内。SCH-LT4（-）组共 18 人，3 人（16.67%）产后维持亚临床甲减，1 人（5.56%）产后出现低 T4 血症，产后 14 人（77.78%）甲功恢复至正常范围内。妊娠期 TSH ＞ 5mIU/L 是亚甲减孕妇产后持续甲功异常的危险因素（[7/11]vs[3/22]，63.63% vs 13.63% p=0.003）。妊娠期甲功正常的随访妇女共 20 人，有 3 人（15%）在产后出现亚甲减，1 人（5%）出现低 T4 血症，16 人（80%）产后甲功维持正常。

结论　大部分妊娠期亚临床甲减妇女产后甲功可以恢复正常，对接受 L-T4 治疗的亚甲减孕妇应该在产后重新评估其甲状腺功能。

COR-16

左甲状腺替代治疗对亚临床甲状腺功能减退患者非酒精性脂肪性肝病的影响

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目的　非酒精性脂肪性肝病（NAFLD）是肝功能酶学异常和慢性肝病最常见的原因，并且与心血管疾病的发生密切相关，严重威胁人类健康。近年来，有研究提示亚临床甲状腺功能减退（简称亚甲减）是 NAFLD 的独立危险因素，那么，通过补充甲状腺激素来纠正亚甲减是否可以改善 NAFLD？目前尚缺乏此类研究。本研究旨在探讨左甲状腺素（L-T4）替代治疗对亚甲减患者 NAFLD 的影响，为 NAFLD 的治疗提供新策略。

方法　本研究基于一项随机对照试验，对其进行事后分析。纳入分析了 363 例亚甲减患者，包括 33 例重度亚甲减患者（TSH ≥ 10 mIU/L，全部接受 L-T4 替代治疗），和 330 例轻度亚甲减患者（4.2 ≤ TSH < 10 mIU/L，其中 181 例接受 L-T4 治疗，149 例未接受治疗）。随访期为 15 个月，观察各组人群在随访期内 NAFLD 的患病率和血清肝酶的变

化。在合并血脂异常的轻度亚甲减患者中进行亚组分析，比较干预组与对照组观察指标的差异。

结果 经 L-T4 治疗后，重度亚甲减患者 NAFLD 的患病率显著下降（从 48.5% 下降至 24.2%，P=0.041）。亚组分析显示，L-T4 干预可显著降低合并血脂异常的轻度亚甲减患者中 NAFLD 的患病率，并可改善肝功：随访 15 个月后，干预组 NAFLD 的患病率从 54.3% 下降至 40.5%，P=0.035，血清丙氨酸氨基转移酶（ALT）水平也显著下降（从 19.93 ± 10.60 下降至 18.07 ± 8.27, P = 0.043）；而对照组 NAFLD 的患病率和血清 ALT 水平均无明显变化。另外，干预组体重、BMI、血清甘油三酯、血清总胆固醇也明显降低，推测 L-T4 可能通过减重、纠正血脂紊乱进一步改善 NAFLD。

结论 在亚甲减患者，尤其是重度亚甲减、或合并血脂异常的轻度亚甲减患者中，L-T4 替代治疗可显著改善 NAFLD 及肝功。提示对合并亚甲减的 NAFLD 患者，补充甲状腺激素可作为控制 NAFLD 的新方法。

COR-17

中国人群恶性甲状腺结节超声诊断效力的分析

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目的 甲状腺超声是评价恶性甲状腺结节的重要检查，然而目前缺乏国人恶性结节超声特征诊断效力的相关研究。本研究旨在评价中国人群中能预测甲状腺结节恶性的超声学特征。

方法 我们选取了从 2011 年 3 月到 2014 年 7 月在北京大学第一医院进行甲状腺超声检查和手术的甲状腺结节患者（其中 424 个恶性结节，338 个良性结节）。运用单变量和受试者工作特征（Receiver operating characteristic, ROC）分析的方法计算低回声、边界不清、实性、纵横比失调、微钙化和结节内血流增多的单一超声特征预测恶性结节的灵敏度、特异度、约登指数、阴性预测值和阳性预测值，以及多种特征组合的 ROC 曲线下面积分析。

结果 研究发现与良性结节患者相比，恶性结节的患者年龄更小（45.1 ± 11.6 岁 vs 51.3 ± 11.9 岁）并且没有明显的传统危险因素（p<0.001,p=0.93）。与术后病理结果对照，任何一项超声特征都不能单独预测恶性结节。边界不清的约登指数在所有超声特征中最高，为 51.9%，其次是低回声为 45.2%。灵敏度最高和次高的特征是实性和低回声（分别为 89.7% 和 89.2%），特异度最高和次高的特征是纵横比失调和微钙化（分别是 98.5% 和 90.6%）。彩色多普勒的结节内血流增多对恶性甲状腺结节评价的效力较弱。ROC 分析后，低回声与边界不清加实性、纵横比失调和微钙化中任一的 3 个超声特征组合的曲线下面积（Areas under the curve, AUC），可以与全部五种超声特征组合的 AUC 相重叠（AUC=0.850-0.901）。

结论 需高度警惕 B 超筛查时甲状腺结节的纵横比失调和微钙化。根据约登指数和 ROC 结果分析，低回声与边界不清加实性、纵横比或微钙化任一的三种超声特征组合有较高的国人恶性甲状腺结节预测价值。

COR-18

S1PR1 阻滞剂 FTY720 在自身免疫性甲状腺炎中的作用及机制研究

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目的 目前已有研究表明 SPHK1/S1P/S1PR1 可参与多种自身免疫疾病的发生发展，对 S1PR1 进行阻断干预可以缓解疾病的严重程度。然而，在碘致自身免疫性甲状腺炎 NOD.H-2^{h4} 小鼠模型中的作用目前还不明确。本研究的主要目的就是要探讨碘值自身免疫性甲状腺炎 NOD.H-2^{h4} 小鼠模型中 FTY720 治疗的免疫学及其分子机制。

方法 对 6-8 周龄健康 NOD.H-2^{h4} 小鼠，取脾脏进行 CD4+T 淋巴细胞磁珠分选并培养，分别给予 S1P 刺激 FTY720 阻断，探讨 S1P 对 STAT3 的激活作用以及 S1P 激活的 CD4+T 细胞内的信号通路。体内实验探讨 FTY720 是否对自身免疫性甲状腺炎具有预防及治疗作用。NOD.H-2^{h4} 小鼠随机分为正常对照组（CON 组），碘致甲炎组（SAT 组），预防组（PRE 组），治疗组（TRE 组）及单纯打药 FTY720 组（FTY 组）。检测各组甲炎发生率，血清 TgAb 水平，及脾脏细胞亚群及 P-STAT3 水平。

结果 S1P 使 CD4+T 细胞内 P-STAT3 的水平增加。FTY720 可阻断 S1P 对 STAT3 的激活作用。进一步证实 S1P 可通过 S1PR1-JAK-2 激活 P-Tyr^{705}-STAT3, 可通过 S1PR1-AKT-mTOR 激活 P-Ser^{727}-STAT3。体内实验证实，经 FTY720 灌胃的 PRE 组和 TRE 甲状腺炎的发生显著低于 SAT 组 (P<0.05)。PRE 组血清 TgAb 始终低于 SAT 组，TRE 组在 14 周 ,16 周时血清 TgAb 显著低于 SAT 组。SAT 小鼠脾脏 Th1,Th17 及 Tfh 细胞亚群显著高于 CON 组（P<0.05），而 PRE 组及 TRE 组 Th1、Th17 及 Tfh 较 SAT 组相比，各细胞亚群比例显著降低，与 CON 组比无统计学差异。SAT 组中 CD4+T 细胞 P-Tyr^{705}-STAT3 和 P-Ser^{727}-STAT3 与 CON 组相比显著增高，PRE 组和 TRE 组 P-Tyr^{705}-STAT3 和 P-Ser^{727}-STAT3 较 SAT 组显著降低。

结论 NOD.H-2^{h4} 小鼠高碘喂养诱导自身免疫性甲状腺炎的同时给予 FTY720 预防性及治疗性处置后，甲状腺炎评

分降低，血清 TgAb 滴度均明显降低。FTY720 主要通过阻断 S1PR1-JAK2 及 S1PR1-AKT-mTOR 通路抑制其对 STAT3 的激活起到治疗作用。

COR-19

亚临床甲状腺机能减退症妇女体外受精结局的研究

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目的　探讨左旋甲状腺素（LT4）替代治疗的 SCH 妇女体外受精（IVF）的结局以及 IVF 对此类人群甲功的影响。

对象及方法 1. 对 2015 年 6 月至 10 月在我院接受 IVF 助孕的 2463 例不孕妇女进行血清促甲状腺素（TSH）测定，分析甲功与 IVF 后早期妊娠结局的关系。2. 纳入初次行 IVF 助孕的 SCH 妇女 67 例，给予 LT4 替代治疗，TSH 控制于 0.2-4.2mIU/l 之后启动 IVF 周期，追踪随访 IVF 后早期妊娠结局。

结果　1.2463 例接受 IVF 助孕的妇女中甲减 /SCH 的患病率为 3.83%。与甲功正常者相比，甲减 /SCH 患者 IVF 后生化妊娠率显著降低（35.71% vs 49.31%,x=17.109,p<0.001）。

2. 接受 LT4 替代治疗的 SCH 妇女 IVF 后生化妊娠率为 (56%)，与同期甲功正常者 IVF 后生化妊娠率（48.78%）相比无显著差异（x=0.793，p=0.373）。

3. 接受 LT4 替代治疗的 SCH 妇女 IVF 前血清 TSH 水平为 1.8mIU/l（0.43，2.57 mIU/L），IVF 周期中 HCG 日降低为 1.05mIU/l（0.366，2.385 mIU/L），生化妊娠后升高为 4.625 mIU/l（1.13-6.88 mIU/L）。

4. 接受 LT4 替代治疗的 SCH 妇女中，TSH0.2-2.5mIU/l 组与 TSH2.5-4.2mIU/l 组之间 IVF 生化妊娠率无显著差异（61.5% vs52.63%，p=0.806）。前者临床妊娠后 TSH ＞ 2.5mIU/l 的比例为 52.38%，后者临床妊娠后 TSH ＞ 2.5mIU/l 的比例为 77.78%。

结论　甲减 / 亚临床甲减可影响 IVF 后早期妊娠结局，LT4 替代治疗有利于提高此类患者的 IVF 成功率。IVF 周期前较严格的 TSH 控制对提高早期妊娠率可能无影响，但可能对临床妊娠后的 TSH 达标有益。

COR-20

妊娠 4-8 周轻度甲状腺功能减退对妊娠并发症的影响

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目的　妊娠合并甲状腺疾病的发病率较高，目前轻度的甲状腺异常对妊娠并发症的影响尚存在争议。本研究旨在探究亚临床甲状腺功能减退症（简称亚临床甲减）、单纯甲状腺过氧化物酶抗体（TPOAb）阳性及低 T4 血症对妊娠并发症的影响；评估应用 L-T4 治疗可否改善妊娠结局。

方法　本研究对 9245 例 4-8 周妊娠妇女根据妊娠期特异的甲状腺功能诊断标准进行甲状腺功能筛查，根据其甲状腺功能及是否同意临床干预进行分组，随访妊娠结局，并应用 SPSS 统计软件进行分析。

结果　在所调查的 9245 例妊娠妇女中，亚临床甲减 342 例（患病率 3.70%）; 单纯 TPOAb 阳性 293 例（患病率 3.17%）; 单纯低 T4 血症 684 例（患病率 7.40%）；与甲状腺正常组相比，亚临床甲减组流产率显著增加（14.29% vs 7.15%，p<0.05）；TPOAb 阳性组流产、早产、低体重儿的发生率显著增加（分别是 13.64% vs 7.15%，p<0.05；10.00% vs 3.01%，p<0.05;7.27% vs 2.90%,p<0.05）；低 T4 血症组巨大儿发生率显著增加（14.95% vs 10.27%，p<0.05）。与未干预组相比，亚临床甲减干预组流产率明显下降（9.43% vs 14.29%），与甲状腺正常组相比无显著差异。与未干预组相比，TPOAb 阳性干预组流产率下降（9.09% vs 13.64%）、早产率下降（2.02% vs 10.00%）、低体重儿的发生率下降（0.00% vs 7.27%），与甲状腺正常组相比均无显著差异。与未干预组相比，低 T4 血症干预组巨大儿的发生率明显下降（9.29% vs 14.95%），与甲状腺正常组相比无显著差异。

结论　妊娠 4-8 周妇女合并轻度甲状腺功能减退对妊娠结局有不良影响，应对妊娠早期妇女进行甲状腺功能筛查，适当、及时的治疗可降低妊娠风险。

COR-21

Graves 病 CD4+T 淋巴细胞中 miR-4443 作用机制研究

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目的　研究 GD 患者 CD4+T 淋巴细胞中 miRNAs 表达谱及 miR-4443 参与 GD 发生、发展的机制。

方法　运用 Microarray 芯片方法检测未治疗的初诊 GD 患者（uGD）及正常志愿者（hCD）外周血 CD4+T 淋巴细胞中 miRNAs 表达谱；根据芯片结果和既往文献报道，挑选 8 个 miRNAs 进行 realtime PCR 扩大样本验证；将 uGD 患者的 miRNAs 相对表达量与 GD 相关临床参数进行相关性分析，选择与 GD 最相关的 miR-4443 进行深入研究；分选 CD4+T 淋巴细胞，转染 miR-4443 mimic 或 inhibitor 后，观察 miR-4443 对 CD4+T 淋巴细胞炎症因子、趋化因子和增殖的影响；通过报告基因，表达分析和小分子干扰 RNA（siRNA）实验证实 miR-4443 作用的靶基因和靶通路。

结果　uGD 和 hCD 的 miRNA 谱存在显著差异；扩大样本验证后发现 miR-4443 与 GD 相关临床参数显著相关；miR-4443 在 uGD 患者中显著上调，随着治疗的进展逐渐恢复正常水平；miR-4443 可增加 CD4+T 淋巴细胞分泌包括 IL-1β、IL-6、IL-17、IFNγ 及 CCL21 在内的多种炎症

和趋化相关细胞因子，可促进 CD4+T 淋巴细胞增殖；miR-4443 可直接与肿瘤坏死因子受体相关因子 4（TRAF4）的 3’ UTR 结合以抑制其表达，从而激活 NF-κB 通路；进一步分析发现 uGD 患者 CD4+T 淋巴细胞中 TRAF4 表达下降，且与 miR-4443 水平显著负相关，当抑制其表达后有类似于过表达 miR-4443 的作用。

结论 GD 患者 CD4+T 淋巴细胞中上调的 miR-4443 通过抑制 TRAF4 的表达以促进 NF-κB 通路活性，从而影响 CD4+T 淋巴细胞的功能，参与 GD 发生、发展的免疫致病过程。

COR-22

短程泼尼松治疗中重度亚急性甲状腺炎 — 一项前瞻，随机，对照，单盲研究

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目的 糖皮质激素作为中重度亚急性甲状腺炎 (SAT) 的常用治疗方案，可快速缓解发热和疼痛。目前尚没有报道短程强的松治疗中重度 SAT，我们评估了这种治疗的有效性及安全性。

方法 这是一项前瞻，随机，对照，单盲研究（ClinicalTrials.gov ID：NCT01837433）。入组 2013 年 8 月至 2014 年 12 月 50 例中重度SAT(评分≥3 分)，随机分两组。实验组：强的松早 20mg 晚 10mg 一周，控制症状后停用，第二周塞来昔布 400mg 首日顿服，余下 6 天塞来昔布 200mg Bid，共服药 2 周。对照组：强的松早 20mg 晚 10mg 一周，控制症状后自第二周每周减量 5mg，至停药，共服药 6 周。所有患者停药后随访 6 月。主要终点：治疗结束时，两组有效性及复发率差异。次要终点：两组停药时，甲状腺、肾上腺皮质功能，血糖，血压，骨代谢，脂类间差异。

结果 基线年龄，性别，严重度评分，血沉，C 反应蛋白，吸碘率 3 小时、24 小时，FT3，FT4，TSH，糖化白蛋白，甘油三酯，总胆固醇，皮质醇 (8am)，收缩压，舒张压，空腹血糖，早餐后 2 小时血糖，晚餐前血糖，睡前血糖，甲状旁腺素指标，P 均 >0.05，无统计学差异。主要终点：两组有效率分别为 69.2%（18/26）和 75%（18/24），P=0.757, 复发率分别为 30.8%（8/26）和 25%（6/24），P 均 >0.05，无统计学差异。次要终点：两组停药时收缩压，甲状旁腺素均 P<0.05，有统计学差异。糖化白蛋白，末梢血糖，甘油三酯，总胆固醇，皮质醇 (8am)，舒张压，P 均 >0.05，无统计学差异。

结论 本研究是第一个评价 1 周泼尼松与标准 6 周治疗中重度 SAT 疗效和安全性的研究，是迄今为止最短程泼尼松治疗 SAT 的研究。研究表明：短疗程与标准疗程一样有效，复发率相似。而骨，血压副作用较少。

COR-23

重组人 II 型肿瘤坏死因子受体 - 抗体融合蛋白治疗甲状腺相关性眼病的临床研究

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目的 探讨重组人 II 型肿瘤坏死因子受体—抗体融合蛋白（益赛普）治疗中重度活动性甲状腺相关性眼病（thyroid associated ophthalmopathy，TAO）的临床疗效及安全性。

方法 40 例中重度活动性 TAO 患者随机分成为两组，分别予益赛普及甲泼尼龙治疗各 12 周，观察并比较两组患者治疗前后临床活动度评分（Clinical activity score，CAS）、眼病指数（Ophthalmomopathy index，OI）及突眼度的改善情况；同时检测两组患者治疗前后血清细胞因子（TNF-α、IL-2、IL-6）水平的变化并比较两组患者不良反应。

结果 益赛普组和甲泼尼龙组均能显著降低 TAO 患者 CAS 评分及 OI 指数（$P < 0.05$），但两组间比较无统计学差异（$P > 0.05$）；两种治疗方法对患者突眼度的改善均不显著（$P > 0.05$）。治疗后两组患者血清 IL-6 及 TNF-α 水平均显著下降（$P < 0.05$），且益赛普组 TNF-α 水平下降明显高于甲泼尼龙组（$P < 0.05$），而两组血清 IL-2 水平在治疗前后均无显著变化（$P > 0.05$）。与甲泼尼龙组相比，益赛普组发生不良反应的比例下降。

结论 易赛普治疗可显著改善 TAO 患者临床症状，疗效与糖皮质激素相当，且耐受性及安全性优于糖皮质激素，为 TAO 的治疗提供新的研究方向。

COR-24

microRNA-20b 在甲状腺乳头癌中的表达及其作用机制

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目的 microRNAs（miRNAs）是一类内源性非编码小分子 RNAs。研究发现部分 miRNAs 在 PTC 中表达异常并参与调控 PTC 细胞的增殖、凋亡、迁移和侵袭。最近研究发现 microRNA-20b（miR-20b）在 PTC 中表达明显下降，其在 PTC 中发挥的生物学功能及作用机制目前尚不明确。本研究旨在探索 miR-20b 在 PTC 中的生物学功能以及 miR-20b 与 MAPK/ERK 信号通路的关系。

方法 通过 qRT-PCR 检测 PTC 和癌旁甲状腺组织中 miR-20b 的表达水平，并研究其与患者临床病理学特征的关系。在甲状腺乳头状癌细胞系 K1 和 TPC-1 中高表达 miR-20b，并通过 MTT 实验和细胞计数检测细胞活力情况；通过 Transwell 实验和划痕实验检测细胞的迁移、侵袭能力。我们进一步预测并验证 miR-20b 的靶基因，探索 miR-20b 的

作用机制。

结果　在 47 对 PTC 及癌旁甲状腺组织中，我们发现 miR-20b 在癌组织中的表达水平显著低于癌旁正常甲状腺组织。miR-20b 的表达下调与 PTC 的颈部淋巴结转移和 TNM 分期 III/IV 期癌肿相关。在 K1 和 TPC-1 细胞中高表达 miR-20b 后，细胞的活力、迁移和侵袭能力明显被抑制。通过 TargetScan 软件，我们发现预测的靶基因中 SOS1 和 ERK2 分别是 MAPK/ERK 通路的上游蛋白和通路的核心蛋白。双荧光素酶报告基因检测显示 SOS1 和 ERK2 是 miR-20b 的靶基因，并且发现 miR-20b 可以通过作用于 SOS1 和 ERK2 抑制 MAPK/ERK 通路的活性。通过 siRNA 抑制 SOS1 和 ERK2 表达后可以产生与高表达 miR-20b 一致的细胞生物学现象，而回补实验显示高表达靶基因 SOS1 和 ERK2 可以部分抑制 miR-20b 的生物学功能，这进一步提示 miR-20b 通过作用于靶基因 SOS1 和 ERK2 抑制 MAPK/ERK 通路的活性，并发挥抑制细胞活力、迁移和侵袭的生物学功能。

结论　在 PTC 组织中 miR-20b 表达显著低于癌旁甲状腺组织，且 miR-20b 的表达下调与 PTC 的颈部淋巴结转移和晚期肿瘤（TNM 分期 III/IV 期）相关。miR-20b 可能通过靶基因 SOS1 和 ERK2 抑制 MAPK/ERK 通路的活性，在 PTC 中发挥抑癌基因的作用。我们结果提示 miR-20b 可能在 PTC 的发生和进展中起到重要的调节作用，有望成为 PTC 治疗的一个新靶点。

COR-25

环磷酰胺联合骁悉序贯治疗激素复发性甲状腺相关性眼病 20 例疗效分析

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目的　观察免疫抑制剂环磷酰胺、骁悉序贯治疗糖皮质激素复发性甲状腺相关性眼病的临床疗效。

方法　回顾性分析 2013 年至 2015 年在我院内分泌科住院诊治的甲状腺相关性眼病患者 20 例，所有患者均曾用足够剂量的糖皮质激素治疗眼部症状好转后再次复发，且 CAS 评分在 3 分或 3 分以上，治疗方法包括低盐饮食、高枕卧位、佩戴有色眼镜、戒烟等，对所有患者进行甲状腺疾病治疗的同时予环磷酰胺静脉冲击后予小剂量骁悉口服治疗，治疗前后检测所有患者的血常规、尿常规、肝功能、肾功能及甲功，评估其突眼度及 CAS 评分变化，疗效判定标准为临床治愈：眼部自觉胀痛、畏光、流泪等症状消失，眼球明显回缩，眼球突出度＜ 18mm，或较前减少 3mm 以上。显效：眼部自觉症状消失，眼球突出度较前减少 2mm 以上。有效：眼部自觉症状好转，眼球突出度减少 1~2mm。无效：眼部自觉症状改善，但眼球突出度无明显变化或较前减少＜ 1mm。应用 SPSS21.0 统计学软件对所得数据进行分析，以 α=0.05 作为显著性检验水准。

结果　1. 治疗前后患者的血常规、尿常规、肝功能、肾功能等均处于正常范围，差异不明显（P ＞ 0.05），甲功经治疗后可维持正常水平；2. 治疗前平均突眼度 19.60 ± 2.18mm，治疗后为 18.00 ± 1.73mm，差异有统计学意义（P ＜ 0.05）；治疗前平均 CAS 评分为 3.95 ± 1.00，治疗后为 0.65 ± 0.93，治疗前后差异有统计学意义（P＜ 0.05）；3. 本研究 20 例患者中，临床治愈 8 例，占 40%；显效 6 例，占 30%；有效 3 例，占 15%；无效 3 例，占 15%，总体好转率为 85%，其中病程较长、眼部病情分级越高的男性患者治疗效果较为明显。

结论　对于糖皮质激素治疗后再次复发的甲状腺相关性眼病患者，应用环磷酰胺及骁悉序贯疗法治疗有效，对突眼和疾病活动性效果好，且副作用较小。

COR-26

妊娠妇女孕早期的铁缺乏可能预示其孕中期低甲状腺素血症和临床甲状腺功能减退症的发生

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目的　由于妊娠期母体对铁的需求量增加，孕妇极易发生铁缺乏。铁缺乏可以减弱含铁酶甲状腺过氧化物酶活性，进而导致甲状腺激素合成减少。本研究旨在探讨妊娠妇女孕期铁缺乏与低甲状腺素血症之间的相关性。

方法　2012-2015 年，孕早期和亚临床甲状腺功能减退症研究，简称 SHEP 研究实施。在辽宁省 19 家医院注册登记了 9964 名孕 4-12 周妊娠妇女和 2272 名育龄期拟妊娠妇女。9964 人中 1834 人参与了随访研究。在排除了多胎妊娠，既往和初访时有甲状腺疾病史和其他慢性病史，服用影响甲状腺功能药物（口服避孕药、糖皮质激素、多巴胺、抗癫痫药等）、孕期服用含碘或含铁的维生素或药物、孕期服用甲巯咪唑、丙基硫氧嘧啶或甲状腺激素治疗者后，我们对 811 人进行了分析，其中 760 人参加了孕中期，350 人参加了孕晚期随访，299 人参与了孕中、晚期随访。所有随访人

群进行了血清 FT4，TSH，TPOAb，TgAb 铁蛋白，转铁蛋白受体，和尿碘的测定。

结果 1、孕早期妇女的铁储备量和 FT4 水平显著高于与育龄期拟妊娠妇女。2、随着妊娠的进展，孕妇的铁储备量持续下降，血清 FT4 水平亦随之下降。3、多元线性回归分析显示：在孕早期和孕中期，血清 FT4 的水平与铁储备量呈显著的正相关，但在孕晚期，两者无相关。4、孕早期铁缺乏的孕妇，孕中期发生低甲状腺素血症和临床甲状腺功能减退症的比例显著高于铁正常妇女。

结论 妊娠妇女孕早期的铁缺乏可能预示其孕中期低甲状腺素血症和临床甲状腺功能减退症的发生。孕早期铁储备不足的孕妇宜监测孕期甲状腺激素水平。

COR-27

不同体质指数人群正常范围内血清甲状腺激素的变化及其意义

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目的 比较不同体质量指数（body mass index，BMI）人群正常范围内血清甲状腺激素水平的差异。探讨血清甲状腺激素水平与 BMI 的关系。

方法 筛查湖南省人民医院体检中心 2014 年 11 月至 2015 年 1 月体检人群共 1479 例，记录一般临床资料，排除甲状腺疾病史及家族史，共 847 例资料完整者完成甲状腺功能检测。采用 2000 年国际肥胖工作组（International obesity task force，IOTF）规定的亚太地区肥胖标准：BMI≥25kg/m^2 为肥胖。其中，甲功正常者 740 例（肥胖者 519 例，非肥胖者 221 例），甲状腺功能异常者 107 例。比较肥胖组与非肥胖组发生甲状腺功能异常的差异。将 740 例甲状腺功能正常者根据 BMI 从低到高进行分组，分为：D1 组（n=221）：18.5~25 kg/m^2；D2 组（n=357）：25~28 kg/m^2；D3 组（n=107）：28~30 kg/m^2；D4 组（n=55）：30 kg/m^2~。比较不同 BMI 各组正常范围内血清甲状腺激素水平的差异。探讨血清甲状腺激素水平与 BMI 的关系。

结果 1. 与非肥胖组比较，肥胖组发生亚临床甲减风险增加（6.02% vs 10.36%），OR 值为 1.804，差异具有统计学意义（$p < 0.05$）。2. 随着 BMI 的逐渐升高，BMI≥25kg/m^2 的肥胖组较正常体重组血清 FT4 下降（$p < 0.05$）。其中，BMI 为 28-30kg/m^2 的肥胖组血清 FT4 最低，而当 BMI 升高至 30 kg/m^2 以上时，血清 FT4 上升（$p < 0.05$）。3. 随着 BMI 的升高，BMI 为 28-30kg/m^2 的肥胖组 FT3/FT4 比值较其他各组明显升高（$p < 0.05$）。

结论 1. 肥胖人群与非肥胖人群比较，发生亚临床甲减的风险增加。2. 在 BMI < 30 kg/m^2 的人群中，随着 BMI 的逐渐升高，血清 FT4 水平下降，FT3/FT4 比值升高，提示随着肥胖程度的加重，甲状腺功能逐步下降，但 T4 转化为 T3 的比例代偿性增加。3. BMI≥30 kg/m^2 的人群较为特殊，其甲状腺激素水平与非肥胖组类似，提示该组人群可能存在对甲状腺轴的独特调节机制。

COR-28

采用 PDCA 循环引导的全程运动干预模式对 2 型糖尿病患者相关代谢指标影响的研究

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目的 探讨采用 PDCA 引导的全程运动干预模式对 2 型糖尿病（T2DM）合并非酒精性脂肪肝（NAFLD）患者定期随访，对其血糖、血脂和生活质量的影响。

方法 选择 T2DM 合并 NAFLD 的患者 121 例，采用随机数字表进行分组。实验组在常规运动的同时，采用 PDCA 循环引导的全程运动干预模式进行随访；对照组进行常规运动模式随访。观察两组随访前、随访后 3 个月、随访后 6 个月的血糖、血脂达标率及生活质量的变化。

结果 随访后 3 个月，实验组 FPG、2hPG、HbA1c、TG、LDL-C 等代谢指标达标率优于随访前（$P < 0.05$）；随访后 6 个月，实验组 FPG、BMI、2hPG、HbA1c、TC、TG、LDL-C、HDL-C 等代谢指标达标率优于对照组（$P < 0.05$）；随访后 6 个月，实验组生活质量总分、心理、生理、社会关系及自身健康状况总体主观感受得分高于随访前（$P < 0.05$）。

结论 采用 PDCA 引导的全程运动干预模式对患者进行定期随访，能提高患者的血糖、血脂的达标率和生活质量。

COR-29

丁酸梭菌对于高脂膳食诱导的肥胖和结肠免疫紊乱的调节作用

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目的 肥胖是一系列代谢紊乱的总称并伴有全身多器官的系统炎症。最近的研究指出高脂膳食会造成肠道的免疫失衡。益生菌尤其是乳酸菌已经被多次报道对肥胖有一定的改善作用。在本研究中，我们的目的是研究一株丁酸梭菌 CGMCC0313.1（CB0313.1）在限制高脂膳食诱导的小鼠肥胖中的作用。

方法 4 周龄 C57BL/6 小鼠随机分成 3 组，分别为正常组、高脂组（喂食高脂饲料）和高脂处理组（高脂饲料同时灌饲 CB0313.1），12 周后检测小鼠体重变化，葡萄糖耐受，空腹血糖、空腹胰岛素水平，肝脏病理切片观察，血清内毒素水平以及结肠炎症指标（长度、结肠炎症因子、短链脂

肪酸水平），Western blot 及 real time PCR 检测结肠紧密连接蛋白和 mRNA 表达。

结果　结果显示，喂食 CB0313.1 的小鼠显示出更少的肝脏中脂质积累，更低的血清胰岛素水平和更好的胰岛素敏感性。不仅如此，CB0313.1 也能逆转高脂膳食诱导的结肠炎症，降低结肠肿瘤坏死因子 α（TNF-α）的水平，提高结肠白细胞介素 10（IL-10）的水平。在调节肠道炎症的同时，CB0313.1 也能通过提高紧密连接蛋白（claudin-1 和 occludin）的表达降低结肠的通透性，减少血液中内毒素的浓度。在结肠内容物中，CB0313.1 够改善高脂膳食造成的结肠中有益短链脂肪酸的浓度的降低。在脂肪组织中，CB0313.1 处理的小鼠显示出更低的促炎性炎症因子和趋化因子的 mRNA 水平。

结论　我们的结果证明了 CB0313.1，一种改善肠道炎症和通透性的益生菌，能够改善高脂膳食诱导的肥胖，胰岛素抵抗以及脂肪组织的炎症。

COR-30

LAMP3 在肝脏脂代谢中的调控作用及机制研究

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目的　阐明。本研究目的在于观察溶酶体相关膜蛋白 3 (lysosome-associated membrane protein 3，LAMP3) 在肝细胞脂代谢中的调控作用，并揭示其调控的分子机制，为代谢紊乱相关疾病的干预治疗提供新的策略与依据。

方法　在游离脂肪酸诱导的肝细胞胰岛素抵抗模型中检测 LAMP3 表达变化；利用重组质粒在 HepG2、Huh7 细胞中过表达 LAMP3，通过 qPCR 和 Western-blot 技术检测 LAMP3 对脂肪代谢过程中关键调控因子的影响，采用甘油三酯试剂盒及油红 O 染色检测细胞内脂肪总量变化；并通过 Western-blot 检测 PI3K/Akt 信号通路关键蛋白，如 pAkt、pPDK1 等在过表达 LAMP3 后的表达变化，探讨 LAMP3 调控脂代谢的分子机制。

结果　游离脂肪酸作用细胞 HepG2、Huh7 后，细胞内甘油三酯含量明显增加，LAMP3 表达也显著升高。细胞 HepG2、Huh7 过表达 LAMP3 后，脂肪合成过程关键调控因子 PPARγ、FASN、ACC1 表达明显上调，而脂肪酸氧化分解关键酶 CPT1A、ACOX1 表达显著下调，同时细胞内甘油三酯含量明显增加。在过表达 LAMP3 的 HepG2 细胞中，PI3K/Akt 信号通路关键蛋白，如 pAkt、pPDK1 表达显著下调，提示 LAMP3 调控脂代谢可能依赖于 PI3K/Akt 信号通路。

结论　本研究阐明了 LAMP3 在肝脂代谢中的重要调控作用，揭示了 LAMP3 可能通过抑制 PI3K/Akt 信号通路抑制肝细胞脂肪酸氧化分解，促进脂肪堆积，加重肝细胞胰岛素抵抗。该研究提示 LAMP3 可能成为肥胖、糖尿病等代谢紊乱相关疾病的潜在干预靶点。

COR-31

Orexin A 及其受体 1 干预 Hep3B 人肝癌细胞葡萄糖摄取和有氧代谢及其分子机制的研究

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目的　增食欲素 A（orexin A）和 B (orexin B) 是与能量代谢密切相关的下丘脑神经肽。通过与两个增食欲素受体（OX1R/OX2R）结合发挥生物学效应。本研究以 Hep3B 人肝癌细胞为研究对象，研究细胞中增食欲素受体的表达。探讨外源性 orexin A 对 Hep3B 细胞葡萄糖摄取和有氧代谢的影响及其可能的分子机制。

方法　体外培养 Hep3B 人肝癌细胞，给予不同浓度的 orexin A (10^{-9}-10^{-7} M) 处理。分别用实时定量 PCR 和免疫印迹检测细胞增食欲素受体基因和蛋白表达。免疫印迹检测细胞中葡萄糖转运蛋白 1（GLUT1）表达；[^{3}H]-2- 脱氧葡萄糖检测细胞对葡萄糖的摄取；实时定量 PCR 检测细胞乳酸脱氢酶（LDHA）、丙酮酸脱氢酶 B（PDHB）、丙酮酸脱氢酶激酶 1（PDK1）mRNA 水平；同时测定细胞乳酸含量以及丙酮酸脱氢酶（PDH）的酶活性。此外，研究 orexin A 对 Hep3B 细胞内 PI3K/Akt/mTOR 通路的影响，加入 Akt 及 mTOR 抑制剂后，检测上述代谢指标的变化。

结果　Hep3B 细胞中有 OX1R 的表达，但未检测到 OX2R。外源性 orexin A 能刺激 Hep3B 细胞 OX1R mRNA 和蛋白的表达，且呈剂量相关。Orexin A 通过 OX1R 活化 PI3K/Akt/mTOR 通路，增加细胞 GLUT1 表达，促进细胞对葡萄糖的摄取。此外，orexin A 增加 PDHB，抑制 LDHA 和 PDK1 的 mRNA 水平；抑制细胞乳酸的含量；增加 PDH 酶活性。但用抑制剂阻断 PI3K 通路后，orexin A 对 Hep3B 细胞的上述作用并未发生明显改变。

结论　Hep3B 人肝癌细胞中有 OX1R 的表达，且对外源性 orexin A 的刺激高度敏感。Orexin A 通过 OX1R 活化 PI3K/Akt/mTOR，上调 GLUT1 表达，增加细胞对葡萄糖的摄取。此外，orexin A 干预 Hep3B 细胞内葡萄糖的代谢方向，促进有氧代谢，抑制糖酵解。orexin A 的这一作用并不依赖于 PI3K/Akt/mTOR 通路。抑制糖酵解能够抑制肿瘤细胞生长，已被视为一种抗癌治疗途径。本研究结果提示增食欲素可能通过对肿瘤细胞糖代谢的干预作用起到抑制肿瘤生长的效应，为靶向能量代谢的肿瘤的治疗和干预提供分子生物学基础，也为揭示代谢性疾病与肿瘤发生发展的分子机制提供新的视野和靶标。

COR-32

胰腺衍生因子 PANDER 与代谢综合征组份聚集相关

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目的 胰腺衍生因子（PANcreatic DERived Factor，PANDER）是一种在胰岛 B 细胞特异性高表达，与胰岛素共分泌的细胞因子，体外实验和动物实验表明 PANDER 与糖脂代谢的调节相关，可能参与 2 型糖尿病、高甘油三酯血症、代谢综合征等的发生发展。本研究观察健康体检人群血清 PANDER 水平，分析血清 PANDER 水平的影响因素，并探讨 PANDER 与血糖、血脂水平、代谢综合征的关系。

方法 健康体检人群中随机招募研究对象 212 例。所有受试者测量血压、身高、体重、腰围，计算体重指数（BMI），测定患者血脂谱，行口服葡萄糖耐量试验，测定空腹血糖、空腹胰岛素及 2 小时血糖。 用 ELISA 法测定血清 PANDER。 MS 诊断采用国际糖尿病联盟（IDF）关于 MS 的全球定义，糖代谢异常与糖尿病的诊断参照 1999 年 WHO 诊断标准。用 HOMA-β 指数评价胰岛 β 细胞功能，用 HOMA-IR 指数、胰岛素敏感性指数 (IAI) 评价胰岛素抵抗。正态分布的计量资料以 ±S 表示，非正态分布资料经对数转换后再进行分析。组间差异采用 t 检验，三组间差异比较采用单因素方差分析，有统计学意义后用 Bonfennio 法校正检验水准；数据间的相关分析采用直线相关分析。以 P < 0.05 为差异具有统计学意义。

结果 在所有受试者中，代谢综合征组份全部正常者 65 人，含一个或以上代谢组份异常者 147 人。血清 PANDER 水平在代谢异常组明显升高（P < 0.05），且与代谢异常组份聚集密切相关 (r = 0. 529, P < 0.001)。PANDER 随代谢综合征异常组份增多而升高。同时，血清 PANDER 与空腹血糖 (r = 0.187, P = 0.046)、餐后 2h 血糖 (r = 0.195, P = 0.035)、HOMA-β 指数 (r = –0.191, P = 0.039)、甘油三酯 (r = 0.305, P = 0.001) 以及高密度脂蛋白 (r = –0.333, P < 0.001) 均显著相关。在校正其他混杂因素后运用多重线性回归分析发现，血清 PANDER 水平是发生空腹血糖受损或糖尿病的危险因素（OR值2.22，95%置信区间1.15-4.42，P = 0.018）。

结论 本人群中血清 PANDER 水平与代谢综合征组份聚集关联，是血糖升高的危险因素，需进一步在大样本中验证。

COR-33

Meta 分析：中国人群中非酒精性脂肪性肝病与维生素 D 水平负相关

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目的 非酒精性脂肪性肝病 (nonalcoholic fatty liver disease, NAFLD) 被认为是胰岛素抵抗 (insulin resistance , IR) 及代谢综合征 (metabolic syndrome , MS) 在肝脏的表现，随着其发病率的日益升高及人们对其认识的不断深入，非酒精性脂肪性肝病成为全球重要的公共健康问题。本研究运用 Meta 分析的研究方法系统评价了中国人群中非酒精性脂肪性肝病与维生素 D 水平的相关性。

方法 通过计算机检索 Pubmed、CNKI、维普、万方、读秀数据库，检索有关非酒精性脂肪性肝病与血清维生素 D 相关性的临床研究，同时对相关会议论文集及纳入的综述性文献的参考文献进行手工检索，时间截止至 2016 年 3 月。根据统一的纳入及排除标准，筛选文献，应用 stata11.0 软件对纳入的文献进行异质性检验、合并效应值，同时进行偏倚估计和敏感性分析。

结果 本研究共纳入 11 篇研究对象为中国人的病例对照及横断面研究，非酒精性脂肪性肝病患者共 3752 例，健康对照共 5360 例。脂肪肝均根据腹部超声的检查进行诊断。Meta 分析结果提示，与对照组相比，NAFLD 患者 25 羟维生素 D（25-hydroxyvitamin D, 25（OH）D）水平降低，SMD：-0.34ng/ml，95% CI:-0.49,-0.18，差异有统计学意义（P=0.000）。根据研究类型亚组分析，结果显示病例 - 对照研究组及横断面研究组 NAFLD 患者 25（OH）D 水平均下降（P<0.05）；根据性别亚组分析，结果示与同性别健康对照组相比，男性及女性 NAFLD 患者 25（OH）D 水平均降低（P<0.05），组间差异无统计学意义（P>0.05）；根据脂肪肝严重程度亚组分析，发现 25（OH）D 水平随着脂肪肝严重程度的增加而降低（P<0.05）。各研究的敏感性分析较稳定，且无明显发表偏倚。

结论 NAFLD 患者 25（OH）D 水平明显低于正常人，且随着脂肪肝严重程度增加而降低。提示维生素 D 可能是 NAFLD 发生和发展的一项保护因素，应关注 NAFLD 患者体内的维生素 D 状况。

COR-34

硒暴露与非酒精性脂肪肝病发病的关联性研究

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目的 动物实验证实硒暴露可使肝酶水平升高、Kupper 细胞激活、肝胰岛素抵抗增加、以及肝甘油三酯浓度升高，提示硒暴露可能和非酒精性脂肪肝的发病相关。本研究调查中老年人群中硒暴露的水平及探讨硒暴露与 NAFLD 发病的关联关系。

方法 研究人群为 REACTION 的子部分：上海崇明地区中老年人群，其中 9930 个体拥有完整调查资料，排除不符合标准的个体后，8850 个体（男性：2739 ；女性：5811

）进入本研究。血浆硒浓度测定采用安捷伦 7500ce 电感耦合等离子体质谱系统，脂肪肝的检测采用腹部超声。

结果　所研究人群中 NAFLD 的患病率为 31.4%。人群血浆硒中位浓度为 213 μg/L (interquartile range: 181.6–247.4 μg/L)。NAFLD 组血浆硒中位水平：270.2 μg/L，而 non-NAFLD 组血浆硒中位水平：192.5 μg/L（ P<0.01 ）。升高的血浆硒水平和升高的 TG、LDL-c、空腹血糖、餐后 2 小时血糖、A1c、HOMA-IR 以及肝酶谱（ALT、AST 及 γ-GT ）相关联 (all P <0.05)。在校正过潜在的影响因素后，相比于第 1 四分位水平人群，处于第 4 四分位血浆硒水平的人群其 NAFLD 发生风险显著升高（OR=1.56，95%CI：1.15-2.19 ）。

结论　东南沿海地区人群血浆硒水平较高，较高的血浆硒水平常伴发代谢紊乱。硒暴露的增加和升高的 NAFLD 发病相关联。

COR-35

儿童期和胎儿期经历饥荒与成年非酒精性脂肪性肝病的相关性研究

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目的　中国在 1959-62 年遭遇了人类历史最严重的饥荒。已有流行病学调查研究发现生命早期的营养事件可以影响成年后慢性疾病发生发展。非酒精性脂肪性肝病（NAFLD ）作为代谢性疾病也呈现逐渐高发的态势。该研究目的是探讨儿童或胎儿期经历营养不良是否与成年后 NAFLD 的患病风险相关，并且是否存在性别差异。

方法　该研究在上海、浙江和江西 16 个地点进行，共纳入 6899 例人群样本。除去小于 40 岁、酗酒史、血吸虫肝病史、病毒性肝炎、继发性 NAFLD 药物使用等，本研究共纳入 5306 例。生于 1959-62 年为胎儿期饥荒暴露（年龄 52-55 岁），出生于 1949-58 年为儿童期暴露（年龄 56-65 岁），出生于 1921-48 年为青年 / 成人期暴露（年龄 66-93 岁），出生于 1963-74 年（年龄 40-51 岁 ）为非饥荒暴露对照组。脂肪变性程度根据 B 超分成正常、轻度和中重度。

结果　非暴露组、胎儿和儿童期暴露组的 NAFLD 患病率分别为 55.9%、55.8% 和 55.4%（男性 ）及 33.0%、46.3% 和 51.7%（女性 ）。女性胎儿和儿童期暴露组的 NAFLD 患病率显著高于非暴露组（P <0.05 ）。校正年龄、城市农村居住地、经济水平、BMI、糖尿病、血脂异常和高血压，和非暴露组相比，女性ALT与胎儿和儿童期暴露存在显著相关（P <0.05 ）。通过 logistic 分析，调整以上因素后，同样只有女性胎儿期（OR 1.77, 95% CI 1.22, 2.57 ）和儿童期暴露组（OR 1.82, 95% CI 1.35, 2.46 ）的中重度 NAFLD 患病风险显著高于非暴露组（P <0.05 ）。男性生命早期未见该相关性。

结论　女性生命早期经历营养不良可能与成年 NAFLD 风险上升有关，结合以往的研究结果说明怀孕女性以及生命早期的婴儿儿童应给予足够的营养保证。

COR-36

小檗碱预防肝脏脂肪沉积向脂肪性肝炎和纤维化发展的机制研究

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目的　本研究拟通过动物模型和细胞模型观察小檗碱对非酒精性脂肪肝的影响，探讨小檗碱预防肝脏脂肪沉积向脂肪性肝炎和纤维化发展的分子机制。

方法　按体重、空腹血糖校准法将 db/db 小鼠随机分为两组，对照组和药物组各 7 只，以灌胃给药的方法分别予羧甲基纤维素钠和盐酸小檗碱（200mg/kg.d ）5 周；C57BL/6 小鼠按体重随机分为三组，普通饲料组、甲硫氨酸胆碱缺乏饮食（MCD ）饲料组、MCD 加小檗碱组各 8 只，后者给药前先给予 MCD 两周，随后继续给予 MCD 饲料，并开始以灌胃给药的方法予羧甲基纤维素钠和盐酸小檗碱（200mg/kg.d ）4 周；C57BL/6 小鼠按体重随机分为三组，分别为对照组，衣霉素注射组（Tunicamycin ），衣霉素注射加小檗碱给药组。小鼠处死后，血清测 TG、TC、ALT、AST 等指标，肝脏组织做 HE 和油红染色，Folch 法检测肝脏脂肪含量，抽提组织总 RNA 并检测与糖脂代谢、内质网应激、炎症和纤维化相关基因 mRNA 水平的表达，通过 Western Blot 方法检测相关基因蛋白水平的表达。分离小鼠肝脏原代细胞，用 OA/PA 诱导脂肪堆积，随后予以 5%BSA 和 BBR 处理，24 后收集细胞测定 TG 水平。

结果　db/db 和 MCD 小鼠模型中，小檗碱组 ALT 和 AST 有显著降低，肝脏脂肪沉积减少，肝组织内总甘油三酯及总胆固醇水平下降，且肝脏中胶原蛋白含量减少；在 db/db 和 MCD 小鼠小檗碱组中，肝脏组织的内质网应激、炎症反应及纤维化相关基因的 mRNA 表达水平显著下降。在上述模型中，内质网应激及炎症相关蛋白在小檗碱组的活性显著降低，脂代谢转录相关蛋白表达显著下降；TUN 注射小鼠模型中，小檗碱可以阻断 TUN 注射组引起的内质网应激，小檗碱组较 TUN 注射组肝脏脂肪沉积、胶原含量减少；db/db、MCD 和 TUN 注射小鼠模型中，小檗碱组肝脏胞核内 ATF6 和 SREBP-1c 表达水平较对照组下降。细胞水平研究的结果显示，BBR 处理组细胞甘油三酯含量减少，而且小檗碱可以通过调控ATF6 进而抑制SREBP-1c的表达。

结论 在体及体外实验均证明，小檗碱是通过抑制内质网应激从而改善肝脏的脂质沉积以及进行性的病理表现如炎症、肝细胞凋亡以及纤维化等症状。对于我们在临床合理应用小檗碱治疗 NAFLD 具有极其重要的意义，并对深入理解 NAFLD 发病过程中内质网应激的重要作用也具有重要的科学影响。

COR-37

Prkar2b 缺失通过上调 creb 及 p38 磷酸化水平激活白色脂肪组织产热

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目的 肥胖的发生发展与能量摄入与消耗失衡相关。白色脂肪棕色化水平激活可上调机体能耗，有助于抵抗肥胖。Prkar2b 是哺乳动物体内编码 PKA 调节亚基 RII beta 的基因，主要表达于脂肪组织及大脑，Prkar2b 基因敲除小鼠能耗增加、体重减轻、抵抗高脂饮食诱导的肥胖及脂肪肝，但机制尚不明确。本研究旨在明确 Prkar2b 缺失是否通过上调白色脂肪组织棕色化水平上调机体产热并探索其机制。

方法 研究利用 PB 转座子构建 prkar2b 失活突变小鼠模型，利用代谢笼、min 核磁等分析小鼠能耗及体质分布；处死并解剖小鼠，分离腹股沟及附睾旁白色脂肪，观察脂肪组织形态学变化及产热基因表达差异；分离腹股沟脂肪组织 SVF 细胞并诱导分化为成熟脂肪细胞，利用油红染色分析脂肪细胞的成脂及分化水平，检测产热基因表达水平。

结果 Prkar2b 失活突变小鼠体重减轻、体脂含量下降、能耗增加、基础体温升高、抵抗高脂饮食诱导的肥胖，并且胰岛素敏感性升高；小鼠腹股沟脂肪组织形态上有显著的棕色样改，组织中 UCP1 及其他产热基因表达显著上调，P38 及 Creb 磷酸化水平显著上调；小鼠附睾旁脂肪组织 UCP1 及产热基因表达上调，但形态上没有表现出明显的棕色样变；由突变小鼠腹股沟分离的原代 SVF 细胞在诱导分化为成熟脂肪细胞后，其 UCP1 及其他产热基因表达显著上调；P38 及 Creb 磷酸化水平显著上调。

结论 本研究提示，在白色脂肪组织中，Prkar2b 失活突变可以引起白色脂肪组织中 UCP1 及其他产热基因表达上调，其机制可能与 P38 及 Creb 磷酸化水平上调有关。Prkar2b 基因突变小鼠抵抗高脂饮食诱导肥胖的能力可能与白色脂肪棕色化水平上调引起的能耗增加相关。

COR-38

代谢正常肥胖转归糖尿病风险的前瞻性队列研究

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目的 了解泸州社区 40 岁以上代谢正常肥胖（MHO）患病率及随访 3 年糖尿病发病率情况。

方法 2011 年 4 月 -8 月采用多级整群抽样方法，对泸州市 3 个社区不同街道 40 岁以上非糖尿病居民进行问卷调查、体格检查和生化检测，于 2014 年 6 月 -10 月对其进行随访调查。

结果 共计纳入 2442 例人群（男性 30.7%）。MHO、代谢正常非肥胖（MHNO）、代谢异常肥胖（MUHO）及代谢异常非肥胖（MUHNO）分别占 14.8%、45.3%、19.5% 和 20.4%，男、女 MHO 患病率分别为 11.2% 和 15.4%。随访 3 年，共计 248 例转归为糖尿病，与 MHNO 相比，MHO、MUHO 及 MUHNO 糖尿病发病风险分别是 MHNO 的 1.64（95%CI，0.99 ~ 2.70），5.23（95%CI，3.72 ~ 7.36），3.93（95%CI，2.74 ~ 5.64）倍，女性 MHO 糖尿病发病风险是 MHNO 2.05（95%CI，1.15 ~ 3.65）倍。MHO 组随访 3 年后 TG、SBP、DBP、FBS 和 OGTT 2h 血糖指标异常百分比分别为 34.3%、39.4%、22.6%、8.3% 及 43.4%，与 MHNO 组相比明显增加（$P < 0.05$）。

结论 ① MHO 在女性和相对低龄的人群中患病率更高，② MHO 组糖尿病发病率明显低于 MUHO、MUHNO 组，女性 MHO 组糖尿病发病率高于 MHNO 组，③与 MHNO 相比，MHO 更易发生代谢异常。

COR-39

二甲双胍对高脂饮食诱导肥胖小鼠肠道菌群、短链脂肪酸及 GLP-1 的影响

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目的 肠道菌群作为环境因素之一参与肥胖等代谢性疾病的发生发展，肠道菌群代谢产物短链脂肪酸（SCFAs）可刺激肠道 L 细胞分泌 GLP-1。二甲双胍对肠道作用是近来研究热点且并未完全阐释清楚，本文旨在了解二甲双胍对高脂饮食诱导肥胖小鼠肠道菌群、SCFAs 及 GLP-1 的影响。

方法 高脂饮食诱导 C57BL/6J 小鼠 11 周建立肥胖模型，分为 3 个组：低脂饮食对照组（LFD-CT，n=8）、高脂饮食对照组（HFD-CT，n=8）和高脂饮食 + 二甲双胍干预组（HFD-Met，n=8），干预 7 周后收集小鼠血清及粪便，ELISA 法检测血清胰岛素、GLP-1，提取粪便细菌基因组 DNA 并扩增 16S rRNA V1-V3 区，Illumina Miseq PE250/PE300 测序，分析肠道菌群结构，气相色谱法（GC）检测粪

便 SCFAs（乙酸、丙酸及丁酸）。SPSS19.0 软件对比分析不同处理组各项检测指标差异。

结果　（1）一般生化指标：与 LFD-CT 组比较，HFD-CT 组体重及血糖升高，血清胰岛素增高（P<0.05），肠道激素 GLP-1 稍有下降，但差异无统计学意义（P=0.635）。与 HFD-CT 组对比，HFD-Met 组体重及血糖明显下降，血清胰岛素降低，肠道激素 GLP-1 水平增高（P<0.05）。（2）肠道菌群：与 LFD-CT 组对比，HFD-CT 组肠道菌群多样性降低，群落结构紊乱。对比 HFD-CT 组，HFD-Met 组厚壁菌门明显减少（P<0.05），拟杆菌门（P=0.185）及疣微菌门（P=0.136）呈增多趋势，菌属 Helicobacter（P=0.033）、Granulicatella（P=0.017）和 Staphylococcus（P=0.015）显著增多，Lachnospiraceae_incertae_sedis（P=0.006）显著减少，Akkermansia（P=0.136）稍有增多。（3）GC：HFD-CT 组 SCFAs 均高于 LFD-CT 组（P<0.05），与 HFD-CT 组相比，HFD-Met 组 SCFAs 均降低（P<0.05）。

结论　1. 二甲双胍影响肥胖小鼠肠道菌群结构，表现为某些菌门及属水平的变化。2. 饮食类型及二甲双胍对小鼠粪便 SCFAs 有显著影响。3. 二甲双胍增高 GLP-1 的机制可能并不是通过肠道菌群 -SCFAs 轴实现的。

COR-40

妊娠期糖尿病与妊娠期甲状腺功能状态的相关性分析

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目的　了解妊娠期甲状腺功能与血糖水平的相关性，明确妊娠期甲状腺功能异常、甲状腺过氧化物酶抗体（Thyroid peroxidase Antibody,TpoAb）阳性是否增加妊娠期糖尿病（Gestational Diabetes Mellitus,GDM）的发病风险。

方法　选取在南方医科大学第三附属医院产检的孕妇 514 名，收集血清游离妊娠期甲状腺激素（Free Thyroxine,FT4）、促甲状腺激素（Thyroid-Stimulating Hormone,TSH）、TpoAb、孕 24-28 周行 75gOGTT 检查结果，统计 GDM、甲功异常的发病率，比较 GDM 组与非 GDM 组甲功异常、TpoAb 阳性在妊娠各期的发病率差异，明确 FT4、TpoAb 水平对 GDM 发病率的影响，并采用 Spearman 秩相关分析 FT4、TSH 与血糖水平的相关性。

结果　① GDM 发病率为 16.3%（84/514）；总的甲功异常发病率为 21.2%（109/514），临床甲亢、亚临床甲亢、临床甲减、亚甲减发病率分别为 3.7%（19/514）、1.9%（10/514）、0.2%（1/514）、15.4%（70/514）；TpoAb 阳性率为 9.7%（40/412）。② GDM 组与非 GDM 组之间的总甲功异常（P=0.523）、TpoAb 阳性率（P=0.305）差异无统计学意义。③妊娠早、中、晚期甲功异常对于 GDM 的发病率差异无统计学意义（P>0.05），妊娠早期 TpoAb 阳性对 GDM 发病率的影响有统计学意义（χ^2=6.362，P=0.012），中晚期 TpoAb 阳性对 GDM 发病率的影响无统计学意义（P>0.05）。④ FT4 与空腹血糖相关（r=-0.148，P=0.01），与 1h、2h 血糖无明显相关性，TSH 与三个血糖点之间无明显相关性。

结论　甲功异常对 GDM 发病无明显预示作用，尚无充分的证据证明妊娠期甲状腺疾病与妊娠期糖尿病之间存在关联，但是妊娠早期 TpoAb 阳性对妊娠期糖尿病发病可能有一定预测作用。

COR-41

腹腔镜下代谢手术治疗肥胖的 2 型糖尿病患者近期疗效观察

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目的　观察肥胖合并 2 型糖尿病（T2DM）患者腹腔镜下代谢手术（LBS）术后的近期临床疗效。

方法　对 26 例肥胖的 T2DM 患者术前及术后 3 个月的临床资料进行对比分析，分别比较腹腔镜下胃旁路术（LGBP）和腹腔镜胃袖状切除术（LSG）两种术式治疗的病情缓解情况及术后并发症发生情况。

结果　1. LBS 术后 3 个月总体体重、腰围、体重指数均较术前显著下降（p<0.01）。术后总体 FPG、2hPG、HbA1c 水平较术前下降（p<0.05）。总体 C2/C0 比值较术前升高（p<0.01）。LGBP 组额外体重减轻百分比、额外体重指数下降百分比均高于 LSG 组（p<0.05）。

2. LBS 治疗 T2DM 术后 3 个月有效率达 95.8%，其中 LGBP 组缓解率为 64.7%，有效率 94.1%；LSG 组缓解率 57.1%，有效率 100%，两组疗效无差异（P>0.05）。LBS 术后总体不良反应发生率为 12.5%。两组不良反应发生率无差异（p>0.05）。

3. LBS 术后 3 个月总体甘油三酯水平较术前降低（p<0.05），高密度脂蛋白胆固醇较术前升高（p<0.05），而低密度脂蛋白胆固醇及总胆固醇水平较术前无变化（p>0.05）。肝脏酶学指标中谷丙转氨酶、γ - 谷氨酰胺转移酶水平较术前降低（p<0.05），而谷草转氨酶及碱性磷酸酶水平无变化（p>0.05）。血肌酐、尿酸水平较术前无变化（p>0.05）。

结论　1. LBS 在有效减轻肥胖的 T2DM 患者体重的同时可明显改善糖代谢及胰岛功能，短期疗效显著，且安全性高。

2. LBS 可改善肥胖的 T2DM 患者的血脂异常，降低肝酶水平，但对血尿酸水平无影响。

3. LGBP 减重效果优于 LSG，二者降糖疗效与术后不良反应无明显差异。

COR-42

SGLT-2 抑制剂达格列净通过抑制 NLRP3 炎症小体活化减轻了糖尿病 ApoE-/- 鼠动脉粥样硬化斑块形成

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目的 本实验旨在观察钠 - 葡萄糖协同转运蛋白 2（SGLT-2）抑制剂 - 达格列净（Dapa）对糖尿病 $ApoE^{-/-}$ 鼠动脉粥样硬化斑块形成的影响及其机制。

方法 $ApoE^{-/-}$ 鼠经腹腔注射链脲佐菌素（STZ）诱导糖尿病，高脂喂养诱发动脉粥样硬化，C57BL/6J 鼠作为对照，分成 C57 正常对照组、$ApoE^{-/-}$ 组、$ApoE^{-/-}$ 糖尿病组、$ApoE^{-/-}$+Dapa 组、$ApoE^{-/-}$ 糖尿病 +Dapa 共 5 组，动物灌胃给予 Dapa（1mg/kg/d）处理 12 周，对照组给予等量生理盐水，收集血清以 ELISA 法检测 IL-1β、IL-18 炎症因子和 NLRP3 炎症小体水平，处死动物后收集各组动物主动脉样本进行油红 O 染色分析斑块面积，HE 染色观察血管病理形态变化，免疫荧光检测主动脉斑块局部巨噬细胞渗出和斑块稳定性变化，取组织标本进行 Western blotting 检测局部组织 NLRP3 炎症小体、IL-1β、IL-18 炎症因子表达改变。

结果 代谢指标检测显示 Dapa 处理减少了 $ApoE^{-/-}$ 糖尿病鼠血糖水平达 43%（$p<0.01$），对非糖尿病鼠血糖也减少了 28%（$p<0.05$）；降低了血清中游离脂肪酸（FFA）和甘油三酯（TG）水平（$p<0.05$）；减少了血液中 IL-1β、IL-18 炎症因子和 NLRP3 炎症小体水平；病理检测显示 Dapa 干预抑制了糖尿病鼠动脉粥样硬化斑块的形成，免疫荧光显示 Dapa 减少了斑块中巨噬细胞的渗出，抑制了平滑肌细胞的减少，提高了斑块的稳定性，减少了血管局部组织中 NLRP3 炎症小体、IL-1β、IL-18 炎症因子的表达。

结论 Dapa 通过降糖调脂减少了血液和主动脉组织中炎症小体 NLRP3 的活化和炎症因子 IL-1β、IL-18 的表达，抑制了主动脉斑块中巨噬细胞的渗出和炎症反应，减轻了糖尿病动脉粥样硬化斑块的形成，提高了斑块的稳定性，可能对糖尿病心血管并发症带来长期的获益。

COR-43

Notch 信号通路在二甲双胍调节 HepG2 人肝癌细胞生物学特性中的作用探讨

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目的 糖尿病患者肿瘤发生风险增加。肝癌作为一种男女共患的恶性肿瘤，在糖尿病患者中的发病风险也明显增高。2 型糖尿病患者首选的口服降糖药物二甲双胍其抗肿瘤特性是近年来的研究热点，但其机制尚未完全清楚，现对其的研究主要集中在单磷酸腺苷活化的蛋白激酶（AMPK）信号通路。本研究是为了探究二甲双胍是否存在其他抗癌旁路，即肿瘤细胞上的 Notch 信号通路是否参与了二甲双胍对 HepG2 人肝癌细胞生物学特性的调节。

方法 ①用不同浓度的二甲双胍（分别为 0mmol/L、5mmol/L、10mmol/L、20mmol/L）干预 HepG2 人肝癌细胞 48h 后，采用 RT-qPCR 及 Western Blotting 检测肿瘤细胞上 4 种 Notch 受体及下游 Hes1 因子 mRNA 及蛋白的表达情况；MTS 比色法及 Annexin V-FITC/PI 双染法流式细胞分别检测 HepG2 细胞的增殖、凋亡情况。②用 DAPT 成功阻断肿瘤细胞上 Notch 信号通路后，再次检测 HepG2 细胞的增殖、凋亡情况。

结果 ①随二甲双胍干预浓度的增高，Notch1 ~ Notch4 受体及 Hes1 因子 mRNA 及蛋白的表达水平逐渐降低，二甲双胍干预浓度在 10mmol/L 及其以上组较二甲双胍 0mmol/L 干预组差异有统计学意义（$P<0.05$）。②二甲双胍呈剂量依赖地方式降低 HepG2 细胞增殖活性，促其凋亡（$P<0.05$）。③ DAPT 阻断 HepG2 细胞上的 Notch 信号通路后，二甲双胍对 HepG2 细胞抑增殖、促凋亡作用增强（$P<0.05$）。

结论 二甲双胍可能通过下调 Notch 信号通路抑制 HepG2 肝癌细胞增殖，促其凋亡。

COR-44

1 例先天性全身脂肪萎缩性糖尿病家系的临床和基因诊治

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目的 通过诊治并分析 1 例先天性全身脂肪萎缩性糖尿病（congenital generalized lipodystrophy, CGL）患者及家系，同时对患者及家系进行全基因组测序分析筛查出突变位点，并通过 Sanger 测序进行验证，探讨患者 CGL 的发病机制，丰富中国人群的 CGL 致病位点的遗传图谱，提高对该罕见遗传病的诊治认识。

方法 对患者的临床资料进行回顾性分析，收集家系的相关临床资料（现病史、既往病史、家族史和体格检查等）、实验室检查（生化、OGTT 及胰岛素、C 肽释放试验、甲状腺功能等）、高胰岛素正糖钳夹试验及影像学检查（腹部核磁共振、肝脏脂肪 B 超定量、肝胆胰脾 B 超、子宫及附件 B 超、超声心动图、心电图等）。采集该家系成员外周血白细胞提取 DNA，进行全基因组测序分析，并通过双脱氧链终止法 (Sanger) 测序进行验证。

结果 本研究中患者出生时消瘦明显，儿时喂养正常。表现为全身皮下脂肪缺如，面容瘦削，两颊内陷，颧骨突出，眼眶深陷。毳毛明显，骨骼肌、肌腱、皮下静脉浅显易见。肝脏肋下 2cm, 脾脏肋下 3cm。实验室检查：空

腹血糖（16.37mmol/L）、糖化血红蛋白（10.6%）、空腹胰岛素（414pmol/L）和C肽(1827pmol/L)、甘油三酯（2.31mmol/L）和谷丙转氨酶（42.1 U/L）高出正常上限；高胰岛素正糖钳夹提示严重胰岛素抵抗；肝脏脂肪B超定量提示肝脏脂肪含量为39.13%。住院期间给予患者胰岛素泵治疗，最大剂量在每天126u；FBG和PBG分别控制在5-6mmol/L，5-9mmol/L，出院后予以诺和锐早16u中18u晚16u皮下注射，长秀霖72u睡前皮下注射；FBG和PBG分别控制在5-6mmol/L，7-8mmol/L。全基因组测序表明患者的BSCL2基因存在Y187C和E189X的复合杂合突变，患者父亲是BSCL2基因的E189X杂合突变携带者，母亲是BSCL2基因的Y187C杂合突变携带者。Sanger测序验证了上述结果，同时提示患者弟弟BSCL2基因型正常。

结论　本研究表明全身皮下脂肪缺如、严重的胰岛素抵抗、糖尿病、高甘油三酯血症和肝脏脂肪变性是CGL的典型临床表现，目前仍以对症治疗为治疗原则，降脂药物控制甘油三酯水平，以大剂量胰岛素为主的降糖方案控制血糖。BSCL2基因复合杂合突变是先天性全身脂肪萎缩性糖尿病的发病机制之一。

COR-45

皮下注射利拉鲁肽通过调节Akt/GSK-3β信号通路改善甲基乙二醛诱导的拟阿尔海默病样病变

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目的　探讨糖代谢产物甲基乙二醛（MG）对小鼠认知能力及对tau蛋白磷酸化的影响；研究利拉鲁肽干预拟阿尔茨海默病（AD）模型是否能改善认知功能，提高其学习和记忆能力，并从整体、组织及分子生物学水平深入探讨可能的机制。

方法　第一部分：SPF级8周龄C57雄性小鼠随机分为溶媒对照组、MG低剂量组、MG中剂量组、MG高剂量组、阳性对照Aβ组，分别采用侧脑室注射生理盐水、0.35μmol MG、0.7μmol MG、1.4μmol MG和410pmolAβ。应用Morris水迷宫探索不同剂量的MG对小鼠认知能力损伤情况，Western-blot检测tau蛋白磷酸化程度及其对相关的调控通路Akt/GSK3β信号的影响。第二部分：SPF级8周龄C57雄性小鼠随机分为溶媒对照组、利拉鲁肽组、模型组、干预组。模型组及干预组采用侧脑室注射0.7μmol MG造成拟AD样病变。应用Morris水迷宫观察皮下注射利拉鲁肽（25nmol/kg/day）8周对小鼠学习和记忆的改善情况，透射电镜观察神经细胞及突触超微结构变化，Westernblot检测海马磷酸化tau蛋白及其相关的调控通路Akt/GSK3β信号的活化程度。

结果　不同剂量的MG能损伤小鼠的认知功能，但各剂量间无显著差别；MG能够通过抑制Akt，激活GSK3β信号通路从而增加tau蛋白磷酸化。利拉鲁肽能够减少CA1区锥体细胞的脂褐素累积和线粒体结构损伤，减轻小鼠海马突触结构的损伤，并且通过降低p-tau(202s)及p-tau(396s)的表达，激活Akt，抑制GSK3β活性，从而改善认知相关功能。

结论　MG可通过调节Akt/GSK3β信号通路诱导tau蛋白磷酸化从而损害认知功能；利拉鲁肽干预后能减少神经元细胞和突触的损伤，降低磷酸化tau蛋白的表达，并促进Akt/GSK3β信号通路活化从而改善认知功能。利拉鲁肽能够改善哺乳动物的认知功能，对促进神经退行性病变个体的健康具有显著的作用。因此，利拉鲁肽有望成为治疗糖尿病相关神经退行性病变的安全、有效的临床药物。

COR-46

胰岛素治疗对2型糖尿病胰岛α细胞功能的影响

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目的　在临床状态下，通过不同治疗方案下2型糖尿病75gOGTT中胰岛素、C肽与胰高血糖素结果，认识胰岛素治疗对胰岛α细胞功能的影响及分析可能的相关因素，以进一步明确2型糖尿病胰岛α细胞的功能特点。

方法　（1）收集持续治疗时间>3个月的住院2型糖尿病患者1956例。（2）通过75gOGTT检测血浆胰岛素、C肽、胰高血糖素水平。（3）筛选出不同治疗方案状态下年龄、性别、HbA1c无统计学差异的2型糖尿病患者，并分别计算并比较各组病程，空腹、0-30分钟AUC（曲线下面积）、30-120分钟AUC的胰岛素、C肽、胰高血糖素，进行不同治疗状态下各组数据的统计学分析。

结果　在年龄、性别、糖化血红蛋白无统计学差异前提下：1. 使用胰岛素组与使用非促泌剂组比较：与非促泌剂治疗组比较，胰岛素治疗组病程较长（$p<0.05$）；血浆胰岛素水平较高（$p<0.05$）；血浆C肽水平较低（$p<0.05$）；血浆胰高血糖素水平较低（$p<0.05$）。2. 使用胰岛素组与使用促泌剂组比较：与促泌剂治疗组比较，胰岛素治疗组病程较长（$p<0.05$）；血浆胰岛素水平较高（$p<0.05$）；血浆C肽水平及胰高血糖素水平较低。3. 使用胰岛素+非促泌剂组与使用非促泌剂组比较：与非促泌剂组比较，胰岛素+非促泌剂组病程较长（$p<0.05$）；血浆胰岛素水平较高（$p<0.05$）；血浆C肽水平较低（$p<0.05$）；血浆胰高血糖素水平在空腹、0-30分钟AUC较高，30-120分钟AUC较低。4. 使用胰岛素+促泌剂组与使用促泌剂组比较：与促泌剂组比较，胰岛素+促泌剂组病程较长（$p<0.05$）；血浆胰岛素水平较高（$p<0.05$）；血浆C肽水平及胰高血糖素水平较低。

结论　1. 在年龄、性别、HbA1c无统计学差异的前提下，使用胰岛素治疗较使用口服药物治疗患者病程明显较

长，胰岛 α 细胞分泌胰高血糖素量少。2. 血浆胰岛素水平受外源性胰岛素影响明显，使用胰岛素治疗患者较使用口服药物治疗患者胰岛 β 细胞分泌胰岛素量少。

COR-47

长期不完全睡眠剥夺对大鼠糖代谢的影响及机制研究

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目的 睡眠不足的人常伴有情绪异常、感知和学习记忆能力的降低，长期睡眠缺乏会导致高血压、心脏病、肥胖症等，甚至引发猝死 . 近年来，大量流行病学研究表明，睡眠障碍与糖代谢之间存在着密切的关系，但睡眠剥夺对糖代谢的具体影响机制还未见报道。本实验拟建立大鼠长期不完全睡眠剥夺模型 , 观察睡眠剥夺对大鼠糖代谢的影响，探讨其机制。

方法 健康 3 月龄雄性 Wistar 大鼠 32 只，随机分为不完全睡眠剥夺 1 组（SD1 组）、不完全睡眠剥夺 2 组（SD2 组）、实验对照组（TC 组）、空白对照组（CC 组）共 4 组，每组 8 只大鼠，利用“小平台水环境法”建立大鼠睡眠剥夺模型。不完全睡眠剥夺 1 组置于持续光照环境中，睡眠剥夺 18h，间歇 6h；不完全睡眠剥夺 2 组置于持续光照环境中，睡眠剥夺 22h，间歇 2h；实验对照组置于持续光照环境中；空白对照组模拟正常作息时间，生活在每天 12h 拟光照，12h 黑暗的环境中。21 天后股动脉放血处死所有大鼠，摘取肝脏称重，留取血液并检测血糖，离心后取血清用化学发光免疫分析法检测总甲状腺素（TT4）、总三碘甲腺原氨酸（TT3）、促甲状腺激素（TSH）、糖皮质激素（Cor）和促肾上腺皮质激素（ACTH），放射免疫分析法检测胰岛素 (INS)，胰高血糖素 (Glu)；生化法检测肝脏谷草转氨酶（AST），谷丙转氨酶（ALT）。

结果 SD1、SD2 组大鼠相比于 CC 组皮毛较暗，行为更加暴躁，摄食量减少，体重减轻，且 SD2 组更加明显。SD2 大鼠血糖 [(5.14 ± 1.18) nmol/L]、INS [(0.07 ± 0.03) ng/ml]、TT4 [(34.94 ± 4.64) nmol/L] 与 CC 组 [分别为 (6.87 ± 0 .50) nmol/L]、[(0.29 ± 0.12) ng/ml]、[(62.63 ± 6.36) nmol/L] 相比，均有明显降低，而 TT3 上升 [(0.95 ± 0.06) nmol/ vs(0.69 ± 0.12) nmol/L]，差异有统计学意义 (P<0.05)、TSH 显示升高趋势、Glu，Cor 和 ACTH 显示降低趋势差异，但差异无统计学意义 (P > 0.05)。TC 组，SD1 组上述指标与 CC 组无统计学差别。SD1、SD2 组大鼠相比于 CC 组，AST，ALT 均有不同程度升高且具有统计学差别。

结论 长期不完全 SD 使大鼠糖代谢紊乱，与多个系统器官的功能变化有关，其中胰岛、甲状腺、肝脏功能变化起重要作用。

COR-48

小檗碱通过 Plac8/ C/EBP β /PRDM16 通路诱导内脏白色脂肪组织棕色化改善 2 型糖尿病地鼠脂诱性胰岛素抵抗的研究

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目的 研究小檗碱对 2 型糖尿病地鼠内脏白色脂肪组织中 Plac8/ C/EBP β /PRDM16 转录通路、白 / 棕脂组织转换通路基因表达的影响并探讨相关治疗机制。

方法 应用高脂饮食及 STZ 制作胰岛素抵抗和 2 型糖尿病地鼠模型，随后分成正常对照组、胰岛素抵抗组、2 型糖尿病组和 2 型糖尿病小檗碱治疗组，治疗 9 周。应用 real-time RT-PCR 方法检测各组地鼠内脏白色脂肪组织中 Plac8/ C/EBP β /PRDM16 转录通路、白 / 棕脂组织转换通路及靶基因的基因表达。

结果 模型地鼠白色脂肪组织中 Plac8、C/EBP β 、SIRT1、GLUT-1、PRDM16、PPAR γ 、PGC-1 α 、PGC-1 β 及棕脂组织特异基因 UCP-1、Cidea、Elovl3 和 PPAR α 的 mRNA 表达降低。Ber 治疗诱导白色脂肪组织中 Plac8/ C/EBP β /PRDM16 信号通路而诱导 PRDM16 信号通路效应，诱导棕脂组织特异基因 mRNA 的表达，抑制白色脂肪选择性基因 mRNA 的表达，诱导白色脂肪棕色化，改善脂诱性胰岛素抵抗。

结论 Plac8/ C/EBP β /PRDM16 转录通路及白 / 棕脂组织转换通路参与脂诱性内脏白色脂肪组织胰岛素抵抗的形成及小檗碱治疗的分子机制。

COR-49

B-rafV600E 介导基因 H3K27 甲基化沉默促进甲状腺癌发生发展的机制研究

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目的 甲状腺乳头状癌是最常见的内分泌系统肿瘤，B-raf^{V600E} 突变是其重要的遗传学改变，另外，表观遗传学在其发生发展中亦发挥重要作用，DNA 启动子区甲基化及组蛋白 H3K27me3 是调控基因表观遗传学沉默的重要机制之一。我们前期研究表明，B-raf^{V600E} 基因突变可导致基因启动子区甲基化水平的异常，因此，本研究旨在明确 B-raf^{V600E} 能否通过调控基因启动子区 H3K27 甲基化调控甲状腺癌的发生发展，并分析其分子机制。

方法　在小鼠 NIH3T3 细胞中过表达 B-raf^{V600E}，利用 ChIP-Seq 及表达谱芯片筛选差异表达基因，利用 western blot 及定量 RT-PCR 检测过表达 B-raf^{V600E} 后组蛋白甲基转移酶（PcG）蛋白的表达改变，并利用抑制剂在甲状腺癌细胞系及 B-raf^{V600E} 介导的甲状腺癌小鼠中明确该突变通过 H3K27me3 下调基因表达的分子机制。

结果　B-raf^{V600E} 较正常 B-raf 能够显著激活 MAPK 信号通路并上调 H3K27 甲基化，芯片结果显示 B-raf^{V600E} 使 1485 个基因表达下调，1742 个基因启动子区 H3K27 甲基化上调，其中 150 个基因的表达下调可能由 H3K27 甲基化所致。同时我们发现 B-raf^{V600E} 过表达组（PcG）蛋白 EZH2、SUZ12 及 JARID2 的表达上调，而在甲状腺癌细胞系中利用抑制剂下调 MAPK 信号通路的活性发现，随着 p-ERK 水平的减少，甲状腺癌细胞系 BCPAP 及 K1 中 H3K27 甲基化水平下降，EZH2、SUZ12 及JARID2 的表达下调。随后我们发现，MAPK 下游转录因子 c-Myc 可能参与对 PcG 蛋白的调控，利用小干扰 siRNA 在 NIH3T3 细胞及甲状腺癌细胞系中下调 c-Myc 能够使 PcG 蛋白表达下调，且 c-Myc 能够直接与 PcG 基因的启动子区结合调控其转录，另一方面，c-Myc 能够与 PcG 基因上游的 microRNAs 结合下调 miR-26a、miR-200b 及 miR-155 的表达，进而上调 PcG 蛋白的表达，最后，我们在 B-raf^{V600E} 基因突变驱动的甲状腺乳头状癌转基因小鼠体内进一步验证了上述的结果。

结论　甲状腺乳头状癌中 B-raf^{V600E} 能够通过上调 H3K27me3 下调基因的表达，c-Myc 通过直接转录激活及下调相关 microRNAs 上调 PcG 蛋白的表达调控 H3K27 甲基化水平。

COR-50

诱导 Balb/c 小鼠对 Graves 病新生口服耐受的研究

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目的　针对目前 Graves 治疗大多针对功能学，而缺乏病因学即自身免疫方向的治疗手段的不足，本研究拟通过给予新生 Balb/c 小鼠口服酵母表达体系生产纯化的重组人 TSHR A 亚基蛋白诱导耐受，并在小鼠成年后诱导 Graves 病，观察比较不同组别小鼠的甲状腺功能，探索诱导小鼠对 Graves 病新生口服耐受的可行性，为 Graves 病甚至自身免疫性疾病的治疗和预防提供新的选择和思路。

方法　给新生 Balb/c 雌性小鼠口服不同剂量（1000 μg、500 μg、100 μg）的由酵母表达体系生产并纯化的重组人 TSHR A 亚基，并在小鼠成年后通过肌肉注射 Ad-TSHR 289 腺病毒的方式诱导 Graves 病模型。成功制备 Graves 病模型后处理小鼠，评价各组小鼠的甲状腺功能，包括放免法检测小鼠血清中 TT4 水平和 TRAb 含量，甲状腺组织病理检查以评估小鼠甲状腺滤泡上皮细胞增生程度。评估各组小鼠的免疫状态：流式细胞术检测小鼠脾 CD4+ 单核细胞群中 CD25+FoxP3+ Tregs 的比例；淋巴增值试验以评估各组小鼠脾淋巴细胞对重组 A 亚基刺激的反应。

结果　大剂量耐受组小鼠Graves病发病率低于模型组，血清 TT4、TRAb 水平低于模型组，甲状腺滤泡上皮增生程度明显较模型组轻；中剂量耐受组和低剂量耐受组的甲状腺功能指标与模型组相比无明显差异。流式细胞术结果显示大剂量耐受组小鼠脾 CD4+ 单核细胞中 Tregs 比例明显高于模型组和对照组，中剂量耐受组和低剂量耐受组与模型组相比无明显差异。淋巴增值试验结果显示大剂量耐受组小鼠脾淋巴细胞对 A 亚基刺激反应比模型组更为敏感，中剂量耐受组和低剂量耐受组小鼠脾淋巴细胞对 A 亚基刺激的反应与模型组无明显差别。

结论　大剂量（1000 μg）重组人 TSHR A 亚基口服免疫新生期 Balb/c 雌性小鼠，可成功诱导出成年后对 Graves 病的免疫耐受模型；中剂量（500 μg）和低剂量（100 μg）的 A 亚基新生期口服免疫不能诱导对 Graves 病的免疫耐受。脾 CD4+ 单核细胞群中 Tregs 比例上调，可能是诱导对 Graves 病免疫耐受的主要机制之一。

COR-51

妊娠早期甲状腺毒症对下一代发育水平的影响

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目的　研究妊娠早期甲状腺毒症，包括妊娠期一过性甲状腺毒症 (gestational transient thyrotoxicosis,GTT) 和 Graves 病，对下一代智力及运动发育水平的影响。

方法　研究对象来自于 2011 年至 2013 年参与《妊娠早期妇女碘铁营养缺乏、亚临床甲状腺激素缺乏：筛查与干预》项目的妊娠 12 周前妇女及同时期于中国医科大学附属第一医院内分泌科门诊就诊的妊娠早期妇女及其子女。在妊娠早期（1-12 周）进行问卷调查、体格检查并检测血清促甲状腺激素（TSH）、游离甲状腺素（FT4）、甲状腺过氧化物酶抗体（TPOAb）、尿碘等指标，分为 GTT 组（12 人），Graves 病组（8 人）及正常对照组（12 人）进行随访，在其子女 12 个月 -30 个月期间应用贝利婴幼儿发展量表进行发育水平测定，包括智力发展指数 (MDI) 和精神运动发展指数 (PDI)。

结果　（1）Graves 病组妊娠早期妇女 FT4 水平与其下一代 PDI 间成负相关（r=-0.805 p=0.016），Graves 病组妊娠早期妇女 TPOAb 水平与其下一代 MDI 间同样成负相关（r=-0.749 p=0.032）。（2）GTT 组与正常对照组妊娠早期 TSH、FT4、TPOAb 与 MDI、PDI 均无显著相关性（$p > 0.05$）。（3）各组间比较 PDI 与 MDI 水平无显著差异（$p > 0.05$）。

结论　妊娠早期 Graves 病患者其 FT4 水平较高，可能影响其子女早期运动发育，而其 TPOAb 水平较高则可能

影响其子女早期智力发育。妊娠期一过性甲状腺毒症对其下一代智力发育及运动发育均无明显影响。加强对妊娠早期甲状腺毒症的监测，鉴别是非常必要的，对于甲状腺功能正常及妊娠期一过性甲状腺毒症患者控制 TSH、FT4、TPOAb 水平对其下一代智力及运动发育水平无显著影响，而对 Graves 病患者早期干预控制 FT4 及 TPOAb 水平可能提高其下一代智力及运动发育水平。

COR-52

巨噬细胞在甲状腺滤泡癌和甲状腺腺瘤中的密度差异及其机制研究

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目的 甲状腺滤泡癌 (follicular thyroid carcinoma, FTC) 与甲状腺腺瘤 (follicular adenoma, FA) 在影像学及细胞形态学上难以鉴别，二者唯一的区别在于是否存在包膜或血管侵犯。大量研究表明肿瘤相关巨噬细胞 (tumor associated macrophage, TAM) 在肿瘤的发生发展中发挥重要作用。而 FTC 与 TAM 的关系尚未见相关报道。因此我们观察 TAM 在 FTC 和 FA 中的密度差异，并分析其与 FTC 临床病理特征之间的关系；分析 FTC 和 FA 分泌的细胞因子谱，研究 FTC 招募巨噬细胞的分子机制，从肿瘤微环境的角度探索 FTC 诊断和治疗的新思路。

方法 收集 61 例 FTC 和 48 例 FA 石蜡标本构建组织芯片，采用免疫组化法观察 CD68/CD163(巨噬细胞表面特异的分子标记物) 阳性细胞数在甲状腺滤泡性肿瘤的差异，观察 TAM 密度及分布特点。采用细胞因子抗体芯片分析 FTC 和 FA 肿瘤细胞的蛋白分泌谱，筛选 FTC 特异高表达的细胞因子，并在组织芯片上分析特异细胞因子的表达情况。观察 FTC 细胞株条件培养基对单核细胞株的趋化作用及 CCL15 中和抗体对上述过程的影响。

结果 CD68 阳性巨噬细胞在 FTC 中的浸润密度显著高于其在 FA 中的密度（9.5 ± 5.4 vs. 4.9 ± 3.4/ 视野，P=0.000），CD163 染色结果表明 FTC 中的巨噬细胞倾向于促进肿瘤发展的 M2 表型；细胞因子芯片发现 FTC 和 FA 高水平分泌多种细胞因子，其中以 CCL15 的表达差异最为明显，组织芯片验证表明 CCL15 在 FTC 中的表达强度显著高于其在 FA 中的表达（P = 0.000），且与甲状腺滤泡性肿瘤组织中浸润的 CD68 阳性巨噬细胞的密度显著相关 (P = 0.007)。FTC 细胞株的条件培养基可趋化单核细胞的迁移，而 CCL15 中和抗体可部分抑制这一作用。

结论 FTC 可能通过分泌 CCL15 招募巨噬细胞，从而参与甲状腺滤泡性肿瘤的恶变过程。

COR-53

鞘磷脂代谢通路 SphK1-S1P 异常激活促进肾上腺皮质癌发生发展

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目的 探讨鞘磷脂代谢信号通路 SphK1-S1P 在肾上腺皮质癌中的表达，并从分子、细胞以及模式动物水平揭示鞘磷脂代谢 SphK1-S1P 通路对肾上腺皮质癌发生发展的作用机制。

方法 利用 qRT-PCR，Western-blot 及免疫组化技术检测肾上腺皮质癌组织标本中 SphK1 的表达并分析其水平与患者临床病理特征及预后之间的关系。我们应用 RNA 干扰技术沉默肾上腺皮质癌细胞系 H295R 和 SW13 细胞中内源性 SphK1 基因的表达，利用 MTT 染色法、平板克隆形成试验、Transwell 小室以及流式细胞仪 Annexin-V/PI 双染法分别检测 SphK1 水平对肾上腺皮质癌细胞体外增殖、迁移、侵袭及凋亡等生物学功能的影响；此外，我们研究 SphK1-S1P 通路小分子抑制剂 FTY720 对肾上腺皮质癌体外细胞增殖、凋亡和迁移等生物学功能的影响，以及肾上腺皮质癌裸鼠移植瘤生长的抑制作用。

结果 免疫组化，qRT-PCR 和 Western-blot 检测结果均显示 SphK1 在肾上腺皮质癌中过度表达。SphK1 的表达水平与患者预后，肿瘤 ENSAT 分期及肿瘤大小等临床病理特征密切相关。细胞实验结果显示在肾上腺皮质癌细胞系 H295R 和 SW13 细胞中敲低 SphK1 后，细胞增殖及侵袭能力显著降低。FTY720 对肾上腺皮质癌细胞及裸鼠动物模型具有显著的增殖抑制作用，有效诱导细胞凋亡发生，还可抑制 PI3K-AKT 及 MAPK 下游信号通路。联合应用 FTY720 和米托坦可协同抑制 SW13 细胞增殖，增强诱导凋亡效应。

结论 本研究首次揭示鞘磷脂代谢通路 SphK1-S1P 在肾上腺皮质癌发生发展中发挥了重要作用，鞘磷脂代谢信号通路可以作为肾上腺皮质癌治疗的潜在靶点。

COR-54

即时尿钾 / 尿肌酐比值在低钾血症病因研究中可能是 24 小时尿钾的替代性指标

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目的 在临床实践中，通常基于收集 24 小时尿钾来评估是否存在肾性失钾。但收集 24 小时尿钾存在诸多干扰因素且较为繁琐导致结果不准确 , 本研究目的是探讨在调查低钾血症病因时即时尿钾 / 尿肌酐比值能否代替 24 小时尿钾。

方法 收集在我科已明确诊断的 60 例低钾血症患者的即时尿、血样本及 24 小时尿样本，排除肾功能不全、应用

利尿剂、心功能不全、血钾者。33 例低钾患者由肾性失钾导致，病因包括原发性醛固酮增多症、肾小管酸中毒、库欣综合征等。非肾性失钾的低钾血症患者共 27 例，包括甲状腺功能亢进症、食欲减退、高胰岛素血症。30 例血钾正常者作为对照组。收集所有患者（低钾患者在补钾之前）弃去晨尿的第二次尿作为即时尿样本，同一天开始收集 24 小时尿样本和血样本。应用 8000-c 701 测定即时尿钾、尿肌酐和血钾，24 小时尿钾由 24 小时尿液钾浓度与收集的 24 小时尿液总量算出。应用 SPSS 22.0 进行数据统计分析。

结果　肾性失钾组和非肾性失钾组的即时尿钾 / 尿肌酐比值和 24 小时尿钾均存在统计学差异（P<0.05 及 P<0.01）。低血钾患者的 24 小时尿钾与即时尿钾 / 尿肌酐比值呈正相关（r=0.694，p<0.001）；对照组的 24 小时尿钾与即时尿钾 / 尿肌酐比值亦呈正相关（r=0.587，p<0.001）。在本研究中，以 24 小时尿钾 >25 mmol 作为肾性失钾的判定标准（准确度 70.0%，灵敏度 100%、特异度 33.3%）。通过 ROC 曲线得出区分肾性与非肾性的即时尿钾 / 尿肌酐比值的最佳切点值为 3.35 mmol/ mmol（准确度 81.6%，灵敏度 75.8%、特异度 88.9%）。

结论　即时尿钾 / 尿肌酐比值可能是区分肾性失钾和非肾性失钾良好的替代性指标。为了进一步明确尿钾 / 尿肌酐比值的最佳切点值以区分低钾血症的原因，需要进行更大样本量的研究。

COR-55

肾上腺髓性脂肪瘤 36 例临床分析

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目的　探讨肾上腺髓性脂肪瘤的诊断及治疗。

方法　回顾性分析 36 例肾上腺髓性脂肪瘤患者的临床资料，总结诊断及治疗经验。36 例患者术前均行常规生化检查、肾上腺皮髓质激素检测、CT 检查，4 例行腹部超声检查，1 例行 MRI 检查。36 例均手术治疗，其中 33 例行腹腔镜手术，3 例行开放性手术。36 例术后均行病理检查。

结果　36 例手术均获成功，肿瘤直径 10-130mm，术后病理 32 例为髓性脂肪瘤，4 例为髓性脂肪瘤伴皮质腺瘤，且伴有皮质激素水平异常。术后随访 2 月 -44 月，肿瘤均未复发。

结论　肾上腺髓性脂肪瘤多无临床症状及内分泌功能，诊断主要依靠影像学检查，治疗方法根据患者临床症状、内分泌激素水平、肿瘤大小综合选择，有手术指证者首选腹腔镜手术，肿瘤直径 ≥8cm 建议开放性手术治疗。肾上腺髓性脂肪瘤合并肾上腺皮质腺瘤罕见，应积极手术治疗。

COR-56

地塞米松抑制试验在原发色素结节性肾上腺皮质病诊断中的作用

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目的　揭示地塞米松抑制试验在原发色素结节性肾上腺皮质病诊断中的作用。

方法　回顾性分析北京协和医院自 2001 年至 2015 年收治的原发色素结节性肾上腺皮质病（PPNAD）20 例，非 ACTH 依赖性肾上腺大结节样增生（AIMAH）30 例和肾上腺皮质醇分泌瘤 88 例的临床资料和地塞米松抑制试验结果。

结果　本组 PPNAD 患者中，占同期我院收治的库欣综合征患者（1360 例）的 1.5%，平均确诊年龄 22 ± 9 岁，AIMAH 患者平均确诊年龄 50 ± 10 岁，肾上腺皮质醇瘤患者平均确诊年龄 34 ± 9 岁。PPNAD 患者行小剂量地塞米松抑制试验（LDDST）后 24 小时 UFC 平均升高 39%。PPNAD 患者服用大剂量地塞米松后 24 小时 UFC 可见明显升高，平均升高 76%。而 AIMAH 或肾上腺皮质醇分泌瘤患者行 DST 后 24 小时 UFC 升高为— 10 至 7%。采用以 24 小时 UFC(服药后)/ UFC(服药前) 对 PPNAD 行 ROC 曲线，LDDST 的 AUCROC 为 0.751，临界值为 1.144，诊断的敏感性为 75.0%，特异性为 76.7%。HDDST 的 AUCROC 为 0.825，临界值为 1.107，诊断的敏感性为 85.0%，特异性为 78.6%。

结论　地塞米松抑制试验特别是 HDDST 对 PPNAD 患者诊断意义较大。

COR-57

先天性低促性腺激素性性腺功能减退症男性患者生精治疗：GnRH 泵优于双促

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目的　脉冲式 GnRH 或促性腺激素（HCG/HMG）均可诱导先天性低促性腺激素性性腺功能减退症（CHH）男性患者产生精子。但是目前尚不明确，哪种治疗产生精子的效果更佳。

方法　这项回顾性研究，纳入 202 CHH 患者，根据不同治疗方案分为 GnRH 组 (n=20) 和 HCG/HMG 组 (n=182)。治疗时间均超过 12 个月；

结果　两组患者总的随访时间分别为 15.6 ± 5.0 (范围 12-27) 个月和 28.7 ± 13.0 (范围 12-66) 个月。两组患者的精子初现时间分别为 6 (95%CI 1.6-10.4) 个月和 18 (95%CI 16.4-20.0) 个月 (P<0.001)。GnRH 组和 HCG/HMG 组，达到精子浓度超过 $\geq 5 \times 10^6$/ml 所需要的治疗时间分别为 14

(95%CI 5.8-22.2)个月和27 (95%CI 18.9-35.1)个月 (P<0.001)。达到精子浓度 ≥10 × 10^6/ml 的治疗时间分别为 18 (95%CI 10.0-26.0) 个月和 39 (95%CI unknown) 个月。与此相应，和 GnRH 组相比，HCG/HMG 组需要更长的时间才能达到睾丸体积 ≥4 ml, ≥8 ml, ≥12 ml and ≥16 ml. 我们对两个组的精子活动度（a+b+c 百分数）进行评价（只选取精子浓度超过 >10^6/ml 的精液样本）：GnRH 组（16 个精液样本）的精子活动度为 43.7 ± 20.4%，而 HCG/HMG 组（153 个精液样本）为 43.2 ± 18.1% (P=0.921)。 随访期间，GnRH 组的睾酮水平低于 HCG/HMG 组，两组分别为 8.3 ± 4.6 和 16.2 ± 8.2 nmol/L（P<0.001）。

结论 和 HCG/HMG 治疗相比，脉冲式 GnRH 可促进 CHH 患者更早产生精子，产生更大的睾丸体积。

COR-58

性腺功能异常的病因构成及疾病谱变迁趋势

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目的 总结近 30 年于解放军总医院内分泌科住院诊治的性腺功能异常患者的病因构成特点，分析疾病谱变迁趋势。

方法 收集 1985 年 1 月 1 日至 2014 年 6 月 31 日因性腺功能异常（包括各种原因导致的性分化异常、青春期发育异常、性腺功能减退等疾病）患者的病例资料，包括：性别、年龄、入院日期、家庭住址、临床诊断、实验室检查、影像学资料等，对其进行回顾性分析。

结果 ① 30 年间于我科住院诊治的性腺功能异常患者共 1233 例，社会性别为男性 790 例 (64.07%)，女性 443 例 (35.93%)，平均初诊年龄 20.79 ± 10.42 岁，高峰为 13-18 岁（38.36%）。②性腺功能异常疾病的就诊人数呈逐年上升趋势，其病因构成复杂，以获得性低促性腺激素性性腺功能减退症 (AHH) 所占比例最高（34.51%），不同时间段疾病病因构成不同，先天性低促性腺激素性性腺功能减退症呈逐年上升趋势（15.20%vs22.24%,P<0.05），垂体柄中断综合征 (PSIS) 呈逐年上升趋势（0vs12.80%，P<0.05），其他疾病的变化无统计学意义。③ 429 例性发育异 (DSD) 常患者，社会性别为男性 298 例（70.24%），女性 131 例（29.76%）；平均初诊年龄 18.90 ± 7.11 岁，较非 DSD 患者的平均初诊年龄小（21.65 ± 11.66 岁，P<0.05），不同年龄段 DSD 的病因构成比例有差别。DSD 病因分类：46,XY DSD 278 例（64.80%），46,XX DSD 86 例（20.05%），性染色体 DSD 65 例（15.15%）。④ DSD 的就诊率呈逐年上升趋势，不同时间段疾病病因构成不同，均以特发性低促性腺激素性性腺功能减退症 (IHH) 多占比例最高（29.31%、30.69%、33.70%）。来自农村的就诊率呈逐年上升趋势（24.14%vs27.73%vs37.04%，P<0.05），而一线、二线城市呈逐年下降趋势。

结论 近 30 年来我院性腺功能异常就诊人数呈逐年上升趋势，这类疾病病因构成复杂，疾病谱有所变化，以获得性低促性腺激素性性腺功能减退症和特发性低促性腺激素性性腺功能减退症所占比例最高。其中性发育异常患者的平均初诊年龄小，其就诊人数亦呈逐年上升趋势，此外来自于农村的患者比例逐渐增加。

COR-59

miR-192 调控高糖培养大鼠肾小球系膜细胞中 MCP-1 表达的作用机制研究

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目的 通过高糖培养大鼠肾小球系膜细胞，观察 miR-192、MCP-1 的表达变化，探讨高糖培养大鼠肾小球系膜细胞诱导 miR-192 高表达调控 MCP-1 的表达的分子机制。

方法 正常糖、高糖或等渗甘露醇培养鼠肾小球系膜细胞 HBZY-1，Real-time PCR 法检测 miR-192/ miR-200b/ miR-200c/Zeb1/MCP-1 的表达，Western blot 法检测蛋白的表达。HBZY-1 细胞分别转染 miR-192-inhibitor 及其对照 miR-192-inhibitor NC 后，高糖处理培养，Real-time PCR 法检测 miR-192/ miR-200b/ miR-200c/Zeb1/MCP-1 的表达，Western blot 法检测蛋白的表达。HBZY-1 细胞分别转染 Zeb1 siRNA 及其对照 Zeb1 si NC 后，高糖处理培养，Real-time PCR 法检测 miR-192/ miR-200b/ miR-200c/Zeb1/MCP-1 的表达，Western blot 法检测 Zeb1 和 MCP-1 蛋白的表达。

结果 ⑴高糖培养大鼠肾小球系膜细胞 HBZY-1 中 miR-192、miR-200b、miR-200c、MCP-1 表达较正常对照组、甘露醇组显著升高，差异均具有统计学意义，P<0.05；Zeb1 表达降低，差异具有统计学意义，P<0.05。甘露醇组与正常对照组无显著性差异。⑵ HBZY-1 细胞转染 miR-192-inhibitor 后，细胞中的 miR-192、miR-200b、miR-200c、MCP-1 表达均下调，差异均具有统计学意义，P<0.05；Zeb1 表达升高，差异具有统计学意义，P<0.05。miR-192-inhibitor NC 转染组与未转染细胞组表达变化趋势一致。⑶ HBZY-1 细胞 Zeb1 表达沉默后，细胞中的 miR-192、miR-200b、miR-200c、MCP-1 表达均显著升高，差异均具有统计学意义，P<0.05。Zeb1 siNC 转染组与未转染组表达变化趋势一致。

结论 高糖诱导大鼠肾小球系膜细胞 miR-192 表达上调，抑制 Zeb1 的表达，上调炎症因子 MCP-1 表达，在糖尿病肾病发病过程中起了一定的作用，抑制 miR-192 有望成为治疗糖尿病肾病的抗炎靶点。

COR-60

Ccrn4l 介导糖尿病肾病近端肾小管损伤的机制

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目的　探讨 Ccrn4l（carbon catabolite repression 4-like）介导糖尿病肾病（diabetic nephropathy, DN）近端肾小管损伤的分子机制。

方法　给予 6 周龄 db/db 小鼠（n=8）及同窝出生的 db/m 小鼠（n=8）正常饮食，观察 16 周后处死小鼠，留取肾脏标本。体外使用正常糖（5.6mM）、高糖（25mM 葡萄糖）、高脂（250uM 棕榈酸）、高糖加高脂（25mM 葡萄糖＋250uM 棕榈酸）、转化生长因子 TGF- β 1（10ng/ul）处理人肾小管上皮细胞株 HK-2，干预 5 天后，收集细胞裂解液中的蛋白和 RNA。使用 SiRNA 干扰技术敲低 HK-2 细胞中 Ccrn4l 的表达水平。应用免疫组化方法检测小鼠肾脏组织中 Ccrn4l、上皮型 - 钙黏附蛋白（E-cadherin）、平滑肌动蛋白（alpha-SMA）的表达水平。Western Blot 检测肾脏和 HK-2 细胞中 Ccrn4l、E-cadherin、NF-kB 抑制因子 alpha（IKB-alpha）蛋白的表达水平。应用实时定量 PCR（RT-PCR）方法检测小鼠肾脏组织和 HK-2 细胞中 Ccrn4l、MCP-1、TNF-alpha 的 mRNA 表达水平。

结果　与对照组相比，db/db 糖尿病小鼠肾脏 Ccrn4l 的基因和蛋白表达水平均显著增高，尤其是在肾小管区域。Db/db 小鼠近端肾小管区域 E-cadherin 的表达下调，同时 alpha-SMA 表达明显增高，提示小管上皮细胞发生间质转分化（EMT）。IKB-alpha 在糖尿病小鼠的肾脏组织中的表达被明显下调，提示 NF-kB 通路被激活。高糖、高脂以及 TGF-β 1 均可以显著上调 HK-2 细胞中 Ccrn4l、MCP-1、以及 TNF-alpha 的表达，同时导致 IKB-alpha 表达下降，HK-2 发生 EMT。然而，敲低 HK-2 细胞中的 Ccrn4l 的表达后，这些改变可以被明显逆转。

结论　Ccrn4l 介导了糖尿病肾病肾小管病变的发生与发展，参与了糖尿病状态下肾脏组织的炎症、纤维化及肾小管上皮向间充质细胞转分化等病理过程。

COR-61

胰岛素泵治疗对冠脉搭桥术后 2 型糖尿病患者血糖控制及住院天数的影响

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目的　合并 2 型糖尿病的冠心病患者大多病变严重，表现为多支病变或（和）左主干病变。冠状动脉搭桥术是为患者建立血运重建的重要治疗措施，但术后患者存在难治性高血糖，如何控制好围手术期血糖对糖尿病患者的冠心病治疗及预后具有重要影响。胰岛素泵治疗在围手术期血糖控制方面有其独特的优势。本研究旨在探讨胰岛素泵治疗与传统的降糖治疗相比对改善冠脉搭桥术患者血糖控制及住院天数的影响。

方法　本研究分析了我院 2014 年 11 月至 2016 年 2 月年在我院心脏成人外科行冠脉搭桥术的 2 型糖尿病患者共 667 例，其中男性 479 例，女性 188 例，平均年龄（60.66 ± 7.92）。冠脉搭桥术后行胰岛素泵治疗患者 185 例，行传统降糖治疗方式患者 482 例（包括胰岛素或胰岛素联合口服药物患者 435 例，口服药治疗患者 44 例，）。采集患者入院时年龄、性别、身高、体重、血压、心率、空腹血糖、糖化血红蛋白、血脂、糖尿病病史、冠心病病史、手术情况、术后的血糖及住院天数等资料。分析两组之间血糖控制及住院天数的差异。

结果　基线资料显示，胰岛素泵治疗组与传统降糖治疗组入院时年龄、性别比例及BMI和空腹血糖无显著差异，仅糖化血红蛋白在传统降糖治疗组略高于胰岛素泵治疗组。胰岛素泵治疗组出院时的空腹血糖明显低于传统降糖治疗组（8.81 ± 2.24 mmol/L vs 10.91 ± 2.65 mmol/L,P<0.01）。总住院天数胰岛素泵治疗组比传统降糖治疗组减少近 3 天（16.81 ± 7.88 天 vs 19.63 ± 7.6 天，P<0.01），主要是减少了术后普通病房的住院天数（5.81 ± 2.79 天 vs 8.53 ± 4.28 天，P<0.01）。治疗期间胰岛素泵治疗组低血糖（任意血糖＜ 3.9 mmol/L）发生率为 0.23%，传统降糖治疗组低血糖发生率为 0.18%，两组比无统计学差异（P ＞ 0.05）。严重低血糖（任意血糖＜ 2.8 mmol/L）发生率两组均为 0 次。

结论　胰岛素泵治疗不仅能够平稳、快速地控制冠脉搭桥术后 2 型糖尿病患者的高血糖，还能够显著减少患者的住院天数，而且这种治疗方法亦不会增加低血糖风险，是冠脉搭桥术后高血糖患者较好的治疗选择。

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糖尿病前期人群十年转归及与性别相关的危险因素分析

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目的　中国非传染性疾病 2010 年监测糖尿病专题调查提示，中国糖尿病前期患病率已高达 50.1%，然而影响糖尿病前期转归的因素仍不十分明确。长期的随访研究可探索介导这种转归的相关因素，因此，我们在一个十年的糖尿病随访样本中研究性别特异的糖尿病前期转归情况及相关的影响因素。

方法　本研究采用分层，多阶段，整群的抽样方法，

于 2003 年从上海市平凉 33 个社区中随机抽取近胜社区、霍新社区、明园村社区和江浦社区进行流行病学研究。从符合筛选资格的 18000 个常驻居民当中，随机抽取了 2200 位居民做为基线人群，2013 年对该人群进行了随访。基线及随访研究内容均包括问卷调查、体格检查及生化检查。问卷调查主要收集人口学信息、生活方式、既往病史及家族史等。体格检查具体包括身高、体重、腰围、臀围、收缩压和舒张压等指标。生化检查时采集研究对象血浆进行空腹葡萄糖检测，同时检测血清检测胰岛素、糖化血红蛋白、肝肾功能、血脂水平等指标。本研究所有数据均使用 SPSS 18.0 进行统计分析。研究的各个阶段均实施严格的质量控制，以保证研究数据的可靠性。

结果 在基线水平一致的情况下，logistic 回归结果显示男性的年龄和运动状态，女性的血糖水平和腰围分别与糖尿病前期转归正常显著相关。在男性群体中，运动积极组糖尿病前期患者转归正常的风险是运动不积极组的 3 倍（95%CI 1.09-8.30）而在女性群体中，腰围每增加一厘米，转归正常的风险减少 6%。同时，在糖尿病前期患者进展为糖尿病的危险因素探究中，男性年龄越大（OR 1.09, 95%CI, 1.03-1.16），TG 水平越高（OR 1.75, 95%CI, 1.24-2.49），餐后血糖越高（OR 1.64, 95%CI, 1.25-2.16），吸烟（（OR 3.29, 95%CI, 1.10-9.78）都使得糖尿病前期进展成糖尿病的风险显著升高。在女性糖尿病前期患者中，基线有高血压病史者（（OR 2.38, 95% CI, 1.13-5.03），有糖尿病家族史（OR 2.74, 95% CI, 1.23-6.12）及基线腰围越大（OR 1.05, 95% CI, 1.01-1.10）进展为糖尿病的风险就越高。

结论 针对不同性别，具有不同危险因素的糖尿病前期患者应采取个体化的干预措施。

COR-63

非酒精性脂肪肝人群发生糖代谢异常风险的前瞻性研究—上海长风研究

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目的 在社区中老年人群中进行前瞻性观察，探讨非酒精性脂肪肝人群发生糖代谢异常的风险。

方法 2014 年 11 月至 2015 年 7 月对 633 例于 2010 年 6 月至 2012 年 9 月参加上海长风社区 45 岁以上中老年多种慢性疾病调查的基线人群进行随访，检测空腹血糖和糖负荷后 2 小时血糖，根据 1999 年 WHO 糖尿病诊断标准，FBG≥6.1mmol/L 和 / 或 2hBG≥7.8mmol/L 定义为糖代谢异常人群。采用超声半定量方法测定肝脏脂肪含量（LFC），以基线 LFC 超过 9.15% 为脂肪肝组，剔除 136 例基线已诊断糖尿病患者，剩余 497 例基线糖代谢正常者（男性 181 例，占 36.4%）进入统计分析，入组分析人群中位随访时间 4.71 年。

结果 1、基线脂肪肝组 181 例，非脂肪肝组 316 例。脂肪肝组糖代谢异常发生率高于非脂肪肝组（43.6% vs 31.6%，P=0.007）。脂肪肝组糖代谢异常发生风险增加 21.3%（RR：1.213，95%CI：1.046 ~ 1.407）。2、按基线肝脏脂肪含量每增加 5% 分组，与 LFC<5% 相比，LFC 5%~10%、10%~15% 和大于 15% 组发生糖代谢异常的 RR 分别为 1.090、1.109 和 1.409（95%CI 分别为 0.933~1.273，0.902~1.365，1.136~1.747）。3、Logistic 回归分析显示，基线 LFC 水平是未来发生糖代谢异常的危险因素，且独立于基线入组时的年龄（RR：1.026，95%CI：1.007~1.046）。

结论 非酒精性脂肪肝增加糖代谢异常的患病风险，肝脏脂肪含量超过 15% 较肝脏脂肪含量小于 5%，发生糖代谢异常的风险增加 40.9%。

COR-64

GLP-1 受体激动剂通过激活 cAMP/PKA/CREB 信号通络对 AGEs 诱导的星形胶质细胞炎症损伤的保护作用

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目的 研究胰高糖素样肽 -1（GLP-1）受体激动剂对 AGEs 造成星形胶质细胞炎性损伤的保护性机制。

方法 体外原代培养大鼠星形胶质细胞，分为 4 组：对照组、AGEs（0、50、100、200、400ug/ml）组、AGEs+GLP-1(10、100、1000ng/ml)组、AGEs+GLP-1R shRNA（敲减 GLP-1R）组。干预结束后对星形细胞进行形态学观察，应用流式细胞仪检测、免疫印迹、免疫荧光、ELISA、PCR 等方法检测细胞增殖凋亡、ROS、TNF-α、IL-1β 等炎症相关因子水平和 cAMP/PKA/CREB 通路相关蛋白的表达，采用单因素方差分析进行多组间均数比较。

结果 AGEs 可以显著增加细胞内 ROS 水平、Caspase-3 活性及 TNF-α 和 IL-1β 等炎性细胞因子的分泌（P<0.01），并呈剂量和时间依赖性（P<0.01）。GLP-1 受体激动剂干预可以显著降低星形胶质细胞 ROS 产生，并降低 Caspase-3 活性、TNF-α 和 IL-1β 的分泌（P<0.01），但对 GLP-1R 敲减的星形胶质细胞无上述作用。进一步的机制研究发现，AGEs 可以显著降低星形胶质细胞中胞内 cAMP、PKA 的活性以及 CREB 磷酸化水平（P<0.01），GLP-1 受体激动剂可逆转 AGEs 引起的 cAMP/PKA/CREB 通路的变化（P<0.01），但在 GLP-1R 敲减的星形胶质细胞未出现上述变化。此外，腺苷酸环化酶抑制剂 SQ22536 或 PKA 抑制剂 RP 预处理均可以显著减弱 GLP-1 受体激动剂对 AGEs 诱导 ROS 生成、TNF-α 和 IL-1β 分泌、caspase-3 激活和细胞死亡的保护作用。

结论 GLP-1 可以通过活化 GLP-1R 介导的 cAMP / PKA / CREB 通路减轻 AGEs 引起的星形胶质细胞的炎性损伤作用，从而发挥中枢神经系统的保护作用。

COR-65

胰岛细胞瘤中微小 RNA-144/ 451 通过靶向 PTEN / Akt 信号通路促进细胞增殖的研究

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目的　胰岛素瘤是功能性胰腺神经内分泌肿瘤的主要类型。功能微小 RNAs（miRNAs）在胰岛素瘤中调控肿瘤的发生和生长的功能仍未知。

方法　我们通过 miRNA 定量 PCR 表达谱分析人正常胰岛和胰岛细胞瘤组织，发现了 114 个差异表达的miRNA。

结果　我们发现了人胰岛细胞瘤组织和人正常胰岛中差异表达的 miRNA。其中有 41 个差异 miRNA 分别归属于 7 个 miRNA 家族，3 个家族中的 28 个 miRNA 个定位在表观遗传调控的印迹染色体 14q32 区域。我们在 8 例人正常胰岛和 25 个胰岛素瘤样本中验证了表达差异最显著的 miRNA-144/ 451。我们的数据表明，在小鼠胰岛 β 细胞中过表达 miRNA-144/ 451 可以通过靶向 PTEN/Akt 信号通路和 CyclinD2 促进细胞增殖。

结论　我们的研究结果强调了功能性 miRNA 在胰岛细胞瘤中的重要性。

COR-66

胰岛 β 细胞特异性 INS1 驱动基因过表达和敲除小鼠模型的构建和表征

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目的　胰岛 β 细胞特异性基因过表达和敲除技术是在体功能基因研究的基础。

方法　我们构建了 Ins1-Cre-DsRed 和 Ins1-rtTA 小鼠模型。这些小鼠模型表达小鼠 Ins1 启动子驱动下的 Cre 重组酶或反向四环素调控的反式激活子（rtTA）而不包含 hGH 小基因。

结果　我们的数据表明，通过和报告小鼠（ROSAmT/mG 或 tetO-HIST1H2BJ/GFP）交配，可以在小鼠胚胎 13.5 天有效的检测到 Cre 介导的重组和 rtTA 介导的激活。而且 Cre 和 rtTA 表达仅限于胰岛 β 细胞而没有发生大脑和其他组织的泄漏。两个转基因小鼠均表现出正常的葡萄糖耐量和胰岛素分泌。

结论　这些结果表明 Ins1-Cre-DsRed 和 Ins1-rtTA 小鼠可用于在胚胎和成年小鼠中敲除或过表达靶基因以推进 β 细胞的研究。

COR-67

miR-375 靶向调控 Mapkap1 在血管紧张素Ⅱ影响胰岛 β 细胞中的作用及机制

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目的　Mapkap1 是 mTORC2 的重要组分，可通过影响 Akt-Ser473 磷酸化影响 Akt 活化，mTORC2-Akt 对于维持胰岛 β 细胞量及功能十分重要。本课题组前期研究显示血管紧张素Ⅱ（AngⅡ）可通过上调miR-375致胰岛 β 细胞凋亡，抑制其增殖。生物信息学软件预测 Mapkap1 基因的 3’ UTR 有 miR-375 的结合位点。本研究初步探讨了 miR-375 靶向调控 Mapkap1 在 Ang Ⅱ影响胰岛 β 细胞中的作用及机制。

方法　双荧光素酶报告基因实验验证 miRNA-375 的靶点，Real time-PCR 分析 miR-375、Mapkap1 mRNA 水平，Western blot 分析 β-actin、Mapkap1、Akt、Phospho-Akt(ser473)、caspase-3、cleaved caspase-3 的蛋白水平，流式细胞术分析细胞凋亡率，放射免疫分析法检测胰岛素分泌量。在小鼠胰岛 β 细胞 MIN6 细胞中转染 miR-375 mimic 或 inhibitor 过表达 / 抑制 miR-375 水平，转染 Mapkap1-TSB(microRNA target site blocker，TSB) 抑制 miR-375 对靶基因 Mapkap1 的负性调控作用，转染 siRNA 抑制 Mapkap1 的表达。

结果　双荧光素酶报告基因实验结果显示 miR-375 mimic 对 Mapkap1 野生型载体的报告荧光有明显的下调作用，相应结合位点突变后，报告荧光有所恢复。在 MIN6 细胞中，转染 miR-375 mimic 后 Mapkap1 蛋白水平明显降低，转染 miR-375 inhibitor 后 Mapkap1 蛋白水平明显升高。Ang Ⅱ处理 MIN6 细胞结果显示 Ang Ⅱ可下调 MIN6 细胞 Mapkap1 蛋白水平，且一定程度上存在浓度依赖性和时间依赖性，然而 Mapkap1 mRNA 的水平无统计学差异。在 MIN6 细胞中，转染 Mapkap1-TSB 使 Ang Ⅱ引起的细胞凋亡减少、Ang Ⅱ作用的细胞胰岛素分泌量升高；转染 Mapkap1 siRNA 能够明显降低 Akt-ser473 磷酸化水平、上调 cleaved caspase-3 水平，使细胞凋亡率显著升高，细胞胰岛素分泌量显著降低。

结论　Ang Ⅱ通过 miR-375 靶向调控 Mapkap1 的表达增加 MIN6 细胞的凋亡、抑制胰岛素分泌。

COR-68

EPC 移植治疗糖尿病兔下肢缺血的血管重建和血管生成相关基因的表达

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目的　探讨内皮祖细胞（EPC）移植治疗糖尿病兔下肢

缺血的效果及机制。

方法 健康日本大耳白兔随机分三组，糖尿病 PBS 对照组（A 组）、糖尿病内皮祖细胞移植治疗组 (B 组)、正常血糖内皮祖细胞移植治疗组 (C 组)。骨髓来源的内皮祖细胞经体外扩增培养 7 天后，通过肌内注射进行细胞移植，细胞标记分析内皮祖细胞移植后的分布及存活情况，十四天后用病理、动脉造影、彩超来评价治疗效果，同时分析对血管生成相关基因的影响，并测定肌浆中 VEGF 浓度。

结果 1 病理示三组毛细血管密度分别为 9.29 ± 1.63 个 / 视野、12.60 ± 2.16 个 / 视野*、12.51 ± 1.56 个 / 视野，血管 / 肌束比值分别为 0.66 ± 0.05、0.83 ± 0.11*、0.90 ± 0.13；2 彩超示三组缺血侧 / 正常侧下肢胫前动脉收缩期峰值流速比值分别为 0.49 ± 0.05、0.57 ± 0.08*、0.60 ± 0.09；3 动脉造影示三组缺血侧下肢动脉显影血管数分别为 6.25 ± 2.82 个、10.25 ± 3.28* 个、10.13 ± 2.36 个；4 血管生成相关基因芯片分析示糖尿病内皮祖细胞移植治疗组与对照组比较上调超过两倍的基因达 27 个，其中包括 VEGF 等多种促血管生成物质。 5 缺血肌肉中 VEGF 的浓度测定示三组结果分别为 0.22 ± 0.05 ng/g、0.30 ± 0.07ng/g* 、0.31 ± 0.08ng/g（*：与 A 组比较 P<0.05，有统计学意义，与 C 组比较 P≥0.05，二者无差别）

结论 内皮祖细胞移植治疗糖尿病动物下肢缺血能有效改善血供、促进血管重建，恢复血流，其治疗机制复杂，多种因子及受体参与其中，血管内皮细胞生长因子（VEGF）在治疗中作用起到了关键作用。

COR-69

应用血清胰岛素与 C 肽指标预测使用外源性胰岛素的 2 型糖尿病患者 IAA 阳性的最佳临界值探讨

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目的 应用 ROC 曲线寻找血清胰岛素及 C 肽指标对预测使用外源性胰岛素的 2 型糖尿病（T2DM) 患者胰岛素自身抗体（IAA）阳性的最佳临界值。

方法 通过对 283 例于 2009 年 -2013 年在华西医院住院并检测过 IAA，使用过外源性胰岛素的 T2DM 患者资料进行研究，按 IAA 测定结果分为阳性组及阴性组，统计其血清胰岛素（Ins）及 C 肽（C-P）、糖化血红蛋白（HbA1c）等测定值及（IAA）结果，比较两组间差异，采用 ROC 曲线评价不同时间点的 Ins 及 C-P 指标对 IAA 阳性的预测切点。

结果 阳性组的空腹胰岛素（Ins-0h）及餐后 2 小时胰岛素（Ins-2h）平均水平为阴性组的 3 倍左右，差异均有统计学意义 (P<0.0001)。空腹 C 肽（C-P-0h）及餐后 2 小时 C 肽（C-P-2h）水平阴性组稍高，差异无统计学意义 (P>0.05)，两组的空腹及餐后 2 小时的血清胰岛素 /C 肽比值（Ins-0h /C-P-0h、Ins-2h/C-P-2h）相比其差异均有统计学意义 (P<0.0001)，阳性组明显高于阴性组，经 Spearman 相关分析提示两组空腹及餐后 2 小时胰岛素、C 肽均存在正相关关系，但阳性组的相关性明显低于阴性组，说明在阳性组中胰岛素与 C 肽值出现“分离”的情况。以 Ins-0h、Ins-2h、Ins-0h /C-P-0h、Ins-2h/C-P-2h 来预测 IAA 阳性的 ROC 曲线下面积分别为 0.804、0.738、0.881、0.865，四个指标与 0.5 相比差异有统计学意义 (P<0.0001)，其中 Ins-0h/C-P-0h 预测效果最好，达到 0.881。当 Ins-0h、Ins-2h、Ins-0h /C-P-0h、Ins-2h /C-P-2h 分别为：5.51、29.68、8.6、17.8 时，预测 IAA 的敏感度分别为：67%、49%、80%、58%，特异度分别为 80%、87%、83%、97%，可见以 Ins-0h/C-P-0h 的比值预测，其灵敏度及特异度均较高。

结论 IAA 阳性组的 Ins、C-P 与阴性组相比呈现出不相匹配、分离的现象，Ins-0h、Ins-2h、Ins-0h /C-P-0h、Ins-2h /C-P-2h 可用来筛查使用外源性胰岛素的 T2DM 患者 IAA 阳性的高风险人群，当 Ins-0h /C-P-0h 为 8.6 时，作为 IAA 阳性的初步预测切点价值最高。

COR-70

糖尿病足创面感染病原菌分布特点及耐药性 15 年变迁

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目的 探讨 DF 创面感染病原菌分布特点及耐药性变迁，指导临床抗生素选择，提高经验性抗感染治疗的有效性。

方法 收集 2000 年 1 月至 2014 年 12 月在南方医科大学南方医院住院治疗的 580 例 DFI 患者的病例资料，回顾性分析其一般临床资料、创面棉拭子微生物培养及药敏结果。580 例 DFI 患者按照溃疡 PEDIS 感染级别分为 PEDIS2 级组，PEDIS3 级组，PEDIS4 级组；根据有无合并下肢动脉缺血和周围神经病变，判断溃疡性质为神经性、缺血性、混合性溃疡；季节采用候温法划分，根据广东省月平均气温将季节划分为春季、夏季、秋季 3 个季节。比较上述各组病原菌分布特点。并根据耐药性变化趋势将资料按年份分为 2 组：2000 ~ 2010 年、2011 ~ 2014 年，分析 15 年来 DFI 病原菌对不同抗生素的耐药性变迁情况。

结果 Logistic 回归分析结果提示 DF 溃疡 PEDIS 感染级别（$P < 0.001$）及季节（$P < 0.01$）共同影响 DFI 病原菌类型。溃疡性质对 DFI 病原菌分布的影响无统计学意义（$P > 0.05$）。PEDIS2 级的 DFI 溃疡在各季节均以 G+ 菌感染为主；PEDIS4 级的 DFI 溃疡在各季节均以 G- 菌感染占优势；而 PEDIS3 级者在春秋季以 G+ 菌感染为主（55.3%），夏季以 G- 菌感染为主（53.3%）（$P < 0.05$）。各个季节 DFI 创面

的混合感染率均随着 PEDIS 级别的增加而上升(P < 0.01)。G+ 菌以葡萄球菌属为主 (44.7%)，对青霉素、氨苄西林完全耐药，对万古霉素、利奈唑胺 100% 敏感 ,15 年来对阿莫西林/克拉维酸钾的耐药率由 15.0% 上升至 48.1% (P < 0.05)；G- 菌以肠杆菌科最常见 (61.3%)，对氨苄西林耐药率最高 (91.3%)，对美罗培南最敏感 (99.5%)，15 年来对头孢噻肟的耐药率由 29.2% 增长至 43.7% (P < 0.05)。

结论　对 DFI 患者经验性抗感染治疗时可综合考虑溃疡 PEDIS 级别与季节因素对感染病原菌类型的影响，并结合不同类型病原菌对抗生素的敏感性特点有针对性地选择抗生素。15 年来我院 DFI 病原菌随着时间变迁对多种抗生素的耐药性较早年有升高趋势，其中 β - 内酰胺类、头孢菌素类尤甚。根据伤口特征合理有针对性地使用抗菌药物，减少抗生素的滥用，对防止、延缓病原菌的耐药性增长，提高抗感染治疗的有效性有重大意义。

COR-71

贝前列素钠联合阿司匹林对 2 型糖尿病大血管病变的作用及安全性研究

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目的　探讨贝前列素钠联合阿司匹林对 2 型糖尿病大血管病变的作用及安全性。

方法　选取 2010 年 07 月至 2012 年 04 月于中山大学孙逸仙纪念医院体检中心以及门诊就诊的 50-75 周岁、2 型糖尿病合并动脉粥样硬化的患者，共纳入 64 例。随机分为双药组(n=32)和单药组(n=32)，双药组服用贝前列素钠(20ug Tid)和阿司匹林(100mg Qd)，单药组仅服用阿司匹林(100mg Qd)。入组时测定踝肱指数、脉搏波速度、颈动脉及下肢动脉 (胫前动脉、足背动脉、胫后动脉) 彩超等。每 3 个月随访 1 次，复查大便潜血，每年复查全部指标。对所有受试者进行为期 4 年的随访，研究结束后，比较各组治疗前后观察指标的差异以及两组间的差异。

结果　1、一般情况及合并用药：用药前及用药 4 年后性别、年龄、糖尿病病程、吸烟史、高血压病史、体质指数、血压、血糖、血脂、肝功能、肾功能等一般情况两组间比较均无统计学差异；两组间合并使用降糖药、降压药和调脂药的患者所占的比例、用药时间比较均无统计学差异。 2、反映动脉粥样硬化早期改变的指标：用药前后及两组间颈动脉内膜中层厚度的比较无统计学差异。 4、反映动脉粥样硬化晚期改变的指标：(1)用药前后及两组间踝肱指数的比较无统计学差异。(2)用药前后下肢动脉(胫前动脉、足背动脉、胫后动脉) 内径比较有统计学差异，且双药组较单药组增大更为显著；两组间下肢动脉内径比较无统计学差异。(3)用药前后下肢动脉狭窄程度比较无统计学差异，除用药 3 年后两组间胫前动脉狭窄程度比较有统计学差异外，其他时间点两组间下肢动脉狭窄程度比较无统计学差异。 5、反映动脉弹性的指标：双药组和单药组用药前后脉搏波速度比较无统计学差异；两组间脉搏波速度的比较有统计学差异，从各时间点看，除用药前外，单药组的脉搏波速度均显著高于双药组。 6、安全性指标：两组间心血管事件、出血等不良事件的发生率比较无统计学差异。

结论　1、与单用阿司匹林相比，贝前列素钠联合阿司匹林对 2 型糖尿病大血管病变的作用可能主要体现为舒张血管及延缓血管管壁僵硬的进展。 2、贝前列素钠联合小剂量阿司匹林治疗的安全性高，未增加出血倾向。

COR-72

SERPINF1 基因新突变导致五个 VI 型成骨不全症的家系研究

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目的　VI 型成骨不全症 (osteogenesis imperfecta, OI) 是常染色体隐性遗传、表现为严重骨骼畸形、血清色素上皮衍生因子 (pigment epithelium-derived factor, PEDF) 含量下降的罕见类型 OI，本研究旨在分析六例 VI 型 OI 患者的表型特征，检测致病基因 SERPINF1 的突变类型，并测定血清 PEDF 含量。

方法　纳入六例来自五个非近亲婚配家系的 OI 患者，评估临床表现、血清钙磷及骨转换指标水平、骨骼 X 线表现及骨密度。采用二代捕获测序技术和 Sanger 测序进行致病基因突变的检测及验证。采用 ELISA 双抗夹心法测定血清 PEDF 含量。

结果　六例患者均婴幼儿起病，年骨折 1.3-14 次，具有脊柱后凸、四肢长骨弯曲等不同程度的骨骼畸形，无蓝巩膜、牙本质发育不全及听力下降；影像学表现为严重骨质疏松、骨骼畸形、爆米花样骨骺等。致病基因检测提示一例患者为第 3 外显子纯合突变，c.271_279dupGCCCTCTCG (p.Ala91_Ser93dup)；一例患者为第 3 内含子和第 5 外显子复合杂合突变，c.283+1G>T，c.498_499delCA (p.Arg167SerfsX35)；一例患者为第 8 外显子纯合突变，c.1202_1203delCA (p.Thr401ArgfsX)；一例患者为第 3 外显子复合杂合突变，c.184G>A (p.Gly62Ser)，c.271_279dupGCCCTCTCG (p.Ala91_Ser93dup)；最后来自同一家系的两例患者为第 4 外显子复合杂合突变，c.390TC (同义突变)，c.397C(p.Gln133X)；父母均为携带者。其中后五例患者均具有 SERPINF1 基因的新突变。上述基因突变可能影响 I 型胶原的合成及破骨细胞的分化。血清 PEDF 含量测定提示其中五例 VI 型患者的血清 PEDF 含量极低，较年龄、性别匹配的 COL1A1/2 基因突变 OI 患者和正常对照均显著下降，六例 SERPINF1 基因突变携带者的血清 PEDF 含量介于上述

两者之间。

结论 本研究首次报道国内 SERPINF1 基因突变导致罕见的常染色体隐性遗传 VI 型 OI 患者的临床特点，并在中国患者中检出了六种该基因的新型突变；此外，血清 PEDF 含量对 VI 型 OI 患者具有重要的诊断价值。

COR-73

200 例成年起病的非手术性甲状旁腺功能减退症临床分析

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目的 探讨成年起病的非手术性甲旁减临床特点。

对象和方法 回顾性分析 1987 年 12 月至 2015 年 12 月于北京协和医院内分泌科门诊就诊的成年起病的 200 例非手术性甲旁减患者临床表现及生化指标，在规律随诊的 128 例患者中分析泌尿系统并发症比例及其影响因素。

结果 男性 81 例，女性 119 例，中位发病年龄 29（18~74）岁，中位确诊时间 4（0~40）年，中位病程 6（0~40）年。初诊时有手足搐搦及手足麻木症状者分别为 81.5%、62.0%，32% 有癫痫发作史。颅内钙化及白内障发生比例分别为 60.9%（98/161）和 74.4%（96/129）。生化指标方面，血钙（1.61 ± 0.30）mmol/L，血磷（1.91 ± 0.39）mmol/L，碱性磷酸酶（66.7 ± 27.0）U/L，游离钙（0.72 ± 0.15）mmol/L，PTH 3（0~20.4）pg/mL，血肌酐（78.7 ± 17.0）μmol/L，24 小时尿钙 71.8（5.0~668）mg。99 例患者测定血镁（0.79 ± 0.17）mmol/L，21 例患者存在低镁血症。所有患者均给予口服钙剂联合维生素 D 及其衍生物治疗，低镁血症者予补镁治疗。规律随诊的 128 例患者中，随访时间 3（0.33~23.0）年，治疗过程出现高钙尿症（＞ 350mg/24h）86 例。在正常尿钙和高钙尿症两组患者间，比较初诊时的病程、年龄、性别比例、颅内钙化、白内障、血钙、血磷、PTH、尿钙及治疗后的血钙、血磷、尿钙的差异，除治疗后尿钙外，余未见明显差异。泌尿系结石 / 钙化 5 例，血肌酐升高 8 例，回归分析提示肾功能下降与年龄、病程相关。

结论 成年起病的非手术性甲旁减临床表现以手足搐搦、手足麻木、癫痫发作多见，易被漏诊或误诊，口服钙剂、维生素 D 及其衍生物可有效缓解临床症状及体征，需密切监测血钙、尿钙、泌尿系超声，以避免出现高钙尿症、泌尿系结石 / 钙化及肾功能不全等并发症。

COR-74

肝脏脂肪含量、肝酶与骨代谢及其标志物的关系研究

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目的 近期研究发现骨骼、脂肪组织及肝脏之间存在着复杂的调控网络。临床上脂肪肝病变与骨量流失之间的关系也正逐步被揭示。本研究采用超声定量肝脏脂肪含量方法，进一步探索社区人群中肝脏脂肪含量、肝酶与骨密度之间的关系。

方法 研究入组 2010-2011 年上海长风社区中老年受试者 2224 例。除外已知合并病毒性肝炎、自身免疫性肝炎、酒精性肝炎及其他慢性肝病，肾功能不全、缺少骨密度数据及绝经前女性的 441 例受试者，共有 1659 例纳入分析。每一受试者均经过详细的既往史及生活运动方式调查、形体参数测定以及血糖、血脂、肝酶等血生化指标测定。肝脏脂肪含量采用本课题组新建立的超声定量肝脏脂肪含量方法测定。腰椎、髋部骨密度及体脂成分采用 GE iDXA 仪器测定。

结果 1) 研究入组 1659 例中老年男性及绝经后女性，其肝脏脂肪含量中位数 4.9%，该人群 NAFLD、代谢综合征、糖尿病患病率分别为 31.8%，29.2% 和 18.7%；2) 相关分析显示校正年龄、体重后，男性受试者超声定量肝脏脂肪含量与腰椎（r=-0.116, P<0.001）、髋部（r=-0.095, P=0.014）及全身骨密度（r=-0.134, P<0.001）呈显著负相关，绝经后女性肝脏脂肪含量与腰椎（r=-0.093,P=0.008）、全身骨密度（r=-0.107，P=0.002）呈显著负相关；3）作为肝脏损伤标志物，男性受试者中血清 ALT 水平与全身 (r=-0.164, P<0.001)、腰椎 (r=-0.102,P=0.005)、髋部骨密度 (r=-0.075,P-0.041) 呈负相关，绝经后女性血清 ALT 与骨密度无显著相关性；4）多元逐步回归分析显示校正年龄、体重、吸烟、饮酒、代谢综合征各组分、体脂百分比后，男性肝脏脂肪含量和肝酶 ALT 仍与身体各部位骨密度、及骨钙素水平呈独立负相关；5）按照有无脂肪肝和有无肝酶异常分组，ALT 异常的 NAFLD 患者其骨密度显著低于 ALT 正常 NAFLD 患者或无 NAFLD 者。

结论 本研究显示肝脏脂肪沉积和炎症可能是中老年男性骨量流失的危险因素，对于合并肝酶升高的男性 NAFLD 患者应筛查骨密度情况。

COR-75

甲状旁腺激素和成纤维生长因子 23 对于表皮角质形成细胞 25 羟维生素 D-1α 羟化酶和 24 羟化酶的调节

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目的 慢性肾脏病（CKD）矿物质和骨代谢异常 (CKD-MBD) 在 CKD 患者中普遍存在。另外 CKD 时肾脏合成 1,25(OH)2D 的能力降低，而 1,25(OH)2D 也可由肾外组

织合成，如表皮，但表皮在CKD时显然不能代偿肾源性1,25(OH)2D的不足。予肾切除患者25(OH)D后，血1,25(OH)2D明显上升。此外予肾切除大鼠注射抗FGF23抗体后，血1,25(OH)2D亦明显升高。这些研究提示，在CKD时肾外组织包括表皮内1,25(OH)2D的合成可能受到了抑制。但表皮1,25(OH)2D的合成是如何受到调节的，并不十分清楚。本研究旨在探讨PTH与FGF23对表皮角质形成细胞1α羟化酶和24羟化酶的调节。

方法　免疫组化检测正常的人表皮组织PTH1R、FGFR1-4、Klotho和FGF23的表达。WB和qRT-PCR检测人表皮角质形成细胞系HaCaT细胞内PTH1R、FGFR1-4、Klotho、1α羟化酶和24羟化酶蛋白及mRNA的表达水平。WB检测ERK1/2、p-ERK1/2、JNK、p-JNK、P38、p-P38、AKT、p-AKT蛋白表达水平。

结果　免疫组化结果表明人表皮组织表达PTH1R、FGFR2-4和klotho，但不表达FGFR1。WB和qRT-PCR结果表明，HaCaT表达PTH1R、FGFR2-4和klotho的蛋白和mRNA，但不表达FGFR1蛋白和mRNA。PTH可抑制HaCaT的1α羟化酶蛋白的表达，但对其1α羟化酶mRNA以及24羟化酶蛋白和mRNA表达无影响。PTH对HaCaT的1α羟化酶蛋白的影响可被PKC抑制剂而非PKA抑制剂所阻碍。另外，FGF23可抑制HaCaT的1α羟化酶蛋白和mRNA的表达，并可促进24羟化酶蛋白和mRNA的表达。FGF23可促进ERK1/2和AKT磷酸化，而对P38和JNK磷酸化无促进作用。ERK1/2抑制剂可阻碍FGF23对HaCaT的1α-羟化酶和24羟化酶蛋白和mRNA的调节。

结论　PTH可促进HaCaT的1α-羟化酶表达，而对其24-羟化酶表达无影响。PTH可能通过激活PKC信号通路促进HaCaT的1α羟化酶表达。FGF23可抑制HaCaT的1α-羟化酶的表达，并可促进其24羟化酶的表达，而FGF23的该作用可能通过激活MAPK ERK1/2实现。

COR-76

50岁以上男性体重指数、体质成分、骨密度的变化特征及其相关性分析

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3. 解放军总医院老年肾内科
4. 解放军总医院老年保健科

目的　探讨50岁以上老年男性随增龄，体质成分(body composition)、体重指数(body mass index, BMI)及骨密度(bone mineral density, BMD)的变化趋势，及其相互关系。

方法　分析我院2009-2011年度门诊358例50岁以上老年男性患者的体质成分及BMD测定资料，根据年龄和BMI分组，比较各年龄组间体质成分的差别，分析体质成分的变化对BMD的影响。

结果　①该人群身高、体重随增龄而降低($p < 0.0001$，$p = 0.0002$)，但BMI各组间无统计学差异；瘦体重指数(Lean mass index, LMI)及非脂肪体重指数(Fat free mass index, FFMI)随增龄而下降(p均< 0.000)，而脂肪体重指数(Fat mass index, FMI)随增龄而增加($p = 0.0145$)；骨矿含量(Bone mass content, BMC)及瘦体重(Lean mass, LM)的绝对值随增龄而降低($p = 0.0031$, $p < 0.0001$)，而脂肪含量(Fat mass, FM)各年龄组间无差异；从体质成分比例上看，随增龄%FM升高，而%LM降低(p均< 0.0001)。②随增龄股骨颈(Femoral neck, FN)和全髋(Total hip, TH)的BMD降低($p < 0.0001$, $p = 0.0027$)，而腰椎1-4(L1-4)的BMD无明显变化。③将BMI分组，随着BMI增加，各部位BMD增高(p均< 0.01)，而骨松及骨量减少的检出率相应减少(p均< 0.01)。④将BMI≥20 < 24 Kg/m2设为1，以骨质疏松症检出率为结局，采用回归分析，提示BMI降低是骨量减少及骨质疏松症的独立危险因素，BMI增加是BMD的保护因素。⑤分别以FMI、LMI和FFMI四分位统计，结果显示：随FMI增高，L1-4部位BMD增高($p = 0.0003$)，而FN和HP的BMD则随着LMI和FFMI的增加而增加(p均< 0.0001)。

结论　50岁以上老年男性，BMI过低更易患骨质疏松症，而体质成分中FMI是腰椎部位的保护因素，LMI和FFMI是髋部BMD的保护因素。

COR-77

运用全基因组外显子测序技术进行垂体柄中断综合征的致病基因研究：一项针对24例典型患者的研究

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目的　垂体柄中断综合征是以不同程度的垂体前叶激素分泌缺乏为主要临床表现的罕见疾病，其影像学特征为垂体柄缺如或纤细，常合并垂体后叶高信号异位、垂体前叶发育不良。近年研究认为其病因与基因突变有关，然而较早前发现的突变基因对该病的解释不到5%，关键致病基因尚未发现。本研究运用全外显子组测序的方法探索致病基因。

方法　对24例临床特征典型的垂体柄中断综合征患者进行全外显子组测序，运用生物信息学方法分析筛选候选基因，并且在另外25例未测序患者中运用一代测序方法进行验证。

结果　24例患者中男性22例，女性2例，平均年龄25 ± 6.02岁，骨龄(SD score) -1.3(-5.0~0.5)，其中2例患者伴有中线发育异常，臀位出生患者比例达45.8%。全体患者均有生长激素缺乏，70.8%的患者同时伴有ACTH缺乏，垂体核磁均有前叶发育不良，后叶异位，以及垂体柄缺失。

经过初步过滤，全外显子组测序捕获了 5300 多个基因突变，其中包括约 4500 个 SNP 与 800 个 Indel 突变。通过通路富集分析，发现突变在 Notch 信号通路上有显著富集。有 41 个基因突变位于与垂体发育、功能相关的 Wnt、Hedgehog 及 Notch 信号通路上，其中 NCOR2、ZIC2、NKD2、MAML3 为高频突变基因，将上述基因运用一代测序方法在剩余 25 例患者上验证，发现 MAML3 突变出现在 11 例患者中，该突变造成 4 个谷氨酰胺的缺失。

结论 垂体柄中断综合征的发病与垂体发育、功能相关的 Wnt、Hedgehog 及 Notch 信号通路的基因突变可能有关，这在以往未曾报道过。

COR-78

失血性休克对 Wistar 大鼠下丘脑 - 垂体 - 甲状腺轴的影响

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目的 通过监测血清 TRH、TSH、T3、T4 水平及垂体 TSHβ mRNA 的表达在失血性休克后的动态改变，探讨急性失血性休克对 wistar 大鼠下丘脑 - 垂体 - 甲状腺轴的影响。

方法 6-8 周龄雄性 Wistar 大鼠 36 只，体重 230-260g，随机分成 5 组，每组 6-8 只，分别为 0 分组（只进行置管而不进行失血，即为对照组）、15 分钟组、30 分钟组、60 分钟组、120 分钟组。实验大鼠均行左侧颈静脉导管置入术，除对照组不需进行失血外，失血均于导管植入后 12-16 小时内进行（对照组直接进行标本采集），并于大鼠自由活动时通过颈静脉置入导管在 3-5min 内完成失血，失血量为 1.8-2.0ml/100g，建立急性失血性休克动物模型，分别于失血后 15 分、30 分、60 分、120 分心脏采血待测血清 TRH、TSH、T3、T4，采血后立即断头，迅速分离并取出垂体，待 Real-time PCR 测垂体组织 TSHβ mRNA 表达。

结果 1、血清 TRH 平均值：与对照组相比 120 分钟组明显升高（$p < 0.05$），实验组各组间差异均无统实计学意义；2、血清 TSH 平均值：与对照组相比 15 分钟组轻度增高、30、60 分组轻度降低（$P > 0.05$），120 分组明显降低（$p < 0.05$），实验组各组间差异均无统实计学意义；3、血清 TT4、FT4 平均值：未见明显变化；4、血清 TT3、FT3 平均值：15 分钟组轻度降低（$p > 0.05$），120 分钟明显降低（$p < 0.05$），实验组各组间差异均无统实计学意义；5、失血性休克后垂体 TSHβ mRNA 较对照组有降低趋势，但无统计学差异。

结论 急性失血性休克导致血清 TSH、T3 的降低；引起血清 TRH 的水平增加；对垂体 TSHβ mRNA 的表达无明显影响。

COR-79

颅咽管瘤神经内分泌功能分级与腺垂体生长激素储备功能评价和重建

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目的 分级评价颅咽管瘤患者占位效应解除后下丘脑 - 垂体 - 靶腺轴功能；评价颅咽管瘤患者占位效应解除后腺垂体生长激素储备功能，及生长激素缺乏对生长发育、内分泌代谢影响；评价颅咽管瘤生长激素缺乏患者在生长激素替代治疗期间的疗效与安全性。

方法 采用前瞻性横断面研究设计，收集 2012 年 2 月至 2015 年 12 月在我院内分泌科住院的颅咽管瘤患者。采集资料，以“颅咽管瘤神经内分泌功能缺陷诊断标准”分级评价上述患者的神经内分泌功能，证实为生长激素缺乏患者予生长激素替代治疗。

结果 收集患者 52 例，中位数年龄 25（17,43）岁，分为 4-17 岁和 18-65 岁两个年龄段。下丘脑 - 垂体 - 靶腺轴功能受损及功能分级评价结果发现 52 例患者均有不同程度的下丘脑功能受损，年龄段 4-17 岁的患者下丘脑功能受损较 18-65 岁年龄段明显；垂体 - 肾上腺轴、垂体 - 甲状腺轴功能受损最为显著，两年龄段无差异。所有 18-65 岁年龄段患者出现垂体 - 性腺轴功能受损，较 4-17 岁年龄段患者增多。神经内分泌功能分级为 2 级的患者占 75%，3 级次之，1 级较少，无 0 级患者。23 例进行 ITT 试验的患者各时间点 GH 均＜ 1ng/ml，提示 GH 绝对缺乏，其中 5 例接受 GH 替代治疗，其身高、体重、腰围治疗前后变化明显，有统计学意义；GH、IGF-1、IGFBP-3 替代后增加，TG、TC、LDL-C 替代后下降，肝功能异常、脂肪肝治疗后改善，随访期间未发现肿瘤复发。

结论 颅咽管瘤患者在占位消除后，其神经内分泌功能受损显著，儿童 / 青少年患者更严重。GH 缺乏患者行 GH 替代治疗后身高得到明显改善，安全性较好。

COR-80

青少年促皮质素依赖性库欣综合征的定位诊断特点

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目的 分析青少年促皮质素 (ACTH) 依赖性库欣综合征 (CS) 患者的临床特点和定位诊断。

方法 回顾性分析 35 例青少年 ACTH 依赖性库欣综合征患者的临床表现、实验室检查和定位诊断方法。

结果 其中 29 例库欣病，6 例异位 ACTH 综合征 (EAS)。和 EAS 患者相比，青少年库欣病患者来诊年龄更大

(15.2 ± 2.7Vs12.8 ± 4.4 岁)，病程更长 (1.9 ± 1.5Vs0.7 ± 0.3 年)，血钾更高 (3.8 ± 0.6Vs2.5 ± 0.7mmol/l)，血浆 ACTH 水平更低 (70.2 ± 67.9Vs193.1 ± 103.3 pg/ml)。采用地塞米松抑制试验 (DST) 服药后 24 小时 UFC 和服药前的比值作为切点，小剂量 DST 的临界值为 0.65，敏感性为 100%，特异性为 70.8%。大剂量 DST 的临界值为 0.54，敏感性为 100%，特异性为 91.7%。若以双侧岩下窦静脉取血 (BIPSS) 时血 ACTH 岩下静脉和外周静脉比值 2 为切点，仅 75% 的青少年库欣病患者符合。

结论　大剂量地塞米松抑制试验对青少年 ACTH 依赖性 CS 患者定位诊断意义较大。

COR-81

114 例垂体柄中断综合征临床分析

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目的　分析垂体柄中断综合征 (PSIS) 临床特征。

方法　回顾性分析了我科 2000 年 1 月至 2015 年 4 月以来收治的 114 例PSIS患者的病例资料，包括主诉、现病史、家族史、查体情况；内分泌功能评估，包括生长激素、性腺五项、皮质醇、促肾上腺皮质激素、游离甲状腺素、促甲状腺激素、胰岛素低血糖兴奋试验、GnRH 兴奋试验；垂体核磁共振检查特征。

结果　114 例患者，男性 102 例 (89.4%)，平均年龄 21.1 ± 6.1years。臀位生产率占 89.9%，身材矮小 89 例 (71.8%)，骨龄延迟 6.13 ± 5.14year，第二性征普遍发育不良。生长激素缺乏、性功能低下、肾上腺功能低下、甲状腺功能低下的比例分别是：100%、94%、84.2%、74.6%，高泌乳素血症比例为 28.1%。存在 3 种以上的垂体激素异常的患者 105 例 (92.1%)。53 例臀位生产患者与 5 例头位生产患者比较，身高、阴茎牵长、睾丸容积、垂体前叶高度、兴奋试验结果差异均无统计学意义 (P<0.05)。

结论　中国的 PSIS 患者的临床表现、症状、激素缺乏程度严重；出生方式不同的患者病情严重程度无显著差异。

COR-82

评价垂体柄中断综合征垂体柄形态变化对垂体前叶功能影响

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目的　比较垂体柄中断综合征患者中垂体柄形态学变化对垂体前叶激素缺乏程度的影响。

方法　对垂体柄中断综合征 (PSIS) 74 例患者，进行完整垂体前叶功能评估包括基础垂体及靶腺激素的测定和兴奋试验。分析垂体柄可见性与垂体前叶功能之间的关系。所有数据均采用 SPSS 19.0 统计学软件分析。

结果　74 名垂体柄中断综合征患者中，中位年龄为 25 (22-28) 岁。其中第二性征缺乏 (97.3%) 为最常见临床表现，其次为身材矮小。生长激素缺乏、性激素缺乏、肾上腺皮质激素缺乏、垂体性甲状腺功能低下的比例分别是 100%,97.2%、88.2% 和 70.3%。垂体柄可见组促黄体生成素 (LH)、促卵泡成熟素 (FSH)、清晨血皮质醇 (F)、24 小时尿游离皮质醇、游离三碘甲状腺原氨酸 (FT3) 及游离甲状腺素 (FT4) 明显高于垂体柄不可见组 (P<0.05)。两组患者分别行 GnRH 兴奋试验及 ITT 后发现，垂体柄可见组 LH、FSH 及血 F 兴奋程度明显优于垂体柄不可见组 (p<0.05)，但生长激素 (GH) 水平与垂体柄不可见组相似。

结论　垂体柄中断综合症的患者均存在一种或者几种激素分泌缺陷，推荐所有患者都应该进行垂体功能评估。垂体柄可见度可作为垂体柄中断综合征中激素水平缺乏严重程度分级指标。

EA-01

Sodium intake regulates glucose homeostasis through the PPAR δ /adiponectin-mediated SGLT2 pathway

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EA-02

NRF2 activation by antioxidant antidiabetic agents accelerates tumor metastasis

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EA-03

Altered peripheral B-lymphocyte subsets in Type 1 diabetes and latent autoimmune diabetes in adults

邓超

中南大学湘雅二医院

EA-04

Efficacy and safety of liraglutide versus sitagliptin, both in combination with metformin, in Chinese patients with type 2 diabetes: a 26-week, open-label, randomised,

active comparator clinical trial

臧丽
解放军总医院

EA-05

Diabetes and risk of arterial stiffness: a mendelian randomization analysis

徐敏
上海交通大学医学院附属瑞金医院

EA-06

Ameliorating endothelial mitochondrial dysfunction restores coronary function via transient receptor potential vanilloid 1-mediated protein kinase A/uncoupling protein 2 pathway

熊诗强
第三军医大学大坪医院

EA-07

GLP-1 receptor agonist promotes brown remodelling in mouse white adipose tissue through SIRT1

徐芬
广东中山大学附属第三医院

EA-08

Impaired pancreatic beta cell compensatory function is the main cause of type 2 diabetes in individuals with high genetic risk: a 9 year prospective cohort study in the Chinese population

严婧
上海第六人民医院

EA-09

Prolactin-stimulated survivin induction is required for beta cell mass expansion during pregnancy in mice

武晓泓
江苏省人民医院

EA-10

Characterization of relatively malignant form of osteopetrosis Ca used by a novel mutation in the PLEKHM1 gene

薄涛
山东省立医院

EA-11

The urinei odine to creatinine as an optimal index of iodine during pregnancy in an iodine adequate area in China

李晨嫣
中国医科大学附属第一医院

EA-12

Cardiovascular risk in early onset type 2 diabetes

高蕾丽
北京大学人民医院

壁报交流

CPO-001

硒蛋白 P 在高碘诱导自身免疫甲状腺炎小鼠甲状腺中的表达

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CPO-002

乌鲁木齐地区正常人群血清 TSH 参考区间的建立

王新玲 , 木尼拉 , 陈翔 , 徐子奇 , 郭艳英 , 艾合买提江 , 热孜万古丽 , 赵红丽

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CPO-003

新疆乌鲁木齐维汉族碘营养水平与甲状腺结节的相关研究

郭艳英 , 王慧丽 , 马福慧 , 王新玲 , 艾合买提江 , 木尼拉 , 热孜万古丽 , 赵红丽 , 邢淑清

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CPO-004

磁共振 T1 mapping 技术对甲减患者弥漫性心肌损伤的定量评估

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CPO-005

12 例原发于甲状腺淋巴瘤病例回顾及分析

张杨 , 高莹 , 袁振芳 , 高燕明 , 郭晓蕙

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CPO-006

先天性甲减致病基因的筛查及其遗传模式的研究

孙凤 , 宋怀东 , 赵双霞 , 张乐乐 , 苑菲菲 , 马誉铷

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CPO-007

慢性肾脏疾病和亚临床甲状腺功能减退之间的关系：一项病例对照研究

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CPO-008

5 例甲状腺功能亢进症合并烟雾病临床资料分析

刘晓钢 [1], 郑丽丽 [1], 马园园 [2], 吴雪 [2], 李珊 [1], 张丽侠 [1], 李冲 [1]

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CPO-009

抗甲状腺药物治疗导致粒细胞缺乏症 36 例患者临床资料分析

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CPO-010

从 TPOAb 阳性值探讨妊娠期甲状腺功能指标的正常值范围

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CPO-011

在甲功正常的非糖尿病人群中甲状腺激素水平与胰岛素抵抗关系的流行病学研究

谷晓岚 , 牛敏 , 高政南

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CPO-012

促甲状腺激素对心肌细胞 SERCA2a 表达影响的研究

董佳佳 , 田利民

甘肃省人民医院内分泌科

CPO-013

HOXC10 高表达促进甲状腺癌侵袭转移以及不良预后的作用研究

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CPO-014

TSH 通过激活 Akt 增加促动脉粥样硬化因子的表达

焉雨濛 , 姜凤伟 , 赖亚新 , 王浩宇 , 刘爱华 , 张媛媛 , 滕卫平 , 单忠艳

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CPO-015

组蛋白去乙酰化酶 SIRT7 在甲状腺癌发生发展中的作用及分子机制

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CPO-016

外周血甲状腺过氧化物酶 mRNA 与甲状腺乳头状癌转移风险的研究

蒋筠 , 顾丽萍 , 李娜 , 王育璠 , 吴艺捷 , 彭永德
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CPO-017

正常人群甲状腺功能与肾小球滤过率的关系探讨

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CPO-018

不孕症妇女甲状腺自身抗体阳性率调查

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CPO-019

自身免疫甲状腺炎患者抑郁与焦虑状态自我评定及特异相关危险因素分析

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CPO-020

中国指南对甲状腺结节手术患者诊治策略的影响

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CPO-021

肿瘤相关长链非编码 RNA 在甲状腺癌中的表达

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CPO-022

北京社区甲状腺炎合并脑病流行病学调查分析

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CPO-023

碘充足地区母体甲状腺球蛋白的妊娠期特异性改变

张晓文 [1], 李晨嫣 [1], 毛金媛 [1], 王薇薇 [1], 谢晓晨 [1], 彭诗乔 [1], 王肇君 [1], 韩成 [1], 张晓梅 [2], 王丹阳 [3], 范晨玲 [1], 单忠艳 [1], 滕卫平 [1]
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CPO-024

住院 2 型糖尿病患者合并甲状腺功能减退的临床特征、危险因素分析及筛查策略的研究

段妍 , 周翔海 , 罗樱樱 , 潘蓉 , 庞梦端 , 刘艳 , 高学营 , 纪立农
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CPO-025

亚临床甲状腺功能减退患者 T1 值升高与心肌损伤的相关性

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CPO-026

姜黄素诱导甲状腺乳头状癌 BCPAP 细胞发生内质网应激

包建东 , 俞惠新 , 张莉 , 程献 , 高岩岩
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CPO-027

甲状腺影像报告与数据系统（Thyroid Image Reporting and Date System，TI-RADS）联合甲状腺细胞病理学 Bethesda 报告系统（Bethesda system for reporting thyriod cytopathology，BSRTC）在诊断甲状腺结节中的应用价值

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CPO-028

甲状腺乳头状微小癌和直径介于 1-2cm 乳头状癌术后复发影响因素的比较

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CPO-029

中医药治疗甲状腺结节组方规律的研究

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CPO-030

ITM2A 介导环境和遗传相互作用促进 Graves 病的发生

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CPO-031

Graves 病合并高钙血症病例报告三例合并文献复习

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CPO-032

甲状腺乳头状癌患者必须接受甲状腺全切及淋巴结全清扫术吗？ ——一项关于甲状腺乳头状癌的预后评估及术式选择的队列临床随访研究

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CPO-033

妊娠期母体低 T4 血症通过抑制 mTOR 信号通路导致后代孤独症的发生

刘爱华，龚珣，肖悦，侯源源，王浩宇，周莹莹，项阳，单忠艳，滕卫平
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CPO-034

碘难治性远处转移分化型甲状腺癌临床分析

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CPO-035

甲状腺乳头状癌中 miR-21 和 miR-181b 的表达与 BRAFV600E 突变及临床病理特征之间的关系

杨光辉，车奎，余霄龙，王萍，王颜刚，侯旭，赵世华
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CPO-036

罕见基因突变引起的家族性白蛋白异常性高甲状腺素血症家系合并高遗传概率及高流产率

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CPO-037

TIRADS 分级与 2015ATA 指南超声分级在评估甲状腺结节中的比较

吴艺捷，刘馨，史秋生，金宇飚，赵立
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CPO-038

甲状腺激素不敏感综合征和原发性甲状旁腺功能减退症临床特点的比较分析

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CPO-039

儿童和青少年甲状旁腺功能亢进症

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CPO-040

糖尿病周围神经病变足底压力的研究

连晓芬，张帆，戴亚丽，林远，卢东辉，韩令川，谢谦，吴佩娴，张宁波
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CPO-041

99mTc-DTPA 肾动态显像及血清胱抑素 C 在糖尿病肾病早期诊断中的应用

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CPO-042

Atgl 基因敲除对 C57BL/6 小鼠肾脏结构和功能的影响及机制研究

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CPO-043

肝主疏泄 ----- 糖尿病假性急腹症从肝医治探讨

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CPO-044

2 型糖尿病患者肌少症与肾功之间的关系

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CPO-045

亚临床甲减与 2 型糖尿病患者颈动脉粥样硬化和糖尿病肾

脏病的相关性研究

许本洋
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CPO-046

高压氧联合黄芪对高糖下视网膜神经节细胞的保护作用

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CPO-047

2 型糖尿病患者认知功能和甲状腺激素水平的相关性分析

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CPO-048

丹红注射液联合常规疗法治疗糖尿病合并脑梗塞患者的临床疗效分析

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CPO-049

创面负压治疗对糖尿病足创面肉芽组织胶原蛋白沉积的影响

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CPO-050

GLP-1 受体激动剂对肥胖 2 型糖尿病体脂含量及其内脏脂肪面积的影响

徐静 , 郑宏庭 *, 王建 , 童强 , 王慧 , 乔巧 , 张瑞 , 白倩 , 黄陈
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CPO-051

SDF-1 通过 PI3K/Akt 和 MAPK/Erk 信号通路对人微血管内皮细胞系功能产生影响

高静 , 李新岩 , 王敏哲 , 邓琼 , 刘贯英 , 杨雪松
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CPO-052

新诊断 2 型糖尿病患者短期胰岛素强化治疗期间的低血糖分析

刘烈华 , 王良娇 , 柯伟健 , 李延兵
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CPO-053

LMNA 基因 D47Y 突变导致家族部分性脂肪萎缩性糖尿病一例

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CPO-054

延伸护理模式在 2 型糖尿病患者出院后的应用

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CPO-055

对 244 例糖尿病患者健康宣教的效果评价

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CPO-056

DPP-IV 抑制剂与甘精胰岛素联合治疗 2 型糖尿病的临床观察

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CPO-057

新型 CB1 受体拮抗剂 ZH-101-S 对糖尿病大鼠肾脏保护作用

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CPO-058

探讨糖尿病酮症酸中毒和高血糖高渗状态患者甲状腺功能的改变与病情的关系

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CPO-059

2 型糖尿病患者尿液胞外囊泡中 TGF-β 1 和 CD2AP 与糖尿

病肾脏病的相关性研究

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CPO-060

新疆维吾尔族 2 型糖尿病患者颈动脉内膜中层厚度与维生素 D 及血清胱抑素 C 水平的关系研究

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CPO-061

氧化型低密度脂蛋白对肝窦内皮细胞整合素 αvβ3 表达的影响及其机制

张琦, 刘静, 许衍甲, 王云芳, 牛瑞兰
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CPO-062

沉默信息调节因子 1 及其下游因子在糖尿病肾脏病变中的表达改变

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CPO-063

快速血酮检测仪检测血 β- 羟丁酸水平对住院糖尿病患者酮症的筛查价值

朱显军, 李蓬秋, 张学军, 鲜杨, 吴冀川, 包明晶, 杨艳, 张磊, 刘丽梅, 曹旭, 杨毅
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CPO-064

中国人胰岛素基因 -23A/T 变异与早发 2 型糖尿病发病相关

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CPO-065

利拉鲁肽在高糖环境下对体外培养的小鼠前成骨细胞 MC3T3-E1 增殖、分化的影响

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CPO-066

去泛素化酶 CYLD 对高糖诱导的肾系膜细胞 NF-KB 炎症信号的调控研究

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CPO-067

二甲双胍作用于 3T3-L1 前脂肪细胞诱导过程中对 v-SNAREs 蛋白家族表达的影响

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CPO-068

脐带间充质干细胞通过诱导 M2 型巨噬细胞改善 2 型糖尿病大鼠的非酒精性脂肪性肝病

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CPO-069

血糖控制不佳的 2 型糖尿病患者加用长效胰岛素或胰岛素增敏剂治疗血糖和肾脏功能变化的长期随访研究

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CPO-070

新疆克拉玛依社区居民慢性病调查分析

吴胜利, 朱玉婧, 黄丽娟, 谢成瑶, 谢爱霞
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CPO-071

GLP-1 受体激动剂 Exendin-4 通过 Sirt1/Foxo-1 信号通路上调 脂联素水平的研究

王安平, 李婷, 安平, 闫文华, 郑华, 母义明
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CPO-072

2 型糖尿病患者血清 miR-130b 水平与尿白蛋白排泄率的相关性研究

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CPO-073

血糖波动对 2 型糖尿病大鼠坐骨神经中神经生长因子及其受体表达的影响

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CPO-074

COPD 合并 2 型糖尿病患者应用糖皮质激素后使用实时动态血糖监测联合胰岛素泵强化控制血糖的研究

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CPO-075

Hsp90 通过内质网应激调控大鼠 INS-1E 细胞脂毒性的机制研究

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CPO-076

初发 2 型糖尿病合并高同型半胱氨酸血症患者的血管内皮功能及其影响因素分析

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CPO-077

SIRT1 在 ghrelin 抑制胰岛素分泌的通路中的作用

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CPO-078

中国前瞻性糖尿病研究 (China PDS) 3 个月随访结果

韩颖[1], 胡大清[2], 陈丽贤[3], 杨乃龙[4], 金晖[5], 侍晓云[6], 李全民[7], 梁琳琅[8], 季锋萍[9], 王斌辉[9], 母义明[10]
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CPO-079

SLCO1B3 基因与 2 型糖尿病患者磺脲类药物疗效之间关系的研究

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CPO-080

磷酸西格列汀和伏格列波糖分别联合二甲双胍及胰岛素对于新诊断 2 型糖尿病临床疗效的随访研究

史春虹 , 张茹 , 白然 , 刘丹 , 王咏波 , 张雪扬 , 王浩 , 杜建玲
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CPO-081

p38 细胞丝裂素活化蛋白激酶 - 内皮型一氧化氮合酶 - 一氧化氮信号通道在人脐静脉内皮细胞凋亡中的保护作用

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CPO-082

津力达颗粒降低血管紧张素 II 以及 Smad2/3 表达改善 1 型糖尿病大鼠肝损伤的机制研究

叶菲 , 刘子毓 , 陈海燕 , 陈向芳 , 刘志民
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CPO-083

16 例糖尿病合并夏科氏骨关节病临床特点分析

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CPO-084

胃袖状切除术通过维持 GLP-1r 通路活性及 L 细胞的分化来改善胰岛 β 细胞的功能

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CPO-085

胰岛素 1 相分泌在类固醇性糖尿病与 2 型糖尿病早期鉴别诊断的研究价值

张姣娇 , 蔡劲薇 , 梁杏欢 , 周嘉 , 李励 , 冼晶 , 黄振兴 , 李素妹 , 蒙丽恒 , 李世春 , 吴昱 , 秦映芬 *
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CPO-086

外周血管介入术对糖尿病足血管狭窄情况改善的疗效评估

张晓 , 郑宏庭 *, 童强 , 徐静 , 周永红 , 王渊
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CPO-087

DPP-4 抑制剂通过胰岛 γ 氨基丁酸影响 Bcl-2 级 Bax 蛋白的表达

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CPO-088

甘肃省兰州市 2 型糖尿病患者以及糖调节受损人群慢性肾脏疾病的患病状况调查

甄东户 , 关聪会 , 汤旭磊
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CPO-089

miR-375 在人胚胎干细胞定向分化为胰岛素分泌细胞过程中对肝细胞核因子 1β 表达的调控作用

杨进 , 魏蕊 , 王海宁 , 刘烨 , 侯文芳 , 高洪伟 , 洪天配
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CPO-090

氧化应激对糖尿病大鼠 Neuritin 水平和坐骨神经功能及超微结构的影响

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CPO-091

TCF7L2 基因多态性与新疆维吾尔族 2 型糖尿病关系的研究

刘浩 , 李惠
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CPO-092

SiRNA 干扰内质网应激 PERK/eIF2α 通路在糖尿病肾病中的作用及机制研究

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CPO-093

侧脑室注射 M35 对 2 型糖尿病大鼠心肌组织 GLUT4 表达的影响

张真稳 [1], 方彭华 [2], 史明仪 [2], 卜平 [2], 王艳 [1], 朱妍 [1]
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CPO-094

白介素—1β 基因 rs1143627-C/T 多态性与糖尿病周围神经病变的相关性

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CPO-095

mTOC1 参与 60% 胰腺切除诱导的 β 细胞代偿性增殖

李文毅 , 张宏利 , 聂爱芳 , 宁光 , 顾燕云 , 汪启迪
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CPO-096

角膜共焦显微镜检查可早期预测 2 型糖尿病周围神经病变

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CPO-097

2 型糖尿病肾病患者体内脂肪细胞因子与骨转换指标之间的相互关系

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CPO-098

IL-6 与 2 型糖尿病肾病密切相关：基于人群的横断面研究

王亚飞 , 胡祥 , 曾天舒 , 盛夏 , 张皎月 , 郑涓 , 陈璐璐
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CPO-099

心磷脂酰基转移酶 1 在糖尿病大鼠不同时期坐骨神经中的表达及意义

李亚坤 [1], 杨俊朋 [3,1], 陈慧晓 [1], 梁萌萌 [1], 张圆 [1], 赵志刚 [2]
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CPO-100

妊娠期糖尿病患者血糖波动特点及其与妊娠结局的相关性

分析

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CPO-101

Pluronic F-127 水凝胶三维培养糖尿病大鼠脂肪干细胞优化分化功能的相关研究

范丽君 , 沈洁 , 林凯桑 , 肖倩蓉 , 李晨钟 , 李章芳 , 韩亚娟
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CPO-102

2 型糖尿病合并脑梗死患者血清同型半胱氨酸等指标特点的分析

姜新 , 夏君 , 谢晓娜 , 王贺元 , 吕然然 , 高影
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CPO-103

USP22 在糖尿病肾病足细胞凋亡和炎症中的作用及机制研究

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CPO-104

糖尿病患者腰臀比与血糖控制及白蛋白尿的相关性研究

王正宜 [1,2], 丁琳 [1,2], 黄小琳 [1,2], 陈颖 [1,2], 孙琬琬 [1,2], 林琳 [1,2], 黄亚 [1,2], 王珀 [1,2], 彭魁 [1,2], 陆洁莉 [1,2], 陈宇红 [1,2], 徐敏 [1,2], 王卫庆 [1,2], 毕宇芳 [1,2], 徐瑜 [1,2], 宁光 [1,2]
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CPO-105

肽基辅氨酰异构酶 B 通过调节胰岛素原折叠对抗内质网应激诱导的 MIN6 细胞凋亡

韦晓 [1], 朱丹 [2], 陈国芳 [1], 曹萌 [1], 茅晓东 [1], 李兴佳 [1], 陈煜 [1], 徐一娇 [1], 杨婉薇 [1], 汪奇峰 [1], 刘超 [1]
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CPO-106

Dab2 在醛固酮腺瘤中表达及病理意义

李平 , 马建强 , 张敏 , 刘光香 , 赵晓智 , 沈山梅 , 朱大龙
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CPO-107

新发现的血管紧张素 II 和胰岛素 / 胰岛素样生长因子 1 的交互作用：协同激活肾上腺皮质 H295 细胞的 ERK1/2 通路

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CPO-108

中国原发性醛固酮增多症患者中三个确诊试验诊断价值的比较

宋颖 , 何文雯 , 杨淑敏 , 程庆丰 , 胡金波 , 甄乾娜 , 李启富
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CPO-109

午夜 1mg 地塞米松抑制试验对肾上腺意外瘤中

李乐乐 , 韩白玉 , 窦京涛 , 杨国庆 , 谷伟军 , 吕朝晖 , 母义明
解放军总医院内分泌科

CPO-110

基因表达谱分析揭示 ERBB2 过表达在嗜铬细胞瘤发病机制中的作用

齐研 [1], 苏颋为 [1], 张霞 [1], 蒋怡然 [1], 袁文祺 [1], 王卫庆 [1], 崔斌 [1,2], 宁光 [1,2]
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CPO-111

多发性内分泌腺瘤病 1 型家系研究

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CPO-112

中国首例 Klinefelter 综合征合并 17α 羟化酶缺陷症病例的诊治

王臻 [1,2,3], 盛志峰 [1,2,3], 刘石平 [1,2,3], 周智广 [1,2,3], 戴如春 [1,2,3]
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CPO-113

15 例 17 羟化酶缺陷症患者临床特点及基因突变研究

韩兵 [1], 范梦夏 [1], 朱惠 [1], 程彤 [1], 朱文娇 [1], 陆颖理 [1], 刘阳 [2], 乔洁 [1]
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CPO-114
应用目标序列捕获测序技术筛查 46, XY 性分化异常疾病的致病基因

刘兆祥 , 茅江峰 , 伍学焱 , 聂敏 , 王曦 , 郑俊杰
中国医学科学院北京协和医学院北京协和医院内分泌科

CPO-115
雄激素不敏感综合征及类固醇 5 α - 还原酶 2 缺乏症的基因突变分析

崔铭萱 , 聂敏 , 茅江峰 , 王曦 , 刘兆祥 , 郑俊杰 , 伍学焱
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CPO-116
地塞米松抑制试验中血尿皮质醇对库欣综合征诊断价值的比较

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CPO-117
6 例 Noonan 综合征患者临床特点及 rhGH 治疗效果分析

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CPO-118
一垂体柄阻断综合征家系基因筛查及文献综述

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山东大学附属省立医院

CPO-119
重组人生长激素对垂体柄中断综合征合并矮身材患者的治疗作用 一项针对 75 例中国患者的回顾性研究

王成芷 , 郭玲玲 , 韩白玉 , 王安平 , 刘红艳 , 苏星 , 郭清华 , 母义明
解放军总医院

CPO-120
垂体柄中断综合征与前动力蛋白受体 2 和前动力蛋白 2 基因突变的相关性分析

韩白玉 [1,2], 李乐乐 [1], 王成芷 [1], 郭清华 [1], 吕朝晖 [1], 母义明 [1], 窦京涛 [1]
1. 解放军总医院内分泌科
2. 解放军 264 医院内分泌科

CPO-121
SSAs 在不具手术适应症的 TSH 瘤患者中的临床应用

沈如飞 , 郑宏庭 *, 段炼 , 田永峰
第三军医大学新桥医院内分泌科

CPO-122
经蝶术后生化未缓解库欣病患者的临诊应对

沈如飞 , 郑宏庭 *, 段炼 , 田永峰
第三军医大学新桥医院内分泌科

CPO-123
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张豫文 [1], 孙首悦 [1], 陈宇红 [1], 贾慧英 [1], 齐研 [1], 郁忠勤 [1], 王卫庆 [2], 宁光 [2]
1. 上海交通大学医学院附属瑞金医院北院内分泌科
2. 上海交通大学医学院附属瑞金医院内分泌科

CPO-124
非酒精性脂肪肝患者肝组织中 irisin 的表达及意义

马圆圆 [1,2], 吴雪 [1,2], 刘晓钢 [1], 张丽侠 [1], 李姗 [1], 王亭亭 [1], 王志芳 [1], 李冲 [1], 李静怡 [1], 韩超 [1], 李付广 [3], 郑丽丽 [1]
1. 郑州大学第一附属医院内分泌与代谢科
2. 河南省高等学校临床医学重点开放实验室
3. 郑州大学基础医学院免疫教研室

CPO-125
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孙英凯 [1], 王计秋 [1], 陈茂培 [1], 柯颖颖 [2], 赵少倩 [1], 刘文 [1], 马勤云 [1], 石娟 [1], 邹曜宇 [3], 宁廷鲁 [3], 张志国 [1], 洪洁 [1], 刘瑞欣 [1], 宁光 [1]
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CPO-126
肝脏中 Cyp17a1 基因调控糖异生的作用和机制

章志建 , 林毅 , 徐浣白 , 顾鸣宇 , 彭永德
上海市第一人民医院

CPO-127

Gitelman 综合征伴胰岛素抵抗一例

于菁，李静，都镇先，王晓黎，王秋月，单忠艳

中国医科大学附属第一医院

CPO-128

脂肪间充质干细胞诱导 M2 型巨噬细胞以促进白色脂肪棕色化并发挥减肥效应

谢宗燕[1,3]，郝好杰[2]，张琪[1,3]，程愈[1]，刘杰杰[2]，韩为东[2]，母义明[1]

1. 解放军总医院内分泌科

2. 解放军总医院分子生物室

3. 南开大学医学院

CPO-129

apelin 通过激活 PI3K-PDE3B 途径抑制胰岛细胞胰岛素分泌

郭琳，李强

哈医大二院

CPO-130

男性高尿酸血症对肾功能正常的肾脏损伤指标研究及降尿酸治疗的影响

龚淑兰，伦语，马晓龙，车奎，迟静薇，陈颖，侯旭，王颜刚

青岛大学附属医院内分泌与代谢病科

CPO-131

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李星[1]，张卫欢[2]，杨丽华[1]，姜勇[1]，李民[1]，王远征[1]，袁振芳[1]，郭晓蕙[1]

1. 北京大学第一医院

2. 开滦总医院

CPO-132

褪黑素改善黑棘皮病合并肥胖患者的胰岛素抵抗及皮肤症状

孙航，宋科秀，陈佳奇，王兴纯，曲伸

同济大学附属上海第十人民医院

CPO-133

血清维生素 D 水平与非酒精性脂肪肝患病风险和肝脏脂肪含量关系的研究—上海长风研究

林寰东，王丹，夏明锋，齐齐格，李小明，马慧，高鑫

复旦大学附属中山医院

CPO-134

肥胖与体重正常女性皮下脂肪组织差异 microRNA 的分析

龚凤英，尚晨，朱惠娟，潘慧，王淳邻，李乃适，王林杰，阳洪波

中国医学科学院，北京协和医学院，北京协和医院内分泌科，卫计委内分泌重点实验室

CPO-135

中国华东地区成年人群血铅水平与 NAFLD 相关性研究

陈驰，翟华玲，王宁荐，陆颖理

上海市第九人民医院

CPO-136

2 型糖尿病人群中 TRIB3 基因 Q84R 功能性多态位点与非酒精性脂肪性肝病发生风险的关联研究

张伟伟，钮忆欣，杨震，李晓永，张洪梅，祝凌妃，方文军，秦利，苏青

上海交通大学医学院附属新华医院内分泌科

CPO-137

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张念荣[1,2]，刘杰[3]，江宇[4]，王林杰[5]，阳洪波[5]，潘慧[5]，朱惠娟[5]，王波[4]，王艳红[4]，尤莉莉[4]，李文歌[2]，李乃适[5]

1. 北京协和医学院

2. 中日友好医院肾内科

3. 中国人民解放军总医院解放军医学院

CPO-138

MicroRNA-124 调控肝脏甘油三酯代谢的功能与机制研究

刘醒[1]，李小英[2]

1. 上海交通大学医学院附属瑞金医院内分泌代谢病临床医学中心

2. 复旦大学附属中山医院内分泌代谢病科

CPO-139

糖代谢异常患者肝脏病理特征

卞华，常薪霞，颜红梅，夏明锋，朱小鹏，高鑫

复旦大学附属中山医院

CPO-140

血清铁蛋白与非酒精性脂肪性肝病的相关性研究

叶艳，田浩明

四川大学华西医院内分泌及代谢病科

CPO-141
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王小春
新疆医科大学第一附属医院

CPO-142
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王倩倩 , 肖元元 , 祝超瑜 , 魏燕燕 , 李旭 , 韩峻峰 , 魏丽 , 贾伟平
上海交通大学附属第六人民医院

CPO-143
胰岛素抵抗和单硝酸异山梨酯对 SHR 心肌细胞凋亡的影响
白冰 [1], 葛龙菲 [2], 田晨光 [1]
1. 郑州大学第二附属医院
2. 郑州市第一人民医院

CPO-144
“安生疗法”治疗代谢综合症 60 例临床观察
苏国盈 , 陈国宁 , 王晓红 , 王继华
无锡安国医院

CPO-145
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周静 , 曾天舒
华中科技大学同济医学院附属协和医院内分泌科

CPO-146
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王雨 , 林志健 , 蔡萌 , 白云飞 , 赵天宇 , 李凡 , 周伟龙 , 张冰
北京中医药大学中药学院

CPO-147
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李园园 [1,2], 于泳 [3], 王菲 [4], 徐潮 [1,2], 张海清 [1,2], 赵萌 [1,2], 刘璐 [1,2], 高聆 [1,2], 赵家军 [1,2]
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3. 山东大学附属省立医院超声科

CPO-148
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田茗源 [1], 李伶 [2], 杨刚毅 [1]
1. 重庆医科大学附属第二医院内分泌与代谢病科
2. 重庆医科大学检验医学院，临床检验诊断学教育部重点实验室

CPO-149
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王伟 [1], 齐燕飞 [2,2]
1. 复旦大学附属中山医院
2. 澳大利亚悉尼大学

CPO-150
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霍晶晶 , 王丽 , 于世家
辽宁中医药大学附属医院 内分泌科

CPO-151
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林忆阳 [1], 林梅芳 [2], 叶洪江 [1], 徐向进 [1]
1. 南京军区福州总医院内分泌科
2. 福建医科大学福总临床医学院

CPO-152
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熊雪莲 [1], 陆炎 [2], 赵洁结 [3], 高鑫 [1], 李小英 [1]
1. 复旦大学附属中山医院内分泌科
2. 复旦大学附属中山医院
3. 上海交通大学医学院附属瑞金医院

CPO-153
代谢综合征患者血清 glypican-4 水平及与其危险因素个数的相关性研究
吴芸秀 , 陈燕娟 , 陈立曙 , 杨毅华
广东省汕头市汕头大学医学院第二附属医院

CPO-154
原发性骨质疏松症血清尿酸水平与骨密度、骨转换
陈琳 , 游利 , 陈瑾瑜 , 潘凌 , 彭永德
上海交通大学附属第一人民医院内分泌代谢科

CPO-155

中国人群中血清铁蛋白水平与代谢综合征和胰岛素抵抗关系研究

陈玲[1], 李玉凤[2], 张放[1], 张思敏[1], 周翔海[1], 纪立农[1]
1. 北京大学人民医院
2. 北京平谷医院

CPO-156

我国脂肪肝等肝病高发的代谢成因与根本防治探讨

郑荣领
首都医科大学附属北京佑安医院 北京市肝病研究所

CPO-157

益气利湿中药对高尿酸血症大鼠肾组织 TGF-B1mRNA 表达影响的实验研究

王丽 , 于世家 , 霍晶晶
辽宁中医药大学附属医院

CPO-158

妊娠期代谢相关性疾病对母儿预后的影响分析

陈芃 , 秦迁 , 王姣 , 王守俊
郑州大学第一附属医院

CPO-159

高龄老年女性骨质疏松患者（≥80 岁）骨代谢特点及使用双膦酸盐的疗效

谷文莎 , 游利
上海交通大学附属第一人民医院内分泌代谢科

CPO-160

甘肃省绝经后女性及老年男性骨质疏松流行现况调查

杨睿斐 , 邵菲菲 , 马雯娟 , 田利民
甘肃省人民医院内分泌科

CPO-161

二甲双胍对成骨细胞功能蛋白表达的影响及其与 PPARγ 的关系

龚姣 , 严孙杰（通讯作者）
福建医科大学附属第一医院

CPO-162

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周映辉 , 张燕 , 郭玥 , 周后德 , 伍西雨 , 袁凌青 , 谢忠建 , 盛志峰
中南大学湘雅二医院

CPO-163

健康青少年人群骨代谢相关指标的特点及参考范围

李尤佳 , 赵晓伟 , 关海霞
中国医科大学附属第一医院内分泌科内分泌研究所

CPO-164

同型半胱氨酸对骨髓间充质干细胞成骨及成脂分化功能的影响

马芳芳 , 冯燕陵 , 姜晓彤 , 汤旭磊
兰州大学第一医院

CPO-165

中国人群中 Wnt1 基因突变所致成骨不全症的家系研究

刘怡 , 吕芳 , 徐晓杰 , 王建一 , 宋玉文 , 姜艳 , 王鸥 , 夏维波 , 邢小平 , 李梅
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CPO-166

肿瘤性骨软化症手术切除肿瘤与药物治疗对骨密度影响的比较

冯娟[1,2], 姜艳[1], 夏维波[1], 王鸥[1], 李梅[1], 邢小平[1], 孟迅吾[1]
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2. 中国医学科学院北京协和医学院

CPO-167

Suppression of plasma free fatty acids reduces myocardial lipid content and systolic function in type 2 diabetes.

xia guo, huanqi ge, hui zheng
Teda International Cardiovascular Hospital

CPO-168

Clinical characteristics of Cardiac structure and function in patients with hypertensive diabetes mellitus

meibiao zhang, shuibing Yang, jingjin Yang
The First People's Hospital of Huaihua, Hunan

CPO-169

A cross-sectional study for prevalence of osteoporosis of postmenopausal women and older men: a study in Gansu province, northwestern of China

Ruifei Yang, Feifei Shao, Wenjuan Ma, Limin Tian
Gansu Provincial Hospital

CPO-170

GLP-1 contributes to increases in PGC-1α expression by downregulating miR-23a to reduce apoptosis

chi wang, qiang li, wei wang, lin guo, chang guo, yiqiong sun, jinchao zhang
The Second Affiliated Hospital of Harbin Medical University

CPO-171

Serum Metabolite Signatures of cardiovascular diseases in prediabetes with hypertension

Wenxin Tong[1], Qiaoling Yang[2], Li Yang[2], Jingyan Tian[1]
1. RuiJin Hospital, Shanghai Jiao Tong University School of Medicine
2. The MOE Key Laboratory for Standardization of Chinese Medicines, Shanghai University of Traditional Chinese Medicine

CPO-172

Immunohistochemical expression of somatostatin receptor subtypes 2 and 5 in TSH-secreting pituitary adenomas from a consecutive case series of pituitary adenomas

Hongjuan FANG, Liyong ZHONG
Department of Endocrinology, Beijing Tiantan Hospital, Capital Medical University

CPO-173

1,25(OH)2D3 Improves Cardiac Dysfunction, Hypertrophy and Fibrosis through PARP1/SIRT1/mTOR Dependent Mechanisms in Type 1 Diabetes

Hua Qu, Huacong Deng
the First Affiliated Hospital of Chongqing Medical University

CPO-174

Combined Therapy of GABA and GLP-1 Prevents the Onset of Diabetes by Promoting β-Cell Regeneration in Mice

Wenjuan Liu[1,2], Wan Yun[1], Jiang Dongdong[1], Cui Qiaoli[1], Wang Zhihong[1], Prud'homme Gerald[2], Liu Rui[1], Wang Qinghua[1,2]
1. Division of Endocrinology and Metabolism, Huashan Hospital, Fudan University, Shanghai, China
2. Division of Endocrinology and Metabolism, St. Michael's hospital, University of Toronto, M5B 1W8

CPO-175

The Proinflammatory Cytokine High-Mobility Group Box-1 Mediates Peripheral Neuropathy In Diabetes Rats

Min Shi, Juan Chen, Xiangcheng Zhang, Ridong Zhang, Jingjing Ma, Hong Zhang
Huai'an First People's Hospital, Nanjing Medical University

CPO-176

Insulin downregulates the transcriptional coregulator CITED2, an inhibitor of proangiogenic function in endothelial cells

Xuanchun Wang[1], Thomas Rathjen[2], Samuel Lockhart[3,2], Ditte Sørensen[4,2], Brian ONeill[2], Nishant Dwivedi[2], Simone Rørdam-Preil[4], Hans Beck[4], Lars Rasmussen[4], Christian Rask-Madsen[2]
1. Huashan Hospital, Fudan University, Shanghai, China
2. Joslin Diabetes Center, Harvard Medical School, Boston, MA, United States
3. Queen's University Belfast, Belfast, United Kingdom

CPO-177

Ectopic Cushing's Syndrome due to Multiple Retroperitoneal Paragangliomas

Yan Xie
Qilu Hospital of Shandong University

CSE美敦力
“全权由我”早餐卫星会

时间： 2016年9月1日 7:30–8:15
地点： 北京国家会议中心 311A
主席： **母义明　教授** (中国人民解放军总医院)

时　间	内　容	讲　者
7:30–8:15	全院血糖管理的实战经验分享	**姬秋和　教授** 西安第四军医大学西京医院

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诺和诺德卫星会

会议时间：9月1日 07:30–08:15

会议地点：三层 311B

大会主席：潘长玉 教授　中国人民解放军总医院

题　　目：餐后新论 — 重视日常危害 提升博弈策略

讲　　者：李全民 教授 中国人民解放军火箭军总医院

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诺和诺德

诺和诺德卫星会

会议时间：9月1日 12:00–12:45

会议地点：一层 多功能厅A Function Hall A

大会主席：洪天配 教授　北京大学第三医院

题　　目：2型糖尿病合并腹型肥胖的综合管理

讲　　者：彭永德 教授 上海交通大学附属第一人民医院

甘李

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您好，感谢您一直以来对甘李药业的关注与支持！

甘李药业是国内唯一一家专注于胰岛素类似物研发及生产的高科技制药公司，长期以来致力于携手医生寻找更好的内分泌疾病治疗方案，为患者提供最优秀的药品和服务，改善患者的生活品质。现有的胰岛素类似物产品涵盖了基础、餐时、预混所有种类。甘精胰岛素——长秀霖®及赖脯胰岛素——速秀霖®上市以来，得到了广大医生及患者的认可。2014年，甘李药业又上市了国内第一支预混胰岛素类似物——速秀霖®25。

如何建立不同类型胰岛素在糖尿病治疗中的地位，在合适的患者中发挥更大的价值，在此，我们诚挚邀请您参加CSE甘李药业卫星会，让我们共同关注糖尿病患者，携手发展糖尿病诊疗事业，您的积极参会和分享将给到大家更多收获。期待您拨冗莅临。

时间：2016年9月1日12:00-12:45

地点：北京国家会议中心　309A

会议日程：

12:00--12:05	主席致辞	邢小平教授　杨涛教授
12:05--12:20	甘李药业产品海外注册进展汇报	吴见青博士(甘李公司研发部)
12:20--12:35	同类胰岛素类似物药效学比较研究	马建华教授
12:35--12:45	会议总结	邢小平教授　杨涛教授

甘李药业股份有限公司

2016年8月

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DPP-4抑制剂
——从过去到未来

捷诺维® 捷诺达® 专题会

9月1日 中午12:00-12:40

北京国家会议中心309B

主席：宁光 院士　赵家军 教授

讲题1——回顾篇

从指南到临床看DPP-4抑制剂的疗效和安全性

邀请讲者：陈璐璐教授

讲题2——展望篇

从中国2型糖尿病患者达标所面临的挑战看西格列汀固定复方制剂的临床应用前景

邀请讲者：王卫庆教授

08-2018-DIAB-1180714-0014

赛诺菲 糖尿病

共同 超越 期望

赛诺菲中国糖尿病事业部

邀请函
INVITATION
2016赛诺菲卫星会

尊敬的嘉宾：

作为糖尿病大国，中国糖尿病领域的不断进步，关乎着千万中国患者的福祉。借助第十七届内分泌大会暨中华医学会第15次全国内分泌学术大会的高端平台，我们将于2016年9月1日12:00-13:35于310室举办来得时/亚莫利卫星会。

本次卫星会特别邀请多位资深教授担任嘉宾讲者，与各位与会者共同分享、探讨糖尿病领域前沿学术成果，我们诚挚地邀请您莅临本次会议，与众多同仁一起交流心得，分享经验。您的莅临将是我们的莫大荣幸！

来得时卫星会

时间：9月1日 12:00-12:45
地点：310室

时间	讲题	讲者
12:00-12:05	开场致词	翁建平
12:05-12:15	承诺 挑战 希翼---从质量改善探寻糖尿病防控出路	翁建平
12:15-12:40	千里之行，始于足下---糖尿病管理的质量改善	李启富
12:40-12:45	讨论与总结	全体

亚莫利卫星会

时间：9月1日 12:50-13:35
地点：310室

时间	讲题	讲者
12:50-12:55	开场致词	陈璐璐
12:55-13:25	磺脲类药物安全性的综合评价	贾京涛
13:25-13:30	讨论	全体
13:30-13:35	总结	陈璐璐

DongBaoDiabetes
东宝糖尿病

第十七届国际内分泌大会
暨中华医学会第十五次全国内分泌学术大会
东宝糖尿病卫星会

胰岛素注射技术现状及新进展

2016年**9**月**1**日　12:00–12:45

北京国家会议中心 **311A**

主席：**纪立农** 教授　北京大学人民医院

讲者：**郭晓蕙** 教授　北京大学第一医院

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欢迎参加
默克午餐卫星会

会议时间： 9月1日12:00-12:45

会议地点： 311B

演讲嘉宾：

母义明教授
解放军总医院

郭立新教授
卫生部北京医院

演讲主题：

- 相得“胰”彰，全程获益
  ——二甲双胍联合胰岛素之证据与策略
- 米格列奈:关注病理核心，实施精确治疗

MERCK

礼来卫星会

尊敬的老师：

欢迎参加礼来卫星会，此次会议的话题围绕“中西方糖尿病治疗的差异”展开，并有2016年最新发布的RCT研究结果公布，相信此次会议会为您带来更多治疗策略上的思考，期待您的出席及精彩互动。

会议时间：9月1日12:00-12:50　会议地点：国家会议中心 306会议室

时间	主题	讲者
12:00-12:05	开场	高　鑫 教授、严　励 教授
12:05-12:25	糖尿病治疗的东西方差异	窦京涛 教授
12:25-12:45	CLASSIFY研究最新介绍——糖尿病临床问题的解析	杨文英 教授
12:45-12:50	问答环节	高　鑫 教授、严　励 教授

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尊敬的_____医师：

您好！

感谢您一直以来对拜耳公司的关心与支持！我们诚挚邀请您参加第十七届国际内分泌大会暨中华医学会第十五次全国内分泌学学术会议拜耳卫星会，期待您的莅临。

拜耳医药保健有限公司

2016年08月

会议日程

会议时间：9月1日 12:00-12:45

会议地点：北京国家会议中心307会议室

会议主席：潘长玉 教授

时 间	内 容	讲 者
12:00-12:05	会议主席致辞	潘长玉 教授
12:05-12:25	审视不同时代心血管结局相关研究所带来的启示	杨文英 教授
12:25-12:45	东西方差异之量体裁衣式2型糖尿病管理	朱大龙 教授

每一顿餐后的关爱都关乎健康的未来

TIME

诺和诺德卫星会

会 议 时 间：9月2日 12:00-12:45

会 议 地 点：一层 多功能厅A Function Hall A

大会主席：王卫庆 教授　上海交通大学医学院附属瑞金医院

题　　目：中国T2DM的血糖管理决策——透过现象看本质

讲　　者：郭晓蕙 教授 北京大学第一医院

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2016 第十七届国际内分泌大会
暨中华医学会第十五次全国内分泌学术大会

欧唐宁®卫星会

会议时间：2016年9月2日 12:00-12:50

会议地点：北京国家会议中心 三楼 报告厅

大会主席：洪天配 教授　王卫庆 教授　　大会讲者：陈璐璐 教授　赵志刚 教授

12:00-12:05	开场致辞	洪天配 教授 北京大学第三医院 王卫庆 教授 上海交通大学附属瑞金医院
12:05-12:25	从AACE ACE指南看利格列汀的全程守护轻松管控	陈璐璐 教授 华中科技大学同济医学院协和医院
12:25-12:45	独特创新——从作用机制与代谢排泄看利格列汀的临床价值	赵志刚 教授 首都医科大学附属北京天坛医院
12:45-12:50	会议总结	洪天配 教授 北京大学第三医院 王卫庆 教授 上海交通大学附属瑞金医院

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诺华卫星会

热点争鸣，全“心”出发

时间:9月2日12:50-13:35　地点:309B会议室

主席

母义明 教授

主任医师，教授，博士生导师
解放军总医院内分泌科主任
中华医学会内分泌学主任委员
中国医师协会内分泌代谢分会副会长
北京市糖尿病专业委员会前任主任委员
《中华内分泌代谢杂志》副总编
《中国前沿医学杂志》副主编

朱大龙 教授

医学博士、教授、博士生导师
二级主任医师，享受国务院津贴
南京鼓楼医院内分泌科行政主任兼大内科主任
中华医学会糖尿病分会候任主任委员
江苏省糖尿病学分会名誉主任委员
江苏省内分泌学会副主任委员
江苏省内分泌代谢疾病重点学科及南京市内分泌代谢疾病临床医学中心学科带头人

讲者

《DPP4抑制剂的“心”选择——全面、平稳、安全》

陈璐璐 教授　武汉协和医院

《肾素-血管紧张素系统与代谢疾病》

严晓伟 教授　北京协和医院

精彩活动　期待参与

诺华卫星会

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有机会获得彭永德教授主编的
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诺华卫星会

新“瑞”绽放，精彩全程

时间:9月2日12:00–12:50　地点:309B会议室

主席

宁光 院士

中国工程院院士，教育部长江特聘教授
973首席科学家，上海交通大学博士生导师上海交通大学医学院附属瑞金医院副院长
卫生部内分泌代谢病重点实验室主任
国家代谢性疾病临床医学研究中心主任
上海市内分泌代谢病研究所所长和上海市内分泌肿瘤重点实验室主任

赵家军 教授

医学博士、主任医师、教授
博士生导师，泰山学者
山东省立医院内分泌科
山东省临床医学研究院内分泌代谢研究所所长
中华医学会内分泌分会侯任主任委员
山东省糖尿病分会主任委员

讲者

《宜合瑞®(二甲双胍/维格列汀单片复方制剂)在2型糖尿病管理中的应用》

彭永德 教授　上海市第一人民医院

《佳维乐--循征证据指导下的全程治疗伙伴》

曾龙驿 教授　中山大学附属第三医院

精彩活动　期待参与

诺华卫星会

参加诺华卫星会
有机会获得母义明教授主编的
《实用临床内分泌诊疗手册》
限量350本

诺华小讲堂

参加诺华展台2场小讲堂
有机会获得彭永德教授主编的
《常见甲状腺疾病使用手册》
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INVITATION

互联网慢病管理困境与未来走势

医云健康将于中华医学会内分泌年会第十五次全国学术会议期间召开卫星会议

会议主持
纪立农教授、朱大龙教授

会议内容

- **互联网慢病管理的困境与出路**
  (母义明教授 12:00-12:20)
- **医云健康在慢病管理中的探索**
  (李启富教授 12:20-12:40)

医云健康愿与各界朋友携手合作,共同发展。
诚挚欢迎各界朋友前来医云健康展位-101参观交流。

时间: 2016年9月2日 12:00-12:45
地点: 北京国家会议中心 310 会议室

Cloudoc
医云健康

DongBaoDiabetes
东宝糖尿病

第十七届国际内分泌大会
暨中华医学会第十五次全国内分泌学术大会
东宝糖尿病卫星会

2016年**9**月**2**日　12:00-12:45

北京国家会议中心 **311A**

主席：**朱大龙** 教授　南京鼓楼医院

互联网形式下糖尿病宣教与患者管理新模式

讲者：**陈　蓉** 经理　通化东宝药业股份有限公司

基于人文关怀的优质医疗服务与糖尿病特殊患者管理

讲者：**王　砚** 教授　云南省第一人民医院

导升明® DOXIUM

欢迎参加默克导升明®卫星会

会议时间： 9月2日 12:00 – 12:45

会议地点： 311B

会议主席： 单忠艳教授 中国医科大学附属第一医院内分泌科

演讲嘉宾： 张新媛教授 北京同仁医院眼科

演讲主题： 导升明®—糖尿病视网膜病变（DR）管理新视角

糖尿病视网膜病变
防“黑”需“早”行动

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口服胰岛素胶囊

第一个被FDA证实可以口服的胰岛素

天麦生物午餐卫星会邀请函

时间：2016年9月2日12:00-13:00

地点：3楼307会议室

主席：著名内分泌领域专家 宁光 教授

讲者：Dr.Miriam Kidron（以色列）& 伊秀林 博士

翻译：叶蕾 副教授

主题：口服胰岛素胶囊FDA II期B临床试验结果 & 口服胰岛素动物实验结果

时间	内容	讲者	单位
12:00-12:05	开场致辞	宁　光 教授	上海瑞金医院
12:05-12:40	口服胰岛素胶囊FDA II期B临床试验结果	Dr.Miriam Kidron 翻译：叶蕾 副教授	Oramed（以色列） 上海瑞金医院
12:40-12:50	口服胰岛素动物实验结果	伊秀林 博士	天津药物研究院
12:50-13:00	总结，散会	宁　光 教授	上海瑞金医院

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对于合适的2型糖尿病患者：

强效降糖 捷出达标

简明处方资料

警告：乳酸性酸中毒
关于完整的黑框警告请详见说明书【注意事项】部分。
1. 乳酸性酸中毒是一种罕见但严重的并发症，可以在本品治疗过程中由于二甲双胍的蓄积而发生。在败血症、脱水、过度饮酒、肝功能受损、肾功能不全和急性充血性心力衰竭等情况下，发生风险增加。
2. 发作时仅伴有非特异性症状，包括全身不适、肌痛、呼吸困难、嗜睡加重和非特异性腹部不适。实验室检查异常包括pH 值下降、阴离子间隙增高和血乳酸水平升高。
3. 一旦怀疑酸中毒，应让患者立即停用本品并住院治疗。

【规格】
西格列汀二甲双胍片（50mg/500mg）：
每片含磷酸西格列汀50mg（以西格列汀计）和盐酸二甲双胍500mg。
西格列汀二甲双胍片（50mg/850mg）：
每片含磷酸西格列汀50mg（以西格列汀计）和盐酸二甲双胍850mg。
【适应症】
本品配合饮食和运动治疗，用于经二甲双胍单药治疗血糖仍控制不佳或正在接受二者联合治疗的2 型糖尿病患者。
【禁忌】
肾病或肾功能异常。已知对磷酸西格列汀、盐酸二甲双胍或本品的任何其它成分过敏。急性或慢性代谢性酸中毒，包括糖尿病酮症酸中毒在内，无论是否伴有昏迷。对于接受影像学检查需要血管内注射含碘造影剂的患者，应暂时停止本品治疗，因为这类造影剂可能造成急性肾功能改变。

【用法用量】
根据患者目前的治疗方案来决定本品的初始剂量。每日服药两次，餐中服药。可供选择的药物剂量有：
50mg西格列汀/500mg盐酸二甲双胍
50mg西格列汀/850mg盐酸二甲双胍
【不良反应】
西格列汀二甲双胍复方制剂中各活性成分的不良反应
西格列汀的已知不良反应
在西格列汀单药治疗的患者中发生率≥5%且比接受安慰剂患者更常见的不良事件（不考虑研究者对因果关系的评估）是鼻咽炎。
二甲双胍的已知不良反应
开始二甲双胍治疗后最常见（>5%）的已确定不良反应是腹泻、恶心/呕吐、胃肠胀气、腹部不适、消化不良、衰弱和头痛。其他少见者为大便异常、低血糖、肌痛、头晕、指甲异常、皮疹。出汗增加、味觉异常、胸部不适、寒战、潮感样症状、潮热、心悸、体重减轻等。二甲双胍可减少维生素B12吸收，但极少引起贫血。本品在治疗剂量范围内，引起乳酸性中毒罕见。
低血糖
当磷酸西格列汀和二甲双胍联用与磺酰脲类或胰岛素同时给药时，报告至少一次低血糖不良反应的患者百分比高于安慰剂和二甲双胍与磺酰脲类或胰岛素同时给药观察到的百分比。
上市后经验
在本品或其成分之一西格列汀上市使用后，有如下其他的不良反应报告。过敏反应，包括过敏症、血管性水肿、疹、风疹、皮肤血管炎和剥脱性皮肤损害，包括Stevens–Johnson综合征；急性胰腺炎，包括致死性和非致死性出血性和坏死性胰腺炎；肾功能恶化，包括急性肾功能衰竭（有时候需要透析）；上呼吸道感染；肝酶水平升高；便秘；呕吐；头痛；关节痛；肌痛；肢体疼痛；背痛。
【药物相互作用】
尚无研究评价本品药代动力学方面的药物相互作用，但是，已有研究评价本品的单独成份西格列汀和二甲双胍。
研究药物相互作用的试验表明，西格列汀对以下药物的药代动力学不会产生临床意义的影响：二甲双胍、罗格列酮、格列本脲、华法林以及口服避孕药。西格列汀不会抑制CYP酶痛CYP3A4、2C8或2C9。体内试验的结果也表明，西格列汀不会抑制CYP2D6、1A2、2C19或2B6，也不会诱导产生CYP3A4。
有些药物容易引起高血糖，从而导致患者的血糖控制不佳。这类药物包括噻嗪类及其他利尿药、皮质类固醇、烟碱酸、甲状腺药物、雌激素、口服避孕药、苯妥英类、烟酸、拟交感神经药、钙离子通道阻滞剂以及异烟肼。如果接受本品治疗的患者还服用了上述药物，则医生应当密切监测患者的血糖，保证血糖控制良好。
【孕妇及哺乳期妇女用药】
服其他口服降血糖药物一样，不推荐妇女在妊娠期服用本品。
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