

icdm 2011

2011 International Conference on Diabetes and Metabolism

10~12 November 2011
Grand Hilton Seoul Hotel, Seoul, Korea

Plenary lecture

- PL1 The diabetic foot in 2011
- PL2 Systemic impact of adipocyte-derived factors: impact on hepatic physiology

Special lecture

- SL New agents in development for therapy of type 2 diabetes

Symposia

- S1 Islet cell death and regeneration
- S2 Brain-peripheral tissue communication
- S3 Recent advances in gut hormone and diabetes
- S4 Diabetes education recognition programs in Asia-Pacific region
- S5 Islet biology: islet in distress and islet imaging
- S6 Translational studies on glucose metabolism
- S7 NAD biology and metabolism
- S8 Exercise and pre-diabetes
- S9 Juvenile diabetes
- S10 Physiology and pathology of lipid metabolism
- S11 Insulin resistance and vascular dysfunction
- S12 Introduction to 2011 KDA clinical recommendation of medical nutrition therapy
- S13 Diabetes prevention program in Asia
- S14 Novel targets in steatosis and steatohepatitis
- S15 Microvascular aspect of diabetic complications
- S16 Diabetes self-management education
- S17 Gestational diabetes mellitus

Welcome to the 2011 International Conference on Diabetes and Metabolism

It is our pleasure to invite the members and guests to the 2011 International Conference on Diabetes and Metabolism which will be held in Grand Hilton Seoul Hotel, Seoul, Korea, from 10th to 12th November 2011.

Korean Diabetes Association (KDA) has arranged these important scientific symposia and the extensive educational programs for physicians, researchers and educators. There will be world-renowned speakers in seventeen symposium sessions including Insulin secretion & biology, Insulinaction & obesity, Clinical diabetes & therapeutics, Epidemiology & genetics, Acute & chronic complication, Behavioral medicine & education and Gestational diabetes mellitus. The pertinent issues in the broad areas of diabetes mellitus and its updated treatment will be discussed throughout the conference.

This international conference is of significant importance for giving an opportunity for all participants to update and exchange knowledge from basic to clinical and to develop a common vision for the future of diabetes treatment through extensive discussions.

Once again, we would like to express our warmest welcome to you for joining the first ICDM 2011. The organizing committee has been working to make ICDM 2011 a truly memorable experience for all participants. We hope you are able to experience and enjoy unique and wonderful cultural attraction during your stay in Seoul. We look forward to meeting you at the ICDM 2011 in Seoul, Korea.

Sincerely yours,



Jin-Woo Kim, MD
President
Korean Diabetes Association



Sung-Woo Park, MD
Chairman, Board of Directors
Korean Diabetes Association

Timetable

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

	Room 1	Room 2	Room 3	Room 4	
November 10 (Thu)					
12:00~	Registration				Registration
14:00~16:00	Policy forum				
16:00~16:30	Coffee break				
16:30~17:10	Sulwon lecture				
17:10~17:40	Satellite symposium 1	Satellite symposium 2	Satellite symposium 3		
17:40~	Welcome reception				
November 11 (Fri)					
	Islet biology & insulin secretion, immunology & transplantation	Insulin action & obesity	Clinical diabetes & therapeutics	Behavioral medicine & education	Poster exhibition
7:00~8:00	Breakfast symposium 1	Breakfast symposium 2			
8:30~10:00	Oral presentation 1	Oral presentation 2	Oral presentation 3	Oral presentation 4	
10:00~10:20	Coffee break				
10:20~10:30	Opening address				
10:30~11:10	Plenary lecture 1				
11:10~11:40	Special lecture				
11:40~12:00	Break (Poster viewing)				
12:00~13:30	Luncheon symposium 1	Luncheon symposium 2			
13:30~15:00	S1 Islet cell death and regeneration	S2 Brain-peripheral tissue communication	S3 Recent advances in gut hormone and diabetes	S4 Diabetes education recognition programs in Asia-Pacific region	
15:00~15:30				S8 Exercise and pre-diabetes	
15:30~15:50	Coffee break				
15:50~16:20	S5 Islet biology: islet in distress and islet imaging	S6 Translational studies on glucose metabolism	S7 NAD biology and metabolism	Current health insurance issues of diabetes management	
16:20~17:50					
18:00~	Dinner				
November 12 (Sat)					
	Epidemiology & genetics	Insulin action & obesity	Acute & chronic complication	Behavioral medicine & education	Poster exhibition
7:00~8:00	Breakfast symposium 3	Breakfast symposium 4			
8:30~10:00	Oral presentation 5	Oral presentation 6	Oral presentation 7	S17 Gestational diabetes mellitus	
10:00~10:20	Coffee break				
10:20~12:20	S9 Juvenile diabetes	S10 Physiology and pathology of lipid metabolism	S11 Insulin resistance and vascular dysfunction	S12 Introduction to 2011 KDA clinical recommendation of medical nutrition therapy	
12:20~14:00	Luncheon symposium 3	Luncheon symposium 4			
14:00~15:00	Plenary lecture 2				
15:00~15:20	Coffee break				
15:20~17:20	S13 Diabetes prevention program in Asia	S14 Novel targets in steatosis and steatohepatitis	S15 Microvascular aspect of diabetic complications	S16 Diabetes self-management education	
17:20~	Closing				

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Plenary lecture 1

Nov. 11(Fri), 10:30~11:10 / Room1,2,3

Chair: Jin Woo Kim 2

The diabetic foot in 2011

Andrew J. M. Boulton (University of Manchester, UK)

Plenary lecture 2

Nov. 12(Sat), 14:00~15:00 / Room1,2,3

Chair: Sung Woo Park 4

Systemic impact of adipocyte-derived factors: impact on hepatic physiology

Philipp E. Scherer (UT Southwestern Medical Center, USA)

Special lecture

Nov. 11(Fri), 11:10~11:40 / Room1,2,3,4

Chair: Sung Woo Park 8

New agents in development for therapy of type 2 diabetes

Robert R. Henry (University of California, San Diego, USA)

Islet biology & insulin secretion, immunology & transplantation

Nov. 11(Fri), 13:30~15:30 / Room1

S1 Islet cell death and regeneration

Chairs: Hyun Chul Lee, In Sun Park 12

S1-1 The role of interleukin-21 in the development of type-1 diabetes Cecile King (The Garvan Institute for Medical Research, Australia)

S1-2 Role of innate immunity in diabetes Myung Shik Lee (Sungkyunkwan University, Korea)

S1-3 Insulin regulation of pancreatic beta cell function and proliferation Rohit N. Kulkarni (Harvard Medical School, USA)

S1-4 Differentiation of pancreatic epithelial cell-derived NOD-iPS cells into functional pancreatic insulin-producing cells

Ssan Goo Cho (Konkuk University, Korea)

Insulin action & obesity

Nov. 11(Fri), 13:30~15:30 / Room2

S2 Brain-peripheral tissue communication

Chairs: Yong-Wook Cho, Min Seon Kim 24

S2-1 Identification of Rho-kinase as a novel regulator of adiposity Young Bum Kim (Harvard Medical School, USA)

S2-2 Organ-organ interaction for metabolic control Wataru Ogawa (Kobe University, Japan)

S2-3 Synaptotagmin, oxytocin and obesity mechanism Dongsheng Cai (Albert Einstein Medical School, USA)

S2-4 Role of GRP78 in regulation of MC4R signaling Ja Hyun Baik (Korea University, Korea)

Clinical diabetes & therapeutics

Nov. 11 (Fri), 13:30~15:30 / Room3

S3 Recent advances in gut hormone and diabetes

Chairs: Yutaka Seino, Young Seol Kim 32

S3-1 Short-form glucose-dependent insulinotropic polypeptide (GIP) is expressed in pancreatic α -cells and gut endocrine cells

Yukihiro Fujita (Asahikawa Medical University, Japan)

S3-2 Evolutionary conserved residues at the GLP-1 receptor core confer ligand-induced receptor activation

Jae Young Seong (Korea University, Korea)

S3-3 IBCAP; discovery of another intestinal hormone with beta cell augmenting activity

Hideo Toyoshima (Jichi Medical University, Japan)

S3-4 Bioconjugated incretin analogues for potential type 2 diabetes therapeutics

Kang Choon Lee (Sungkyunkwan University, Korea)

Behavioral medicine & education

Nov. 11 (Fri), 13:30~15:00 / Room4

S4 Diabetes education recognition programs in Asia-Pacific region

Chairs: Jeong Tae Woo, Lim Keuky 40

S4-1 Recognition programs of diabetes educator and teams in Taiwan

Neng Chun Yu (Taiwanese Association of Diabetes Educators, Taiwan)

S4-2 Diabetes education: the learning roadmap for diabetes educators in Singapore

Brenda Lim (Association of Diabetes Educators, Singapore)

S4-3 Recognition programs; an Australian experience

Jane Giles (Diabetes Outreach-Country Health SA, Australia)

S4-4 The status of diabetes education programs and clinics in Korea

Kyu Jeung Ahn (Kyung Hee University, Korea)

Islet biology & insulin secretion, immunology & transplantation

Nov. 11 (Fri), 15:50~17:50 / Room1

S5 Islet biology: islet in distress and islet imaging

Chairs: Kwang Won Kim, Dong Seop Choi 48

S5-1 Control of insulin granule exocytosis

Susumu Seino (Kobe University, Japan)

S5-2 Imaging of inflammation in endogenous islets and islets in transplanted grafts

Anna Moore (Massachusetts General Hospital, USA)

S5-3 Preventive effects of endothelial progenitor cells on the early graft loss after islet transplantation

Hye Seung Jung (Seoul National University, Korea)

S5-4 *In vivo* positron emission tomography (PET) imaging of endogenous pancreatic beta cell mass in healthy and type 1 diabetic subjects

Gary Cline (University of Yale, USA)

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Insulin action & obesity

Nov. 11(Fri), 15:50~17:50 / Room2

S6 Translational studies on glucose metabolism

Chairs: Young Kil Choi, In Kyu Lee 56

S6-1 PGC-1 coactivators: orchestrators of skeletal muscle metabolism

Zoltan P. Arany (Harvard Medical School, USA)

S6-2 Amino acid regulation of insulin sensitivity

Feifan Guo (Shanghai Institute for Nutritional Sciences, China)

S6-3 Functional analysis of key regulators in hepatic glucose metabolism

Seung-Hoi Koo (Sungkyunkwan University, Korea)

S6-4 Mitochondrial dysfunction in white adipose tissue and systemic insulin resistance

Min Ho Shong (Chungnam National University, Korea)

Clinical diabetes & therapeutics

Nov. 11(Fri), 15:50~17:50 / Room3

S7 NAD biology and metabolism

Chairs: Hong Kyu Lee, Min Young Chung 64

S7-1 Mitochondrial deacetylase Sirt3 as novel therapeutic for age-associated diseases

Bong Hyun Ahn (LG Life Sciences Ltd, Korea)

S7-2 Control of the NAD⁺ redox state by the pyruvate dehydrogenase kinases

Robert A. Harris (Indiana University, USA)

S7-3 SIRT1 and/or AMPK activators as new drug candidates against metabolic disease from natural products

Won Keun Oh (Chosun University, Korea)

Behavioral medicine & education

Nov. 11(Fri), 15:00~16:20 / Room4

S8 Exercise and pre-diabetes

Chairs: Young Kun Kim, Yong Seong Kim 70

S8-1 Physical activity in type 2 diabetes prevention programs

Sang Woo Oh (Dong Guk University, Korea)

S8-2 Role of physical activity in pre/hypertension: accumulation of 10 min walks

Saejong Park (The Korea Institute of Sport Science, Korea)

S8-3 Exercise and type 2 diabetes: ACSM and ADA joint position statement

Seok Won Park (CHA University, Korea)

Epidemiology & genetics

Nov. 12(Sat), 10:20~12:20 / Room1

S9 Juvenile diabetes

Chairs: Sei Won Yang, Byung-kyu Suh 76

S9-1 Recent topics from multicenter collaborative studies in Japan

Shin Amemiya (Saitama Medical University, Japan)

S9-2 Genetics in diabetes - contribution to the classification and management

Jee Suk Yu (Darkook University, Korea)

S9-3 Obesity and insulin resistance in children and adolescents

Eun Young Kim (Chosun University, Korea)

S9-4 Epidemiologic changes of juvenile diabetes in Korea

Hyun-Wook Chae (Yonsei University, Korea)

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Insulin action & obesity

Nov. 12(Sat), 10:20~12:20 / Room2

S10 Physiology and pathology of lipid metabolism

Chairs: Seoung Yeon Kim, Hyoung Woo Lee 84

S10-1 Islet hormone secretion regulation and energy homeostasis Weiping Han (Singapore Bioimaging Consortium, A*STAR, Singapore)

S10-2 Role of SIRT1 deacetylase and microRNA-34a in regulation of hepatic metabolism

Jongsook Kim Kemper (University of Illinois at Urbana-Champaign, USA)

S10-3 Diet-induced obesity and adipose tissue inflammation

Alan Chait (University of Washington Seattle, USA)

S10-4 The role of immune cells in the development of obesity-induced inflammation and insulin resistance

Jong Soon Lee (Harvard Medical School, USA)

Acute & chronic complication

Nov. 12(Sat), 10:20~12:20 / Room3

S11 Insulin resistance and vascular dysfunction

Chairs: You Hern Ahn, Bong Yun Cha 92

S11-1 Insulin action and resistance in the microcirculation

Zhenqi Liu (University of Virginia, USA)

S11-2 Insulin resistance and new strategies to suppress vascular smooth muscle cell proliferation

In Kyu Lee (Kyungpook National University, Korea)

S11-3 Metabolic syndrome, adipokines and vascular inflammation

Kyung Mook Choi (Korea University, Korea)

S11-4 Which lipid particles are atherogenic under diabetic condition?; Lipid traffics in idabetics

Ki Hoon Han (University of Ulsan, Korea)

Behavioral medicine & education

Nov. 12(Sat), 10:20~12:20 / Room4

S12 Introduction to 2011 KDA clinical recommendation of medical nutrition therapy

Chairs: Soon Hyun Shinn, In Joo Kim 100

S12-1 Introduction to 2011 KDA clinical recommendation of medical nutrition therapy (MNT)

Chong Hwa Kim (Sejong General Hospital, Korea)

S12-2 New version of KDA dietary recommendations-MNT, energy intake and carbohydrate

Hee Jung Ahn (Eulji Hospital, Korea)

S12-3 New version of KDA dietary recommendations-protein, fat, vitamin and mineral

Young Ran Lee (Kangnam Sacred Heart Hospital, Korea)

S12-4 New version of KDA dietary recommendations-fiber, sodium, alcohol and sweeteners

Young-Mi Park (Seoul National University Bundang Hospital, Korea)

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Epidemiology & genetics

Nov. 12(Sat), 15:20~17:20 / Room1

S13 Diabetes prevention program in Asia

Chairs: Moon-Gi Choi, Michael Hirst 110

S13-1 Introduction to diabetes in Asia and Ansong-Ansan community cohort epidemiologic study

Nam Han Cho (Ajou University, Korea)

S13-2 Lesson from diabetes prevention program in India and China

Byoung Joon Kim (Konyang University, Korea)

S13-3 Japan diabetes prevention program (JDPP) and Japan diabetes outcome intervention trial-1 (J-DOIT1)

Naoki Sakane (National Hospital Organization Kyoto Medical Center, Japan)

Insulin action & obesity

Nov. 12(Sat), 15:20~17:20 / Room2

S14 Novel targets in steatosis and steatohepatitis

Chairs: Tai Hee Lee, Ki Up Lee 116

S14-1 Myricocin prevents non-alcoholic steatohepatitis in mice fed methionine-choline-deficient diet

Ki Up Lee (University of Ulsan, Korea)

S14-2 Selenoprotein P as a hepatokine that causes insulin resistance

Toshinari Takamura (Kanazawa University, Japan)

S14-3 Blockade of mineralocorticoid receptor ameliorates glucose metabolism and steatohepatitis in a novel mice model of non-alcoholic steatohepatitis

Tsutomu Wada (University of Toyama, Japan)

S14-4 Protection against hepatic steatosis and systemic insulin resistance by conditional knockdown of p70 S6 kinase in liver

Eun Ju Bae (Woosuk University, Korea)

Acute & chronic complication

Nov. 12(Sat), 15:20~17:20 / Room3

S15 Microvascular aspect of diabetic complications

Chairs: Hyung Joon Yoo, Duk-Kyu Kim 124

S15-1 Pharmaceutical elevation of NAD⁺ level and metabolic diseases

Woo Jin Park (Gwangju Institute of Science and Technology, Korea)

S15-2 Management of diabetic foot problems in the western pacific region

Shigeo Kono (Kyoto Medical Center, Japan)

S15-3 Diabetic nephropathy; new opportunities and new therapeutics

Merlin C Thomas (Baker IDI Heart and Diabetes Institute, Australia)

S15-4 HbA1c variability as a risk of microvascular complication in diabetes

Hirohito Sone (University of Tsukuba Institute of Clinical Medicine, Japan)

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Behavioral medicine & education

Nov. 12(Sat), 15:20~17:20 / Room4

S16 Diabetes self-management education

Chairs: Sung Koo Kang, Kang Hee Sim 132

S16-1 Essential guidelines for pediatric diabetes education by an experienced educator

Eun Kyung Kwon (Samsung Seoul Hospital, Korea)

S16-2 Diabetes self-management education for older adults: general principles and practical application

Hyang Mi Jang (Gangnam Severance Hospital, Korea)

S16-3 The effects of diabetes education which was reinforced on patient lifestyle modification

Jeong Rim Lee (Seoul Asan Medical Center, Korea)

S16-4 Foot care for diabetics

Bok Rye Song (Seoul St. Mary's Hospital, Korea)

Behavioral medicine & education

Nov. 12(Sat), 8:30~10:00 / Room4

S17 Gestational diabetes mellitus

Chairs: Hak Chul Jang, Moon Young Kim 140

S17-1 Genetics of gestational diabetes mellitus

Sung Hoon Kim (Kwandong University, Korea)

S17-2 T2DM after GDM pregnancy: early vs. late converters

Soo Heon Kwak (Seoul National University, Korea)

S17-3 Maternal obesity and fetal macrosomia

Kyung Ju Lee (CHA University, Korea)

S17-4 Evolving paths to fetal metabolic programming

Eun Sook Oh (Mizmedi Hospital, Korea)

Current health insurance issues of diabetes management

Nov. 11(Fri), 16:20~17:50 / Room4

Chair: Tae Sun Park 149

The payment status for the glucose test-strips on the type 1 diabetes patients

Young Ko (National Health Insurance Corporation, Korea)

Status after applying a new insurance benefits standard for diabetes drugs

Gyu Im Kim (Health Insurance Review & Assessment Service, Korea)

Action plan of quality assessment program in diabetes care

Hyun Ja Yoo (Health Insurance Review & Assessment Service, Korea)

Contents

2011 International Conference on Diabetes and Metabolism
Korean Diabetes Association

Satellite symposium 1	Nov. 10(Thu), 17:10~17:40 / Room1	Chair: Dong-Sun Kim	154
A New Alternative in DPP4 inhibition Jeffrey Wayne Stephens (Swansea University, UK)			
Satellite symposium 2	Nov. 10(Thu), 17:10~17:40 / Room2	Chairs: Hak Chul Jang, Sung Rae Kim	156
A PROspective comparative clinical study to evaluate efficacy and safety of PITavastatin in patients with metabolic syndrome: PROPIT study Sung Hee Choi (Seoul National University, Korea)			
Satellite symposium 3	Nov. 10(Thu), 17:10~17:40 / Room1	Chair: Dong-Sun Kim	158
Diagnosis and management of diabetic neuropathy Andrew James Michael Boulton (University of Manchester, UK)			
Breakfast symposium 1	Nov. 11(Fri), 7:00~8:00 / Room1	Chair: Jae Myung Yu	160
Back to the fundamentals: MOA, PK, and PD of DPP-4 inhibitors Young Min Cho (Seoul National University, Korea)			
Breakfast symposium 2	Nov. 11(Fri), 7:00~8:00 / Room2	Chair: Moon Kyu Lee	162
Vildagliptin has a better metabolic impact than Sitagliptin on mean amplitude glycaemic excursion Giuseppe Paolisso (Second University of Naples, Italy) Beneficial impact of direct renin inhibition on renal and cardiovascular disease Hans-Henrik Parving (University of Copenhagen, Denmark)			
Breakfast symposium 3	Nov. 12(Sat), 7:00~8:00 / Room1	Chair: Dong Seop Choi	166
What's new & controversy on statin treatment in diabetes? Chang Beom Lee (Hanyang University, Korea)			
Breakfast symposium 4	Nov. 12(Sat), 7:00~8:00 / Room2	Chair: Yong Ki Kim	168
Updates on the clinical usefulness of sitagliptin Jeong Hyun Park (Inje University, Korea)			
Luncheon symposium 1	Nov. 11(Fri), 12:00~13:30 / Room1	Chair: Hyun Chul Lee	170
Overcoming barriers now in successful management of type 2 diabetes Eun Seok Kang (Yonsei University, Korea)			
Luncheon symposium 2	Nov. 11(Fri), 12:00~13:30 / Room2	Chair: Sun Woo Kim	172
Recent issues on hypertension management and role of aprovel Dae Jung Kim (Ajou University, Korea)			
Luncheon symposium 3	Nov. 12(Sat), 12:20~14:00 / Room1	Chair: Kyung Soo Ko	174
What is your choice for glycemic control? proven or new Sin Gon Kim (Korea University, Korea)			
Luncheon symposium 4	Nov. 12(Sat), 12:20~14:00 / Room2	Chair: Joong-Yeol Park	176
The treatment of atherogenic dyslipidemia in patients with diabetes mellitus Giuseppe M.C. Rosano (IRCCS San Raffaele, Italy)			

Oral Presentation

Islet biology & insulin secretion, immunology & transplantation
Oral presentation 1

Nov. 11(Fri), 8:30~10:00 / Room1
Chairs: Yu Bae Ahn, Sung-Hee Ihm 181

- OP1-1 The incretin effect measured by isoglycemic intravenous glucose infusion in Korean subjects with normal glucose tolerance and type 2 diabetes mellitus**
Tae Jung Oh*, Min Young Kim, Ji Yon Shin, Kyong Soo Park, Young Min Cho
Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea
- OP1-2 Preventing the rejection of pancreatic islet grafts using a siRNA-nanoparticle probe**
Anna Moore*, Ping Wang, Mehmet V. Yigit, Zdravka Medarova, Alana Ross, Guangping Dai
Molecular Imaging Laboratory, MGH/MIT/HMS Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts 02129, USA
- OP1-3 Acute induction of insulin resistance with glucosamine infusion increases pancreatic islet blood flow in anesthetized rats**
Xiang Gao*, Monica Sandberg and Leif Jansson, Leif Jansson
Uppsala University
- OP1-4 Long-term metabolic consequences of 50% partial pancreatectomy for benign pancreatic tumors with or without islet autotransplantation**
Sang-Man Jin^{1*}, Seung-Hoon Oh³, Soo Kyoung Kim¹, Hye Seung Jung⁴, Seong-Ho Choi², Jae Hyeon Kim¹, Myung-Shik Lee¹, Moon-Kyu Lee¹, Kwang-Won Kim¹
Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine¹, Department of Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine², Samsung Biomedical Research Institute³, Department of Internal Medicine, Seoul National University College of Medicine⁴
- OP1-5 Genetic partial insufficiency of mitochondrial respiratory chain (OXPHOS) function in pancreatic beta cells induce islet hyperplasia**
Yong Kyung Kim^{1*}, Soung Jung Kim¹, Min Jeong Ryu¹, Min Hee Lee¹, Seong Eun Lee¹, Min Jeong Choi¹, Hyo Kyun Chung¹, Koon Soon Kim¹, Hyun Jin Kim¹, Ki Ryang Kweon², Chul-Ho Lee³, Min Ho Shong¹
Research Center for Endocrine & Metabolic Diseases, Chungnam National University School of Medicine, Daejeon¹, Department of Biochemistry, Chungnam National University School of Medicine, Daejeon², Animal Model Center, Korea Research Institute of Bioscience & Biotechnology (KRIBB), Daejeon³
- OP1-6 Suppression of Perk improves hyperglycemia and recovers autophagic activity in β cell-specific Atg7 knockout mice**
Min Joo Kim*, Shin Hee Hong, Ho Young Kan, Ye Jin Lee, Hakmo Lee, Sung Soo Chung, Kyong Soo Park, Hack C. Jang, Seong Yeon Kim, Hye Seung Jung
Department of Internal Medicine, Seoul National University College of Medicine
- OP1-7 Inhibition of fatty acid translocase cluster determinant 36 (FAT/CD36) prevents glucotoxicity in INS-1 cells**
Byung Sam Park^{1*}, Sang Hyun Park¹, Hyun Hee Chung¹, Ye Jin Seo², Ji Sung Yoon¹, So Young Park², Yong Woon Kim², Jong Yeon Kim², Hyoung Woo Lee¹, Kyu Chang Won¹
Department of Internal Medicine, Yeungnam University College of Medicine¹, Department of Physiology, Yeungnam University College of Medicine²

Acute & chronic complication
Oral presentation 2

Nov. 11(Fri), 8:30~10:00 / Room2
Chairs: Min Ho Song, Kwan woo Lee 182

- OP2-1 The relationship of the between a venous return time, PWV and physical inactivity duration in T2DM with hemiplegia**
Akira Kimura*, Isao Kobayashi
Gunma PAZ college Graduate School off Health Sciences

- OP2-2 The association of urinary tubular markers and urinary angiotensinogen with albuminuria in early nephropathy of type 2 diabetes**
Bo Gwang Choi^{1*}, Ji Hyun Kang¹, Yun Kyung Jeon¹, Sang Soo Kim¹, Bo Hyun Kim¹, Yong Ki Kim², In Joo Kim¹, In Joo Kim¹
Department of Internal Medicine, School of Medicine, Pusan National University¹, Kim Yong Ki Internal Medicine Clinic²
- OP2-3 The association of bladder cancer with pioglitazone in Korean subjects with T2D might be different from that in Caucasian population**
Sun Ok Song*, Kwang Joon Kim, Hyun Min Kim, Eun Young Lee, Jae Hoon Moon, Eun Seok Kang, Bong Soo Cha, Hyun Chul Lee, ByungWan Lee
Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea
- OP2-4 8-hydroxy-2-deoxyguanosine prevents plaque formation in a partial ligated ApoE knockout mouse, an acute model of atherosclerosis**
Joo Young Huh^{1*}, Hanjoong Jo³, Sun Choi¹, Myung-Hee Chung⁴, Hunjoo Ha²
College of Pharmacy, Division of Life & Pharmaceutical Sciences¹, Department of Bioinspired Science, Ewha Womans University, Seoul, Korea², Division of Cardiology, Department of Medicine, Emory University, Atlanta, USA³, Department of Pharmacology, Seoul National University College of Medicine, Seoul, Korea⁴
- OP2-5 NOD2 deficiency enhances neointimal formation in response to vascular injury**
Min-Young Kwon^{1*}, Xiaoli Liu³, Seon-Jin Lee³, Young-Ho Kang¹, Ki-Up Lee², Mark A. Perrella³, Su Wol Chung¹
School of Biological Sciences, University of Ulsan, South Korea¹, Department of Internal Medicine, School of Medicine, University of Ulsan, South Korea², Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA³
- OP2-6 Effect of 6-gingerol on vascular inflammation and atherosclerosis associated with diabetes mellitus**
So Hun Kim*, Qing Song Jin, Hyun Ae Lim, Seung Youn Lee, Seong Bin Hong, Yong Seong Kim, Moonsuk Nam
Department of Internal Medicine, Inha University School of Medicine, Incheon, Korea
- OP2-7 Vaspin protects vascular endothelial cells against free fatty acid-induced apoptosis through a phosphatidylinositol 3-kinase/Akt pathway**
Chang Hee Jung^{1*}, Woo Je Lee¹, Jenie Yoonoo Hwang¹, So Mi Seol², Yun Mi Kim², Yoo La Lee², Joong-Yeol Park¹
Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Asan Institute of Life Sciences, University of Ulsan College of Medicine, Asan Medical Center²

Clinical diabetes & therapeutics (I)

Nov. 11(Fri), 8:30~10:00 / Room3

Oral presentation 3

Chairs: Kyo Il Suh, Kyung Wan Min 184

- OP3-1 The effects of caloric restriction on fetuin-A and cardiovascular risk factors in rats and humans: a randomized controlled trial**
Sae Jeong Yang^{1*}, Kyung Mook Choi¹, Hee Jung Ahn², So Young Lee¹, Baek-Hui Kim³, Kyeong Jin Kim¹, Sun Hwa Kim¹, Jae Hee Ahn¹, Ho Cheol Hong¹, Hae Yoon Choi¹, Myoung Jin Cho¹, Yoonjung Kim¹, Chai Ryoung Eun¹, Joohyung Kim¹, Hye Jin Yoo¹, Hee Young Kim¹, Ji A Seo¹, Sin Gon Kim¹, Nan Hee Kim¹, Sei Hyun Baik¹, Dong Seop Choi¹, Kyung Wan Min⁴
Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University¹, Diabetes Center, Eulji Hospital², Department of Pathology, College of Medicine, Korea University³, Eulji University School of Medicine⁴
- OP3-2 Increased selenoprotein P levels in subjects with visceral obesity and non-alcoholic fatty liver disease**
Ho Cheol Hong*, Dong Seop Choi, Sei Hyun Baik, Sin Gon Kim, Nan Hee Kim, Ji A Seo, Hee Young Kim, Hye Jin Yoo, Sae Jeong Yang, Chai Ryoung Eun, Yoon Jung Kim, Hae Yoon Choi, Myoung Jin Cho, Joo Hyung Kim, Jae Hee Ahn, Sun Hwa Kim, Kyeong Jin Kim, Kyung Mook Choi
Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University, Seoul, Korea

- OP3-3 Association of adiponectin, resistin, and vascular inflammation analysis with 18F-fluorodeoxyglucose positron emission tomography**
Hae Yoon Choi*, Dong Seop Choi, Sei Hyun Baik, Sin Gon Kim, Nan Hee Kim, Ji A Seo, Hee Young Kim, Hye Jin Yoo, Sae Jeong Yang, Chai Ryoung Eun, Ho Cheol Hong, Yoon Jung Kim, Myong Jin Cho, Joo Hyung Kim, Jae Hee Ahn, Sun Hwa Kim, Kyeong Jin Kim, Kyung Mook Choi
Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University, Seoul, Korea
- OP3-4 Clinical characteristics of sleep disorders in patients with type 2 diabetes**
Tae Suk Kim^{1*}, Ohk Hyun Ryu², Moon Gi Choi², Seong Jae Kim³, Jung Hie Lee³, Eun Hee Cho¹
Department of Internal Medicine, School of Medicine, Kangwon National University, Korea¹, Department of Internal Medicine, College of Medicine, Hallym University Chuncheon, Korea², Department of Psychiatry, School of Medicine, Kangwon National University, Korea³
- OP3-5 The increment of postprandial TG levels in Korean subjects with prediabetes and type 2 diabetes according to their metabolic syndrome status**
Kyeong Hye Park*, Kwang Joon Kim, Byung-Wan Lee, Eun Seok Kang, Bong Soo Cha, Hyun Chul Lee, Byung-Wan Lee
Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine
- OP3-6 Adequate glycemic control in intensive care unit**
Sang Hyun Park*, Byung Sam Park, Hyun Hee Chung, Ji Sung Yoon, Kyu Chang Won, Hyoung Woo Lee
Department of Internal Medicine, Yeungnam University
- OP3-7 Higher morning to evening ratio in total dose of twice daily biphasic insulin analogue might be effective in achieving glucose control in patients with poorly controlled type 2 diabetes**
Yong-ho Lee^{1*}, Hea Jin Kwon², Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-Wan Lee¹
Yonsei University College of Medicine¹, Severance Hospital²

Behavioral medicine & education

Nov. 11(Fri), 8:30~10:00 / Room4

Oral presentation 4

Chairs: Yeon-Ah Sung, Bong Soo Cha **186**

- OP4-1 Prevalence of metabolic syndrome and cut-off values according to the physical fitness levels in Korean adult males**
Yeo-jin Moon^{1*}, Seung-chul Rhim³, Ho-Seung Lee⁴, Young-Soo Jin⁴, Hae-Mi Jee², Yong-Hwan Kim⁴, Sung-Woo Park⁵, Chul-Young Park⁵
Diabetes Mellitus Center, Kangbuk Samsung Hospital¹, Department Medical, University of Ulsan College of Medicine, Seoul², Department of Neurological Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea³, Sports Health Medical Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul⁴, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine⁵
- OP4-2 Development and evaluation of an integrated self-management program for women with gestational diabetes mellitus**
Hee Sook Kim^{1*}, Sue Kim², Jeong Eun Park³, Sung Hoon Kim³
College of Nursing, Seoul National University¹, College of Nursing, Yonsei University, Korea², Diabetes Center, Division of Endocrinology & Metabolism, Department of Medicine, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine, Seoul, Korea³
- OP4-3 Factors influencing physical activity behavior among Iranian women with type 2 diabetes using the extended theory of reasoned action**
Alireza Didarlo^{1*}, Rasool Gharaaghaji Asl³, Hossian Habibzadeh⁴, Shamsaddin Niknami⁵, Reza Pourali⁶, Davood Shojaeizadeh²
Department of Health and Social Medicine, Uremia University of Medical Sciences, Uremia, Iran¹, Department of Health Education and promotion, Tehran University Medical Sciences, Tehran, Iran², Department of Biostatistics and Epidemiology, Uremia University of Medical Sciences, Uremia, Iran³, Department of Nursing, Uremia University of Medical Sciences, Uremia, Iran⁴, Department of Health Education and Promotion, Tarbiat Modares University, Tehran, Iran⁵, Department of Health and Social Medicine, Uremia University of Medical Sciences, Uremia, Iran⁶

OP4-4 WITHDRAWN

OP4-5 Dietary pattern consisting of a variety of foods reduces the risk of metabolic syndrome

Inkyung Baik^{1*}, Nam H Cho³, Myoungsook Lee⁴, Chol Shin²

Department of Foods and Nutrition, College of Natural Sciences, Kookmin University¹, Department of Internal Medicine, Korea University Ansan Hospital, Ansan², Department of Preventive Medicine, Ajou University School of Medicine, Suwon³, Department of Food and Nutrition, Research Institute of Obesity Sciences, Sungshin Women's University⁴

OP4-6 The effects of a lifestyle intervention program according to implementation of session goal in Korean male with metabolic syndrome

Sun Young Kim^{1*}, Ji Yeon Kang¹, Ill-Keun Park¹, Youn Koun Chang¹, Yoo Kyoung Park², Yun Mi Paek¹, Tae In Choi¹

Radiation Health Research Institute, Korea Hydro & Nuclear Power Co., Ltd, Korea¹, Department of Medical Nutrition, Kyung Hee University, Yongin, Republic of Korea²

OP4-7 The study on the carbohydrate consumption of Korean T2DM patients

Hee Young Kim^{1*}, Eun Mi Kim², Jinsun Choi¹, Ji-Hoon Choi³, Seung-hyun Yoo³, Won-Jun Kim³, Se-Eun Park³, Chul-Young Park³, Won-Young Lee³, Ki-Won Oh³, Sung-Woo Park³, Sun-Woo Kim³

Diabetes Mellitus Center, Kangbuk Samsung Hospital¹, Department of Dietetic, Kangbuk Samsung Hospital², Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine³

Epidemiology & genetics

Nov. 12(Sat), 8:30~10:00 / Room1

Oral presentation 5

Chairs: Yong Soo Park, Moon Suk Nam **188**

OP5-1 Arsenic exposure and prevalence of diabetes mellitus in Korean adults: Analyses based on the Fourth Korea National Health and Nutrition Examination Survey (KNHANES), 2008-2009

Sang Youl Rhee^{1*}, Sang Ouk Chin¹, Moon Chan Choi¹, Suk Chon¹, You-Choel Hwang¹, In-Kyung Jeong¹, Seungjoon Oh¹, Kyu Jeung Ahn¹, Ho Yeon Chung¹, Sung Woon Kim¹, Jin-Woo Kim¹, Young Seol Kim¹, Jeong-taek Woo¹
Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine¹, Research Institute of Endocrinology, Kyung Hee University²

OP5-2 The value of the apolipoprotein B/A1 ratio in the diagnosis of metabolic syndrome in a Korean population

Min-Jung Lee^{1*}, Jenie Yoonoo Hwang¹, Ji Hee Yu¹, Mi Seon Shin¹, Sung Jin Bae², Joong-Yeol Park¹, Hong-Kyu Kim², Woo Je Lee¹

Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Department of Health Screening and Promotion Center, University of Ulsan College of Medicine, Asan Medical Center²

OP5-3 The target level of A1c in type 2 diabetes patients with medical disease might not be less than 7% of HbA1c

Sun Ok Song^{1*}, Kwang Joon Kim², Hyun Min Kim¹, Seok Hannah¹, Eun Young Lee¹, Da Ham Kim¹, Jae Hoon Moon¹, Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-wan Lee¹

Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea¹, Severance Executive Healthcare Clinic²

OP5-4 The association of non-alcoholic fatty liver disease and cardiac structural and functional changes in Koreans

Chai Ryoung Eun^{1*}, Ji A Seo¹, Hyunjoon Cho¹, Ho Cheol Hong¹, Hae Yoon Choi¹, Myong Jin Cho¹, Yoon Jung Kim¹, Joo Hyung Kim¹, Sae Jeong Yang¹, Hye Jin Yoo¹, Hee Young Kim¹, Hyung Joon Yim², Sin Gon Kim¹, Kyung Mook Choi¹, Sei Hyun Baik¹, Dong Seop Choi¹, Seong Hwan Kim³, Nan Hee Kim¹

Endocrinology, Korea University Medical School, Korea¹, Hepatology, Korea University Medical School, Korea², Cardiology, Korea University Medical School, Korea³

OP5-5 Low vitamin D status is closely associated with nonalcoholic fatty liver disease in the subjects with diabetes or insulin resistance

Sun Hwa Kim^{1*}, Ji A Seo¹, Chai Ryoung Eun¹, Hyunjoo Cho¹, Ho Cheol Hong¹, Hae Yoon Choi¹, Myong Jin Cho¹, Yoon Jung Kim¹, Joo Hyung Kim¹, Sae Jeong Yang¹, Hye Jin Yoo¹, Hee Young Kim¹, Hyung Joon Yim², Sin Gon Kim¹, Kyung Mook Choi¹, Sei Hyun Baik¹, Dong Seop Choi¹, Chol Shin³, Nan Hee Kim¹
Division of Endocrinology, Department of Internal Medicine, Korea University Medical School, Republic of Korea¹, Division of Hepatology, Department of Internal Medicine, Korea University Medical School, Republic of Korea², Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Korea University Medical School, Republic of Korea³

OP5-6 Gene expression pattern in transmitochondrial cytoplasmic hybrid cells harboring type 2 diabetes-associated mitochondrial DNA haplogroups

Soo-Heon Kwak^{1*}, Seungwoo Hwang², Jong Bhak³, Hae Sun Kang¹, You Ri Lee¹, Bo Kyung Koo¹, Kyong Soo Park¹, Hong Kyu Lee⁴, Young Min Cho¹
Department of Internal Medicine, Seoul National University College of Medicine¹, Korean Bioinformation Center, Korea Research Institute of Bioscience and Biotechnology², Theragen BiO Institute³, Department of Internal Medicine, Eulji University College of Medicine⁴

OP5-7 Low visfatin levels are associated with exacerbated insulin resistance and impaired insulin secretion in overweight and normal weight Korean women with gestational diabetes mellitus

Sunmin Park^{1*}, Sung-Hoon Kim²
Hoseo University¹, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine²

Insulin action & obesity

Nov. 12(Sat), 8:30~10:00 / Room2

Oral presentation 6

Chairs: Soon Jib Yoo, Ho Sang Shon 189

OP6-1 Effects of adiposity on insulin resistance and metabolic disturbance in women with and without polycystic ovary syndrome

Hye Jin Lee^{1*}, Jee-Young Oh¹, Young Sun Hong¹, Hye Won Chung², Yeon-Ah Sung¹
Division of Endocrinology, Department of Internal Medicine, Ewha Womans University School of Medicine¹, Department of Obstetrics and Gynecology, Ewha Womans University School of Medicine²

OP6-2 Zfp521 as a negative regulator of preadipocyte commitment

Sona Kang*, Rana Gupta, Shingo Kajimura, Evan Rosen
Beth Israel Deaconess Medical Center, Harvard Medical School

OP6-3 Ciliogenesis of hypothalamic neuron is impaired in obesity and regulated by leptin

Mi-seon Shin^{1*}, Yu Mi Han², Gil Myoung Kang², Sae Bom Lee², Hyun-Kyong Kim², So Young Gil², Joong Yeol Park¹, Ki Up Lee¹, Hyuk Whan Koh³, Min-seon Kim¹
Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Appetite Regulation Laboratory, Asan Institute for Life Science², Age-Related & Brain Diseases Research Center, Kyung Hee University³

OP6-4 Effects of exercise without calorie restriction on insulin action and ectopic fat in obese boys: A randomized controlled trial

SoJung Lee^{1*}, Nancy Guerra¹, Jennifer Kuk², Fida Bacha¹, Chris Boesch³, Silva Arslanian¹
Division of Weight Management and Wellness, Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA¹, School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada², Magnetic Resonance Spectroscopy and Methodology, Department of Clinical Research, University Bern, Bern, Switzerland³

OP6-5 Role of Rho-kinase on insulin secretion in pancreatic β -cells

Byung-Jun Sung*, Moon-Kyu Lee, Kwang-Won Kim, Myung-Shik Lee, Jea Hyun Kim, Se Won Kim, Mi Yeon Kim, Moon-Kyu Lee
Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center

OP6-6 Resveratrol promotes the mitochondrial activity with over-expression of ER-alpha in brown adipocyte

Cheol Ryong Ku*, Cheol Ryong Ku, Eun Jig Lee, Eun Jig Lee
Endocrinology, Severance Integrative Research Institute for Cerebral & Cardiovascular Diseases, Yonsei University College of Medicine, Seoul, Korea

OP6-7 eNamt regulates body weight homeostasis through hypothalamic Sirt2-mediated inhibition of Foxo1

So Young Gil^{1*}, Gil Myung Kang¹, Byung Soo Youn³, Hyun-Kyong Kim¹, Churl Namkoong¹, Hyukki Chang⁴, Ji Hee Yu², Ji-Youn Chung², Joong-Yeol Park², Ki-Up Lee², Min Seon Kim¹
Apeptide Regulation National Research Laboratory, Asan Institute for Life Sciences, University of Ulsan College of Medicine, Seoul, Korea¹, Department of Internal Medicine, University of Ulsan College of Medicine, Seoul, Korea², AdipoGen Inc., Incheon 406-840, Korea³, Department of Human Movement Science, Seoul Women's University, Seoul, Korea⁴

Clinical diabetes & therapeutics (II)

Nov. 12(Sat), 8:30~10:00 / Room3

Oral presentation 7

Chairs: Sung-Soo Koong, Young Duk Song **191**

OP7-1 Effects of exenatide (Exendin-4) on glycemic control over 12 weeks in patients with Korean type 2 diabetes treated with metformin and a sulfonyleurea

Kwang Joon Kim^{*}, Hea Jin Kwon, Sun Ok Song, Hyun Min Kim, Eun Young Lee, Eun Seok Kang, Bong Soo Cha, Hyun-Chul Lee, Byun-Wan Lee
Division of Endocrinology, Department of Internal Medicine, Yonsei University College of Medicine

OP7-2 The effect of rosiglitazone on LRP1 expression and amyloid β uptake in human brain microvascular endothelial cells: a possible role of low-dose thiazolidinedione for dementia treatment

Jae Hoon Moon^{1*}, Hyung Jun Kim², Ae Hee Yang², Hyun Min Kim¹, Byung-Wan Lee¹, Eun Seok Kang¹, Hyun Chul Lee¹, Bong Soo Cha¹
Department of Internal Medicine, Yonsei University College of Medicine¹, Brain Korea 21 for Medical Science, Yonsei University College of Medicine

OP7-3 Comparison of efficacy and safety of once-daily dosing and on-demand use of udenafil for type 2 diabetes patients with erectile dysfunction

Soon Hyun Park^{1*}, Sung Woo Park², Bong Yeon Cha³, Je Byung Park⁴, Kyung Wan Min⁵, Yeon Ah Sung⁶, Tae Hwa Kim⁷, Hyun Jin Kim⁸, Jae Min Lee¹, Jae Hyuk Lee¹, Kang Seo Park¹
Department of Internal Medicine, Eulji University School of Medicine, Daejeon¹, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul², Department of Endocrinology & Metabolism, College of Medicine the Catholic University of Korea³, Department of Internal Medicine, Gachon University of Medicine and Science Graduate School of Medicine, Incheon⁴, Department of Internal Medicine, Eulji University School of Medicine, Seoul⁵, Department of Endocrinology, Ewha Woman's University School of Medicine, Seoul⁶, Department of Internal Medicine, College of Medicine, Hanyang University, Seoul⁷, Departments of Internal Medicine, Chungnam National University School of Medicine, Daejeon⁸

OP7-4 Anti-diabetic actions of a non-agonist PPAR γ ligand blocking Cdk5-mediated phosphorylation

Jang Hyun Choi^{1*}, Alexander S. Banks¹, Patrick R. Griffin², Bruce Spiegelman¹
Department of Cancer Biology and Division of Metabolism and Chronic Disease, Dana-Farber Cancer Institute and Department of Cell Biology, Harvard Medical School, Boston, Massachusetts 02115, USA¹, Department of Molecular Therapeutics, The Scripps Research Institute, Scripps Florida, Jupiter, Florida 33458, USA²

OP7-5 Efficacy and safety of linagliptin (5 mg) compared to placebo in combination with metformin and sulphonylurea over 24 weeks in type 2 diabetic patients of Korean ethnicity: A post-hoc analysis

Sin Gon Kim^{1*}, Jeong Hyun Park², Hyoung Woo Lee³, Sung Woo Park⁴, Doo Man Kim⁵, Moon Suk Nam⁶, Tae Sun Park⁷, Duk Kyu Kim⁸, Kwan Woo Lee⁹, Jeong Taek Woo¹⁰, Kun Ho Yoon¹¹, Ji Soo Lee¹², Dong Seop Choi¹
Department of Endocrinology and Metabolism, Korea University College of Medicine, Seoul¹, Department of Internal Medicine College of Medicine Inje University, Busan², Department of Internal Medicine, Yeungnam University College of Medicine, Daegu³, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunwan University School of Medicine, Seoul⁴, Department of Internal Medicine, Hallym University Sacred Heart Hospital, Seoul⁵, Department of Endocrinology and Metabolism, Inha University College of Medicine, Incheon⁶, Department of Internal Medicine Chunbuk National University College of Medicine, Jeonju⁷, Department of Internal Medicine, Dong-A University College of Medicine, Busan⁸, Department of Endocrinology and Metabolism, Ajou University School of Medicine, Gyeonggi-Do⁹, Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul¹⁰, Department of Internal Medicine The Catholic University of Korea, Seoul, Korea¹¹, Boehringer-Ingelheim Korea, Department of Medicine¹²

OP7-6 Modest reversal of metabolic syndrome manifestations with vitamin D correction: A 12-month prospective study

Nasser Al-Daghri*, Khalid Alkharfy

Biomarkers Research Program, Biochemistry Department, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia (KSA); Prince Mutaib Chair for Biomarkers of Osteoporosis, King Saud University, Riyadh, KSA

OP7-7 Enhanced carbohydrate craving in diabetic patients

Ji Hee Yu^{1*}, Mi-Seon Shin¹, Jenie Yoonoo Hwang¹, Chang Hee Jung¹, Eun Hee Koh¹, Woo Je Lee¹, Joong-Yeol Park¹, Ki-Up Lee¹, Jeong Rim Lee², So-Yoon Yoon³, Min-Seon Kim¹

Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Ulsan College of Medicine, Seoul, Korea¹, Outpatient Nursing 1 Team, Nursing Department, Asan Medical Center, Seoul, Korea², Diabetics and Nutrition Services Team, Asan Medical Center, Seoul, Korea³

Poster Presentation

Islet biology & insulin secretion, immunology & transplantation

197

PE1 Genome-wide identification of palmitate-regulated immediate early genes and target genes in pancreatic beta-cells reveals a central role of NF- κ B

Hyung Jin Choi^{1*}, Seungwoo Hwang², Se-Hee Lee¹, You Ri Lee¹, Jiyon Shin¹, Kyong Soo Park¹, Young Min Cho¹
Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea¹, Korean Bioinformation Center, Korea Research Institute of Bioscience and Biotechnology, Daejeon, Korea²

PE2 Gliclazide does not fully prevent 2-deoxy-D-ribose-induced oxidative damage because it does not restore glutathione content in a pancreatic β -cell line

Gwanpyo Koh^{1*}, Sang Ah Lee¹, Dae-Hoo Lee¹, Hyoun-Jung Chin²
Jeju National University Hospital¹, Hankook General Hospital²

PE3 Molecular mechanisms of early growth response protein-1 (EGR-1) expression by quercetin in INS-1 beta-cells and the role of EGR-1 in cell proliferation

Jae Min Cho*, Seo-Yoon Chang, Yang-Hyeok Jo, Myung-Jun Kim
Departments of Physiology, College of Medicine, The Catholic University of Korea

PE4 Protective effect of GLP-1 analogue (exenatide) in mouse pancreatic β -cell line: a role of SREBP1c

Seok-Woo Hong^{1*}, Jin-Mi Lee¹, Ji-Hun Choi², Se-Eun Park², Eun-Jung Rhee², Cheol-Young Park², Ki-Won Oh², Sung-Woo Park², Sun-Woo Kim², Won-Young Lee²
Institute of Medical Research, Kangbuk Samsung Hospital¹, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital²

PE5 Effect of combination of metformin and fenofibrate on glucose homeostasis in diabetic Goto-Kakizaki rats

Tae Jung Oh*, Ji Yon Shin, Kyong Soo Park, Young Min Cho
Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

PE6 Effects of Resveratrol on the pancreatic islets in an animal model of type 2 diabetes

Young-Eun Lee^{1*}, Eun-Mi Lee¹, Esder Lee¹, Ki-Ho Song¹, Yu-Bae Ahn¹, Guolian Li², Zhenqi Liu², Seung-Hyun Ko¹
Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea¹, Department of Internal Medicine, University of Virginia Health System, Charlottesville, VA²

PE7 Transplantation of insulin secreting cells differentiated from human adipocyte-derived stem cells into type 2 diabetes mice

Ji Sun Nam^{1*}, Hyun Mi Kang², Jiyoung Kim², Seah Park², Haekwon Kim², Shin Ae Kang¹, Jong Suk Park¹, Kyung Wook Kim¹, Chul Woo Ahn¹, Kyung Rae Kim¹, Chul Woo Ajm¹
Department of Internal Medicine, Yonsei University College of Medicine¹, Department of Biotechnology, Seoul Women's University²

- PE8 Autologous islet transplantation after partial pancreatectomy can improve insulin secretion and induce better glycemic control than oral hypoglycemic agents**
Ji Won Yoon^{1*}, Shin Hee Hong¹, Jung Hee Kim¹, Min Joo Kim¹, Yenna Lee¹, Eun Ky Kim¹, Hak Mo Lee¹, Sung Soo Chung¹, Hyo Cheol Kim¹, Jin Young Jang¹, Kyoung Bun Lee¹, Kyong Soo Park¹, Seong Yeon Kim¹, Hye Seung Jung¹
Department of Internal Medicine, Seoul National University College of Medicine¹, Department of Radiology, Seoul National University College of Medicine², Department of Surgery, Seoul National University Hospital³, Department of Pathology, Seoul National University College of Medicine⁴
- PE9 Altered glucagon levels in early diabetes**
Jung Hwan Park^{*}, Sang Mo Hong, Chang Bum Lee, Yong Soo Park, Woong Hwan Choi, You Hern Ahn, Tae Wha kim, Dong Sun Kim
Department of Internal Medicine, College of Medicine, Hanyang University, Seoul, Korea
- PE10 A case of insulin autoimmune syndrome in patient with Hashimoto's thyroiditis**
Sang-Yoon Kim^{1*}, Sang-Jin Kim¹, Mi-Kyung Kim¹, Hye-Soon Kim¹, Won-Ki Baek², Dae-Kyu Song³, Ho-Chan Cho¹
Department of Internal Medicine, Keimyung University DongSan Medical Center, Daegu, Korea¹, Department of Microbiology, Keimyung University School of Medicine², Department of Physiology, Keimyung University School of Medicine³
- PE11 A case of autoimmune polyglandular syndrome type IIIA including type 1 diabetes with concomitant pseudohypoparathyroidism**
Sang-Jin Kim^{1*}, Sang-Yoon Kim¹, Won-Ki Baek², Dae-Kyu Song³, Ho-Chan Cho¹
Department of Internal Medicine, Keimyung University DongSan Medical Center, Daegu, Korea¹, Department of Microbiology, Keimyung University School of Medicine², Department of Physiology, Keimyung University School of Medicine³

Acute & chronic complication

199

- PE12 The role of estrogen-related receptor gamma (ERRg) in the development of vascular calcification**
Ji-Hyun Kim^{1*}, Han-Jong Kim¹, Joon-Young Kim³, Young-Keun Choi³, Chae-Myeong Ha¹, Sun Joo Lee¹, Chang Joo Oh¹, Jeong-Kook Kim¹, Eonju Jeon², Hyun-Ae Seo², Jong Ho Kim², Yeon Kyung Choi², Keun-Gyu Park², In-Kyu Lee¹
Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, South Korea¹, Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea², Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea³
- PE13 Cilostazol inhibits plasminogen activator inhibitor type 1 expression in liver**
Yun-A Jung^{1*}, Hye Soon Kim¹, Sang Yoon Kim¹, Keun Gyu Park², In Kyu Lee², Mi-Kyung Kim¹
Department of Internal Medicine and Institute for Medical Science, Keimyung University School of Medicine¹, Department of Internal Medicine, Kyungpook National University School of Medicine²
- PE14 Peroxisomal dysfunction exacerbated renal injury in diabetic catalase null mice**
Inah Hwang^{1*}, Jiyoun Lee¹, Jehyun Park¹, Hi Bahl Lee², Ye-Shih Ho³, Hunjoo Ha¹
Department of Bioinspired Science, Division of Life & Pharmaceutical Sciences, the Center for Cell Signaling & Drug Discovery Research, and College of Pharmacy, Ewha Womans University, Seoul, Korea¹, Kim's Clinic and Dialysis Unit, Myrang, Korea², Institute of Environmental Health Sciences, Wayne State University, Detroit, Michigan, USA³
- PE15 Protective effect of alpha-lipoic acid on vascular calcification**
Chae-Myeong Ha^{1*}, Han-Jong Kim², Joon-Young Kim², Young-Keun Choi¹, Sun Joo Lee¹, Chang Joo Oh¹, Jeong-Kook Kim¹, Ji-Hyun Kim¹, Udayakumar Karunakaran¹, Ji Yun Jeong³, Eonju Jeon³, Hyun-Ae Seo³, Jong-Ho Kim³, Yeon-Kyung Choi³, Jung-Guk Kim³, Keun-Gyu Park³, In-Kyu Lee³
Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, South Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea³

- PE16 Epicardial adipose tissue thickness assessed by cardiac magnetic resonance is an independent indicator for coronary artery stenosis, but not silent myocardial ischemia in asymptomatic type 2 diabetic patients**
Hyun Min Kim^{1*}, Kwang Joon Kim¹, Jae Hoon Moon¹, Hye-Jeong Lee², Young Jin Kim², Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-Wan Lee¹
Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea¹, Department of Radiology, Yonsei University College of Medicine, Seoul, Korea²
- PE17 The role of apolipoprotein B/apolipoprotein A1 ratio in predicting occult coronary atherosclerosis detected by multi-detector computed tomography**
Chang Hee Jung^{1*}, Jenie Yoonoo Hwang¹, Mi Seon Shin¹, Ji Hee Yu¹, Eun Hee Kim², Sung Jin Bae², Dong Hyun Yang³, Joon-Won Kang³, Joong-Yeol Park¹, Woo Je Lee¹, Hong-Kyu Kim²
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- PE18 The combination effect of pioglitazone and alpha lipoic acid on the peripheral nerves in experimental diabetic rats**
Kyung Ae Lee^{*}, Kyung Taek Park, Hea Min Yu, Heung Yong Jin, Hong Sun Baek, Tae Sun Park
Division of Endocrinology and Metabolism, Department of Internal Medicine, Research Institute of Clinical Medicine, Chonbuk National University Medical School, Jeonju
- PE19 Brachial-ankle pulse wave velocity and metabolic syndrome in Korean adults**
Ho Chan Cho^{1*}, Sang Jin Kim¹, Won Ki Baik², Dae Kyu Song², Hyun Sook Jang³, Pil Sook Park⁴, Byung Yeol Chun⁵, Dong Hoon Shin⁶
Department of Internal Medicine, Keimyung University Dongsan Medical Center, Daegu, South Korea¹, Chronic Disease Research Center, Keimyung University School of Medicine², Department of Home Economics Education, Kyungpook National University³, Department of Food and Nutrition, College of Science and Engineering, Kyungpook National University⁴, Department of Health Promotion Research Center, Kyungpook National University⁵, Department of Preventive Medicine, Keimyung University School of Medicine⁶
- PE20 Association between ankle-brachial index and nerve conduction study in type 2 diabetic patients**
Min Young Chung^{*}, Doo Young Lee, Jung sik Moon, Jin Ook Chung, Dong Hyeok Cho, Dong Jin Chung
Department of Internal Medicine, Chonnam National University Medical School
- PE21 Association between plasma leptin levels and chronic complications in type 2 diabetic patients**
Dong Jin Chung^{*}, Doo Young Lee, Jung Sik Moon, Jin Ook Chung, Dong Hyeok Cho, Min Young Chung
Department of Internal Medicine, Chonnam National University Medical School
- PE22 Hyperglycemic hyperosmolar syndrome in young diabetic patient accompanied by acute pyelonephritis and nephrogenic diabetes insipidus**
Jin Ook Chung^{*}, Doo Young Lee, Jung Sik Moon, Dong Hyeok Cho, Dong Jin Chung, Min Young Chung
Department of Internal Medicine, Chonnam National University Medical School
- PE23 Effect of sulforaphane on transforming growth factor- β /Smad in hepatic fibrosis**
Chang Joo Oh^{1*}, Joon-Young Kim², Ae-Kyung Min², Young-Keun Choi¹, Sun Joo Lee¹, Ji-Hyun Kim¹, Jeong-Kook Kim¹, Chae-Myeong Ha¹, Udayakumar Karunakaran¹, Jong Ho Kim³, Yeon Kyung Choi³, Eonju Jeon³, Hyun-Ae Seo³, Ji Yun Jeong³, Han-Jong Kim², In-Kyu Lee¹
Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, South Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea³

- PE24 The prevalence and clinical implications of painful diabetic neuropathy in Korea**
Jong Chul Won^{1*}, Huyk Sang Kwon², Chong Hwa Kim³, Ji Hyun Lee⁴, Tae Sun Park⁵, Bong Yun Cha², Kyung Soo Ko¹
Department of Internal Medicine, Cardiovascular and Metabolic Disease Center, Sanggye Paik Hospital, College of Medicine, Inje University, Seoul¹, Department of Internal Medicine, College of Medicine, Catholic University, Seoul², Department of Internal Medicine, Sejong General Hospital, Bucheon³, Department of Internal Medicine, College of Medicine, Catholic University, Daegu⁴, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju⁵
- PE25 The relation of lipid profiles and carotid intima media thickness in Korean type 2 diabetic patients**
Won Chul Ha*, Tae Seo Sohn, Su Jin Oh, Hyun Shik Son
The Catholic University of Korea, Uijeongbu St, Mary's Hospital
- PE26 The relationship between serum adipocyte fatty acid-binding protein, tumor necrosis factor- α and change of renal function in healthy adult**
Hee kwan Won*, Se Eun Park, Eun Jung Rhee, Cheol Young Park, Ki Won Oh, Sung Woo Park, Sun Woo Kim, Won Young Lee
Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sunkyunkwan University School of Medicine
- PE27 Diagnostic value of absence of coronary artery calcification in asymptomatic patients with type 2 diabetes**
Jaechan Leem*, Jung Eun Jang, Eun Hee Koh, Woo Je Lee, Min-Seon Kim, Joong-Yeol Park, Ki-Up Lee
Department of Internal Medicine, University of Ulsan College of Medicine, Seoul, Korea
- PE28 Exendin-4 modulates sclerostin level induced by rosiglitazone in osteocyte-like cells**
Ju-Young Kim*, Ji-Hyun Kim, Dong-Mee Lim, Youn-Zoo Cho, Keun-Young Park, Byung-Joon Kim
Division of Endocrinology, Department of Internal Medicine, Konyang University School of Medicine, Daejeon, Korea
- PE29 Association of serum adipokine levels with cardiac autonomic neuropathy, in Korean type 2 diabetic patients**
Chan Hee Jung*, Bo Yeon Kim, Chul Hee Kim, Sung Koo Kang, Ji Oh Mok
Soonchunhyang University School of Medicine, Bucheon
- PE30 Relationship with serum adipokine levels and microangiopathies in Korean type 2 diabetic patients**
Chan Hee Jung*, Bo Yeon Kim, Ji Oh Mok, Sung Koo Kang, Chul Hee Kim
Soonchunhyang University School of Medicine, Bucheon
- PE31 Effect of intrathecally administered cholera toxin in sepsis-induced hypoglycemia**
Yun-Beom Sim^{1*}, Soo-Hyun Park¹, Jin-Koo Lee², Seon-Mi Kim¹, Yu-Jung Kang¹, Sung-Su Kim¹, Su-Jin Kim¹, Ji-Young Seo¹, Chea-Ha Kim¹, Su-Min Lim¹, Hong-Won Suh¹
Department of Pharmacology, Institute of Natural Medicine, College of Medicine, Hallym University¹, Department of Pharmacology, College of Medicine, Translational Research Center, Institute of Bio-Science and Technology, Dankook University²
- PE32 The relationship between A1c variability and coronary angiographic finding in T2DM**
Jaejoon Kim*, Yeojeong Song, Mingu Chon, Jajun Goo, Kyoung-nyoun Kim, Jayoung Lee, Jihoon Kang, Jihye Suk, Taeik Kim, Mikyung Kim, Mikyung Kim
Dep. of Internal Medicine, Maryknoll Medical Center
- PE33 The relationship of thyroid stimulating hormone and free thyroxine levels with coronary angiographic finding in type 2 diabetes with normal thyroid function**
Jayoung Lee*, Mikyung Kim, Jajun Goo, Yeojeong Song, Mingu Chon, Jaejoon Kim, Kyoung-nyoun Kim, Jihoon Kang, Jihye Suk, Taeik Kim, Mikyung Kim
Dep. of Internal Medicine, Maryknoll Medical Center
- PE34 Association of serum adipocyte-specific fatty acid binding protein (A-FABP) with fatty liver index as predictive indicator of Non-alcoholic fatty liver disease(NAFLD)**
Won Seon Jeon*, Cheol Young Park, Se Eun Park, Eun Jung Rhee, Ki Won Oh, Sun Woo Kim, Sung Woo Park, Won Young Lee, Won Young Lee
Kangbuk Samsung Hospital

- PE35 High glucose and fatty acid increases BMP4 expression in human endothelial cells**
Hyuk-Sang Kwon*, Oak-Kee Hong, Soon-Jib Yoo, Mee-Kyung Kim, Ki-Hyun Baek, Ki-Ho Song, Kun-Ho Yoon, Ho-Young Son, Kwang-Woo Lee, Bong-Yun Cha
Department of Internal Medicine, The Catholic University of Korea
- PE36 The association between regional arterial stiffness and chronic kidney disease in type 2 diabetes**
Won Jun Kim*, Mi Hae Seo, Won Sun Jeon, Ji Hoon Choi, Hee Kwan Won, Seung Hyun Yoo, Se Eun Park, Eun Jung Rhee, Won Young Lee, Ki Won Oh, Sung Woo Park, Sun Woo Kim, Cheol-Young Park
Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine
- PE37 LDL particle size and microvascular complications in type 2 diabetes mellitus**
Eun-Hee Jang*, Seok-Jong Lee, Mee-Kyoung Kim, Ki-Hyun Baek, Ki-Ho Song, Kwang-Woo Lee, Hyuk-Sang Kwon
Yeouido St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea

Clinical diabetes & therapeutics

206

- PE38 Association of circulating metabolic intermediates with inflammatory and oxidative stress markers and arterial stiffness in male patients with newly-diagnosed type 2 diabetes**
Chang Young Ha^{1*}, Ji Young Kim³, Jean Kyung Paik², Oh Yoen Kim³, Eun Jig Lee⁴, Jong Ho Lee²
Interdisciplinary Course of Science for Aging, Graduate School, Yonsei University¹, Research Laboratory of Clinical Nutrigenetics/Nutrigenomics, Dept. of Food & Nutrition, College of Human Ecology, Yonsei University², Yonsei University Research Institute of Science for Aging, Yonsei University³, Division of Endocrinology, Yonsei University College of Medicine⁴
- PE39 Metabolic characteristics in Korean type 2 diabetic patients according to fatty liver and/or visceral obesity**
Eun Young Lee^{1*}, Sena Hwang¹, Young Ju Choi², Byung Wook Huh², Byung-Wan Lee¹, Eun Seok Kang¹, Bong Soo Cha¹, Eun Jig Lee¹, Hyun Chul Lee¹, Kap Bum Huh²
Department of Endocrinology and Metabolism, Yonsei University College of Medicine¹, Huh's Diabetes Center and 21st Century Diabetes and Vascular Research Institute²
- PE40 Dietary calorie restriction improves RBP4 and is associated with reduced visceral fat but not with hepatic lipid in obese women with type 2 diabetes**
Hee Jung Ahn^{1*}, Jin Young Jang¹, Hee Geum Seok¹, Jae Hyuk Lee², Gang Seo Park², Kyung Ah Han², Kyung Wan Min²
Diabetes Center, Eulji Hospital¹, Department of Internal Medicine, Eulji University School of Medicine²
- PE41 Aerobic exercise improves RBP4 and is associated reduced visceral fat in obese women with type 2 diabetes**
Kyung Hwa Cha^{1*}, Hee Jung Ahn¹, Jin Young Jang¹, Hee Geum Seok¹, Jae Hyuk Lee², Gang Seo Park², Kyung Ah Han², Kyung Wan Min²
Diabetes Center, Eulji Hospital¹, Department of Internal Medicine, Eulji University School of Medicine²
- PE42 Low serum magnesium levels were associated with the development of type 2 diabetes In women with history of gestational diabetes mellitus: The Korean National Diabetes Program (KNDP) study**
Sae Jeong Yang^{1*}, Tae Nyun Kim³, Sei Hyun Baik¹, Kwan Woo Lee⁴, Moon Suk Nam⁵, Yong Soo Park⁶, Jeong Taek Woo⁷, Young Seol Kim⁷, Sung-Hoon Kim²
Department of Internal Medicine, Korea University College of Medicine¹, Department of Medicine, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine², Department of Medicine, Haeundae Hospital, Inje University College of Medicine³, Department of Internal Medicine, Ajou University College of Medicine⁴, Department of Internal Medicine, Inha University College of Medicine⁵, Department of Internal Medicine, Hanyang University College of Medicine⁶, Department of Internal Medicine, Kyung Hee University College of Medicine⁷
- PE43 Influences of different gastrointestinal tract reconstruction approaches on postoperative pancreatic β -cell function in patients with type 2 diabetes mellitus**
Chao Zheng*, Jinli Cai, Zhenzai Cai
Department of endocrinology, Second Affiliated Hospital of Wenzhou Medical College, Wenzhou, China

- PE44 A case of brittle diabetes mellitus associated with circulating anti-insulin antibody**
Hee Kyung Kim*, Soo-Jung Kim, Jee-Hee Yoon, Ho-Cheol Kang
Department of Internal Medicine, Chonnam National University Hwasun Hospital, Chonnam University Medical School, Gwangju, South Korea
- PE45 Effect of lifestyle modification on serum chemerin concentration in overweight and obese adults with type 2 diabetes**
So Hun Kim^{1*}, Seung Hwan Lee², Justin Y. Jeon², Seung Youn Lee¹, Young Ju Suh³, Seong Bin Hong¹, Yong Seong Kim¹, Moonsuk Nam¹
Department of Internal Medicine, Inha University School of Medicine, Incheon, Korea¹, Department of Sport and Leisure Studies, Yonsei University, Seoul, Korea², Center for Clinical Research, Inha University School of Medicine, Incheon, Korea³
- PE46 The comparative study of dipeptidyl peptidase-IV inhibitor and sulfonylurea on the effect of improving glucose variability and oxidative stress in type 2 diabetic patients with inadequate glycemic control on metformin**
Hun-Sung Kim*, Jeong-Ah Shin, Jin-Sun Jang, Juyoung Shin, Jae-Hyoung Cho, Ho-Young Son, Kun-Ho Yoon
The Catholic University of Korea, Seoul, Korea
- PE47 The effect of telephone counseling on glycemic control in diabetes using insulin treatment**
Nam Keong Kim^{1*}, Ho Young Lee², Sang Jin Kim², Mi Kyung Kim², Ho Chan Cho², Hye Soon kim²
Department of Internal Medicine, Andong Hospital¹, Department of Internal Medicine and Institute for Medical Science, Keimyung University School of Medicine²
- PE48 A case of fulminant type 1 diabetes mellitus with HLA DRB1*0405/*0406-DQB1*0302/*0401**
Ye-Ri So*, Yu Chul Hwang, Yu Chul Hwang, Ho Yeon Chung, In-Kyung Jeong
Department of Endocrinology and Metabolism, Kyung Hee University Hospital at Gangdong
- PE49 HbA1c reflects dyslipidemia in older nondiabetic Korean adults**
JiHye Shin^{1*}, HaeJung Lee², SangYong Kim¹, HakYeon Bae¹, JinHwa Kim¹
Division of Endocrinology and Metabolism, Chosun University Hospital, Gwangju, Republic of Korea¹, Diabetes Center, Chosun University Hospital, Gwangju, Republic of Korea²
- PE50 The effect of seasonal vitamin D supplementation on glycemic control in Korea**
Ohk Hyun Ryu*, Juri Park, Jun Goo Kang, Sung Hoon Yu, Chul Sik Kim, Seong Jin Lee, Eun Gyoung Hong, Doo Man Kim, Sung Hee Ihm, Jae Myung Yu, Hyung Joon Yoo, Moon Gi Choi
Hallym University College of Medicine, Internal Medicine
- PE51 Achieving rate to low-density lipoprotein cholesterol goals in diabetic patients in real world clinical setting**
Min Jeong Kwon*, Eun Ju Lee, Jung Hae Ko, Tae Kyun Kim, Soon Hee Lee, Jeong Hyun Park
Department of Internal Medicine, College of Medicine, Inje University
- PE52 Clinical characteristics of patients admitted to emergency department with hypoglycemia**
Kyung Taek Park*, Tae Sun Park, Ji Hyun Park, Heung Yong Jin, Kyung Ae Lee, Hea Min Yu, Hong Sun Baek
Chonbuk National University Hospital, Department of Internal Medicine, Division of Endocrinology and Metabolism
- PE53 Usefulness of one-hour plasma glucose level in diabetes diagnosis in association with A1C**
Yang Ho Kang*, Dong Won Yi, Seok Man Son
Division of Endocrinology and Metabolism, Department of Internal Medicine, Pusan National University Yangsan Hospital, Pusan National University School of Medicine, Yangsan, Korea
- PE54 In addition to hypertension and high HbA1c, aspirin therapy and older age are risk factors of diabetic nephropathy**
Yu-Wen Cheng^{1*}, Shih-Liang Chang², Usman Malik¹
Lee's General Hospital, Miaoli, Taiwan¹, Department of Medicinal Botanicals and Health Applications, Da-Yeh University, Changhua, Taiwan²
- PE55 The clinical features of central obesity according to gender differences in patients with type 2 diabetes**
Hyeryun Jung*, Seung Jun Lee, Eui Dal Jung, Ji Hyun Lee, Ho Sang Shon, Jihyun Lee
Department of Internal Medicine, School of Medicine, Catholic University of Daegu

- PE56 The favorable effects of Kimchi on metabolic parameters in patients with type 2 diabetes mellitus**
So-Yeon An^{1*}, Min Suk Lee¹, Yong Jun Choi¹, Tae Ho Kim¹, Hye-Kyoung Lee¹, Won Sun Hwang¹, Sun Jung Choe¹, Seung Jin Han¹, Hae Jin Kim¹, Dae Jung Kim¹, Kwan-Woo Lee¹
Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, Republic of Korea¹, Division of Endocrinology, Department of Internal Medicine, Kwandong University, College of Medicine, Myongji Hospital, Goyang, South Korea², Department of Food Services and Clinical Nutrition, Ajou University School of Medicine, Suwon, Republic of Korea³
- PE57 The optimal cutoff value of waist circumference based on insulin resistance and visceral fat thickness in Korean type 2 diabetes**
Jung Soo Lim^{1*}, Young Ju Choi², Eun Jig Lee¹, Kap Bum Huh²
Endocrinology, Yonsei University College of Medicine¹, Huh's Diabetes Center and the 21 Century Diabetes and Vascular Research Institute²
- PE58 Urinary chiro- and myo-inositol levels as a marker for type 2 diabetes mellitus**
Hye Won Jang^{1*}, Kyu Ri Park², Min Kyeong Kim¹, Kyong Hye Joung¹, Tae Kyun Kim¹, Koon Soon Kim¹, Hyun Jin Kim¹, Young Suk Jo¹, Minho Shong¹, Bon Jeong Ku¹, Bon Jeong Ku¹
Department of Internal Medicine, Chungnam National University School of Medicine¹, Daejeon-Chungnam Branch, Korean Association of Health Promotion²
- PE59 Effects of the pravastatin on serum adiponectin levels and multimeric adiponectin in patients with type 2 diabetes mellitus and hypercholesterolemia**
Ji Hyun Kim^{*}, Ma Rie Rhee, Jung Ah Shin, Sung Soo Lee, Jung Min Lee, Soon Jib Yoo, Kun Ho Yoon, Sang Ah Chang
Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea
- PE60 DPP-4 inhibitor plus metformin treatment blunt glucose excursion more effectively than metformin alone or sulfonylurea plus metformin**
Sun Ok Song^{1*}, Kwang Joon Kim², Hyun Min Kim¹, Eun Young Lee¹, Jae Hoon Moon¹, Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-wan Lee¹
Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine¹, Severance Executive Healthcare Clinic², Korea
- PE61 Cathepsin K, L expression in adipocytes is upregulated by palmitate via TNF α and IL-6**
Jeong Seon Yoo^{1*}, Young-Mi Lee¹, Eun-Hae Lee¹, Shin-Young Lee¹, Ji-Woon Kim¹, Ki-cheon Jeong², Shin Ae Kang¹, Joo Young Nam², Jong Suk Park¹, Young Duk Song², Kyung Rae Kim¹, Hyun Chul Lee¹, Chul Woo Ahn¹
College of Medicine Yonsei University¹, NHIC Ilsan Hospital²
- PE62 Sarcopenic phenotype in patients with newly diagnosed type 2 diabetes**
Hee Kyoung Jeong^{*}, Jang Won Son, Seong Su Lee, Sung Rae Kim, Soon Jib Yoo
Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Bucheon, Korea
- PE63 The usability of 1,5-anhydroglucitol in diagnosis of diabetes**
Mee Kyoung Kim^{*}, Hyuk-Sang Kwon, Ki-Hyun Baek, Eun Hee Jang, Kwang Woo Lee, Ki-Ho Song
Yeouido St. Mary's Hospital, The Catholic University of Korea, Seoul, Korea
- PE64 Resolution of type 2 diabetes following IFN-a therapy for chronic hepatitis C**
Juri Park^{*}, Hyung Joon Yoo, Moon Gi Choi, Sung Hee Ihm, Jae Myung Yoo, Eun Gyung Hong, Seong Jin Lee, Chul Sik Kim, Ohk Hyun Ryu, Jun Goo Kang, Sung Hoon Yu, Doo-Man Kim
Hallym University Medical Center
- PE65 The effect of ACEI or ARB on contrast medium induced acute kidney injury after coronary angiography in type 2 diabetes**
Jajun Goo^{*}, Yeojeong Song, Mingu Chon, Jaejoon Kim, Kyoung-nyoun Kim, Jayoung Lee, Jihoon Kang, Jihye Suk, Taeik Kim, Mikyung Kim, Mikyung Kim
Dep. of Internal Medicine, Maryknoll Medical Center, Busan, Korea

- PE66 Relationship between microangiopathy and brachial-ankle pulse wave velocity(baPWV) in type 2 diabetic patients**
Eunju Lee*, Taekyun Kim, Minjeong Kwon, Soonhee Lee, Jeonghyun Park
Department of Internal Medicine, College of Medicine, Inje University, Busan, Korea
- PE67 A case of hypoglycemia with type 2 diabetes mellitus having taken metformin and vildagliptin**
Mi Yeon Kang*, Jung Min Kim, Jae Won Bum
St. Carollo Hospital
- PE68 Three cases of fulminant type 1 diabetes developed after drug-induced hypersensitivity syndrome**
Chao Zheng*, Xiaoying Wu
Department of Endocrinology, Second Affiliated Hospital of Wenzhou Medical College, Wenzhou, China
- PE69 Unusual two cases diagnosed with different types of diabetes presenting similar clinical symptom**
Sutoung Park*, Younggu Kim, Eunju Lee, Taekyun Kim, Minjeong Kwon, Soonhee Lee, Jeonghyun Park
Department of Internal Medicine, College of Medicine, Inje University, Busan, Korea
- PE70 Clinical characteristics of the DPP4 inhibitors responders in Korean subjects with type 2 diabetes**
Tae Jung Oh*, Bae Jae Hyun, Yeong Gi Kim, Young Min Cho, Kyong Soo Park, Seong Yeon Kim, Hye Seung Jung
Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea
- PE71 Effects of nutrition education on the dietary compliance recognition and blood glucose control in patients with type 2 diabetes mellitus**
Mi Ja Kim^{1*}, Sun Yung Ly¹, Kyoung Hye Yu¹
Dept. of Culinary Nutrition, Woosong University¹, Dept. of Food and Nutrition, Chungnam National University², Dept. of Food and Nutrition, Daejeon Health Science College, Daejeon, Korea³
- PE72 Associated factors with the glycemic control in subjects with type 2 diabetes on insulin therapy**
Soo Kyoung Kim^{1*}, Jung Tae Sik¹, Jung Jung Hwa¹, Lee Sang Min¹, Kim Ho-Su¹, Chung Hye Soo², Kwon Sam², Jeong Gui-Hwa³, Cho Sung-Rae³, Jong Ryeal Hahm¹
Department of Internal Medicine, School of Medicine, Gyeongsang National University¹, Division of Endocrinology and Metabolism, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine², Division of Endocrinology and Metabolism, Changwon Fatima Hospital³
- PE73 The effects of a DPP-IV inhibitor on glucose control and islet function in Korean patients with type 2 diabetes**
Juyoung Shin*, Jin Sun Jang, Hun Sung Kim, Ho Young Son, Bong Yeon Cha, Kun Ho Yoon, Jae Hyoung Cho
Seoul St. Mary's Hospital
- PE74 Current status of therapeutic target achievement according to duration of diabetes in Korean type 2 diabetic patients**
Ji Hye Suk^{1*}, Mi Kyung Kim¹, Ja Young Park², Sung Pyo Son³, Sun Hae Shin³, Min Chul Kim⁴, Bo Hyun Kim⁵, Jun Hyeob Ahn⁶, Kwang Jae Lee⁷, Min Jung Kwon⁸, Sun Hee Lee⁸, Jeong Hyun Park⁸, In Joo Kim⁵, Chang Won Lee²
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- PE75 Which oral anti-diabetic drug or combinations is more safe and effective on adding insulin glargine in chronic uncontrolled type 2 diabetic patients?**
Jun Goo Kang^{1*}, Cheol-Young Park², Suk Chon³, Junghyun Noh⁴, Seung Joon Oh³, Chang Beom Lee⁵, Sung Woo Park¹
Department of Endocrinology and Metabolism, Hallym University School of Medicine, Hallym University Sacred Heart Hospital, GyeongGi, South Korea¹, Department of Endocrinology and Metabolism, Sungkyunkwan University School of Medicine, Kangbuk Samsung Hospital, Jongro, South Korea², Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine, Seoul, Republic of Korea³, Department of Endocrinology and Metabolism, Inje University, Ilsan Paik Hospital, Goyang, Republic of Korea⁴, Department of Endocrinology and Metabolism, Hanyang University School of Medicine, Seoul, Korea⁵

- PE76 Efficacy of exenatide in clinical practice in Korean type 2 diabetic patient**
Jin-sun Jang*, Bong-Yun Cha, Ho-Young Son, Kun-Ho Yoon, Jae-Hyoung Cho, Juyoung Shin, Jae-Hyoung Cho
Department of Endocrinology & Metabolism, Seoul St. Mary's Hospital, The Catholic University of Korea
- PE77 Prevalence of type 2 diabetes mellitus and glucose intolerance among persons with chronic liver diseases in Mongolia**
Byambatseren Jambaljav^{1*}, Tuul N², Yanjmaa S¹, Tsetsgee Dagvadorj¹
Department of Endocrinology, State Central Clinical Hospital of Mongolia¹, Department of Gastroenterology, State Central Clinical Hospital of Mongolia²

Behavioral medicine & education

216

- PE78 Performance of 7 point SMBG based on structured testing program study in clinical practice**
Kyoung Soo Kim*, Kyoung Soo Kim, Hyun-jung Yu, Mi-Suk Kim, Young-Suk Kim, Mi-Ryung Kim, Jihye Suk, Mikyung Kim, Young Suk Kim
Meryknoll Medical Center
- PE79 The relationship between health condition and health-related quality of life of adult diabetes patients**
Hae-Jung Lee^{1*}, So-Hui Kim¹, Hak-Yeon Bae², Sang-Yong Kim², Jin-Hwa Kim², Jong Park³
Doctoral Student, Health Sciences, Chosun University¹, Department of Internal Medicine, College of Medicine, Chosun University², Department of Preventive Medicine, College of Medicine, Chosun University³
- PE80 Myo-inositol, glycemic index, and insulin index of Korean fruits for DM patients**
Jung-Eun Yim^{1*}, Jee-Hyun Ryu¹, Wan-Hee Suk¹, Young-Seol Kim¹, Cheon-Seok Park¹, Ryowon Choue²
Dept. of Food and Nutrition, College of Natural Science, Changwon National University¹, Dept. of Medical Nutrition, Graduate school of East-West Medical Science, Kyung Hee University², Research Institute of Medical Nutrition, Kyung Hee University³, Dept. of Endocrine and Metabolism, College of Medicine, Kyung Hee University⁴, Dept. of Food Engineering, Kyung Hee University⁵
- PE81 The effect of information provision on lifestyle changes for impaired fasting glucose persons**
Jinsun Choi^{1*}, Eun Mi Kim², Seung Eun Lee¹, Yeo-jin Moon¹, Ji-hoon Choi³, Seung-hyun Yoo³, Won-jun Kim³, Se-eun Park³, Chul-Young Park³, Won-Young Lee³, Ki-Won Oh³, Sung-Woo Park³, Sun-Woo Kim³
Diabetes Mellitus Center, Kangbuk Samsung Hospital¹, Department of Dietetic, Kangbuk Samsung Hospital², Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine³
- PE82 Evaluation of diabetes education in patients with type 2 diabetes in Mongolia**
Enkhjargal Yanjmaa^{1*}, Kh,Altaisaikhan¹, Altaisaikhan Khasag¹
Lecturer School of Nursing HSUM¹, Diabetes Educator of SCCH²
- PE83 Comparison of accuracy of SMBG and self-management according to type of diabetes**
Jeong Eun Park^{1*}, Kang Hee Sim², Joo Wha Yoo³, Jung Hwa Lee⁴, Hyang Mi Jang⁵, Na Ri Roh⁶, Hee Sook Kim⁷
Diabetes Center, Cheil General Hospital & Women's Healthcare Center, Kwandong University, Seoul, Korea¹, Diabetes Education Unit, Samsung Medical Center, Seoul, Korea², Department of Nursing, Seoul National University Hospital, Seoul, Korea³, Diabetes Center, Kyunghee University Hospital at Gangdong, Seoul, Korea⁴, Diabetes Center, Gangnam Severance Hospital, Yonsei University, Seoul, Korea⁵, Division of Nursing, Yonsei University Health System, Seoul, Korea⁶, College of Nursing, Seoul National University, Seoul, Korea⁷
- PE84 Status on drug use patterns of diabetes mellitus in Bogra Diabetic Hospital of Bangladesh: An explorative survey among physicians and patients on knowledge and use**
Md. Ariful Haque Mollik^{1*}, Md. Saifur Rahman², Md. Abdur Razzak³, Md. Rohimul Faruque⁴, Azmal Ibna Hassan⁵, Dilara Ferdousi⁶
Peoples Integrated Alliance Bangladesh¹, Biogene Life Care Bangladesh², Jönköping University Sweden³, Bangladesh Development Service Center Bangladesh⁴, Practical Academy on Wise Education and Research Foundation Bangladesh⁵, University of Skövde Sweden⁶

- PE85 Analysis of the factors affect to dietary intake and blood sugar in diabetic patients**
Min Young Noh^{1*}, So Won Jung¹, Ji-sun Lee¹, Bok Rye Song², Kun Ho Yoon², Ho Young Son²
Department of Nutrition, The Catholic University of Korea, Seoul St. Mary's Hospital¹, Department of Internal Medicine, The Catholic University of Korea College of Medicine, Seoul, Korea²
- PE86 Basal characteristics and satisfaction of campers attending 2030 diabetes**
Hye Jin Lee^{1*}, Kyoung Ah Kim³, So Hun Kim⁴, Sin Gon Kim⁵, Chul Sik Kim⁶, Jong Chul Won⁷, Jae Myung Yu⁸, Sang Ah Chang⁹, Jae Hyeon Kim¹⁰, Eun Hee Kim¹¹, Sun Ah Park⁸, Seon Yeong Park¹², Koung Ok Yun¹³, So Yoon Yoon¹⁴, Eun Young Lee¹⁵, Jung Min Lee¹⁶, Jung Hwa Lee¹⁷, Hea Kyong Jin¹⁸, Soo Jeong Han¹⁹, Jeong Mi Lee²⁰, In Bin Jung²¹, Choon Hee Chung²
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- PE87 Alcohol intake and insulin resistance among vitamin D deficient diabetic patients**
HyunWook Cho^{*}, HeeJa Ko, HyunOk Park, GiYeon Lee, BoYoung Yone, EunKyoung Han, HaeYeon Lee, SungWan Chun, YeoJoo Kim, SangJin Kim, SungWan Chun
Soonchunhyang University Cheonan Hospital
- PE88 The correlation between patients' own assessments of their diabetes self-management and actual glycemic control**
Ju Hee Lee^{1*}, Jung Hun Ohn¹, Eun Shil Hong¹, Bo Kyung Koo², Sang Wan Kim², Ka Hee Yi², Min Kyong Moon²
Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea¹, Department of Internal Medicine, Seoul National University Boramae Hospital, Seoul, Korea²
- PE89 The effect of hypoglycemic experience during admission period on the self management of hypoglycemia**
Young Na^{*}, Hye-Sun So, Eun-Hee Jang, Mee-Kyoung Kim, Hyuk-Sang Kwon, Ki-Hyun Baek, Kwang-Woo Lee, Ki-Ho Song
Yeouido St. Mary's Hosipital, The Catholic University, Seoul, Korea
- PE90 Changes in cardiometabolic risk factors and dietary quality after web-based education program in metabolic syndrome men**
Ji Yeon Kang^{1*}, Suk Hee Sung¹, Yoo Kyoung Park², Tae In Choi¹, Yun Mi Paek¹
Division of Endocrinology & Metabolism, Department of Internal Medicine
- PE91 Effectiveness of decrease of diabetes risk in male workers using web-based education program**
Ji Yeon Kang^{1*}, Ji Young Lee¹, Yoo Kyoung Park², Tae In Choi¹, Yun Mi Paek¹
Radiation Health Research Institute, Korea Hydro & Nuclear Power Co., Ltd, Korea¹, Research Institute of Clinical Nutrition, Kyung Hee University, Seoul, Korea²
- PE92 Physical activity and obesity in type 2 diabetes**
Seungyeon Lee^{*}, Sohun Kim, Moonsuk Nam, Yongseong Kim, Seongbin Hong
Department of Internal Medicine, Inha University School of Medicine
- PE93 Development of a dietary index for Korean adults and its association with the risk of metabolic syndrome: The Korean Diet Index for Adults (KODIA)**
Inkyung Baik^{1*}, Nam H Cho³, Myoungsook Lee⁴, Chol Shin²
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Epidemiology & genetics

220

- PE94 A 20-week, randomized, multicenter, non-inferiority clinical trial to compare mitiglinide with voglibose in a basal-plus regimen with long-acting insulin glargine in patients with type 2 diabetes**
Jang-Won Son^{1*}, Soon-Jib Yoo¹, In-Kyu Lee², Jeong-taek Woo³, Sei Hyun Baik⁴, Hak Chul Jang⁵, Kwan Woo Lee⁶, Bong Soo Cha⁷, Yeon-Ah Sung⁸, Tae Sun Park⁹, Kun-Ho Yoon¹
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- PE95 The predictors of neonatal birth weight of Korean women with gestational diabetes mellitus**
Hee Sook Kim*, Jeong Eun Park, Sung Hoon Kim
College of Nursing, Seoul National University¹, Diabetes Center, Division of Endocrinology & Metabolism, Department of Medicine, Cheil General Hospital², Diabetes Center, Division of Endocrinology & Metabolism, Department of Medicine, Cheil General Hospital³
- PE96 The comparison of the insulin resistance and the prevalence of metabolic syndrome between North Korean Refugees and South Korean**
Joo Hyung Kim^{1*}, Dong Seop Choi¹, Sei Hyun Baik¹, Kyung Mook Choi¹, Nan Hee Kim¹, Ji A Seo¹, Hee Young Kim¹, Hye Jin Yoo¹, Sae Jung Yang¹, Yoon Jung Kim¹, Myongjin Cho¹, Chae Ryung Eun¹, Hae Yoon Choi¹, Ho Chul Hong¹, Yun Jeong Lee², Sin Gon Kim¹
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- PE97 Therapeutic effects of NecroX compound on nonalcoholic steatohepatitis by suppressing mitochondrial reactive oxygen species**
Hyo Kyun Chung^{1*}, Yong Kyung Kim¹, Ji-Hoon Park², Soung Jung Kim¹, Min Jeong Ryu¹, Min Hee Lee¹, Seong Eun Lee¹, Min Jeong Choi¹, Koon Soon Kim¹, Bon Jeong Koo¹, Ki Ryang Kweon², Chul-Ho Lee³, Hyun Jin Kim¹, Young Suk Jo¹, Minho Shong¹
Research Center for Endocrine & Metabolic Diseases, Chungnam National University School of Medicine, Daejeon¹, Department of Biochemistry, Chungnam National University School of Medicine, Daejeon², Animal Model Center, Korea Research Institute of Bioscience & Biotechnology (KRIBB), Daejeon³
- PE98 Vitamin D receptor gene polymorphisms and HLA DRB1*04 interaction in Saudi type 2 diabetes patients**
Nasser Al-Daghri*, Omar Al-Attas
Biomarkers Research Program, Biochemistry Department, College of Science, King Saud University, Riyadh 11451, Kingdom of Saudi Arabia (KSA); Prince Mutaib Chair for Biomarkers of Osteoporosis, King Saud University, Riyadh 11451, KSA; Center of Excellence in Biotechnology Research, King Saud University 11451, KSA
- PE99 Type 2 diabetes risk assessment in Mongolia**
Munkhtur Yadmaa^{1*}, Enkhjargal Yanjmaa², Sersumaa Purevdorj³
Central Regional Electricity Transmission Grid State Owned Stock Company¹, School of nursing HSUM², Chingeltei Health Center³
- PE100 Long-term changes of the prevalence and control rate of hypertension among Korean adults with diagnosed diabetes: 1998-2008 Korean National Health and Nutrition Examination Survey (KNHANES)**
Jae-Seung Yoon^{1*}, Seung-Hyun Ko¹, Yu-Bae Ahn¹, Sun-Hye Ko¹, Won-Chul Lee², Yong-Moon Park²
Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea¹, Department of Preventive Medicine, The Catholic University of Korea²
- PE101 Observations on the traditional phytotherapy for gestational diabetes among the inhabitants of the Narayanganj district in Bangladesh**
Md. Ariful Haque Mollik^{1*}, Md. Torikul Islam², Krishna Nando Bhattacharyya³, Bivash Chandra Panday⁴
Peoples Integrated Alliance Bangladesh¹, Tarash Kalyan Sangstha Bangladesh², America Bangladesh Friendship Forum United States of America³, Practical Academy on Wise Education and Research Foundation Canada⁴

- PE102 CA19-9 level according to fasting glucose level in general population**
Bu Kyung Kim*, Yo-Han Park, Young Sik Choi
Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea
- PE103 The effect of metabolic syndrome and smoking on arterial stiffness**
Bu Kyung Kim*, Yo-Han Park, Young Sik Choi
Department of Internal Medicine, Kosin University College of Medicine, Busan, Korea
- PE104 Association of pyruvate dehydrogenase kinase 4 gene polymorphisms with type 2 diabetes and metabolic syndrome**
Seong-Su Moon*, Young Sil Lee
Department of Internal Medicine, Dongguk University School of Medicine
- PE105 Association analysis of the gene SNPs related to both obesity risk and physical fitness**
Hyun-Jun Kim*, Tae Gil Yang, Yeong Geun Kim, Dong Hoon Lee
Department of Physical Education, Kyungnam University
- PE106 Association of lipid and lipoprotein profiles with future development of type 2 diabetes in non-diabetic Korean subjects: A 4-year retrospective, longitudinal study**
Mihae Seo^{1*}, Ji Cheol Bae², Se Eun Park¹, Eun Jung Rhee¹, Cheol Young Park¹, Ki Won Oh¹, Sung Woo Park¹, Sun Woo Kim¹, Won Young Lee¹
Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea¹, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea²
- PE107 Explosive increase in diabetes health care utilization in Korea; 1990-2008**
Kyung Sun Park^{1*}, Sei-Rok Doh², Soo-Kyung Kim¹, Yong-Wook Cho¹, Seok Won Park¹
Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea¹, Korea Institute of Health and Social Affairs, Center for Health and Social Affairs Statistics, Seoul, Korea²
- PE108 Prevalence of diabetic complication and clinical characteristics in newly diagnosed Korean type 2 diabetic patients: Korean type 2 diabetes prospective cohort study**
Moon Chan Choi*, Sang Ouk Chin, Sang Youl Rhee, Suk Chon, You Cheol Hwang, In-Kyung Jeong, Seungjoon Oh, Kyu Jeung Ahn, Ho Yeon Chung, Jeong-taek Woo, Sung-Woon Kim, Jin-Woo Kim, Young Seol Kim
Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine
- PE109 The association between socio-economic status and the prevalence of diabetes mellitus in the Korean population**
Bo Kyung Koo*, Jung Hun Ohn, Eun Shil Hong, Sang Wan Kim, Ka Hee Yi, Min Kyong Moon
Seoul National University, College of Medicine¹, BORAMAE Medical Center²

Insulin action & obesity

224

- PE110 Peroxiredoxin 3 is a key molecule regulating adipocyte oxidative stress, mitochondrial biogenesis, and adipokine expression**
Joo Young Huh^{1*}, Kong-Joo Lee², Hunjoo Ha²
College of Pharmacy, Division of Life & Pharmaceutical Sciences¹, Department of Bioinspired Science, Ewha Womans University, Seoul, Korea²
- PE111 Effects of pyruvate dehydrogenase kinase 2 (PDK2) deficiency on hepatic steatosis induced by the high fat diet**
Younghoon Go^{1*}, Younghoon Go¹, Nam Ho Jeoung⁴, Ji-yun Jeong³, Ae-Kyung Min², Hyeon-Ji Kang¹, Bo Yoon Park¹, Eon-Ju Jeon³, Hyun-Ae Seo³, Jong Ho Kim³, Yeon Kyung Choi³, Keun-Gyu Park³, Robert A. Harris⁵, In-Kyu Lee³, In-Kyu Lee¹
Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea³, Department of Fundamental Medical and Pharmaceutical Sciences, Catholic University of Daegu, Daegu, Korea⁴, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Roudebush VA Medical Center, Indianapolis, U.S.A.⁵

- PE112 Various oscillation patterns of serum FGF21 concentrations in healthy volunteers**
Sang Ah Lee^{1*}, Eun Hee Kim², Mi-Seon Shin², Jenie Yoonoo Hwang², Eun Hee Koh², Woo Je Lee², Joong-Yeol Park², Eunheui Jeong², Min-Seon Kim²
Department of Internal Medicine, Jeju National University School of Medicine¹, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine²
- PE113 PRMT1 regulates hepatic gluconeogenesis via FoxO1**
Dahee Choi^{*}, Kyoung-Jin Oh, Hyesook Han, Seung-Hoi Koo
Department of Molecular Cell Biology, Sungkyunkwan University School of Medicine
- PE114 A crucial role for TCF4M, a short splice variant of TCF7L2, in regulation of hepatic glucose metabolism**
Kyoung-Jin Oh^{*}, Jinyoung Park, Seung-Hoi Koo
Department of Molecular Cell Biology, Sungkyunkwan University School of Medicine 300 Chunchun-dong, Jangan-gu, Suwon, 440-746, Gyeonggi-do, Korea
- PE115 WITHDRAWN**
- PE116 WITHDRAWN**
- PE117 cAMP responsive element binding protein 3-like 3 (CREB-H) decreases hepatic lipogenesis**
Ae-Kyung Min^{2*}, Young Hoon Go³, Hyeon Ji Kang³, Bo Yoon Park³, Udayakumar Karunakaran³, Ji Yun Jeong¹, Eon Ju Jeon¹, Hyun Ae Seo¹, Keun Gyu Park¹, In-Kyu Lee¹
Department of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, Korea³
- PE118 Inhibitory effects of AG330 on adipocyte differentiation and obesity**
Hyeon-Ji Kang^{1*}, Younghoon Go¹, Ae-Kyung Min², Bo-Yoon Park¹, Hyun-Ae Seo³, Ji Yun Jeong³, Eon Ju Jeon³, Keun-Gyu Park³, In-Kyu Lee³
Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, Korea¹, Department of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, Korea², Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Korea³
- PE119 Anti-atherogenic effect of S-adenosylmethionine through heme oxygenase-1 induction ameliorating endoplasmic reticulum stress in endothelial cells**
Jaechan Leem^{*}, Jung Eun Jang, Eun Hee Koh, Woo Je Lee, Min-Seon Kim, Joong-Yeol Park, Ki-Up Lee
Department of Internal Medicine, University of Ulsan College of Medicine, Seoul, Korea
- PE120 Effect of high glucose on IGFBP-5 expression in cardiac fibroblast**
Seung Eun Song^{*}, So Young Park, Yong Woon Kim, Jong Yeon Kim, Kyung Oh Doh, So Young Park
Department of Physiology, Yeungnam University College of Medicine¹, Aging-associated Vascular Disease Research Center, Yeungnam University College of Medicine, Daegu 705-717, Korea²
- PE121 WITHDRAWN**
- PE122 Association between serum free thyroxine and coronary artery calcification in healthy euthyroid subjects**
Eun Sook Kim^{*}, Je-Ho Han, Sungdae Moon
Division of Endocrinology, Department of Internal Medicine, Incheon St. Mary's Hospital, the Catholic University of Korea, Incheon, Korea
- PE123 The effect of fenofibrate on the morphology of the mitochondria of liver in obese (OLETF) rats**
Su Kyung Park^{1*}, Hye-Jeong Lee², Mi-Kyoung Park¹, Duk Kyu Kim¹
Department of Internal medicine, College of Medicine, Dong-A University¹, Department of Pharmacology, College of Medicine, Dong-A University²
- PE124 The increases in hepcidin and fat accumulation in pancreas of the high fat/iron overloaded mice**
Joo Sun Choi^{*}, Hyo Jung Lee, In-Uk Koh, Jihyun Song
Division of Metabolic Diseases, Center for Biomedical Sciences, Korea National Institute of Health, Chungbuk 363-951, Korea

- PE125 Role of AMP-activated protein kinase in biosynthesis of S-Adenosyl-L-methionine in liver**
Hye-Jeong Lee^{1*}, Eunhui Seo¹, Ae-wha Seo¹, So-Young Park¹, Sang-Oh Choi¹, Soo-Kyoung Park², Mi-Kyoung Park², Duk Kyu Kim²
Department of Pharmacology, Dong-A University College of Medicine¹, Department of Internal Medicine, Dong-A University College of Medicine²
- PE126 Ectopic expression of olfactory receptor in human endothelial cell**
Jenie Hwang*, Chang Hee Jung, Woo Je Lee, Yoon-Mi Kim, Joong-Yeol Park
University of Ulsan, School of Medicine, Asan Medical Center
- PE127 Effects of acetyl-L-carnitine on fatty acid metabolism and insulin resistance in high fat diet-fed mice**
Jung-Hee Hong*, Jae Hyun Kim, Myung-Shik Lee, Kwang-Won Kim, Moon-Kyu Lee
Division of Endocrinology and Metabolism, Department of Medicine, Samsung Medical Center
- PE128 Association between metabolic risk factors and dietary intakes by the obesity level in male workers**
Yun Mi Paek*, Yun Mi Paek, Tae In Choi
Radiation Health Research Institute, Korea Hydro & Nuclear Power Co., Ltd, Korea
- PE129 Exendin-4 increased canonical wnt/ β -catenin signaling pathway, resulting in decrease of SREBP and PPAR γ in hepatocytes**
Jinmi Lee^{1*}, Seok-Woo Hong¹, Ji-Hun Choi², Se-Eun Park², Eun-Jung Rhee², Cheol-Young Park², Ki-Won Oh², Sung-Woo Park², Sun-Woo Kim², Won-Young Lee²
Institute of Medical Research, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea¹, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea²
- PE130 Visfatin induces sickness responses in the brain**
Byong Seo Park*, Sung Ho Jin, Byung Ju Lee
Department of Biological Sciences, College of Natural Sciences, University of Ulsan, Ulsan, Republic of Korea
- PE131 The increase of microRNA-96 induced by mitochondrial dysfunction causes insulin resistance in hepatocytes through the translational repression of IRS-1**
Hyo Jin Jeong*, Wan Lee
Department of Biochemistry, Dongguk University School of Medicine, Kyungju, Korea
- PE132 Hypothalamic vaspin/SERPIN12 mediates the anorexigenic action of leptin**
Gil Myoung Kang^{1*}, Byung Soo Youn³, Ju Young Lee¹, Hyun Kyong Kim¹, Ji Hee Yu², Mi-Seon Shin², So Young Gil¹, Joong-Yeol Park², Ki-Up Lee², Min seon Kim²
Asan Institute for Life Sciences¹, Department of Internal Medicine, University of Ulsan College of Medicine², Adipogen Inc., Incheon 406-840, Korea³
- PE133 The effects of growth hormone treatment on leptin, adiponectin and interleukin 1 β (IL1 β) changes in hypopituitarism patients**
Kyung Wook Kim*, SY Nam, CW Ahn, BS Cha, ES Lee, SK Lim, KR Kim, HC Lee
Yonsei University Hospital
- PE134 Exendin-4 directly ameliorates steatohepatitis by improvement of fat metabolism and insulin signaling**
In-Kyung Jeong^{1*}, Sung Jig Lim², You-Cheol Hwang¹, Kyu Jeung Ahn¹, Ho Yeon Chung¹, Min-Kyung Chae³, Hyung-Joon Yoo³, Seung-Hyun Koh⁴, Myung-Joon Kim⁵, Suk Chon¹, Seungjoon Oh¹, Jeong-taek Woo¹, Sung Woon Kim¹, Jin-Woo Kim¹, Young Seol Kim¹
Department of Endocrinology & Metabolism, Graduate School of Medicine, KyungHee University, Korea¹, Department of Pathology, Graduate School of Medicine, KyungHee University, Korea², Department of Internal Medicine, Hallym University, Korea³, Department of Endocrinology and Metabolism, Catholic Medical School, Korea⁴, Department of physiology, Catholic Medical School, Korea⁵
- PE135 The usefulness of fat mass index to diagnose the metabolically un-healthy obese people**
Sang Mo Hong*, Chang Beom Lee, Yong Soo Park, Dong Sun Kim, You Hern Ahn, Tae Wha Kim, Woong Hwan Choi
Endocrinology and Metabolism, Hanyang University College of Medicine, Seoul, Korea

PLENARY LECTURES



Andrew J.M. Boulton

- Department of Medicine, University of Manchester, UK
- E-mail: Andrew.j.Boulton@man.ac.uk

• Education and Appointments

- 1976 MB, BS (with Honours), University of Newcastle-upon-Tyne
- 1979 MRCP (UK)
- 1981-1986 Senior Medical Registrar, Royal Hallamshire and Northern General Hospitals, Sheffield
- 1983-1984 Visiting Assistant Professor of Medicine, Division of Endocrinology, University of Miami, School of Medicine, Miami, Florida
- 1985 MD (PhD equivalent), University of Newcastle-upon-Tyne
- 1986-1995 Senior Lecturer, then Reader (from 1991) in Medicine, University of Manchester, and Consultant Physician, Manchester Royal Infirmary
- 1992 FRCP
- 2003 DSc(Hon), University of Cluj, Romania
- 1995- Professor of Medicine, University of Manchester and Consultant Physician, Manchester Royal Infirmary, Oxford Road, Manchester, Manchester, M13 9WL, UK
- 2002- Professor of Medicine, University of Miami, Diabetes Research Institute, Suite 3054, 1450 North West 10th Avenue, Miami, FL 33136, USA

• Research Interests

Diabetic complications, diabetic neuropathy, diabetic foot.
GCP training July 2009.

• Brief List of Publications

Author of more than 400 papers and 8 books on the above topics.

The diabetic foot in 2011

Andrew J.M. Boulton

University of Manchester, UK

Diabetic foot problems remain the commonest cause for hospital admission amongst diabetic patients in Western countries and recent data from Norway confirmed the high mortality in patients with a history of foot ulcers even after adjustment for other co-morbidities. In order to prevent foot ulcers an understanding of their pathogenesis is essential and good prospective data confirmed that the following are amongst the many risk factors for foot ulceration: Peripheral neuropathy, peripheral vascular disease, past history of foot ulceration or amputation, other microvascular complications (especially nephropathy), and foot deformity. Recent data suggests that patients with diabetes who are on dialysis for end stage diabetic nephropathy are amongst the highest risk of all subjects for development of foot problems. All patients with diabetes therefore should undergo an annual comprehensive diabetic foot examination to assess their risk of developing future ulcers or other problems. New tests including the Vibratip and the Ipswich touch test will be considered along with more traditional screening methods. It is important to classify foot

ulcers using a standard validated system such as the University of Texas wound classification system. In the Middle East and other African countries, neuropathic foot ulcers predominate: these are frequently plantar and the most important aspects of management are removing callous and dead tissue from the ulcer and its margins and removing pressure from the wound by using appropriate offloading techniques. There is an increasing evidence base to support the use of adjunctive therapies for more complex diabetic foot ulcers such as negative pressure wound therapy using vacuum assisted closure, and hyperbaric oxygen in predominantly ischaemic ulcers with no chance for vascular reconstruction. Infections should be assessed clinically and treated with appropriate targeted antimicrobial therapy. Most important in the management of the diabetic foot remains team work with the patient together with supporting physicians, surgeons, physical therapists, podiatrists, nurses and other health care professionals working together.



Philipp E. Scherer

- Touchstone Diabetes Center, UT Southwestern Medical Center, USA
- E-mail: Philipp.scherer@utsouthwestern.edu

• Education and Appointments

1987	Biocenter, Univ of Basel, Basel, Switzerland	MS
1992	Biocenter, Univ of Basel, Basel Switzerland	PhD
1992-1996	Whitehead Inst., Mass Inst. Techn., Cambridge, MA	Postdoctoral Fellow
1997-2007	Albert Einstein College of Medicine, New York	Assistant/Assoc./Full Professor
2007-present	UT Southwestern Medical Center of Dallas	Professor, Int. Med. & Cell Bio

• Research Interests

Current efforts in my laboratory are focused on the integrated physiology of the adipocyte and the impact on whole body energy homeostasis, inflammation and cancer. I have had a longstanding interest in adipocyte-derived factors (adipokines) and adipocyte physiology. As such, we have focused our efforts on adipose tissue and the cells that adipose tissue-derived factors target, such as hepatocytes, cardiac myocytes and beta cells. We are approaching these questions with a multi-pronged approach that includes cell biological and biochemical approaches as well as the use of mouse genetics, with the ultimate goal to apply the findings to clinical questions related to diabetes and its sequelae.

• Brief List of Publications

- Holland, W.L., Miller, R.A., Wang, Z.V., Sun, K., Barth, B.M., Bui, H.H., Davis, K.D., Bikman, B.T., Halberg, N., Rutkowski, J.M., Wade, M.R., Tenorio, V.M., Kuo, M.S., Brozinick, J.T., Zhang, B.B., Birnbaum, M.J., Summers, S.S. and P. E. Scherer. 2011. Receptor-mediated activation of ceramidase activity initiates the pleiotropic actions of adiponectin. *Nature Medicine* Jan;17(1):55-63.
- Holland W.L., Bikman B.T., Wang L.P., Liu Y., Sargent K.M., Fontenot G.K., Pagliassotti M.J., Clegg D.J., Scherer P.E. and S.A. Summers. 2011. Toll-like receptor 4 in the control of lipid utilization: TLRs induce insulin resistance by promoting the synthesis of sphingolipids. *J. Clin. Invest.* (in press).
- Sun, K., Kusminski, C.M. and P. E. Scherer. 2011. Adipose Tissue Remodeling and Obesity, *J. Clin. Invest.* 121(6):2094-101
- Park, J., Euhus, D. and P.E. Scherer. 2011. Paracrine and Endocrine Effects of Adipose Tissue on Cancer Development and Progression, *Endocrine Reviews* (in press)
- Atzori, L., Griffin, J.L., Scherer, P.E. and I. Irminger-Finger. 2011. Editorial for the directed issue: "Metabolic pathways in cancer" *Int J Biochem Cell Biol.* (in press)
- Hamilton, M.P., Gore, M.O., Ayers, C.R., Wu, X., McGuire, D.K. and P. E Scherer. 2011. Adiponectin and cardiovascular risk profile in patients with type 2 diabetes mellitus: Parameters associated with adiponectin complex distribution. *Diab Vasc Dis Res.*, (in press)
- Deng, Y. and P. E. Scherer. 2010. Adipokines as novel biomarkers and regulators of the metabolic syndrome. *Ann N Y Acad Sci.*;1212(1):E1-E19.
- Landskroner-Eiger, S., Park, J., Israel, D., Pollard, J.W. and P. E. Scherer. 2010. Morphogenesis of the Developing Mammary Gland: Stage-Dependent Impact of Adipocytes. *Dev Biol.*; 344(2):968-78
- Park, J.Y., Kusminski, C.M., Chua, S. C. and P.E. Scherer. 2010. Leptin receptor signaling supports cancer cell metabolism through suppression of mitochondrial respiration in vivo. *American J. Path.* 177:3133-3144
- P.E. Scherer. 2010. Community Corner - Anti-Diabetes Wars: New Hope (Commentary); *Nat. Medicine*, 16 (9): 973
- Xu, Y., Berglund, E.D., Holland, W.L., Chuan, J-C, Fukuda, M., Rossi, J., Jones, J.E., Zigman, J.M., Lowell, B.B., Scherer, P.E. and J. K. Elmquist. 2010. 5-HT2CRs Expressed by Pro-opiomelanocortin Neurons Regulate Insulin Sensitivity in Liver. *Nat Neurosci.*;13(12):1457-920.

Systemic impact of adipocyte-derived factors: impact on hepatic physiology

Philipp E. Scherer

UT Southwestern Medical Center, USA

Aims: The transcription factor Xbp1 is the most conserved component of the unfolded protein response (UPR) pathway. Its spliced form, Xbp1s, is potently induced in liver in the postprandial state. The relevance of this induction remains unclear.

Methods: To examine the specific pathways under the control of the Xbp1s in the context of homeostasis in liver, we generated a mouse model with liver specific, inducible Xbp1s overexpression (LIXs).

Results: Acute expression of Xbp1s in hepatocytes leads to profound systemic changes in fuel utilization, rapid development of hypoglycemia and hepatic steatosis. The de-

fective metabolic adaptation LIXs animals is particularly apparent during the transition from the fed to the fasted state. This physiologic maladaptation is driven by an Xbp1s-driven upregulation of a number of target genes.

Conclusion: Our results provide the first evidence that Xbp1s plays a critical role in fuel switch in hepatocytes through modulation of carbohydrate metabolism, highlighting the Xbp1s pathway as a regulatory nexus to connect the UPR with whole body energy homeostasis. Adipocyte-derived factors can modulate this process very significantly.

SPECIAL LECTURE



Robert R. Henry

- VA San Diego Healthcare System, Chief, Section of Diabetes, Endocrinology & Metabolism, USA
- E-mail: Robert.Henry2@va.gov

• Education and Appointments

1969-1971	University of Winnipeg, Manitoba, Canada, Pre-Medical Science
1971-1975	University of Manitoba Medical School - M.D.
1975-1981	University of Manitoba Medical School
1980	University of Manitoba Medical School, Internal Medicine Residency 3 years (ABIM)
1981	University of Manitoba Medical School, Endocrinology Residency 2 years (FRCP(C))
1981-1982	University of Manitoba, Health Sciences Center, Assistant Clinical Professor of Medicine
1982-1983	University of Colorado Health Sciences Center, Diabetic Research Unit, Visiting Assistant Professor of Medicine
1984-1985	University of California, San Diego, Visiting Assistant Research Endocrinologist
1985-1991	University of California, San Diego, Assistant Professor of Medicine, In Residence
1991-1997	University of California, San Diego, Associate Professor of Medicine, In Residence
1993-1994	University of Edinburgh, Royal Infirmary, Visiting Professor of Medicine
1997-present	University of California, San Diego, Professor of Medicine, In Residence

• Brief List of Publications

1. Zimering, M, Anderson, R, Ge, L, Moritz, T, On behalf of the Veterans Affairs Diabetes Trial (VADT). (2011) Increased plasma basic fibroblast growth factor is associated with coronary heart disease in adult type 2 diabetes mellitus. *Metabolism Clinical and Experimental* (60) 284-91.
2. Saremi A, Moritz T, Anderson R, Abraira C, Duckworth W, Reaven P, On behalf of the Veterans Affairs Diabetes Trial (VADT). (2011) Rates and Determinants of Coronary and Abdominal Aortic Artery Calcium Progression in the Veterans Affairs diabetes Trial (VADT). *Diabetes Care* (33)12, 2642-47.
3. Anderson RJ, Bahm GD, Moritz TE, Kaufman D, Abraira C, Duckworth W. On behalf of the Veterans Affairs Diabetes Trial (VADT). (2011) Blood Pressure and Cardiovascular Disease Risk in the Veterans Affairs Diabetes Trail. *Diabetes Care* (34)1, 34-8.
4. DeFronzo RA, Tripathy D, Schwenke DC, Banerji M, Bray GA, Buchanan TA, Clement SC, Henry RR, Hodis HN, Kitabchi AE, Mack WJ, Mudaliar S, Ratner RE, Williams K, Stentz FB, Musi N, Reaven PD; ACT NOW Study. (2011) Pioglitazone for diabetes prevention in impaired glucose tolerance. *N Engl J Med* 24;364(12):1105-15.
5. Shah PK, Mudaliar S, Chang AR, Aroda V, Andre M, Burke P, Henry RR. Effects of intensive insulin therapy alone and in combination with pioglitazone on body weight, composition, distribution and liver fat content in patients with type 2 diabetes. *Diabetes Obes Metab*. 2011 Jan 27. Doi: 10.1111/j.1463-1326.2011.01370.x. (Epub ahead of print)
6. Peristein T, Henry RR, Mather K, Rickels M, Abate N, Grundy S, Mai Y, albu J, Marks J, Pool J, Creager M. The Effect of angiotensin Receptor Blockade on Endothelial Dysfunction and Insulin Resistance in Obese Hypertensive Patients. (Submitted)
7. Folsom JH, Sasaki A, Mudaliar S, Henry RR, Torres M, Golshan S, Glorioso DK, Jeste DV. (2011) Increased Framingham 10-year risk of coronary heart disease in older patients with psychosis. *Schizophrenia Research* 125(2-3):295-9. Epub 2010 Nov 19. Update
8. Henry RR, Smith SR, Schwartz SL, Mudaliar SR, List JF, Duan RY, Chen RS. (2011) Effects of saxagliptin on β -cell stimulation and insulin secretion in patients with type 2 diabetes. *Diabetes Obes Metab* 13:850-58.

New agents in development for therapy of type 2 diabetes

Robert R. Henry

University of California, San Diego, USA

Although there are numerous oral and injectable anti-diabetic agents available for the treatment of type 2 diabetes, many patients are unable to achieve and maintain acceptable glucose levels and minimize diabetic complications. Currently, there are numerous compounds with unique mechanisms of action that have progressed to phase 3 development. This includes the oral once-daily dual PPAR alpha/gamma agonist aleglitazar, the long acting once weekly GLP-1 injectable agonists exenatide QW, albiglutide, and delaglutide, and the sodium glucose co-transporter 2 receptor inhibitors dapagliflozin and canagliflozin. Aleglitazar combines the glucose lowering and cardiovascular (CV) risk factor benefits of PPAR gamma agonism with the beneficial lipid effects of PPAR alpha

activation. A large multi-national study of type 2 diabetes and acute coronary syndrome is currently underway. The once weekly GLP-1 agonists reduce A1c by 1.0-1.5% with associated weight loss of 3-5% body weight and possibly less nausea and vomiting. Their use results in CV risk factor benefits and several large CV event trials are underway. The once-daily SGLT2 inhibitors reduce proximal tubule glucose reabsorption and increase glycosuria, reducing A1c by 0.6-0.9% and body weight by 3-5%. Their use is associated with a small but consistent increase in genitourinary infections. The benefits and limitations of each class of medications will be reviewed as will their potential use in the management of type 2 diabetes.

SYMPOSIA



Cecile King

- Department of Immunology, Garvan Institute of Medical Research, Australia
- E-mail: c.king@garvan.org.au

• Education and Appointments

1993-1997	Institute for Child Health Research, UWA, Perth, Western Australia.	PhD candidate
1995-1996	Employer: University of Western Australia, Department of Microbiology and Immunology	Laboratory Demonstrator /Tutor
1997-2001	Department of Immunology, The Scripps Research Institute.	Research Associate
2002-2004	Department of Immunology, The Scripps Research Institute.	Senior Research Associate
2005-present	Department of Immunology, The Garvan Institute of Medical Research	Research Fellow
2006-present	The University of New South Wales	Adjunct senior Lecturer

• Research Interests

Type-1 diabetes, autoimmunity, cytokines, T cell subsets, T helper cell differentiation

• Brief List of Publications

1. Cecile King (2011). A fine romance: T follicular helper cells and B cells. *Immunity* 24;34(6):827-9.
2. Badami E, Sorini C, Coccia M, Usuelli V, Molteni L, Bolla AM, Scavini M, Mariani A, King C, Bosi E, Falcone M (2011). Defective Differentiation of Regulatory FoxP3+ T Cells by Small-Intestinal Dendritic Cells in Patients With Type 1 Diabetes. *Diabetes*, 2011 Jun 6.
3. Cho JH, Kim HO, Webster K, Palendira M, Hahm B, Kim KS, King C, Tangye S, Sprent J (2011).
4. Calcineurin-dependent negative regulation of CD94/NKG2A expression on naive CD8+ T cells. *Blood*, 2011 May 3.
5. Helen McGuire, Alexis Vogelzang, Cindy S Ma, William E. Hughes, Pablo Silveira, Stuart G Tangye, David Fulcher, Daniel Christ, Marika Falcone and Cecile King (2011). Diabetogenic CD4+ T cells comprise a novel T helper subset that co-express interleukin-21 and the chemokine receptor CCR9. *Immunity*, 2011 Apr 22;34(4):602-15.
6. Cecile King (2011). Regulation of T follicular helper cells. *Trends in Immunology*. Invited review in Press
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| S1-1 |

The role of interleukin-21 in the development of type-1 diabetes

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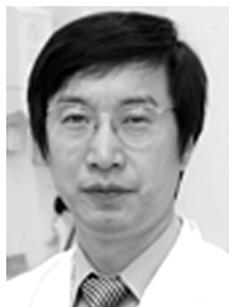
Objective: Type 1 diabetes is an incurable chronic autoimmune disease. While transplantation of pancreatic islets may serve as a surrogate source of insulin, recipients are subjected to a life of immunosuppression. Interleukin-21 is necessary for type 1 diabetes in NOD mice. We examined the efficacy of an IL-21 targeted therapy on prevention of diabetes in NOD mice, in combination with syngeneic islet transplantation and the role of IL-21 in islet allograft rejection. In addition, we identified which immune cells were required to respond to IL-21 for the development of diabetes.

Research Design and Methods: Diabetic NOD mice were treated with IL-21R/Fc, an IL-21 neutralizing chimeric protein combined with syngeneic islet transplantation. Survival of allogeneic islet grafts in IL-21R deficient mice was also assessed. The role of IL-21 was determined by the selective deletion on IL-21R on CD8+ T cells.

Results: Evidence is provided that IL-21 is continually

required by the autoimmune infiltrate, such that insulinitis was reduced and reversed, and diabetes inhibited by neutralization of IL-21 at a late preclinical stage. Recovery from autoimmune diabetes was achieved by combining neutralization of IL-21 with islet transplantation, resulting in both the protection of transplanted islets as well as the recovery of endogenous beta cell function in diabetic mice. Furthermore, IL-21-responsiveness by CD8+ T cells was sufficient to mediate islet allograft rejection and was critical for the development of diabetes in NOD mice.

Conclusions: Neutralization of IL-21 in NOD mice can inhibit diabetes, and when paired with islet transplantation, this therapeutic approach restored normoglycemia. The influence of IL-21 on a graft-mounted immune response was robust, since the absence of IL-21 signaling prevented islet allograft rejection. These findings suggest that therapeutic manipulation of IL-21 may serve as a suitable treatment for patients with type 1 diabetes.



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• Education and Appointments

1981	Seoul National University	MD
1990	Seoul National University	Ph.D.
1995	Scripps Research Institute	Research Associate
-present	Samsung Medical Center, Sungkyunkwan University	Professor

• Research Interests

Cell death, innate immunity, autophagy

• Brief List of Publications

1. Inami Y, Waguri S, Sakamoto A, Kouno T, Nakada K, Hino O, Watanabe S, Ando J, Iwadate M, Yamamoto M, Lee M-S, Tanaka K, Komatsu M. Persistent activation of Nrf2 through p62 in hepatocellular carcinoma cells. *J Cell Biol* 193:275-284, 2011
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| S1-2 |

Role of innate immunity in diabetes

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While it is generally agreed that apoptosis of pancreatic β -cells is the final step in type 1 diabetes (T1D), it has not been clearly elucidated which molecule(s) are the real culprit(s) in T1D. Combinations or synergism between $\text{IFN}\gamma$ + $\text{TNF}\alpha$ or $\text{IFN}\gamma$ + $\text{IL-1}\beta$ has been claimed as the death effectors. Dissection of the molecular mechanism explaining such a synergism suggests an important role for STAT1 as a signal transducer in β -cell death by cytokines and a disparate role for $\text{NF-}\kappa\text{B}$, one of the most important signaling pathways in innate immunity, according to the effector cytokines. In contrast to the final step, the initial step in the development of T1D has been elusive. Recently, we observed that late apoptotic β -cells with secondary necrosis elicited inflammation in macrophages through TLR2, one of the most important receptors for innate immune res-

ponses. Late apoptotic cells induced maturation of dendritic cells and activation of autoreactive T cells through TLR2/MyD88/ $\text{NF-}\kappa\text{B}$ signaling. *TLR2*-knockout mice showed defective priming of diabetogenic T cells by apoptotic β -cells. Furthermore, TLR2 deficiency conferred a significant protection against T1D, suggesting islet inflammation via innate immune receptors could be one of the initial events in T1D.

While islet inflammation has been regarded to be specific for T1D, recent papers reported that islet inflammation and innate immunity contribute to the development of T2D as well. Besides TLR activation, role for NLR activation and inflammasomes in T2D has been shown. Further investigation will be necessary to clarify the role of innate immunity in T1D and T2D.



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• Education and Appointments

1990	St. Johns. Medical College, Bangalore University	M.D., Medicine
1996	Royal Postgraduate Medical School University of London, England (PI: SR Bloom MD)	Ph.D., Biochemistry
1997-1999	Joslin Diabetes Center, Boston (PI: CR Kahn MD)	Post-Doc Fellowship, Cell. & Mol. Physiology
1986-1990	Resident Intern, Victoria Hospital; Research Officer, St John's Medical College, Bangalore Clinical Registrar & Research Fellow, Division of Endocrinology, Hammersmith Hospital, London Research Fellow/Research Associate, Joslin Diabetes Center and Harvard Medical School, Boston	
2000-2003	Instructor in Medicine, Harvard Medical School, Boston	
2000-	Principle Investigator, Joslin Diabetes Center, Boston	
2002-	Director, Specialized Assay Core, DERC, Joslin Diabetes Center, Boston	
2003-	Member, Fellowship Committee, Joslin Diabetes Center, Boston	
2004-	Member, IACUC Committee, Joslin Diabetes Center, Boston	
2004-2008	Assistant Professor of Medicine, Harvard Medical School, Boston	
2004-	Faculty Member, BBS Graduate Program, Harvard Medical School, Boston	
2004-	PhD/PQ Examiner, Harvard Univ.; Univ. Melbourne; Univ. Mass; Univ. Toronto	
2007-	Adjunct Faculty Member, Harvard Stem Cell Institute, Harvard Medical School, Boston	
2009-	Associate Professor of Medicine, Harvard Medical School, Boston	

• Research Interests

My research interests are focused on investigating signalling pathways impacting growth and function of pancreatic islet cells with the long-term goal of improving therapeutic approaches for the treatment of type 1 and type 2 diabetes and obesity-associated diabetes. I spend 85% of my total time towards research, 10% towards teaching and 5% towards administrative responsibilities.

• Brief List of Publications

1. Hinault, Kawamori D, Liew CW, Maier B, ... Mirmira R, Scrable H, Kulkarni RN*. Delta 40 isoform of p53 controls β -cell proliferation and glucose homeostasis in mice. *Diabetes* 60(4):1210-22, 2011. (*corresponding)
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| S1-3 |

Insulin regulation of pancreatic beta cell function and proliferation

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The pancreatic islets play a critical role in the maintenance of glucose homeostasis by regulating hormone secretion and synthesis from the endocrine pancreas. While it has been recognized that insulin regulates the function and metabolism of classical target tissues including the liver, skeletal muscle, and adipose a large body of scientific evidence gathered over the last decade points to insulin action in non-classical tissues including the pancreatic beta and alpha cells and the brain. The signaling pathways and key proteins that are involved in the effects of insulin in the regulation of insulin secretion and synthesis, proinsulin

processing, beta cell proliferation, and mitochondrial function are not fully explored. In this presentation I will discuss data from experiments aimed at understanding the link between growth factor (insulin and insulin-like-growth-factor-I) signaling and proinsulin processing, beta cell proliferation and insulin secretion in mouse and human islets and also provide evidence for the effects of exogenous insulin on beta cell function in healthy humans and in humans with impaired glucose tolerance or type 2 diabetes. These data have direct implications for a role for insulin in regulating beta cell biology.



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• Education and Appointments

1987-1991	Department of Genetic Engineering, Korea University	B.A.
1991-1993	Department of Genetic Engineering, Korea University	M.S.
1993-1998	Department of Genetic Engineering, Korea University	Ph.D.
1997-2000	CDRC, Graduate school of Biotechnology, Korea University	Senior Research Scientist
2000-2001	Mount Sinai School of Medicine, New York, USA	Post-Doctoral Fellow
2001-2003	Graduate school of Biotechnology, Korea University	Research Professor
2003-2007	Department of Animal Biotechnology, Konkuk University	Assistant Professor
2006-Present	Brain Korea 21 (BK21) Team, Dept. of Animal Biotechnology, Konkuk University	Director
2007-Present	Department of Animal Biotechnology, Konkuk University	Associate Professor
2011-Present	Institut Pasteur Korea	Visiting Professor

• Research Interests

Major: Generation of disease-specific induced pluripotent stem cells (iPSC)

We are studying about various signaling pathways involved in apoptosis and development, which will present helpful information in developing new therapy for cancer or other human diseases. Recently, we are focusing on generation of disease-specific induced pluripotent stem cells (iPSC) including diabetes-specific iPSC and characterization of the signaling pathways regulating cell proliferation, differentiation, or cell death of stem cells and cancer or cancer stem cells.

• Brief List of Publications

1. Chang Hyun Lee, Jung-Hyun Kim, Hyun Joo Lee, Kilsoo Jeon, HyeJin Lim, Hye yeon Choi, Eung-Ryoung Lee, Seung Hwa Park, Jae-Yong Park, Sunghoi Hong, Soonhag Kim*, Ssang-Goo Cho*. (2011) The generation of iPSC (induced pluripotent stem) cells using non-viral magnetic nanoparticle-based transfection. *Biomaterials*. 32 (2011) 6683-6691.
2. Deug-Nam Kwon, Mi-Ryung Park, Jong-Yi Park, Ssang-Goo Cho, Chankyu Park, Jae-Wook Oh, Hyuk Song, Jae-Hwan Kim, Jin-Hoi Kim. (2011) Characterization of a putative cis-regulatory element that controls transcriptional activity of the pig uroplakin II gene promoter. *Biochem. Biophys. Res. Commun.* 410(2): 264-269.
3. Eung-Ryoung Lee, Jung-Hyun Kim, Hye Yeon Choi, Kilsoo Jeon, and Ssang-Goo Cho. (2011). Cytoprotective effect of eriodictyol in UV-irradiated keratinocytes via phosphatase-dependent modulation of both the p38 MAPK and Akt signaling pathways. *Cell. Physiol. Biochem.* 27(5): 513-524.
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7. Kyung Tae Noh, Ssang-Goo Cho, and Eui-Ju Choi. (2010). Knockdown of apoptosis signal-regulating kinase 1 modulates basal glycogen synthase kinase-3 β kinase activity and regulates cell migration. *FEBS Lett.* 584 (2010): 4097-4101.

| S1-4 |

Differentiation of pancreatic epithelial cell-derived NOD-iPS cells into functional pancreatic insulin-producing cells

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Objective: The non-obese diabetic (NOD) mouse is a classical animal model for autoimmune type 1 diabetes (T1D), and exhibit clinical or immunological features that closely mimic those of human T1D patients. Thus, the prospect of induced pluripotent stem cells (iPSCs) as a therapeutic modality against established T1D should be verified in NOD mouse model.

Research Design and Methods: Here, we demonstrate a proof of concept for cellular therapy using NOD mouse-derived iPSCs (NOD-iPSCs). We generated iPSCs from NOD mouse-derived MEFs (NMs) or pancreas-derived-epithelial cells (NPEs) by constitutive expression of Oct4, Sox2, KLF4, and c-Myc genes, and applied directed differentiation protocols to differentiate the NOD-iPSCs toward functional pancreatic beta cells. Finally, we investigated whether the NOD-iPSC-derived insulin-producing cells could normalize hyperglycemia in transplanted diabetic mice.

Results: The NOD-iPSCs showed typical embryonic stem cell (ESC)-like characteristics such as expression of stemness markers, in vitro differentiation, teratoma formation, and generation of chimeric mice. Next, we tried a step-wise differentiation of the NOD-iPSCs to insulin producing cells, and found that NPE-iPSCs more efficiently differentiated into this cell type than the NM-iPSCs or even ESCs. Transplantation of the differentiated NPE-iPSCs into diabetic model

mice resulted in kidney engraftment of insulin-producing cells and normalization of blood glucose levels.

Conclusions: We propose that these NOD-iPSCs will provide a useful tool for investigating genetic susceptibility to autoimmune diseases and for generating a cellular interaction model of T1D. These data support the potential application of patient-derived iPSCs in autologous beta-cell transplantation in the treatment of diabetes.

INTRODUCTION

Type 1 diabetes (T1D), a polygenic autoimmune disease, has been linked to more than 25 loci and results from the destruction of the pancreatic beta cells through insulinitis (1). At present, pancreatic islet transplantation is a promising therapeutic option for T1D patients, but cell replacement therapy for T1D requires a source of glucose-responsive insulin-secreting cells (2). Although embryonic stem cells (ESCs) have been reported to differentiate into pancreatic beta-like insulin producing cells (3), cells derived from immunologically unmatched ESCs could be the targets of both allograft reactions and the autoimmune response that caused the initial cell destruction. An alternative source of insulin-producing cells may be the patient-derived iPSCs and an autologous approach would eliminate the possibility of allo-immune rejection of transplanted cells. We hypothesized that a combination of the cell reprogramming and differentiation techniques could be used for generation of

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patient-specific iPSCs and differentiation into pancreatic beta-like cells. Such cells could provide a promising resource for cell therapy to treat diabetes. The non-obese diabetic (NOD) mice spontaneously develop autoimmune T1D, which has many similarities to human autoimmune diabetes and is a valuable model for investigation of the pathogenesis and genetic susceptibility to T1D (4). Given the similarity to human T1D, we chose this model to test the effectiveness of a cell therapy approach.

RESEARCH DESIGN AND METHODS

1. Mice and cells

NOD/ShiJcl and NOD/scid mice were purchased from the Korean Research Institute of Bioscience and Biotechnology. In order to isolate mouse embryonic fibroblasts (MEFs), 14 Day - 7 embryos from NOD mice were used as previously described (5). To isolate pancreas-derived epithelial cells (PEs), a pancreas tissue from an 8 week old NOD mouse was used as previously described (6).

NMs and NPEs were infected with the concentrated self-inactivating human immunodeficiency virus (HIV) type-1 based lentiviral vectors encoding Oct4, Sox2, KLF4, and c-Myc under the control of EF-1 (elongation factor-1 alpha) promoter.

2. Bisulfite DNA sequencing, genotyping, flow cytometry, and RT-PCR analyses

Genomic DNA was purified from ESCs, NOD-iPSCs and NMs by using the Genomic DNA prep kit (QIAGEN) and DNA was utilized for bisulfite conversion using the EpiTect Bisulfite kit (QIAGEN), according to the manufacturer's protocol. The genotypes of the established NOD-iPSCs were determined using microsatellite markers (Mouse genome informatics; MGI). For Multi-color flow cytometry analysis, cells were trypsinized, washed twice in PBS, and then stained using the Multi-color flow cytometry kit (R&D systems). Total RNA was isolated using TRI reagent and cDNA was subjected to PCR amplification with specific primers.

3. Spontaneous differentiation and teratoma assay

To induce differentiation into the three embryonic layers, cells were cultured in suspension to form embryoid bodies (EBs) in low attachment dishes. The cells were subjected to an 8 day induction procedure (4-/4+) that consisted of 4 days of culture as aggregates without RA followed by 4 days of culture with RA. For teratoma formation assay, NOD- iPSCs were injected intramuscularly into hind leg of NOD/scid mice. Teratomas were excised 5 weeks after injection.

4. Eight cell stage injection and embryo transfer

B6D2F1 (C57BL/6 x DBA/2) and ICR male and female mice were used to produce in vitro fertilized eight-cell embryos. For eight-cell embryo injection, embryo injections were performed on eight-cell embryos before obvious compaction using an OLYMPUS micromanipulator.

5. Differentiation of the NOD-iPSCs into pancreatic beta-like cells and transplantation

ESCs and NOD-iPSCs were plated onto Matrigel-coated dishes and incubated for 3 days with X-Vivo 10 supplemented with BSA containing activin A. Then, the differentiated cells were cultured for 2 days in F12/Iscove's modified Dulbecco's medium (1:1) supplemented with BSA and insulin-transferrin-selenium (ITS) with RA. After RA induction, the cells were cultured in DMEM supplemented with BSA and ITS, together with bFGF and EGF and in DF 12 medium with ITS, bFGF and nicotinamide. The insulin levels in culture supernatants were measured using the rat/mouse ELISA kit (EZRMI-13K; Linco). Before transplantation, streptozotocin was injected intraperitoneally into NOD/scid mice and the differentiated cells were transplanted into the left subcapsular renal space. Grafts were removed 5 weeks after transplantation and analyzed by H/E staining or immunohistochemistry (immunofluorescence and DAB-nickel reactions).

RESULTS & DISCUSSION

The non-obese diabetic (NOD) mouse model is a classical animal model for autoimmune T1D, and exhibit clinical or immunological features that closely mimic those of human T1D patients. Thus, the prospect of induced pluripotent stem cells (iPSCs) as a therapeutic modality against established T1D should be verified in NOD mouse model. However, NOD mouse strain was known to be notoriously nonpermissive for derivation of ES cells.

First, we prepared MEFs (mouse embryonic fibroblasts) or PEs (pancreas-derived epithelial cells) from NOD mice and analyzed the expression level of pancreas-specific genes, such as HNF3b, PDX-1, and Pax6 using quantitative RT-PCR analysis (Fig. 1). Compared with the NOD-MEFs (NMs) and control ESCs (G4-2), NOD-PEs (NPEs) showed high expression of the pancreas-specific genes. We established NOD-iPSC lines and applied a chemically defined stepwise method to differentiate the NOD-iPSCs into functional pancreatic beta-like insulin producing cells. The dif-

ferentiated NOD-iPSCs expressed diverse pancreatic beta cell markers and secreted insulin in response to glucose and KCl stimulation. Moreover, when transplanted into diabetic mice, the NOD-iPSC-derived insulin-producing cells ameliorated hyperglycemia. Taken together, these results indicate that NPE-iPSC-derived insulin-producing cells when transplanted into the left subcapsular renal space were able to secrete insulin in vivo and to lower blood glucose levels in the STZ-treated diabetic mice.

Our data suggest that as an alternative to the Edmonton protocol, a combination of the cell reprogramming and differentiation techniques could be used to generate genetically matched patient-specific pancreatic beta cells which would create an unlimited source of beta cells, and reduce the requirement for immune-suppression drugs. Although the NOD mouse strain is considered a nonpermissive strain for ES cell derivation (7) due to requirement of specific exogenous factors to maintain the ICM-like pluripotent state (8), we could efficiently establish NOD-iPSC lines from both NMs and NPEs using lentiviral expression system, in which Oct4, Sox2, Klf4, and c-Myc genes are constitutively ex-

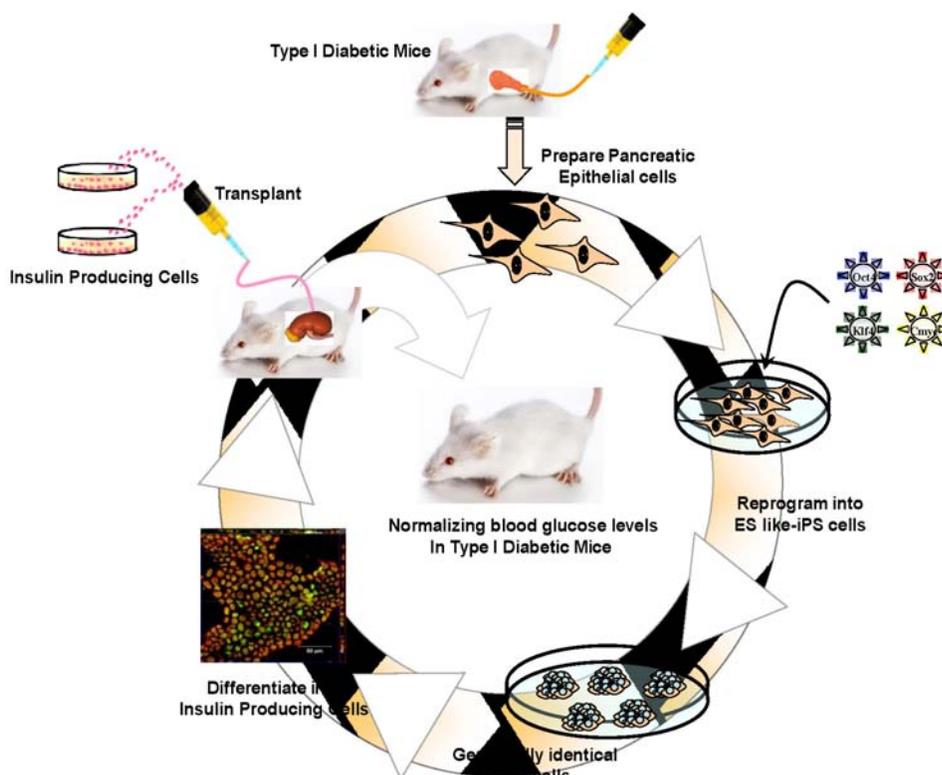


Fig. 1. A scheme summarizing the differentiation of pancreatic epithelial cell-derived NOD-iPSCs (NPE-iPSC) into functional pancreatic insulin-producing cells and the further transplantation results. The NPE-iPSC-derived insulin-producing cells which were transplanted into the left subcapsular renal space were able to secrete insulin in vivo and to lower blood glucose levels in the STZ-treated diabetic mice.

pressed under the control of EF-1 promoter. In our study, significant expression of endogenous Klf4 and c-Myc genes was detected in NMs and NPEs, while endogenous expression of Oct4 and Sox2 genes was not detected in the NOD mouse-derived cells. As previously reported (8), the strong expression of the endogenous Klf4 and c-Myc in NMs and NPEs may be important for successful production of the NM-iPSCs and NPE-iPSCs.

Moreover, our data showed that the generation efficiency of iPSCs from NPEs was at least 2-fold higher than that from MEFs. We also could detect apparent expression of Nanog and *cripto* in NPEs but not in NMs, suggesting the possibility that the endogenous expression of Nanog and *cripto* in NPEs may accelerate reprogramming (9). We found that the NPE-iPSCs more efficiently differentiated into pancreatic beta-like insulin-producing cells, compared with NM-iPSCs and NPE-iPSCs. Based on several different direct differentiation methods, we could develop the optimized stepwise differentiation protocol, which led to successful differentiation of NOD-iPSCs into insulin-producing cells. Interestingly, we could find differences of gene expression pattern between the differentiated NM-iPSCs and NPE-iPSCs. Our data validated that the expression of pancreatic specific genes in differentiated NPE-iPSCs were higher than that in differentiated NM-iPSCs or G4-2 ESCs. Our results suggest the possibility that genetically matched iPSCs retain a transient transcriptional and epigenetic memory of their cellular origin, which can substantially affect their potential to differentiate into specific cell types, as previously reported in other types of cells (10). Although our results suggest that cells differentiated from patient-derived iPSCs may be an effective therapy in the treatment of T1D, further studies are needed to address the long-term safety and ef-

fect of these disease model-derived iPSCs.

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9. Theunissen TW, van Oosten AL, Castelo-Branco G, Hall J, Smith A, Silva JC: Nanog overcomes reprogramming barriers and induces pluripotency in minimal conditions. *Curr Biol* 21:65-71
10. Kim K, Doi A, Wen B, Ng K, Zhao R, Cahan P, Kim J, Aryee MJ, Ji H, Ehrlich LI, Yabuuchi A, Takeuchi A, Cunniff KC, Hongguang H, McKinney-Freeman S, Naveiras O, Yoon TJ, Irizarry RA, Jung N, Seita J, Hanna J, Murakami P, Jaenisch R, Weissleder R, Orkin SH, Weissman IL, Feinberg AP, Daley GQ: Epigenetic memory in induced pluripotent stem cells. *Nature* 467:285-290

PLENARY LECTURES

SPECIAL LECTURE

SYMPOSIA

SATELLITE SYMPOSIA

ORAL PRESENTATIONS

POSTER EXHIBITIONS

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• Education and Appointments

1990-1996	University of Tsukuba, Tsukuba, Japan	Doctoral student/Research Fellow
1999-2003	Harvard Medical School, Boston, MA	Instructor
1999-	Beth Israel Deaconess Medical Center, Boston, MA	Staff Scientist
2007-	Gachon University of Medicine & Science, Korea	Adjunct Professor
2003-	Harvard Medical School, Boston, MA	Assistant Professor

• Research Interests

Major: Pathogenesis of obesity and type 2 diabetes, Molecular mechanism of insulin/leptin resistance

• Brief List of Publications

1. Kim MS, Pak YK, Jang PG, Namkoong C, Choi YS, Han SM, Kim SW, Kim HS, Park JY, Kim YB, Lee KU. Role of Forkhead Transcription Factor FOXO1 in the Regulation of Food Intake and Energy Balance. *Nature Neuroscience* 2006; 6:901-906.
2. Ongusaha P, Kim HG, Kwak JC, Der CJ, Ridley AJ, Dotto GP, Kim YB, Aaronson SA, Lee SW. RhoE Is a Pro-Survival p53 Target Gene that Inhibits ROCK I-Mediated Apoptosis in Response to Genotoxic Stress. *Current Biology* 2006; 16:2466-2472.
3. Vianna CR, Huntgeburth M, Coppari R, Choi CS, Lin J, Krauss S, Barbatelli G, Tzameli I, Kim YB, Cinti S, Shulman GI, Spiegelman BM, Lowell B. Hypomorphic mutation in PGC1 β causes mitochondria dysfunction and liver insulin resistance. *Cell Metabolism* 2006; 4:453-464.
4. Zabolotny JM, Kim YB. Silencing insulin resistance through SIRT1. *Cell Metabolism* 2007; 6:247-249,
5. Handschin C, Choi CS, Chin S, Kim S, Kawamori D, Kurpad AJ, Neubauer N, Hu J, Mootha VK, Kim YB, Kulkarni RN, Shulman GI, Spiegelman BM. Abnormal glucose homeostasis in skeletal muscle-specific PGC-1 α knockout mice reveals skeletal muscle-pancreatic β cell cross-talk. *J Clin Invest* 2007; 117:3463-3474
6. Ongusaha P, Kim HG, Kwak JC, Der CJ, Kim YB, Jame Liao, Lee AW. Identification of ROCK1 as an upstream activator of JIP-3-JNK signaling axis in response to UVB damage. *Science Signaling* 2008;1; ra 14
7. Lee DH, Shi J, Jeoung NH, Kim MS, Zabolotny JM, Lee SW, White MF, Wei L, Kim YB. Targeted disruption of ROCK1 causes insulin resistance in vivo. *J Biol Chem* 2009;284:11776-11780
8. Kienesberger PC, Lee DH, Flier JS, Haemmerle G, Zechner R, Kim YB*, Kershaw EE*. Adipose triglyceride lipase deficiency is associated with tissue specific changes in insulin signaling. *J Biol Chem* 2009; 284: 30218-30229 *co-corresponding author
9. Shiuchi T, Haque MS, Okamoto S, Inoue T, Kageyama H, Lee S, Toda C, Suzuki A, Bachman ES, Kim YB, Sakurai T, Yanagisawa M, Shioda S, Imoto K, Minokoshi Y. Hypothalamic orexin stimulates feeding-associated glucose utilization in skeletal muscle via sympathetic nervous system. *Cell Metabolism* 2009; 10:466-480
10. Chun KH, Lee KD, Lee DH, Jung Y, RR Henry, Ciaraldi TP, Kim YB. In vivo activation of ROCK1 by insulin is impaired in skeletal muscle of human with type 2 diabetes. *Am J Physiol Endocrinol Metab* 2011; 300:E536-542
11. Shin HJ, Park YH, Kim SU, Moon, HB, Park DS, Sun HN, Han YH, Lee CH, Lee DS, Song IS, Lee DH, Kim M, Kim NS, Kim DG, Kim JM, Kim SK, Kim YB*, Yu DY*. Hepatitis B Virus X protein induces Insulin Resistance via Activating Gluconeogenesis *J Biol Chem* 2011(in press) *co-senior author
12. Shizuoka S, Choi CS, Shimizu N, Kim M, Zhang T, Dong HH, Kim YB, Kaneki M. Liver-specific iNOS expression is sufficient to cause hepatic insulin resistance and hyperglycemia in mice. *J Biol Chem* 2011 (in press)

| S2-1 |

Identification of Rho-kinase as a novel regulator of adiposity

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Harvard Medical School, USA

Obesity is often accompanied by an eating disorder, which contributes to dysregulation of body-weight homeostasis and energy balance. The hypothalamus is a key site that plays an essential role in the physiologic regulation of food intake and body weight. It is established that impaired leptin signaling in the hypothalamus causes hyperphagia, which hence promotes adiposity and weight gain. Over the past decade, there have been intensive efforts to identify mediators of leptin action in the hypothalamus that control feeding behavior, energy expenditure, and glucose metabolism. In the hypothalamus, the arcuate nucleus is a key

site of leptin action that is critical for feeding regulation and energy balance. Indeed, it is now evident that leptin signaling in POMC- and AgRP/NPY-producing neurons in the hypothalamic arcuate nucleus are required for normal body-weight homeostasis. Our studies identify Rho-kinase as a new regulator of leptin action that is necessary for the homeostatic regulation of feeding and adiposity. This talk will focus the physiological role of Rho-kinase in hypothalamic control of energy metabolism and feeding behavior, with particular emphasis to Rho-kinase's effect on POMC- and AgRP neuron.



Wataru Ogawa

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• Education and Appointments

- 1979-1984 Kobe University School of Medicine, M.D
- 1991-1994 Kobe University Graduate School of Medicine (Internal Medicine). Ph.D.
- 1991-1994 Postdoctoral fellow, Department of Molecular Pharmacology, Stanford University Medical School
- 1997-2002 Assistant Professor, Second Department of Internal Medicine, Kobe University School of Medicine
- 2002-2003 Assistant Professor, Department of Diabetes, Digestive and Kidney Diseases, Kobe University School of Medicine
- 2003-2007 Associate Professor, Department of Diabetes, Digestive and Kidney Diseases, Kobe University School of Medicine
- 2007-2009 Associate Professor, Department of Internal Medicine, Division of Diabetes, Metabolism and Endocrinology, Kobe University School of Medicine
- 2010- Associate Professor

• Research Interests

Molecular mechanism of insulin action and insulin resistance

• Brief List of Publications

1. Takashima M, Ogawa W, Hayashi K, Inoue H, Kinoshita S, Okamoto Y, Sakaue H, Wataoka Y, Emi A, Senga Y, Matsuki Y, Watanabe E, Hiramatsu R, Kasuga M et al. Role of KLF15 in regulation of hepatic gluconeogenesis and metformin action. *Diabetes*. 59:1608-1615, 2010
2. Hosooka T, Noguchi T, Kotani K, Nakamura T, Sakaue H, Inoue H, Ogawa W, Tobimatsu K, Takazawa K, Sakai M, Matsuki Y, Hiramatsu R, Yasuda T, Lazar MA, Yamanashi Y, Kasuga M. Dok1 mediates high-fat diet-induced adipocyte hypertrophy and obesity through modulation of PPAR-gamma phosphorylation. *Nat Med*. 14:188-193, 2008
3. Okamoto Y, Ogawa W, Nishizawa A, Inoue H, Teshigawara K, Kinoshita S, Matsuki Y, Watanabe E, Hiramatsu R, Sakaue H, Noda T, Kasuga M. Restoration of glucokinase expression in the liver normalizes postprandial glucose disposal in mice with hepatic deficiency of PDK1. *Diabetes*. 56:1000-1009, 2007
4. Inoue H, Ogawa W, Asakawa A, Okamoto Y, Nishizawa A, Matsumoto M, Teshigawara K, Matsuki Y, Watanabe E, Hiramatsu R, Notohara K, Katayose K, Okamura H, Kahn CR, Noda T, Takeda K, Akira S, Inui A, Kasuga M. Role of hepatic STAT3 in brain-insulin action on hepatic glucose production. *Cell Metab*. 3:267-275, 2006.
5. Hashimoto N, Kido Y, Uchida T, Asahara S, Shigeyama Y, Matsuda T, Takeda A, Tsuchihashi D, Nishizawa A, Ogawa W, Fujimoto Y, Okamura H, Arden KC, Herrera PL, Noda T, Kasuga M. Ablation of PDK1 in pancreatic beta cells induces diabetes as a result of loss of beta cell mass. *Nat Genet*. 38:589-593, 2006
6. Mori T, Sakaue H, Iguchi H, Gomi H, Okada Y, Takashima Y, Nakamura K, Nakamura T, Yamauchi T, Kubota N, Kadowaki T, Matsuki Y, Ogawa W, Hiramatsu R, Kasuga M. Role of Kruppel-like factor 15 (KLF15) in transcriptional regulation of adipogenesis. *J Biol Chem*. 280:12867-12675, 2005
7. Inoue H, Ogawa W, Ozaki M, Haga S, Matsumoto M, Furukawa K, Hashimoto N, Kido Y, Mori T, Sakaue H, Teshigawara K, Jin S, Iguchi H, Hiramatsu R, LeRoith D, Takeda K, Akira S, Kasuga M. Role of STAT-3 in regulation of hepatic gluconeogenic genes and carbohydrate metabolism in vivo. *Nat Med*. 10:168-174, 2004

| S2-2 |

Organ-organ interaction for metabolic control

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Organ-organ interaction is essential for the regulation of metabolic control. The liver is a major target of insulin and plays a central role in the regulation of glucose metabolism. Insulin-induced suppression of hepatic glucose production is known to be achieved not only by the direct effect of the hormone but also by its indirect action on other organs. We have found that an increase in the plasma insulin concentration activate the transcription factor STAT3 in the liver. This effect of insulin was mediated not by the direct action of insulin but by the hormone's effects in the brain, and the increase in hepatic IL-6 induced by the brain-insulin action is essential for the activation of STAT3. The inhibition of gluconeogenic genes induced by intracerebral ventricular insulin infusion was impaired in mice with liver-specific STAT3 deficiency or in mice with IL-6 deficiency. These results indicate that IL-6-STAT3 signaling in the liver contributes to insulin action in the brain, leading

to the suppression of hepatic glucose production. Skeletal muscle is essential for fatty acid metabolism. Oxidation of fatty acid in skeletal muscle is increased in response to exercise and the transcriptional coactivator PGC-1 α is thought to participate in this process. We have identified two alternative variants of PGC-1 α . The alternative variants are dominant exercise-induced isoforms of PGC-1 α in skeletal muscle, and their induction is dependent on β 2-adrenergic stimuli. Mice with selective deficiency in the alternative variants developed age-dependent obesity with insulin resistance. Energy expenditure, fat mass loss and the ability for fatty acid oxidation in skeletal muscle induced by exercise or by β -adrenergic stimuli were markedly attenuated in the mutant mice. Our results thus suggest that the alternative variants of PGC-1 α control fat mass and whole body insulin sensitivity through the regulation of the exercise adaptation of skeletal muscle.



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• Education and Appointments

1988-1993	Nanjing Medical College	Bachelor degree student
1994-1997	Nanjing Medical University	Master degree student
1997-2000	Shanghai Jiaotong University	PhD student
2000-2005	Joslin Diabetes Center/Harvard Medical School	Post-doc
2005-2008	University of Wisconsin-Madison Medical School	Assistant Professor
2008-present	Albert Einstein College of Medicine	Associate Professor

• Research Interests

Central nervous system basis of obesity and type 2 diabetes

• Brief List of Publications

1. Zhang X, Zhang G, Zhang H, Karin M, Bai H, Cai D. Hypothalamic IKK β /NF- κ B and ER stress link overnutrition to energy imbalance and obesity. *Cell*, 134 (7): 61-73, 2008. (Highlighted by preview in *Cell*, highlighted as a top-10 article of Faculty 1000)
2. Cai D. NF- κ B-mediated metabolic inflammation in peripheral tissues versus the central nervous system. *Cell Cycle*, 8 (16): 2542-2548, 2009.
3. Purkayastha S, Zhang H, Zhang G, Ahmed Z, Wang Y, Cai D. Dysregulation of peripheral insulin action and blood pressure by brain endoplasmic reticulum stress. *Proc. Natl. Acad. Sci. U.S.A.*, 108(7): 2939-2944, 2011.
4. Zhang G, Bai H, Zhang H, Dean C, Wu Q, Li J, Guariglia S, Meng Q, Cai D. Neuropeptide exocytosis involving synaptotagmin-4 and oxytocin in hypothalamic programming of obesity and metabolic diseases. *Neuron*, 69 (3): 523-535, 2011. (Highlighted as featured *Neuron* article and by preview in *Neuron* 69: 401-403, 2011; Highlighted as a top-2% article by Faculty 1000)
5. Purkayastha S, Zhang G, Cai D. Uncoupling the mechanisms of obesity and hypertension by targeting hypothalamic IKK β /NF- κ B. *Nature Medicine*, 17 (7): 883-7, 2011. (Highlighted as *Nature Medicine* news, highlighted by a preview in *Cell Metabolism*, 14 (7): 3-4, 2011)
6. Zhang H, Zhang G, Gonzalez, F, Park S, Cai D. Hypoxia-Inducible Factor Directs POMC Gene to Mediate Hypothalamic Glucose Sensing and Energy Balance Regulation. *PLoS Biology*, 9 (7), 2011. (Highlighted as a primer report by *PLoS Biology*.)
7. Meng Q, Cai D. Defective hypothalamic autophagy mediates central pathogenesis of obesity via IKK-beta/NF-kappaB pathway. *Journal of Biological Chemistry*. 2011, July 15 ahead of Epub.
8. Zhang G, Meng Q, Cai D. Resting-stage oxytocin release in circadian control of body weight and metabolic balance. *American Journal of Physiology (Endocrine and Metabolism)*, 2011, August 9 ahead of Epub.
9. Cai D. Neurons link aging and obesity to hypertension? *Aging*, (invited review article, in process).
10. Cai D. Release mechanism of brain neuropeptides, a new era in metabolic research. *Journal of Communicative & Integrative Biology*, (invited review article, in process).
11. Cai D. Metabolic effects of hypothalamic oxidative stress and inflammation. *Annals of the New York Academy of Sciences*, (invited review article, in process).

| S2-3 |

Synaptotagmin, oxytocin and obesity mechanism

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Albert Einstein Medical School, USA

Energy and body weight homeostasis are critically regulated by the hypothalamus. A key regulatory basis is the operation of the neural system comprising first-order neurons in the arcuate nucleus and second-order neurons in the paraventricular nucleus (PVN). Metabolic factors such as hormones and nutrients act on first-order neurons to induce initial signals, and therefore activate second-order neurons to exert metabolic effects. Second-order neurons can employ both neurotransmitter and neuropeptide pathways to control energy intake and expenditure; however, it remains unclear whether and how neurotransmitter/neuropeptide release in second-order neurons are regulated. Oxytocin (OXT) neurons are a group of PVN neurons which respond to various first-order signals, and mice deficient of OXT or OXT receptor are obese. In the meanwhile, recent research has appreciated the different roles of local (somato-dendritic) vs. systemic (axonal) OXT release. In this context, we discovered that synaptotagmin-4 (Syt4) is

a negative regulator of OXT release, and this regulatory process is physiologically relevant to body weight control and obesity development. Detailed findings include: (1) Syt4 is distinctly expressed in hypothalamic OXT neurons to suppress OXT exocytosis, in particular the local (somato-dendritic) release of OXT in the PVN; (2) High-fat diet (HFD) feeding increases Syt4 vesicular binding to impair OXT release, and this effect is particularly prominent for the somato-dendritic Syt4-OXT system; (3) Lentiviral Syt4 overexpression in the PVN is obesogenic; (4) Syt4 knockout mice are obesity resistant; (5) Local (intra-brain) delivery of OXT is catabolic due to food intake reduction and energy expenditure increase. Based on these findings, we conclude that hypothalamic Syt4-OXT system represents an exocytotic basis for the hypothalamic control of energy and body weight balance, and change of this system can lead to development of obesity and related diseases.



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• Education and Appointments

2006-present	College of Life Sciences and Biotechnology, Korea University	Full Professor
2003-2006	College of Life Sciences and Biotechnology, Korea University	Associate Professor
2002-2003	Medical Research Center, College of Medicine, Yonsei University	Associate Professor
1996-2002	Medical Research Center, College of Medicine, Yonsei University	Assistant Professor
1992-1995	IGBMC (Institut de Genetique et de Biologie Moleculaire et Cellulaire), CNRS, Strasbourg, France	Post-Doctoral Fellow
1992	Université de Paris VI (Pierre et Marie Curie), Paris, France	Ph.D. in Molecular and Cellular Pharmacology
1985-87	Université de Paris VI (Pierre et Marie Curie), Paris, France	M.S in Biochemistry
1985	Yonsei University, Dept. of Biochemistry	B.S. in Biochemistry

• Research Interests

Major: Signaling and Physiological Functions of Neurotransmitters and Their Receptors

1. Dopaminergic Signaling in Neuro-psychiatric Disorders.
2. Melanocortin Signaling in central control of obesity

• Brief List of Publications

1. Yoon S, Chang MS, Choi MH, Baik JH. Wnt5a Binds to the Dopamine D2 Receptor and Regulates Dopamine Neuron Development via ERK Activation. *Journal of Biological Chemistry*, 286 (18), 15641-15651 (2011)
2. Kim HK, Youn BS, Shin MS, Namkoong C, Park KH, Baik JH, Kim JB, Park JY, Lee K, Kim YB, Kim MS. Hypothalamic Angpt14/Fiaf Is a Novel Regulator of Food Intake and Body Weight. *Diabetes*, 2010(59), 2772-2780. (2010)
3. Kim KS, Yoon YR, Lee HJ, Yoon S, Kim SY, Shin SW, Juan JA, Kim MS, Choi SY, Woong S, Baik J-H. Enhanced Hypothalamic Leptin Signaling in Mice lacking dopamine D2 receptors. *Journal of Biological Chemistry*, 285(12), 8905-8917. (2010)
4. Yun HM, Baik JH, Kang IS, Jin C, Rhim H. Physical interaction of Jab1 with human serotonin 6 G-protein-coupled receptor and their possible roles in cell survival. *Journal of Biological Chemistry*, 285(13), 10016-10029. (2010)
5. Jang PG, Namkoong C, Kang GM, Hur MW, Kim SW, Kim GH, Kang Y, Jeon MJ, Kim EH, Lee MS, Karin M, Baik JH, Park JY, Lee KU, Kim YB, Kim MS. NF- κ B activation in hypothalamic POMC neurons is essential in illness- and leptin-induced anorexia. *Journal of Biological Chemistry*, 285(13), 9706-9715. (2010)
6. Yoon S, Noh JS, Choi S-Y, Baik JH. Effects of Atypical Antipsychotic Drugs on Body Weight and Food Intake in Dopamine D2 Receptor Knockout Mice. *Biochemical and Biophysical Research Communications*, 393, 235-241. (2010)
7. Yoon KW, Cho J-H, Lee JK, Kang Y-H, Chae JS, Kim YM, Kim J, Kim EK, Kim S E, Baik JH, Naik UP., Cho S-G, Choi E-J. CIB1 functions as a Ca²⁺ -sensitive modulator of stress-induced signaling by targeting ASK1. *Proc Natl Acad Sci USA*, 106(41), 17389-94. (2009)
8. Kim SY, Lee HJ, Kim YN, Yoon S, Lee JE, Sun W, Choi EJ, Baik JH. Striatal-Enriched Protein Tyrosine Phosphatase Regulates Dopaminergic Neuronal Development via Extracellular Signal-Regulated Kinase signaling. *Experimental Neurology*, 214(1), 69-77. (2008) (corresponding author)
9. Choi J, Ha CM, Choi EJ, Jeong CS, Park JW, Baik JH, Park JY, Costa M.E., Ojeda S.R., and Lee BJ. KAP3, a kinesin superfamily-associated protein, is preferentially expressed in glutamatergic neurons and contributes to the excitatory control of female puberty. *Endocrinology* 149, 6146-6156. (2008)
10. Kim DH, Shin SW, Baik JH. Role of third intracellular loop of the melanocortin 4 receptor in the regulation of constitutive activity. *Biochem Biophys Res Commun*. 365(3), 439-445. (2008)

| S2-4 |

Role of GRP78 in regulation of MC4R signaling

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The melanocortin 4 receptor (MC4R) is essential for the central regulation of energy homeostasis. We have previously shown that the third intracellular loop of MC4R (MC4Ri3) is important in regulation of MC4R signaling. We identified that MC4Ri3 interacts with glucose-regulated protein 78 (GRP78), an ER stress-inducible molecular chaperone. We observed that GRP78 is expressed in paraventricular nucleus of hypothalamus, where MC4R is ex-

pressed also. Under ER stress condition, down-regulation of GRP78 by using siGRP78, significantly inhibited the internalization of MC4R and in brain, the MC4R-GRP78 interaction in hypothalamus was reduced. These data suggest that GRP78 may play an important role in control of MC4R signaling. [supported by the NRF Korea (Grant No. 2009-0083608)]



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• Education and Appointments

1987-1993	Shiga University of Medical Science, JAPAN	Medical (MD) Student
1993-1995	University Hospital, Shiga University of Medical Science	Resident (Internal Medicine)
1995-1999	Graduate School, Shiga University of Medical Science	Graduate (PhD) Student
2002-2007	University of British Columbia, CANADA	PDF, Research Associate
2007-Present	Asahikawa Medical University, JAPAN	Assistant Professor

• Research Interests

Diabetes, Incretins, Gut physiology (Gut endocrine cells, Gut stem cells), Diabetic Complications

• Brief List of Publications

1. Fujita Y, Haneda M. Molecular mechanism of insulin secretion facilitated by incretin. *Nippon Rinsho*. 2011 May;69(5):808-12
2. Takiyama Y, Harumi T, Watanabe J, Fujita Y, Honjo J, Shimizu N, Makino Y, Haneda M. Tubular injury in a rat model of type 2 diabetes is prevented by metformin: a possible role of HIF-1 α expression and oxygen metabolism. *Diabetes*. 2011 Mar;60(3):981-92
3. Isoe T, Makino Y, Mizumoto K, Sakagami H, Fujita Y, Honjo J, Takiyama Y, Itoh H, Haneda M. High glucose activates HIF-1-mediated signal transduction in glomerular mesangial cells through a carbohydrate response element binding protein. *Kidney Int*. 2010 Jul;78(1):48-59.
4. Gage BK, Riedel MJ, Karanu F, Rezaia A, Fujita Y, Webber TD, Baker RK, Wideman RD, Kieffer TJ. Cellular reprogramming of human amniotic fluid cells to express insulin. *Differentiation*. 2010 Sep-Oct;80(2-3):130-9
5. Fujita Y, Asadi A, Yang GK, Kwok YN, Kieffer TJ. Differential processing of pro-glucose-dependent insulinotropic polypeptide in gut. *Am J Physiol Gastrointest Liver Physiol*. 2010 May;298(5):G608-14.
6. Fujita Y, Wideman RD, Asadi A, Yang GK, Baker R, Webber T, Zhang T, Wang R, Ao Z, Warnock GL, Kwok YN, Kieffer TJ. Glucose-dependent insulinotropic polypeptide is expressed in pancreatic islet alpha-cells and promotes insulin secretion. *Gastroenterology*. 2010 May;138(5):1966-75.
7. Fujita Y, Wideman RD, Speck M, Asadi A, King DS, Webber TD, Haneda M, Kieffer TJ. Incretin release from gut is acutely enhanced by sugar but not by sweeteners in vivo. *Am J Physiol Endocrinol Metab*. 2009 Mar;296(3):E473-9.
8. Fujita Y, Chui JW, King DS, Zhang T, Seufert J, Pownall S, Cheung AT, Kieffer TJ. Pax6 and Pdx1 are required for production of glucose-dependent insulinotropic polypeptide in proglucagon-expressing L cells. *Am J Physiol Endocrinol Metab*. 2008 Sep;295(3):E648-57.
9. Wideman RD, Fujita Y, Kieffer TJ. 'Insulin-expressing engineered cell lines and primary cells: surrogate b cells from liver, gut, and other sources.' *Current Opinion in Organ Transplantation*, 12:67-72, 2007

| S3-1 |

Short-form glucose-dependent insulinotropic polypeptide (GIP) is expressed in pancreatic α -cells and gut endocrine cells

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Aims: Incretins, glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are gastrointestinal hormones that are released in response to nutrient intake and promote insulin secretion via G-protein coupled receptors. Interestingly, a subset of enteroendocrine cells expresses both GIP and GLP-1. Proglucagon is differently processed in the gut and the pancreas. We sought to determine whether GIP also might be expressed as an isoform and co-expressed with proglucagon in pancreatic α -cells.

Methods: We assessed GIP expression via RT-PCR, in situ hybridization, and immunohistochemistry. We measured GIP release from isolated islets via the bioassay, compared the biological activities of full-length and short-form GIP, and assessed the impact of immunoneutralization of islet GIP on glucose-stimulated insulin secretion in isolated islets. We also investigated whether short-form GIP is expressed in the gut.

Results: GIP mRNA was detected in mouse islets. GIP protein localized to pancreatic α -cells of mouse, human,

and snake, based on immunohistochemical analyses. However, immunoreactivity was detected in islets from pro-hormone convertase (PC) 2 knockout but not wild-type mice by a C-terminal GIP antibody. Intriguingly, we found short-form GIP expression with PC2 especially in the lower gut. Bioactive GIP was released from mouse and human islets after arginine stimulation. In several diabetic animal models, GIP expression is concomitant with α -cells expansion in the islets. In the perfused mouse pancreas, GIP1-42 and GIP1-30 had equipotent insulinotropic actions. Finally, immunoneutralization of GIP secreted by isolated islets decreased glucose-stimulated insulin secretion.

Conclusions: GIP is expressed in and released from pancreatic islets; in α -cells, PC2 processes proGIP to a short-form but bioactive form of GIP that differs from the full-length, PC1/3-derived GIP form from K-cells. Short-form GIP is also expressed in the gut. Islet-derived GIP promotes islet glucose competence and also could support islet development and survival.



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• Education and Appointments

1986-1990	Department of Zoology, College of Natural Sciences, Seoul National University, Seoul, Korea	BS
1990-1992	Department of Molecular Biology, College of Natural Sciences Seoul National University, Seoul, Korea	MS
1992-1996	Department of Molecular Biology, College of Natural Sciences Seoul National University, Seoul, Korea	PhD
1996-1997	Research Center for Cell Differentiation, Seoul National University	Postdoc
1997-1999	Division for Clinical & Experimental Endocrinology, University of Göttingen, Germany	Postdoc
2000-2005	Hormone Research center, School of Biological Sciences and Technology, Chonnam National University	Assistant Professor
2005-2011	Graduate School of Medicine, Korea University	Associate Professor
2011-present	Graduate School of Medicine, Korea University	Professor

• Research Interests

Major: Neuroendocrinology
 Molecular interaction between G-protein-coupled receptors and their ligands.
 Coevolution of G-protein-coupled receptors and peptide ligands.
 Identification of ligands for orphan G-protein-coupled receptors.

• Brief List of Publications

1. Zhao E, McNeilly JR, McNeilly AS, Fischer-Colbrie R, Basak A, Seong JY, Trudeau VL (2011) Secretoneurin Stimulates the Production and Release of Luteinizing Hormone in Mouse L beta T2 Gonadotropin Cells. *Am J Physiol Endocrinol Metab* (in press)
2. Park E, Iaccarino C, Lee J, Kwon I, Baik SM, Kim M, Seong JY, Son GH, Borrelli E, Kim K (2011) Regulatory roles of hnRNP M and Nova-1 in the alternative splicing of the dopamine D2 receptor pre-mRNA. *J Biol Chem* (in press)
3. Kim HD, Choe HK, Chung S, Kim M, Seong JY, Son GH, Kim K (2011) Class-C SOX Transcription Factors Control GnRH Gene Expression via the Intronic Transcriptional Enhancer. *Mol Endocrinol*. 25(7):1184-1196
4. Servili A, Page YL, Leprince J, Caraty A, Escobar S, Parhar IS, Seong JY, Vaudry H, Kah O (2011) Organization of two independent kisspeptin systems derived from evolutionary-ancient kiss genes in the brain of zebrafish. *Endocrinology* 152(4):1527-40
5. Kim D-K, Cho EB, Moon MJ, Park S, Hwang J-K, Kah O, Sower SA, Vaudry H, Seong JY (2011) Revisiting the evolution of gonadotropin-releasing hormones and their receptors in vertebrates: Secrets hidden in genomes. *Gen Com Endocrinol* 170:68-78
6. Kim JE, You DJ, Lee C, Ahn C, Seong JY, Hwang JI (2010). Suppression of NF-kappaB signaling by KEAP1 regulation of IKKbeta activity through autophagic degradation and inhibition of phosphorylation. *Cell Signal* 22:1645-1654
7. Tsutsui K, Bentley GE, Kriegsfeld LJ, Osugi T, Seong JY, Vaudry H. (2010) Discovery and evolutionary history of GnIH and kisspeptin: New key neuropeptides controlling reproduction. *J Neuroendocrinology* 22:716-727

| S3-2 |

Evolutionary conserved residues at the GLP-1 receptor core confer ligand-induced receptor activation

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Aims: Glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) play important roles in insulin secretion through their receptors, GLP1R and GIPR. Although GLP-1 and GIP are attractive candidates for treatment of type 2 diabetes and obesity, little is known regarding the molecular interaction of these peptide ligands with their receptors. Here, we determined specific amino acid residues in the heptahelical core domain of GLP1R responsible for interaction with ligand and receptor activation.

Methods: We generated chimeric and point-mutated GLP1R/GIPR together with chimeric GLP-1/GIP peptides. Ligand-receptor interaction was systematically determined using HEK293T cells transfected with the receptor plasmid and a cAMP-responsive element-driven luciferase reporter plasmid.

Results: We found that transmembrane helix 2 (TMH2),

extracellular loop 1 (ECL1), and ECL2 within the core of GLP1R are necessary for specific ligand binding and receptor activation. Based on amino acid sequence comparison of these regions of vertebrate GLP1Rs and GIPRs, we further constructed site-directed mutated receptors, revealing that Ile¹⁹⁶ of TMH2, Leu²³² and Met²³³ of ECL1, and Asn³⁰² of ECL2 in GLP1R confer specific GLP-1 binding and receptor activation. Using GLP-1/GIP chimeric peptides, we found that His¹ of GLP-1 interacts with Asn³⁰² of GLP1R, and Thr⁷ of GLP-1 has close contact with a binding pocket formed by Ile¹⁹⁶, Leu²³², and Met²³³ of GLP1R.

Conclusion: This study is the first to demonstrate molecular determinants within the core of the receptors conferring ligand binding and receptor activation, which may provide critical clues for development of nonpeptide agonists for treatment of diabetes mellitus and obesity.



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• Education and Appointments

- 1985 Graduated from University of Tokyo, School of Medicine
- 1985 Residency at 3rd Department of Internal Medicine, University of Tokyo
- 1986 Residency at Tokyo Metropolitan Komagome Hospital
- 1987 Research Associate at the Department of Virology & Oncology Laboratory, Cancer Institute, Japanese Foundation for Cancer Research
- 1990 Associate Professor, Hematology & Oncology Group, The 3rd Department of Internal Medicine, University of Tokyo
- 1993 Research Associate at Molecular and Cell Biology Laboratory (Prof. Tony Hunter), The Salk Institute for Biological Studies (La Jolla, USA)
- 2000 Associate Professor, Department of Internal Medicine, Metabolism and Endocrinology, Graduate School of Comprehensive Human Sciences, University of Tsukuba
- 2006 Associate Professor, Division of Endocrinology and Metabolism, Department of Medicine, Saitama Medical Center, Jichi Medical University
- 2010 Visiting Associate Professor, Division of Functional Genomics & Systems Medicine, Research Center for Genomic Medicine, Saitama Medical University

• Research Interests

Diabetes, Endocrinology, Internal Medicine

• Brief List of Publications

1. Yamamoto T, Shimano H, Inoue N, Nakagawa Y, Matsuzaka T, Takahashi A, Yahagi N, Sone H, Suzuki H, Toyoshima H, Yamada N. Protein Kinase A Suppresses Sterol Regulatory Element-binding Protein-1C Expression via Phosphorylation of Liver X Receptor in the Liver. *J Biol Chem.* 2007 Apr 20;282(16):11687-95.
2. Nakakuki M, Shimano H, Inoue N, Tamura M, Matsuzaka T, Nakagawa Y, Yahagi N, Toyoshima H, Sato R, Yamada N. A transcription factor of lipid synthesis, sterol regulatory element-binding protein (SREBP)-1a causes G(1) cell-cycle arrest after accumulation of cyclin-dependent kinase (cdk) inhibitors. *FEBS J.* 2007 Sep;274(17):4440-52.
3. Ohgaki S, Iida K, Yokoo T, Watanabe K, Kihara R, Suzuki H, Shimano H, Toyoshima H, Yamada N. Identification of ISG12b as a putative interferon-inducible adipocytokine which is highly expressed in white adipose tissue. *J Atheroscler Thromb.* 2007 Aug;14(4):179-84.
4. Matsuzaka T, Shimano H, Yahagi N, Kato T, Atsumi A, Yamamoto T, Inoue N, Ishikawa M, Okada S, Ishigaki N, Iwasaki H, Iwasaki Y, Karasawa T, Kumadaki S, Matsui T, Sekiya M, Ohashi K, Hasty AH, Nakagawa Y, Takahashi A, Suzuki H, Yatoh S, Sone H, Toyoshima H, Osuga J, Yamada N. Crucial role of a long-chain fatty acid elongase, Elov16, in obesity-induced insulin resistance. *Nat Med.* 2007 Oct;13(10):1193-202.
5. Inoue N, Yahagi N, Yamamoto T, Ishikawa M, Watanabe K, Matsuzaka T, Nakagawa Y, Takeuchi Y, Kobayashi K, Takahashi A, Suzuki H, Hasty AH, Toyoshima H, Yamada N, Shimano H. Cyclin-dependent kinase inhibitor, p21WAF1/CIP1, is involved in adipocyte differentiation and hypertrophy, linking to obesity and insulin resistance. *J Biol Chem.* 2008 Jul 25;283(30):21220-9.
6. Watanabe K, Okamoto F, Yokoo T, Iida KT, Suzuki H, Shimano H, Oshika T, Yamada N, Toyoshima H. SPARC is a major secretory gene expressed and involved in the development of proliferative diabetic retinopathy. *J Atheroscler Thromb.* 2009 Apr;16(2):69-76.
7. Yoshida M, Dezaki K, Yamato S, Aoki A, Sugawara H, Toyoshima H, Ishikawa SE, Kawakami M, Nakata M, Yada T, Kakei M. Regulation of voltage-gated K⁺ channels by glucose metabolism in pancreatic beta-cells. *FEBS Lett.* 2009 Jul 7;583(13):2225-30.

| S3-3 |

IBCAP; discovery of another intestinal hormone with beta cell augmenting activity

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Aims: Success of incretin related drugs, such as GLP-1 analogs and DPP IV inhibitors, has brought worldwide attention to intestine as a hormone secreting organ and major therapeutic target in metabolic syndrome and diabetes. We are working on a novel intestine-specific secretory hormone, IBCAP (intestine derived beta-cell augmenting promoter), identified by ourselves.

Methods: Oligo-cap Signal Sequence Trap (Oligo-cap SST) strategy developed in our laboratory was used to clone IBCAP gene. Biological activity and significance of IBCAP was evaluated through northern blot analysis, GSIS (glucose stimulated insulin secretion), recombinant-adenovirus expression system, and by developing transgenic and knock-out animals of the gene.

Results: We demonstrated that the factor has insulin secretion promotive effect, and furthermore, adenovirus-

mediated expression in STZ treated type 1 diabetes model mice decreased blood glucose concentration and increased the area of pancreatic β -cells of the mice. Transgenic mice over-expressing the factor revealed to have increased area and number of pancreatic islets, where, analysis of the knock-out mice of the gene was shown to have decreased amount. Thus, we named this factor as intestine derived beta-cell augmenting promoter (IBCAP).

Conclusion: Our results demonstrated that IBCAP is a novel intestine-specific secretory protein with incretin-like activity, which can activate glucose dependent insulin secretion and also can increase pancreatic islets. IBCAP may have a role as a major player that controls the number and amount of pancreatic islets, and should be another strong candidate of therapeutic use in diabetes and pancreas β -cell regeneration.



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• Education and Appointments

1981	Sungkyunkwan University	Ph.D. in Pharmacy,
1982-1991	Chonnam National University, College of Pharmacy	Associate Professor
1989-1990	University of Kentucky, College of Pharmacy	Visiting Professor
1992-present	Sungkyunkwan University, College of Pharmacy	Professor
1995-present	Pharmaceutical Development and Technology (Informa)	Editorial Board Member
1996-1998	Sungkyunkwan University, College of Pharmacy	Dean
2001-2005	Pharmaceutical Research (AAPS journal, Springer)	Editorial Board Member
2002-present	AAPS PharmSciTech (AAPS e-journal)	Editorial Board Member
2003-present	American Association of Pharmaceutical Scientists (AAPS)	Fellow
2006-present	Center of Excellence for Future Pharmaceutical Education and Research (BK21)	Director

• Research Interests

Major: Drug Delivery System

1. PEGylation and bioconjugation of peptide and protein drugs and their drug delivery system.
2. Monoclonal antibody-based drug targeting; immunotoxin and immunoconjugate
3. Analytical method development for drug delivery system
4. Development of sustained release dosage forms of peptide and protein drugs

• Brief List of Publications

1. Jiang HH, Kim TH, Lee S, Chen X, Youn YS, Lee KC. PEGylated TNF-related apoptosis-inducing ligand (TRAIL) for effective tumor combination therapy. *Biomaterials*, 2011, 32:8529-8537
2. Kim TH, Youn YS, Jiang HH, Lee S, Chen X, Lee KC. PEGylated TNF-Related Apoptosis-Inducing Ligand (TRAIL) Analogs: Pharmacokinetics and Anti-tumor Effects. *Bioconjug. Chem.* 2011, 22:1631-7.
3. JH Ahn, EJ Park, HS Lee, KC Lee, and DH Na, Reversible blocking of amino groups of octreotide for the inhibition of formation of acylated peptide impurities in poly(lactide-co-glycolide) delivery systems, *PharmSciTech*, 2011, in press
4. Kim H, Lee J, Kim TH, Lee ES, Oh KT, Lee DH, Park ES, Bae YH, Lee KC, Youn YS. Albumin-Coated Porous Hollow Poly(Lactic-co-Glycolic Acid) Microparticles Bound with Palmitoyl-Acylated Exendin-4 as a Long-Acting Inhalation Delivery System for the Treatment of Diabetes. *Pharm Res.* 2011 28:2008-19.
5. TH Kim, HH Jiang, S Lee, YS Youn, CW Park, Y Byun, X Chen and KC Lee. Mono-PEGylated Dimeric Exendin-4 as High Receptor Binding and Long-Acting Conjugates for Type 2 Anti-diabetes Therapeutics. *Bioconjug Chem.* 2011: 22(4):625-32.
6. Nguyen MK, Huynh CT, Gao GH, Kim JH, Huynh DP, Chae SY, Lee KC, Lee DS. Biodegradable oligo(amido-amine/ β -amino ester) hydrogels for controlled insulin delivery. *Soft Matter.* 7 (2011) 2994-3001.
7. Kim I, Kim TH, Ma K, Park ES, Oh KT, Lee ES, Lee KC, Youn YS. A 4-arm polyethylene glycol derivative conjugated with exendin-4 peptide and palmitylamine having dual-function of size-increase and albumin-binding for long hypoglycemic action. *Regul Pept.* 2011:167(2-3):239-45.
8. Lim SM, Kim TH, Jiang HH, Park CW, Lee S, Chen X and Lee KC, Improved biological half-life and anti-tumor activity of TNF-related apoptosis-inducing ligand (TRAIL) using PEG-exposed nanoparticles. *Biomaterials* 2011: 32, 3538-3546.

| S3-4 |

Bioconjugated incretin analogues for potential type 2 diabetes therapeutics

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Incretin-based diabetic therapies are considered to be one of the most effective approaches because of multiple gluco-regulatory functions and disease-modifying potentials of the incretin hormones, such as GLP-1 and exendin-4. However, there also exist several practical limitations of the incretin-based diabetic therapies, typically including the relatively short biological half-lives and absence of injection-free treatments due to the relatively low bioavailability on the non-parenteral administrations.

Bioconjugated GLP-1

In case of GLP-1, the extremely short biological half-life owing to the enzymatic degradation by DPP IV must be overcome for the successful clinical applications. To address these issues, we employed the site specific conjugations to produce the enzyme-resistant or orally-available GLP-1 adducts with minimal loss of its intrinsic bioactivities. The PEGylation of GLP-1 resulted in the dramatically improved proteolytic resistance against DPP IV enzyme, and the significantly enhanced circulation half-life rendered the protracted hypoglycemic activities in vivo.

Bioconjugated Exendin-4

Owing to the DPP IV resistant characteristics, exendin-4 showed relatively long elimination half-life of 2.4 h in human. However, considering life-long drug treatment of type 2 diabetes and recent advanced clinical outcomes by using long-acting incretin mimetics, the improved anti-diabetic therapies can be achieved by the developing long-acting exendin-4 derivatives. The site-specific PEGylation of exendin-4 was the most effective modality to produce long-acting incretin mimetics in vivo. Furthermore, the conformationally preserved PEGylation of exendin-4 by using branched PEG (20 kDa) with short PEG spacer arm (3 kDa) resulted in the extremely protracted hypoglycemic and antiobesity efficacies in vivo. Various experimental approaches revealed that site-specific conjugated exendin-4s by bile acids or fatty acids showed improved antidiabetic potentials such as long-circulating character and protracted hypoglycemic efficacies.

Conclusively, our novel and innovative studies revealed that the bio-conjugations of incretin mimetics can be reasonable approaches to develop the clinically efficient incretin-based biotherapeutics for the type 2 diabetic therapy.



Neng Chun Yu

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• Education and Appointments

1986	China Medical University graduated
1990	Specialist in Internal Medicine
1992	Specialist in Endocrine and Metabolism
1995-1997	Department Chief of Diabetes Metabolism Division Lotong Poh-Ai Hospital
1996	Certified Diabetes Educator
1997-2006	Department Chief of Diabetes Center Lotong ST. MARY'S Hospital

• Research Interests

1. Diabetes education
2. Benchmarking and quality improvement in diabetes
3. Self monitoring of blood glucose

• Brief List of Publications

1. Yu NC, Su HS, Tsai ST, Lin BJ, Shiu RS, Hsieh YC, Sheu WH-H. ABC control of diabetes: Survey data from National Diabetes Health Promotion Centers in Taiwan. *Diabetes Research and Clinical Practice* 2009;84:194-200
2. Yu NC. Long term follow up of hemoglobin A1c in 13 cases with G6PD deficiency in a diabetes clinic, Symposium of A1C in diagnosis and clinical implication, Chinese Taipei Diabetes Association, Nov/11/2010, Oral presentation
3. Yu NC, Chen S-M, Li Y-H, F S-H. Survey Of Subcutaneous Lipohypertrophy In 514 Insulin Treated Patients, 6th International Huaxia Congress of Endocrinology, Dec/10/2010, Oral presentation.
4. Tsai ST, Yu NC, Lin Boniface J, Tai TY. *Glucose Profile by Self-Monitoring*, ISBN:9789862412268, Common Wealth Magazine, Taipei, Nov/2010

| S4-1 |

Recognition programs of diabetes educators and teams in Taiwan

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Taiwanese Association of Diabetes Educators, Taiwan

Aims: Sharing the experience of recognition programs of diabetes educators and teams in Taiwan

Methods: Summary the historical and most updated regulation and result of recognition programs from data bank of Taiwanese Association of Diabetes Educators

Results: The pilot diabetes team program enrolled 2 hospitals in 1991 and expanded gradually under the support of DOH, the recognition program of diabetes educators and teams started since 1997. The criteria for certification of educators include core curriculum courses, 50 hours CME, a written test, 80 hours internship and a finally oral test, during the period the HCPs must maintain their own clinical case management for one year. The number of CDEs had increased from 240 to 4428 (48% of all members) during 1997-2010. There are 167 recognition Diabetes Health Promotion Institutes organized by CDEs and 1059 (hospital 252, GP 807) Diabetes Shared Care Teams in Taiwan in

2011, these teams cover 30% of diabetes population and make better care performance than those who do not attain the recognition program.

Conclusion: Recognition programs of diabetes educators and teams play an important role in diabetes chronic care model. The diabetes educators support self-management of patients effectively, the training courses and qualification system ensure the medical decisions are given under guidelines or consensus by educators, the trained HCPs work together to organize their own delivery system with same standard. The outcome of diabetes care is reviewed periodically through information system by TADE and NHI. Every country has their own strategy to combat diabetes, training and recognition system of both diabetes educators and teams are important for HCPs to establish a effective diabetes care system, hopefully together we can overcome the disease burden from diabetes.



Brenda Lim

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• Education and Appointments

1985-1988	Staff Nurse - Paediatric /ENT/Orthopaedic Ward - Tan Tock Seng Hospital
1988-1995	Staff Nurse/Senior Staff Nurse - Paediatric Ward - National University Hospital
1995-2001	Diabetes Nurse Educator - Diabetes Clinic - National University Hospital
2001-2005	Clinic Manager in Diabetes Centre -Tan Tock Seng Hospital
2005-2010	Operations Manager in Dept of Endocrinology/Geriatric Medicine/Oncology Medical/Occupational Health in Tan Tock Seng Hospital
2010-present	Director of Nursing in National Skin Centre

• Research Interests

Special interest in Diabetes Mellitus, Healthcare Services and Dermatology.

• Brief List of Publication

1. Rinkoo Dalan, Michelle Jong, Siew-Pang Chan, Robert Hawkins, Robin Choo, Brenda Lim, May L Tan, Melvin Ks Leow. High-sensitivity C-reactive protein levels and Type 2 Diabetes in urban North Indians. The Journal of the Endocrinology & Metabolism, 2009

| S4-2 |

Diabetes education: the learning roadmap for diabetes educators in Singapore

Brenda Lim

Association of Diabetes Educators, Singapore

Diabetes education has been recognized as an essential element of preventive and disease management delivering across clinics and hospitals. With the increasing demands of nurses as educators for preventive and chronic disease management, it is important to establish a learning roadmap in preparing the transition role of a nurse to a diabetes educator.

In the recent years, many hospitals and primary health-care institutions in Singapore have provided the learning roadmap for diabetes education and various specialized professional nursing development. The learning also often

takes into consideration of the characteristics of nurses with respect to their professional development for career path.

The institution support is the key to the development of role of nurses as educators. Today, with the establishment of the learning roadmap for diabetes educators in Singapore, many nurses have successfully integrated into the role of diabetes educators with competent and confident to assume responsibility for educating different population groups in a variety of setting such as children and adolescent, gestational, adult and elderly diabetes care and education.



Jane Giles

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• Education and Appointments

1989	Royal Adelaide Hospital	General Registered Nurse
1994	Deakin University - Victoria	Graduate Certificate (Diabetes Education)
1998	Diabetes Outreach - Country Health SA	Manager
1998	Australian Diabetes Educators Association	Credentialed Diabetes Educator (Re-credentialed, 2001, 2004, 2007 & 2010)
1999	University of South Australia	Master of Nursing (Advanced Nursing Practice)
1999-current	University of South Australia and Flinders University	Guest Lecturer
2000-2008	Australian Diabetes Educators Association	Vice President 2005-2006 President 2007-2008
2004	University of South Australia	Bachelor of Education (Adult Education & Educational Computing)
2006-2009	Diabetes Australia	Board Director

• Research Interests

Major: Education of health professionals / education and support of people with diabetes in rural areas.

• Brief List of Publications

1. Von derBorsch J & Giles J (2011) Education priorities for alcohol and diabetes, *Diabetes Management Journal*, 35, (in press).
2. Giles J (2010) Nursing roles in initiating and adjusting insulin, *Diabetes Management Journal*, 32, p 24
3. Giles J (2009) Australian diabetes map, *The Australian Diabetes Educator*, 12(4), pp 11-12.
4. Giles J, Visentin V & Phillips P (2009) Building and supporting a diabetes education workforce, *Proceedings of the 10th National Rural Health Conference*, editor Gordon Gregory, Cairns Qld, 17-20 May 2009. Canberra: National Rural Health Alliance, 2009.
5. Giles J, Visentin K & Hill P (2008) Diabetes Care, In *A Practice Manual for Community Nursing in Australia*, Chap 12, Ed Kralik D, Trowbridge K & Smith J, Wiley-Blackwell, Melbourne
6. Price N & Giles J (2008) Sickday management for people with diabetes, *Diabetes Management Journal*, Mar Vol 22, p. 6
7. Phillips P, Giles J & Martin W (2007) Why don't you..? Yes, but..? *The Australian Diabetes Educator*, 10 (2) p.14-15
8. Giles J & Phillips P (2007) Microalbuminuria - Getting the best specimen, *The Australian Diabetes Educator*, 10 (2) p.38
9. Cornelius S & Giles J (2007) ADEA International Partnerships Committee; Supporting neighbouring countries to enhance diabetes education, *The Australian Diabetes Educator*, 10 (2) p.31-32

| S4-3 |

Recognition programs; an Australian experience

Jane Giles

Diabetes Outreach - Country Health SA, Australia

Credentiailling by health professional organisations is primarily a process used to verify the qualifications and experience of health professionals to determine their ability to provide safe, high quality health care services. Credentiailling has the potential to improve safety for consumers of health services by ensuring clinicians practice within the bounds of their training and competency, and engage in planned continuing professional education. It also enables recognition of advanced training and practice capacity. Health professional associations use 'credentiailling' in different ways to address recognition issues related to an extension of the health professionals primary qualification.

In 1986 the Australian Diabetes Educators Association commenced a national credentiailling program for its members as a way of recognising those diabetes educators who had developed an advanced level of knowledge, skill and competency. The program at that time was based on the

diabetes educator being able to demonstrate training and experience in diabetes education. Re-credentiailling was based on demonstrating continuing professional development in various areas over a three-year cycle. In 2001, the program underwent a significant review. This review resulted in the applicant being required to complete a Post Graduate Certificate in Diabetes Education, 1800 hours of diabetes education practice and a portfolio of continuing professional education in the year proceeding the application. In 2008, a mentoring program was added to the credentiailling process. Mentoring aimed to further build rigor related in competency. An applicant now needs to be part of a mentoring relationship with a credentiailled diabetes educator for a period of not less than 6 months. Re-credentiailling remains on a 3 year cycle and continues to be based on demonstrating continuing professional education and professional contribution.



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• Education and Appointments

1981-1987	Kyung Hee University, College of Medicine	M.D.
1994-1997	Kyung Hee University, Graduate School	Ph.D.
1991-1995	Kyung Hee University Hospital	Residency in Internal Medicine
1995-1998	Samsung Seoul Hospital	Fellowship of Endocrinology and Metabolism
1998-1999	Kwandong University, College of Medicine	Assistant Professor
1999-2005	Eulji University, School of Medicine	Associate Professor
2006-present	Kyung Hee University, School of Medicine	Professor

• Research Interests

Major: Endocrinology and Metabolism, islet transplantation

• Brief List of Publications

1. Kang, H., Ahn, K.J., Choi, J.Y., Park, H.J., Park, S.J. & Lee, S.K., Efficacy of insulin glargine in perioperative glucose control in type 2 diabetic patients. *Eur J Anaesthesiol*, 2009, 26, 666-70.
2. Nam Ju Lee, S.E.L., Cheung-Seog Park, Hyun-Jong Ahn, Kyu Jeung Ahn, Yong Seek Park, Upregulation of Heme Oxygenase-1 as an Adaptive Mechanism against Acrolein in RAW 264.7 Macrophages. *Mol. Cell. Toxicol*, 2009, 5, 7.
3. Park, K.S., Ahn, K.J., Kim, B.J., Kim, H.J., Yoo, S.M., Kim, J.Y., Lee, K.H., Baik, H.W. & Lee, S.K., Circulating concentrations of monocyte chemoattractant protein-1 are associated with menopause status in Korean women. *Clin Chim Acta*, 2009, 403, 92-6.
4. Lee, S.R., Choi, M.C. & Ahn, K.J., A case of multiple endocrine neoplasia type 1 with primary liver gastrinoma. *J Korean Med Sci*, 2010, 25, 953-6.
5. Y.-C. Hwang, I.-K.J., S. Chon*, S. Oh*, K. J. Ahn, H. Y. Chung, J.-T. Woo*, S.-W. Kim*, J.-W. Kim* and Y. S. Kim*, Fulminant Type 1 diabetes mellitus associated with acute hepatitis A. *Diabetic Medicine*, 2010, 27, 2.
6. Ahn, KJ, Insulin therapy in Highly insulin resistance type 2 Diabetes Mellitus. *Korean Diabetes Journal*, 2010, 34, 6.
7. Hwang YC, Jeong IK, Ahn KJ, Chung HY. Circulating osteocalcin level is associated with improved glucose tolerance, insulin secretion and sensitivity independent of the plasma adiponectin level. *Osteoporos Int*. 2011 Jun 9. [Epub ahead of print]
8. Chon S, Choi MC, Lee YJ, Hwang YC, Jeong IK, Oh S, Ahn KJ, Chung HY, Woo JT, Kim SW, Kim JW, Kim YS. Autoimmune hypoglycemia in a patient with characterization of insulin receptor autoantibodies. *Diabetes Metab J*. 2011 Feb;35(1):80-5. Epub 2011 Feb 28
9. Yoon KH, Shin JA, Kwon HS, Lee SH, Min KW, Ahn YB, Yoo SJ, Ahn KJ, Park SW, Lee KW, Sung YA, Park TS, Kim MS, Kim YK, Nam MS, Kim HS, Park IeB, Park JS, Woo JT, Son HY. Comparison of the efficacy of glimepiride, metformin, and rosiglitazone monotherapy in korean drug-na?ve type 2 diabetic patients: the practical evidence of antidiabetic monotherapy study. *Diabetes Metab J*. 2011 Feb;35(1):26-33. Epub 2011 Feb 28.
10. Kim HJ, Chun KH, Kim DJ, Han SJ, Kim YS, Woo JT, Park Y, Nam MS, Baik SH, Ahn KJ, Lee KW. Utilization patterns and cost of complementary and alternative medicine compared to conventional medicine in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2011 Jul;93(1):115-22. Epub 2011 Apr 27.
11. Kim SK, Kwon SB, Yoon KH, Ahn KJ, Kang JG, Jung HS, Kang ES, Kim JH, Kim KW. Assessment of glycemic lability and severity of hypoglycemia in Korean patients with type 1 diabetes. *Endocr J*. 2011;58(6):433-40. Epub 2011 Apr 20.

| S4-4 |

The status of diabetes education programs and clinics in Korea

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Diabetes is a chronic disease can have a profound affect on the overall health, quality of life and longevity of patients. In poorly controlled diabetes, stroke, heart disease, blindness, kidney failure, leg disease and amputations are all common. Making an early diagnosis, monitoring and controlling blood sugar is the best way to delay or prevent most of chronic complications of diabetes, improving quality of life.

The aim of patient education is for people with diabetes to improve their knowledge, skills and confidence, enabling them to take increasing control of their own condition and integrate effective self-management into their daily lives. High-quality structured education can have a profound effect on health outcomes and can significantly improve quality of life.

Lots of hospitals or clinics in Korea have education programs for diabetic patients and their families. KDA has certification program for Diabetes educator and Diabetes education hospital recognition program. KDA were investigated the status of diabetes education in regional hospitals

by online survey. 130 hospitals were requested and received responses from 78 hospitals including 58 diabetes recognition program certified hospital. 55% of educators were certificate holders, and these doctors, nurses, nutritionists, social workers etc. Regarding the type of education program, the group education was 99% and the individual education was 87%. Physician educators teach contents include what is diabetes, its complications and medical management. Nurse educators teach contents include self-care-management, smbg, foot care, exercise and lifestyle modification. Dietician educators teach contents include medical nutritional therapy. Social worker educators teach contents include psychological and stress management. But a few hospitals have a follow-up and monitoring program, such as improvement of A1c, hypertension, lipid profile and weight reduction.

Because diabetes education is an integral part of diabetes prevention and care, we need to make an effort to standardize and structured the education system.



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• Education and Appointments

1974	Kobe University School of Medicine, Kobe, Japan	Doctor of Medicine (M.D.)
1976	Kitano Hospital, Osaka, Japan	Clinical Fellow
1978	Kyoto University School of Medicine, Kyoto, Japan	Fellow
1982	Kyoto University School of Medicine, Kyoto, Japan	Doctor of Medicine (D.M.Sci.)
1982	The University of Michigan, Ann Arbor, USA	Postdoctoral Research Fellow
1991	The University of Chicago, Chicago, USA	Associate Professor
1998	The University of Chicago, Chicago, USA	Assistant Professor
2003-present	Div. of Cellular and Molecular Medicine, Kobe University Graduate School of Medicine, Kobe, Japan	Professor
2008-present	Div. of Diabetes and Endocrinology, Kobe University Chiba University School of Medicine, Chiba, Japan Graduate School of Medicine, Kobe, Japan	Professor Professor

• Research Interests

1. Mechanisms of insulin secretion
2. Regenerative medicine of pancreatic beta-cells
3. Mechanisms of the development of diabetes
4. Development of novel therapies for diabetes

• Brief List of Publications

1. Seino S et al. Dynamics of insulin secretion and the clinical implications for obesity and diabetes. *J Clin Invest.* 121: 2118-2125, 2011
2. Minami K et al. Tracing phenotypic reversibility of pancreatic beta-cells in vitro. *J Diabetes Invest.* 1: 242-251, 2010
3. Iwasaki M, et al. Establishment of new clonal pancreatic beta-cell lines (MIN6-K) useful for study of incretin/cyclic adenosine monophosphate signaling. *J Diabetes Invest.* 1: 137-142, 2010
4. Seino S et al. Sulfonylurea action re-revisited. *J Diabetes Invest.* 1: 37-39, 2010
5. Yasuda T et al. Rim2 alpha determines docking and priming states in insulin granule exocytosis. *Cell Metab.* 12: 117-129, 2010
6. De Marinis YZ et al. GLP-1 inhibits and adrenaline stimulates glucagon release by different modulation of N- and L-type Ca2+ channel-dependent exocytosis. *Cell Metab.* 11: 543-553, 2010
7. Seino S et al. Pancreatic beta-cell signaling: toward better understanding of diabetes and its treatment. *Proc Jpn Acad Ser B Phys Biol Sci.* 86: 563-577, 2010
8. Garnot Z et al. LKB1 regulates pancreatic beta cell size, polarity, and function. *Cell Metab.* 10: 296-309, 2009
9. Zhang CL et al. The cAMP sensor Epac2 is a direct target of anti-diabetic sulfonylurea drugs *Science.* 325: 607-610, 2009
10. Fujimoto W et al. Niflumic acid-sensitive ion channels play an important role in the induction of glucose-stimulated insulin secretion by cyclic AMP in mice. *Diabetologia.* 52: 863-872, 2009
11. Sugawara K et al. Rab11 and its effector Rip11 participate in regulation of insulin granule exocytosis. *Genes Cells.* 14: 445-456, 2009
12. Seino S et al. Roles of cAMP signaling in insulin granule exocytosis. *Diabetes Obes Metab.* 11 Suppl 4: 180-188, 2009

| S5-1 |

Control of insulin granule exocytosis

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Clarification of the mechanisms of insulin secretion provides a basis for better understanding and treatment of diabetes. Exocytosis of insulin granules is the final step of the secretory process of insulin secretion. Glucose-induced insulin secretion (GIIS) is the most important mechanism of insulin secretion. GIIS occurs in a biphasic manner: a rapid, sharp phase (first phase), followed by a slow, sustained phase (second phase). According to an existing model, the first phase of insulin secretion results from a readily releasable (RRP) pool comprising docked granules, the second phase from a reserve pool (RP) comprising granules located a distant way from the plasma membrane. However, in contrast the existing model, we have found that both phases in GIIS are caused mainly by restless newcomer (the granules that are fused immediately without docking). In addition to GIIS, potentiation of GIIS is critical for normal regulation of insulin secretion. It is now known that incretin/cAMP signaling potentiates insulin granule exocytosis by protein kinase A (PKA)-independent as well as PKA-dependent mechanisms, the former involving Epac2 (also referred to as cAMP-GEFII), a guanine-nucleotide-exchange factor (GEF) for Rap1. Epac2/Rap1 signaling potentiates insulin granule exocytosis probably by increasing the size of RRP. We have also found that Epac2 also is a direct target of sulfonylureas (SUs).

We previously reported that Epac2 binds to Rim2 (Rab3-interacting molecule 2, now renamed Rim2 α). We have studied Rim2 α null mice and Rim2 α -deficient clonal pancreatic β -cells, to clarify the role of Rim2 α in insulin granule exocytosis. We have found that although interaction of Rim2 α and Rab3 is required for docking, it is unnecessary for glucose-induced insulin granule exocytosis. This is consistent with the finding that glucose-in-

duced insulin granule exocytosis is caused by the granules that are newly recruited by stimulation and immediately fused to the plasma membrane without docking (*restless newcomer above*). We have also found that Rim2 α interacts with Munc13-1 at basal state and that Munc13-1 dissociates from this Rim2 α /Munc13-1 complex by glucose stimulation to activate Syntaxin1, which can form a SNARE complex with SNAP-25 and VAMP-2, which is essential for fusion of insulin granules to the plasma membrane, indicating that Rim2 α primes insulin granules for exocytosis. Thus, Rim2 α plays a critical role in determining docking and priming states in insulin granule exocytosis.

In this symposium, control of insulin granule exocytosis will be discussed, based on our studies.

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• Education and Appointments

1978-1983	Moscow Sate University, Moscow Russia	Student
1983-1990	Institute of Biochemistry, Russian Academy of Sciences	Graduate student
1991-1997	Massachusetts General Hospital/Harvard Medical School	Postdoctoral Research Scientist
1997-2006	Massachusetts General Hospital/Harvard Medical School	Instructor, Assistant Professor
2006-date	Massachusetts General Hospital/Harvard Medical School	Associate Professor, Director, Molecular Imaging Laboratory

• Research Interests

Major: Molecular Imaging

• Brief List of Publications

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6. Medarova Z, Kumar, M, Ng, SW, Junzheng, Y, Barteneva N, Evgenov N, Petkova V, Moore A. Multifunctional magnetic nanocarriers for image-tagged siRNA delivery to intact pancreatic islets. *Transplantation*, 2008
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| S5-2 |

Imaging of inflammation in endogenous islets and islets in transplanted grafts

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A key element of the pathology of Type 1 diabetes is the death or dysfunction of insulin producing cell in pancreatic islets, caused by autoimmune destruction. Initial inflammation in pancreatic islets begins before the onset of diabetes and persists for many years with no obvious clinical symptoms. Prominent features of inflammation include accumulation of diabetogenic T cells in the islets and vascular damage.

Islet transplantation has recently emerged as a powerful tool to restore normoglycemia in diabetic patients. However, on-going autoimmune events cause inflammation in islet grafts leading to significant islet loss after transplantation. Inflammation in transplanted islets has features similar to that happening in endogenous islets. Specifically,

accumulation of immune cells causes vascular destruction that ultimately leads to the graft loss.

In vivo imaging is a powerful tool, which allows scientists and clinicians to "look" inside the body without surgical intervention. It is widely used to detect and follow various pathologies including cancer, Alzheimer disease, stroke and others. It would be highly advantageous if similar tools could be applied for the detection, monitoring, and treatment of diabetes. Imaging could play a crucial role in identifying inflammation in both endogenous and transplanted islets. This presentation will focus on novel developments in non-invasive imaging of endogenous pancreatic islets as well as islets in transplants during inflammation and associated changes in islet microenvironment.



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• Education and Appointments

1999	Seoul National University College of Medicine	M.D.
2007	Seoul National University College of Medicine	Ph.D.
2009-present	Seoul National University College of Medicine	Assistant Professor

• Research Interests

Major: islet cell biology, islet transplantation

• Brief List of Publications

1. Mechanism for anti-oxidative effects of thiazolidinediones in pancreatic β -cells. Chung SS, Kim M, Lee JS, Ahn BY, Jung HS, Lee HM, Park KS. *Am J Physiol Endocrinol Metab*. 2011 Aug 16. [Epub ahead of print]
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| S5-3 |

Preventive effects of endothelial progenitor cells on the early graft loss after islet transplantation

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There has been successful demonstration of islet cell isolation from a cadaveric donor's pancreas, transplantation into subjects with diabetes, and thereby improvement in glucose regulation. The Edmonton case series suggest that approximately two-thirds of the recipients enjoy insulin independence 1 year after receiving islet infusion. Even so, worldwide efforts to advance the therapy have served to break through hurdles yet to clear. One of the obstacles is the shortage of sources of islets. There can be two approaches to overcome the limitation of islets: protecting the islets in the course of the tough isolation process to maximize isolation yield; another is saving the islets lost in the early post-transplant period, which are as much as 50-60% of the grafts.

Intravascular infusion of islets results in nonspecific inflammatory and coagulation pathways promoting a so-called instant blood-mediated inflammatory reaction (IBMIR). Various methods preventing IBMIR have been applied to enhance islet survival and engraftment. Endothelial cells are known to protect against complement-mediated

lysis and activation of coagulation. Endothelial progenitor cells (EPC) seem to have lower profile of procoagulation in some environment compared to mature endothelial cells. In addition, endothelial progenitor cells display a unique ability to promote angiogenesis although the underlying molecular mechanism remains poorly understood. These suggest that endothelial progenitor cells might be a better source to protect IBMIR and enhance islet vasculogenesis. Therefore, we tested effects of composite pig islet-human endothelial progenitor cell grafts in vitro and in vivo. These 'endothelial progenitor cell coats' reduced components of IBMIR and improved blood glucose levels in STZ-diabetic athymic (nu/nu) nude mice. On morphologic examination, we identified more islet grafts colocalized with human EPC in the liver.

Therefore, if optimal EPC-islet coculture method would be identified, EPC-coating can be applied to control the strong innate immune response induced by islet grafts, and clinical islet transplantation would be more available and feasible strategy for the cure of diabetes.



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• Education and Appointments

1978	University of Missouri-Columbia	B.S.
1988	University of Missouri-Rolla	Chemistry/Biology Ph.D.
1987-89	Yale University (Chemistry Department)	Physical Organic Chem.
1989-2000	Yale University School of Medicine	Post-doctoral Candidate Research Scientist
2000-present	Yale University School of Medicine	Associate Professor

• Research Interests

1. Mechanisms coupling mitochondrial metabolism with intracellular signaling to regulate insulin secretion from pancreatic islet β -cells.
2. Non-invasive imaging of pancreatic beta-cell mass.

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| S5-4 |

***In vivo* positron emission tomography (PET) imaging of endogenous pancreatic beta cell mass in healthy and type 1 diabetic subjects**

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Developing treatments to prevent loss of, or restore, pancreatic islet β -cell mass (BCM) in type 1 diabetic (T1DM) patients is hampered by a lack of robust methods for the non-invasive imaging of BCM. MR imaging approaches have the advantage of imaging without the use of ionizing radiation, are relatively economical, are amendable to longitudinal studies of changes in BCM, and proof-of-principle for imaging endogenous BCM has been demonstrated in rodents. Compared to MRI, PET and SPECT imaging have the inherent drawback of requiring the use of ionizing radiation. However, the enhanced sensitivity, combined with the judicious use of selective imaging agents, has proven the value of these methods for receptor-targeting imaging. The key for imaging then lies in identifying a receptor that is highly-enriched in the target tissue and developing a receptor-specific ligand that can be readily labeled with a PET-detectable radionuclide. Strategies to image BCM by PET and SPECT have explored the efficacy of small molecule and β -cell-specific antibody and antibody-fragment radioligands targeted to β -cell specific receptor binding sites. Of the radioligands identified to date, only those targeting Vesicular Monoamine Transporter type-2 (VMAT2) have met those criteria justifying phase 1 clinical evaluation

for use to quantitatively image BCM in humans.

We evaluated [^{18}F]FP-DTBZ for VMAT2-directed imaging and quantification of BCM in 7 T1DM and 9 healthy controls matched for age and body mass index. Dynamic PET data were acquired on the HR+ for up to six hours after administration of radiotracer. Regional time-activity curves, with metabolite-corrected arterial data, were analyzed using compartmental models to estimate the total volume of distribution (V_T) in tissue, an index of total tracer uptake relative to arterial plasma concentration. Binding potential (BP_{ND}), a ratio of specific to non-displaceable uptake, was calculated for pancreatic subregions using the renal cortex as a reference region devoid of specific binding. Beta-cell function was assessed by an arginine stimulus test. Mean V_T and BP_{ND} in pancreas were reduced markedly in the T1DM subjects, whereas V_T in kidney did not differ significantly between groups. Both pancreatic binding parameters correlated with beta-cell function as reflected by the arginine-elicited increase in circulating C-peptide. These findings demonstrate that quantitative evaluation of endogenous beta-cell mass can be performed clinically with [^{18}F]FP-(+)-DTBZ PET.



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• Education and Appointments

1985-1989	Harvard College, Cambridge, MA	BA	Biochemical Sci.
1989-1998	Harvard Medical School, Boston, MA	MD	Medicine
1989-1992	Mass. Institute of Tech., Cambridge, MA		Health, Sci. & Tech.
1991-1995	Harvard Graduate School, Cambridge, MA	PhD	Biol. & Biomed Sci.
1998-2001	Clinical Resident in Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts		
2001-2005	Clinical Fellow in Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts		
2002-	Medical Staff, Melrose Wakefield Hospital, Melrose, Massachusetts		
2005-2007	Research Fellow in Cancer Biology, Dana-Farber Cancer Institute and Harvard Medical School, Boston, Massachusetts		
2005-2007	Instructor, Department of Medicine, Division of Cardiology, Brigham & Women's Hospital, Boston, Massachusetts		
2008-	Assistant Professor, Department of Medicine, Division of Cardiology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts		
2009-	Assistant Professor, Program in Biochemical and Biological Sciences, Harvard Medical School, Boston, Massachusetts		

• Brief List of Publications

1. Rowe GC, Jang C, Patten IS, Arany Z. (2011). PGC-1beta Regulates Angiogenesis in Skeletal Muscle. *Am J Physiol Endocrinol Metab.* 2011 Mar 1. [Epub ahead of print] PMID: 21364124
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7. Arany, Z.*, S.-Y. Foo, Y. Ma, J. Ruas, A. Bommi-Reddy, G. Girnun, M. Cooper, D. Laznik, J. Chinsomboon, S. Rangwala, K. H. Baek, A. Rosenzweig, and B.M. Spiegelman*. (2008) "HIF-independent regulation of VEGF and angiogenesis by the transcriptional coactivator PGC-1 α ." *Nature.* 451: 1008-13. *co-corresponding authors PMID: 18288196
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| S6-1 |

PGC-1 coactivators: orchestrators of skeletal muscle metabolism

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Mitochondria in skeletal muscle are thought to play a critical role in insulin sensitivity. Current models posit that accumulation of incompletely oxidized and unesterified fatty acids drive much of insulin resistance. Fatty acids are almost entirely consumed by mitochondria, underscoring the key role played by these organelles. The transcriptional coactivators PGC-1 α and PGC-1 β are potent regulators of mitochondrial biology in muscle, and have thus been promoted as potential important modifiers of glucose

homeostasis. The possible role that these coactivators play in insulin resistance will be discussed, including data from multiple gain-of-function and loss-of-function genetically modified mouse models. In addition, the PGC-1 coactivators also regulate numerous ancillary programs important for mitochondrial function, including nutrient transport and vascular homeostasis. Mechanisms by which the PGC-1s, and endurance exercise, regulate vascular homeostasis in muscle will be discussed.



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• Education and Appointments

1997-2001	University of Tokyo, Dept. of Neurochemistry	Ph.D
2001-2002	University of Minnesota, Dept. of Psychiatry	Postdoctoral Fellow
2002-2005	Beth Israel Deaconess Medical Center and Harvard Medical School, Division of Endocrinology	Postdoctoral Fellow
2005-2007	Pennsylvania State University, Dept. of Biology	Research Assistant Professor
2007-present	Shanghai Institute for Nutritional Sciences, Chinese Academy of Science	Principle Investigator, Professor, PhD advisor

• Research Interests

The long term goal of our research interest is to understand the cellular and molecular mechanisms underlying genetic and nutritional regulation of metabolic diseases including obesity, diabetes, and fatty liver. This will be achieved by using molecular and cellular biology techniques in animal models and cell lines. Currently, our lab research interest focuses on elucidating the mechanisms of central and peripheral regulation of altered lipid metabolism under leucine deprivation. These studies will certainly provide important evidence for the better understanding, and hopefully lead to the possible nutritional prevention or treatment of certain metabolic diseases, such as obesity, diabetes and fatty liver.

• Brief List of Publications

1. Cheng Y#, Zhang Q #, Meng Q, Xia T, Huang Z, Wang C, Liu B, Chen S, Xiao F, Du Y, and Guo F*. Leucine deprivation stimulates fat loss via increasing corticotrophin releasing hormone (CRH) expression in the hypothalamus and activating sympathetic nervous system (SNS). *Molecular Endocrinology*. Accepted
2. H, Meng Q, Xiao F, Chen S, Yu J, Wang C, and Guo F*. ATF4 deficiency protects mice from high-carbohydrate diet-induced liver steatosis. *Biochemical Journal*. Published online. DOI: 10.1042/BJ20110263
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| S6-2 |

Amino acid regulation of insulin sensitivity

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Insulin resistance is a common feature of many metabolic diseases, including type 2 diabetes mellitus and non-alcoholic fatty liver diseases. Various strategies have been proposed to treat insulin resistance, including lifestyle modifications and pharmacological interventions. Recently, there has been a growing interest in treating insulin resistance with dietary manipulation of micronutrients, including branched-chain amino acids (BCAAs), including leucine. Several studies have shown that dietary supplementation of leucine influences insulin sensitivity.

By contrast, our research has focused on the effect of eliminating leucine from the diet. We recently observed that leucine deprivation increases whole-body insulin sensitivity and insulin signaling in liver. Furthermore, we show

that leucine deprivation improves hepatic insulin sensitivity by sequentially activating GCN2 and decreasing mTOR signaling. In addition, we found that activation of AMPK also contributes to increased hepatic insulin sensitivity under leucine deprivation. Finally, we show that leucine deprivation improves insulin sensitivity under insulin-resistant conditions. This study describes mechanisms underlying increased hepatic insulin sensitivity under leucine deprivation. Furthermore, we demonstrate a novel function for GCN2 in the regulation of insulin sensitivity. These observations provide a rationale for short-term dietary restriction of leucine for the treatment of insulin resistance and associated metabolic diseases.



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• Education and Appointments

1988-1992	Dept. of Chemistry, Seoul National University, Korea	BA
1993-1995	Dept. of Chemistry, Seoul National University, Korea	MS
1995-2000	Dept. of BMBB, University of Minnesota, USA	Ph.D.
2000-2001	Dept. of BMBB, University of Minnesota, USA	Postdoctoral Fellow
2001-2002	Dept. of Mol Pharm, Stanford University, USA	Postdoctoral Fellow
2002-2005	Salk Institute for Biological Studies, USA	Research Associate
2005-2009	Sungkyunkwan University School of Medicine	Assistant Professor
2009-Present	Sungkyunkwan University School of Medicine	Associate Professor

• Research Interests

Major: Biochemistry, Metabolism, Transcription, Liver

• Brief List of Publications

1. Dongryeol Ryu*, Woo-Young Seo*, Young-Sil Yoon*, Yo-Na Kim, Su Sung Kim, Hye-Jin Kim, Tae-Sik Park, Cheol Soo Choi# and Seung-Hoi Koo#. ER stress promotes LIPIN2-dependent hepatic insulin resistance. *Diabetes*. 60(4):1072-81. 2011 (*co-first authors, #co-corresponding authors)
2. Kyoung-Jin Oh*, Jinyoung Park*, Su Yeon Lee, Injae Hwnag, Jae Bum Kim, Tae-Sik Park, Heon-Jeong Lee, and Seung-Hoi Koo. Atypical antipsychotic drugs perturb AMPK-dependent regulation of hepatic lipid metabolism. *Am J Physiol Endocrinol Metab*. 300(4):E624-32. 2011 (*co-first authors)
3. Young-Sil Yoon, Min-Woo Lee, Dongryeol Ryu, Jeong Ho Kim, Hui Ma, Woo-Young Seo, Yo-Na Kim, Su Sung Kim, Chul Ho Lee, Tony Hunter, Cheol Soo Choi, Marc R. Montminy# and Seung-Hoi Koo#. Suppressor of MEK null (SMEK)/protein phosphatase 4 catalytic subunit (PP4C) is a key regulator of hepatic gluconeogenesis. *Proc Natl Acad Sci U S A*. 107(41):17704-9. 2010 (#co-corresponding authors)
4. Ji-Min Lee*, Woo-Young Seo*, Kwang-Hoon Song, Dipanjan Chanda, Yong Deuk Kim, Don-Kyu Kim, Min-Woo Lee, Dongryeol Ryu, Yong-Hoon Kim, Jung-Ran Noh, Chul-Ho Lee, John Y. L. Chiang, Seung-Hoi Koo# and Hueng-Sik Choi#. AMPK-dependent repression of hepatic gluconeogenesis via disruption of CREB/CRTC2 complex by orphan nuclear receptor SHP. *J Biol Chem*. 285(42): 32181-91. 2010 (*co-first authors, #co-corresponding authors)
5. Min-Woo Lee*, Dipanjan Chanda*, Jianqi Yang, Hyunhee Oh, Su Sung Kim, Young-Sil Yoon, Sungpyo Hong, Keun-Gyu Park, In-Kyu Lee, Cheol Soo Choi, Richard W. Hanson, Hueng-Sik Choi# and Seung-Hoi Koo#. Regulation of hepatic gluconeogenesis by an ER-bound transcription factor, CREBH. *Cell Metab*. 11(4):331-339. 2010 (*co-first authors, #co-corresponding authors)
6. Balachandar Nedumaran*, Gwang Sik Kim*, Sungpyo Hong, Young-Sil Yoon, Yong-Hoon Kim, Chul-Ho Lee, Young Chul Lee, Seung-Hoi Koo# and Hueng-Sik Choi#. Orphan Nuclear Receptor DAX-1 acts as a novel corepressor of LXR α and inhibits hepatic lipogenesis. *J Biol Chem*. 285(12):9221-32. 2010 (*co-first authors, #co-corresponding authors)
7. Balachandar Nedumaran*, Sungpyo Hong*, Yuan-Bin Xie, Yong-Hoon Kim, Woo-Young Seo, Min-Woo Lee, Chul-Ho Lee, Seung-Hoi Koo# and Hueng-Sik Choi#. DAX-1 acts as a novel corepressor of orphan nuclear receptor HNF4 α and negatively regulates the gluconeogenic enzyme gene expression. *J Biol Chem*. 284(40): 27511-23. 2009 (*co-first authors, #co-corresponding authors)

| S6-3 |

Functional analysis of key regulators in hepatic glucose metabolism

Seung-Hoi Koo

Sungkyunkwan University, Korea

Liver plays a major role in maintaining glucose homeostasis in mammals. Under fasting conditions, glucagon promotes hepatic glucose production in part by activating gluconeogenic programs at the transcriptional level. We have previously described a role of CREB coactivator CRTC2/TORC2 in the regulation of hepatic gluconeogenesis by controlling key enzyme gene expression including PEPCK and G6Pase. Families of AMPK-related kinases such as SIK1 or SIK2 were shown to be involved in this process by catalyzing serine 171 phosphorylation of CRTC2/TORC2, which promotes its cytoplasmic retention and subsequent degradation process. Conversely, hepatic protein phosphatase 4 reverses this process to promote de novo glucose production from the liver. Uncontrolled activation of CRTC2 by insulin resistance has been attributed to the hyper-

glycemia and the progression of type 2 diabetes, and both inactivation of SIK activity and enhancement of PP4 activity were observed at least in rodent animal models. Further analysis are necessary to delineate the relative importance of various kinases and phosphatases implicated in this process.

In this talk, we would like to discuss a recent progress regarding the regulatory mechanisms for CRTC2-dependent glucose metabolism using animal models. In addition, potential new regulatory mechanisms to modulate CRTC2 activity will be discussed. Mechanistic analysis for the CRTC2-dependent hepatic glucose metabolism would provide the valuable information for developing potential therapeutic means for the treatment of type 2 diabetes.



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• Education and Appointments

1980-1986	College of Medicine, Chungnam National University	B.A. Degree
1987-1989	Postgraduate School, Chungnam National University	Master Degree
1992-1998	Postgraduate School, Chungnam National University	Ph. Degree
2001-present	Laboratory of Endocrine Cell Biology, National Research Laboratory Program, Ministry of science and technology	Chief
2004-present	Department of Internal Medicine, School of Medicine, Chungnam National University	Professor
2004-2010	Division of Endocrinology-Metabolism, Department of Internal Medicine, Chungnam National University hospital	Chief
2010-present	Research Center for Endocrine and Metabolic Diseases, Ministry of Health & Welfare	Director
2011-present	Chungnam National University School of Medicine	Vice-president

• Research Interests

Major: Division of Endocrinology-Metabolism
 Endocrine Metabolic Diseases, Thyroid, Osteoporosis, Diabetes, metabolic syndrome

• Brief List of Publications

1. Lee JH, Koh H, Kim M, Kim Y, Lee SY, Karess RE, Lee SH, Shong M, Kim JM, Kim J, Chung J Energy-dependent regulation of cell structure by AMP-activated protein kinase. *Nature*. 2007 Jun 21;447(7147) :1017-1020
2. Kwon MC, Koo BK, Moon JS, Kim YY, Park KC, Kim NS, Kwon MY, Kong MP, Yoon KJ, Im SK, Ghim J, Han YM, Jang SK, Shong M, Kong YY Crif1 is a novel transcriptional coactivator of STAT3. *EMBO J*. 2008 Feb 20;27(4):642-653
3. Hwang JH, Kim DW, Jo EJ, Kim YK, Jo YS, Park JH, Yoo SK, Park MK, Kwak TH, Kho YL, Han J, Choi HS, Lee SH, Kim JM, Lee I, Kyung T, Jang C, Chung J, Kweon GR, Shong M Pharmacological Stimulation of NADH Oxidation Ameliorates Obesity and Related Phenotypes in Mice. *Diabetes*. 2009 Apr;58(4):965-974
4. Kim SY, Jeoung NH, Oh CJ, Choi YK, Lee HJ, Kim HJ, Kim JY, Hwang JH, Tadi S, Yim YH, Lee KU, Park KG, Huh S, Min KN, Jeong KH, Park MG, Kwak TH, Kweon GR, Inukai K, Shong M, Lee IK Activation of NAD(P)H:quinone oxidoreductase 1 prevents arterial restenosis by suppressing vascular smooth muscle cell proliferation. *Circ Res*. 2009 Apr 10;104(7):842-850
5. Kim YH, Hwang JH, Noh JR, Gang GT, Kim DH, Son HY, Kwak TH, Shong M, Lee IK, Lee CH Activation of NAD(P)H:quinone Oxidoreductase Ameliorates Spontaneous Hypertension in an Animal Model via Modulation of eNOS Activity. *Cardiovasc Res*. 2011 Apr 18

| S6-4 |

Mitochondrial dysfunction in white adipose tissue and systemic insulin resistance

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Insulin resistance is an underlying cause of type 2 diabetes. Mitochondrial dysfunction characterized by impaired oxidative phosphorylation (OXPHOS) has been proposed as an etiological mechanism of insulin resistance. However, the cause and initiating organ of OXPHOS dysfunction in the development of systemic insulin resistance has yet to be identified. Chronic inflammation of white adipose tissue (WAT) is a critical process in the development of systemic insulin resistance in excessive adiposity. Furthermore, dysfunction of cellular organelles, including mitochondria and endoplasmic reticulum (ER), is considered to be the underlying cause of insulin resistance and type 2 diabetes. Adipose mitochondrial mass is suppressed in the insulin resistant state and improvement of insulin

resistance with a PPAR γ agonist is associated with increased adipose mitochondrial biogenesis. These results strongly suggest that the dysregulation of mitochondrial function in adipose tissue plays a critical role in the development of insulin resistance and diabetes. To determine whether adipose OXPHOS deficiency plays an etiological role in systemic insulin resistance, the metabolic phenotypes of mice with OXPHOS-deficient adipose tissue were analyzed. In this symposium, detailed analytical results on systemic insulin resistance will be discussed in mice model of adipose mitochondrial dysfunction. These findings indicate that OXPHOS reserves in adipose tissue determine metabolic and inflammatory responses and can cause systemic inflammation and insulin resistance.



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• Education and Appointments

1998-2000	Kyungpook National University, Korea	M.S.
2000-2003	The Catholic University, Seoul, Korea	Ph.D.
2004-2004	Youngman University, Korea	Research Professor
2004-2008	NHLBI, NIH, USA	Visiting Fellow
2009-Present	LG Life Sciences Ltd. / R&D Park	Senior Scientist

• Research Interests

Major: Drug discovery, Mitochondrial disease
 innovative drug discovery, Metabolic disease, Mitochondrial disease, cancer

• Brief List of Publications

1. Kim HJ, Koo SY, Ahn BH, Park O, Park DH, Seo DO, Won JH, Yim HJ, Kwak HS, Park HS, Chung CW, Oh YL and Kim SH (2010) Neceox as a Novel Class of Mitochondrial Reactive Oxygen Species and ONOO⁻ Scavenger. *Arch Pharm Res* 2010 Nov; 33(11):1813-1823.
2. Liu J, Cao L, Chen J, Song S, Lee IH, Quijano C, Liu H, Keyvanfar K, Chen H, Cao LY, Ahn BH, Kumar NG, Rovira II, Xu XL, van Lohuizen M, Motoyama N, Deng CX, Finkel T. (2009) Bmi1 regulates mitochondrial function and the DNA damage response pathway. *Nature*. 2009 May 21; 459(7245):387-92.
3. Park MH, Ahn BH, Hong YK, Min do S. (2009) Overexpression of phospholipase D enhances matrix metalloproteinase-2 expression and glioma cell invasion via protein kinase C and protein kinase A/NF-kappaB/Sp1-mediated signaling pathways. *Carcinogenesis*. 2009 Feb; 30(2):356-65.
4. Ahn BH, Kim HS, Song S, Lee IN, Liu J, Vassilopoulos, Deng CX, Finkel T. (2008) A role the Mitochondrial deacetylase Sirt3 in regulating energy homeostasis. *Proc Natl Acad Sci U S A*. 2008 Sep 23; 105(38):14447-52.
5. Jacobs KM, Pennington JD, Bisht KS, Aykin-Burns N, Kim HS, Mishra M, Sun L, Nguyen P, Ahn BH, Leclerc J, Deng CX, Spitz DR, Gius D. (2008) SIRT3 interacts with the daf-16 homolog FOXO3a in the mitochondria, as well as increases FOXO3a dependent gene expression. *Int J Biol Sci*. 2008 Sep 5;4(5):291-9.
6. Jang YH, Ahn BH, Namkoong S, Kim YM, Jin JK, Kim YS, Min DS. (2008) Differential regulation of apoptosis by caspase-mediated cleavage of phospholipase D isozymes. *Cell Signal*. 2008 Dec;20(12):2198-207.
7. Ahn BH, Park MH, Lee YH, Min DS. (2007) Phorbol myristate acetate-induced Egr-1 expression is suppressed by phospholipase D isozymes in human glioma cells. *FEBS Lett*. 2007 Dec 22;581(30):5940-4.
8. Ahn BH, Park MH, Lee YH, Kwon TK, Min DS. (2007) Up-regulation of cyclooxygenase-2 by cobalt chloride-induced hypoxia is mediated by phospholipase D isozymes in human astrogloma cells. *Biochim Biophys Acta*. 2007 Dec; 1773(12):1721-31.
9. Jin JK, Ahn BH, Na YJ, Kim JI, Kim YS, Choi EK, Ko YG, Chung KC, Kozlowski PB, Min DS. (2007) Phospholipase D1 is associated with amyloid precursor protein in Alzheimer's disease. *Neurobiol Aging*. 2007 Jul; 28(7): 1015-27.
10. Shin SY, Choi HY, Ahn BH, Min do S, Son SW, Lee YH. (2007) Phospholipase Cgamma1 stimulates transcriptional activation of the matrix metalloproteinase-3 gene via the protein kinase C/Raf/ERK cascade. *Biochem Biophys Res Commun*. 2007 Feb 16; 353(3):611-6.
11. Nemoto S, Combs CA, French S, Ahn BH, Fergusson MM, Balaban RS, Finkel T. (2006) The mammalian longevity-associated gene product p66shc regulates mitochondrial metabolism. *J Biol Chem*. 2006 Apr 14; 281(15): 10555-60.
12. Ahn BH, Min G, Bae YS, Bae YS, Min DS. (2006) Phospholipase D is activated and phosphorylated by casein kinase-II in human U87 astrogloma cells. *Exp Mol Med*. 2006 Feb 28; 38(1):55-62.

| S7-1 |

Mitochondrial deacetylase Sirt3 as novel therapeutic for age-associated diseases

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Sirtuins post-translationally modulate the function of many cellular proteins that undergo reversible acetylation-deacetylation cycles, affecting physiological responses that have implications for treating diseases of ageing. Potent small-molecule modulators of sirtuins have shown efficacy in pre-clinical models of metabolic, neurodegenerative and inflammatory diseases, and so hold promise for drug discovery efforts in multiple therapeutic areas. Here, we demonstrate a role for the mitochondrial NAD-dependent deacetylase Sirt3 in the maintenance of basal ATP levels and as a regulator of mitochondrial electron transport. We note that Sirt3(-/-) mouse embryonic fibroblasts have a reduction in basal ATP levels. Reconstitution with wild-type but not a deacetylase-deficient form of Sirt3 restored ATP levels in these cells. Furthermore in wild-type mice, the resting level of ATP correlates with organ-specific Sirt3 protein expression. Remarkably, in mice lacking Sirt3, basal levels of ATP in the heart, kidney, and liver were reduced >50%. We

further demonstrate that mitochondrial protein acetylation is markedly elevated in Sirt3(-/-) tissues. In addition, in the absence of Sirt3, multiple components of Complex I of the electron transport chain demonstrate increased acetylation. Sirt3 can also physically interact with at least one of the known subunits of Complex I, the 39-kDa protein NDUFA9. Functional studies demonstrate that mitochondria from Sirt3(-/-) animals display a selective inhibition of Complex I activity. Furthermore, incubation of exogenous Sirt3 with mitochondria can augment Complex I activity. These results implicate protein acetylation as an important regulator of Complex I activity and demonstrate that Sirt3 functions in vivo to regulate and maintain basal ATP levels. Potent small-molecule modulators of sirtuins have shown efficacy in preclinical models of metabolic, neurodegenerative and inflammatory diseases, and so hold promise for drug discovery efforts in multiple therapeutic areas.



Robert A. Harris

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• Education and Appointments

1962	Iowa State University, Ames, IA	B.S.
1964	Purdue University, Lafayette, IN	M.S.
1965	Purdue University, Lafayette, IN	Ph.D.
1966-1970	University of Wisconsin, Madison, WI	Postdoctoral
1970-1975	Associate Professor, Department of Biochemistry, Indiana University School of Medicine	
1975-2008	Professor of Biochemistry and Molecular Biology, Indiana University School of Medicine	
1992-present	Grace M. Showalter Professor of Biochemistry, Indiana University School of Medicine	

• Brief List of Publications

1. Schneider, van Geyte, Frais, Kiss, Aragonés, Mazzone, Mairbäur, Debock, Jeoung, ollenhauer, Georgia-dou, Bishop, Roncal, Sutherland, Jordan, Gallez, Weitz, Harris, Maxwell, Baes, Ratcliffe, and Carmeliet. 2010. Loss of silencing of the PHD1 prolyl hydroxylase protects livers of mice against ischemia/reperfusion injury. *Gastroenterology* 138, 1143-1154 (2010).
2. Acin-Perez, R., Hoyos, B., Zhao, F., Vinogradov, V., Fischman, D.A., Harris, R.A., Leitges, M., Wongsirirotj, N., Blaner, W.S., Manfredi, G., and Hammerling, U. Control of oxidative phosphorylation by vitamin A illuminates a fundamental role in mitochondrial energy homeostasis. *FASEB Journal* 24: 627-636 (2010).
3. Halim, N.D., McFate, T., Okagaki, P., Korotchkina, L.G., Patel, M.S., Jeoung, N.H., Harris, R.A., Schell, M.J., and Verma, A. Phosphorylation status of pyruvate dehydrogenase distinguishes metabolic phenotypes of rat cerebral cortical astrocytes and neurons. *Glia* 58: 1168-1176 (2010).
4. Harris, R.A. Carbohydrate Metabolism I. Major Metabolic Pathways and their Control. In *Textbook of Biochemistry with Clinical Correlations* (Devlin, T.M., ed.) John Wiley & Sons, 7th Edition, pp. 591-646 (2010).
5. Harris, R.A. and Crabb, D.W. Metabolic Interrelationships. In *Textbook of Biochemistry with Clinical Correlations* (Devlin, T.M., ed.) John Wiley & Sons, 7th Edition, pp. 839-882 (2010).
6. Jeoung, N.H., and Harris, R.A. Role of pyruvate dehydrogenase kinase 4 in regulation of blood glucose levels. *Korean Diabetes Journal* 34: 274-283 (2010).
7. Kim, H., Kim, H-J., Lee, K., Kim, J-M, Kim, H.S., Kim, J-R., Choi, Y-K., Lee, S.J., Kim, J.Y., Harris, R.A., Jeong D., and Lee, I. Alpha-lipoic acid attenuates vascular calcification via reversal of mitochondrial function and restoration of Gas6/Axl/Akt survival pathway. *J. Cell. Mol. Med.* DOI: 10.1111/j.1582-4934.2011.01294.x (2011).
8. Dunford, E., Herbst, E., Jeoung, N.H., Gittings, W., Inglis, J.G., Vandenboom, R., LeBlanc, P.J., Harris, R.A., and Peters, S.J. The effect of pyruvate dehydrogenase (PDH) kinase 2 ablation on PDH activation during muscle contraction: the effect PDH kinase 1 compensation. *Am. J. Physiol.* 300: R1487-R1493 (2011).
9. Liangpunsakul, S., Sozio, M.S., Harris, R.A., Ross, R.A., Zeng, Y., and Crabb, D.W. Activation of carbohydrate response element binding protein (ChREBP) by ethanol. Submitted (2011).
10. Ussher, J.R., Wang, W., Gandhi, M., Oka, T., Keung, W., Jaswal, J.S., Clanachan, A.S., Dyck, J.R.B., Harris, R.A., and Lopaschuk, G.D. Stimulation of glucose oxidation yields dramatic protection against acute myocardial infarction. Submitted (2011).
11. Herbst, E.A., Dunford, E.C.E., Harris, R.A., Vandenboom, R., Leblanc, P.J., Roy, B.D., Jeoung, N.H., and Peters, S.J. Role of pyruvate dehydrogenase kinase 4 in regulating PDH activation during acute muscle contraction. Submitted (2011).
12. Hwang, B., Wu, P., and Harris, R.A. Additive effects of clofibrac acid and pyruvate dehydrogenase kinase isoenzyme 4 (PDK4) deficiency on hepatic steatosis in mice fed a high-saturated fat diet. Submitted (2011).

| S7-2 |

Control of the NAD⁺ redox state by the pyruvate dehydrogenase kinases

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The pyruvate dehydrogenase complex (PDC) is relatively active in the fed state to direct pyruvate into the citric acid cycle and lipid synthesis. In the starved state PDC is shut down by phosphorylation by pyruvate dehydrogenase kinases (PDKs) to conserve three carbon substrates for gluconeogenesis. This helps maintain blood glucose levels during starvation but contributes to hyperglycemia in diabetes. Studies with PDK4 knockout (KO) and PDK2/PDK4 double knockout (DKO) mice have established the importance of the PDKs in setting fasting blood glucose levels. Loss of control of PDC in PDK KO mice lowers pyruvate levels and limits the synthesis of oxaloacetate by pyruvate carboxylase. Not surprisingly, therefore, the phenotype of the PDK2/PDK4 DKO mice resembles that of children with pyruvate carboxylase deficiency. Although lack of substrate (pyruvate) is responsible for reduced pyruvate carboxylase flux in the PDK2/PDK4 DKO mice whereas lack of functional enzyme activity is responsible in pyruvate carbox-

ylase deficiency, both are characterized by hypoglycemia due to reduced synthesis of the oxaloacetate required for glucose synthesis. Both are also characterized by elevated tissue and blood lactate/pyruvate ratios and therefore elevated cytoplasmic NADH/NAD⁺ ratios due to reduced availability of oxaloacetate for the malate/aspartate shuttle, by lower mitochondrial NADH/NAD⁺ ratios due to a decrease in the availability of oxaloacetate for the citric acid cycle, and by an increase in serum citrulline levels due to a decrease in the availability of oxaloacetate and therefore aspartate for the urea cycle. This study shows that regulation of PDC activity by the PDKs is critically important for pyruvate carboxylase activity which in turn is critically important for setting normal cytoplasmic and mitochondrial NAD⁺ redox states and for maintaining activity of the malate-aspartate shuttle, lactate/alanine gluconeogenesis, and urea synthesis.



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• Education and Appointments

1984-1988	Department of Pharmacy, Chungnam National University	BS
1988-1991	Department of Pharmacy, Chungnam National University	MS
1994-1999	Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST)	Doctor
2002-2004	Department of Biochemistry, Baylor College of Medicine	Post-Doc.
1991-2005	Korea Research Institute of Bioscience and Biotechnology (KRIBB)	Research Scientist
2005-2007	Korea Research Institute of Bioscience and Biotechnology (KRIBB)	Principal Research Scientist
2007-	College of Pharmacy, Chosun University	Professor

• Research Interests

Major: Metabolic syndrome, Natural products, Pharmacognosy

• Brief List of Publications

1. Nguyen PH, Kang HW, Le TVT, Chae J, Kim SK, Kwon KI, Lim SI, Oh WK. Simple process for the decrease of myristicin content from *Myristica fragrans* and its activity with AMP-activated protein kinase (AMPK). *Journal of Food Biochemistry*, 2011 (in press, Correspondence).
2. Noh JR, Kim YH, Gang GT, Hwang JH, Lee HS, Ly SY, Oh WK, Song KS, Lee CH. Hepatoprotective effects of Chestnut (*Castanea crenata*) inner shell extract against chronic ethanol-induced oxidative stress in C57BL/6 mice. *Food Chem Toxicol.*, 49(7), 1537-1543, 2011.
3. Nguyen PH, Dao TT, Kim J, Phong DT, Ndinth DT, Mbafor JT, Oh WK. New 5-deoxyflavonoids and their inhibitory effects on protein tyrosine phosphatase 1B (PTP1B) activity. *Bioorganic & Medicinal Chemistry*, 19(11), 3378-3383, 2011 (Correspondence).
4. Khanal P, Oh WK, Yun HJ, Namgoong GM, Ahn SG, Kwon SM, Choi HK, Choi HS. p-HPEA-EDA, a phenolic compound from virgin olive oil, induces apoptosis of human colon cancer cells by activation of AMP-activated protein kinase. *Carcinogenesis*, 32(4), 545-553, 2011.
5. Namkoong S, Kim TJ, Jang IS, Kang KW, Oh WK, Park J. Alpinumisoflavone induces apoptosis and suppresses ERK/MAPK and NF- κ B pathways in lung tumor cells. *Biol Pharm Bull.*, 34(2), 203-208, 2011.
6. Dao TT, Nguyen PH, Lee HS, Kim EH, Park J, Lim SI, Oh WK. Chalcones as novel influenza A (H1N1) neuraminidase inhibitors from *Glycyrrhiza inflata*. *Bioorganic & Medicinal Chemistry Letters*, 21(1), 294-298, 2011 (Correspondence).
7. Nguyen TNA, Dao TT, Thung BT, Choi H, Kim E, Park J, Lim SI, Oh WK. Influenza A (H1N1) Neuraminidase Inhibitors from *Vitis amurensis*. *Food Chemistry*, 124(2), 437-443, 2011 (Correspondence).
8. Nguyen PH, Na M, Dao TT, Ndinth DT, Mbafor JT, Park J, Cheong H, Oh WK. New stilbenoid with inhibitory activity on viral neuraminidases from *Erythrina addisoniae*. *Bioorganic & Medicinal Chemistry Letters*, 20(22), 6430-6434, 2010 (Correspondence).
9. Oh WK, Cho KB, Hien TT, Dao TT, Kim TH, Kim HS, Han HK, Kwon SM, Ahn SG, Yoon JH, Kim TH, Kim YG, Kang KW. Amurensin G, a potent natural SIRT1 inhibitor, rescues doxorubicin responsiveness via down-regulation of multidrug resistance 1. *Molecular Pharmacology*, 78(5), 855-864, 2010 (First author).
10. Noh JR, Gang GT, Kim YH, Yang KJ, Hwang JH, Lee HS, Oh WK, Song KS, Lee CH. Antioxidant Effects of the Chestnut (*Castanea crenata*) inner shell extract in t-BHP-treated HepG2 cells, and CCl₄- and high fat diet-treated mice. *Food Chem Toxicol.*, 48(11), 3177-3183, 2010.

| S7-3 |

SIRT1 and/or AMPK activators as new drug candidates against metabolic disease from natural products

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As secondary substances from natural products are generally low-toxic's small molecules with high potential for chemical novelty and biological interests, extensive studies on medicinal plants may result in the investigation of new compounds with drug-like properties. The main objective of our team using natural plants as research source is finding active compounds on metabolic syndrome.

AMPK (AMP-activated protein kinase) and NAD⁺-dependent deacetylase (SIRT's) activated in response to reduced nutrient availability were selected as our interesting drug targets. Recently, many studies indicate that SIRT's and AMPK activators would mimic or potentiate the exercise-related effects. AMPK is activated when the AMP concentration rises, and also by upstream kinases such as LKB1 and CaMKK, while SIRT's is activated by reduced NAD⁺ content in the cells. Sirtuins have also emerged as therapeutic targets to treat age-related diseases.

Active compounds on AMPK and SIRT's have to control the energy homeostasis conserved from unicellular to the complex multicellular organisms. Furthermore, as metabolic disease has a character to be sustained for a lifetime from onset with disease, safety (low toxicity) as the potential values of natural products was assignable.

During we have been screened potentiated materials on the activity of SIRT's (SIRT1-7) from natural products, many papers were reported about controversy on whether the resveratrol or its derivatives as SIRT1 activator is a true or not? Thus, we tried to make screening method for finding of SIRT's activities by co-transfection of p53 and SIRT's, or by also determination of NAD⁺ content as end product. In this seminar, we will introduce some candidates by our methods, and also recent results by compounds isolated as SIRT's and/or AMPK activators on aging cells and animal models.



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• Education and Appointments

1985-1991	Seoul National University	MD
1998-2000	Seoul National University	Master of Science
2000-2002	Seoul National University	PhD
1991-1995	Seoul National University Hospital	Internship & Residency
1998-1999	Seoul National University Hospital	Fellowship
Currently	Korean Society for the Study of Obesity	Secretary General
Currently	Korean Society for Cancer Prevention	Chairman of Division of Clinical Cancer Prevention
Currently	Korea Health Promotion Foundation	Director
Currently	Korean Institute of Dietary Education Evaluation	Director
Currently	Advisor to Korea Health of Ministry, KFDA and others	

• Research Interests

Major: Obesity, Metabolic Syndrome, Clinical Nutrition, and Cancer Prevention

• Brief List of Publications

1. Park HS, Park CY, Oh SW, Yoo HJ. Prevalence of obesity and metabolic syndrome in Korean adults. *Obes Rev.* 2008 Mar;9(2):104-7.
2. Kim HJ, Lee S, Kim TW, Kim HH, Jeon TY, Yoon YS, Oh SW, Kwak H, Lee JG. Effects of exercise-induced weight loss on acylated and unacylated ghrelin in overweight children. *Clin Endocrinol (Oxf).* 2008 Mar;68(3):416-22.
3. Yun YH, Lim MK, Won YJ, Park SM, Chang YJ, Oh SW, Shin SA. Dietary preference, physical activity, and cancer risk in men: national health insurance corporation study. *BMC Cancer.* 2008 Dec 11;8:366
4. Jang EJ, Park SW, Park JS, Park SJ, Hahm KB, Paik SY, Sin MK, Lee ES, Oh SW, Park CY, Baik HW. The influence of the eradication of *Helicobacter pylori* on gastric ghrelin, appetite, and body mass index in patients with peptic ulcer disease. *J Gastroenterol Hepatol.* 2008 Dec;23 Suppl 2:S278-85.
5. Kim KH, Kim YJ, Lee S, Oh SW, Lee K, Park Y, Kim HJ, Kwak H. Evaluation of plasma leptin levels & BMI as predictor of postpartum weight retention. *Kim KH, Kim YJ, Lee S, Oh SW, Lee K, Park Y, Kim HJ, Kwak H. Indian J Med Res.* 2008 Nov;128(5):595-600.
6. Won JC, Park CY, Lee WY, Lee ES, Oh SW, Park SW. Association of plasma levels of resistin with subcutaneous fat mass and markers of inflammation but not with metabolic determinants or insulin resistance. *J Korean Med Sci.* 2009 Aug;24(4):695-700.
7. Lee ES, Yoon YS, Park CY, Kim HS, Um TH, Baik HW, Jang EJ, Lee S, Park HS, Oh SW. Eradication of *Helicobacter pylori* increases ghrelin mRNA expression in the gastric mucosa. *J Korean Med Sci.* 2010 Feb;25(2):265-71.
8. Park SS, Yoon YS, Oh SW. Health-related quality of life in metabolic syndrome: The Korea National Health and Nutrition Examination Survey 2005. *Diabetes Res Clin Pract.* 2011 Mar;91(3):381-8.
9. Rhee MY, Yang SJ, Oh SW, Park Y, Kim CI, Park HK, Park SW, Park CY. Novel genetic variations associated with salt sensitivity in the Korean population. *Hypertens Res.* 2011 May;34(5):606-11.
10. Oh SW, Park CY, Lee ES, Yoon YS, Lee ES, Park SS, Kim Y, Sung NJ, Yun YH, Lee KS, Kang HS, Kwon Y, Ro J. Adipokines, insulin resistance, metabolic syndrome, and breast cancer recurrence: a cohort study. *Breast Cancer Res.* 2011 Mar 30;13(2):R34.
11. Shin SJ, Lim CY, Rhee MY, Oh SW, Na SH, Park Y, Kim CI, Kim SY, Kim JW, Park HK. Characteristics of sodium sensitivity in Korean populations. *J Korean Med Sci.* 2011 Aug;26(8):1061-7.

| S8-1 |

Physical activity in type 2 diabetes prevention programs

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Type 2 diabetes is reaching epidemic proportions worldwide, but its primary prevention and treatment are still a challenge. The risk of developing type 2 diabetes is inversely associated with regular exercise, and there is strong evidence that physical exercises, coordinately with diet or independently, prevent or delay progression to type 2 diabetes. There is a growing consensus on the issue that physical exercise should be part of therapeutic strategy to slow the development of type 2 diabetes in high-risk in-

dividuals and to improve glucose control in type 2 diabetes. For these purposes, exercise programs should have both aerobic and resistance components. Recently, well organized recommendations on this issue were suggested by several experts groups. All of these are based on the growing evidences on this issue. In this presentation, I will review these evidences especially focusing the primary prevention of type 2 diabetes.



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• Education and Appointments

2007-present	Korea Institute of Sports Science, Korea Sports Promotion Foundation	Researcher
2011-present	Graduate School of Physical Education, Kyung Hee University	Adjunct professor
2003-present	American College of Sports Medicine (ACSM)	ACSM Certified Clinical Exercise Specialist® (CES)
2006	Indiana University, Bloomington, IN, USA	Ph.D in clinical exercise physiology
2001	Indiana University, Bloomington, IN, USA	MS in exercise physiology
1996	Kyung Hee University, Seoul, Korea	BS in Chemistry

• Research Interests

Major: Clinical exercise physiology; Exercise physiology; Sports medicine
health and disease in exercise, especially exercise prescription for hypertension; health and disease in young elite Korean athletes

• Brief List of Publications

1. Park, S., Kim, J.K., Cho, H.M., Kim, H.G., Beekley, M.D., & Nho, H.S. (2010). Increase in maximal oxygen uptake following 2-week walk training with blood flow occlusion in athletes. *European Journal of Applied Physiology*; 109, 591-600.
2. Kim, K. Park, S. Kim, K. Jun, T. Park, D. & Kim, K. (2010). Salivary cortisol and IgA responses during golf competition vs. practice in elite male and female junior golfers. *Journal of Strength and Conditioning Research*; 24, 852-858.
3. Kim, K. Chung, J., Park, S. & Shin, J.P. (2009). Psychological stress response during competition between elite and non-elite Korean Junior Golfers. *International Journal of Sports Medicine*; 30, 503-508.
4. Lee, J., Cho, H.S., Park, S., & Kim, W.K. (2009). Regular exercise produced cardioprotective effects on rat's heart with hypertension induced by L-NAME administration. *Clinical and Experimental Hypertension*; 31, 364-375.
5. Lee, H, Nho, H., Jim, J., Choi, H, Park, S. (2008). Post-exercise hypotension in dipping and non-dipping type blood pressure. *The Korean Journal of Physical Education*; 47, 811-819.
6. Park, S., Rink, L.D. & Wallace, J.P. (2008). Accumulation of physical activity: blood pressure reduction between 10 min walking sessions. *Journal of Human Hypertension*: 22, 475-482.
7. Park, S., Rink, L.D. & Wallace, J.P. (2006). Accumulation of physical activity leads to a greater blood pressure reduction than a single continuous session, in prehypertension. *Journal of Hypertension*: 24, 1761-1770

| S8-2 |

Role of physical activity in pre/hypertension: accumulation of 10 min walks

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Although physical activity (PA) is an essential factor in the prevention and management of type 2 diabetes, individuals with type 2 diabetes still remain inactive. In 2007, the updated PA recommendations included the accumulation of several short bouts (10 min or more) of moderate-intensity physical activity (PA_{accum}). Despite the updated recommendation, limited scientific evidence exists on its effectiveness of PA_{accum} on health outcomes including high blood pressure (BP).

Purpose: To examine the effects of the PA_{accum} vs. a single continuous session (PA_{cont}) on BP reduction in men with hypertension and prehypertension.

Methods: Twenty three men (35.9±9.4 yrs; 137.8±9.3/88.4±7.8 mm Hg) with hypertension and prehypertension participated in a randomized cross-over design. Men completed three treatments: a control and two PA sessions, the PA_{accum} (four 10-min walk 50-min apart at 50% of VO_{2peak}) and the PA_{cont} (40-min walk at 50% of VO_{2peak}). Two PA sessions were separated by >7 days. After each treatment, participants wore an ambulatory BP monitor beginning at the same time of day for 24 hrs. Systolic (S) and diastolic (D) BP were averaged for 24 hrs, daytime (06:00-22:00 hr) and nighttime (22:00-06:00 hr). One-way ANOVAs with repeated measures were used to determine

the effects of each PA treatment on the BP reduction ($p < 0.05$).

Results: Main effects were found in 24-hr ($p < 0.0001$), daytime ($p = 0.001$) and nighttime SBP ($p = 0.032$) and 24-hr ($p = 0.021$) and daytime DBP ($p = 0.023$) while none were found in nighttime DBP ($p = 0.082$). The 24-hr SBP was decreased 3.0 mmHg following the PA_{accum} and 4.7 mm Hg following the PA_{cont}, respectively. The 24-hr DBP was decreased 2.3 mmHg following the PA_{accum} and 2.3 mm Hg following the PA_{cont}, respectively. Daytime SBP was decreased 2.9 mmHg following the PA_{accum} and 4.5 mm Hg following the PA_{cont}. Daytime DBP was decreased 2.3 mmHg following the PA_{accum} and 2.3 mm Hg following the PA_{cont}, respectively. Nighttime SBP was 4.5 mm Hg following the PA_{cont}. In addition, SBP was significantly reduced following the 2nd (-6.5 mm Hg), and the 3rd (-6.1 mm Hg) short sessions compared to the baseline (142.6±11.1 mm Hg) in hypertension.

Conclusion: The accumulation of physical activity reduced BP for 24 hrs in men with hypertension and prehypertension. The PA_{accum} was as effective as the PA_{cont} in reducing 24-hr and daytime SBP and DBP. Accumulating 10-min brisk walks appears to be effective for the treatment and prevention of hypertension.



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• Education and Appointments

1983-1989	Yonsei University	MD
1994-1998	Graduate School, Yonsei University	PhD
2003-2006	University of Pittsburgh, Dept of Epidemiology Health ABC Study, NIA, NIA	MPH, DrPH
2010-	CHA University	Professor

• Research Interests

Major: Diabetes Epidemiology, Diabetes in older adults, Sarcopenia and frailty

• Brief List of Publications

1. Kim SK, Choi YJ, Huh BW, Kim CS, Park SW, EJ Lee, Cho YW, Huh KB: The ratio of Waist-to-calf circumference and carotid atherosclerosis. *Diabetes Care*, Accepted
2. Rhee EJ, Choi JH, Yoo SH, Bae JC, Kim WJ, Choi ES, Park SE, Park CY, Park SW, Oh KW, Park SW, Kim SW, Lee WY: The Association of Unintentional Changes in Weight, Body Composition, and Homeostasis Model Assessment Index with Glycemic Progression in Non-Diabetic Healthy Subjects. *Diabetes Metab J.* 35(2):138-148, 2011
3. Kim SK, Oh HJ, Kim JW, Lee YK, Kim SK, Park SW, Kim YL, Park WK, Cho YW: The clinical characteristics of newly diagnosed early onset (<40 years old) diabetes in outpatients' clinic. *Korean Diabetes J.* 34(2):119-125, 2010
4. Kim SK, Kim DJ, Kim SH, Lee YK, Park SW, Cho YW, Huh KB: Normal range of alanine aminotransferase concentration is associated with carotid atherosclerosis. *Diabetes Res Clin Pract.* 88:111-116, 2010
5. Delmonico MJ, Harris TB, Visser M, Park SW, Conroy MB, Velasquez-Mieyer P, Boudreau R, Manini TM, Nevitt M, Newman AB, Goodpaster BH: Longitudinal study of muscle strength, quality, and adipose tissue infiltration. *Am J Clin Nutr* 90:1579-85, 2009 (IF 6.74)
6. Kim SK, Park SW, Hwang IJ, Lee YK, Cho YW: High fat stores in ectopic compartments in men with newly diagnosed type 2 diabetes: An anthropometric determinant of carotid atherosclerosis and insulin resistance. *Int J Obesity* 34:105-110, 2010 (IF 3.64)
7. Park SW, Goodpaster BH, Lee JS, Kuller L, Boudreau R, de Rekeneire N, Harris TB, Kritchevsky S, Tylavsky FA, Nevitt M, Cho YW, Newman AB: Excessive loss of skeletal muscle mass in older adults with type 2 diabetes. *Diabetes Care* 32:1993-1997, 2009 (IF 7.8)
8. Park SW, Kim SK, Cho YW, Kim DJ, Song YD, Choi YJ, Huh BW, Choi SH, Jee SH, Cho MA, Lee EJ, Huh KB: Insulin resistance and carotid atherosclerosis. *Atherosclerosis* 205:309-313, 2009 (IF 4.287)
9. Choi YJ, Kim HC, Kim HM, Park SW, Kim J, Kim DJ: Prevalence and management of diabetes mellitus in Korean Adults. *Diabetes Care* 32:2016-20, 2009 (IF 7.8)
10. Kim SK, Kim SH, Park KS, Park SW, Cho YW: Regression of the increased common carotid artery intima media thickness in subclinical hypothyroidism after thyroid hormone replacement. *Endocr J* 56:753-758, 2009 (IF 1.14)
11. Kim SK, Park SW, Kim SH, Cha BS, Lee HC, Cho YW: Visceral fat amount is associated with carotid atherosclerosis even in type 2 diabetic men with a normal waist circumference. *Int J Obesity* 33:131-135, 2008 (IF 3.64)
12. Kim SK, Kim HJ, Ahn CW, Park SW, Cho YW, Lim SK, Lee HC, Cha BS: Hyperleptinemia as a robust risk factor of coronary artery disease and metabolic syndrome in type 2 diabetic patients. *Endocr J.* 55:1085-92, 2008 (IF 1.14)

| S8-3 |

Exercise and type 2 diabetes: ACSM and ADA joint position statement

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Although physical activity (PA) is a key element in the prevention and management of type 2 diabetes, many with this chronic disease do not become or remain regularly active. High-quality studies establishing the importance of exercise and fitness in diabetes were lacking until recently, but it is now well established that participation in regular PA improves blood glucose control and can prevent or delay type 2 diabetes, along with positively impacting lipids, blood pressure, cardiovascular events, mortality, and quality of life. Structured interventions combining PA and modest weight loss have been shown to lower risk of type 2 diabetes by up to 58% in high-risk populations. Most benefits of PA on diabetes management are realized through acute and chronic improvements in insulin action, accomplished with both aerobic and resistance training. The benefits of physical training are discussed, along with recommendations for varying activities, PA-associated blood glucose management, diabetes prevention, gestational diabetes mellitus, and safe and effective practices for PA with diabetes-related complications.

Exercise plays a major role in the prevention and control of insulin resistance, prediabetes, gestational diabetes mellitus, type 2 diabetes, and diabetes-related health complications. Both aerobic training and resistance training improve insulin action, at least acutely, and can assist with management of blood glucose levels, lipids, blood pressure, cardiovascular risk, mortality, and quality of life, but exercise must be undertaken regularly to have continued benefits and likely include regular training of varying types. Most people with type 2 diabetes can perform exercise safely, as long as certain precautions are taken. The inclusion of an exercise program or other means of increasing overall PA is critical for optimal health in individuals with type 2 diabetes.

Both the American College of Sports Medicine (ACSM) and the American Diabetes Association (ADA) reviewed the relevant, published research and developed the recommendations. ACSM and ADA joint position statement will be introduced and discussed in detail.



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• Education and Appointments

1972	Graduated from Keio University Faculty of Medicine	MD
1983	Degree, from Keio University	PhD
1986-1998	Yamanashi Medical University	Assistant Professor
1998-2007	Yamanashi Medical University	Associate Professor
2007-present	Saitama Medical University	Professor

• Research Interests

Major: Pediatric endocrinology and diabetes mellitus
Genetic or etiologic background of pediatric and adolescent diabetes mellitus.
Advanced technology for diabetes indices and treatment.

• Brief List of Publications

1. Amemiya S (editor in chief): The management of pediatric and adolescent diabetes mellitus (ver. 3); Consensus Guideline, Ed by The Japan Diabetes Society and The Japanese Society for Pediatric Endocrinology, Nankodo, Tokyo June 2011 (in Japanese)
2. Sugihara S, Ogata T, Amemiya S on behalf of The Japanese Study Group of Insulin Therapy for Childhood and Adolescent Diabetes (JSGIT): Genetic Characteristics on HLA-Class II and Class I among Japanese Type 1A and Type 1B Diabetic Children and Their Families. *Pediatric Diabetes* (in press)
3. Levy-Marchal C, Arslanian S, Cutfield W, Sinaiko A, Druet C, Marcovecchio ML, Chiarelli F, on behalf of ESPE-LWPES-ISPAD-APPES-APEG-SLEP-JSPE and the Insulin Resistance in Children Consensus Conference Group (Amemiya S as a delegate of JSPE): Insulin Resistance in Children: Consensus, Perspective and Future Directions *J Clin Endocrinol Metab* 95(12): 5189-5198,2010
4. Yagasaki H, Kobayashi K, Saitou T, Nagamine K, Mitsui Y, Mochizuki M, Kobayashi K, Cho H, Ohyama K, Amemiya S, Nakazawa S. : Nocturnal blood glucose and IGFBP-1 changes in type 1 diabetes: Differences in the dawn phenomenon between insulin regimens. *Exp Clin Endocrinol Diabetes*. 118(3):195-199, 2010
5. Rosenbloom AL, Silverstein JH, Amemiya S, Zeitler P, Klingensmith GJ: ISPAD Clinical Practice Consensus Guidelines 2009 Compendium Type 2 diabetes mellitus in children and adolescents, *Pediatric Diabetes* 10:S12-S17-S32,2009
6. Tajima T, Ohtake A, Hoshino M, Amemiya S, Sasaki N, Ishizu K, Fujieda K. OTX2 loss of function mutation causes anophthalmia and combined pituitary hormone deficiency with a small anterior and ectopic posterior pituitary. *J Clin Endocrinol Metab* 94(1):314-319,2009
7. Sugihara S, Sasaki N, Amemiya S, Kohno H, Tanaka T, Matsuura N, The Committee for Medical Treatment of Childhood-onset Type 2 Diabetes mellitus, The Japanese Society for Pediatric Endocrinology: Analysis of birth weight at birth and at diagnosis of childhood-onset type 2 diabetes mellitus in Japan. *Pediatric Diabetes* 9: 4(part 1):281-290, 2008

| S9-1 |

Recent topics from multicenter collaborative studies in Japan

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Aims: To clarify the genetic or etiologic factors in Japanese pediatric and adolescent patients with diabetes mellitus.

Methods: The multicenter collaborative studies were conducted in the Japanese Society for Pediatric Endocrinology, JSPE. Regarding the genetic susceptibility to type 1 diabetes mellitus, T1DM, third cohort since 2007 in a study group was investigated in comparison with a part of their family members. And regarding the etiologic background in T2DM, the data collected in 2003 were examined especially focused on relationships between birth weight, incidence of either obese or non-obese diabetes mellitus and their family history with diabetes.

Results: HLA haplotypes specific to Japanese pediatric T1DM were demonstrated that the susceptible alleles for Type 1A with pancreatic autoantibody were DRB1 * 0901, * 0405, * 0802, DQB1 * 0303, * 0401, * 0302, and DPB1 * 0201, * 0301. The protective alleles were also confirmed. In the transmission disequilibrium test (TDT), the suscep-

tible DRB1 and DQB1 alleles, and the protective DRB1, DQB1 and DPB1 alleles were confirmed.

Among patients initially diagnosed as Type 1B without pancreatic autoantibody with their age of onset at less than 5 years-old, 5 out of 34 patients were revealed to have monogenic diabetes, one and four *INS* gene mutations.

As to the etiologic basis of Japanese pediatric and adolescent T2DM, non-obese case account for 20 to 30 %, less family history of diabetes and more history of low-birth weight.

Conclusions: Japanese T1DM showed specific and unique HLA haplotypes. Since patients with *INS* gene mutation were diagnosed beyond 5 months-old or later, monogenic diabetes has to be explored in case of Type 1B. Since babies with low-birth weight less than 2500g were shown at risk of T2DM, we have to watch and advocate the risk of T2DM for young ladies expecting their babies in near future.



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• **Education and Appointments**

1989	College of medicine, Seoul National University, Seoul, Korea	M.D.
2002	Degree of PhD in Medical Science, Seoul National University, Seoul, Korea	Ph.D.
1994	Residency training, Department of Pediatrics, Seoul National University Children's Hospital, Seoul, Korea	Residency
1996-1997	Fellowship, Department of Pediatric Endocrinology, Seoul National University Children's Hospital, Seoul, Korea	Fellowship
2005-2007	Post-Doctoral fellowship, University of Colorado School of Medicine Barbara Davis Center for Childhood Diabetes, Denver, CO, USA	Post-Doctoral fellowship
2001-	Department of pediatrics, College of Medicine, Dankook University, Cheonan, Korea	Associate professor

• **Research Interests**

Major: Diabetes: Immunogenetics of type 1 diabetes
 Genetic diagnosis of several monogenic diseases with endocrinologic and/or neurologic manifestations including MODY, congenital hypothyroidism
 Growth and development
 Puberty

• **Brief List of Publications**

1. Park JY, Oh JS, Yu J. Autoantibody Positivity and Clinical Characteristics of Diabetes Mellitus in Childhood. *J Korean Soc Pediatr Endocrinol* 2011;16:119-27.
2. Jung MH, Yu J, Shin CH, Suh BK, Yang SW, Lee BC. Association of cytotoxic T lymphocyte antigen-4 gene polymorphisms and HLA class II alleles with the development of type 1 diabetes in Korean children and adolescents. *J Korean Med Sci* 2009; 24: 1004-9.
3. Hong KB, Park JY, Chang YP, Yu J. Thyroid dysfunction in premature infants. *Korean J Pediatr* 2009;52:991-8.
4. Yu J, Steck AK, Babu S, Yu L, Miao D, McFann K, Hutton J, Eisenbarth GS, Klingensmith G. Single nucleotide transcription factor 7-like 2 (TCF7L2) gene polymorphisms in anti-islet autoantibody-negative patients at onset of diabetes. *J Clin Endocrinol Metab* 2009;94(2): 504-10.
5. Wang J, Miao D, Babu S, Yu J, Barker J, Klingensmith G, Rewers M, Eisenbarth GS, Yu L. Prevalence of autoantibody-negative diabetes is not rare at all ages and increases with older age and obesity. *J Clin Endocrinol Metab* 2007;92(1):88-92.
6. Kang SY, Shin CH, Yang SW, Park MH, Yu J. Human leukocyte antigen(HLA) genotypes and thyroid autoimmunity in Korean patients with type 1 diabetes. *Korean J Pediatr* 2005;48(6):624-33.
7. Barker JM, Yu J, Yu L, Wang J, Miao D, Bao F, Hoffenberg E, Nelson JC, Gottlieb PA, Rewers M, Eisenbarth GS. Autoantibody "subspecificity" in type 1 diabetes: risk for organ-specific autoimmunity clusters in distinct groups. *Diabetes Care* 2005;280:850-5.
8. Yu J, Shin CH, Yang SW, Park MH, Eisenbarth GS. Analysis of children with type 1 diabetes in Korea: high prevalence of specific anti-islet autoantibodies, immunogenetic similarities to Western populations with "unique" haplotypes, and lack of discrimination by aspartic acid at position 57 of DQB. *Clin Immunol* 2004;113:318-25.

| S9-2 |

Genetics in diabetes - contribution to the classification and management

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Dankook University, Korea

Diabetes mellitus (DM) can be classified as type 1, type 2, and other specific types according to the underlying causes. Most childhood DM was usually thought of as type 1 DM (T1DM), but the incidence of type 2 DM (T2DM) in childhood is increasing and it can also be caused by monogenic defect.

The topic will cover some of the genetic findings in the field of neonatal and childhood diabetes. It includes HLA study, the study about *TCF7L2* polymorphism, and the mutations of the gene *KCNJ11*, glucokinase (*GCK*) and *HNF1A*.

We studied the expression of anti-islet autoantibodies and HLA-DR and -DQ genotypes in Korean children with T1DM. The positivity of the anti-ICA512, anti-GAD65, and anti-insulin autoantibodies in the newly onset T1DM patients (n=15) was high, and all of them had one or more of the autoantibodies. HLA analysis showed higher frequencies of HLA-DRB1*0301, *0405, *09012 and -DQB1*0201, *0401, *03032 alleles in T1DM compared to controls ($P < 0.05$).

We looked at the association of HLA status with the expression of antiislet autoantibodies using the samples of 478 relatives (SOC: sibling-offspring cohort) of patients with T1DM as well as 793 newborns from the general population (NEC: newborn nonrelative cohort) selected for the expression of specific HLA haplotypes. The presence of persistent autoantibodies was strongly related to HLA status and family history of T1DM. In contrast, the expression of transient antiislet autoantibodies did not differ by family history of DM, and none of the DR3/4(DQ2/8) relatives and DR3/4(DQ2/8) newborns expressed transient autoantibodies. The research indicates that children can express

transient anti-islet autoantibodies, but such transient autoantibodies are relatively infrequent and are not correlated with known genetic risk factors for T1DM.

We also designed the study to evaluate whether two T2DM-associated single nucleotide polymorphisms (SNPs) of transcription factor 7-like 2 (*TCF7L2*) gene are associated with the development of islet autoantibody-negative diabetes vs. islet autoantibody-positive diabetes in young patients. Autoantibody against GAD65, ICA512bdc, insulin, and ZnT8 transporter, and cytoplasmic islet cell antibody were assayed in patients with new onset diabetes seen at the Barbara Davis Center using sera obtained within 2 week of diagnosis. We genotyped two noncoding variants in the *TCF7L2* gene, rs12255372 and rs7903146, in diabetic subjects and normal controls. A total of 140 patients (15.7%) were negative for all islet autoantibodies among 893 subjects less than age 25 at the onset of diabetes. The allele and genotype frequencies of two SNPs showed that these are associated (odds ratio up to 4) with the development of diabetes in the autoantibody-negative diabetic cohort, but not in the autoantibody-positive diabetic cohort. *TCF7L2* type 2 diabetes susceptibility alleles are associated with islet autoantibody-negative but not autoantibody-positive new onset diabetes in young patients. And we could find the monogenic defects in the persistently autoantibody negative DM patients who was initially thought as having T1DM.

Genetic study in addition to the antiislet autoantibody test could be valuable in diagnosing specific DM for the proper management as well as understanding of the pathogenesis.



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• Education and Appointments

1991	College of Medicine, Chosun University, Gwang-Ju, Korea	M.D
1994-1998	Department of Pediatrics, Chosun University Hospital, Gwang-Ju, Korea	Residency
2000	Chosun University Postgraduate School, Gwang-Ju, Korea	Ph.D
2007-2008	Division of cellular and molecular physiology, Joslin Diabetes Center, Harvard University, Boston, MA, USA	Postdoctoral research fellow
2001-Present	Department of Pediatrics, School of Medicine, Chosun University	Associate Professor

• Research Interests

Major: Pediatric endocrinology

• Brief List of Publications

1. Ji Young Moon, Kyung Rae Moon, Sang Kee Park, Yoon Young Chung, Eun Young Kim. Changes in Neuropeptide Y-immunoreactive cells in the hypothalamus and Cajal interstitial cells in the small intestine of rats with high-fat diet. *Korean J Pediatr Gastroenterol Nutr* 2011;14: 171-180
2. Wanzhu Jin, Alison B Goldfine, Jose Jimenez-Chillar, Eun Young Kim, Robert R Henry, Theodore P Ciaraldi, Edward Moon, Tanner Boes, Merve Emecan, Conner Fitzpatrick, Anish Sen, Ankit Shah, Martha Vokes, Joshua Schroeder, Elizabeth Tatro, ME Patti. Increased SRF transcriptional activity in human and mouse skeletal muscle is a signature of insulin resistance. *J Clin Invest* 2011;121:918-929
3. Eun Young Kim, Wonhee Lee, Chang Hoon Song, Sang Kee Park. Correlation of Clinical Characteristics and Levels of Adiponectin and Resistin in Human Cord Blood of Fetuses of Women with Gestational Diabetes and Pregnancy-induced Hypertension. *J Korean Soc Pediatr Endocrinol* 2010;15:64-70
4. Jussi Pihlajamaki, Tanner Boes, Eun Young Kim, Allison B Goldfine, Farrell Dearie, Brian W Kim, Joshua Schroeder, Imad Nasser, Edward Mun, Peter J Park, Antonio C Bianco, Mary Elizabeth Patti. Thyroid hormone related regulation of gene expression in human fatty liver. *J Clin Endocrinol Metab* 2009;94:3521-3529.
5. Eun Young Kim. Insulin Resistance and Intracellular Thyroid Hormone Dysfunction. *J Korean Soc Pediatr Endocrinol* 2009;14:94-99

| S9-3 |

Obesity and insulin resistance in children and adolescents

Eun Young Kim

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Recently, the prevalence of obesity and metabolic syndrome is rapidly increasing among children and adolescents in Korea. The prevalence of obesity in Korean children is estimated to be around 10%, and the incidence of metabolic syndrome was 30 to 40% in overweight or obese children and adolescents in Korea. Korea has been undergoing considerable changes in the lifestyle influencing on obesity and metabolic syndrome along with rapid economic growth. The lifestyle trends contributing to both of these phenomena include changes in dietary patterns and habits with western dietary pattern and high-fat intake, decreasing of physical activity, and increasing sedentary behaviors. Over-intake of nutrients induces fat deposition in liver and skeletal muscle as well as adipose tissue, and it can alter energy metabolism. We have recently observed that in cultured myotubes, induction of insulin resistance by exposure to saturated fatty acids reduced TR expression and DNA binding activity, and TR α 1 expression was decreased in human type 2 diabetes mellitus. Thyroid hormone stimulates metabolic rate, protein catabolism, fatty acid oxida-

tion and nuclear-encoded mitochondrial OXPHOS gene expression. We hypothesized that thyroid hormone mediated transcription may be reduced in insulin resistance induced by high fat diet (HFD), and thus may contribute to impaired expression of oxidative metabolic genes linked to insulin resistance *in vivo*. We have shown that HFD effects on subsets of T3-responsive genes in laboratory rats suggest that obesity associated with HFD may alter the pattern of coactivator/corepressors within the TR transcriptional complex. These results indicate that HFD induce intracellular T3 resistance, and then may exacerbate metabolic disturbance. Furthermore, T3 responsive genes are down-regulated in the liver of humans with obesity and diabetes. Since childhood obesity leads to the higher prevalence of obesity in adulthood, which increases the risk of metabolic syndrome, the medical profession must be actively involved with educating the parents and the community in order to raise their awareness of the importance of healthy life styles and dietary habits.



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• Education and Appointments

2001	Yonsei University College of Medicine	MD
2003-2007	Severance Hospital	Residency(Pediatrics)
2007-2010	Severance Hospital	Clinical research fellow(Pediatric endocrinology)
2010-	Gangnam Severance Hospital	Assistant professor

• Research Interests

Major: Beta cell function in type 1 diabetes, Pancreatic beta cell apoptosis

• Brief List of Publications

1. Serum kisspeptin levels in Korean girls with central precocious puberty. Rhie YJ, Lee KH, Eun SH, Choi BM, Chae HW, Kwon AR, Lee WJ, Kim JH, Kim HS. *J Korean Med Sci.* 2011 Jul;26(7):927-31. Epub 2011 Jun 20.
2. Insulin-like growth factor-binding protein-3 mediates high glucose-induced apoptosis by increasing oxidative stress in proximal tubular epithelial cells. Yoo EG, Lee WJ, Kim JH, Chae HW, Hyun SE, Kim DH, Kim HS, Oh Y. *Endocrinology.* 2011 Aug;152(8):3135-42. Epub 2011 Jun 7.
3. Sexual precocity in hypomelanosis of Ito: mosaicism-associated case report and literature review. Park JM, Kim HJ, Kim T, Chae HW, Kim DH, Lee MG. *Int J Dermatol.* 2011 Feb;50(2):168-74.
4. Effects of a structured exercise program on insulin resistance, inflammatory markers and physical fitness in obese Korean children. Chae HW, Kwon YN, Rhie YJ, Kim HS, Kim YS, Paik IY, Suh SH, Kim DH. *J Pediatr Endocrinol Metab.* 2010 Oct;23(10):1065-72.
5. Insulin-like growth factor binding protein-3 induces G1 cell cycle arrest with inhibition of cyclin-dependent kinase 2 and 4 in MCF-7 human breast cancer cells. Kim HS, Lee WJ, Lee SW, Chae HW, Kim DH, Oh Y. *Horm Metab Res.* 2010 Mar;42(3):165-72.

| S9-4 |

Epidemiologic changes of juvenile diabetes in Korea

Hyun-Wook Chae

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The worldwide incidence of type 2 diabetes (T2D) and obesity have increased for last decades. Childhood obesity has increased substantially and the prevalence of childhood and adolescence onset T2D has been increased rapidly.

From the Korea National Health and Nutrition Examination Survey (KNHNES) 2005, the incidence of childhood and adolescent obesity was 9.7% (boys 11.3%, girls 8.0%), which is 1.7 times higher than KNHNES 1997. Furthermore, the incidence of obese boys aged 10-14 years is 17.9%. Therefore, the incidence of metabolic syndrome (MS) was increased up to 4.7-14.0% in those aged 12 to 19 years. The prevalence of MS in obese children was 37.5% by modified pediatric ATP III standard in 2003, which is not lower than US results. The epidemiologic changes of juvenile diabetes in Korea show similar consequence. In a regional study, the incidence of diabetes was 0.12 patients per 100,000 under 15 years old in 1980 and increased up to 4.73 ones in 2005, and the proportion of T2D was increased up to 21.4%.

The development of T2D in children and adolescents is possibly related to puberty, obesity, family history, and defects in insulin secretion besides insulin resistance. Impaired glucose tolerance (IGT) was prevalent among obese children, while beta cell function was relatively preserved. The obese children with high normal levels in oral glucose tolerance test may have a gradual deterioration in glucose stimulated insulin response and have an increased risk of IGT and T2D. The proportion of Korean children born small for gestation age (SGA) was gradually increasing and T2D, dyslipidemia, hypertension, cardiovascular disease might be more frequent among SGA children. The SGA children with catch-up growth in height and high BMI showed higher insulin resistance and the long term complication might be developed in adolescence or early adult life.

Childhood obesity and T2D are increasing in Korea simultaneously. Early intervention is important to prevent both immediate and long-term effects on health and well-being.



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• Education and Appointments

2008-present	Singapore Bioimaging Consortium, A*STAR	Head
2005-2008	Singapore Bioimaging Consortium, A*STAR	Deputy Head
2003-2005	UT Southwestern Medical Center	Research Assistant Professor
1999-2003	HHMI and UT Southwestern Medical Center	HHMI Associate
1996-1999	University of Pittsburgh	Research Associate
1992-1996	Cornell University	Ph.D. Student

• Research Interests

Research in my lab aims to uncover the molecular basis of diabetes and obesity that provides targets for drug development, and to develop animal models of diabetes, obesity and metabolic syndrome linked neurodegeneration that allow evaluation of therapeutic interventions. We use molecular genetics, cell biology, and physiology techniques to analyze genetically modified animals and cell lines. The major research directions are:

- * Molecular mechanisms of endocrine hormone secretion
- * Molecular basis of diabetes and obesity
- * Metabolic syndromes and neurodegeneration

• Brief List of Publications

1. Liu T, Sun L, Xiong Y, Shang S, Guo N, Teng S, Wang Y, Liu B, Wang C, Wang L, Zheng L, Han W*, Zhang CX*, Zhou Z*: Calcium triggers quantal release simultaneously from two types of vesicles in a single astrocyte. *The Journal of Neuroscience* (accepted for publication), 2011. (*co-corresponding authors)
2. Gustavsson N, Wang Y, Kang Y, Seah T, Radda GK, Han W: Synaptotagmin-7 as a positive regulator of glucose-induced glucagon-like peptide-1 secretion. *Diabetologia* 54(7):1824-1830, 2011.
3. Gustavsson N, Seah T, Lao Y, Radda GK, Südhof TC, Han W: Delayed onset of hyperglycemia in a mouse model with impaired glucagon secretion demonstrates that dysregulated glucagon secretion promotes hyperglycemia and type 2 diabetes. *Diabetologia* 54(2):415-423, 2011.
4. Gustavsson N, Wang X, Seah T, Wang Y, Xu J, Radda GK, Südhof TC, Han W: Neuronal Calcium sensor synaptotagmin-9 is not involved in the regulation of glucose homeostasis or insulin secretion. *PLoS ONE* 5(11):e15414, 2010.
5. Wei S, Xu Y, Shi H, Wong SH, Han W, Talbot K, Hong W, Ong WY: EHD1 is a synaptic protein that modulates exocytosis through binding to snapin. *Molecular and Cellular Neuroscience* 45(4):418-429, 2010.
6. Lou PH, Yang G, Huang L, Cui Y, Pourbahrami T, Radda GK, Li C, Han W: Reduced body weight and increased energy expenditure in transgenic mice over-expressing the soluble leptin receptor. *PLoS One* 5(7):e11669, 2010.
7. Han W, Chuang K-H, Chang YT, Olivo M, Velan SS, Townsend D, Bhakoo K, Radda GK: Imaging metabolic syndrome. *EMBO Molecular Medicine* 2(6):196-210, 2010.
8. Yang L, Gan Z, Zhao L, He Z, Xu J, Li W, Gao X, Wang X, Han W, Chen L, Xu T, Liu Y: An essential role for RNA editing enzyme ADAR2 in glucose-regulated insulin exocytosis. *The FASEB Journal* (accepted for publication), 2010.
9. Han W, Li C: Linking type 2 diabetes and Alzheimer's disease. *Proceedings of the National Academy of Sciences of the United States of America* 107(15):6557-6558, 2010.
10. Kostromina E, Gustavsson N, Wang X, Lim CY, Radda GK, Li C, Han W: Glucose intolerance and impaired insulin secretion in pancreas-specific STAT3 KO mice are associated with reduced microvasculature around pancreatic islets. *Endocrinology* 151(5):2050-2059, 2010.
11. Lu J, Gustavsson N, Li Q, Radda GK, Südhof TC, Han W: Generation of transgenic mice for in vivo detection of insulin-containing granule exocytosis and quantification of insulin secretion. *Journal of Innovative Optical Health Sciences* 2(4):397-405, 2009.

| S10-1 |

Islet hormone secretion regulation and energy homeostasis

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Type 2 diabetes is caused by relative deficiency of insulin secretion and is associated with dysregulation of glucagon secretion during the late stage of diabetes development. Secretion of insulin and glucagon is triggered by elevated intracellular calcium levels. Although the precise mechanism by which the calcium signal is coupled to insulin and glucagon granule exocytosis is unclear, synaptotagmin-7 (Syt7) has been shown to be a positive regulator of calcium-dependent insulin and glucagon secretion, and may function as a calcium sensor for insulin and glucagon granule exocytosis. Deletion of Syt7 leads to impaired glucose-stimulated insulin secretion and nearly abolished Ca^{2+} -dependent glucagon secretion in mice. Under non-stressed

resting state, however, Syt7 KO mice exhibit normal insulin level but severely reduced glucagon level. We studied energy expenditure and metabolism in Syt7 KO and control mice using indirect calorimetry. Syt7 KO mice had lower body weight and body fat content, and exhibited higher oxygen consumption and basal metabolic rate. Respiratory exchange ratio (RER) was lower in Syt7 KO mice, suggesting an increased use of lipid in their energy production. These results show that the lean phenotype in Syt7 KO mice was mostly attributed to increased lipolysis and energy expenditure, and suggest that reduced glucagon level may have broad influence on the overall metabolism in the mouse model.



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• Education and Appointments

1979-1983, 1986	Seoul National University, Seoul Korea	B.S. and M.S.
1986-1991	University of Illinois at Urbana-Champaign	Ph.D.
1991-1998	University of Illinois at Urbana-Champaign Stanford University	Post-doctoral researcher
1998-2000	University of Illinois at Urbana-Champaign	Principal Research Scientist
2000-2006	University of Illinois at Urbana-Champaign	Research Assistant Professor

• Research Interests

Major: Molecular Endocrinology

Nuclear receptors and transcriptional cofactors controlling hepatic lipid and glucose metabolism:

1. Molecular regulation of FXR activity in health and disease
2. SHP action in metabolic regulation: Physiology and Mechanism.
3. Novel Regulatory Networks Controlling Hepatic Metabolism through SIRT1 and microRNAs

• Brief List of Publications

1. J. Miao#, SE Choi#, SM Seok, L.Yang, W.Zuercher, Y.Xu, T.Willson, H. E.Xu, and J. K. Kemper .(2011) (# these authors contributed equally to this study). Ligand-dependent regulation of the activity of the orphan nuclear receptor, Small Heterodimer Partner (SHP), in the repression of bile acid biosynthetic CYP7A1 and CYP8B1 genes, *Molecular Endocrinology* , 25, 1159-1169.
2. D. Kanamaluru, Z. Xiao, S. Fang, S. Choi, D.Kim, T. Veenstra, and J. K. Kemper .(2011) Arginine methylation by PRMT5 at a naturally-occurring mutation site is critical for metabolic regulation by Small Heterodimer Partner. *Molecular and Cellular Biology*, selected as a spotlight paper, 31, 1540-1550.
3. J. K. Kemper . (2011) Regulation of FXR Transcriptional Activity in Health and Disease: Emerging Roles of FXR Cofactors and Post-Translational Modifications. Invited review, *Biochimia et Biophysica Acta*, 1812, 842-850.
4. B. Ponugoti#, D. Kim#, Z. Smith, J. Miao, M. Zang, S. Y. Wu, C. M. Chiang, T. D. Veenstra, and J. K. Kemper. (2010)(# these authors contributed equally to this study), SIRT1 deacetylates and inhibits SREBP-1c activity in regulation of hepatic lipid metabolism. *J. Biol Chem*, 285: 33959-70.
5. J. Lee and J. K. Kemper. (2010) Controlling SIRT1 expression by microRNAs in health and metabolic disease. Invited review, *Aging*, 2: No 8, 1-8.
6. J. Lee, A. Padhye#, A. Sharma#, G. Song#, J. Miao, Y. Mo, L. Wang, and J. K. Kemper. (2010) (# these authors contributed equally to this study), FXR inhibition of MiR-34a expression positively regulates hepatic SIRT1 levels, *J. Biol Chem*, 285, 12604-12611.
7. J. K. Kemper (also corresponding author), Z.Xiao#, B.Ponugoti#, J. Miao #, S. Fang, D. Kanamaluru, S. Tsang, S. Wu, C. M. Chiang, and T. D. Veenstra. (2009) (# these authors contributed equally to this study). FXR acetylation is normally dynamically regulated by p300 and SIRT1 but is constitutively elevated in metabolic disease states. *Cell Metabolism*, 10, 392-404.
Selected as an Editor's Choice by *Science Signaling*.
Selected as a Faculty of 1000 Recommended Article
8. J.Miao, S. Fang, J. Lee, C. Comstock, K. E. Knudsen, and J. K. Kemper. (2009) Functional specificity of Brm and Brg-1 Swi/Snf ATPases in the feedback regulation of hepatic bile acid biosynthesis. *Mol. Cell. Biol.*, 6170-6181.
9. J. Miao, Z. Xiao, D. Kanamaluru, G. Min, P. M. Yau, T. D. Veenstra, E.Ellis, S. Strom, K. Suino-Powell, E. Xu, and Kemper JK. (2009), Bile acid signaling pathways increase stability of Small Heterodimer Partner (SHP) by inhibiting ubiquitin-proteasomal degradation. *Genes and Development*, 23:986-996
Selected as a Faculty of 1000 Recommended Article.

| S10-2 |

Role of SIRT1 deacetylase and microRNA-34a in regulation of hepatic metabolism

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Aims: SIRT1 is an NAD⁺-dependent deacetylase implicated in beneficial metabolic effects and longevity. We have examined how SIRT1 controls hepatic lipid metabolism by deacetylating and altering the activities of two important metabolic regulators, a key lipogenic activator SREBP-1c and the bile acid receptor and negative regulator of lipogenesis, FXR. We also examined how hepatic SIRT1 is negatively regulated by elevated microRNA-34a (miR-34a) in obesity and further examined the miR-34a/SIRT1 regulatory axis as a potential therapeutic target.

Methods: Proteomic, biochemical, and functional studies were utilized to examine the effects of SIRT1-regulated acetylation of SREBP-1c and FXR on liver metabolism. Downregulation and overexpression of miR-34a were utilized to test if miR-34a directly targets both SIRT1 and Nampt1, a critical enzyme increasing cellular NAD⁺ levels. Anti-miR-34a experiments were performed in dietary obese mice.

Results: Acetylation of SREBP-1c at Lys-289/309, regulated by p300 acetylase and SIRT1 deacetylase, increased its lipogenic activity by enhancing protein stability and

binding to lipogenic genes. In contrast, FXR acetylation at Lys-217 decreased transactivation activity by inhibiting its heterodimerization with RXR α and DNA binding. Remarkably, acetylation levels of SREBP-1c and FXR were highly elevated in obese mice, which have markedly decreased SIRT1 levels and abnormally elevated miR-34a levels. Further studies suggested that miR-34a targets SIRT1 and Nampt1 by directly binding to the 3'UTR of their mRNAs, and downregulation of the elevated miR-34a in obesity restored SIRT1, Nampt1, and NAD⁺ levels with decreased lipogenesis, increased insulin and glucose tolerance, improved ER stress, and decreased inflammation.

Conclusion: These results suggest that SIRT1 suppresses hepatic lipogenesis by inhibiting SREBP-1c and activating FXR via protein deacetylation. Reducing acetylation of these proteins by targeting SIRT1 may be useful for treating metabolic disorders. Furthermore, targeting the aberrantly regulated miR-34a/SIRT1-Nampt1 axis with anti-miR-34a may have potential for treating metabolic disorders.



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• Education and Appointments

MBChB - 1967	University of Cape Town, South Africa	
MD Thesis - 1972	University of Cape Town, South Africa	
1968	University of Cape Town, South Africa	Intern
1969-73	Royal Postgraduate School, London, England	Registrar and Research Fellow
1973-75	London Hospital	Lecturer
1975-77	University of Washington	Senior Fellow
1977-80	University of Washington	Assistant Professor
1980-85	University of Washington	Associate Professor
1985-	University of Washington	Professor
1996-	University of Washington	Head, Division of Metabolism, Endocrinology and Nutrition

• Research Interests

Major: Lipids, diabetes and atherosclerosis; adipose tissue biology; lipoprotein proteoglycan interactions

• Brief List of Publications

1. Yoon, J., Subramanian, S., Ding, Y., Wang, S., Goodspeed, L., Sullivan, B., Kim, J., O'Brien, K., Chait, A.: Chronic insulin therapy reduces adipose tissue macrophage content in LDL-receptor-deficient mice. *Diabetologia* 54:1252-60, 2011.
2. Chiba, T., Chang, M., Wang S., Wight T., McMillen T., Oram J., Vaisar T., Heinecke J., DeBeer, F., De Beer, M., Chait, A.: Serum amyloid A facilitates the binding of high-density lipoprotein from mice injected with lipopolysaccharide to vascular proteoglycans. *Arterioscler. Thromb. Vasc. Biol.*, 31:1326-32, 2011.
3. Little, P.J., Chait, A., Bobik, A.: Cellular and cytokine-based inflammatory processes as novel therapeutic targets for the prevention and treatment of atherosclerosis. *Pharmacol Ther.* 131:255-68, 2011.
4. Subramanian, S., Goodspeed, L., Wang, S., Kim, J., Zeng, L., Ioannou, G., Haigh, W., Yeh, M., Kowdley, K., O'Brien, K., Pennathur, S., Chait, A.: Dietary cholesterol exacerbates hepatic steatosis and inflammation in obese LDL receptor-deficient mice. *J Lipid Res.*, 2011. Epub - ahead of print.
5. Handa, P., Tateya, S., Rizzo, N.O., Cheng, A.M., Morgan-Stevenson, V., Han, C.Y., Clowes, A.W., Daum, G., O'Brien, K.D., Schwartz, M.W., Chait, A., Kim, F.: Reduced vascular nitric oxide-cGMP signaling contributes to adipose tissue inflammation during high-fat feeding. *Arterioscler. Thromb. Vasc. Biol.* - In press.
6. Callegari, A., Liu, Y., White, C.C., Chait, A., Gough, P., Raines, E.W., Cox, D., Kavanagh, T.J., Rosenfeld, M.E.: Gain and loss of function for glutathione synthesis: Impact on advanced atherosclerosis in apolipoprotein E-deficient mice. *Arterioscler. Thromb. Vasc. Biol.* 2011 Epub - ahead of print.
7. Chait, A., Subramanian, S.: Hypertriglyceridemia secondary to obesity and diabetes. *Biochim. Biophys. Acta.* - In press.
8. Schauer, I.E., Knaub, L., Lloyd, M., Watson, P., Gliwa, C., Lewis, K., Chait, A., Klemm, D., Gunter, J., Bouchard, R., McDonald, T., O'Brien, K., and Reusch, J.: CREB downregulation in vascular disease: a common response to cardiovascular risk. *Arterioscler. Thromb. Vasc. Biol.* 30:733-741, 2010.
9. Campbell, L.A., Yaraei, K., Van Lenten, B., Chait, A., Blessing, E., Kuo, C., Nosaka, T., Ricks, J., Rosenfeld, M.: The acute phase reactant response to respiratory infection with *Chlamydia pneumoniae*: implications for the pathogenesis of atherosclerosis. *Microb. Infect.* 12:598-606, 2010.

| S10-3 |

Diet-induced obesity and adipose tissue inflammation

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Atherosclerotic cardiovascular disease is a common consequence of type 2 diabetes and the metabolic syndrome, both of which are associated with visceral obesity, adipose tissue inflammation, insulin resistance, dyslipidemia and atherosclerosis. We have used *in vitro* and *in vivo* models to help understand the link between obesity and these downstream consequences.

Adipocyte hypertrophy induced *in vitro* by exposure of differentiated 3T3-L1 cells to high glucose conditions or certain saturated fatty acids results in increased expression of the monocyte chemotactic factors, MCP-1 and the extra-hepatic isoform of serum amyloid A (SAA), SAA₃. Stimulation of expression of these molecules requires generation of reactive oxygen species by NADPH oxidase 4

and activation of NF κ B. Similar changes in adipose tissue were evoked *in vivo* by feeding LDL receptor deficient mice a high fat, high sucrose cholesterol-containing diet, which resulted in adipocyte hypertrophy, obesity, and macrophage accumulation in visceral fat. MCP-1 and SAA expression increased, consistent with these molecules playing a role in macrophage recruitment to adipose tissue. Moreover, the mice became insulin resistant, had evidence of systemic inflammation (with increased levels of the hepatic isoform of SAA) and developed atherosclerosis.

These findings suggest that diet-induced obesity and adipose tissue inflammation can lead to insulin resistance and atherosclerosis by a mechanism that involves the local production of MCP-1 and SAA in adipose tissue.



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• Education and Appointments

1983	Seoul National University, Seoul, Korea	BA
1985	Seoul National University, Seoul, Korea	MS
1993	Boston University, Boston, USA	Ph.D.
1999	Joslin Diabetes Center/Harvard Medical School	Instructor
2006	Joslin Diabetes Center/Harvard Medical School	Assistant Investigator
2010	Joslin Diabetes Center/Harvard Medical School	Assistant Professor

• Research Interests

Major: Immunology in insulin resistance/Type 2 Diabetes

• Brief List of Publications

1. Nishi, M, Werner E, Frantz JD, Dhe-Paganon S, Hansen L, Lee J, Shoelson SE. Mechanism for human SH2-b dimerization and activation of JAK2. *Mol Cell Biol* 2005;25:2607-21.
2. Goldfine AB, Silver R, Aldhahi W, Cai D, Lee J, Shoelson SE. Use of salsalate to target inflammation in the treatment of insulin resistance and Type 2 Diabetes. *Clin Trans Sci* 2008;1:36-43.
3. Feuerer M, Herrero H, Cipolletta D, Naaz A, Wong J, Nayer A, Lee J, Goldfine A, Benoist C, Shoelson S, MathisD. Lean, but not obese, fat is enriched for a unique population of regulatory T cells that affect metabolic parameters. *Nat Med* 2009;15:930-9.
4. Herrero H, Shapiro H, Nayer A, Lee J, Shoelson SE. Inflammation and adipose tissue macrophages in lipodystrophic mice. *Proc Natl Acad Sci USA* 2010;107:240-5.

| S10-4 |

The role of immune cells in the development of obesity-induced inflammation and insulin resistance

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Subacute chronic inflammation has been implicated as an important player to mediate the development of obesity-induced insulin resistance in animal models as well as in human. However, there are many questions remained to be answered. Our major question has been "Which cells mediate the development of obesity-induced inflammation?" Although insulin responsive cells such as adipocytes, hepatocytes, myocytes and β cells are important for glucose homeostasis, recent studies strongly suggest that obesity-induced inflammation is mainly regulated by immune cells, especially in adipose tissue. Indeed, most of immune cell

types including macrophages, T and B cells and mast cells are found in adipose tissue and the number of these cells are increased with obesity. It has been also shown that inflammation in adipose tissue is maintained by the balance of pro-inflammatory cells (M1 macrophages, mast cells and CD 8 T cells) and anti-inflammatory cells (M2 macrophages and regulatory T cells). I will further discuss our recent findings for the new role of immune cells including adipose tissue macrophages in the development of obesity-induced insulin resistance.



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• Education and Appointments

1986	Hunan Medical University	M.D.
2008	University of Virginia	Associate Professor of Medicine
2010	University of Virginia	Associate Chief, Division of Endocrinology

• Research Interests

Insulin action and cardiovascular complications of diabetes

• Brief List of Publications

1. Zheng C, Zhou Z, Yang L, Lin J, Huang G, Li X, Zhou W, Wang X, Liu Z. Fulminant type 1 diabetes mellitus exhibits distinct clinical and autoimmunity features from classical type 1 diabetes mellitus in Chinese. *Diabetes/Metabolism Research and Reviews*. 2011, 27(1):70-8.
2. Wang N, Ko S-H, Chai W, Li G, Barrett EJ, Tao L, Cao W, and Liu Z. Resveratrol recruits rat muscle microvasculature via a nitric oxide-dependent mechanism that is blocked by tumor necrosis factor- α . *Am J Physiol Endocrinol Metab* 2011; 300(1):E195-201.
3. Liu J, Jahn LA, Fowler DE, Barrett EJ, Cao W, and Liu Z. Free fatty acids induce insulin resistance in both cardiac and skeletal muscle microvasculature in humans. *J Clin Endocrinol Metab*. 2011; 96(2):438-46.
4. Hong T, Ning J, Yang X, Liu H-Y, Han J, Liu Z, and Cao W. Fine-tuned regulation of the PGC-1 α gene transcription by different intracellular signaling pathways. *Am J Physiol Endocrinol Metab* 2011, 300(3):E500-E507.
5. Wang AP, Li X, Zheng Y, Liu BL, Huang G, Yan X, Liu Z, and Zhou Z. Thiazolidinediones protect mouse pancreatic β -cells directly from cytokine-induced cytotoxicity through PPAR γ -dependent mechanisms. *Acta Diabetol* 2011, [Epub ahead of print]
6. Cao W, Ning J, Liu HY, Hong T, and Liu Z. Excess exposure to insulin is the primary cause of insulin resistance and its associated atherosclerosis. *Curr Mol Pharmacol*. 2011 Jan 18 [Epub ahead of print]
7. Ning J, Hong T, Ward A, Pi J, Liu Z, Liu H-Y, and Cao W. Constitutive role for IRE1 α -XBP1 signaling pathway in the insulin-mediated hepatic lipogenic program. *Endocrinology* 2011, 152(6):2247-2255
8. Chai W, Liu J, Jahn LA, Fowler DE, Barrett EJ, and Liu Z. Salsalate attenuates free fatty acids-induced microvascular and metabolic insulin resistance in humans. *Diabetes Care* 2011, 34(7):1634-8
9. Xiang Y, Zhou P, Li X, Huang G, Liu Z, Xu A, Leslie RD, and Zhou Z. Heterogeneity of altered cytokine levels across the clinical spectrum of diabetes in China. *Diabetes Care* 2011, 34(7):1639-41
10. Ning J, Hong T, Yang X, Liu Z, Liu H-Y, and Cao W. Insulin and insulin signaling play a critical role in fat induction of insulin resistance in mouse. *Am J Physiol Endocrinol Metab* 2011 [E-pub ahead of print]
11. Barrett EJ, Wang H, Upchurch CT, and Liu Z. Insulin regulates its own delivery to skeletal muscle by feed-forward actions on the vasculature. *Am J Physiol Endocrinol Metab* 2011 [E-pub ahead of print]
12. Ko S-H, Cao W, and Liu Z. Management of hypertension and microvascular insulin resistance in diabetes. *Current Hypertension Reports* 2010; 12(4):243-51.
13. Cohn WF, Ropka ME, Pelletier SL, Barrett JR, Kinzie MB, Harrison MB, Liu Z, Miesfeldt S, Tucker AL, Worrall BB, Gibson J, Mullins IM, Elward KS, Franko J, Guterbock TM, Knaus WA. Health Heritage $\text{\textcircled{C}}$, a web-based tool for the collection and assessment of family health history: initial user experience and analytic validity. *Public Health Genomics*. 2010; 13(7-8):477-91.

| S11-1 |

Insulin action and resistance in the microcirculation

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University of Virginia, USA

Microvasculature exerts profound effects on tissue metabolism and survival. It regulates tissue perfusion to ensure adequate delivery of nutrients, oxygen and hormones, and provides endothelial exchange surface area between the plasma and tissue interstitium. Under normal physiology, insulin plays a major role in the regulation of microvascular perfusion in muscle by fine-tuning its signals through the PI3-kinase/Akt/eNOS pathway and the MAPK pathway. Activation of the PI3-kinase pathway leads to eNOS phosphorylation and NO production, resulting in dilation of the precapillary arterioles and increased capillary perfusion. On the other hand, activation of the MAPK pathway causes vasoconstriction due to increased production of vasoconstrictor endothelin-1. Insulin's vasodilatory action in the microvasculature is closely related with its metabolic action. Insulin-mediated capillary recruitment clearly precedes insulin-stimulated glucose uptake in muscle and blockade of insulin-mediated capillary recruitment decreases insulin-stimulated glucose disposal by ~40%.

Microvascular insulin resistance is well established in obesity and diabetes and may play important role in the

development of diabetes and the related macro- and micro-vascular complications. In the insulin resistant states, insulin action through the PI3-kinase pathway is blunted while its signals through the MAPK pathway remains intact or even enhanced, a phenomenon referred to as selective insulin resistance. This leads to a decreased NO bioavailability and same or enhanced endothelin-1 production, tilting the balance between endothelin-1 and NO production and resulting in increased vasoconstriction and decreased muscle microvascular perfusion. The underlying mechanisms are under active investigation. Inflammation and free fatty acids have clearly been implicated as the culprits. Both are capable of causing oxidative stress and inflammation, and blunting insulin-mediated muscle microvascular recruitment. The angiotensin system also potently regulates muscle microvascular perfusion and thus insulin delivery/action. Balancing angiotensin II's actions on the type 1 receptors (vasoconstriction) and type 2 receptors (vasodilation) may aid in improved insulin delivery/action in diabetes.



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• **Education and Appointments**

2005-present	Dept. of Int. Med., Kyungpook National Univ. Hospital, Korea	Professor / Staff
1998-2005	Dept. of Int. Med., Keimyung Univ. Med. School / DSMC, Korea	Professor / Staff
1994-1995	Joslin Diabetes Center, Harvard Medical school, Boston	Research Fellow
1982-1986	Internal Medicine, Dongsan Medical Center, Daegu, Korea	Intern, Residency
1987-1988	Joslin Diabetes Center, Harvard Medical school, Boston,	Clinical Fellow
1983-1988	School of Medicine, Kyungpook National University, Korea	Master & Ph.D.
1978-1982	School of Medicine, Kyungpook National University, Korea	M.D.

• **Research Interests**

Major: Endocrinology, Diabetes
 Metabolic syndrome, vascular complications, obesity, mitochondrial function

• **Brief List of Publications**

1. Kim YH, Hwang JH, Noh JR, Gang GT, Kim DH, Son HY, Kwak TH, Shong M, Lee IK, Lee CH. Activation of NAD(P): quinone oxidoreductase ameliorates spontaneous hypertension in an animal model via modulation of eNOS activity. *Cardiovasc Res.* 2011 Aug 1;91(3):519-27
2. Kim H, Kim HJ, Lee K, Kim JM, Kim HS, Kim JR, Ha CM, Choi YK, Lee SJ, Kim JY, Harris R, Jeong D, Lee IK. Alpha-lipoic acid attenuates vascular calcification via reversal of mitochondrial function and restoration of Gas6/Axl/Akt survival pathway. *J Cell Mol Med.* Epub 2011 Mar 1
3. Misu H, Takamura T, Takayama H, Hayashi H, Matsuzawa-Nagata N, Kurita S, Ishikura K, Ando H, Takeshita Y, Ota T, Sakurai M, Yamashita T, Mizukoshi E, Yamashita T, Honda M, Miyamoto K, Kubota T, Kubota N, Kadowaki T, Kim HJ, Lee IK, Minokoshi Y, Saito Y, Takahashi K, Yamada Y, Takakura N, Kaneko S. A liver-derived secretory protein, selenoprotein P, causes insulin resistance. *Cell Metab.* 2010 Nov 3;12(5):483-95
4. Min AK, Kim MK, Seo HY, Kim HS, Jang BK, Hwang JS, Choi HS, Lee KU, Park KG, Lee IK. Alpha-lipoic acid inhibits hepatic PAI-1 expression and fibrosis by inhibiting the TGF-beta signaling pathway. *Biochem Biophys Res Commun.* 2010 Mar 12;393(3):536-41.
5. Kim MK, Chanda D, Lee IK, Choi HS, Park KG. Targeting orphan nuclear receptor SHP in the treatment of metabolic diseases. *Expert Opin Ther Targets.* 2010 Apr;14(4):453-66. Review
6. Kim HJ, Kim JY, Lee SJ, Kim HJ, Oh CJ, Choi YK, Lee HJ, Do JY, Kim SY, Kwon TK, Choi HS, Lee MO, Park IS, Park KG, Lee KU, Lee IK. {alpha}-Lipoic Acid Prevents Neointimal Hyperplasia Via Induction of p38 Mitogen-Activated Protein Kinase/Nur77-Mediated Apoptosis of Vascular Smooth Muscle Cells and Accelerates Postinjury Reendothelialization. *Arterioscler Thromb Vasc Biol.* 2010 Nov;30(11):2164-72.
7. Kim JE, Song SE, Kim YW, Kim JY, Park SC, Park YK, Baek SH, Lee IK, Park SY. Adiponectin inhibits palmitate-induced apoptosis through suppression of ROS in endothelial cells: involvement of cAMP/PKA and AMPK. *J Endocrinol.* 2010 Oct;207(1):35-44.
8. Seo HY, Kim MK, Min AK, Kim HS, Ryu SY, Kim NK, Lee KM, Kim HJ, Choi HS, Lee KU, Park KG, Lee IK. Endoplasmic Reticulum Stress-Induced Activation of Activating Transcription Factor 6 Decreases cAMP-Stimulated Hepatic Gluconeogenesis via Inhibition of CREB. *Endocrinology.* 2010 Feb;151(2):561-8.

| S11-2 |

Insulin resistance and new strategies to suppress vascular smooth muscle cell proliferation

In-Kyu Lee

Kyungpook National University, Korea

In patients with diabetes, the American Diabetes Association reports (2006) that heart disease was responsible for 68 percent of diabetes-related deaths on those over 65 years of age. In fact, diabetes increases the risk of coronary, cerebrovascular, and peripheral arterial disease up to fourfold. Accumulating evidences showed that main pathogenesis of the increased cardiovascular manifestation in the diabetic is related with hyperglycemia and insulin resistance. These patients required more revascularization procedures com-

pared with the general population at an earlier point in time and had a more prone to restenosis and failure, which is secondary to a heightened formation of neointimal hyperplasia. Neointimal formation, the leading cause of restenosis, is caused by proliferation of vascular smooth muscle cells (VSMCs). In this presentation, several new molecules prevented VSMC's proliferation *in vitro* and *in vivo* caused by mainly G1 cell cycle arrest via an AMPK dependent and independent mechanism.



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• Education and Appointments

2001-2004	Korea University	Assistant Professor
2004-2009	Korea University	Associate Professor
2005-2006	University of Texas	Research Fellow
2009-	Korea University	Professor

• Research Interests

Major: Adipokines, metabolic syndrome

• Brief List of Publications

1. Yang SJ, Kim SE, Choi HY, Kim TN, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. High-sensitivity C-reactive protein in the low- and intermediate-Framingham risk score groups: Analysis with 18F-Fluorodeoxyglucose positron emission tomography. *Int J Cardiol* 2011; In press
2. Yang SJ, Hwang SY, Choi HY, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Serum selenoprotein P levels in patients with type 2 diabetes and prediabetes: Implications for insulin resistance, inflammation, and atherosclerosis. *J Clin Endocrinol Metab* 2011; In press
3. Yoo HJ, Park MS, Yang SJ, Kim TN, Lim KI, Kang HJ, Song W, Baik SH, Choi DS, Choi KM. The differential relationship between fat mass and bone mineral density by gender and menopausal status: the KSOS study. *J Bone Miner Metab* 2011; In press
4. Yang SJ, Hong HC, Choi HY, Yoo HJ, Gho GJ, Whang TG, Baik SH, Choi DS, Kim SM, Choi KM. Effects of three-month combined exercise program on fibroblast growth factor 21 and fetuin-A levels and arterial stiffness in obese women. *Clin Endocrinol* 2011; In press
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| S11-3 |

Metabolic syndrome, adipokines and vascular inflammation

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Atherosclerosis is one of the leading causes of morbidity and mortality in the world. Rupture of atherosclerotic plaques is the primary mechanism of myocardial infarction or cerebrovascular accidents. Plaque rupture is the consequence of vulnerable atherosclerotic plaque. Inflammatory state and composition of an atherosclerotic plaque are more important determinants of acute clinical events than the degree of stenosis. Therefore, non-invasive imaging tools to detect vulnerable atherosclerotic plaque are urgently needed. Recently, MRI and CT showed great improvement to identify atherosclerotic vascular disease. Especially, multi-slice CT has been shown to provide excellent anatomical and morphological images of coronary

arteries. Furthermore, positron emission tomography with fluoro-deoxyglucose (FDG-PET) has become one of the advanced imaging techniques for the detection of vascular inflammation that reflect vulnerable plaques. Therefore, hybrid imaging with both PET and CT especially provides combined functional and structural vascular imaging.

Recently, we performed several clinical studies using PET/CT in Koreans. The results suggest that PET/CT might be a novel non-invasive modality to assess vascular inflammation in CV risk group such as type 2 diabetes or metabolic syndrome. Furthermore, adipokines derived from visceral adipose tissue might be important factor that was associated with vascular inflammation.



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• **Education and Appointments**

1983-1989	Medical College, Seoul National University	
1989-1990	Internship	Seoul National University Hospital
1990-1994	Residency	Department of Internal Medicine, Seoul National University Hospital
1994-1996	Clinical and Research Fellowship	Division of Cardiology, Department of Internal Medicine, Seoul National University Hospital
1996-1999	Visiting Scientist	Department of Medicine, University of California, San Diego, USA
1999-2001	Postdoctoral Fellow	Department of Medicine, University of California, San Diego, USA
2001-2001	Project Scientist (proposed)	Department of Medicine, University of California, San Diego, USA
2001-present	Associate Professor	Division of Cardiology, Asan Medical Center, Department of Internal Medicine, College of Medicine, University of Ulsan, Seoul, Republic of Korea

• **Brief List of Publications**

1. Kang SJ, Mintz GS, Park DW, Lee SW, Kim YH, Lee CW, Han KH, Kim JJ, Park SW, Park SJ. Tissue characterization of in-stent neointima using intravascular ultrasound radiofrequency data analysis. *Am J Cardiol.* 2010 Dec 1;106(11):1561-5.
2. Kang SJ, Mintz GS, Park DW, Lee SW, Kim YH, Lee CW, Han KH, Kim JJ, Park SW, Park SJ. Late and very late drug-eluting stent malapposition: serial 2-year quantitative IVUS analysis. *Circ Cardiovasc Interv.* 2010 Aug;3(4):335-40.
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| S11-4 |

Which lipid particles are atherogenic under diabetic condition?; Lipid traffics in diabetics

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Diabetic conditions considerably change the traffics of lipid particles in fasting and non-fasting conditions. Insulin inhibits the action of protein kinase in adipocytes and suppresses the release of free fatty acid (FFA) and reduces the uptake of glucose. The overload of FFA stimulates hepatocytes to synthesize the release the representative triglyceride(TG)-rich lipoprotein particles (TRLs) such as VLDL. The translocation of TG to HDL and LDL particles results in the catabolism of HDL particles and transformation to more atherogenic small-dense LDL.

Diabetic conditions also increase the production of chylomicron (CM), which induces postprandial hyperTGemia, through regulating multiple steps of CM production in the

intestinal epithelial cells. The uptake of cholesterol as well as triglyceride is important for the formation of CM and ,interestingly, GLP-1, not GLP-2, may suppress the CM formation.

So-called lipotoxicity which can be represented as FFA overload, not only induces overproduction of TRLs in the live and gut, but also increases insulin resistance in the liver and the peripheral organs. Conversely, hyperglycemia itself and insulin resistance increase the severity of lipotoxicity as well. Therefore, controlling the overload of both lipid and glucose may eventually alleviate the atherogenic and dyslipidaemic conditions observed in diabetic conditions.



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• **Education and Appointments**

1988-1994	College of Medicine, Chonbuk National University	
1999-2001	Master Course of Medical Science, Graduate School, Chonbuk National University	
2002-2007	Ph.D. Course of Medical Science, Graduate School, Chonbuk National University, Majored in diabetology	
1998-2002	Internal medicine, Medical College of Chonbuk National University Hospital	Resident
2002-2003	Endocrinology & Metabolism, Medical College of Chonbuk National University Hospital	Fellow

• **Research Interests**

Major: Diabetes, Diabetic neuropathy, atherosclerosis

• **Brief List of Publications**

1. Autoimmune Hypoglycemia in a Type 2 Diabetic Patient With Anti-Insulin and Insulin Receptor Antibodies. *Diabetes Care* 27: 288-289,2005
2. Autoimmune Hypoglycemia in a Type 2 Diabetic Patient With Anti-Insulin and Insulin Receptor Antibodies: Response to Sahin, Tutuncu, and Guvener. *Diabetes Care* 27: 1247,2005
3. Aortic pulse wave velocity measurement is more reliable test than carotid intima-media thickness in predicting coronary artery disease in diabetic patients. 2006 *Diabetes* vol.55 supplement 1. A601
4. Power Spectral Analysis Of Heart Rate Variability In Patients With Diabetes In Korea. 2007 *Diabetes* vol.56 supplement 1. A612
5. The effects of exercise, performed fed and fasted state on plasma glucose and hormone in subjects with Type 2 diabetes. 2007 *Diabetes* vol.56 supplement 1. A639
6. Switching patients no longer adequately controlled on basal insulin analogue to biphasic insulin aspart30 offered improved glycemic control. *Diabetes*, June 2008 vol.57 supplement 1 A162
7. Effect of anti-platelet agents on pulse wave velocity in people with type 2 diabetes. *Diabetes*, June 2008 vol.57 supplement 1 A180

| S12-1 |

Introduction to 2011 KDA clinical recommendation of medical nutrition therapy

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Korean diabetes association (KDA) has been actively involved in the development and dissemination of diabetes care standards, guidelines, and related documents for many years. A balanced review and analysis of the literature on a scientific or medical topic related to diabetes. A comprehensive examination by a panel of experts of a scientific or medical issue related to diabetes. The category now also includes task force, workgroup, and expert committee reports. Recommendations are assigned ratings of A, B, or C, depending on the quality of evidence. Expert opinion (E) is a separate category for recommendations in which there is as yet no evidence from clinical trials, in which clinical trials may be impractical, or in which there is conflicting evidence.

KDA released standards of medical care in diabetes in 2007. These standards of care are revised May 2011 by the KDA's multidisciplinary Professional Practice Committee, incorporating new evidence.

Medical nutrition therapy (MNT) is an integral component of diabetes prevention, management, and selfmanagement education. In addition to its role in preventing and controlling diabetes, KDA recognizes the importance of nu-

trition as an essential component of an overall healthy lifestyle. Individuals who have prediabetes or diabetes should receive individualized MNT as needed to achieve treatment goals, preferably provided by a registered dietitian familiar with the components of diabetes MNT. Achieving nutrition-related goals requires a coordinated team effort that includes the active involvement of the person with prediabetes or diabetes. Because of the complexity of nutrition issues, it is recommended that a registered dietitian who is knowledgeable and skilled in implementing nutrition therapy into diabetes management and education be the team member who provides MNT.

Clinical trials/outcome studies of MNT have reported decreases in A1C at 3-6 months ranging from 0.25% to 2.9% with higher reductions seen in type 2 diabetes of shorter duration. Multiple studies have demonstrated sustained improvements in A1C at 12 months and longer when an Registered Dietitian provided follow-up visits ranging from monthly to three sessions per year.

This sessions provided new version of 2011 KDA Clinical recommendation of medical nutrition therapy.



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• Education and Appointments

1998	MD degree from Duksung Women's University, Department of Food and Nutrition
2001	Master degree from Duksung Women's University, Department of Food and Nutrition
2006	Ph D degree from Duksung Women's University, Department of Food and Nutrition
2001-present	Registered Dietitian in Diabetes Center, Nowon Eulji Hospital

• Brief List of Publications

1. Ahn HJ, Kan KA, Jang JY, Lee JH, Park KS, Min KW. Small rice bowl-based meal plan for energy and macronutrient intake in Korean Men with type 2 diabetes; A pilot study. *Diabetes Metab J* 2011;35:273-81.
2. Ahn HJ, Min KW, Cho YO. Assessment of vitamin B6 status in Korean patients with newly diagnosed type 2 diabetes. *Nutr Res Pract* 2011;5:24-9.
3. Ahn HJ, Han KA, Kwon HR, Min KW. The small rice bowl-based meal plan was effective at reducing dietary energy intake, body weight, and blood glucose levels in Korean women with type 2 diabetes mellitus. *Korean Diabetes J* 2010;34:340-9.
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5. Ahn HJ, Eom YK, Han KA, Kwon HR, Kim HJ, Park KS, Min KW. The effects of small sized rice bowl on carbohydrate intake dietary patterns in women with type 2 diabetes. *Korean Diabetes J* 2010;34:1-8.

| S12-2 |

New version of KDA dietary recommendations - MNT, energy intake and carbohydrate

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Diabetes medical nutrition therapy (MNT) is integral to diabetes care and management. Individuals with diabetes need MNT recommendations that are supported by scientific evidence. To achieve positive outcomes, a coordinated team effort that provides continued education. We will review the updated version of 2011 KDA MNT recommendations for effects of MNT, energy intake and carbohydrate.

Prospective studies support MNT as a cost-effective therapy in reaching treatment goals. MNT provided by registered dietitians is reported to lower A1C -0.25~-2.9%, depending to the type and duration of diabetes.

Because of the correlation with obesity and insulin resistance, body weight reduction is an important therapeutic method for overweight or obese individuals with pre-diabetes or diabetes. Short-term studies have demonstrated that moderate weight loss in individuals with type 2 diabetes is associated with improved insulin resistance, blood glucose, lipid and blood pressure.

Although, numerous studies have attempted to identify the optimal mix of macronutrients distribution, including carbohydrate, it has not been established. For achieving glycemic control, monitoring total carbohydrate intake re-

mains a key strategy in individuals with diabetes. Korean National Health and Nutrition Examination surveys (KNHANES) reported that 65% of daily energy intake is from carbohydrate in the Koreans. Therefore, we emphasized that the amount of carbohydrate intake is more important than the type of carbohydrate. The use of the glycemic index and glycemic load may provide a modest additional benefit for glycemic control over that observed when total carbohydrate is considered alone.

In conclusion, numerous studies have proved the effectiveness of MNT provided by RD, therefore, the updated recommendations were not subjected to objections and no changes were made from the previous recommendations. However, with regards to body weight reduction, low energy intake of elderly from previous recommendation was deleted due to lack of evidence and obese subjects were recommended to reduce the energy intake to achieve the moderate weight reduction (reduction of 7% of initial weight). As previous recommendations reported, the updated recommendations stressed more importance on the total amount of carbohydrate intake than the type of carbohydrate intake.



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• Education and Appointments

1992	Graduated from Department of Food and Nutrition, Duksung Women University, Seoul, Korea	
2002	Graduated from Yonsei University, Graduate School of Human Environmental	
1992-2004	Sejong Hospital	Dietitian
2004-present	Kangnam Sacred Heart hospital	Dietitian Director
2006-2007	Korean Diabetes Association	Nutrition Committee
2008-2009	Korean Diabetes Association	Education Committee
2010-present	Korean Diabetes Association	Nutrition Committee
2008-present	Nutrition Society of diabetes education	Director

| S12-3 |

New version of KDA dietary recommendations- protein, fat, vitamin and mineral

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Diabetes is a chronic illness that requires continuing medical care and ongoing patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications. MNT is an integral component of diabetes prevention, management, and diabetes complications. Nutrition Committee gave an expansive review of diabetes treatment guidelines developed by Diabetes Associations in United States, Japan, Canada and the International Diabetes Federation through the workshops. Nutrition Committee has also reedited diabetes treatment guidelines through investigation of comprehensive review, search for national and international diabetes-related references. This will introduce a revised edition of clinical nutrition guideline of protein, fat, and vita-

min / mineral.

<Recommendation>

- Protein should provide 15-20% of total energy intake however limiting protein intake to 0,8 g/kg daily if the person is proteinuria greater than 1g/day (B)
- No more than 25% of total energy intake should come from fat. Restrict saturated fats to <7% of total daily energy intake and restrict trans fat intake to a minimum. Cholesterol intake to less than 200mg a day.(B)
- Routine vitamin and mineral supplementation is not necessary. In the case of an identified deficiency, limited dietary intake or special need, supplementation may be recommended (B)

Table 1. KDA evidence grading system for clinical practice recommendations

Level of evidence	Description
A	<p>Recommendation is clear evidence</p> <ul style="list-style-type: none"> • Evidence from a well-conducted generalizable, randomized controlled trials that are adequately powered, multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	<p>Recommendation is evidence reliable</p> <ul style="list-style-type: none"> • Supportive evidence from well-conducted prospective cohort studies • Supportive evidence from a well-conducted case-control study
C	<p>Recommendation is evidence availability</p> <ul style="list-style-type: none"> • Evidence from randomized clinical trials with small organizations • Observational study or case reports
E	Expert consensus or clinical experience



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• Education and Appointments

- 2001 MD degree from Catholic University, Department of Food and Nutrition, Korea
- 2007 Master degree from Kyunghee University Graduate School of East-West Medical, Department of Medical Nutrition, Korea
- 2009- A committee member of food and nutrition, Korean Diabetes Association
- 2003- Clinical Dietitian, Seoul National University Bundang Hospital

| S12-4 |

New version of KDA dietary recommendations- fiber, sodium, alcohol and sweeteners

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The new standards of medical care for diabetes are modified by the KDA to provide patients with diabetes, clinicians and other individuals who are interested in diabetes care. To introduce the recent version of dietary recommendations in 2011, the revised standards of dietary fiber, sodium, alcohol and sweeteners are listed below.

Fiber

- The recommended dietary fiber intake is 20-25g/day (12g/1,000 kcal/day) from in various fiber sources because dietary fiber helps prevent diabetes and regulate blood glucose levels. [B]

Fiber helps prevent diabetes and regulate blood glucose levels. Meta-analyses of studies showed higher cereal fiber intakes may decrease diabetes risk. Likewise, according to another study of the randomized controlled trial, high intake of dietary fiber improves glycemic control. The dietary fiber intake recommended to 14g/1,000 kcal/day, a half amount of grain should be cereal, by the American Diabetes Association (ADA). Also, 25-50g/day, in various sources including soluble fiber and cereal fiber, by the Canadian Diabetes Association (CDA) and 20-25g/day by the Japanese Diabetes Society (JDS) were recommended. The KDA recommended that diabetic patients consume 12g/1,000kcal/day of dietary fiber which is based on the Dietary Reference Intakes for Koreans (KDRIs).

Sodium

- Limit sodium intake to <4,000mg/day (<10g of salt) to prevent high blood pressure and to regulate appetite; however, for individuals with diabetes and hypertension, heart complications or cardiovascular disease, limit sodium intake to <2,000-3,000mg/day (<5-7.5g of salt). [B]

Controlling blood pressure and blood glucose levels are associated to complications of diabetes. Therefore, it is important to limit sodium intake to 4,000mg/day; however, for diabetic patients with renal complications or cardiovascular disease (CVD), the dietary sodium intake of <2,000-3,000mg/day (<5-7.5g of salt) is recommended. Meta-analyses of studies about the effect of salt reduction on blood pressure, blood pressures in both hypertensive and normotensive groups decreased when their dietary sodium intake limited to 6g/day, and the risk for CVD and stroke deaths reduced in low salt group. The KDRIs needed a guideline to prevent lifestyle disease due to excessive sodium intake of Korean. Therefore, the daily sodium intake by WHO/FAO which is <2,000mg/day (<5g of salt) to prevent chronic diseases related to diet was suggested as the daily sodium intake for Korean. For patients with diabetes and symptomatic renal failure, the dietary sodium intake of <2,000mg/day is recommended, and <2,300mg/day for hypertensives and normothensives to reduce the risk of CVD by the ADA. Nevertheless, the average amount of sodium intake in Korea is 4,500mg/day which is 2.3 higher than the guideline of sodium intake by WHO. Therefore, it is recommended an individualized sodium in-

take upon eating habits in Korean.

Alcohol

- Limit alcohol consumption to a moderate amount (one or two drinks per day) for patients with diabetes who can control their blood glucose; however, for diabetic patients with liver disease, hyperlipidemia, and obesity, alcohol consumption should be restricted. [E]

There is no restriction of alcohol consumption for patients with diabetes who do not have diabetes complications or renal disease and who can control their glucose levels; however, diabetic patients who are taking oral hypoglycemic agents or insulin may have a risk of hypoglycemia. For patients who cannot control their drinking habits, their alcohol consumption should be restricted because excessive drinking aggravates glycemic control. Alcohol consumption should be limited to one drink per day for women and two drinks per day for men. Patients should eat breakfast and should check their blood glucose levels to reduce risk of hypoglycemia in the morning after drinking.

Sugar Alcohols and Sweetener

- Sugar alcohols and sweeteners are safe when consumed within the daily intake guidelines by the KFDA. [A]

Generally, the calorie of sugar alcohol is 2kcal/g which is lower than the calorie of carbohydrate which is 4kcal/g. FDA classified sugar alcohols are a Generally Recognized As Safe (GRAS). Sweeteners are safe if patients consume within the acceptable daily intake (ADI) by the Joint Expert Committee of Food Additives (JECFA) of FAO/WHO and the safety of sweeteners for patients with diabetes is approved by ADA and CDA.

The recommendation of medical nutrition therapy for sugar alcohols and sweeteners were newly published by KDA in 2011 while the recommendations of fiber, sodium, and alcohol have slightly changed from the recommendations in 2007. The new recommendations will be a beneficial guideline for health care providers and patients with diabetes. Therefore, the health care providers should be knowledgeable about updated MNT to educate and provide people with diabetes.

PLENARY LECTURES

SPECIAL LECTURE

SYMPOSIA

SATELLITE SYMPOSIA

ORAL PRESENTATIONS

POSTER EXHIBITIONS

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• Education and Appointments

2013-2015	The International Diabetes Federation Western Pacific	Chairman
2010-2012	The International Diabetes Federation Western Pacific	Chairman elect
2000-Present	Department of Preventive Medicine, Ajou University	Professor
2001-2009	The International Diabetes Federation Western Pacific Region	Executive Director
1997-present	The Center for Clinical Epidemiology, Ajou University Medical Center	Director
2002-2007	Department of Preventive Medicine, Ajou University School of Medicine	Chairman
1989-1994	Department of Medicine, Northwestern University Medical School	Assistance Professor
1984-1989	University of Pittsburgh	Clinical Epidemiology
1977-1983	East Tennessee State University	Medicine

• Research Interests

Major: Diabetes epidemiology

• Brief List of Publications

Published more than 100 SCI publications and 15 Medical Text books in Diabetes, Gestational diabetes, Osteoporosis, Metabolic syndrome, and GWAS studies from the cohort research.

| S13-1 |

Introduction to diabetes in Asia and Ansung-Ansan community cohort epidemiologic study

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Diabetes has risen dramatically in the world from an estimated 30 million cases in 1985 to 177 million in 2000, which is further expected to increase to some 380 million by 2025. Furthermore, diabetes development with higher rates being reported in Asians, Hispanics, African Americans and indigenous peoples of the USA, Canada, Australia and Pacific regions. This presentation covers overview of diabetes epidemiology in Asia and special focus on the 10 year prospective ongoing cohort study from Korea.

A total of 10,038 Korean men and women in the age range 40-69 yr voluntarily participated in this community-based prospective study. All subjects underwent a 75-g oral glucose tolerance test at baseline and at each biennial follow-up. The crude incidence densities in rural men were 20.5, 24.5 and 31.5 per 1,000 person-years in 40th, 50th and 60th respectively. In urban men the rates were 28.3, 42.3 and 55.9 per 1,000 person-years respectively in similar age groups. The incident density of T2DM was lower in women with 13.8, 20.1 and 27.1 in rural whereas the urban women presented with 18.3, 33.4 and 52.9 per 1,000 person-years in 40, 50, and 60th age groups. The overall incidence density of T2DM for 8 years was 26.0 per 1000 person-years. That was 1,113 new T2DM cases were identi-

fied in 43,634 person-years at risk. The stepwise discriminative analysis identified the eleven independent predictive variables; hemoglobin A1c (HbA1c), urban living, systolic blood pressure, homeostasis model assessment (HOMA) index of β -cell function and insulin resistance, alanine transaminase (ALT), triglyceride, age, family history of diabetes, smoking and waist circumference. It yielded a statistically significant function of $\lambda=0.826$, $\chi^2=1125.3$, $P < 0.001$. This function showed that the rate of correct prediction was 72.9%, specificity of 73.9% and sensitivity of 63.8% for diabetes.

The putative risk factors identified in Korean studies are very similar to the risk factors identified from the other countries, including genetic background. The scientific evidence suggests that the dramatic increase in the incidence and prevalence of T2DM in Korea is related to the economic development of Korea, which has a direct influence on health policy, as well as an individual's health behaviors. We expect to observe the current diabetes rates until the key risk factors are present for long enough in our society, at which point we would expect to start observing a more gradual increase in both the incidence and prevalence of T2DM in Korea.



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• Education and Appointments

1983-1989	Kyunghee University, School of Medicine	
1989-1990	Kyunghee University Hospital	Medical Intern
1993-1997	Kyunghee University Hospital	Medical Resident
1993-1996	Kyunghee University	M.Sc., Medical Science
1998-2000	Kyunghee University (Endocrinology)	Ph.D., Medical Science
1997-1999	Endocrinology, Samsung Medical Center	Research Fellow
1999-2001	Eulji University School of Medicine	Instructor
2003-2006	National Institutes of Health	Visiting Fellowship
2001-2008	Eulji University School of Medicine	Assistant Professor
2008-2011	Konyang University School of Medicine	Associate Professor
2011-Present	Konyang University School of Medicine	Professor

• Research Interests

Major: Pathophysiology of Diabetes Mellitus, Incretin hormone, GLP-1, Islet biology and islet transplantation

• Brief List of Publications

1. So-Ra Jung, No-Joon Song, Hyun Sook Hwang, Jae Jin An, Yong-Jun Cho, Hae Young Kweon, Seok-Woo Kang, Kwang Gill Lee, Keejung Yoon, Byung-Joon Kim, Chu Won Nho, Soo Young Choi, Kye Won Park. Silk peptides inhibit adipocyte differentiation through 1 modulation of the Notch pathway in C3H10 T1/2 cells. *Nutrition Research*, 2011
2. Soo Jin Yang, Jung Mook Choi, Lisa Kim, Byung-Joon Kim, Jin Hee Sohn, Won Jun Kim, Se Eun Park, Eun Jung Rhee, Won Young Lee, Ki Won Oh, Sung Woo Park, Sun Woo Kim, Cheol-Young Park. Chronic administration of ezetimibe increases active glucagon-like peptide-1 and improves glycemic control and pancreatic beta cell mass in a rat model of type 2 diabetes. *Biochemical and Biophysical Research Communications* 407:153-157. 2011
3. Dong Mee Lim, Ju Young Kim, Kang Woo Lee, Keun Young Park, Byung Joon Kim. GLP-1 Can Protect Proinflammatory Cytokines Induced Beta Cell Apoptosis through the Ubiquitination. *Endocrinol Metab* 26:142-149, 2011
4. Kim ST, Kim BJ, Lim DM, Song IG, Jung JH, Lee KW, Park KY, Cho YZ, Lee DH, Koh GP. Basal C-peptide Level as a Surrogate Marker of Subclinical Atherosclerosis in Type 2 Diabetic Patients. *Diabetes Metab J*. 35(1):41-49. 2011
5. Kyung Jin Choi, Dong Su Cho, Ju Young Kim, Byung Joon Kim, Kyung Moo Lee, Shin Hye Kim, Dong Kwan Kim, Se Hoon Kim, and Hyung Seo Park. Ca^{2+} -induced Ca^{2+} Release from Internal Stores in INS-1 Rat Insulinoma Cells. *Korean J Physiol Pharmacol*. 15(1):53-9. 2011
6. Byung Joon Kim. Obesity and Sex Hormones. *Korean J Obes* 19(4):113-118. 2010
7. Ju-Young Kim, Dong-Mee Lim, Chan Il Moon, Kyung-Jin Jo, Seong-Kyu Lee, Haing-Woon Baik, Ki-Ho Lee, Kang-Woo Lee, Keun-Young Park, and Byung-Joon Kim. Exendin-4 Protects Oxidative Stress-Induced b-Cell Apoptosis through Reduced JNK and GSK3b Activity. *J Korean Med Sci* 25: 1626-1632. 2010
8. Jeong SU, Kang DG, Lee DH, Lee KW, Lim DM, Kim BJ, Park KY, Chin HJ, Koh G: Clinical Characteristics of Type 2 Diabetes Patients according to Family History of Diabetes. *Korean Diabetes J* 34:222-228. 2010
9. Kim BJ, Zhou J, Martin B, Carlson OD, Maudsley S, Greig NH, Mattson MP, Ladenheim EE, Wustner J, Turner A, Sadeghi H, Egan JM. Transferrin fusion technology: a novel approach to prolong biological half-life of insulinotropic peptides. *J Pharmacol Exp Ther*. 334(3):682-692. 2010

| S13-2 |

Lesson from diabetes prevention program in India and China

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The prevalence and incidence of type 2 diabetes is increasing worldwide. Although major pathogenesis of type 2 diabetes is progressive insulin resistance and relative insulin deficiency, underlying features are interaction between a genetic predisposition and behavioral and environmental factor. Despite many candidate genes are evaluating, the genetic basis of type 2 diabetes has not to be identified. But we have strong evidence that we prevent occurrence of type 2 diabetes through modified nongenetic risk factors as obesity and physical inactivity.

For prevention of disease, Primary prevention, action to protect against disease and disability, is more important than secondary tertiary prevention. In Type 2 diabetes, Education about diabetes, weight control and encourage of physical activity in non diabetic family member of type 2 diabetes and impaired glucose tolerance. Today, I will summarize and discuss about two primary prevention studies, Indian diabetes prevention program (IDPP) from India and Da Qing IGT and Diabetes Study in China.

Indian diabetes prevention program (IDPP) was a community-based, prospective, randomized, controlled clinical trial performed in Indian subjects who were diagnosed IGT over 3 years. The study groups were divided standard

health care advice group (control), lifestyle modification group (LSM), metformin treated group (MET), and LSM plus MET group. The relative risk reduction for diabetes was 28.5% with LSM, 26.4% with MET and 28.2% with LSM + MET as compared with the control group. Only lifestyle modification (LSM) involving diet and enhanced physical activity helped to delay or prevent the progression of IGT to diabetes. Also, LSM was potent methods to prevent diabetic progression as compare to metformin drug.

China Da Qing Diabetes Prevention Study was a large-scale randomized trials performed in Chinese people with impaired glucose tolerance for 2-year intervals over a 6-year period. This study was stated from 1986 and Study groups were divided diet only, exercise only, or diet plus exercise. In 1992, this study reported that life style modification reduced cumulative incidence of diabetes in all groups. Also, risk of developing diabetes reduced 31% ~ 42 % in intervention groups. After 20 year follow up, incidence of diabetes in intervention group still had 43% lower than control group.

The life style modification in IGT subjects can prevent or delayed diabetes and these medication can be effective for a long period.



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• Education and Appointments

1983-1989	Jichi Medical School	M.D.
1999	First Department of Internal Medicine, Kyoto Prefectural University of Medicine	Ph.D.
2001-2003	Division of Molecular Epidemiology, Kobe University Graduate School of Medicine	Assistant Professor
2003-present	Division of Preventive Medicine, Clinical Research Institute, National Hospital organization Kyoto Medical Center	Division Director
2010-present	Faculty of Sport and Health Science, Ritsumeikan University	Visiting Professor

• Research Interests

Diabetes prevention, Diabetes Education, Molecular Epidemiology, beta3-agonists

• Brief List of Publications

1. Sakane N, Sato J, Tsushita K, Tsujii S, Kotani K, Tsuzaki K, Tominaga M, Kawazu S, Sato Y, Usui T, Kamae I, Yoshida T, Kiyohara Y, Sato S, Kuzuya H; Japan Diabetes Prevention Program (JDPP) Research Group: Prevention of type 2 diabetes in a primary healthcare setting: three-year results of lifestyle intervention in Japanese subjects with impaired glucose tolerance. *BMC Public Health*. 2011;11(1):40.
2. Tsuzaki K, Kotani K, Sano Y, Fujiwara S, Takahashi K, Sakane N: The association of the Clock 3111 T/C SNP with lipids and lipoproteins including small dense low-density lipoprotein: results from the Mima study. *BMC Med Genet*. 2010;11:150.
3. Fujiwara S, Kotani K, Brantley PJ, Tsuzaki K, Matsuoka Y, Domichi M, Sano Y, Kajii E, Sakane N: Dietary salt reduction in rural patients with albuminuria using family and community support: the Mima study. *Asia Pac Fam Med*. 2010;9(1):6.
4. Tsuzaki K, Kotani K, Fujiwara S, Sakane N: Adiponectin and lipoprotein particle size. *Diabetes Care*. 2010;33(1):e11.
5. Gugliucci A, Kotani K, Taing J, Matsuoka Y, Sano Y, Yoshimura M, Egawa K, Horikawa C, Kitagawa Y, Kiso Y, Kimura S, Sakane N: Short-term low calorie diet intervention reduces serum advanced glycation end products in healthy overweight or obese adults. *Ann Nutr Metab*. 2009;54(3):197-201.
6. Tsuzaki K, Kotani K, Nagai N, Saiga K, Sano Y, Hamada T, Moritani T, Yoshimura M, Egawa K, Horikawa C, Kitagawa Y, Kiso Y, Sakane N: Adiponectin gene single-nucleotide polymorphisms and treatment response to obesity. *J Endocrinol Invest*. 2009;32(5):395-400.
7. Sakane N, Fujiwara S, Sano Y, Domichi M, Tsuzaki K, Matsuoka Y, Hamada T, Saiga K, Kotani K: Oxidative stress, inflammation, and atherosclerotic changes in retinal arteries in the Japanese population; results from the Mima study. *Endocr J*. 2008;55(3):485-8.
8. Hamada T, Kotani K, Fujiwara S, Sano Y, Domichi M, Tsuzaki K, Sakane N: The common -55 C/T polymorphism in the promoter region of the uncoupling protein 3 gene reduces prevalence of obesity and elevates serum high-density lipoprotein cholesterol levels in the general Japanese population. *Metabolism*. 2008;57(3):410-5.

| S13-3 |

Japan diabetes prevention program (JDPP) and Japan diabetes outcome intervention trial-1 (J-DOIT1)

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The incidence of type 2 diabetes mellitus (T2DM) is increasing in Japan. Although Japanese have a lower prevalence of obesity than Westerners, a tendency to gain weight due to lifestyle changes coupled with an aging of the population seems to be closely related to the rapid expansion of the diabetic population. There is thus an urgent need for effective public health strategies to combat this situation in Japan. In both the Diabetes Prevention Program and Finnish Diabetes Prevention Study, considerable efforts were made by well-trained staff to achieve changes in lifestyle among participants. How to translate the findings of clinical research into real-world practice is a key issue to be addressed. Japan Diabetes Prevention Program (JDPP) was performed to test whether a lifestyle intervention program, carried out in a primary healthcare setting using existing resources, can reduce the incidence of type 2 diabetes in Japanese with impaired glucose tolerance (IGT). Through health checkups in communities and workplaces,

304 middle-aged IGT subjects with a mean body mass index (BMI) of 24.5 kg/m² were recruited and randomized to the intervention group or control group. The lifestyle intervention was carried out for 3 years by public health nurses using the curriculum and educational materials provided by the study group. After 1 year, the intervention had significantly improved body weight and daily non-exercise leisure time energy expenditure. The 3-year cumulative incidence tended to be lower in the intervention group (14.8% vs. 8.2%). Japan Diabetes Outcome Intervention Trial-1 (J-DOIT1), a large-scale cluster randomized controlled trial, is designed to test whether goal-focused lifestyle coaching delivered by telephone can prevent development of T2DM in high-risk individuals. The large number of participants was recruited and cohort has been successfully randomized. These trials are expected to contribute to evidence-based real-world preventive practice.



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• **Education and Appointments**

1980	College of Medicine, Seoul National University	M.D.
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1981-1984	Seoul National University Hospital, Department of Internal Medicine	Resident
1984-1986	Seoul National University Hospital, Division of Endocrinology and Metabolism	Clinical Fellow
1986-1988	University of Calgary, Canada	Research Fellow
1989-present	Department of Internal Medicine, Asan Medical Center University of Ulsan College of Medicine	Clinical staff Instructor -- Professor

• **Research Interests**

Major: Pathogenesis of diabetes and metabolic syndrome

• **Brief List of Publications**

1. Kim MS, Pak YK, Jang PG, Namkoong C, Choi YS, Won JC, Kim KS, Kim SW, Kim HS, Park JY, Kim YB, Lee KU. Role of hypothalamic Foxo1 in the regulation of food intake and energy homeostasis. *Nat Neurosci.* 2006 Jul;9(7):901-6
2. Yeom SY, Kim GH, Kim CH, Jung HD, Kim SY, Park JY, Pak YK, Rhee DK, Kuang SQ, Xu J, Han DJ, Song DK, Lee JW, Lee KU, Kim SW. Regulation of insulin secretion and beta-cell mass by activating signal cointegrator 2. *Mol Cell Biol.* 2006 Jun;26(12):4553-63. (co-correspondence)
3. Koh EH, Park JY, Park HS, Jeon MJ, Ryu JW, Kim M, Kim SY, Kim MS, Kim SW, Park IS, Youn JH, Lee KU: Essential role of mitochondrial function in adiponectin synthesis in adipocytes. *Diabetes* 2007 56:2973-81, 2007
4. Park KG, Min AK, Koh EH, Kim HS, Kim MO, Park HS, Kim YD, Yoon TS, Jang BK, Hwang JS, Kim JB, Choi HS, Park JY, Lee IK, Lee KU: Alpha-lipoic acid decreases hepatic lipogenesis through AMPK-dependent and -independent pathways. *Hepatology* 2008 48(5):1477-86.
5. Won JC, Park JY, Kim YM, Koh EH, Seol S, Jeon BH, Han J, Kim JR, Park TS, Choi CS, Lee WJ, Kim MS, Lee IK, Youn JH, Lee KU. Peroxisome proliferator-activated receptor-gamma coactivator 1-alpha overexpression prevents endothelial apoptosis by increasing ATP/ADP translocase activity. *Arterioscler Thromb Vasc Biol.* 2010; 30:290-297.
6. Koh EH, Kim M, K C R, Kim H, Park HS, Oh KS, Park IS, Lee WJ, Kim MS, Park JY, Youn JH, Lee KU. eNOS plays a major role in adiponectin synthesis in adipocytes. *Am J Physiol Endocrinol Metab.* 2010; 30, E846-853.
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| S14-1 |

Myriocin prevents non-alcoholic steatohepatitis in mice fed methionine-choline-deficient diet

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Methionine and choline-deficient diet (MCD)-induced fatty liver is one of the best studied animal models of non-alcoholic fatty liver disease (NAFLD). In particular, this model is important for understanding the mechanism of NAFLD progression, since long-term administration of MCD has been shown to cause NASH, liver cirrhosis and hepatocellular carcinoma. We recently found that sterol regulatory element binding protein-1c-induced lipogenesis is important in the early stages, while increased fatty acid uptake and decreased fatty acid oxidation become more important in the later stages of NAFLD in mice fed MCD. Oversupply of fatty acid, when not coupled with mitochondrial oxidation, can lead to increased biosynthesis of sphingolipids, including ceramide, and diacylglycerol.

ATP synthesized in the mitochondria is exchanged for cytosolic ADP by adenine nucleotide translocator (ANT) to provide a continuous supply of ADP to mitochondria. We

previously reported that PGC-1 α reduces cell apoptosis and ROS generation in endothelial cells treated with excessive fatty acid by increasing ATP/ADP translocase activity of ANT and ANT1 expression (ATVB 30:290, 2010). In this study, we found that myriocin, an inhibitor of ceramide synthesis, significantly reduced fatty acid-induced decreases in ATP/ADP translocase activity. Based on these findings, we examined possible preventive effect of myriocin on MCD-induced NAFLD. As we expected, myriocin prevented steatosis and steatohepatitis in mice fed MCD for 6 weeks. MCD significantly increased ANT1 expression but decreased ATP/ADP translocase activity. Conversely, myriocin treatment significantly increased ATP/ADP translocase activity. In order to demonstrate that ANT activity is important for prevention of NAFLD and maintenance of mitochondrial function in hepatocytes, we are doing experiments using ANT1 over-expressing transgenic mice.



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• Education and Appointments

1992-1988	Faculty of Medicine, Kanazawa University
1988-1992	Kanazawa University Graduate School of Medical Science Awarded the degree of PhD in Internal Medicine
1993-1997	Department of Biochemistry, Tohoku University (Prof. Hiroshi Okamoto)
1994-1997	Special Researcher, Japan Society for the Promotion of Science
1997-2000	Medical staff, the First Department of Internal Medicine, Kanazawa University Hospital
2000-2001	Assistant Professor, Department of Endocrinology and Metabolism, Kanazawa University Hospital
2001-	Associate Professor, Department of Disease Control and Homeostasis, Kanazawa University Graduate School of Medical Science

• Research Interests

Type 2 diabetes, insulin resistance, obesity, fatty liver disease

• Brief List of Publications

1. Misu H, Takamura T, et al.: A liver-derived secretory protein, selenoprotein p, causes insulin resistance. *Cell Metab* 12:483-495, 2010
2. Hamaguchi E, Takamura T, et al.: Histological course of nonalcoholic fatty liver disease in Japanese patients: tight glycemic control, rather than weight reduction, ameliorates liver fibrosis. *Diabetes Care* 33:284-286, 2010
3. Ootsuji H, Honda M, Kaneko S, Usui S, Okajima M, Okada H, Sakai Y, Takamura T, et al.: Altered hepatic gene expression profiles associated with myocardial ischemia. *Circ Cardiovasc Genet* 3:68-77, 2010
4. Komura T, Sakai Y, Honda M, Takamura T, Matsushima K, Kaneko S: CD14+ monocytes are vulnerable and functionally impaired under endoplasmic reticulum stress in patients with type 2 diabetes. *Diabetes* 59:634-643, 2010
5. Sakurai M, Takamura T, et al.: Abnormal liver function tests and metabolic syndrome--is fatty liver related to risks for atherosclerosis beyond obesity? *Intern Med* 48:1573-1574, 2009
6. Sakurai M, Takamura T, et al.: Middle-aged Japanese women are resistant to obesity-related metabolic abnormalities. *Metabolism* 58:456-459, 2009
7. Sakurai M, Miura K, Takamura T, et al.: J-shaped relationship between waist circumference and subsequent risk for Type 2 diabetes: an 8-year follow-up of relatively lean Japanese individuals. *Diabet Med* 26:753-759, 2009
8. Nakamura S, Takamura T, et al.: Palmitate induces insulin resistance in H4IIEC3 hepatocytes through reactive oxygen species produced by mitochondria. *J Biol Chem* 284:14809-14818, 2009
9. Ando H, Takamura T, et al.: The hepatic circadian clock is preserved in a lipid-induced mouse model of non-alcoholic steatohepatitis. *Biochem Biophys Res Commun* 380:684-688, 2009
10. Ando H, Takamura T, et al.: Clock gene expression in peripheral leucocytes of patients with type 2 diabetes. *Diabetologia* 52:329-335, 2009

| S14-2 |

Selenoprotein P as a hepatokine that causes insulin resistance

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The liver plays a central role in energy metabolism and is the major site for the production of various secretory proteins. We have identified selenoprotein P (SeP) as a novel liver-derived hormone involved in the development of insulin resistance. SeP functions as a selenium supply protein produced by the liver; however, the role of SeP in glucose metabolism has not yet been established.

Results: 1) Comprehensive gene expression analyses revealed that hepatic expression of *SeP* correlated with insulin resistance in humans. 2) Serum levels of SeP were significantly elevated in people with type 2 diabetes compared with normal subjects. 3) Administration of purified SeP protein impaired insulin-induced Akt phosphorylation in both H4IIEC hepatocytes and C2C12 myocytes. 4) Hyperinsulinemic-euglycemic clamp studies showed that injection with purified SeP protein increased endogenous glucose production and decreased peripheral glucose disposal in mice. 5) Treatment with SeP reduced phosphor-

ylation of AMPK α and ACC in both H4IIEC hepatocytes and mouse liver. 6) Treatment with SeP suppressed fatty acid beta oxidation and its related gene expression without affecting AMP/ATP concentration. 7) When constitutively active-AMPK was over-expressed, SeP was unable to impair insulin stimulated Akt phosphorylation in H4IIEC hepatocytes. 8) Treatment with SeP increased the levels of protein phosphatase 2C (PP2C), a negative regulator of AMPK phosphorylation, in H4IIEC hepatocytes. 9) Both genetic deletion and RNA interference-mediated knockdown of SeP improved systemic insulin sensitivity and glucose tolerance in mice.

Conclusion: The liver-derived hormone SeP contributes to insulin resistance and hyperglycemia in type 2 diabetes. AMPK has been shown to mediate metabolic actions of hormones secreted by adipose tissue such as adiponectin and leptin. Also, SeP impairs insulin signaling in hepatocytes, at least partly, by inactivating AMPK.



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• Education and Appointments

2005-present	Department of Clinical Pharmacology, Faculty of Pharmaceutical Science, University of Toyama	Assistant Professor
2001-2005	First Department of Internal Medicine, Toyama Medical & Pharmaceutical University	Clinical and Research Fellow
2001	Toyama Medical & Pharmaceutical University of Medical Science	Ph.D.
1995	Toyama Medical & Pharmaceutical University of Medical Science	M.D.

• Research Interests

Insulin resistance, Obesity, Hepatic steatosis, Energy homeostasis

• Brief List of Publications

1. Wada T, Hoshino M, Kimura Y, Ojima M, Nakano T, Koya D, Tsuneki H, Sasaoka T, Both type I and II IFN induces insulin resistance by inducing different isoform of SOCS expression in 3T3-L1 adipocytes. *Am J Physiol Endocrinol Metab.* 300: E1112-E1123, 2011
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3. Wada T, Hori S, Sugiyama M, Fujisawa E, Nakano T, Tsuneki H, Nagira K, Saito S, Sasaoka T. Progesterone inhibits glucose uptake by affecting diverse steps of insulin signaling in 3T3-L1 adipocytes. *Am J Physiol Endocrinol Metab.* 298:E881-E888, 2010.
4. Soeda Y, Tsuneki H, Muranaka H, Mori N, Hosoh S, Ichihara Y, Kagawa S, Wang X, Toyooka N, Takamura Y, Uwano T, Nishijo H, Wada T, Sasaoka T, The inositol phosphatase SHIP2 negatively regulates insulin/IGF-I actions implicated in neuroprotection and memory function in mouse brain. *Mol Endocrinol.* 24:1965-1977, 2010.
5. Tsuneki H, Wada T, Sasaoka T. Role of orexin in the regulation of glucose homeostasis. *Acta Physiol.* 198:335-348, 2010.
6. Wada T, Ohshima S, Fujisawa E, Koya D, Tsuneki H, Sasaoka T. Aldosterone inhibits insulin-induced glucose uptake by degradation of IRS1 and IRS2 via an ROS-mediated pathway in 3T3-L1 adipocytes. *Endocrinology.* 150:1662-1669, 2009.
7. Ikubo M, Wada T, Fukui K, Ishiki M, Ishihara H, Asano T, Tsuneki H, Sasaoka T. Impact of lipid phosphatases SHIP2 and PTEN on the time- and Akt-isoform-specific amelioration of TNF α -induced insulin resistance in 3T3-L1 adipocytes. *Am J Physiol Endocrinol Metab.* 296:E157-E164, 2009.
8. Wada T, Azegami M, Sugiyama M, Tsuneki T, Sasaoka T. Characteristics of signalling properties mediated by long-acting insulin analogue glargine and detemir in target cells of insulin. *Diabetes Res Clin Pract.* 81:269-277, 2008.
9. Kagawa S, Soeda Y, Ishihara H, Oya T, Sasahara M, Yaguchi S, Oshita R, Wada T, Tsuneki H, Sasaoka T. Impact of transgenic overexpression of SH2-containing inositol 5'-phosphatase 2 on glucose metabolism and insulin signaling in mice. *Endocrinology.* 149:642-650, 2008.
10. Tsuneki H, Murata S, Anzawa Y, Soeda Y, Tokai E, Wada T, Kimura I, Yanagisawa M, Sakurai T, Sasaoka T. Age-related insulin resistance in hypothalamus and peripheral tissues of orexin knockout mice. *Diabetologia.* 51:657-667, 2008.

| S14-3 |

Blockade of mineralocorticoid receptor ameliorates glucose metabolism and steatohepatitis in a novel mice model of non-alcoholic steatohepatitis

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Aim: Since the appropriate mice model reflecting human non-alcoholic steatohepatitis (NASH) with the phenotypes of metabolic syndrome is not generally available, we established a novel mice model of NASH by utilizing liver-specific transgenic mice expressing sterol response element binding protein 1c (SREBP1c) fed high-fat and fructose diet (HFFD). We examined the impact of eplerenone, a selective mineralocorticoid receptor (MR) antagonist, administration on the metabolisms and hepatic fibrosis in the mice.

Methods: Four groups of mice were prepared; C57Bl/6j fed regular diet (WTRD); Liver specific SREBP1c Tg mice fed regular diet (TgRD), Tg mice fed HFFD (Tg^{HFFD}); and Tg mice fed HFFD with eplerenone (Tg^{HFFD+Ep}). After 12 weeks of feeding, mice phenotypes were analyzed.

Results: Tg^{HFFD} showed increased body weight and epididymal fat weight with elevation of blood pressure and dyslipidemia, which was significantly ameliorated by

eplerenone. The treatment significantly improved insulin resistance and hepatic gluconeogenesis after pyruvate loading in Tg^{HFFD}. Tg^{HFFD} mice showed enlarged adipocyte size and apparent macrophage infiltration with crown like structure formation in the epididymal fat tissue. Importantly, Tg^{HFFD} mice demonstrated distinctive histological feature of NASH in the liver including macrovesicular steatosis with lobular inflammation and hepatic fibrosis. Eplerenone effectively ameliorated these histological changes and suppressed inflammation in both liver and adipose tissue. In rat primary kupffer cells, aldosterone augmented lipopolysaccharide-induced TNF α production, and it was suppressed by pretreatment with eplerenone.

Conclusion: We established a novel mice model of NASH with phenotypes of metabolic syndrome. Eplerenone effectively ameliorated metabolic abnormalities, steatohepatitis, and hepatic fibrosis in the mice.



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• Education and Appointments

1987-1991	Seoul National University, College of Pharmacy	Bachelor
1991-1993	Seoul National University, College of Pharmacy	Master
2002-2007	Seoul National University, College of Pharmacy	PhD
1993-2002	Dong-A Pharmaceutical Company	Senior Researcher
2005-2007	Research Institute of Pharmaceutical Sciences, SNU	Researcher
2007-2008	Seoul National University, College of Pharmacy	Postdoc
2007-2008	DukSung Women's University	Instructor
2008-2011	University of California, San Diego	Postdoc
2011-present	WooSuk University	Assistant Professor

• Research Interests

Major: insulin resistance, insulin signaling, hepatic steatosis, inflammation

• Brief List of Publications

1. Bae EJ, Xu J, Oh DY, Bandyopadhyay G, Lagakos W, Olefsky JM (2011) Liver specific p70 S6 kinase depletion protects against hepatic steatosis and systemic insulin resistance. (submitted)
2. Oh DY, Morinaga H, Bae EJ, Talukdar S, Olefsky JM (2011) Increased in vivo macrophage tracking in obese mice. (under revision)
3. Fan W, Morinaga H, Kim JJ, Bae EJ, Spann NJ, Heinz S, Glass CK, Olefsky JM (2010) FoxO1 regulates Tlr4 inflammatory pathway signalling in macrophages. *EMBO Journal* 29(24):4223-36
4. Oh DY, Talukdar S, Bae EJ, Imamura T, Morinaga H, Fan W, Li P, Lu WJ, Watkins SM, Olefsky JM. (2010) GPR120 is an Omega-3 polyunsaturated fatty acid receptor and mediates potent anti-inflammatory and insulin sensitizing effects. *Cell* 142(5):687-98
5. Li P, Lu M, Nguyen MT, Bae EJ, Chapman J, Feng D, Hawkins M, Pessin JE, Sears DD, Nguyen AK, Amidi A, Watkins SM, Nguyen U, Olefsky JM. (2010) Functional heterogeneity of CD11c-positive adipose tissue macrophages in diet-induced obese mice. *J Biol Chem*. 285(20):15333-45.
6. Yoshizaki T, Schenk S, Imamura T, Babendure JL, Sonoda N, Bae EJ, Oh D, Lu M, Milne JC, Westphal C, Bandyopadhyay G, Olefsky JM. (2009) SIRT1 inhibits inflammatory pathways in macrophages and modulates insulin sensitivity. *Am J Physiol Endocrinol Metab*. 298(3):E419-28.
7. Hwang SH, Ki SH, Bae EJ, Kim HE, Kim SG. (2009) Role of adenosine monophosphate-activated protein kinase-p70 ribosomal S6 kinase-1 pathway in repression of liver X receptor-alpha-dependent lipogenic gene induction and hepatic steatosis by a novel class of dithiolethiones. *Hepatology*. 49(6):1913-1925.
8. Nam M, Lee WH, Bae EJ, Kim SG. (2008) Compound C inhibits clonal expansion of preadipocytes by increasing p21 level irrespectively of AMPK inhibition. *Arch Biochem Biophys*. 479(1):74-81.
9. Chung HJ, Kang HE, Bae EJ, Lee I, Kim SG, Lee MG. (2008) Effects of E. Coli lipopolysaccharide on the pharmacokinetics of ipriflavone and its metabolites, M1 and M5, after intravenous and oral administration of ipriflavone to rats: decreased metabolism of ipriflavone due to decreased expression of hepatic CYP1A2 and 2C11. *J Pharm Sci*. 97(11):5024-5036.
10. Bae EJ, Yang YM, Kim SG. (2008) Abrogation of hyperosmotic impairment of insulin signaling by a novel class of 1,2-dithiole-3-thiones through the inhibition of S6K1 activation. *Mol Pharmacol*. 73(5):1502-1512.

| S14-4 |

Protection against hepatic steatosis and systemic insulin resistance by conditional knockdown of p70 S6 kinase in liver

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Obesity associated hepatic steatosis is manifested by selective insulin resistance where lipogenesis remains sensitive to insulin, whereas, the ability of insulin to suppress glucose production is impaired. P70 S6 kinase (S6K), the downstream substrate of mammalian target of rapamycin, has been highlighted as a molecular link between obesity and insulin resistance. To elucidate the physiological role of S6K in selective insulin resistance, we have created a mice model of liver specific knockdown of S6K by systemic delivery of adeno-associated virus carrying short hairpin small interference RNA for S6K and examined the effects of S6K deficiency on hepatic steatosis and systemic insulin resistance in C57BL/6 mice. S6K knockdown in liver (L-S6K-KD) resulted in rapid lowering of blood glucose and fasting plasma insulin concentrations, without changes in food intake or body weight. This improvement was accom-

panied by enhanced glycogen content in liver. L-S6K-KD mice fed high fat diet showed improved glucose tolerance and insulin sensitivity compared to control. This insulin sensitization took place in liver, skeletal muscle, and adipose tissue as assessed by the hyperinsulinemic-euglycemic clamp technique. Additionally, L-S6K-KD mice showed amelioration of steatosis as demonstrated by triglyceride measurements and Oil Red O staining. This was associated with down-regulation of key lipogenic genes upon refeeding after a 21 hr fasting with a robust increase in insulin signal transduction in liver. Importantly, S6K deficiency mediated a significant increase in epididymal fat mass, under refeeding conditions, which is the opposite to the decrease in liver weight. In conclusion, our results demonstrate the importance of S6K for the development of hepatic steatosis and systemic insulin resistance in obese mice.



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• Education and Appointments

1984	Seoul National University	BS
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1993	University of Virginia, USA	PhD
1996	Johns Hopkins University	Postdoc
1996-1999	Gwangju Institute of Science and Technology	Assistant Professor
1999-2006	Gwangju Institute of Science and Technology	Associate Professor
2006-present	Gwangju Institute of Science and Technology	Professor
2009-2001	Gwangju Institute of Science and Technology	Dean

• Research Interests

Major: Molecular Biology
Gene therapy for heart failure and neuronal degenerative diseases

• Brief List of Publications

1. Hyeeseon Cha, Ji Myoung Kim, Jae Gyun Oh, Moon Hee Jeong, Chang Sik Park, Hyeon Joo Jeong, Byung Keon Park, Young-Hoon Lee, Dongtak Jeong, Dong Kwon Yang, Oliver Y. Bernecker, Do Han Kim, Roger J. Hajjar, and Woo Jin Park (2008) PICOT is a critical regulator of cardiac hypertrophy and cardiomyocyte contractility. *Journal of Molecular and Cellular Cardiology*. 45(6):796-803
2. Seung Hee Lee, Dong Kwon Yang, Bo Youn Choi, Young-Hoon Lee, Seon-Young Kim, Dongtak Jeong, Roger J. Hajjar, and Woo Jin Park (2009) The transcription factor Eya2 prevents pressure overload-induced adverse cardiac remodeling. *Journal of Molecular and Cellular Cardiology*. 46(6):596-605
3. Hyeeseon Cha, Hyeon Joo Jeong, Seung Pil Jang, Joo Yeon Kim, Dong Kwon Yang, Jae Gyun Oh, and Woo Jin Park (2010) Parathyroid hormone accelerates decompensation following left ventricular hypertrophy. *Experimental and Molecular Medicine*. 42(1): 61-68
4. Pyoung Oh Yoon, Min-Ah Lee, Hyeeseon Cha, Moon Hee Jeong, Jooyeon Kim, Seung Pil Jang, Bo Youn Choi, Dongtak Jeong, Dong Kwon Yang, Roger J. Hajjar, and Woo Jin Park (2010) The opposing effects of CCN2 and CCN5 on the development of cardiac hypertrophy and fibrosis. *Journal of Molecular and Cellular Cardiology*. 49(2):294-303
5. Hye-Eun Han, Saravanan Sellamuthu, Bae Hyun Shin, Yong Jae Lee, Sungmin Song, Ji-Seon Seo, In-Sun Baek, Jeomil Bae, Hannah Kim, Yung Joon Yoo, Yong-Keun Jung, Woo Keun Song, Pyung-Lim Han, and Woo Jin Park (2010) The Nuclear Inclusion a (NIa) Protease of Turnip Mosaic Virus (TuMV) Cleaves Amyloid- β . *PloS One*. 5(12):e15645.
6. Inju Park, Cecil Han, Sora Jin, Boyeon Lee, Heejin Choi, Jun Tae Kwon, Dongwook Kim, Jihye Kim, Ekaterina Lifirsu, Woo Jin Park, Zee Yong Park, Do Han Kim and Chunghee Cho (2011) Myosin regulatory light chains are required to maintain the stability of myosin II and cellular integrity. *Biochemical Journal*. 434(1):171-80.
7. Sumita Mishra, Vivek Chander, Priyam Banerjee, Jae G Oh, Ekaterina Lifirsu, Woo Jin Park, Do Han Kim, and Arun Bandyopadhyay (2011) Interaction of annexin A6 with alpha actinin in cardiomyocytes. *BMC Cell Biology*. 12:7.
8. Saravanan Sellamuthu, Bae Hyun Shin, Hye-Eun Han, Sang Min Park, Hye Jin Oh, Seong-Hwan Rho, Yong Jae Lee, and Woo Jin Park (2011) An Engineered Viral Protease Exhibiting Substrate Specificity for a Polyglutamine Stretch Prevents Polyglutamine-Induced Neuronal Cell Death. *PloS One*. 6(7):e22554.
9. Changwon Kho, Ahyoung Lee, Dongtak Jeong, Jae Gyun Oh, Antoine H. Chaanine, Eddy Kizana, Woo Jin Park, and Roger J. Hajjar (2011) SUMO1-dependent modulation of SERCA2a in heart failure. *Nature*

| S15-1 |

Pharmaceutical elevation of NAD⁺ level and metabolic diseases

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Numerous previous studies showing that Sirt1, an NAD⁺-dependent class III histone deacetylase, exerts a wide spectrum of beneficial effects in a variety of cellular processes have prompted intensive efforts to develop efficient modalities for the activation of Sirt1. In the present study, we found that oral administration of an anticancer drug to mice elevated the cellular NAD⁺ level in the hearts. This change was accompanied by enhanced Sirt1 activity, as determined by increased deacetylation of known Sirt1 substrates. Pressure overload-induced cardiac hypertrophy was significantly inhibited by the treatment of the drug. Under the sustained pressure overload, this drug prevented

deterioration of mitochondrial integrity and function, concomitant with elevated expression of genes associated with mitochondrial biogenesis and fatty acid metabolism, further supporting the involvement of Sirt1. Adverse cardiac remodeling resulting from pressure overload, myocardial infarction, and ischemia-reperfusion was also significantly ameliorated. The elevated glucose level in db/db mice was completely normalized by this drug. Notably this drug did not increase the body weight. We suggest that this drug is an efficient modulator of Sirt1 activity and that it may be effective in the treatment of metabolic diseases including heart failure and diabetes.



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• Education and Appointments

1978-1984	Shinsyu University School of Medicine (M.D., 1984)	
1987-1992	Kyoto University Graduate School of Medicine (Ph.D., 1992)	
1997-2003	WHO-collaborative Centre for Diabetes, Kyoto National Hospital	Medical Staff
2007-Present	Kyoto University Graduate School of Medicine	Clinical Professor of Medicine
	WHO- collaborative Centre for Diabetes, National Hospital Organization, Kyoto Medical Center	Director

• Research Interests

Major: Diabetic Foot

• Brief List of Publications

1. Characteristics of Diabetic Foot in the Western Pacific Region - ASIPAC foot study - *Diabetologia* 53(suppl),1: S457-S458, 2010 S.Kono et al.
2. Urinary cystatin C as a potential risk marker for cardiovascular disease and chronic kidney disease in patients with obesity and metabolic syndrome. *Clin J Am Soc Nephrol*, 6(2):265-73, 2010 S.Kono et al.
3. Salivary cortisol levels are associated with outcomes of weight reduction therapy in obese Japanese patients *Metabolism* (in press) S.Kono et al.
4. Diabetic foot (Clinical guidelines) Japan Diabetes Society (Nankodo) 2010; 115-125,2010 Kono S
5. The management of diabetic foot in Japan The Japan Society of Diabetic Complications 24(2)187-190, 2010 Kono S
6. Diabetic foot- conservative treatment- *The kidney* 32(1)20-25,2009 Kono S
7. The progress in diabetes mellitus- diabetic foot problems *The Journal of the Japanese Society of Internal Medicine* 98(4)75-81, 2009 Kono S
8. Neuro-musclar disease and diabetes *Journal of Japan Diabetes Society* 51(3)207-209, 2008 Kono S
9. Patient-oriented approach of diabetic froot problems *The Japanese Journal of Dermatology* 116(13)2191-2194,2006 Kono S
10. Diabetic Foot-diagnosis and treatment *Clinical Endocrinology* 53(12)152-156, 2005 Kono S

| S15-2 |

Management of diabetic foot problems in the Western Pacific region

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Aims: The number of diabetic foot lesions and consequently amputations is increasing in the world. More than 1.3 million people with diabetes are amputated because of diabetic foot problems every year. This means that every 20 seconds a lower limb is lost somewhere in the world. Much progress has been made in the last 20 years in our understanding of the pathogenesis and management of diabetic foot problems. Multidisciplinary treatment has succeeded to reduce amputation rate in tertiary foot centers. However, in the Western Pacific Region (WPR) there are no foot care specialists such as podiatrists and there is much ignorance amongst medical staff as to how to identify and educate those at risk and treat those who develop problems.

Methods: In order to increase awareness and reduce amputations, we have launched the study (ASIPAC FOOT

STUDY) to investigate the characteristics of diabetic patients with foot ulcers and their lifestyles in WPR.

Results & Conclusion: The characteristics of diabetic foot patients and their lifestyles in WPR were much different in some points from those in other regions. Diabetic foot patients with PAD seem to be increasing in this region, while smoking rates are high and revascularization is seldom applied. In order to reduce amputations, it is essential to increase awareness of diabetic foot and tobacco problems, and improve the skills of screening and education of high risk patients and management of foot ulcer through regional practical guideline and professional training program. For this purpose, IDF-WPR has promoted new diabetic foot care project by organizing IDF-WPR recognized diabetic foot clinics and centers in member countries, closely collaborating with WHO.



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• Education and Appointments

MBChB	University of Otago, NZ
PhD	University of Melbourne, Australia
FRACP	Royal Australian College of Physicians
Adjunct Professor	Dept of Epidemiology and Preventive Medicine, Monash University, Australia

• Research Interests

Diabetic Complications, Chronic kidney disease, Diabetes-associated atherosclerosis
Advanced glycation end products (AGEs), Renin angiotensin system (RAS)

• Brief List of Publications

1. Groop PH, Thomas MC, Moran JL, Wadèn J, Thorn LM, Mäkinen VP, Rosengård-Bärlund M, Saraheimo M, Hietala K, Heikkilä O, Forsblom C; FinnDiane Study Group. The presence and severity of chronic kidney disease predicts all-cause mortality in type 1 diabetes. *Diabetes*. 2009 Jul;58(7):1651-8.
2. Thomas MC, Macisaac RJ, Jerums G, Weekes A, Moran J, Shaw JE, Atkins RC. Nonalbuminuric renal impairment in type 2 diabetic patients and in the general population (national evaluation of the frequency of renal impairment co-existing with NIDDM [NEFRON] 11). *Diabetes Care*. 2009 Aug;32(8):1497-502.
3. Thomas MC, Cooper ME. Into the light? Diabetic nephropathy and vitamin D. *Lancet*. 2010 Nov 6;376(9752):1521-2.
4. Thomas MC, Pickering RJ, Tsorotes D, Koitka A, Sheehy K, Bernardi S, Toffoli B, Nguyen-Huu TP, Head GA, Fu Y, Chin-Dusting J, Cooper ME, Tikellis C. Genetic Ace2 deficiency accentuates vascular inflammation and atherosclerosis in the ApoE knockout mouse. *Circ Res*. 2010 Oct 1;107(7):888-97.
5. Thomas MC, Moran J, Forsblom C, Harjutsalo V, Thorn L, Ahola A, Wadèn J, Tolonen N, Saraheimo M, Gordin D, Groop PH; for the FinnDiane Study Group. The Association Between Dietary Sodium Intake, ESRD, and All-Cause Mortality In Patients With Type 1 Diabetes. *Diabetes Care*. 2011 Apr;34(4):861-6.
6. Ekinci EI, Clarke S, Thomas MC, Moran JL, Cheong K, Macisaac RJ, Jerums G. Dietary Salt Intake and Mortality in Patients With Type 2 Diabetes. 2011 Mar;34(3):703-9.
7. Herman-Edelstein M, Thomas MC, Thallas-Bonke V, Saleem M, Cooper ME, Kantharidis P. Dedifferentiation of immortalized human podocytes in response to transforming growth factor- β : a model for diabetic podocytopathy. *Diabetes*. 2011 Jun;60(6):1779-88.
8. Thomas MC, Söderlund J, Lehto M, Mäkinen VP, Moran JL, Cooper ME, Forsblom C, Groop PH; on behalf of the FinnDiane Study Group. Soluble receptor for AGE (RAGE) is a novel independent predictor of all-cause and cardiovascular mortality in type 1 diabetes. *Diabetologia*. 2011 May 24
9. Toffoli B, Pickering RJ, Tsorotes D, Wang B, Bernardi S, Kantharidis P, Fabris B, Zauli G, Secchiero P, Thomas MC. Osteoprotegerin promotes vascular fibrosis via a TGF- β 1 autocrine loop. *Atherosclerosis*. 2011 May 27
10. Forsblom C, Thomas MC, Moran J, Saraheimo M, Thorn L, Wadèn J, Gordin D, Frystyk J, Flyvbjerg A, Groop PH; on behalf of the FinnDiane Study Group. Serum adiponectin concentration is a positive predictor of all-cause and cardiovascular mortality in type 1 diabetes. *J Intern Med*. 2011 May 26.

| S15-3 |

Diabetic nephropathy; new opportunities and new therapeutics

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In individuals with diabetes, the presence and severity of kidney disease adversely affects their well-being, significantly contributes to burden of morbidity and increases their risk of a premature death. Indeed, excess mortality associated with diabetes is almost entirely confined to those with chronic kidney disease. Similarly, myocardial infarction and stroke are over 2-10 times more common in diabetic patients with kidney disease than in those without normal renal function. The efficiency of current management strategies for the treatment of diabetic nephropathy, even in optimal combination, is partial, at best. Although substantial progress has been made towards understanding the pathogenesis of diabetic nephropathy, at present there are no new drugs that provide the solutions we want for

our patients. Even when used in combination with standard medical care, current data indicate that renal complications are at best only modestly reduced, at the expense of additional pill burden and exposure to off-target effects. Given the ever-growing burden of diabetic kidney disease, there is a substantial opportunity for better and more targeted (smarter) therapeutic interventions against oxidative stress, inflammation, endothelial dysfunction, AGE accumulation, activation of PKC, the renin angiotensin system, and other key pathogenic pathways. Moreover, shifting the focus to the primary prevention of kidney disease in diabetes, rather than simply its treatment is vital for the ongoing health of the 300 million patients with diabetes worldwide.



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• Education and Appointments

1990-	University of Tsukuba Hospital	Resident
1997-	University of Michigan Medical Center	Research Fellow
1999-	University of Tsukuba Institute of Clinical Medicine	Assistant Professor
2006-	Ochanomizu University	Associate Professor
2009-	Current position	

• Research Interests

Clinical epidemiology of diabetes and other metabolic diseases.

• Brief List of Publications

1. Heianza Y, Sone H, et al. HbA1c 5.7-6.4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (TOPICS 3): a longitudinal cohort study. *Lancet* (in press)
2. Kawasaki R, Sone H, et al. Incidence and progression of diabetic retinopathy in Japanese adults with type 2 diabetes: 8 year follow-up study of the Japan Diabetes Complications Study (JDACS). *Diabetologia* (in press)
3. Katayama S, Sone H, et al. Low Transition Rate from Normo- and Low Microalbuminuria to Proteinuria in Japanese Type 2 Diabetics: the Japan Diabetes Complications Study (JDACS). *Diabetologia* 54:762-766, 2011
4. Heianza Y, Sone H, et al. Low Serum Potassium Levels and Risk of Type 2 Diabetes: Toranomon Hospital Health Management Center Study 1 (TOPICS 1). *Diabetologia* 54:762-766, 2011
5. Kodama S, Sone H, et al. Alcohol Consumption and Risk of Atrial Fibrillation: A Meta-analysis. *J Am Coll Cardiol* 57:427-36, 2011
6. Sone H, et al. Long-term lifestyle intervention lowers incidence of stroke in Japanese patients with type 2 diabetes: a nationwide multicenter randomised controlled trial. (the Japan Diabetes Complications Study). *Diabetologia* 53:419-428, 2010
7. Kodama S, Sone H, et al. The Association between Serum Uric Acid and Development of Type 2 Diabetes Mellitus. A Meta-Analysis. *Diabetes Care* 32:1737-1742, 2009
8. Kodama S, Sone H, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women. *JAMA* 301: 2024-2035, 2009
9. Sone H, et al. Waist circumference as a cardiovascular and metabolic risk in Japanese patients with type 2 diabetes. *Obesity* 17: 585-92, 2009
10. Kodama S, Sone H, et al. Influence of Fat and Carbohydrate Proportions on the Metabolic Profile in Patients with Type 2 Diabetes: A Meta-analysis. *Diabetes Care* 32:959-965, 2009

| S15-4 |

HbA1c variability as a risk of microvascular complication in diabetes

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Backgrounds and Aim: Although glycemic instability has been considered as a potential risk factor for development of microvascular complications in diabetes, clinical evidence has been inconsistent. In addition, although HbA1c variability has been reported to be predictive of microvascular complications in type 1 diabetes, whether it applies to type 2 diabetes is unknown. Therefore, we examine the association between A1C variability and development of microalbuminuria, as defined by an albumin-to-creatinine ratio ≥ 3 mg/g in at least two of three consecutive urine samples, in patients with type 2 diabetes.

Methods: A1C was measured in 669 serially registered normoalbuminuric adults aged 20-79 with type 2 diabetes. The association between A1C variability (intrapersonal SD

of serially collected A1C) with development of microalbuminuria was determined by Cox regression analysis after adjustment for other risk factors for microalbuminuria.

Results: Microalbuminuria occurred in 167 subjects during the 5.6 ± 2.3 -year observation period. Even after adjustment for mean A1C, A1C variability was a significant predictor of microalbuminuria independently of the mean A1C. The effects of these two variables were quite similar (hazard ratio 1.31 for every 1 SD increase [95% CI 1.11-1.54], $p=0.001$, and 1.32 [1.11-1.57], $p=0.001$, respectively).

Conclusion: A1C variability affects the development of nephropathy independently of mean A1C in type 2 diabetes.



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• Education and Appointments

1992-1996	Bachelor's degree, Chung-Ang University	
1996-1999	Children's ward, Samsung Medical Center	Nurse
2003-2007	Mastercourse, Nursing, Chung-Ang University	
2003	Obtained a certification as a Diabetes Educator	
2009	Obtained a certification as a Child Health Advanced Nurse Practitioner	
1999-present	Department of Pediatrics, Samsung Medical Center	Child Health Advanced Nurse Practitioner

• Research Interests

Major: Children with diabetes

• Brief List of Publications

Parenting Stress and Guilty Feeling for Mothers Having Children with Rare Genetic Metabolic Disease, Journal of Korean Clinical Nursing Research, 2008

| S16-1 |

Essential guidelines for pediatric diabetes education by an experienced educator

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The purpose of pediatric diabetes education is to provide children with type1 diabetes and their family in diabetes self-care and crisis management with appropriate knowledge and skills so that they can improve clinical outcomes and their health status.

In addition to the necessary knowledge and management skills, it is very important for educators to consider psychosocial factors in pediatric diabetes education. Therefore, to promote self-care motivation, flexible self-management skills and active engagement with caregivers in pediatric diabetes patients and their families, I propose 7 key guidelines that educators can incorporate in their pediatric diabetes education programs.

1. You must consider child's growth in education.

Patients and their parents tend to reduce food intake just to keep glucose level low. To prevent growth delay, maintain adequate food intake to meet the total daily calorie requirements even if it leads to higher insulin dosages.

2. Provide good role models or examples to give hope and encourage them.

3. Advise parents not to get angry or sad in front of a child, when they show hyperglycemia. Otherwise, children may hide their glucose score.

4. **Make them understand that facing hyperglycemia with courage is more important than hiding the score.** They should know that the most important thing is to check blood glucose right away and to reduce glucose level with appropriate insulin administrations when hyperglycemia is suspected.

5. Emphasize that people who are prepared can overcome diabetes.

Encourage them to carry 3 items (glucometer, some sugar and ultra short acting insulin) always like friends. They should cope with hypo or hyperglycemia at any time.

6. Emphasize that they can control and battle diabetes.

Some children do not check blood sugar intentionally due to anxiety over hyperglycemia, which will lead to a defeat.

7. Help them not to worry about what others might think of their self-care activities.

If they avoid checking blood sugar or injecting insulin in public places, they would gradually skip these self-care activities. Although it depends on their personality, it is important to keep.



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• Education and Appointments

2006	The Graduate School of Public Health, Yonsei University	Health Promotion & Education
2004-	Gangnam Severance Hospital, Yonsei University	Diabetes Nurse Educator
2004	Korean Diabetes Association	Certified Diabetes Educator
2008-2009	Korean Diabetes Association	Committee Member, Committee of Education
2008	Korean Nurses Association	Geriatric Nurse Practitioner
2010-	Korean Association of Diabetes Nurse Educators	Information Director

• Research Interests

Major: Diabetes Education

| S16-2 |

Diabetes self-management education for older adults: general principles and practical application

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Diabetes is an important health condition for the aging population; at least 20% of patients over the age of 65 years have diabetes, and this number can be expected to grow rapidly in the coming decades. As the number of elderly people is increasing in Korea, the prevalence of diabetes is also increasing.

Diabetes Self-Management education (DSME) is another important element of care for older adults with Diabetes and family members and their caregivers. In chronic illnesses such as diabetes, day-to-day care responsibilities fall mostly on patients. However, when patients are unable to assume full responsibility for their self-care, family members, friends, or other caregivers may need to be involved.

As educators, it is important to be aware of current Diabetes Self-Management education(DSME) guidelines for older adults and how these guidelines can be incorporated in a clinical setting. Older individuals with diabetes have higher rates of premature death, functional disability, and coexisting illnesses such as hypertension, CHD, and stroke than those without diabetes. Older adults with diabetes are also at greater risk than other older adults for several common geriatric syndromes, such as polypharmacy, depres-

sion, cognitive impairment, urinary incontinence, injurious falls, and persistent pain. Optimal care for older adults includes individualized DSME that accommodates the clinical and functional variables found within this population. It is important when prioritizing treatment goals to take patients' quality of life into consideration.

AADE was recommended as follows. The full spectrum of treatment strategies should be used with older persons just as they are for younger persons while considering the person's preferences and quality-of-life issues. Adequate time for education, considering the unique needs of the older person with diabetes, should be made available and reimbursed by third-party payers. Long-term care facilities with a more home-like environment are desirable, allowing flexibility with mealtimes, liberalized diets, and improved quality of life. Education for the resident, staff, and family members is needed as more facilities move toward this type of setting. Screening for common geriatric conditions that have a significant impact on health status of older adults with diabetes should be conducted regularly by the health care provider and diabetes educator.



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• Education and Appointments

2001-Present	Asan Medical Center	Diabetes Clinical Nurse Specialist
2000-Present	Korea Association of Diabetes Nurse Educators	Board of Directors
2007-Present	Korea Diabetes Association	Member of Publication Committee(sub)
2004-2006	Korea Diabetes Association	Member of Education Committee
2000-2003	Graduate School of Education, Ewha Womans University	MS, Ed.

• Research Interests

Major: Diabetes education

• Brief List of Publications

1. Jeong-Rim, Lee, Soon-Ai, Kim, Joo-Wha, Yoo, Yang-kyo, The Present Status of Diabetes Education and the Role Recognition as a Diabetes Educator of nurses in Korea, Diabetes research and clinical practice, Vol 77(Suppl 1, s199-204), 2008
2. Hong Myeong Hee, Yoo Joo Wha, Kim Soon AI, Lee Jeong Rim, Roh Na Ri, Park Jeong Eun, Gu Mee Ock, A Study of Knowledge and Diffusion of Knowledge for Nursing care of Diabetes mellitus among Clinical Nurses. Journal of Korean Clinical Nursing Research Vol.15 No.3. 61-74, December, 2009

| S16-3 |

The effects of diabetes education which was reinforced on patient lifestyle modification

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Introduction: The ultimate goal of this diabetes education program is to help diabetics change their health related behaviors in addition to learning more about the condition they have. In order to make any significant change in the lives of their patients, diabetes educators need to focus on clear, realistic goals which can be easily attained by patients. In 2010, we performed a survey on patient lifestyle preferences in order to determine which aspects would be most easily modifiable. In this presentation, I will introduce our study outcomes and review the other studies' results which focused on patient lifestyle modification.

The study: Our study aimed to determine which lifestyle preferences patients' would consider to be most modifiable.

Method: From June 7th to July 7th of the year 2010, a 29-item questionnaire was conducted on patients with diabetes who participated in a personalized diabetes education program under the supervision of a tertiary hospital in Seoul, South Korea. The questionnaire included the following four categories: 13 items regarding their eating habits, four items pertaining to their exercise habits, two items regarding taking their medication, and 10 items related to diabetes self-management. The participants were asked to choose which items they would be most willing to change and what would be most easily modifiable.

Results: A total of 201 patients agreed to participate in

this survey. When asked which aspect of their lives would be most easily modifiable, 56% of participants selected eating habits, 22.0% selected diabetes self-management (including self-monitoring of blood glucose(SMBG)), 19.9% selected exercise habits, and 1.2% selected taking their medication more regularly.

The most frequently selected item under the category of eating habits was 'Eating three regular meals rather than eating between meals'(represented by 10.4% of participants). Regarding their exercise habits, 'Doing regular exercise for more than 30 minutes every other day each week' (13.4%) was the most frequently selected item and was the most preferred item.

Conclusion: In this study, more than 50% of the participants' chose eating habits as the behavior that they could most easily change. The most frequently chosen item was 'Doing regular exercise for more than 30 minutes every other day each week'.

Although it is difficult to change one's lifestyle, which includes eating and exercise habits, diabetes educators might find it helpful to focus on the individual patients' preferences in order to successfully accomplish behavior change. In the review of other studies', results which focused on lifestyle modification revealed that diabetes educators need to create their own patient-friendly strategies that patients can successfully and continuously implement into their lifestyle care plan.



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• Education and Appointments

1982-1986

Nursing College, The Catholic University

1996-1998

Postgraduate School of Public Health, The Catholic University

1986-

Seoul St. Mary's Hospital

| S16-4 |

Foot care for diabetics

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The care of health foot has had a influence on the importance of managing diabetes. But if patients don't treat your foot quickly when you have minor injuries of foot. Patients will be face to dangerous situation like leg amputated.

However, patients can be prevented many problems such as foot complication through managing of health foot.

Therefore so Korean Diabetes Association has opened a campaign to help the habits of healthy foot and checked foot problems. The result is that 14% will develop a serious foot problem at one time or another that can threaten their limbs or even their life. In particular, higher incidence in young age groups 20s. They don't wear socks in the usual and appropriate footwear. Diabetic foot affected by poor circulation and neuropathy, and they are susceptible to

infection. To make matters worse, these problems can feed on each other. More than 50,000 people with diabetes lose a limb to diabetes each year in United States. If poor glucose are impaired blood circulation disorders and nerve damage and ulcers will be proceed. Eventually patients become a state of leg amputated. It is not easy for patients to screen diabetic foot, because patients a lot of chance. For example when patients visit to hospital, medical teams are busy so they are not interested in patient problems. By keeping your blood glucose levels under control, taking care of your feet with daily foot inspections, visiting they doctor regularly, wearing properly fitting shoes, being alert to early warning signs of neuropathy or circulation problem, and treating any problem that arise, you can prevent ulcers and infection from occurring.



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• Education and Appointments

1989	Kyung Hee University School of Medicine	M.D.
1999	Kyung Hee University School of Medicine	Ph.D.
2000-2003	Joslin Diabetes Center, Harvard Medical School, Boston, MA	Postdoctoral Fellow
2004-2007	Department of Medicine, Sungkyunkwan University School of Medicine	Associate Professor
2007-2009	Department of Medicine, Kwandong University College of Medicine	Associate Professor
2009-present	Department of Medicine, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine	Professor of Medicine

• Research Interests

Major: Genetics of Diabetes
 Monogenic diabetes, Gestational Diabetes Mellitus, Diabetes in pregnancy

• Brief List of Publications

1. Kim JY, Cheong HS, Park BL, Baik SH, Park S, Lee SW, Kim MH, Chung JH, Choi JS, Kim MY, Yang JH, Cho DH, Shin HD, Kim SH. Melatonin Receptor 1 B Polymorphisms associated with the risk of Gestational Diabetes Mellitus. *BMC Med Genet.* 2011 Jun 10;12(1):82.
2. Kim SH, Kim MY, Yang JH, Park SY, Yim CH, Han KO, Yoon HK, Park S. Nutritional risk factors of early development of postpartum prediabetes and diabetes in women with gestational diabetes mellitus. *Nutrition.* 2011 Jul-Aug;27(7-8):782-8.
3. Park JE, Park S, Daily JW, Kim SH. Low gestational weight gain improves infant and maternal pregnancy outcomes in overweight and obese Korean women with gestational diabetes mellitus. *Gynecol Endocrinol.* 2010 Dec 29. [Epub ahead of print]
4. Rhee SY, Kim JY, Woo JT, Kim YS, Kim SH. Familial Clustering of Type 2 Diabetes in Korean Women with Gestational Diabetes Mellitus. *Korean J Intern Med.* 2010 ;25(3):269-272
5. Shin HD, Park BL, Shin HJ, Kim JY, Park S, Kim B, Kim SH. Association of KCNQ1 Polymorphisms with the Gestational Diabetes Mellitus in Korean Women. *J Clin Endocrinol Metab.* 2010 Jan;95(1):445-9.
6. Borowiec M, Liew CW, Thompson R, Boonyasrisawat W, Hu J, Mlynarski WM, El Khattabi I, Kim SH, Marselli L, Rich SS, Krolewski AS, Bonner-Weir S, Sharma A, Sale M, Mychaleckyj JC, Kulkarni RN, Doria A. Mutations at the BLK locus linked to maturity onset diabetes of the young and β -cell dysfunction. *Proc Natl Acad Sci U S A.* 2009 Aug 25;106(34):14460-5.
7. Yu SH, Park S, Kim HS, Park SY, Yim CH, Han KO, Yoon HK, Jang HC, Chung HY, Kim SH: The prevalence of GAD antibodies in Korean women with gestational diabetes mellitus and their clinical characteristics during and after pregnancy. *Diabetes Metab Res Rev* 2009 May;25(4):329-34
8. Kim HS, Hwang SH, Choi ES, Park SY, Yim CH, Han KO, Yoon HK, Chung HY, Kim KS, Bok J, Lee JY, SH Kim. Mutation screening of HNF1A gene in Korean women with gestational diabetes mellitus. *Korean Diabetes J* 2008;32:38-43.

| S17-1 |

Genetics of gestational diabetes mellitus

Sung-Hoon Kim

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Recent advances in the field of genetics have allowed from the identification of genes for monogenic diabetes to find the contribution of many susceptibility genes on the development of common form of diabetes. Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy, affecting 2-5% of all pregnant women. The prevalence of GDM has been increasing over the last decade. It is manifested when insulin secretion is unable to compensate pregnancy-induced increased insulin resistance, but the pathogenesis of GDM is still not completely understood. We have shown the familial clustering of type 2 diabetes in Korean women with GDM. This suggests that similar genetic factors may play a role in the pathogenesis of these conditions. However, genetic studies on GDM are relatively scarce compared with type 2 diabetes. Our data

support that mutations in MODY3 (HNF1A) gene are often present with GDM. In addition, we reported the association of KCNQ1 gene polymorphisms, which may affect β -cell dysfunction, with GDM. Another gene we studied is MTNR1B, which is known that genetic variations of this gene are associated with type 2 diabetes and fasting glucose levels. We found significant associations between the two genetic variants of MTNR1B and GDM and its related phenotypes. Results of genome-wide association study in GDM will show more about the genes are responsible to the development of GDM. Identification of the genetic etiology underlying GDM may not only lead to better understanding of the mechanisms that contribute the pathophysiology of the disease but also develop personalized treatment and prevent complications for the mother and fetus.



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• Education and Appointments

1996-2002	Seoul National University College of Medicine	MD
2002-2003	Seoul National University Hospital	Medical Internship
2003-2007	Seoul National University Hospital	Internal Medicine Residency
2007-2009	Gyeonggi Provincial Office	Epidemic Intelligence Service Officer
2009-2010	Gyeonggi Provincial Office	Secretary of Public Health Promotion
2010-Present	Seoul National University Hospital	Clinical Fellow

• Research Interests

Major: Gestational diabetes mellitus, Type 2 diabetes mellitus, Genetics, Epidemiology

• Brief List of Publications

1. Moon SS, Lee YS, Kim JG, Kim SW, Jeong JY, Jeon EJ, Seo HA, Park KS, Kwak SH, Lee IK. Relationship of 11 β -hydroxysteroid dehydrogenase type 1 and hexose-6-phosphate dehydrogenase gene polymorphisms with metabolic syndrome and type 2 diabetes. *Endocr J.* 2011 Aug 23. [Epub ahead of print]PubMed [citation] PMID: 21869537
2. Kwak SH, Park BL, Kim H, German MS, Go MJ, Jung HS, Koo BK, Cho YM, Choi SH, Cho YS, Shin HD, Jang HC, Park KS. Association of Variations in TPH1 and HTR2B with Gestational Weight Gain and Measures of Obesity. *Obesity (Silver Spring).* 2011 Aug 11. doi: 10.1038/oby.2011.253. [Epub ahead of print]PubMed [citation] PMID: 21836641
3. Kim HI, Kim JT, Yu SH, Kwak SH, Jang HC, Park KS, Kim SY, Lee HK, Cho YM. Gender differences in diagnostic values of visceral fat area and waist circumference for predicting metabolic syndrome in Koreans. *J Korean Med Sci.* 2011 Jul;26(7):906-13. Epub 2011 Jun 20. PubMed [citation] PMID: 21738344, PMCID: PMC3124721
4. Lim S, Shin H, Song JH, Kwak SH, Kang SM, Won Yoon J, Choi SH, Cho SI, Park KS, Lee HK, Jang HC, Koh KK. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998-2007. *Diabetes Care.* 2011 Jun;34(6):1323-8. Epub 2011 Apr 19. PubMed [citation] PMID: 21505206, PMCID: PMC3114326
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6. Hwang S, Kwak SH, Bhak J, Kang HS, Lee YR, Koo BK, Park KS, Lee HK, Cho YM. Gene expression pattern in trans-mitochondrial cytoplasmic hybrid cells harboring type 2 diabetes-associated mitochondrial DNA haplogroups. *PLoS One.* 2011;6(7):e22116. Epub 2011 Jul 13. PubMed [citation] PMID: 21765942, PMCID: PMC3135611 (Co-first author)
7. Kwak SH, Park KS, Lee KU, Lee HK. Mitochondrial metabolism and diabetes. *Journal of Diabetes Investigation.* 2010;October;1(5):161-169.
8. Lee HK, Cho YM, Kwak SH, Lim S, Park KS, Shim EB. Mitochondrial dysfunction and metabolic syndrome-looking for environmental factors. *Biochim Biophys Acta.* 2010 Mar;1800(3):282-9. Epub 2009 Nov 13. Review. PubMed [citation] PMID: 19914351
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| S17-2 |

T2DM after GDM pregnancy: early vs. late converters

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Nearly half of women with gestational diabetes mellitus (GDM) progress to type 2 diabetes mellitus (T2DM) within 10 years after pregnancy. However, susceptibility to T2DM as well as time to progression after GDM pregnancy varies individually. The clinical and genetic factors determining this variability are not fully understood yet.

We investigated the antepartum clinical, metabolic, and genetic differences among early converters (who were diagnosed as T2DM at postpartum 2 months), late converters (who progressed to T2DM more than 1 year later), and non-converters after GDM pregnancy. The study was a prospective longitudinal cohort study involving 843 Korean women with GDM pregnancy. Oral glucose tolerance test (OGTT) was performed at 2 months postpartum and annually for median of 47 months. Study subjects were genotyped for 21 genetic variants in *PPARG*, *IGF2BP2*, *CDKAL1*, *SLC30A8*, *CDKN2A/2B*, *HHEX*, *TCF7L2*, *KCNQ1*, *KCNJ11*, and *FTO*.

Among the 843 GDM women, 105 (12.5%) progressed to T2DM early postpartum. Among the 418 women who

had follow up visits for more than one year, 116 (27.8%) progressed to diabetes. Increased body mass index, family history of T2DM were significantly associated with risk of T2DM. In a sub-study involving 86 GDM women who undertook abdominal fat CT, increased visceral-to-subcutaneous fat ratio was associated with development of T2DM. Early converters had higher glucose and lower insulin concentration during diagnostic OGTT performed at pregnancy compared to late converters. The early converters had significantly decreased 1-hour insulinogenic index compared to late converters. Genetic variants in *HHEX* were associated with early conversion to diabetes and variants in *CDKAL1* were associated with late conversion to diabetes.

In conclusion, we found that a significant proportion of GDM women progress to T2DM after parturition and women who progress to T2DM early post-partum have decreased insulin secretory capacity compared to late converters. These differences might be explained in part by genetic predisposition.



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• Education and Appointments

1988-1994	Medical Degree, College of Medicine, Korea University, Seoul, Korea
1994-1995	Korea Veterans Hospital, Seoul, Korea, Internship
1995-1999	Department of Obstetrics and Gynecology, Korea University Medical Center, Seoul, Korea, Residency
2001-2003	Department of Obstetrics and Gynecology, Korea University Medical Center, Seoul, Korea, Clinical Fellow
2001-2003	Master's Degree, Graduate School of Korea University College of Medicine, Seoul, Korea Majored in Obstetrics
2003-2004	Department of Obstetrics and Gynecology, Clinical Instructor, CHA General Hospital, Seoul, Korea
2003-2007	Ph. D., Graduate School of Korea University College of Medicine, Seoul, Korea
2004-present	Department of Obstetrics and Gynecology, Pochon CHA University, Assistant Professor, CHA general Hospital, Seoul, Korea
2007-2007	Advanced Healthcare Management Program, Seoul National University Hospital, Seoul, Korea
2008-2009	Section of Cellular and Molecular Physiology, Joslin Diabetes Center, Harvard Medical School, Boston, MA, USA, Research Fellow

• Research Interests

1. Gestational diabetes in pregnancy; relationship maternal obesity and fetal development and growth: Study for Proper diagnostic strategy of gestational diabetes in Korea suggested by International Association of Diabetes and Pregnancy study Group (IADPSG); Multicenter Study
2. Childhood Asthma and Allergic Diseases Cohort Study; Multicenter Study
3. Electrophysiological study for diagnosis and treatment of Uterine Atony in postpartum hemorrhage

• Brief List of Publications

1. Kyung Ju Lee, Mi Kyoung Lee, Seo Young Lee, Woo Sik Lee Yoon Hee Lee. Spontaneous rupture of the membrane in a monochorionic pregnancy resulting in a pseudo-monoamniotic pregnancy with a cord entanglement. *Journal of Obstetrics and Gynecologic Research*, 2011 in press
2. Mi kyung Kim, Junguk Hur, Seo Young Lee, Yoo Lee Kim, Kyung Sun Park, Seok Won Park, Kyung Ju Lee. Maternal obesity and associated risk of adverse pregnancy outcomes in women with hyperglycemia. *Korean Journal of OB and Gyn*, 2011 in press
3. Seo-Young Lee, Junguk Hur, Kyung Ju Lee. Pregnancy outcomes and relationship between maternal weight gain and fetal birth weight in Korean pregnant women at risk for gestational diabetes. *Journal of Women's Medicine(Korean Journal of OB and Gyn)* 2011; 6
4. Seo-Young Lee, Mi-kyoung Kim, Myoung-Joo Kim, Seo-yeon Park, Kyung Ju Lee. A case report of severe pre-eclampsia with HELLP syndrome in preterm pregnancy complicated by acute pulmonary edema, acute renal failure, highly elevated liverenzymes suggesting ischemic hepatitis and coagulopathy. *Korean Society of Maternal Fetal Medicine*. 2011;3
5. Kyung Ju Lee. Tip of differentiation between discordant twin and twin to twin transfusion syndrome. *The Korean Society of Ultrasound in Obstetrics and Gynecology*. 2011;4

| S17-3 |

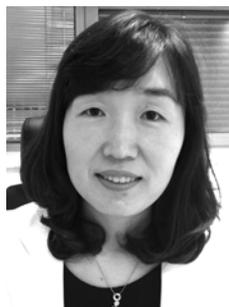
Maternal obesity and fetal macrosomia

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CHA University, Korea

In these days overweight or obesity in women of reproductive age is rapidly increasing worldwide and they are more likely to gain excess weight during pregnancy. Overweight or obesity is considered as a common high-risk obstetric condition along with gestational diabetes, hypertensive disorder during pregnancy, operative delivery and poor fetal outcomes. Especially, obesity can predispose to the development of fetal macrosomia, which may lead to

childhood obesity. Asian women have different characteristics of obesity than western women. This study presents the similarities and differences, between the Korean and Western obese women, in the maternal BMI and pregnancy outcomes including fetal macrosomia related to maternal weight gain. In addition, I will discuss the maternal management for better pregnancy outcomes in obese pregnant women.



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• Education and Appointments

1995	Catholic University Medical College	M.D
2000	Catholic University Medical School, Graduate School	Master
2005	Catholic University Medical School, Graduate School	PhD
1996-2000	St. Mary's Hospital in Catholic University	Residency
2000-2002	St. Mary's Hospital in Catholic University	Clinical Fellow
2002-present	MizMedi Hospital	Clinical Staff
2008-2009	Case Western Reserve University, Cleveland, OH, USA	Visiting Scholar
2009-2010	Cleveland Clinic, Cleveland, OH, USA	Visiting Scholar

• Research Interests

Major: Gestational Diabetes Mellitus

• Brief List of Publications

1. Increased Placental TNF-alpha gene expression in Mice with Gestational Diabetes Mellitus. Submission to Hormone and Metabolic Research)
2. Eun Sook Oh, Jung Hee Han, Sung Min Han, Eun Jung Rhee, Ki Won Oh, Won Young Lee. Plasma concentrations of resistin are higher in women with gestational diabetes mellitus and gestational impaired glucose tolerance than in normal pregnant women Korean J of Diabetes. 2009; 33(4):302-10
3. Eun Sook Oh, Ki Hyun Baek, Won Young Lee, Ki Won Oh, Hye Soo Kim, Je Ho Han, Moo Il Kang, Kwang Woo Lee, Ho Young Son, Sung Koo Kang, The Effect of Oxidative Stress on the Proliferation and Differentiation of Human Bone Marrow Stromal Cell-Derived Osteoblasts. J Kor Soc Endocrinol 2006; 21(3):222-232
4. Oh ES, Rhee EJ, Oh KW, Lee WY, Baek KH, Yoon KH, Kang MI, Yun EJ, Park CY, Choi MG, Yoo HJ, Park SW. Circulating osteoprotegerin levels are associated with age, waist-to-hip ratio, serum total cholesterol, and low-density lipoprotein cholesterol levels in healthy Korean women. Metabolism. 2005 Jan;54(1):49-54

| S17-4 |

Evolving paths to fetal metabolic programming

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Jergen Pedersen suggested that fetal overgrowth was related to increased transplacental transfer of glucose, stimulating the release of insulin by the fetal beta cell and subsequent macrosomia. Optimal maternal glucose control decreased perinatal mortality and morbidity. However, over the last 2 decades, there have been increases in maternal obesity and subsequently gestational diabetes mellitus (GDM) and type 2 diabetes. Neonates of women with well-controlled GDM have significantly increased fat mass. Also, the infants of women with diabetes or pregravid obesity are at increased risk of obesity and glucose tolerance as children and adolescents. Therefore, the maternal metabolic environment may have long-term effects on the developing fetus (ie, perinatal metabolic programming).

Triglycerides (TAG) represent the primary component of lipid stores in fetal adipose tissue. Storage of TAG in fetal adipose tissue may occur from either glucose or free fatty acid (FFA). Glucose is directly transferred from the maternal circulation across the placenta for hepatic and adipose

de novo lipogenesis. FFAs are derived from the maternal circulation through direct placental transfer or after hydrolysis of TAG. The hypothesis that lipids contribute to fetal fat accretion is also supported by data showing that placental cells incubated in vitro with oleate as a substrate accumulate lipids. Also, an up-regulation of pathways regulating lipid transport and synthesis is seen in the placenta of obese/GDM women.

Adipose tissue and the placenta express a common repertoire of cytokine, which open novel perspectives for understanding the pregnancy-induced insulin resistance. It emphasizes the importance of functional interplays between the placenta and maternal adipose tissue in GDM. The environment of elevated IL-6 in systemic maternal and cord blood, as well as in maternal adipose tissue and the placenta, may play a role in metabolic inflammation. Further studies in this field may provide a clue for understanding the inflammatory processes in GDM and obesity and potentially in utero programming of obesity.

**CURRENT HEALTH INSURANCE ISSUES
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The payment status for the glucose test-strips on the type 1 diabetes patients

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Status after applying a new insurance benefits standard for diabetes drugs

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Action plan of quality assessment program in diabetes care

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SATELLITE SYMPOSIA



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• Education and Appointments

2009-present	Swansea University, Swansea, Wales, UK	Reader in Medicine/Consultant
2009-20011	Wales Deanery, Wales, UK	Associate Dean
2005-2009	Swansea University, Swansea, Wales, UK	Senior clinical Lecturer/Consultant
1997-2005	North Thames rotation, London, UK	Specialist Registrar
2001-2004	University College London	Diabetes UK Research Fellow

• Research Interests

Major: Diabetes, Endocrinology, Obesity.
 Genetics of cardiovascular disease; type 2 diabetes; obesity; oxidative stress; inflammation; exercise and diabetes; adipose biology; clinical trials.

• Brief List of Publications

1. Yiannakouris N, Cooper JA, Shah S, Drenos F, Ireland HA, Stephens JW, Li KW, Elkeles R, Godsland IF, Kivimaki M, Hingorani AD, Kumari M, Talmud PJ, Humphries SE. IRS1 gene variants, dysglycaemic metabolic changes and type-2 diabetes risk. *Nutr Metab Cardiovasc Dis*. 2011 Sep 12. [Epub ahead of print].
2. Stephens JW, Bodvarsdottir TB, Wareham K, Prior SL, Bracken RM, Lowe GD, Rumley A, Dunseath G, Luzio S, Deacon CF, Holst JJ, Bain SC. Effects of short-term therapy with glibenclamide and repaglinide on incretin hormones and oxidative damage associated with postprandial hyperglycaemia in subjects with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2011 Aug 9. [Epub ahead of print].
3. Brophy S, Davies H, Dunseath G, Stephens JW, Platts J, Lane H, Beaverstock C, Wakeman L, Russell I, Williams M, Williams DR. Experience of the introduction of routine antibody testing in primary care and of running a trial for latent autoimmune diabetes in adults (LADA). *Diabetes Res Clin Pract*. 2011 Jul;93(1):e49-52.
4. Harrison SC, Cooper JA, Li K, Talmud PJ, Sofat R, Stephens JW, Hamsten A; on behalf of the HIFMECH Consortium, Sanders J, Montgomery H, Neil A; on behalf of the Simon Broome Research Consortium, Humphries SE. Association of a sequence variant in DAB2IP with coronary heart disease. *Eur Heart J*. 2011 Mar 28. [Epub ahead of print].
5. Bracken RM, West DJ, Stephens JW, Kilduff LP, Luzio S, Bain SC. Impact of pre-exercise rapid-acting insulin reductions on ketogenesis following running in Type 1 diabetes. *Diabet Med*. 2011 Feb;28(2):218-22.
6. Prior SL, Jones DA, Gill GV, Bain SC, Stephens JW. Association of the adiponectin rs266729 C>G variant and coronary heart disease in the low risk 'Golden Years' type 1 diabetes cohort. *Diabetes Res Clin Pract*. 2011 Mar;91(3):e71-4.
7. Tang TS, Prior SL, Li KW, Ireland HA, Bain SC, Hurel SJ, Cooper JA, Humphries SE, Stephens JW. Association between the rs1050450 glutathione peroxidase-1 (C > T) gene variant and peripheral neuropathy in two independent samples of subjects with diabetes mellitus. *Nutr Metab Cardiovasc Dis*. 2010 Dec 23. [Epub ahead of print].
8. West DJ, Stephens JW, Bain SC, Kilduff LP, Luzio S, Still R, Bracken RM. A combined insulin reduction and carbohydrate feeding strategy 30 min before running best preserves blood glucose concentration after exercise through improved fuel oxidation in type 1 diabetes mellitus. *J Sports Sci*. 2011 Feb;29(3):279-89.
9. Brophy S, Davies H, Stephens JW, Prior SL, Atkinson M, Bain S, Williams R. Adiponectin levels in people with Latent Autoimmune Diabetes-a case control study. *BMC Res Notes*. 2010 Nov 22;3:317.
10. R, Brenton K, Harris B, Ham R, Rees G, Gorvett T, Boregowda K, Stephens JW, Price DE. Foot ulceration in a secondary care diabetic clinic population: a 4-year prospective study. *Diabetes Res Clin Pract*. 2010 Nov;90(2):e37-9.

A new alternative in DPP4 inhibition

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Linagliptin is a highly selective DPP-4 inhibitor which is administered once a day and since it is largely excreted by the bile and gut no dosage adjustment is necessary with renal or hepatic impairment. Clinical studies have demonstrated a sustained reduction in HbA1c up to 102 weeks duration (mean reduction in HbA1c 0.8%). The efficacy on HbA1c reduction has also been demonstrated in patients over the age of 65 years (-0.60%) and over 75 years (-0.83%) compared to placebo. Cardiovascular safety has been examined in a prospective, pre-specified meta-analysis of 2977 patients. The results showed that linagliptin compared to other oral therapies was associated with a risk ratio of 0.34 (95% CI: 0.15-0.74). Treatment with linagliptin is not associated with significant hypoglycaemia ($\leq 1\%$) even in subjects with renal impairment. No deterioration in renal or liver function has been observed within subjects

with mild to severe renal or liver disease. Linagliptin offers the benefits of glycaemic control, safety and weight neutrality observed with other DPP-4 inhibitors with the additional benefits of safety and efficacy without dose adjustment in renal and hepatic impairment and in an elderly population together with the re-assurance of cardiovascular safety. Within the presentation we will discuss case histories illustrating where linagliptin may fit within the routine clinical management of type 2 diabetes. We will also examine particular patient types who might especially benefit from therapy with linagliptin. These might include younger patients with obesity and coronary heart disease or associated risk factors; patients with declining renal and hepatic function; older patients at risk of hypoglycaemia or with renal impairment and established CHD.



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• Education and Appointments

1991-1997	Yonsei University College of Medicine	MD
1997-2003	Yonsei University College of Medicine, Severance Hospital	Intern, Residency, Clinical Fellow
2003-2004	National Insurance Ilsan Hospital	Faculty
2004.9-2007.09	Seoul National University, College of Medicine, Bundang Hospital	Instructor
2007.10-current	Seoul National University, College of Medicine & Bundang SNU Hospital	Assistant Professor

• Research Interests

Major: adipokine, insulin resistance, lipid metabolism, atherosclerosis, diabetes, metabolic syndrome

• Brief List of Publications

1. Choi SH, Ginsberg HN. Increased very low density lipoprotein (VLDL) secretion, hepatic steatosis, and insulin resistance. *Trends Endocrinol Metab.* 2011 Nov;22(9) 353-63
2. Choi SH, Kim TH, Lim S, Park KS, Jang HC, Cho NH. Hemoglobin A1c as a diagnostic tool for diabetes screening and new-onset diabetes prediction: a 6-year community-based prospective study. *Diabetes Care* 2011 Apr 34(4): 944-9
3. Choi SH, Kwak SH, Lee Y, Moon MK, Lim S, Park YJ, Jang HC, Kim MS. Plasma vaspin concentrations are elevated in metabolic syndrome in men and are correlated with coronary atherosclerosis in women. *Clin Endocrinology.* 2011 May [pub ahead of print]
4. Lee YH, Choi SH(co-first), Lee KW, Kim DJ. Apolipoprotein B/A1 ratio is associated with free androgen index and visceral adiposity and may be an indicator of metabolic syndrome in male children and adolescents. *Clin Endocrinol.* 2011 May 74(5):579-86
5. Choi YJ, Choi SH (co-first), Kim HJ, Han SJ, Hwang JS, Chung YS, Lee KW, Cho HK, Kim DJ. A higher burden of small low-density lipoprotein particles is associated with profound changes in the free androgen index in male adolescents. *J Korean Med Sci.* 2011 Apr; 26(4):534-9
6. Han SH, Choi SH* (co-first), Cho BJ, Lee Y, Park YJ, Moon MK, Lee HK, Kang SW, Han DS, Kim YB, Jang HC, Park KS. Serum fibroblast growth factor-21 concentration is associated with residual renal function and insulin resistance in end-stage renal disease patients receiving long-term peritoneal dialysis. *Metabolism* 2010 Nov;59(11):1656-62
7. Cho NH, Lim S, Kim HR, Chan JC, Jang HC, Choi SH, Cigarette Smoking Is an Independent Risk Factor for Type 2 Diabetes; a community based prospective study. *Clin Endocrinol (Oxf).* 2009 Nov;71(5):679-85.
8. Choi SH, An JH, Lim S, Koo BK, Park SE, Chang HJ, Choi SI, Park YJ, Park KS, Jang HC, Shin CS, Lower bone mineral density is associated with higher coronary calcification and coronary plaque burdens by multidetector-row coronary computed tomography in pre-and post-menopausal women. *Clin Endocrinol.* 2009 Nov;71(5):644-51.
9. Lim S*, Choi SH*(co-first), Choi EK, Chang SA, Koo YH, Chun EJ, Choi SI, Jang HC, Chang HJ, Comprehensive evaluation of coronary arteries by multidetector-row cardiac computed tomography according to the glucose level of asymptomatic individuals. *Atherosclerosis.* 2009 Jul;205(1):156-62.
10. Choi SH, Hur KY, Kim DJ, Kang ES, Lim SK, Huh KB, Lee HC, New staged diabetes management program considering individual beta cell function and insulin resistance ameliorated hyperglycemia in Korean type 2 diabetes mellitus. *Clin Endocrinol.* 2008 Oct; 69(4):549-55
11. Choi SH, Kwak SH, Youn BS, Lim S, Lee HY, Lee NS, Lee HK, Park KS, Kim YB, Jang HC, Higher Plasma Retinol Binding Protein-4 and Lower Adiponectin Concentrations are Associated with Insulin Resistance in Women with Previous Gestational Diabetes Mellitus. *J Clin Endocrinol Metab* 2008 Aug; 93(8):3142-8
12. Choi SH, Lee YJ, Park YJ, Lee EJ, Lim S, Park DJ, Kim SE, Park KS, Jang HC, Cho BY, Retinol Binding Protein-4 Elevation Is Associated with Serum TSH Level in Normal Glucose Tolerant Elderly Subjects Independently from Obesity. *J Clin Endocrinol Metab* 2008 Jun; 93(6):2313-8

A PROspective comparative clinical study to evaluate efficacy and safety of PITavastatin in patients with metabolic syndrome: PROPIT study

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This is a 48 weeks, prospective, randomized, multicenter trial in patients with metabolic syndrome (MS) with mild hyperlipidemia to investigate the effect of pitavastatin +life style modification vs. life style modification only on the progression of MS and other metabolic parameters such as

visceral fat amount, diabetes, adipokines. We screened 289 patients and enrolled 187 patients from 10 sites in Korea. This is the first announcement of the result of PROPIT study, which is recently finished in September, 2011.



Andrew J.M. Boulton

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• Education and Appointments

- 1976 MB, BS (with Honours), University of Newcastle-upon-Tyne
- 1979 MRCP (UK)
- 1981-1986 Senior Medical Registrar, Royal Hallamshire and Northern General Hospitals, Sheffield
- 1983-1984 Visiting Assistant Professor of Medicine, Division of Endocrinology, University of Miami, School of Medicine, Miami, Florida
- 1985 MD (PhD equivalent), University of Newcastle-upon-Tyne
- 1986-1995 Senior Lecturer, then Reader (from 1991) in Medicine, University of Manchester, and Consultant Physician, Manchester Royal Infirmary
- 1992 FRCP
- 2003 DSc(Hon), University of Cluj, Romania
- 1995- Professor of Medicine, University of Manchester and Consultant Physician, Manchester Royal Infirmary, Oxford Road, Manchester, Manchester, M13 9WL, UK
- 2002- Professor of Medicine, University of Miami, Diabetes Research Institute, Suite 3054, 1450 North West 10th Avenue, Miami, FL 33136, USA

• Research Interests

Diabetic complications, diabetic neuropathy, diabetic foot.
GCP training July 2009.

• Brief List of Publications

Author of more than 400 papers and 8 books on the above topics.

Diagnosis and management of diabetic neuropathy

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University of Manchester, UK

The diabetic neuropathies are common and chronic sensorimotor diabetic peripheral neuropathy (DPN) affects up to 50% of older type 2 diabetic patients. Up to half of these individuals may have painful symptoms of whom up to 20% will require some form of pharmacological therapy. The diagnosis of DPN remains a clinical one with exclusion of other causes of neuropathy important as no tests can determine that the neuropathy in any patient is caused by the diabetes. The most troublesome neuropathic symptoms include burning discomfort, altered temperature sensation (feet feel very hot or very cold), hyperaesthesiae, tingling, prickling and sudden shooting, stabbing pains. Examination usually reveals a stocking distribution sensory loss although in acute sensory neuropathy, the clinical examination may be normal. Evidence suggests that blood glucose flux, with erratic fluctuations of blood glucose during the

day and night, contributes to the pathogenesis of neuropathic pain. With respect to treatments, the first step is to try and achieve optimal, stable glycaemic control: sudden improvement in control may however actually worsen neuropathic symptomatology. In addition to achieving stable glycaemic control, most patients require some form of pharmacological intervention and first line drugs include anti-epileptics such as Gabapentin and Pregabalin, the anti-depressant and dual reuptake inhibitor, Duloxetine, or the tricyclic drug Amitriptyline. Strong evidence from randomised controlled trials supports the use of each of the above agents. For those patients with resistant neuropathic pain, synthetic Opioids such as Tramadol, or stronger drugs such as slow release Oxycodone may be useful in the short term. To date, no specific pathogenetic treatments are licensed in the UK for the management of neuropathic pain.



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• Education and Appointments

1996	Graduated from Seoul National University College of Medicine	MD
2004	Graduate School, Seoul National University	PhD
2003-2004	Seoul National University Hospital	Clinical Instructor
2004-2010	Seoul National University Hospital	Clinical Assistant Professor
2009-2010	University of British Columbia, Vancouver, B.C., Canada	Visiting Professor
2010-present	Seoul National University College of Medicine	Assistant Professor

• Research Interests

Major: Incretin, Insulin therapy, Diabetes

• Brief List of Publications

1. Hwang S, Kwak SH, Bhak J, Kang HS, Lee YR, Koo BK, Park KS, Lee HK, Cho YM. Gene Expression Pattern in Transmitochondrial Cytoplasmic Hybrid Cells Harboring Type 2 Diabetes-Associated Mitochondrial DNA Haplogroups. *PLoS ONE* 2011; 6(7):e22116. doi:10.137
2. Speck M, Cho YM (co-first author), Asadi A, Rubino F, Kieffer TJ. Duodenal-jejunal bypass protects GK rats from β -cell loss and aggravation of hyperglycemia and increases enteroendocrine cells coexpressing GIP and GLP-1. *Am J Physiol Endocrinol Metab*. 2011 May;300(5):E923-32
3. Cho YM, Kieffer TJ. New aspects of an old drug: metformin as a glucagon-like peptide 1 (GLP-1) enhancer and sensitiser. *Diabetologia*. 2011 Feb;54(2):219-22
4. Yang JS, Kim JT, Jeon J, Park HS, Kang GH, Park KS, Lee HK, Kim S, Cho YM. Changes in Hepatic Gene Expression upon Oral Administration of Taurine-Conjugated Ursodeoxycholic Acid in ob/ob Mice. *PLoS ONE* 5(11): e13858. doi:10.1371
5. Cho YM, Kieffer TJ. K-cells and glucose-dependent insulinotropic polypeptide in health and disease. *Vitam Horm*. 2010;84:111-50
6. Cho YM, Koo BK, Son HY, Lee KW, Son HS, Choi DS, Kim BW, Kim YK, Lee MK, Lee HC, Min KW, Chung MY, Baek HS, Kim Y, Yoo HJ, Park KS, Lee HK. Effect of the combination of mitiglinide and metformin on glycemic control in patients with type 2 diabetes mellitus. *J Diabetes Invest* 2010 Aug; 1(4): 143-8
7. Cho YM, Kim TH, Lim S, Choi SH, Shin HD, Lee HK, Park KS, Jang HC. Type 2 diabetes-associated genetic variants discovered in the recent genome-wide association studies are related to gestational diabetes mellitus in the Korean population. *Diabetologia*. 2009 Feb;52(2):253-61

Back to the fundamentals: MOA, PK, and PD of DPP-4 inhibitors

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There is plethora of incretin-based therapeutics including GLP-1 analogues and dipeptidyl peptidase-4 (DPP-4) inhibitors. Currently, five DPP-4 inhibitors are available in clinical practice worldwide. Sitagliptin is a beta-phenethylamine with an IC_{50} of 9.96 nM for DPP-4 inhibition; vildagliptin and saxagliptin are cyanopyrrolidines with IC_{50} s of 5.28 nM and 3.37 nM, respectively; alogliptin is an aminopiperidine with an IC_{50} of 6.9 nM; linagliptin is a xanthine derivative with an IC_{50} of approximately 1 nM. Among them, vildagliptin and saxagliptin have much shorter plasma half-lives (approximately 2-3 hrs), but these drugs form firm covalent bonds with DPP-4 enzymes, resulting in extended duration of action. DPP-4 belongs to the DASH (DPP-4 activity- and/or structure homologues) enzymes, which also include DPP-8, DPP-9, and fibroblast activation protein (FAP). Since it has been reported that a DPP-8/9 inhibitor and a non-selective DPP inhibitor produce serious toxicity (i.e., alopecia, thrombocytopenia, anemia, splenomegaly, and death), a high selectivity to the catalytic domain of DPP-4 is of paramount importance. In this regard, alogliptin and linagliptin have the highest selectivity, followed by sitagliptin. The relative selectivity of DPP-4 over DPP-8 and DPP-9 is modest in vildagliptin and saxagliptin. The potency and duration of DPP-4 inhibition are different among DPP-4 inhibitors. Sitagliptin inhibits DPP-4 activity by 97% over 24 hrs, allowing for once daily dosing. Other

DPP-4 inhibitors also exhibit >80% inhibitory activity at its peak action (-95% for vildagliptin, -80% for saxagliptin, and -93% for linagliptin). To assure the adequate DPP-4 inhibition over 24 hrs, vildagliptin needs to be administered twice daily. Saxagliptin is metabolized by CYP3A4, yielding active metabolites. Vildagliptin is metabolized by hydrolysis, which produces inactive metabolites. Sitagliptin, alogliptin, and linagliptin are not appreciably metabolized. Most part of ingested sitagliptin and alogliptin is excreted unchanged through urine, whereas linagliptin is predominantly excreted through bile and feces. The characteristic elimination mechanism of linagliptin allows no dose modification when prescribed for patients with renal dysfunction. In terms of safety, sitagliptin has been the most extensively examined. So far, sitagliptin appears not to be associated with increased risk of pancreatitis, infection, malignancy, and cardiovascular diseases. DPP-4 inhibitors, in general, are not associated with hypoglycemia and weight gain, which are common side effects of most antidiabetic medicines. Caution should be exercised for some adverse events particularly associated with individual DPP-4 inhibitor (e.g., hepatic toxicity for vildagliptin, lymphocytopenia for saxagliptin). When prescribing DPP-4 inhibitors, pharmacokinetics, pharmacodynamics, clinical efficacy, safety, and evidence should be taken into account.



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• Education and Appointments

1988-1992	Assistant Professor at the School of Medicine at University "Federico II" in Naples, Italy
1992-1995	Associate Professor of Emergency Medicine at 2 nd University of Naples - Italy
1995-2000	Associate Professor of Geriatric Medicine at 2 nd University of Naples - Italy
2000-present	Full Professor of Internal Medicine (at 2 nd University of Naples)
2002	Coordinator of the Geriatric Physiopathology PhD program
2002	Director of Geriatric Residency Program
2006-	Director of the pre-medicine program of medical school
2010-	Member of National Council of Health for Italian Minister of Health
2010	Dean of School of Medicine of II University of Naples, Naples, Italy

• Brief List of Publications

1. Maggio M, Ceda GP, Lauretani F, Cattabiani C, Avantaggiato E, Morganti S, Ablondi F, Bandinelli S, Dominguez LJ, Barbagallo M, Paolisso G, Semba RD, Ferrucci L. Magnesium and anabolic hormones in older men. *Int J Androl*. 2011 Jun 15. doi: 10.1111/j.1365-2605.2011.01193.x. [Epub ahead of print] PubMed PMID: 21675994.
2. Barbieri M, Boccardi V, Esposito A, Papa M, Vestini F, Rizzo MR, Paolisso G. A/ASP/VAL allele combination of IGF1R, IRS2, and UCP2 genes is associated with better metabolic profile, preserved energy expenditure parameters, and low mortality rate in longevity. *Age (Dordr)*. 2011 Feb 22. [Epub ahead of print] PubMed PMID: 21340542.
3. Boccardi V, Ambrosino I, Papa M, Fiore D, Rizzo MR, Paolisso G, Barbieri M. Potential role of TCF7L2 gene variants on cardiac sympathetic/parasympathetic activity. *Eur J Hum Genet*. 2010 Dec;18(12):1333-8. Epub 2010 Jul 21. PubMed PMID: 20648057; PubMed Central PMCID: PMC3002850.
4. Rizzo MR, Marfella R, Barbieri M, Boccardi V, Vestini F, Lettieri B, Canonico S, Paolisso G. Relationships between daily acute glucose fluctuations and cognitive performance among aged type 2 diabetic patients. *Diabetes Care*. 2010 Oct;33(10):2169-74. Epub 2010 Jun 23. PubMed PMID: 20573753; PubMed Central PMCID: PMC2945154.
5. Paolisso G. Pathophysiology of diabetes in elderly people. *Acta Biomed*. 2010;81 Suppl 1:47-53. Review. PubMed PMID: 20518191.
6. Ciarambino T, Ferrara N, Castellino P, Paolisso G, Coppola L, Giordano M. Effects of a 6-days-a-week low protein diet regimen on depressive symptoms in young-old type 2 diabetic patients. *Nutrition*. 2011 Jan;27(1):46-9. Epub 2010 May 15. PubMed PMID: 20472399.
7. Boccardi V, Rizzo MR, Marfella R, Papa M, Esposito A, Portoghese M, Paolisso G, Barbieri M. -94 ins/del ATTG NFKB1 gene variant is associated with lower susceptibility to myocardial infarction. *Nutr Metab Cardiovasc Dis*. 2010 Mar 19. [Epub ahead of print] PubMed PMID: 20304615.

Vildagliptin has a better metabolic impact than Sitagliptin on mean amplitude glycaemic excursion

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Aims: Vildagliptin (50 mg) given 2 times daily was compared to sitagliptin (100 mg) one time daily in order to investigate the effect on glucose control evaluated by 24 h glycaemic holter.

Methods: 30 consecutive patients were randomly assigned to take vildagliptin and sitagliptin for 2 weeks. At baseline and after the treatment all patients were submitted to 24 hour glycaemic holter recording.

Results: Vildagliptin and Sitagliptin resulted in similar effect on fasting and post,prandial glucose level decline; similar effect were also observed on glycated haemoglobin. Indeed, vildagptin showed a stronger effect ($p < 0.01$) on mean amplitude glycaemic excursion (MAGE) decline.

Conclusion: Vildaglitpin rather sitagliptin have a more extensive effect on glucose control since it is able to have a more appropriate control on MAGE.



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• Education and Appointments

- 1969-1983 Trained at Different University Hospitals in Copenhagen
- 1977 Specialised in Internal Medicine at Different University Hospitals in Copenhagen
- 1984 Endocrinology at the University of Copenhagen
- 1983-2011 Chief physician at Steno Diabetes Center
- 1997- Appointed Professor of Diabetic Vascular Diabetic Complications (Personal Chair) at the University of Aarhus, Denmark
- 2007- Chief Physician Department of Medical Endocrinology, National Hospital, University of Copenhagen

• Research Activity

- 2008 - Aliskiren combined with losartan in type 2 diabetes and nephropathy
- 2008 - Aliskiren reduces renin system activity in patients with hypertension, type 2 diabetes and albuminuria
- 2008 - Renoprotective effects of direct renin inhibition compared to and in combination with rbesartan in patients
- 2008 - Renoprotective effects of the direct renin inhibitor aliskiren, irbesartan and the combination in patients with type 2 diabetes, hypertension and albuminuria
- 2008 - The combination of aliskiren, a direct renin inhibitor, and losartan in patients with type 2 diabetes and nephropathy
- 2008 - The effect of direct renin inhibition alone and in combination with angiotensin II receptor blockade on markers of the renin-angiotensinaldosterone system
- 2008 - Time course of the antiproteinuric and antihypertensive effects of direct renin inhibition in type 2 diabetes

Beneficial impact of direct renin inhibition on renal and cardiovascular disease

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The cardiovascular (CV) and renal disease are closely linked. For example, urinary albumin-to-creatinine ratio (UACR) provides a sensitive measure of albuminuria and is also a significant predictor of CV events. Reductions in albuminuria have been shown to be associated with improvement in renal function and a reduction in the risk of end-stage renal failure. Furthermore, there are strong correlations between reductions in albuminuria and improved CV outcomes in patients with hypertension.

The randomized, double-blind, placebo-controlled Aliskiren in the eValuation of prOteinuria In Diabetes (AVOID) study was a longer-term and more robust study, which provided evidence of the potential for renal protection with aliskiren. In the AVOID study, 599 patients with mild-to-moderate hypertension, type 2 diabetes and nephropathy initially received losartan 100 mg and optimal antihypertensive therapy for 3 months. Patients were then randomized to receive addition of either aliskiren or placebo for further 6 months. At the study endpoint, aliskiren 300 mg (on top of losartan 100 mg and optimal antihypertensive therapy) reduced UACR by 20% compared with placebo ($p < 0.001$). Furthermore, a significantly greater number of aliskiren-treated patients achieved at least a 50% reduction in UACR from baseline compared with placebo (24.7 vs 12.5%, respectively; $p < 0.001$). As the patients in the AVOID study received losartan 100 mg and optimal antihypertensive therapy, BP was relatively well-controlled as baseline with mean BP of 135/78 mmHg and 134/77 mmHg in the aliskiren and the placebo groups,

respectively. At the study endpoint, reductions from baseline in BP were not significantly different between the aliskiren and placebo groups. These results indicate that the ability of aliskiren to reduce UACR is independent of its BP-lowering efficacy.

Recently, the effect of Aliskiren in patients with symptomatic heart failure was evaluated in the ALOFT study. The study showed that addition of Aliskiren 150 mg daily to an ACEi or ARB and beta blocker had a favourable neurohormonal effect and appeared to be well tolerated (no significant increases in hyperkalaemia, renal dysfunction or symptomatic hypotension). Aliskiren provided significant reductions in the levels of BNP, which were five times greater than with addition of placebo.

Left ventricular (LV) hypertrophy, a marker of cardiac end-organ damage, is associated with an increased risk of CV morbidity and mortality. In the ALLAY study the effect of Aliskiren and Losartan and their combination was evaluated on the reduction of LV mass in 465 patients with hypertension. The study revealed that Aliskiren was as effective as Losartan in producing LV mass regression.

The primary objective of the ALTITUDE trial is to determine whether Aliskiren 300 mg once daily, reduces CV and renal morbidity and mortality, compared with placebo when added to conventional treatment (including ACEi or ARB). ALTITUDE is an event-driven trial that aims to randomize 8,600 high-risk type 2 diabetic patients with a planned follow-up time of 48 months.



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• Education and Appointments

1991-1992	Hanyang University Hospital, College of Medicine, Seoul, Korea	Internship
1993-1997	Hanyang University Hospital, College of Medicine, Seoul, Korea (Internal Medicine)	Residency
1997-2000	Hanyang University Guri Hospital, Guri, Korea (Endocrinology)	Clinical Fellowship
2000-2005	Hanyang University Medical School, Seoul, Korea (Endocrinology)	Assistant Professor
2005-2010	Hanyang University Medical School, Seoul, Korea (Endocrinology)	Associate Professor
2009-2011	Harvard University, School of Public Health (Department of Nutrition), Boston, MA USA	Visiting Scholar
2010-Present	Hanyang University Medical School, Seoul, Korea (Endocrinology)	Professor
2011	MIT (Massachusetts Institute of Technology) Media Lab, Cambridge, MA USA	Researcher

• Research Interests

Major: Obesity and metabolic syndrome

Life style modification through wireless health care system for the management of prediabetes and metabolic syndrome

• Brief List of Publications

1. Kim SH, Kim TH, Lee JS, Koo TY, Lee CB, Yoon HJ, Shin DH, Park SS, Sohn JW. Adiposity, adipokines, and exhaled nitric oxide in healthy adults without asthma. *J Asthma* 48(2):177-82, 2011
2. Lee YJ, Lee H, Jee SH, Lee SS, Kim SR, Kim SM, Lee MW, Lee CB, Oh S. Serum osteocalcin is inversely associated with adipocyte-specific fatty acid-binding protein in the Korean metabolic syndrome research initiatives. *Diabetes Care* 33(7):e90, 2010
3. Lee CB, Koh HC. Modification of the cardiovascular response of posterior hypothalamic adenosine A(2A) receptor stimulation by adenylate cyclase and KATP channel blockade in anesthetized rats. *Auton Neurosci* 12:146;70-5, 2009
4. Kang JG, Lee CB, Park HS, Park CY. Relationship between Circulating Obestatin levels and Obesity in Obese Patients. *Kor J Obesity* 18:1;8-14, 2009
5. Lee CB. Obesity and type 2 Diabetes. *Review Clin Diabetes* 9:155-61, 2008
6. Lee CB. Chapter 2 Energy metabolism and body weight homeostasis *Clinical obesity* 3rd ed p50-61, 2008
7. Lee SY, Park HS, Kim DJ, Han JH, Kim SM, Cho GJ, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ. Appropriate waist circumference cutoff points for central obesity in Korean adults. *Diabetes Res Clin Pract* 75:72-80, 2007

What's new & controversy on statin treatment in diabetes?

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Patients with type 2 diabetes or metabolic syndrome often have mixed dyslipidemia accompanied by cardiovascular risk factors. Dyslipidemia in the patient with type 2 diabetes contributes to atherosclerotic risk and coronary heart disease. There were several large meta-analyses that provide strong evidence of benefit of statin in CV risk patients, with a little evidence of any hazard.

A large meta-analysis from the Cholesterol Trialists' Collaboration (CTT) included 21 studies with more than 130,000 patients, comparing statins vs placebo controls, and another five studies, with approximately 40,000 patients, examining different statin doses. As a result, there was a 22% proportional reduction in the risk of major vascular events for each 1 mmol/L reduction in LDL cholesterol. It implies that 2-3 mmol/L reduction would reduce risk of vascular events by about 40-50%. Additional reductions in LDL cholesterol with more intensive therapy further reduce the incidence of these major vascular events and do not increase the risk of developing cancer and myopathy (except SEARCH and A to Z trial).

Recently, a meta-analysis of the high-profile statin trials testing an increase of the risk of diabetes issued on the Journal of the American Medical Association. The idea for this meta-analysis began two years ago when the signal

for diabetes risk was observed in JUPITER trial. The group later performed an analysis of some of the early statin trials comparing the lipid-lowering drugs with placebo in 90,000 individuals and observed a significant 9% increase in the risk of diabetes mellitus. The trials included in this newest meta-analysis were five trials including PROVE-IT, A to Z, TNT, IDEAL, and SEARCH, that together included 32,752 patients without diabetes at baseline. In conclusion, 1,449 patients treated with high-dose statin therapy developed diabetes compared with 1300 patients assigned to moderate-dose statin therapy. The odds ratio for new-onset diabetes was 1.12 (95% CI 1.04-1.22). Regarding the benefit, 3,134 patients treated with high-dose statin therapy and 3,550 patients treated with moderate-dose therapy had a cardiovascular event and the relative reduction was 16%.

Therefore, we should see an off-target effect. Right now we have no obvious mechanism on the risk of diabetes mellitus by statins. However, the benefit of statins for reducing important macrovascular events is so overwhelming that the balance is clearly on the side of benefit. While monitoring HbA1c levels when treating patients with high-dose statin therapy, we clinicians should continue the statin treatment, especially for the patients at high risk for cardiovascular events.



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• Education and Appointments

1989	College of Medicine, Inje University	MD
1991	Busan Paik Hospital, Inje University	Residency of Internal Medicine
1995	Busan Paik Hospital, Inje University	Clinical Fellow
1996	College of Medicine, Inje University	Full Time Instructor
1999	College of Medicine, Inje University	Assistant Professor
2003	University of Utah, USA	Research Associate
2004	College of Medicine, Inje University	Associate Professor
2010	College of Medicine, Inje University	Professor
2010	Paik Diabetes Center, Inje University	Director

• Research Interests

Major: Gene Therapy
 Diabetic complications, Beta cell regeneration

• Brief List of Publications

1. JH Park et al. Nateglinide and acarbose for post-prandial glucose control after optimizing fasting glucose with insulin glargine in patients with type 2 diabetes. *Diabetic Medicine*, in-press, 2010
2. JH Park et al. The effect of chromium on rat insulinoma cells in high glucose conditions. *Life Science*, in-press, 2010
3. JH Park et al. EGCG and quercetin protected INS-1 cells in oxidative stress via different mechanisms. *Frontiers in Bioscience E2*, 657-664, 2010
4. JH Park et al. REVIEW: Ultrasound-mediated gene delivery. *Expert Opinion on Drug Delivery*, 321-330, 2010
5. JH Park et al. Post-prandial lipid levels for assessing target goal achievement in type 2 diabetic patients taking statin. *J Korean Med Sci*, 387-392, 2010
6. JH Park et al. The effect of glucose fluctuation on apoptosis and function of INS-1 pancreatic beta cells. *Korean Diabetes J*, 47-54, 2010

Updates on the clinical usefulness of sitagliptin

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The increasing burden of type 2 diabetes mellitus (T2DM) and inadequate control in the majority of patients has necessitated for newer therapeutic options. There have been recent exciting advances in the treatment of T2DM, targeting the enteroinsular axis with incretin-based therapies that include the dipeptidyl peptidase IV (DPP-IV) inhibitors. The background, pharmacodynamic and pharmacokinetic profile of sitagliptin and important clinical trials with this drug will be discussed briefly. This lecture is intended to provide a schematic overview of the DPP-IV inhibitor sita-

gliptin, its clinical use and an personal opinion about its place in the treatment algorithm of diabetes management. Sitagliptin is a well-tolerated, moderately efficacious, weight-neutral oral antidiabetic agent, with a low incidence of hypoglycemia. It may have a particular role in the management of type 2 diabetic patients with kidney or liver dysfunction. Animal studies indicate a protective effects on the pancreatic beta cells, and possible beneficial effects on the cardiovascular system, but these remain to be proven in humans in the near future.



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• Education and Appointments

1999-2003	Severance Hospital	Residency
2003-2005	Yonsei University College of Medicine	Clinical Fellow
2005-2006	Yonsei University College of Medicine	Instructor
2006-2010	Yonsei University College of Medicine	Assistant Professor
2010-Present	Yonsei University College of Medicine	Associate Professor
2009-2011	Beth Israel Deaconess Medical Center, Harvard Medical School	Visiting Professor

• Research Interests

Major: Pharmacogenetics, Posttransplantation Diabetes

• Brief List of Publications

1. Leptin replacement improves postprandial glycemia and insulin sensitivity in HIV-infected lipotrophic men treated with pioglitazone: a pilot study. *Metabolism Clinical and Experimental* 60(7):1045-1049, 2011
2. Effects of Leptin and Adiponectin on Pancreatic Beta Cell Function. *Metabolism Clinical and Experimental* 2011 In Press
3. Circulating vaspin and visfatin are not affected by acute or chronic energy deficiency or leptin administration in human subjects. *European Journal of Endocrinology* 164(6):911-917, 2011
4. Low-risk ZnT-8 allele (W325) for post-transplantation diabetes mellitus is protective against cyclosporin A-induced impairment of Beta-cell insulin secretion capacity. *The Pharmacogenomics Journal* 11(3):191-198, 2011
5. Effects of Pioglitazone on Subclinical Atherosclerosis and Insulin resistance in Nondiabetic Renal Allograft Recipients. *Nephrology Dialysis Transplantation* 25(3):976-984, 2010
6. Association of Common type 2 Diabetes Risk Gene Variants and Posttransplantation Diabetes Mellitus in Renal Allograft Recipients in Korea. *Transplantation* 88(5):693-698, 2009
7. Effect of ABCA1 Variant on Atherogenic Dyslipidemia in Patients with Type 2 Diabetes Treated with Rosiglitazone. *Diabetic Medicine* 26(6):577-581, 2009
8. The C609T variant NQO1 is associated with carotid artery plaques in patients with type 2 diabetes. *Molecular Genetics & Metabolism* 97(5):85-90, 2009
9. Association between polymorphisms in SLC30A8, HHEX, CDKN2A/B, IGF2BP2, FTO, WFS1, CDKAL1, KCNQ1 and Type 2 Diabetes in the Korean population. *Journal of Human Genetics* 53(11-12):991-998, 2008
10. LPIN1 Polymorphism is associated with Rosiglitazone Response in Patients with Type 2 Diabetic patients. *Molecular Genetics & Metabolism* 95(1-2):96-100, 2008
11. Rosiglitazone inhibits the early stage of glucolipotoxicity-induced beta-cell apoptosis. *Hormone Research* 70(3):165-173, 2008
12. A Polymorphism in the Zinc Transporter Gene, SLC30A8, Confers Resistance against Posttransplantation Diabetes Mellitus in Renal Allograft Recipients. *Diabetes* 57(4):1043-1047, 2008
13. Adiponectin gene polymorphism 45T >G is associated with carotid artery plaques in patients with type 2 diabetes mellitus. *Metabolism Clinical and Experimental* 57(2):274-279, 2008
14. Lithospermic Acid B Ameliorates the Development of Diabetic Nephropathy in Type 2 Diabetic Rats. *European Journal of Pharmacology* 579(1-2):418-425, 2008
15. A Variant of the Transcription Factor 7-like 2 (TCF7L2) Gene and the Risk of Post-transplant Diabetes Mellitus (PTDM) in Renal Allograft Recipients. *Diabetes Care* 31(1):63-68, 2008

Overcoming barriers now in successful management of type 2 diabetes

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The worldwide burden of type 2 diabetes is high, increasing and underestimated and the poor metabolic control type 2 diabetes is associated with a high risk for microvascular and macrovascular complications. It is important to treat to HbA1c target goals by helping individuals lower their FPG and PPG with a reduced risk of hypoglycaemia and weight gain. Because of the progressive pathophysiology of type 2 diabetes, oral antidiabetic agents often fail to provide sustained glycemic control, indicating the need for new therapies. Saxagliptin is an oral dipeptidyl peptidase-4 inhibitor, recently approved for the treatment of T2DM. By inhibiting dipeptidyl peptidase-4, saxagliptin increases concentrations of the intact forms of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic

polypeptide (GIP). Saxagliptin also improves beta-cell function, increases postprandial insulin secretion and reduces postprandial glucagon secretion. Saxagliptin is generally well tolerated with weight-neutral effects and a low incidence of hypoglycemia. Multicenter randomized trials have shown that saxagliptin as monotherapy, as initial therapy with metformin or as add-on therapy with metformin, a sulfonylurea or a thiazolidinedione leads to significant decreases in HbA1c levels, fasting and postprandial plasma glucose levels. Saxagliptin 5 mg was noninferior to sitagliptin 100 mg when added to metformin, with HbA1c reductions of 0.52% and 0.62% from mean baseline values of 7.7% and 7.7%, respectively. In addition Saxagliptin has been shown to have cardiovascular safety.



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Education and Appointments

1987-1993	Yonsei University College of Medicine	MD
1997-2001	Severance Hospital	Residency; Internal Medicine
2001-2002	Yonsei University, Dept. of Internal Medicine (endocrinology)	Clinical Fellow
2003-present	Ajou University School of Medicine, Dept. of Endocrinology	Associate Professor

Research Interests

Major: Epidemiology of obesity, metabolic syndrome and diabetes

Brief List of Publications

1. Lee EH, Lee YW, Lee KW, Kim DJ, Kim SK. Development and psychometric evaluation of a diabetes-specific quality-of-life (D-QOL) scale. *Diabetes Res Clin Pract*. 2011 Sep 8. [Epub ahead of print] PubMed PMID: 21907441. (as a coauthor)
2. Choi YJ, Choi SE, Ha ES, Kang Y, Han SJ, Kim DJ, Lee KW, Kim HJ. Involvement of visfatin in palmitate-induced upregulation of inflammatory cytokines in hepatocytes. *Metabolism*. 2011 Jun 9. [Epub ahead of print] PubMed PMID: 21664630. (as a coauthor)
3. Kim TH, Choi SE, Ha ES, Jung JG, Han SJ, Kim HJ, Kim DJ, Kang Y, Lee KW. IL-6 induction of TLR-4 gene expression via STAT3 has an effect on insulin resistance in human skeletal muscle. *Acta Diabetol*. 2011 Feb 4. [Epub ahead of print] PubMed PMID: 21293887. (as a coauthor)
4. Jung JG, Choi SE, Hwang YJ, Lee SA, Kim EK, Lee MS, Han SJ, Kim HJ, Kim DJ, Kang Y, Lee KW. Supplementation of pyruvate prevents palmitate-induced impairment of glucose uptake in C2 myotubes. *Mol Cell Endocrinol*. 2011 Oct 15;345(1-2):79-87. Epub 2011 Jul 23. PubMed PMID: 21802492. (as a coauthor)
5. Kim HJ, Chun KH, Kim DJ, Han SJ, Kim YS, Woo JT, Park Y, Nam MS, Baik SH, Ahn KJ, Lee KW. Utilization patterns and cost of complementary and alternative medicine compared to conventional medicine in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2011 Jul;93(1):115-22. Epub 2011 Apr 27. (as a coauthor)
6. Choi SE, Kim TH, Yi SA, Hwang YC, Hwang WS, Choe SJ, Han SJ, Kim HJ, Kim DJ, Kang Y, Lee KW. Capsaicin attenuates palmitate-induced expression of macrophage inflammatory protein 1 and interleukin 8 by increasing palmitate oxidation and reducing c-Jun activation in THP-1 (human acute monocytic leukemia cell) cells. *Nutr Res*. 2011 Jun;31(6):468-78. Epub 2011 Jun 17. (as a coauthor)
7. Kim EK, An SY, Lee MS, Kim TH, Lee HK, Hwang WS, Choe SJ, Kim TY, Han SJ, Kim HJ, Kim DJ, Lee KW. Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients. *Nutr Res*. 2011 Jun;31(6):436-43. PubMed PMID: 21745625. (as a coauthor)
8. Kim JY, Hong JW, Rhee SY, Kim CS, Kim DJ, Lee EJ. Carotid atheromatic plaque is commonly associated with hypopituitary men. *Pituitary*. 2011 Jun;14(2):105-11. Epub 2010 Oct 28. (as a coauthor)
9. Han SJ, Choi SE, Kang Y, Jung JG, Yi SA, Kim HJ, Lee KW, Kim DJ. Effect of sitagliptin plus metformin on β -cell function, islet integrity and islet gene expression in Zucker diabetic fatty rats. *Diabetes Res Clin Pract*. 2011 May;92(2):213-22. Epub 2011 Feb 23. (as a corresponding author)
10. Lee YH, Choi SH, Lee KW, Kim DJ. Apolipoprotein B/A1 ratio is associated with free androgen index and visceral adiposity and may be an indicator of metabolic syndrome in male children and adolescents. *Clin Endocrinol (Oxf)*. 2011 May;74(5):579-86. doi: 10.1111/j.1365-2265.2010.03953.x. (as a corresponding author)
11. Choi YJ, Choi SH, Kim HJ, Han SJ, Hwang JS, Chung YS, Lee KW, Cho HK, Kim DJ. A Higher Burden of Small Low-density Lipoprotein Particles is Associated with Profound Changes in the Free Androgen Index in Male Adolescents. *J Korean Med Sci*. 2011 Apr;26(4):534-9. Epub 2011 Mar 28. (as a corresponding author)
12. Kim CJ, Kim DJ, Park HR. Effects of a Cardiovascular Risk Reduction Intervention With Psychobehavioral Strategies for Korean Adults With Type 2 Diabetes and Metabolic Syndrome. *J Cardiovasc Nurs*. 2011 Mar-Apr;26(2):117-28. Epub 2010 Nov 10. (as a coauthor)
13. Kim TH, Kim EK, Lee MS, Lee HK, Hwang WS, Choe SJ, Kim TY, Han SJ, Kim HJ, Kim DJ, Lee KW. Intake of brown rice lees reduces waist circumference and improves metabolic parameters in type 2 diabetes. *Nutr Res*. 2011 Feb;31(2):131-8. (as a coauthor)

Recent issues on hypertension management and role of arole

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Angiotensin receptor blockers (ARBs) have shown a blood pressure lowering efficacy which is at least comparable with other drug classes, including ACE inhibitors (ACE-I), beta-blockers, calcium channel blockers and diuretics. ARBs also have a lower side effect profile than other hypertensive agents and patients on ARBs are more persistent with therapy. According to recent evaluation from Canadian real-life database, ARB-based therapies were more associated with better persistence and adherence rates and a lower risk of CV events with superior BP control than non-ARB-based therapies. In this study, the effect of irbesartan was superior to the rest of ARBs. Given poor adherence with therapy has been recognized as a causal factor of failure of hypertension control, excellent persistence should be one of the important reasons to choose ARB for hypertension management.

The ARB irbesartan has demonstrated a high efficacy in lowering blood pressure, which has been shown to be at least comparable with ACE-Is and superior to other ARBs such as losartan and valsartan. This means in turn, a better cost-effectiveness for irbesartan than for valsartan and los-

artan in the management of hypertension. In addition, irbesartan has been shown to be effective in both early and late stage diabetic nephropathy. While both losartan and irbesartan are registered for the treatment of late stage diabetic nephropathy, irbesartan is also registered for early stage diabetic nephropathy.

Additionally, irbesartan improves metabolic parameters in hypertensive patients with metabolic syndrome. The effect on metabolic risk factors was more prominent in diabetic patients with metabolic syndrome, which made irbesartan an optimal treatment option for these types of patients.

Despite of additional benefit of ARBs, serious concerns about the safety of ARBs has been recently raised especially in terms of cancer incidence. In this presentation, the recent controversial opinions on the association of ARBs and cancer will be addressed.

Taken together, the data from randomized clinical trials and observational data from real-life clinical practice provides further evidence of the true value of irbesartan compared to other ARBs in the management of hypertension.



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• Education and Appointments

1993	College of Medicine, Korea University	M.D.
2005	Postgraduate School, College of Medicine, Korea University	Ph.D
2008-2009	Korean Diabetes Association	Senior Vice-Secretary General
2007-present	Editorial board, Endocrinology and Metabolism	Member
2010-present	Editorial board, World Journal of Diabetes	Member
2010-present	Division of Endocrinology and Metabolism, Internal Medicine Department, College of Medicine, Korea University	Section Chief
2011-present	Clinical Research Management, Korea University Clinical Trial Center	Director

• Research Interests

Major: clinical diabetes, clinical trials and epidemiologic study

His clinical activities are mainly directed toward clinical diabetes, clinical trials and epidemiologic study. Now, he is a principal investigator of a very unique immigrant study named North Korea Refugees in South Korea (NORNS) Study. The purpose of this study is to find out the prevalence and the epidemiological causes of various life-style related disease, such as diabetes and metabolic syndrome in this immigrant cohort. His work has been published widely in noted International and Korean medical journals. As the principal investigator and co-investigator for lots of multinational studies evaluating oral anti-diabetic agents, his research interests are extended to inflammatory markers and the array of complications associated with type 2 diabetes and metabolic disorders.

What is your choice for glycemic control? proven or new

Sin Gon Kim

Korea University, Korea

Advances in the therapy of type 2 diabetes mellitus (DM) have generated oral glucose-lowering agents that target different pathophysiologic processes in type 2 DM. Based on their mechanisms of action, glucose-lowering agents are subdivided into agents that increase insulin secretion, reduce glucose production, increase insulin sensitivity, and

enhance GLP-1 action. It is also possible to classify these drugs into the proven or new. In this lecture, I would like to summarize and compare the strength and weakness of the proven (esp, sulfonylurea and metformin) or new drugs (esp, incretin related drugs).



Giuseppe M.C. Rosano

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• Education and Appointments

1988	University of Rome "La Sapienza" with full honors	MD in Medicine and Surgery
1992	University of Rome "La Sapienza" with full honors	Specialization in Cardiology
1997	University of London	PhD in Medical Sciences
1990-1994	Royal Brompton Hospital, London	Research Registrar
1994-1997	University of Reggio Calabria	Lecturer, Chair of Clinical Pharmacology
1997-2000	Department of Cardiology Istituto H San Raffaele, Milano	Senior Lecturer
2000	Center of Clinical and Experimental Medicine, IRCCS San Raffaele, Roma	Director
2006	Cardiovascular of the European Medicine Agency	Vice Chairman
2007	TUFTS University of Boston, USA	Adjunct Professor in Cardiology
2010	Department of Medical Sciences, IRCCS San Raffaele, Roma	Director

• Research Interests

Major: Cardiology

Cardiovascular Pharmacology, Cardiac metabolism, Cardiovascular disease in the elderly and in women, Cardiovascular effect of sex hormones, Vascular Physiology, Ischemic heart disease, Heart failure

• Brief List of Publications

Author of 4 books and of 26 chapters in books and over 220 publications in peer reviewed Journals

The treatment of atherogenic dyslipidemia in patients with diabetes mellitus

Giuseppe M.C. Rosano

IRCCS San Raffaele, Italy

Patients with type 2 diabetes mellitus have an increased incidence of atherosclerotic cardiovascular disease. This increase is attributable, in part, to associated risk factors, including hypertension and dyslipidemia. The latter is characterized by elevated plasma triglyceride levels, low levels of high-density lipoprotein (HDL) cholesterol, and small, dense low-density lipoprotein (LDL) particles. Although most patients with diabetes have a dyslipidemia characterized by high triglycerides and low HDL (atherogenic dyslipidemia), most doctors will prescribe an agent aimed at reducing LDL and will not pursue any further adjustment of the lipid profile.

Although statins are effective in patients with type 2 diabetes, rates of cardiovascular events remain elevated in such patients even after statin treatment. Fibrate therapy

in patients with type 2 diabetes reduced the rate of coronary heart disease events in the Veterans Affairs HDL Intervention Trial and in patients without evident coronary artery disease in the Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) trial.

Previous fibrate studies in subjects with diabetes did not address the role of such drugs in patients receiving statin therapy. The ACCORD Lipid study showed that in high-risk patients with type 2 diabetes, combination treatment with fenofibrate and simvastatin reduced the rate of cardiovascular events, as compared with treatment with a statin alone.

Therefore, fenofibrate must be considered as a mainstay in the treatment of diabetic patients with atherogenic dyslipidemia.

ORAL PRESENTATIONS

Oral presentation 1. Islet biology & insulin secretion,
[OP1-1~OP1-7] immunology & transplantation
8:30~10:00 11 Nov 2011 (Room 1)

Oral presentation 2. Acute & chronic complication
[OP2-1~OP2-7] 8:30~10:00 11 Nov 2011 (Room 2)

Oral presentation 3. Clinical diabetes & therapeutics (I)
[OP3-1~OP3-7] 8:30~10:00 11 Nov 2011 (Room 3)

Oral presentation 4. Behavioral medicine & education
[OP4-1~OP4-7] 8:30~10:00 11 Nov 2011 (Room 4)

Oral presentation 5. Epidemiology & genetics
[OP5-1~OP5-7] 8:30~10:00 12 Nov 2011 (Room 1)

Oral presentation 6. Insulin action & obesity
[OP6-1~OP6-7] 8:30~10:00 12 Nov 2011 (Room 2)

Oral presentation 7. Clinical diabetes & therapeutics (II)
[OP7-1~OP7-7] 8:30~10:00 12 Nov 2011 (Room 3)

OP1-1 Islet biology & insulin secretion, immunology & transplantation

The incretin effect measured by isoglycemic intravenous glucose infusion in Korean subjects with normal glucose tolerance and type 2 diabetes mellitusTae Jung Oh*, Min Young Kim, Ji Yon Shin,
Kyong Soo Park, Young Min ChoDepartment of Internal Medicine, Seoul National University
College of Medicine, Seoul, Korea

Objective The incretin effect is decreased in patients with type 2 diabetes (T2D) compared to healthy subjects, where it is normally responsible for 50-70% of postprandial insulin secretion. There has been no study directly measuring the incretin effect in non-Caucasian subjects. We examined the effect and secretion of incretin hormones in Korean subjects with normal glucose tolerance (NGT) and T2D by oral glucose tolerance tests (OGTTs) and isoglycemic intravenous glucose infusion (IIGI) tests.

Methods Nine healthy subjects with NGT and nine patients with T2D were enrolled. β Cell insulin secretory responses to oral and intravenous glucose stimulus were measured by 75g OGTTs and corresponding IIGI tests. The incretin effect was calculated by difference between incremental area under the curve (iAUC) of insulin during OGTTs and IIGI tests divided by iAUC of insulin during OGTTs. Plasma levels of glucose dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) were measured by ELISA.

Results The insulinogenic index was lower in T2D than NGT (0.10 ± 0.02 vs. 0.46 ± 0.08 , $P < 0.001$) and the insulin resistance assessed by HOMA was higher in T2D (2.64 ± 0.52 vs. 0.83 ± 0.09 , $P = 0.001$). AUC of GIP and intact GLP-1 were comparable between NGT and T2D (69900 ± 10880 vs. 70400 ± 8515 , $P = 0.905$ for GIP; 770.0 ± 16.81 vs. 820.9 ± 66.28 , $P = 0.191$ for GLP-1, $n = 4$ for NGT and $n = 5$ for T2D). The incretin effect was significantly reduced in T2D compared with NGT subjects ($35 \pm 3\%$ vs. $51 \pm 6\%$, $P = 0.02$). The gastrointestinal-mediated glucose disposal was also decreased in T2D ($29.0 \pm 5.8\%$ vs. $62.0 \pm 4.3\%$, $P = 0.002$). The incretin effect was negatively associated with body weight (Spearman correlation $\rho = -0.77$; $P = 0.016$) only in the T2D group.

Conclusion The secretion of GIP and GLP-1 in response to oral glucose is not reduced but the incretin effect is significantly reduced in Korean patients with T2D.

OP1-2 Islet biology & insulin secretion, immunology & transplantation

Preventing the rejection of pancreatic islet grafts using a siRNA-nanoparticle probeAnna Moore*, Ping Wang, Mehmet V. Yigit, Zdravka Medarova,
Alana Ross, Guangping DaiMolecular Imaging Laboratory, MGH/MIT/HMS Athinoula A. Martinos Center for
Biomedical Imaging, Department of Radiology, Massachusetts General Hospital,
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Objective Islet transplantation has recently emerged as an acceptable clinical modality for restoring normoglycemia in Type 1 diabetic patients. In this study we explored the potential of gene therapy utilizing RNA interference for improving islet graft survival after transplantation. We targeted beta-2 microglobulin (B2M) - a key component of MHC class I complex - with the purpose of alleviating immune rejection using siRNA-nanoparticle probe for islet labeling prior to transplantation followed by in vivo monitoring by MR imaging.

Methods A probe (MN-siB2M) consisted of therapeutic (siRNA to human β 2-microglobulin, B2M) and imaging (magnetic nanoparticles, MN for MRI) moieties. In vitro testing included stimulation of the islets for 48 hours with rhIFN γ followed by incubation with the probe. B2M gene silencing and protein expression were determined by RT-PCR and Western blot, respectively. In vivo experiments included transplantation of STZ-induced diabetic B2M deficient NOD/scid mice under the left kidney capsule with MN-B2M labeled human islets followed by adoptive transfer with splenocytes from NOD mice to induce immune rejection. In vivo imaging included longitudinal MRI followed by histology.

Results Delivery of the MN-siB2M probe to the islets resulted in specific reduction of B2M mRNA and protein expression and in preventing CD8+ T cells response in vitro. Transplantation of MN-siB2M-labeled islets in diabetic mice restored normoglycemia. Islet grafts were clearly identified on MR images and demonstrated significantly lower graft volume loss in the animals transplanted with MN-siB2M-labeled islets than in controls.

Conclusion In vitro data demonstrated significant silencing of B2M in human pancreatic islets after labeling with MN-siB2M probe. In vivo MRI revealed that the MN-siB2M probe could notably prevent the islet graft from adoptively transferred immuno-rejection compared to controls. The described siRNA-nanoparticle theranostic imaging strategy could lead to significant improvement of islet survival in vivo after transplantation. This study was supported by NIH 5R01DK080784.

OP1-3 Islet biology & insulin secretion, immunology & transplantation

Acute induction of insulin resistance with glucosamine infusion increases pancreatic islet blood flow in anesthetized rats

Xiang Gao*, Monica Sandberg and Leif Jansson, Leif Jansson

Uppsala University

Objective Conditions with increased demands for insulin secretion, including experimental type 2 diabetes, is associated with increased pancreatic islet blood perfusion. The mechanisms are mainly neural, but also locally formed products, such as nitric oxide, are involved. To what extent high blood flow affects islet function has been difficult to study. The aim of this study was to evaluate if an acutely increased peripheral insulin resistance induces an islet blood flow increase. This would enable us to further study the mechanisms and functional consequences of this on islets.

Methods Anesthetized Sprague-Dawley rats were infused for 2 h with glucosamine (6 mg/kg/h). After it, blood glucose concentrations, serum insulin concentrations and the regional blood flow values were measured. Some rats, both saline- and glucosamine-infused, were given an intravenous injection of 30% D-glucose 117 min after initiating the infusion to induce hyperglycemia (control animals received 1 ml saline). Thus 4 groups of animals were studied: infusion with saline+bolus at 117 min with saline; saline+glucosamine (normoglycemic rats) saline+glucose and glucosamine+glucose (hyperglycemic rats).

Results After 2h blood glucose concentrations were unaffected whereas serum insulin concentrations were almost doubled. Pancreatic islet blood flow, measured with microsphere technique, was higher in glucosamine-infused rats than in control rats, whilst the other organ blood flow values were unaffected. The normal glucose-induced increase in islet blood flow was unchanged after glucose administration, whereas subcutaneous fat blood flow was diminished compared to control animals. The reactivity of islet arterial smooth muscle cells, studied in single-islet perfusion system, was higher in glucosamine-infused rats.

Conclusion Acute glucosamine-infusion leads to insulin resistance and this leads to selective increase in pancreatic islet blood flow. This model may be used to further explore the regulation of islet blood perfusion during impaired glucose tolerance.

OP1-4 Islet biology & insulin secretion, immunology & transplantation

Long-term metabolic consequences of 50% partial pancreatectomy for benign pancreatic tumors with or without islet autotransplantationSang-Man Jin^{1*}, Seung-Hoon Oh³, Soo Kyoung Kim¹,
Hye Seung Jung⁴, Seong-Ho Choi², Jae Hyeon Kim¹,
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Internal Medicine, Seoul National University College of Medicine⁴

Objective Partial pancreatectomy with resection extent of about 50% is increasingly performed for benign pancreatic tumors. We aimed to examine the long-term metabolic consequences of 50% partial pancreatectomy performed for benign pancreatic tumors and to determine if IAT has a preventive role for the development of impaired glucose metabolism.

Methods Thirty-eight patients without pre-operative diabetes underwent 50% partial pancreatectomy for benign tumors with (IAT group, $n = 20$) or without (control group, $n = 18$) islet autotransplantation (IAT). Median follow-up duration was 47 months (range, 2-119). Normal glucose tolerance (NGT) and impaired glucose tolerance (IGT) were determined based on fasting blood glucose level, glucose level at 120 min in the 75g-oral glucose tolerance test (OGTT 120-min glucose) and A1C.

Results The OGTT 120-min glucose levels became ≥ 200 mg/dL in 13 patients (34%). The OGTT 120-min glucose levels were estimated to remain 200mg/dL were old age ($p = 0.02$) and high pre-operative insulin resistance ($p = 0.007$). Among the 24 patients with pre-operative A1C of < 0.05 and INS ($p < 0.05$) index at 2 years after operation were associated with NGT.

Conclusion About 50% partial pancreatectomy has a major long-term metabolic consequence in humans, IAT might have benefit in some patients with 50% partial pancreatectomy in the cases with effective isolation of functionally intact islet.

OP1-5 Islet biology & insulin secretion, immunology & transplantation

Genetic partial insufficiency of mitochondrial respiratory chain (OXPHOS) function in pancreatic beta cells induce islet hyperplasia

Yong Kyung Kim^{1*}, Soyoung Jung Kim¹, Min Jeong Ryu¹, Min Hee Lee¹, Seong Eun Lee¹, Min Jeong Choi¹, Hyo Kyun Chung¹, Koon Soon Kim¹, Hyun Jin Kim¹, Ki Ryang Kweon², Chul-Ho Lee³, Min Ho Shong³

Research Center for Endocrine & Metabolic Diseases, Chungnam National University School of Medicine, Daejeon¹, Department of Biochemistry, Chungnam National University School of Medicine, Daejeon², Animal Model Center, Korea Research Institute of Bioscience & Biotechnology (KRIBB), Daejeon³

Objective The beta cell mass is dynamically regulated by balanced neogenesis, replication and beta cell death. However, the interrelationship between beta cell mass and function of cellular organelle, such as mitochondria is not completely understood. To investigate role of suboptimal mitochondrial respiratory chain function on beta cell mass in islet, we have developed the heterozygote mice with reduced mitochondrial Oxphos function by deleting CRIF1, a critical protein for Oxphos translation and biogenesis in mice.

Methods The mice bearing islet beta cell-specific mitochondrial dysfunction were developed by breeding the CRIF1flox/flox mice with RIP2-Cre mice. We have observed the beta cell mass in these mice fed with normal chow diet (NCD) for 22 weeks. Metabolic phenotypes including body weight, food intake, IPGTT and histomorphological islet analysis were performed at 14, 18, 22 wks.

Results The beta cell-specific homozygote CRIF1 deficiency resulted diabetic hyperglycemia with severe islet failure after 7 wks. However, heterozygote CRIF1-deficient mice showed normal glucose tolerance and insulin secretion until 22 wks similar to wild type mice. Interestingly, CRIF1 heterozygote mice in 18wks revealed marked islet hyperplasia characterized with increased beta cell mass. Islet area of CRIF1 heterozygote mice showed 30% increase at 18 wks, 45% increase at 22 wks.

Conclusion This study suggested that suboptimal mitochondrial Oxphos function in beta cell play a intrinsic intracellular condition that drives and stimulates islet hyperplasia, beta cell proliferation.

OP1-6 Islet biology & insulin secretion, immunology & transplantation

Suppression of Perk improves hyperglycemia and recovers autophagic activity in β cell-specific Atg7 knockout mice

Min Joo Kim*, Shin Hee Hong, Ho Young Kan, Ye Jin Lee, Hakmo Lee, Sung Soo Chung, Kyong Soo Park, Hack C. Jang, Seong Yeon Kim, Hye Seung Jung

Department of Internal Medicine, Seoul National University College of Medicine

Objective Autophagy is an intracellular process that degrades unnecessary organelles and recycles them for cellular homeostasis. Pancreatic β cell-specific Atg7 (autophagy-related 7) knockout mice showed β cell mass reduction and β cell dysfunction, causing insulin deficiency and hyperglycemia. ER (endoplasmic reticulum) has a close relation to autophagy. Autophagy can be activated by ER stress and degrade ER under conditions of severe ER stress. In this study, we generated conditional knockout mice of Perk and Atg7 to investigate whether deficiency of PERK, a constituent of ER stress response, can alter β cell mass and function in β cell-specific Atg7 knockout mice.

Methods β cell-specific Atg7 knockout mice (Atg7^{-/-}) were crossed with Perk^{+/-} mice to generate double-knockout mice. Blood glucose levels and body weight were monitored weekly. Intraperitoneal glucose tolerance test was carried out at 20 weeks of age, and then pancreas tissue was harvested to observe the morphological changes.

Results The additional heterozygous deletion of Perk ameliorated hyperglycemia, increased serum insulin levels, and improved disrupted islet architectures in Atg7^{-/-} mice. Phosphorylation of PERK was significantly decreased in the Perk^{+/-};Atg7^{-/-} mice, compared to that in the Perk^{+/-};Atg7^{-/-} mice. However, the expression of CHOP was not different between the two groups. Accumulation of ubiquitin aggregation and p62, markers for impaired autophagy in β cells, were significantly decreased in the Perk^{+/-};Atg7^{-/-} mice compared to those in the Perk^{+/-};Atg7^{-/-} mice.

Conclusion We demonstrated that suppression of Perk improved the impairment of structure and function of islets in the Atg7^{-/-} mice, resulting in recovery from the hyperglycemia. These

Results were suggested due to the improvement of autophagic activity. Further studies on the relationship between ER stress and autophagy in pancreatic β cells are ongoing.

OP1-7 Islet biology & insulin secretion, immunology & transplantation

Inhibition of fatty acid translocase cluster determinant 36 (FAT/CD36) prevents glucotoxicity in INS-1 cells

Byung Sam Park^{1*}, Sang Hyun Park¹, Hyun Hee Chung¹, Ye Jin Seo², Ji Sung Yoon¹, So Young Park², Yong Woon Kim², Jong Yeon Kim², Hyoung Woo Lee¹, Kyu Chang Won¹

Department of Internal Medicine, Yeungnam University College of Medicine¹, Department of Physiology, Yeungnam University College of Medicine²

Objective The mechanisms of glucotoxicity involve several transcription factors and are, at least in part, mediated by generation of chronic oxidative stress (8). Several recent studies (6,7) supported that the Fatty Acid Translocase Cluster Determinant 36 (FAT/CD36) increases uptake of free fat acid in high glucose state in several cells. Yet, little is known about the relation between glucotoxicity and CD36 in the islets. The purposes of the present study were to determine whether prolonged exposure of pancreatic islets to glucotoxic condition disrupts CD36 or increases CD36, we also wanted to evaluate a role of CD36 in pancreatic islets against glucotoxicity.

Methods We checked intracellular peroxide levels, insulin transcription factors, insulin mRNA, glucose stimulated insulin secretion (GSIS) and CD36 of INS-1 cells. INS-1 cells were transfected of CD36 siRNA for inhibition of CD36 in INS-1 cells.

Results The intracellular peroxide levels of the pancreatic islets were increased in the high glucose (30 mM glucose in INS-1 cell) media compared to 5.6 mM glucose media. The insulin mRNA levels and GSIS were decreased in INS-1 cells exposed to high glucose media compared to 5.6 mM glucose media. The insulin mRNA levels, PDX-1 and GSIS were decreased in INS-1 cells exposed to glucotoxic condition (30 mM glucose) compared to 5.6 mM glucose media. And, at INS-1 cells exposed to glucotoxic condition, CD 36 was significant increased compared to normal glucose media at 12 hours. After transfection of CD36 siRNA, CD 36 was significantly decreased compared to control and insulin mRNA and GSIS were significantly increased compared to without CD36 siRNA in INS-1 cells.

Conclusion These results suggest that the influx of fatty acid to islet at early high glucose condition can be increased by increasing of CD36. Therefore, at islets exposed to high glucose and high fatty acid may be exacerbating beta cell dysfunction via increasing of CD 36 and inhibition of CD36 may be prevent glucotoxicity in INS-1 cells.

OP2-1 Acute & chronic complication

The relationship of the between a venous return time, PWV and physical inactivity duration in T2DM with hemiplegia

Akira Kimura*, Isao Kobayashi

Gunma PAZ college Graduate School off Health Sciences

Objective The purpose of this study was to examine whether the specific physical inactivity Duration hours(PID) changed venous return time (VRT), pulse wave velocity (PWV) of Elderly hemiplegic people in Type2 Diabetes Mellitus during 8 weeks.

Methods A participant: It was experimental study in Randomized Clinical Trial. The participant was chosen among client (n=197) in a nursing home at random. We got an agreement from a participant, male thirty four people. Participants in the intervention group (IG; n=14) was educated the physical activity, in the control group (CG; n=20), only the PA was estimated. Average Age: 73±8y, BW: 51.6±10.3kg, BH: 156.±6cm, HbA1c: 6.5±2.8%(JDS). It Analyses an odds ratio using each PID (14, 16 and 18) hours to PID under 12 hours on frequency of change of VRT, PWV. The participants of positive change in VRT on Back Knee Surface and baPWV were after intervention period.

Results "PID under 12" was normalization more than PID over 14 VRT of the unaffected side after intervention period significantly. p=.029. Odds ratio was 0.182. 95%CI: 0.038 to 0.864. After the period of intervention, ratios other than "PID over 14" did not show normalizing for VRT of "PID under 12" in the unaffected side. Ratios other than "PID over 14" did not show normalizing for VRT of "PID under 12" in the affected side, too.

Conclusion In type2 Diabetes Mellitus in Elderly hemiplegic people in, the effective ratio of physical inactivity duration is under 12 hours, may improve only VRT of unaffected side limb after 8weeks period significantly. An over 12 hours physical activity may only specific influence to affected side limb PWV and VRT. This finding will bring the diabetes education, independent living feasible value for these people.

OP2-2 Acute & chronic complication

The association of urinary tubular markers and urinary angiotensinogen with albuminuria in early nephropathy of type 2 diabetes

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Department of Internal Medicine, School of Medicine, Pusan National University¹, Kim Yong Ki Internal Medicine Clinic²

Objective The aim of this study was to evaluate the association of urinary tubular markers and urinary angiotensinogen with albuminuria in early nephropathy of type 2 diabetes.

Methods Urine levels of tubular markers (kidney injury molecule [KIM]-1, neutrophil gelatinase-associated lipocalin [NGAL], liver-fatty acid-binding protein [L-FABP], and interleukin-18 [IL-18]), and marker of intrarenal renin-angiotensin system (RAS) status (angiotensinogen) were determined in 118 patients with type 2 diabetes mellitus and 25 non-diabetic controls with estimated glomerular filtration rate (eGFR) ≥ 60 ml/min/1.73 m².

Results Urinary levels of KIM-1, NGAL, IL-18 and angiotensinogen were significantly higher in macroalbuminuria group compared with control and normo- and microalbuminuria groups but not significantly different between control and normoalbuminuria group. We could not analysis with values of urinary L-FABP due to large proportion of values below the detectable cut-off range. All urinary tubular markers were positively correlated with urinary angiotensinogen and ACR, respectively. By stepwise multiple regression analysis, the urinary ACR as a dependent variable, and the urinary KIM-1, angiotensinogen, and IL-18 were included in the model (R²=37.9%). After adjusting for clinical parameters, the urinary KIM-1, angiotensinogen, and IL-18 were remained in the model (R²=49.4%).

Conclusion Urinary tubular markers, such as KIM-1, IL-18 were the independent factors affecting albuminuria in early course of nephropathy in type 2 diabetes and might reflect the activation of intrarenal RAS.

OP2-3 Acute & chronic complication

The association of bladder cancer with pioglitazone in Korean subjects with T2D might be different from that in Caucasian population

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Objective Many studies have suggested the increased risk for cancer in subjects with type 2 diabetes (T2D). Growing concerns have issued on increased risk of bladder cancer in diabetic subjects who were on pioglitazone. We investigated the association of bladder cancer with pioglitazone.

Methods Retrospectively, we recruited Severance hospital data of subjects with T2D from November 2005 to June 2011. First, we collected the data on bladder cancer with or without diabetes. Second, we analyzed the kinds of hypoglycemic agents in subjects with T2D. Third, we investigated the prevalence of bladder cancer in subjects with T2D. Finally, we conducted case-control analysis using age, sex-matched exact sampling between diabetic subjects with bladder cancer on pioglitazone-dependent and pioglitazone-independent using Pearson's Chi-square test and Fisher's exact test.

Results Total numbers of diabetic subjects were 53,745. In patients with T2D, bladder cancer was found in 507 subjects. We excluded 176 subjects because they were benign conditions or diagnosed with diabetes following bladder cancer. Of the 6078 diabetic subjects who were on pioglitazone, 63 subjects had history of bladder cancer. Of the 63 subjects, 33 subjects were excluded because they started pioglitazone after diagnosis with bladder cancer. The prevalence of bladder cancer in pioglitazone-dependent subjects was 0.49% (30/6078), and that in pioglitazone-independent was 0.64% (301/47491) (p=0.225). The odds ratio of bladder cancer in pioglitazone-dependent to pioglitazone-independent was 1.286 (95% CI 0.883-1.873).

Conclusion Our study suggests that the association of bladder cancer with pioglitazone in Korean subjects with T2D might be different from that in Caucasian population.

OP2-4 Acute & chronic complication

8-hydroxy-2-deoxyguanosine prevents plaque formation in a partial ligated ApoE knockout mouse, an acute model of atherosclerosis

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Objective Abnormal proliferation and migration of vascular smooth muscle cells (VSMCs) along with extracellular matrix (ECM) accumulation are important pathogenic mechanisms involved in development and progression of atherosclerosis. Inflammation and oxidative stress are known to be related in this process, but an effective therapeutic modality remains elusive. 8-hydroxy-2-deoxyguanosine (8-OHdG), a marker of oxidative stress, has been recently rediscovered to possess anti-oxidative and anti-inflammatory effect.

Methods In this study, we investigated the effects of 8-OHdG in partial carotid ligation model, a more physiologically relevant model of disturbed flow.

Results Partially ligated ApoE knockout mice fed high-fat diet developed an advanced lesion in 2 weeks and orally administered 8-OHdG significantly reduced plaque formation along with reduced superoxide formation, monocyte/macrophage infiltration, and ECM accumulation. Further studies with primary VSMCs showed that 8-OHdG inhibited proliferation, migration, and production of ECM and reactive oxygen species. 8-OHdG ameliorated angiotensin II-induced Rac1 activity and molecular docking study confirmed that 8-OHdG stabilizes Rac1-GEF complex indicating involvement of Rac1 in anti-atherogenic effect of 8-OHdG.

Conclusion Our results showed a novel role of orally active 8-OHdG in suppressing plaque formation and VSMC activation through inhibition of Rac1, which emphasizes a new therapeutic avenue to benefit atherosclerosis.

OP2-5 Acute & chronic complication

NOD2 deficiency enhances neointimal formation in response to vascular injury

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Objective Nucleotide-binding oligomerization domain protein 2 (NOD2) stimulates diverse inflammatory responses resulting in differential cellular phenotypes. To identify the role of NOD2 in vascular arterial obstructive diseases, we investigated the expression and pathophysiological role of NOD2 in a vascular injury model of neointimal hyperplasia.

Methods We first analyzed for neointimal hyperplasia following femoral artery injury in NOD2^{+/+} and NOD2^{-/-} mice. To study the expression of NOD2 in VSMCs, we isolate VSMCs from NOD2^{+/+} and NOD2^{-/-} aorta. The migration and proliferation were investigated in NOD2^{+/+} and NOD2^{-/-} VSMCs. We also characterized the signaling pathways in response to PDGF-BB in NOD2^{+/+} and NOD2^{-/-} VSMCs.

Results We first analyzed for neointimal hyperplasia following femoral artery injury in NOD2^{+/+} and NOD2^{-/-} mice. NOD2^{-/-} mice showed a 2.86-fold increase in neointimal formation that was mainly composed of SM alpha-actin positive cells. NOD2 was expressed in vascular smooth muscle cells (VSMCs) and NOD2^{-/-} VSMCs showed increased cell proliferation in response to mitogenic stimuli, PDGF-BB or fetal bovine serum (FBS), compared with NOD2^{+/+} VSMCs. Furthermore, NOD2 deficiency markedly promoted VSMCs migration in response to PDGF-BB and this increased cell migration was attenuated by a PI3 kinase inhibitor. However, PKC and JNK inhibitors exerted negligible effects. Moreover, muramyl dipeptide-stimulated NOD2 prevented PDGF-BB-induced VSMCs migration.

Conclusion Functional NOD2 is expressed in VSMCs, and NOD2 deficiency promoted VSMCs proliferation, migration, and neointimal formation after vascular injury. These results provide evidence for the involvement of NOD2 in vascular homeostasis and tissue injury, serving as a potential molecular target in the modulation of arteriosclerotic vascular disease.

OP2-6 Acute & chronic complication

Effect of 6-gingerol on vascular inflammation and atherosclerosis associated with diabetes mellitus

So Hun Kim*, Qing Song Jin, Hyun Ae Lim, Seung Youn Lee, Seong Bin Hong, Yong Seong Kim, Moonsuk Nam

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Objective 6-gingerol, a major component of ginger has been shown to have anti-oxidative and anti-inflammatory effects, but there are no data evaluating the effect of 6-gingerol on endothelial cell dysfunction and the development of atherosclerosis associated with diabetes. In this study, we examined whether 6-gingerol has protective effects on hyperglycemia and cytokine induced endothelial cell activation and atherosclerosis.

Methods Intracellular ROS, the expression of redox enzymes, inflammation related-signals and monocyte adhesion to endothelial cells were examined after incubation of HUVECs in hyperglycemia(25.2 mM glucose) or TNF alpha with or without 6-gingerol. A total of 28 B6.KORApoe^{sh1} mice were allocated into four groups: Apoe non-diabetic placebo group (AP group, n=6), Apoe non-diabetic 6-gingerol treated group (AG group, n=6), Apoe diabetic placebo group (ASP group, n=8) and Apoe diabetic 6-gingerol treated group (ASG group, n=8). 10 mg/kg/d of 6-gingerol was given orally for the AG and ASG group for 8 weeks and quantification of atherosclerotic lesions in the mouse aorta was done.

Results 20uM 6-gingerol was able to decrease lipid peroxidation increased by hyperglycemia. Reactive oxygen species formation induced by hyperglycemia or TNF- α was decreased by 6-gingerol. 6-gingerol was not able to increase the level of Cu/ZnSOD, MnSOD, catalase, glutathione peroxidase(GPx), glutathione-S-transferase(GST). 6-gingerol prevented I κ B degradation and reduced NF κ B nuclear translocation induced by hyperglycemia and TNF alpha in HUVECs. 6-gingerol was able to decrease the expression of ICAM-1 and VCAM-1 and monocyte adhesion to endothelial cells induced by glucose and TNF alpha. The severity of aortic atherosclerosis was decreased by 6-gingerol in both non diabetic and diabetic Apoe mice (AP 24.7% vs. AG 18.2%, p=0.003, ASP 29.5% vs. ASG 21.9%, p=0.02).

Conclusion 6-gingerol has protective effects on endothelial activation and atherosclerosis associated with diabetes mellitus making it a possible therapeutic approach to this disorder.

OP2-7 Acute & chronic complication

Vaspin protects vascular endothelial cells against free fatty acid-induced apoptosis through a phosphatidylinositol 3-kinase/Akt pathwayChang Hee Jung^{1*}, Woo Je Lee¹, Jenie Yoonoo Hwang¹, So Mi Seol², Yun Mi Kim², Yoo La Lee², Joong-Yeol Park¹Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Asan Institute of Life Sciences, University of Ulsan College of Medicine, Asan Medical Center²

Objective Vaspin, an adipocytokine recently identified in a rat model of type 2 diabetes, has been suggested to have an insulin-sensitizing effect. However, the exact mechanism underlying this action has not been fully elucidated. Furthermore, the specific function of vaspin is largely unknown, especially in vascular cells. We examined whether vaspin affects the insulin-signaling pathway in cultured endothelial cells and is capable of preventing free fatty acid (FFA)-induced apoptosis in endothelial cells through its insulin sensitizing effect, specifically, through its stimulatory effect on PI3-kinase/Akt signaling pathways.

Methods We used human aortic endothelial cells (HAECs) and linoleic acid was used as the representative FFA. Analyses of apoptosis were performed using various methods including cell death ELISA, caspase 3 assay, Annexin V FACSscan, TUNEL analysis and Western blotting for cleaved caspase 3, cleaved PARP and Bcl-xL.

Results Vaspin significantly increased Akt phosphorylation and prevented the impairment of Akt phosphorylation by linoleic acid (LA) in insulin-stimulated endothelial cells, which effects were abolished by pretreatment with the PI3-kinase inhibitor, wortmannin. Moreover, pretreatment with vaspin prevented LA-induced apoptosis in insulin-stimulated endothelial cells; this anti-apoptotic effect of vaspin was also eliminated by pretreatment with wortmannin.

Conclusion The present study indicates that vaspin protects vascular endothelial cells from FFA-induced apoptosis through upregulation of the PI3-kinase/Akt signaling pathway. Our study is the first to demonstrate that vascular cells can be targets of vaspin. Our results further suggest that vaspin could have beneficial effects on the atherosclerosis.

OP3-1 Clinical diabetes & therapeutics (I)

The effects of caloric restriction on fetuin-A and cardiovascular risk factors in rats and humans: a randomized controlled trialSae Jeong Yang^{1*}, Kyung Mook Choi¹, Hee Jung Ahn², So Young Lee¹, Baek-Hui Kim³, Kyeong Jin Kim¹, Sun Hwa Kim¹, Jae Hee Ahn^{1,4}, Ho Cheol Hong¹, Hae Yoon Choi¹, Myoung Jin Cho¹, Yoonjung Kim^{1,5}, Chai Ryoung Eun¹, Joohyung Kim¹, Hye Jin Yoo¹, Hee Young Kim¹, Ji A Seo¹, Sin Gon Kim¹, Nan Hee Kim¹, Sei Hyun Baik¹, Dong Seop Choi¹, Kyung Wan Min⁴Division of Endocrinology and Metabolism, Department of Internal Medicine, College of Medicine, Korea University¹, Diabetes Center, Eulji Hospital², Department of Pathology, College of Medicine, Korea University³, Eulji University School of Medicine⁴

Objective The secreted liver protein fetuin-A is associated with insulin resistance, metabolic syndrome, type 2 diabetes, and atherosclerosis. We examined the effect of caloric restriction (CR) on fetuin-A level and concomitant changes in conventional and novel cardiovascular risk factors in rats and humans.

Methods The effects of CR on hepatic steatosis and fetuin-A mRNA expression were evaluated in obese OLETF rats and control LETO rats. We performed a randomized controlled clinical trial to examine the circulating fetuin-A level and cardiovascular risk parameters including visceral fat area (VFA), atherogenic lipid profile, inflammatory markers, adipokines, brachial artery endothelial function, and carotid intima-media thickness (CIMT) in 76 overweight women with diabetes before and after 12 weeks of CR.

Results CR significantly reduced hepatic steatosis and fetuin-A expression, as well as weight, glucose, and triglyceride level, in OLETF rats. Furthermore, in human subjects, circulating fetuin-A levels were significantly decreased after 12 weeks of CR, accompanied by improvements in VFA, blood pressure, glucose, lipid profiles, and liver function. The CR group also showed significantly decreased apolipoprotein B, leptin, and insulin resistance compared to those in the control group, although endothelial function and CIMT were not different. Multiple regression analysis showed that the changes in fetuin-A were independently associated with changes in hsCRP, adiponectin, and HOMA-IR, in addition to CR (R²=24.6%).

Conclusion CR significantly reduced the hepatic expression of fetuin-A and its circulating levels and improved several cardiovascular risk factors in obese rats and humans with type 2 diabetes.

OP3-2 Clinical diabetes & therapeutics (I)

Increased selenoprotein P levels in subjects with visceral obesity and non-alcoholic fatty liver disease

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Objective Selenoprotein P (SeP) has recently been reported as a novel hepatokine that regulates insulin resistance and systemic energy metabolism in rodents and humans. We explored the associations between SeP, visceral obesity, and non-alcoholic fatty liver disease (NAFLD).

Methods We examined serum SeP concentrations in subjects with increased visceral fat area (VFA) or liver fat accumulation measured using computed tomography (CT). Our study subjects included 120 non-diabetic individuals selected from participants of the Korean Sarcopenic Obesity Study (KSOS). In addition, we evaluated the relationship between SeP and cardiometabolic risk factors, including homeostasis model of insulin resistance (HOMA-IR), high sensitivity C-reactive protein (hsCRP), adiponectin values, and brachial-ankle pulse wave velocity (baPWV).

Results Subjects with NAFLD showed increased levels of HOMA-IR, hsCRP, VFA, and several components of metabolic syndrome and decreased levels of adiponectin and HDL-cholesterol compared to those of controls. Serum SeP levels were positively related to VFA, hsCRP, and baPWV and negatively related to the liver attenuation index. Not only subjects with visceral obesity but also those with NAFLD exhibited significantly increased SeP levels (P<0.001). In multiple logistic regression analysis, the subjects in the highest SeP tertile showed a higher risk for NAFLD compared to those in the lowest SeP tertile, even after adjusting for potential confounding factors (odds ratio=7.48, 95% CI=1.72-32.60, P=0.007).

Conclusion Circulating SeP levels are increased in subjects with NAFLD as well as in those with visceral obesity and may be a novel biomarker for NAFLD.

OP3-3 Clinical diabetes & therapeutics (I)

Association of adiponectin, resistin, and vascular inflammation analysis with 18F-fluorodeoxyglucose positron emission tomography

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Objective Adiponectin and resistin are adipokines that are linked to obesity, inflammation, and atherosclerosis. 18F-Fluorodeoxyglucose (FDG) positron emission tomography is a promising imaging technique that can be used to evaluate vascular inflammation.

Methods We measured adiponectin and resistin levels, as well as traditional cardiovascular risk factors, in 60 obese subjects and 60 nonobese controls. In addition, we compared carotid intima-media thickness and target-to-background ratio (TBR) measured using 18F-fluorodeoxyglucose-positron emission tomography/computed tomography.

Results The mean TBR values were significantly higher in the obese group compared with normal subjects, although their mean carotid intima-media thickness levels were not significantly different. Serum adiponectin levels showed a significant negative correlation with mean TBR values ($r=-0.215$, $P=0.020$), whereas resistin levels were positively correlated with mean TBR values ($r=0.214$, $P=0.021$). Multiple linear regression analysis showed that mean TBR values were independently associated with body mass index, high-sensitivity C-reactive protein, and resistin levels ($R^2=0.308$).

Conclusion Adiponectin and resistin may be useful as biomarkers to reflect vascular inflammation. In particular, resistin levels were independently associated with vascular inflammation even after adjusting for other cardiovascular risk factors.

OP3-4 Clinical diabetes & therapeutics (I)

Clinical characteristics of sleep disorders in patients with type 2 diabetes

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Objective Sleep disturbances are very common in modern society. The aim of this study was to investigate the prevalence, and clinical features of sleep disorders in type 2 diabetic patients.

Methods Study subjects were recruited from the two out-patient diabetes clinics of University hospitals. To investigate the prevalence of sleep disorders, questionnaires for insomnia, restless leg syndrome, sleep apnea subscale of Sleep Disorders Questionnaire (SDQ-SA), Pittsburgh Sleep Quality Index (PSQI), Korean version of Epworth Sleepiness Scale (K-ESS), and Korean version of Beck Depression Inventory (K-BDI) were surveyed to 614 type 2 diabetic patients.

Results There is 381 male (62.1%) patients. Patients had a mean age of 59.7 ± 11.1 years, with a mean body mass index (BMI) of 24.9 ± 3.4 kg/m². The mean duration of diabetes was 10.5 ± 9.1 years. The questionnaires showed insomnia occurred in 48.2% and excessive daytime sleepiness occurred in 8.5% of the patients. Forty-nine percent of type 2 diabetic patients were poor sleepers. Restless leg syndrome was reported in 15.6% and depressed mood was observed in 28.5% of type 2 diabetic patients. Insomnia was associated with age, female sex, caffeine intake and duration of diabetes. Restless leg syndrome was associated with female sex and duration of diabetes. Poor sleep was associated with female sex, and duration of diabetes. The duration of diabetes more than 15 years was associated with higher incidence of insomnia, poor sleep and depressed mood compared to the duration of diabetes less than 5 years. The highest BMI group (≥ 30) had a more sleep apnea compared to the lowest BMI group (< 20).

Conclusion We found that the sleep disorders were very common in type 2 diabetic patient. Awareness and identifying the sleep complaints in type 2 diabetic patients is necessary to improve their quality of life.

OP3-5 Clinical diabetes & therapeutics (I)

The increment of postprandial TG levels in Korean subjects with prediabetes and type 2 diabetes according to their metabolic syndrome status

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Objective Diabetic dyslipidemia, elevated TG and decreased HDL, is tightly linked to characteristics of metabolic syndrome (MetS). We already showed that postprandial TG (ppTG) was strongly correlated to fasting TG. Furthermore, ppTG was more strongly associated with insulin resistance than fasting TG. Because Korean T2D showed somewhat different pathogenesis (i.e, insulin deficiency is a strong contributing factor than insulin resistance), it would be worthwhile investigation determining the factors which may contribute to the increment of triglycerides after standardized diet based on metabolic status.

Methods To investigate the relationship between ppTG and other metabolic parameters, the authors analyzed plasma TG levels and various demographic and metabolic parameters in 171 newly diagnosed, drug naïve prediabetes and diabetes after ingestion of a standardized liquid meal formula (total 500 kcal, 17.5 g fat, 68.5 g carbohydrate, and 17.5 g protein).

Results According to the presence of MetS, diabetic subjects were divided into two subgroups. Diabetic subjects with metabolic syndrome (MetS(+)) seemed to have higher fasting TG, ppTG and delta TG but there were no statistical significance. Pearson's correlation method showed that both fasting TG and ppTG were strongly correlated to in both groups. Diabetic subject without metabolic syndrome (MetS(-)) HOMA-IR was correlated with both fasting TG and ppTG but not in MetS(+) group. Multivariate analysis showed HOMA-IR was predictable factor for ppTG in MetS(-) group but not in MetS(+) group.

Conclusion We postulated that TG increment in postprandial period might be influenced by the additional effects of insulin resistance and central obesity. The influence of the factors for Metabolic syndrome were different according to their metabolic syndrome status, not MetS(+) group but MetS(-) group was associated with insulin resistance.

OP3-6 Clinical diabetes & therapeutics (I)

Adequate glycemic control in intensive care unit

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Objective Hyperglycemia associated with insulin resistance is common in critically ill patients, even those who have not previously had diabetes. Factors contributing to hyperglycemia in critical illness include the release of stress hormones and exogenous administration, such as epinephrine and cortisol. Hyperglycemia has been linked with worse outcomes in patients not known to have diabetes who are admitted to the intensive care unit (ICU). But, trials examining the effects of tighter glucose control have had conflicting results. Although some guidelines suggested a target levels are generally between 140 and 180 mg/dl, it remains unclear whether intensive glucose control improves the prognosis of patients in a ICU.

Methods We conducted an observational study of 1224 patients (male: 798, female: 426) admitted to the ICU, from 1 January 2009 to 31 December 2010, compared mortality and morbidity according to serum glucose.

Results Among 1224 patients, 319 patients were diagnosed with diabetes and 296 patients were dead in ICU, 557 patients received intravenous insulin therapy and 118 received oral hypoglycemic agents. The outcome variables between diabetes and non diabetes were no significant difference. Serum glucose levels were categorized into quartiles (group1: < 100 mg/dl, group2: 100~199 mg/dl, group3: 200~299 mg/dl, group4: ≥ 300 mg/dl). Mortality between groups showed significant low mortality in group1 and group2 ($p < 0.05$) compared with group3. The relationship between ICU outcome and the level of hemoglobin A1c were no significant.

Conclusion It is suggested that, adequate (100~199mg/dl) blood glucose control reduce morbidity and mortality among patients in the ICU. Large multicenter trials and prospective studies are needed to confirm these results.

OP3-7 Clinical diabetes & therapeutics (I)

Higher morning to evening ratio in total dose of twice daily biphasic insulin analogue might be effective in achieving glucose control in patients with poorly controlled type 2 diabetes

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Objective The aims of study are to investigate not only the glucose-lowering effectiveness of twice-daily premixed insulin lispro 25 (Mix25), but also the optimal divided ratio of total Mix25 dose in Korean patients with poorly controlled type 2 diabetes.

Methods In this retrospective study, we retrieved subjects who were on intensive insulin therapy with twice-daily Mix25 regimen for at least 24 weeks. Changes of HbA1c and other clinical and laboratory parameters were evaluated. The subjects were divided into two groups according to dose ratio of pre-breakfast to pre-dinner insulin at 24 weeks: Group I, pre-breakfast:pre-dinner insulin dose ratio= 40:60~55:45; Group II, 56:44~75:25.

Results A total of 143 subjects were ultimately analyzed in this study. There were significant reductions in HbA1c at 12 and 24 weeks ($-2.4 \pm 2.0\%$ and $-2.3 \pm 2.2\%$, respectively, both $p < 0.001$) and 34% of patients had reached the target glycemic goal (HbA1c < 7%) after 24 weeks of twice-daily Mix25 treatment. Compared to Group I, Group II showed significant reductions in postprandial glucose at 12 weeks, and HbA1c levels at 24 weeks (Group I vs. Group II, 209.2 ± 73.2 mg/dl, $7.7 \pm 1.4\%$ vs. 174.2 ± 81.1 mg/dl, $7.2 \pm 1.0\%$, respectively). Of the independent factors, duration of diabetes and history of sulfonylurea use were independently associated with achieving target HbA1c levels less than 7%.

Conclusion Twice-daily Mix25 is an effective option for Korean type 2 diabetic subjects with uncontrolled hyperglycemia. Higher pre-breakfast/pre-dinner dose ratio (56:44~75:25) might be taken into consideration as an initial protocol to accomplish better glycemic control in twice-daily Mix25.

OP4-2 Behavioral medicine & education

Development and evaluation of an integrated self-management program for women with gestational diabetes mellitus

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Objective The purpose of the study was to develop an integrated self-management program which could cover expected weaknesses from separately controlled obstetrics and internal medicine departments and evaluate the positive effects of each on self-management, glycemic control, and maternal identity in women with gestational diabetes mellitus (GDM).

Methods The integrated self-management program was developed to synthesize contents and methods in the management of glycemic control and maternal identity approach. The study period for this program was five weeks and included small group meetings and supportive counseling by telephone. The program was conducted 3 out of 5 times for 1 hour small group meeting and 2 out of 5 times by telephone-counseling. The integrated self-management program was verified by an expert panel. A total of 55 GDM women were recruited from Cheil General Hospital, Seoul, Korea and were assigned to an experimental (n=28) or control group (n=27). The participants were 24-30 weeks pregnant women who had been diagnosed as GDM as of July 30, 2010. Exclusion criteria were a history of diabetes mellitus not related to pregnancy or the presence of high risk disease such as pregnancy induced hypertension. The study was a quasi-experimental pre-post design. Self-management and maternal identity were measured before and after the study. Glycemic control was measured by 2-h postprandial glucose and HbA1c. Self-management and maternal identity were measured by structured questionnaires. χ^2 -tests and Mann-Whitney U tests were used to compare the differences between the two groups.

Results Although there was no significant reduction in HbA1c ($z = -1.179$, $p = .238$), there were statistically significant increases in self-management ($z = 3.802$, $p < .001$) and maternal identity ($z = 4.489$, $p < .001$), and decreased 2-h postprandial glucose levels ($z = -2.434$, $p < .015$) in the experimental group compared to control group.

Conclusion These findings suggest that participation in an integrated self-management program for GDM women improves self-management, maternal identity, and glycemic control. Further studies are needed to identify the effects of an integrated self-management program on pregnancy and neonatal outcomes, and to suggest repeated research for pregnant women to suggest care of GDM management.

OP4-1 Behavioral medicine & education

Prevalence of metabolic syndrome and cut-off values according to the physical fitness levels in Korean adult males

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Objective The purpose of this study was to find out the odds ratio of the metabolic syndrome and the associated cut-off values of the physical fitness factors (VO2max, grip strength, flexibility, lower extremity power, balance) of the adult males.

Methods This study subjects consisted of 5,525 (20-30¹=572; 40-50¹=4,090; 60-70¹=863) participants, aged between 20 to 79. 5,525 subjects were tested for the cardiorespiratory fitness (VO2max), grip strength, flexibility, lower extremity power (vertical jump), balance as well as blood pressure and waist circumference. Metabolic syndrome was diagnosed based on the diagnostic criteria of WHO and ATPIII. Logistic regression analysis was used in order to calculate the metabolic prevalence rate by odd ratio for the ages 20 to 30, 40 to 50, and 60 to 70. The cut off values of such groups were analyzed via ROC curves.

Results For the participants aged 20 to 30, the prevalence rate of the metabolic syndrome increased by 5.9 folds when VO2max was lower than 28.6 ml/kg/min, 3.8 folds when lower extremity power was lower than 42.0 cm, 2.4 folds when balance was lower than 18.2 seconds. For 40 to 50, the prevalence rate of the metabolic syndrome increased by 1.7 folds when VO2max was lower than 27.9 ml/kg/min, 1.3 folds when flexibility was lower than 1.0 cm, 1.5 folds when lower extremity power was lower than 36.0 cm, and 1.3 folds when balance was lower than 8.0 seconds. For 60 to 70, the prevalence rate of the metabolic syndrome increased by 1.9 folds when flexibility was lower than -7.0 cm, 1.7 folds when lower extremity power was lower than 33.0 cm, 2.1 folds when balance was lower than 8.0 seconds.

Conclusion Therefore, participating in the multiple exercise regime to increase the various fitness factors may help decrease the prevalence of metabolic syndrome.

OP4-3 Behavioral medicine & education

Factors influencing physical activity behavior among Iranian women with type 2 diabetes using the extended theory of reasoned action

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Objective Findings of most studies indicate that the only way to control diabetes and prevent its debilitating effects is continuous performance of self-care behaviors. Among these behaviors, physical activity is one of the non-pharmacological methods that affect diabetes treatment and because of its positive effects on diabetic patients, nowadays, it is increasingly considered by researchers and practitioners. This study aimed at determining factors influencing physical activity among diabetic women, using the extended theory of reasoned action in Iran.

Methods An eligible sample of 352 women with type 2 diabetes, referring to a Diabetes Clinic in Khoy, Iran, participated in the study. Appropriate instruments were designed to measure the desired variables (knowledge of diabetes, personal beliefs, subjective norms, perceived self-efficacy, behavioral intention and physical activity behavior). Reliability and validity of the instruments were examined and approved. Statistical analyses of the study were conducted by inferential statistical techniques (independent t-test, correlations and regressions) in SPSS package.

Results The findings of this investigation indicated that, among the constructs of the model, self-efficacy was the strongest predictor of intentions among women with type 2 diabetes that both directly and indirectly, affects physical activity. In addition to self-efficacy, diabetic patients' physical activity also is influenced by other variables of the model and sociodemographic factors.

Conclusion Our findings suggest that the high ability of the theory of reasoned action extended by self-efficacy in forecasting and explaining physical activity can be a base for educational intervention. Thus, for improving diabetics' physical activity behavior and finally controlling the disease, applying educational interventions based on the proposed model is necessary.

OP4-4

WITHDRAWN

OP4-6 Behavioral medicine & education

The effects of a lifestyle intervention program according to implementation of session goal in Korean male with metabolic syndrome

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Objective This study examined how the implementations of session goal contribute to subject's outcomes after a lifestyle intervention program for 12 weeks in males with metabolic syndrome (MetS).

Methods The intervention study on 30 male workers aged 36-58 years (mean aged: 47.2±6.6) with MetS were participated in this study from March to June, 2011. The intervention program conducted 5 face-to-face counseling during the 12 weeks program. The subjects were divided into three groups according to their implementation of session goal levels: Low-implementation group (LI, 70%). Anthropometric parameters, biochemical parameters and nutrient intakes were examined at baseline and at the end of the 12 weeks intervention program.

Results After 12 weeks intervention program, diastolic blood pressure (DBP), waist, intakes of energy, fat and sodium and the number of components of MetS were significantly decreased (P<0.05). According to implementation goal levels, HDL, LDL, percent of body fat, systolic blood pressure (SBP) and DBP were significantly decreased in the HI group (P<0.05). In LI group, total cholesterol (TC) was significantly increased, however DBP and intakes of protein and sodium were significantly decreased (P<0.05). Especially, the HI group had a greater levels of changes in TC, HDL, LDL, SBP, DBP and intakes of fiber compared to the LI and MI group (P<0.05). The number of components of MetS were significantly decreased in HI group (P<0.05), but the change levels were not significantly different among three groups.

Conclusion The lifestyle intervention program is effective in decrease risk of MetS, especially in the high implementation group. Therefore, we suggest that it is necessary to set up a suitable disease session goals at application of protocol and a systematic strategy for increasing implementation level.

OP4-5 Behavioral medicine & education

Dietary pattern consisting of a variety of foods reduces the risk of metabolic syndrome

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Objective To identify major dietary patterns among Korean adults and assess its associations with the development of metabolic syndrome (MS).

Methods A prospective cohort study included 5,251 Koreans aged 40 to 69 years participating in the Korean Genome Epidemiology Study. At baseline, all individuals were free of MS and reported having no history of cardiovascular disease, cancer, diabetes mellitus, hypertension, and dyslipidemia. Incident MS cases were ascertained through biennial examinations during a follow-up period from April 17, 2003 to March 12, 2009. Dietary patterns and its factor loading scores were generated by factor analysis using the dietary information on a food frequency questionnaire. We used pooled logistic regression models to estimate multivariate relative odds (RO) and 95% confidence interval (CI) for the associations of factor loading scores and average daily intake of specific foods with MS risk.

Results Two major dietary patterns, so-called "varied diet" and "unvaried diet", were identified. After controlling for potential confounding factors, factor loading scores for "varied diet", which was contributed to by fish, seafood, vegetables, grains, legumes, meat and poultry, fruits, dairy products, and nuts, were inversely associated with MS risk (p-value for trend: <0.05) while those for "unvaried diet" had no association. Individuals in the highest quintile of the "varied diet" scores showed 0.76 (0.60-0.97) as a multivariate RO (95% CI) of MS risk compared with those in the bottom quintile. In analysis for MS components, such beneficial effects of eating "varied diet" were found to be driven by inverse associations with abdominal obesity, low HDL-cholesterol, and high fasting glucose. Consumption of dairy products and nuts was inversely associated with MS risk (p-value for trend: <0.01 and <0.001, respectively).

Conclusion Data from present study may support for the fundamental concept across dietary guidelines worldwide to recommend a variety of foods for protection of MS.

OP4-7 Behavioral medicine & education

The study on the carbohydrate consumption of Korean T2DM patients

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Objective The amount of carbohydrate intake has influenced on glycemic control of diabetic patient. There is needed to pay special attention to the CHO intake in Koreans those who consumed higher CHO than in western populations. We examined the CHO consumption of Korean adults with T2DM.

Methods Subjects were 300 adult T2DM patients (male159, female141). We were taken 3-day food diary and collected anthropometric & biochemical data. We divided the subjects to 4 groups based on quartile of CHO composition and compared the characteristics.

Results The mean CHO composition of total subjects was 60.5±7.3%. The range of CHO composition of 2nd quartile was similar to the recommendation of Korean Diabetic Association (quartile1 ≤55.5%, quartile2 55.6-60.6%, quartile3 60.7-64.6%, quartile4 ≥64.7%). The proportion of female was higher than that of male in the highest quartile. The ranking order of food groups contributing CHO intake of total subjects was grains, vegetables, fruits, potatoes/starch & sugars. There were significant differences in ranking order according to group. Food group ranked to 2 was vegetables in quartile1 & quartile2, but was fruits in quartile3 & quartile4. The % CHO derived from grains were higher in quartile3 & quartile4 compared with quartile1 & quartile2. Also the % CHO derived from potatoes/starch was higher in quartile4 compared with the other groups. FBS & HbA1c level of quartile1 were lower than those of the other groups although there were no significant differences. Serum TG level of quartile3 was significantly higher compared with the other groups. Total cholesterol level of quartile1 & quartile3 was significantly higher compared with the other groups.

Conclusion In this study, we found there were differences in CHO consumption of T2DM patients. These results suggest that it is important to give attention to CHO consumption in nutrition counseling. Further study will be needed on CHO consumption in Korean T2DM patients.

OP5-1 Epidemiology & genetics

Arsenic exposure and prevalence of diabetes mellitus in Korean adults: Analyses based on the Fourth Korea National Health and Nutrition Examination Survey (KNHANES), 2008-2009Sang Youl Rhee^{1*}, Sang Ouk Chin¹, Moon Chan Choi¹, Suk Chon¹, You-Choel Hwang¹, In-Kyung Jeong¹, Seungjoon Oh¹, Kyu Jeung Ahn¹, Ho Yeon Chung¹, Sung Woon Kim¹, Jin-Woo Kim¹, Young Seol Kim¹, Jeong-taek Woo¹Department of Endocrinology and Metabolism, Kyung Hee University School of Medicine¹, Research Institute of Endocrinology, Kyung Hee University²**Objective** A causal relationship between environmental, low level arsenic exposure and the incidence of diabetes mellitus (DM) has been suggested, but little research has been conducted worldwide.**Methods** We analyzed the glucose tolerance status and creatinine adjusted urine total arsenic concentrations in 3,602 subjects ≥ 20 years who were registered for the Korea National Health and Nutrition Examination Survey, 2008-2009.**Results** Various demographic parameters such as gender, age, resident area, smoking, alcohol, occupation, and serum mercury concentration were associated with urine arsenic concentrations. After adjusting for these variables as confounders, urine arsenic concentrations in subjects with DM were significantly higher than those in subjects with normal glucose tolerance and those with impaired fasting glucose ($p < 0.001$). Compared with the lowest ($< 70.68 \mu\text{g/g}$ creatinine) quartile, the odds ratios and 95% confidence intervals for DM were 1.105 (0.727-1.678), 1.417 (0.944-2.125), and 1.558 (1.030-2.358) for urine arsenic concentrations 70.68 to < 117.71 , 117.71 to < 193.44 , and $\geq 193.44 \mu\text{g/g}$ creatinine, respectively, after multiple adjustment. Furthermore, the urine total arsenic concentration was inversely associated with the insulin secretion index, HOMA2 %B ($\beta = -0.033$, $p = 0.032$).**Conclusion** The findings suggest that environmental low level arsenic exposure, possibly involving beta cell dysfunction, is associated with an increased risk for DM in the Korean population.

OP5-2 Epidemiology & genetics

The value of the apolipoprotein B/A1 ratio in the diagnosis of metabolic syndrome in a Korean populationMin-Jung Lee^{1*}, Jenie Yoonoo Hwang¹, Ji Hee Yu¹, Mi Seon Shin¹, Sung Jin Bae², Joong-Yeol Park¹, Hong-Kyu Kim², Woo Je Lee¹Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Department of Health Screening and Promotion Center, University of Ulsan College of Medicine, Asan Medical Center²**Objective** The ratio of apolipoprotein B (apoB) to apolipoprotein A1 (apoA1) has been reported to be associated with the metabolic syndrome (MetS) and to be a useful biomarker for future cardiovascular disease (CVD). However, the optimal apoB/A1 cut off for determining subjects with MetS has remained undetermined. We therefore assessed whether the apoB/A1 ratio can be used as an indicator of MetS and determined its optimal cut off for identifying subjects with MetS in a Korean population.**Methods** This study was a cross-sectional study. We collected the data regarding to conventional risk factors and serum levels of apoB and apoA1 in 10,940 subjects who participated in a routine health screening examination.**Results** After adjustment for confounding variables, the likelihood of MetS was significantly higher in the highest than in the lowest apoB/A1 quartile, both in men (odds ratio [OR]= 4.07, 95% CI=3.42-4.84) and women (OR=8.41, 95% CI=5.85-12.08). The optimal apoB/A1 ratio for detection of MetS in men was 0.65, with a sensitivity of 63.5% and a specificity of 61.3% (area under the curve=0.67, 95% CI=0.66-0.68, $P < 0.001$), whereas the optimal ratio in women was 0.62, with a sensitivity of 67.9% and a specificity of 61.9% (area under the curve=0.70, 95% CI=0.69-0.71, $P < 0.001$).**Conclusion** The apoB/A1 ratio is independently associated with MetS in a Korean population. Ratios > 0.65 in men and > 0.62 in women are markers of MetS, independent of conventional risk factors. Measurements of apoB/A1 ratios may be particularly useful for determining MetS risk in clinical practice.

OP5-3 Epidemiology & genetics

The target level of A1c in type 2 diabetes patients with medical disease might not be less than 7% of HbA1cSun Ok Song^{1*}, Kwang Joon Kima², Hyun Min Kim¹, Seok Hannah¹, Eun Young Lee¹, Da Ham Kim¹, Jae Hoon Moon¹, Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-wan Lee¹Division of Endocrinology and Metabolism, Department of Internal Medicine, Yonsei University College of Medicine, Republic of Korea¹, Severance Executive Healthcare Clinic²**Objective** We tried to investigate vulnerable medical conditions, and both its threat hold of A1c and glucose fluctuation associated with severe hypoglycemia in Korean type 2 diabetic patients.**Methods** In this retrospective study, we recruited well-documented 42 patients presenting with severe hypoglycemia (group I) from EM admission and randomly selected 81 control subjects (group II) for nested case-control study.**Results** In group I, the mean age, A1c and GA were 71.8 ± 7.8 years, $6.83 \pm 1.42\%$, and $18.9 \pm 7.2\%$, respectively. The followings are chronic medical conditions; 43.2% of chronic kidney disease (CKD), 15.9% of cancer, 11.4% of others (adrenal insufficiency, COPD, MI, hyperthyroidism, r/o insulinoma). In group II, the mean age, sex, A1c and GA were similar to those in group I due to matching for sex, age and A1c. 38.5% of group I had underline medical disease. There were significant differences in BMI (22.14 vs. 24.66 kg/m^2 , $p = 0.02$), Hb (10.73 vs. 13.03 mg/dL , $p < 0.001$), Cr (2.63 vs. 1.07 mg/dL , $p = 0.002$), total cholesterol (157 vs. 139 mg/dL , $p = 0.016$), albumin (3.67 vs. 4.48 mg/dL , $p < 0.001$), eGFR (50.7 vs. 68.7 mg/dL , $p < 0.001$) between group I and II. In addition, A1c of past 3 months were significantly higher in group I ($8.06 \pm 2.41\%$) than that of group II ($6.87 \pm 1.01\%$, $p = 0.006$). In the multiple logistic regression analysis, we included conventional variables (age, diabetes duration, Cr, BMI) and founded parameters (Hb, total cholesterol, eGFR, albumin, A1c) which differ significantly between two groups as independent factors. As a result, hemoglobin, eGFR and variation in A1c were found to be independently associated with development of severe hypoglycemia.**Conclusion** About 75% of subjects with severe hypoglycemia admitted in EM had medical history of CKD, cancer, others. The independent factors predicting severe hypoglycemia were rapid intensified glucose control, anemia and azotemia. We suggest that the target level of A1c in type 2 diabetes patients with medical disease might not be less than 7% of HbA1c.

OP5-4 Epidemiology & genetics

The association of non-alcoholic fatty liver disease and cardiac structural and functional changes in KoreansChai Ryoung Eun^{1*}, Ji A Seo¹, Hyunjo Cho¹, Ho Cheol Hong¹, Hae Yoon Choi¹, Myong Jin Cho¹, Yoon Jung Kim¹, Joo Hyung Kim¹, Sae Jeong Yang¹, Hye Jin Yoo¹, Hee Young Kim¹, Hyung Joon Yim², Sin Gon Kim¹, Kyung Mook Choi¹, Sei Hyun Baik¹, Dong Seop Choi¹, Seong Hwan Kim¹, Nan Hee Kim¹Endocrinology, Korea University Medical School, Korea, Republic of¹, Hepatology, Korea University Medical School, Korea, Republic of², Cardiology, Korea University Medical School, Korea, Republic of³**Objective** We aimed to assess if non-alcoholic fatty liver disease (NAFLD) is associated with early changes of cardiac structure and function, and if these associations are different according to the obesity status in a population-based study.**Methods** The subjects consisted of 1916 Koreans aged over 45 years from the Korean Genome Epidemiology Study, which is an ongoing population-based study. Subjects with LV systolic dysfunction or known cardiovascular diseases were excluded. The severity of fatty liver was assessed by liver minus spleen attenuation score (LSA) using abdominal CT scan. Fatty liver was defined by LSA less than 5. Echocardiography was used to assess LV structure (LV mass) and systolic (LV ejection fraction) and diastolic function, by pulse-wave Doppler (E/A ratio; ratio of early to late diastolic mitral flow velocity) and tissue Doppler imaging (Ea; early diastolic velocity). Obesity was defined by body mass index (BMI) ≥ 25 .**Results** LV mass was higher, and E/A ratio and Ea were lower in subjects with NAFLD than those without [LV mass index (mean \pm SD), 90.0 ± 17.2 vs. $86.2 \pm 16.3 \text{ g/m}^2$, $p < 0.001$; E/A ratio, 0.98 ± 0.26 vs. 1.10 ± 0.33 , $p < .0001$; Ea, 6.72 ± 1.48 vs. $7.59 \pm 1.76 \text{ cm/s}$, $p < 0.001$ in subjects with or without NAFLD, respectively]. Ea was lower in those with NAFLD regardless of obesity status [Ea in the non-obese group, 7.02 ± 1.56 vs. 7.86 ± 1.77 , (with vs. without NAFLD, $p < .0001$); obese group 6.58 ± 1.43 vs. $7.05 \pm 1.59 \text{ cm/s}$ (with vs. without NAFLD, $p < .0001$)]. However, ejection fraction and other parameters of conventional Doppler indices were comparable in both groups. In the regression analysis, the presence of NAFLD was associated with decreased Ea ($\beta = -0.415$, $p < 0.001$) after adjusting for age, sex, BMI, systolic blood pressure and medications for diabetes or hypertension.**Conclusion** NAFLD was associated with cardiac diastolic dysfunction. This is evident not only in obese, but also in non-obese subjects.

OP5-5 Epidemiology & genetics

Low vitamin D status is closely associated with nonalcoholic fatty liver disease in the subjects with diabetes or insulin resistance

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Objective To explore associations between serum 25-hydroxyvitamin D [25(OH)D] concentrations and non-alcoholic fatty liver disease (NAFLD) according to the presence of diabetes or insulin resistance in adult Koreans.

Methods A total of 1081 adults (344 men and 736 women, aged 47-77 years, including 283 diabetic subjects) were enrolled from the Korean Genome Epidemiology Study, a population-based cohort in Ansan city. Serum 25(OH)D concentrations were measured in all subjects. Using computed tomography, visceral obesity was defined as visceral abdominal fat area (VF) $\geq 100\text{cm}^2$ and NAFLD was diagnosed by the liver attenuation index (LAI, the difference between the mean hepatic and splenic attenuation) < 5 Hounsfield Unit.

Results Log[25(OH)D] levels were negatively associated with waist circumference, fasting insulin, homeostasis model assessment of insulin resistance (HOMA-IR), triglycerides, and VF and positively associated with LAI in total or diabetic subjects. However, in nondiabetics, only triglycerides levels were negatively associated with 25(OH)D. In the diabetic subjects, the odds ratios (ORs) for visceral obesity and NAFLD increased sequentially across decreasing quartiles of 25(OH)D [Q1 vs Q4; OR for visceral obesity 2.50 (95% CI:1.18-5.32 p=0.0139); OR for NAFLD 3.34 (95% CI:1.53-7.33, p=0.0016)] after adjusting for age, sex, season, exercise, vitamin supplementation, body mass index, HOMA-IR and medication for diabetes, hypertension and dyslipidemia. In contrast, there was no significant increase of adjusted ORs in nondiabetic subjects. When we classified nondiabetic subjects by HOMA-IR, significant positive association between 25(OH)D and LAI was observed only in the high HOMA-IR group (HOMA-IR ≥ 2.5 , n=207, $\beta=0.0059$, p=0.0172) but no association was observed in the low HOMA-IR group (HOMA-IR < 2.5 , n=592, $\beta=0.0018$, p>0.4).

Conclusion In the subjects with diabetes or high insulin resistance, low vitamin D status is closely associated with NAFLD.

OP5-6 Epidemiology & genetics

Gene expression pattern in transmitochondrial cytoplasmic hybrid cells harboring type 2 diabetes-associated mitochondrial DNA haplogroups

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Objective Decreased mitochondrial function plays a pivotal role in the pathogenesis of type 2 diabetes mellitus (T2DM). Recently, it was reported that mitochondrial DNA (mtDNA) haplogroups confer genetic susceptibility to T2DM in Koreans and Japanese. Particularly, mtDNA haplogroup N9a is associated with a decreased risk of T2DM, whereas haplogroups D5 and F are associated with an increased risk.

Methods To examine functional consequences of these haplogroups without being confounded by the heterogeneous nuclear genomic backgrounds of different subjects, we constructed transmitochondrial cytoplasmic hybrid (cybrid) cells harboring each of the three haplogroups (N9a, D5, and F) in a background of a shared nuclear genome. We compared the functional consequences of the three haplogroups using cell-based assays and gene expression microarrays.

Results Cell-based assays did not detect differences in mitochondrial functions among the haplogroups in terms of ATP generation, reactive oxygen species production, mitochondrial membrane potential, and cellular dehydrogenase activity. However, differential expression and clustering analyses of microarray data revealed that the three haplogroups exhibit a distinctive nuclear gene expression pattern that correlates with their susceptibility to T2DM. Pathway analysis of microarray data identified several differentially regulated metabolic pathways. Notably, compared to the T2DM-resistant haplogroup N9a, the T2DM-susceptible haplogroup F showed down-regulation of oxidative phosphorylation and up-regulation of glycolysis.

Conclusion These results suggest that variations in mtDNA can affect the expression of nuclear genes regulating mitochondrial functions or cellular energetics. Given that impaired mitochondrial function caused by T2DM-associated mtDNA haplogroups is compensated by the nuclear genome, we speculate that defective nuclear compensation, under certain circumstances, might lead to the development of T2DM.

OP5-7 Epidemiology & genetics

Low visfatin levels are associated with exacerbated insulin resistance and impaired insulin secretion in overweight and normal weight Korean women with gestational diabetes mellitus

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Objective Obesity, older age, previous gestational diabetes mellitus (GDM), and family history of diabetes are risk factors but poor predictors of GDM. Therefore, we evaluated whether secretion patterns of adipokines or gestational hormones might be linked to risk for GDM among Korean women.

Methods Non-GDM and GDM participants were divided into normal and overweight groups according to prepregnancy BMI above or below 23 kg/m² at 24-28 weeks of pregnancy. Glucose tolerance, insulin resistance and secretory capacity, anthropometric and dietary data, and serum levels of adipokines and gestational hormones were determined.

Results GDM was associated mainly with increased insulin resistance in overweight women and decreased insulin secretory capacity in normal weight women. Serum adiponectin and resistin levels were lower in GDM women than non-GDM women. In addition, serum visfatin was markedly decreased in both overweight and normal weight GDM women. Serum C-reactive protein levels were higher in overweight GDM subjects than overweight non-GDM women while serum progesterone was greater in GDM women than non-GDM women. These differences were involved in higher energy and saturated fat intakes in both normal weight and overweight GDM women than non-GDM women.

Conclusion GDM in normal-weight Korean women is primarily due to poor insulin secretory capacity, but in overweight GDM women it was primarily due to insulin resistance. Low visfatin levels appear to be a common risk factor for both types of GDM. More research is needed to confirm that low levels of visfatin are involved in the etiology of GDM.

OP6-1 Insulin action & obesity

Effects of adiposity on insulin resistance and metabolic disturbance in women with and without polycystic ovary syndrome

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Objective Approximately 50 to 70% of women with polycystic ovary syndrome (PCOS) have some degree of insulin resistance, and obesity worsens the insulin resistance and metabolic disturbance. Metabolic consequences of PCOS share with those of obesity, therefore defining the causality is difficult. The aim of this study is to evaluate the effect of change of adiposity on insulin sensitivity and metabolic disturbance and to investigate the factors associated with insulin resistance in women with PCOS and controls.

Methods We consecutively recruited 144 women with PCOS (age: 26 ± 5 yr, body mass index, BMI: 24.4 ± 4.0 kg/m²) and 145 control (age: 25 ± 5 yr, BMI: 23.0 ± 3.6 kg/m²), which were divided into 2 groups (lean: BMI < 23 kg/m², overweight/obese (ow/ob): BMI ≥ 23 kg/m²) according to BMI respectively. Anthropometric measures, 75g oral glucose tolerance test (OGTT) were performed and ISI 0.120 (ISI) was calculated for index of insulin sensitivity. We evaluated the $\Delta\text{ISI}/\Delta\text{BMI}$ and $\Delta\text{metabolic features}/\Delta\text{BMI}$.

Results Table. ISI was significantly lower both in lean and ow/ob women with PCOS compared to BMI-matched controls (P<0.05). The multiple regression analysis revealed that BMI ($\beta=-0.375$) and PCOS status ($\beta=-0.423$) were significantly associated with ISI (P<0.05).

Conclusion The increase of BMI could induce the insulin resistance and metabolic disturbance, and both adiposity and PCOS status might affect the insulin resistance. Therefore long-term lifestyle modification might be needed to prevent weight gain and following deterioration of the insulin resistance and metabolic disturbance.

OP6-2 Insulin action & obesity

Zfp521 as a negative regulator of preadipocyte commitment

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Objective To determine the role of Zfp521 in adipose development.**Methods** Gain- and loss-of-function study was performed in 3T3-L1 or C3H10T1/2 cells. In addition, number of primitive preadipocytes and brown adipose tissue mass was quantified in Zfp521 wild type and null embryos. To confirm whether the action of Zfp521 is cell autonomous, competition assay was performed by transplanting F442A cells that are transduced with scramble and Zfp521 hairpin. To determine whether interaction with Ebf1 is required for Zfp521 to inhibit adipogenesis, adipogenic potential was evaluated with overexpression of wild type or truncation mutant of Zfp521 that lacks the Ebf1-interaction domain.**Results** We show that Zfp521 cell autonomously inhibits adipogenesis in vitro and in vivo. We show that Zfp521 directly binds and inhibits the proadipogenic transcription factor Ebf1 in the undifferentiated state. As differentiation proceeds, Ebf1 represses the expression of Zfp521 via binding to a key intronic enhancer, identifying a feedback loop between Zfp521 and EBF1 in the adipogenic transcriptional cascade.**Conclusion** We identify that Zfp521 is a negative regulator of adipose development through Ebf1.

OP6-4 Insulin action & obesity

Effects of exercise without calorie restriction on insulin action and ectopic fat in obese boys: A randomized controlled trialSoJung Lee^{1*}, Nancy Guerra¹, Jennifer Kuk², Fida Bacha¹, Chris Boesch³, Silva Arslanian¹Division of Weight Management and Wellness, Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA¹, School of Kinesiology and Health Science, York University, Toronto, Ontario, Canada², Magnetic Resonance Spectroscopy and Methodology, Department of Clinical Research, University Bern, Bern, Switzerland³**Objective** The effect of regular exercise alone for reducing risk factors for type 2 diabetes and ectopic fat in the liver and skeletal muscle is unknown in youth. Further, the effect of different exercise modalities on obesity-related metabolic risk is unclear. We examined the effects of aerobic versus resistance training without calorie restriction on insulin action, intrahepatic triglyceride (IHTG) and skeletal muscle lipid in obese boys.**Methods** Forty-one obese boys [BMI \geq 95th percentile (34.7 ± 4.5 kg/m²), age: 12-18 yrs] were randomly assigned to one of three groups for 3 months: aerobic exercise (AE, 180 min/week, n=14), resistance exercise (RE, 180 min/week, n=16) or a non-exercise control group (n=11). IHTG were assessed by proton magnetic resonance spectroscopy and intermuscular fat was measured by computed tomography. Insulin sensitivity (IS) and insulin secretion were evaluated by a 3-hour hyperinsulinemic-euglycemic and a 2-hour hyperglycemic clamp, respectively.**Results** Body weight did not change ($P > 0.05$) in the AE (-0.7 ± 1.4 kg) and RE (-0.2 ± 0.7 kg) groups and increased significantly ($P < 0.05$) in the control group (2.9 ± 0.7 kg). Compared with controls, cardiorespiratory fitness increased ($P < 0.05$) (AE: 32% and RE: 25%) and visceral fat (AE: 17% and RE: 14%) and intermuscular fat (AE: 13% and RE: 25%) decreased ($P < 0.05$) in both exercise groups. Further, compared with controls, significant ($P < 0.05$) reduction in IHTG (2.9 to 1.8%) and IS (2.9 to 3.7 mg/kg/min per μ U/ml) were only observed in the RE group. There were no changes in acute insulin secretion in the exercise groups.**Conclusion** Regular exercise without calorie restriction, and independent of exercise modality, is associated with significant improvement in cardiorespiratory fitness and reductions in visceral adiposity and intermuscular fat in previously sedentary, obese, high-risk boys. Resistance exercise has beneficial effects on reducing liver fat and insulin resistance.

OP6-3 Insulin action & obesity

Ciliogenesis of hypothalamic neuron is impaired in obesity and regulated by leptinMi-seon Shin^{1*}, Yu Mi Han², Gil Myoung Kang², Sae Bom Lee², Hyun-Kyong Kim², So Young Gil², Joong Yeol Park¹, Ki Up Lee¹, Hyuk Whan Koh³, Min-seon Kim¹Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center¹, Appetite Regulation Laboratory, Asan Institute for Life Science², Age-Related & Brain Diseases Research Center, Kyung Hee University³**Objective** Genetic ciliopathies such as the Bardet-Biedel Syndrome and Alström syndrome manifest obesity. Moreover, mice with defective ciliogenesis in hypothalamic neurons develop central leptin resistance and obese phenotype. In the present study, we conversely investigated the effects of obesity, feeding manipulation and leptin on the ciliogenesis of the hypothalamic neurons.**Methods** Hypothalamus was collected from the high fat diet-induced obese (DIO) mice and leptin deficient ob/ob mice treated with or without leptin (1 mg/kg for 5 days). Cilia were stained using antibody against the type 3 adenylyl cyclase (AC-III). The number and length of cilia were analyzed using the Image-Proplus⁸ program. Two hypothalamic neuron cells (N1 cells and primary cultured cells) were used to investigate the effect of leptin on ciliogenesis. To confirm the importance of ciliogenesis in leptin signaling, small inhibitory RNAs (siRNA) specific to ciliary proteins IFT88 and Kif3a were injected into the bilateral mediobasal hypothalamus.**Results** Both the numbers and lengths of cilia were significantly decreased in hypothalamus but not in the hippocampus from the DIO mice. Similarly, ob/ob mice had impaired ciliogenesis in the hypothalamus, which was reversed by 7 days-leptin treatment. Furthermore, 24 h-fasting reduced cilia number and length in the hypothalamus which was recovered by regaining of food intake. In vitro, leptin treatment stimulated ciliogenesis in hypothalamic neuron cells through the phosphatidylinositol-3 kinase (PI3K)-dependent mechanisms. Leptin-induced anorexia and Stat3 activation were significantly attenuated in mice injected with IFT88- and Kif3a-siRNA, suggesting that hypothalamic ciliogenesis is critical for central leptin actions.**Conclusion** Hypothalamic neuronal ciliogenesis was significantly impaired in both genetic and acquired obese animal models but stimulated by food intake and leptin treatment. Our findings firstly demonstrate that metabolic conditions dynamically regulate hypothalamic ciliogenesis.

OP6-5 Insulin action & obesity

Role of Rho-kinase on insulin secretion in pancreatic β -cells

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Objective It was reported that inhibition of Rho-kinase activity causes insulin resistance by reducing insulin-stimulated glucose uptake in skeletal muscle in vivo. However, it is still unknown whether Rho-kinase inhibit insulin secretion and if so, what the main mechanism is. In this study, we aimed to identify the effects of Rho-kinase inhibition on insulin secretion from pancreatic β -cells.**Methods** We transfected Rho-kinase siRNA into β -cells for 48 hrs and we performed glucose induced insulin secretion (GIIS) assay, perfusion and intra-cellular calcium staining (Fluo-4 staining) for verification of the effects of Rho-kinase on insulin secretion. In addition, we observed cell proliferation (BrdU uptake assay), cell viability (MTT assay), cell apoptosis (TUNEL assay) and cell cycle (flow cytometry) of β -cells.**Results** After Rho-kinase siRNA transfection, insulin secretion was significantly decreased in response to high glucose stimulation compared with control group. Moreover, same result was confirmed in isolated rat pancreatic islets after Rho-kinase RNAi transfection. In addition, Rho-kinase RNAi reduced cell viability and proliferation. However, cell necrosis and cell cycle were not affected.**Conclusion** Our results suggest that inhibition of Rho-kinase impairs the insulin secretion by marked down regulation of intracellular Ca²⁺ level. Also, Rho-kinase is related to cell viability and proliferation of β -cells. However, it did not affect necrosis and apoptosis of β -cells.

OP6-6 Insulin action & obesity

Resveratrol promotes the mitochondrial activity with over-expression of ER-alpha in brown adipocyte

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Objective Resveratrol (3,5,4'-trihydroxystilbene; RSV) is one kind of polyphenolic phytoalexin that has many effects on metabolic diseases. Given the importance of brown adipose tissue (BAT) for energy expenditure, we investigated the role of RSV on brown adipocyte in vivo and in vitro conditions.

Methods 7-week-old male Otsuka Long Evans Tokushima Fatty (OLETF) rats were divided into 4 groups: (1) Standard diet (SD); (2) SD+RSV; (3) High fat diet (HFD); (4) HFD+RSV. RSV (10 mg/kg body weight, daily) was administered in aqueous suspension orally for 27 weeks via oral sonde. Fasting glucose concentration was measured and an intraperitoneal insulin tolerance test was performed at an every month. At 34 weeks old age, interscapular BATs of OLETF rats were isolated for weighing, histological evaluation, and protein analysis. For in vitro study, interscapular BAT was isolated from 7-week-old male Sprague Dawley (SD) rats.

Results Although there was no difference in body weight, RSV improved the insulin sensitivity in OLETF rats fed with SD or HFD. Furthermore, treatment of RSV on OLETF rats increased the weight of BAT, augmented the differentiation of BAT and the expression of uncoupling protein-1 (UCP-1) in BAT. With the increment of UCP-1, RSV increased the expression of ER-alpha in BAT of OLETF rats. At oil red O staining, RSV prevented the deposit of lipid droplets in the space between each brown adipocyte. Treatment of RSV on primary cultured BAT from SD rats, showed the same results concerning the UCP-1 and ER-alpha.

Conclusion RSV promotes the mitochondrial activity with over-expression of ER-alpha in brown adipocyte. Further study evaluating the relationship between the mitochondrial activity and the ER-alpha could be helpful in understanding the anti-obesity effect of RSV.

OP6-7 Insulin action & obesity

eNamp regulates body weight homeostasis through hypothalamic Sirt2-mediated inhibition of Foxo1

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Nicotinamide adenine dinucleotide (NAD) is an essential coenzyme in a broad range of biological functions including transcriptional regulation via NAD-dependent deacetylase sirtuins. Intracellular NAD is produced through de novo synthesis or via salvage pathways. Nicotinamide phosphoribosyltransferase (Nampt), also known as visfatin or pre-B cell enhancing factor (PBEF), catalyzes a rate-limiting step in the NAD salvage pathway. We investigated a potential involvement of Visfatin/eNampt in central regulation of energy balance. Central and peripheral administration of the Nampt peptide (extracellular Nampt/eNampt) and a Nampt enzymatic product nicotinamide mononucleotide (NMN) inhibited food intake and weight gain in mice. In contrast, administration of the Nampt inhibitor FK866 resulted in hyperphagia and blocked eNampt-induced anorexia and weight loss, suggesting that enhanced Nampt activity produces a negative energy balance. Interestingly, central and peripheral administration of Nampt increased NAD in hypothalamus, liver, blood. In the hypothalamic neurons, treatment with eNampt and NMN strongly promoted the nuclear export and degradation of the transcription factor Foxo1, thereby repressing its transcriptional activities on genes encoding key appetite-regulating neuropeptides such as neuropeptide Y, Agouti-related protein and proopiomelanocortin. Moreover, these effects were mediated through Sirt2-induced Foxo1 deacetylation. Together, these findings indicate that eNampt modulates body weight metabolism by regulating hypothalamic Sirt2 and Foxo1 activities. Nampt is a critical regulator in the circadian clock machinery. Notably, plasma eNampt levels displayed a circadian rhythm with a nocturnal rise in mice, which was reciprocal to the circadian changes in hypothalamic Foxo1 levels. Therefore, eNampt may function as an important molecular link between the circadian and metabolic systems.

OP7-1 Clinical diabetes & therapeutics (II)

Effects of exenatide (Exendin-4) on glycemic control over 12 weeks in patients with Korean type 2 diabetes treated with metformin and a sulfonylurea

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Objective Unlike most antihyperglycaemic drugs, glucagon-like peptide-1 (GLP-1) receptor agonists have a glucose-dependent action and promote weight loss. However, in clinical settings, there are only few data which showed the efficacy and safety of exenatides combined with both sulfonylurea and metformin. Hence, we evaluate the efficacy and safety of exenatide, an exendin-based GLP-1 receptor agonist with oral hypoglycemic agent (metformin+sulfonylurea) in Korean type 2 diabetic (T2DM) patients.

Methods Adults with inadequately controlled T2DM on maximally tolerated doses of metformin, sulfonylurea, or both, were enrolled in this study and exenatide 5microg once daily and 10 microg twice a day (n=81) in a 12-weeks. All patients took both sulfonylurea and metformin daily. The primary and secondary outcome were change in HbA1c and weight. For assessment of the exploratory endpoint, lipid profile were measured.

Results Mean baseline HbA1c for the study population was 8.0%. Exenatide reduced mean HbA1c significantly after 12weeks, (-0.4%, p-value: 0.017); Exenatide failed to show reducing mean fasting plasma glucose and postprandial glucose (fasting glucose: 140.0→144.6, postprandial glucose: 214.6→203.0, p-value: ns, respectively). Exenatide promoted weight losses (-2.4 kg, p-value<0.001) effectively and quickly. Furthermore, this drug reduce total cholesterol and LDL cholesterol (-15.7mg/dl, p-value<0.001, 12.3, p-value<0.001). The drugs was well tolerated, but among 81 patients, 18 patients (22%) was dropped out (nausea: 3, Diarrhea: 3, poor glucose control: 2, discomfort with injection treatment: 5, hypoglycemia: 2, decreased renal function: 1).

Conclusion As published before, Exenatide significantly reduced A1C in patients with T2DM unable to achieve adequate glycemic control with maximally effective doses of combined metformin-sulfonylurea therapy. Interestingly, weight loss is significantly higher and faster in Korean T2DM patients than in patients enrolled in clinical trial, (-2.4kg vs -1.4kg at 12 weeks). Furthermore, exenatides improve lipid profile, especially lowering LDL cholesterol.

OP7-2 Clinical diabetes & therapeutics (II)

The effect of rosiglitazone on LRP1 expression and amyloid beta uptake in human brain microvascular endothelial cells: a possible role of low-dose thiazolidinedione for dementia treatment

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Objective Accumulation of amyloid beta (Aβ) in the brain is known to be involved in the pathogenesis of Alzheimer's disease (AD). Low-density lipoprotein receptor-related protein 1 (LRP1) in brain microvascular endothelial cells is known to be a transporter that export Aβ across the blood-brain barrier (BBB). In this study, the effect of rosiglitazone, a peroxisome proliferator-activated receptor-γ (PPARγ) agonist on the expression and function of LRP1 was investigated in primary human brain microvascular endothelial cells (HBMECs).

Methods HBMECs were treated with various concentration of rosiglitazone for 48 h. The expression of LRP1 in HBMECs was investigated through immunoblotting and RT-PCR. Luciferase assay using the LRP1 promoter-reporter vector was performed. The cellular uptake of Aβ40 and Aβ42 was also evaluated.

Results Rosiglitazone up-regulated the amount of LRP1 mRNA and the protein expression in HBMECs in a dose-dependent manner in up to 10 nM of rosiglitazone concentration. Luciferase assay showed that rosiglitazone activated the transcription of the LRP1 promoter by PPARγ. Aβ40 and Aβ42 uptake through LRP1 in HBMECs also increased by rosiglitazone. This increase of the LRP1 promoter activity and Aβ uptake was observed in up to 10 nM of rosiglitazone concentration. At concentrations above 20 nM of rosiglitazone, the LRP1 expression, the LRP1 promoter activity, and Aβ uptake in HBMECs were not altered compared to those in non-treated cells. The effective range of rosiglitazone concentration on LRP1 expression and function in HBMECs was much lower than that in adipocytes or hepatocytes.

Conclusion In conclusion, this study suggests a new therapeutic application of rosiglitazone for AD at much lower dose than the average doses used for T2DM treatment. This "low-dose rosiglitazone treatment" is expected to reverse the key pathogenesis of AD through enhancing clearance of Aβ in the brain.

OP7-3 Clinical diabetes & therapeutics (II)

Comparison of efficacy and safety of once-daily dosing and on-demand use of udenafil for type 2 diabetes patients with erectile dysfunction

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Objective Recent clinical studies show that once-daily dosing of phosphodiesterase type 5 (PDE5) inhibitor is an effective treatment option for erectile dysfunction. We compared the efficacy and safety between once-daily dosing and on-demand use of udenafil for type 2 diabetes patients with erectile dysfunction.

Methods A multi-center, randomized, open-label, parallel group, 12-week study was conducted. Patients who have shown improvement with on-demand 200mg udenafil according to Sexual Encounter Profile(SEP) diary Q2, Q3 were randomized into 200mg on-demand(n=80) or 50mg once-daily(n=81) for 8 weeks and 4 weeks of treatment-free period was followed. Udenafil was controlled in order to match the same total dose in both groups. The primary efficacy endpoint was the change of the International Index of Erectile Function(IIEF) erectile function domain(EFD) score. Secondary efficacy endpoints included changes of the SEP diary Q2, Q3, IIEF Q3, Q4, other domains of IIEF, the Global Assessment Question(GAQ), shift to normal rate(EFD \geq 26). Vascular endothelial markers were assessed at baseline and after 8 weeks of treatment.

Results Both groups showed significant improvement in IIEF-EFD score after 8 weeks of treatment compared to the score at screening visit(p<0.0001). There was no significant difference between two groups. And the effect was not maintained during the treatment-free follow-up period. Similar results were observed in secondary efficacy end points. There was also no significant difference in vascular endothelial markers. Daily udenafil was well tolerated and showed non-significant tendency for fewer adverse drug reactions. Flushing and headache were the most frequent adverse events.

Conclusion Both methods of medication improved erectile dysfunction in diabetes patients without significant difference. Daily udenafil was not only well tolerated but also not inferior to on-demand udenafil.

OP7-4 Clinical diabetes & therapeutics (II)

Anti-diabetic actions of a non-agonist PPAR γ ligand blocking Cdk5-mediated phosphorylation

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Objective PPAR γ is the functioning receptor for the thiazolidinedione (TZD) class of anti-diabetes drugs including rosiglitazone and pioglitazone. These drugs are full classical agonists for this nuclear receptor, but recent data have shown that many PPAR γ -based drugs have a separate biochemical activity, blocking the obesity-linked phosphorylation of PPAR γ by Cdk5.

Methods We developed novel synthetic compounds that have a unique mode of binding to PPAR γ . Then, we tested their effects on i) blocking Cdk5-mediated PPAR γ phosphorylation, ii)transcriptional activation of PPAR γ , iii) anti-diabetic activity in vivo, iv) the side effects caused by TZD class drugs such as fluid retention or weight gain.

Results Here we describe novel synthetic compounds completely lack classical transcriptional agonism and block the Cdk5-mediated phosphorylation in cultured adipocytes and in insulin-resistant mice. Moreover, one such compound, SR1664, has potent anti-diabetic activity while not causing the fluid retention and weight gain that are serious side effects of many of the PPAR γ drugs. Unlike TZDs, SR1664 also does not interfere with bone formation in culture.

Conclusion These data illustrate that new classes of anti-diabetes drugs can be developed by specifically targeting the Cdk5-mediated phosphorylation of PPAR γ .

OP7-5 Clinical diabetes & therapeutics (II)

Efficacy and safety of linagliptin (5 mg) compared to placebo in combination with metformin and sulphonylurea over 24 weeks in type 2 diabetic patients of Korean ethnicity: A post-hoc analysis

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Objective Linagliptin is a once daily orally administered DPP4 inhibitor with a unique xanthine backbone structure which is primarily excreted in bile and gut. The aim of this study was to assess efficacy and safety of a linagliptin in combination with metformin and sulphonylurea (SU) in Korean patients with Type 2 diabetes mellitus (T2DM).

Methods This is a post hoc analysis of Korean-subgroup patients from a 24-week, randomized, double-blind, placebo-controlled, parallel group study examined the efficacy and safety of linagliptin(5mg,qd) in T2DM patients in combination of metformin plus SU. In Korea, this study was conducted at 11 centers with 174 patients. All patients had a 2-week placebo run-in before being randomized to linagliptin+metformin+SU (n=122) or placebo+metformin +SU (n=52).

Results After 24-week treatment, adjusted mean changes in HbA1c from baseline (approximately 8.2%) in patients receiving linagliptin and metformin plus SU combination, and placebo and metformin plus SU combination were -0.87 \pm 0.74%, 0.03 \pm 0.90% respectively. Mean FPG change from baseline in linagliptin and placebo group were -19.8 \pm 63.4 mg/dl and +16.9 \pm 56.3mg/dl respectively. The overall incidence of adverse events was comparable across treatment groups.

Conclusion Treatment with linagliptin added to the combination of metformin and SU improved glycemic control with substantial reductions in HbA1c, FPG in Korean sub-group and the glycemic control effect with Linagliptin in Korean patients with T2DM are consistent with results seen in the overall study population.

OP7-6 Clinical diabetes & therapeutics (II)

Modest reversal of metabolic syndrome manifestations with vitamin D correction: A 12-month prospective study

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Objective Numerous cross-sectional studies have noted significant negative associations between circulating levels of vitamin D and cardio-metabolic risk factors, highlighting potential extra-skeletal functions of this sterol hormone. Prospective studies, however, have been limited and hence no cause and effect relations can be inferred. This study aims to determine whether vitamin D correction can reverse already established manifestations of the metabolic syndrome (MetS).

Methods A total of 59 adult non-diabetic, overweight and obese Saudis (31 males, 28 females) were randomly recruited in this prospective 1-year interventional study. Anthropometry and biochemical evaluation were performed, including determination of serum vitamin D, calcium and phosphorus concentrations, as well as fasting blood glucose and lipid profile. Subjects were advised to regularly expose themselves to sunlight and increase intake of vitamin D-rich foods. All measurements were repeated 6 and 12 months later.

Results At the initial baseline visit, the prevalence of both low HDL-C and hypertension was significantly increased among patients with vitamin D deficiency (p<0.05), even after adjusting for gender and BMI. Overall prevalence of MetS patients by the modified NHANES ATP III definition decreased from 25.2% to 13.0% and this was largely due to a parallel decrease in the prevalence of low HDL-cholesterol, triglycerides and hypertension.

Conclusion Optimization of vitamin D levels through sun exposure and increased intake of a vitamin D-rich diet can lead to an improved cardio-metabolic profile, offering a promising non-pharmacologic approach in the prevention of MetS manifestations.

Enhanced carbohydrate craving in diabetic patients

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Objective Food craving, an excessive desire for foods, is known to be associated with obesity. Clinical observation indicates enhanced food craving in diabetic patients, which is a big obstacle for glycemic control. However, there is no report on food craving in diabetic patients. Therefore, we investigated food craving in type 2 diabetic (T2DM) patients and compared with non-diabetic controls.

Methods Total 275 (171 T2DM patients and 104 age- and sex-matched non-diabetic controls) had completed the food craving survey. The survey was comprised of the general trait of food cravings questionnaires (G-FCQ-T) to assess a general desire for food and the state of food cravings questionnaires (FCQ-S) with visual stimulation of high-carbohydrate, low-fat (HCLF) foods and low-carbohydrate, high-fat (LCHF) foods. To test if glycemic control state may affect G-FCQ-T and FCQ-S, we evaluated the correlation between HbA1c and craving scores.

Results G-FCQ-T score was significantly higher in T2DM patients than in non-diabetic controls (51.3 ± 1.1 vs. 47.3 ± 1.2 , $p=0.013$), although this difference was abolished after adjusting for BMI (adjusted $p=0.195$). Notably, T2DM patients had higher FCQ-S- HCLF score compared with non-diabetic controls (41.1 ± 0.8 vs. 38.2 ± 0.8 , $p=0.013$). In contrast, FCQ-S-LCHF score was significantly lower in T2DM patients than in non-diabetic controls (35.7 ± 0.8 vs. 38.0 ± 0.9 , $p=0.033$). These results were statistically significant even if BMI was adjusted (adjusted $p=0.027$; adjusted $p=0.005$). Both G-FCQ-T and FCQ-S- HCLF scores were positively correlated with HbA1c whereas there was no correlation between FCQ-S-LCHF and glycemic control index.

Conclusion Diabetic patients have increased craving for high carbohydrate foods but not for low carbohydrate and high fat foods. Poor glycemic control is associated with higher carbohydrate craving scores.



POSTER EXHIBITIONS

[PE1~PE11] Islet biology & insulin secretion,
immunology & transplantation

[PE12~PE37] Acute & chronic complication

[PE38~PE77] Clinical diabetes & therapeutics

[PE78~PE93] Behavioral medicine & education

[PE94~PE109, PE135] Epidemiology & genetics

[PE110~PE134] Insulin action & obesity

PE1 Islet biology & insulin secretion, immunology & transplantation

Genome-wide identification of palmitate-regulated immediate early genes and target genes in pancreatic beta-cells reveals a central role of NF- κ BHyung Jin Choi^{1*}, Seungwoo Hwang², Se-Hee Lee¹, You Ri Lee¹, Jiyon Shin¹, Kyong Soo Park¹, Young Min Cho¹Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea¹, Korean Bioinformatics Center, Korea Research Institute of Bioscience and Biotechnology, Daejeon, Korea²**Objective** Free fatty acid (FFA)-induced pancreatic β -cell dysfunction plays a key role in the pathogenesis of type 2 diabetes. We conducted gene expression microarray analysis to comprehensively investigate the transcription machinery of palmitate-regulated genes in pancreatic β -cells in vitro.**Methods** Mouse pancreatic β TC3 cells were treated with palmitate in the presence or absence of cycloheximide (CHX), which blocks protein synthesis and thereby allows us to distinguish immediate early genes (IEGs) from their target genes.**Results** The microarray experiments identified 34 palmitate-regulated IEGs and 74 palmitate-regulated target genes. In silico promoter analysis revealed that transcription factor binding sites for NF- κ B were over-represented, regulating approximately one-third of the palmitate-regulated target genes. In cells treated with CHX, nfkb1 showed considerable up-regulation by palmitate, suggesting that NF- κ B could be an IEG. Functional enrichment analysis of 27 palmitate-regulated genes with NF- κ B binding sites showed an over-representation of genes involved in immune response, inflammatory response, defense response, taxis, regulation of cell proliferation, and regulation of cell death pathways. Electrophoretic mobility shift assay confirmed that palmitate stimulates NF- κ B activity both in the presence and absence of CHX.**Conclusion** We conclude that NF- κ B is an important IEG that may contribute to the regulation of inflammation and cell proliferation/death in pancreatic β -cells in response to palmitate.

PE2 Islet biology & insulin secretion, immunology & transplantation

Gliclazide does not fully prevent 2-deoxy-D-ribose-induced oxidative damage because it does not restore glutathione content in a pancreatic β -cell lineGwanpyo Koh^{1*}, Sang Ah Lee¹, Dae-Hoo Lee¹, Hyoun-Jung Chin²Jeju National University Hospital¹, Hankook General Hospital²**Objective** 2-Deoxy-D-ribose (dRib) is a powerful reducing sugar that rapidly increases oxidative stress and apoptosis in pancreatic β -cells. Gliclazide is an antidiabetic agent with antioxidant properties and N-acetyl-L-cysteine (NAC) is a glutathione precursor. We compared the effects and mechanisms of gliclazide and NAC in protecting against dRib-induced oxidative damage in a β -cell line.**Methods** HIT-T15 cells were cultured with various concentrations of dRib for 6 or 24 h after pretreatments with gliclazide or NAC.**Results** Using trypan blue vital staining and flow cytometry with annexin V/PI staining, gliclazide treatment slightly reversed dRib-induced cell death and apoptosis and NAC treatment markedly reduced both measures. Likewise, flow cytometry using DHR 123 staining showed that the levels of dRib-induced reactive oxygen species (ROS) were partially suppressed by gliclazide and completely inhibited by NAC. Using electron spin resonance spectrometry, gliclazide and NAC scavenged hydroxyl radicals generated by the Fenton reaction to a similar degree. NAC, but not gliclazide, completely restored the intracellular glutathione depleted by dRib using monochlorobimane fluorescence and glutathione assays.**Conclusion** Gliclazide and NAC scavenged ROS to a similar degree but gliclazide could not restore the intracellular glutathione content as effectively as NAC. Thus, gliclazide treatment suppressed dRib-induced oxidative damage in HIT-T15 cells less than NAC did.

PE3 Islet biology & insulin secretion, immunology & transplantation

Molecular mechanisms of early growth response protein-1 (EGR-1) expression by quercetin in INS-1 beta-cells and the role of EGR-1 in cell proliferationJae Min Cho^{*}, Seo-Yoon Chang, Yang-Hyeok Jo, Myung-Jun Kim

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Objective Early growth response-1 (EGR-1), one of immediate early response genes, is involved in diverse cellular response. We recently reported that quercetin increased catalytic subunit of γ -glutamylcysteine ligase (GCLC) via the interaction of EGR-1 to GCLC promoter in INS-1 beta-cells. Therefore, this study investigated molecular mechanisms of quercetin-induced EGR-1 expression and the role of EGR-1 in cell proliferation in INS-1 cells.**Methods** The expression of EGR-1 protein was detected by Western blot analysis. Additionally, EGR-1 mRNA expression and EGR-1 promoter activity were observed by Northern blot analysis and luciferase assay, respectively. Knock-down of PKA and p38 MAPK was verified by real-time PCR. To examine the transcriptional regulation of EGR-1 by SRE sites, we assessed by EMSA and mutagenesis.**Results** Quercetin significantly induced EGR-1 protein and its mRNA expressions. This induction of EGR-1 was completely blocked by pretreatment with a PKA inhibitor, H-89 and partially blocked by a p38 inhibitor, SB203580. Additionally, the siRNA-mediated inhibition of PKA and p38 resulted in significant reduction of quercetin-induced EGR-1 promoter activity. Study using truncated EGR-1 promoter constructs showed that serum response element (SRE) sites, not cAMP response element site, were essential for EGR-1 transcription. However, electrophoretic mobility shift assay showed that quercetin did not affect the band intensity of DNA-protein complex on SRE site of EGR-1 promoter. Also, immune-shift assay using serum response factor (SRF) and phospho-SRF antibodies showed no difference between control and quercetin-treated groups. Meanwhile, quercetin significantly increased cell proliferation rate and the overexpression of EGR-1 increased the expression of cyclin D1, a key regulator of G1 to S phase progression.**Conclusion** Collectively, quercetin-induced EGR-1 expression is largely dependent on PKA and partly on p38 MAPK pathway, and SRE sites of EGR-1 promoter are involved in EGR-1 transcriptional activity, and quercetin may promote cell proliferation via the increase in EGR-1 and cyclin D1 expressions.

PE4 Islet biology & insulin secretion, immunology & transplantation

Protective effect of GLP-1 analogue (exenatide) in mouse pancreatic β -cell line: a role of SREBP1cSeok-Woo Hong^{1*}, Jin-Mi Lee¹, Ji-Hun Choi², Se-Eun Park², Eun-Jung Rhee¹, Cheol-Young Park², Ki-Won Oh², Sung-Woo Park², Sun-Woo Kim², Won-Young Lee²Institute of Medical Research, Kangbuk Samsung Hospital¹, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital²**Objective** Exendin-4 (Ex-4), a long-acting agonist of glucagon-like peptide-1, is a novel anti-diabetic drug that stimulates insulin secretion and enhances β -cell mass, but the mechanisms involved are not fully understood. In present study, we investigated protective effect of exendin-4 against lipotoxicity, mediated by repression of SREBP1c, regulator of genes expression involved in fat and cholesterol synthesis.**Methods** To observe effect of Ex-4, we evaluated modulation of markers of function, apoptosis and mediating cell signal pathway in MIN6 cells, which were cultured in DMEM medium containing palmitate (400 μ M) with or without Ex-4 (100 nM). We also examined roles of SREBP1c in lipotoxicity model by knockdown with si-RNA.**Results** We found that Ex-4 improved β -cell function and survival as well as induction of insulin signaling (Akt) in palmitate-treated MIN6 cells. This improvement was accompanied by decreased expression and activity of SREBP1c. Moreover repression of SREBP1c by Ex-4 was depended on Akt signal pathway. Knockdown of SREBP1c using si-RNA remarkably decreased lipotoxicity by palmitate in MIN6 cells.**Conclusion** These data lead us to conclude that Ex-4 improves β -cell function and survival in pancreatic β -cell line, by blocking SREBP1c expression and activity through activation of Akt signal pathway.

PE5 Islet biology & insulin secretion, immunology & transplantation

Effect of combination of metformin and fenofibrate on glucose homeostasis in diabetic Goto-Kakizaki rats

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Objective Metformin has recently been suggested to modulate the enteroinsular axis by increasing plasma GLP-1 levels and increasing the expression of glucagon-like peptide-1 (GLP-1) receptors in pancreatic beta cells in a peroxisome proliferator-activated receptor (PPAR)- α -dependent manner. We investigated whether a PPAR- α agonist, fenofibrate, has an additive or synergistic effect, when added to metformin treatment.

Methods We divided the diabetic Goto-Kakizaki (GK) rats into 4 treatment groups including metformin (n=5, 150mg/kg for 2 weeks then 300mg/kg for following 2 weeks), fenofibrate (n=5, 150mg/kg for 4 weeks), metformin plus fenofibrate (n=4), and control (n=5). Fed state blood glucose levels, body weight, food intake were monitored. We performed oral glucose tolerance tests (OGTT) and intraperitoneal glucose tolerance tests (IPGTT) with exenatide injection after 4 weeks treatment.

Results Body weight, food intake, fed state blood glucose levels and HbA1c were not significantly different among groups. During OGTTs, metformin markedly reduces blood glucose levels; whereas fenofibrate increased blood glucose levels at 120 min. In addition, fenofibrate attenuated the glucose lowering effect of metformin during OGTTs. Four-week treatment of metformin did not improve the exenatide sensitivity during IPGTTs, while fenofibrate or fenofibrate plus metformin treatment decreased the exenatide sensitivity.

Conclusion Contrary to our expectation, a PPAR- α agonist, fenofibrate, did not exhibit an additive or synergistic effect on glucose lowering action of metformin in GK rats. Moreover, fenofibrate decreased the exenatide sensitivity during IPGTTs. Further study is needed to explore the effect of fenofibrate on the enteroinsular axis.

PE7 Islet biology & insulin secretion, immunology & transplantation

Transplantation of insulin secreting cells differentiated from human adipocyte-derived stem cells into type 2 diabetes miceJi Sun Nam^{1*}, Hyun Mi Kang², Jiyoung Kim², Seah Park², Haekwon Kim², Shin Ae Kang¹, Jong Suk Park¹, Kyung Wook Kim¹, Chul Woo Ahn¹, Kyung Rae Kim¹, Chul Woo Ajm¹Department of Internal Medicine, Yonsei University College of Medicine¹, Department of Biotechnology, Seoul Women's University²

Objective We evaluated the efficacy of cell therapy using insulin secreting cells differentiated from human eyelid adipocyte-derived stem cells (hEA-ISC) into type 2 diabetes mice in terms of glucose lowering effect, survival benefit, and its effect on other metabolic parameters.

Methods After differentiating hEA using ISI media, these cells were transplanted into renal capsules of type 2 diabetes mice established by low dose streptozotocin injection followed by a high fat diet. Serial blood glucose levels and intra-peritoneal glucose tolerance test were done, and metabolic parameters were assessed. Transplanted kidneys were analyzed for human gene expression, and pancreata for mouse insulin reserve.

Results Mice that received differentiated cells (DC) showed a significant lowering of blood glucose level and improved glucose tolerance compared to those that received undifferentiated cell (UDC) and sham operated mice. There was a survival benefit, with 10 out of 15 mice surviving in DC group while 6 out of 15 in UDC group and none of 8 sham mice surviving at 60 days after transplantation. Significantly increased levels of human insulin and human c-peptide were detected in sera of DC mice (both $p < 0.001$). Human genes were expressed in kidneys of transplanted mice, including INS, GLUT1, GLU2, NeuroD1, Pdx1, and GK. Also, DC and UDC mice showed a significantly lower serum IL-6 level compared to sham group (both $P < 0.05$), and DC mice showed a tendency toward lower triglyceride and free fatty levels compared to sham group ($P = 0.093$ and 0.065 , respectively).

Conclusion Cell therapy using differentiated hEAs is effective in lowering blood glucose level in type 2 diabetes mouse by increasing circulating insulin level, and it also has a favorable effect on metabolic parameters and inflammatory markers. The cause and effect relationship remains to be determined.

PE6 Islet biology & insulin secretion, immunology & transplantation

Effects of Resveratrol on the pancreatic islets in an animal model of type 2 diabetesYoung-Eun Lee^{1*}, Eun-Mi Lee¹, Esder Lee¹, Ki-Ho Song¹, Yu-Bae Ahn¹, Guolian Li², Zhenqi Liu², Seung-Hyun Ko¹Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea¹, Department of Internal Medicine, University of Virginia Health System, Charlottesville, VA²

Objective Resveratrol (3,5,4'-trihydroxystilbene) has been shown to have anti-inflammation, anti-cancer, and the cardiovascular protective effects. In the present study, we aimed to investigate whether resveratrol possesses any beneficial effects on pancreatic islets in an animal model of type 2 diabetes mellitus.

Methods db/db and db/dm mice were orally treated with resveratrol (RSV, 20 mg/kg daily) for 12 weeks. Body weight measurement and oral glucose tolerance test were performed. After sacrifice, pancreatic beta cell mass was quantified by point count method, and the amount of islet fibrosis was obtained. Oxidative stress marker (isoprostane and 8-OHdG) was measured using 24 hr urine sample.

Results Resveratrol treatment for 12 weeks significantly decreased in the level of blood glucose level after glucose challenge. Pancreas weight and beta cell mass was significantly higher in RSV-treated db/db group, compared to control db/db mice. Islet fibrosis area also reduced in RSV-treated db/db mice. Oxidative stress marker was significantly decreased in RSV-treated group (8-OHdG level; db-RSV vs. db-control, 84.6 ± 39.9 vs. 37.3 ± 15.6 mg/24 hrs, $P < 0.05$).

Conclusion Resveratrol treatment improved glycemic status, and attenuated the beta cell loss, destructive changes of pancreatic islets, and oxidative stress in an animal model of type 2 diabetes. The present findings suggest that resveratrol may be considered as an effective therapeutic agent for the treatment of diabetes mellitus.

PE8 Islet biology & insulin secretion, immunology & transplantation

Autologous islet transplantation after partial pancreatectomy can improve insulin secretion and induce better glycemic control than oral hypoglycemic agentsJi Won Yoon^{1*}, Shin Hee Hong¹, Jung Hee Kim¹, Min Joo Kim¹, Yenna Lee¹, Eun Ky Kim¹, Hak Mo Lee¹, Sung Soo Chung¹, Hyo Cheol Kim¹, Jin Young Jang¹, Kyoung Bun Lee¹, Kyong Soo Park¹, Seong Yeon Kim¹, Hye Seung Jung¹Department of Internal Medicine, Seoul National University College of Medicine¹, Department of Radiology, Seoul National University College of Medicine², Department of Surgery, Seoul National University Hospital³, Department of Pathology, Seoul National University College of Medicine⁴

Objective After partial pancreatectomy (Px), effects of autologous islet transplantation (ITx) have not been directly compared to those of oral anti-diabetic drugs (OAD) in terms of insulin secretion. This is an interim analysis of a study comparing the effects of ITx and OAD after distal Px.

Methods Non-diabetic subjects who underwent distal Px for benign tumors were enrolled to either ITx or control group. The subjects in the ITx group received autologous islets 1~2 days after Px through portal vein. During the follow-up, metformin was started if diabetes mellitus developed, and then vildagliptin was added if required. Metabolic parameters were monitored before and after Px for 12 months.

Results Nine patients were enrolled in the ITx group, and 16 in the control. Extent of pancreas resection was higher in the ITx group (59.8 ± 6.1 vs. $34.6 \pm 16.8\%$, $p < 0.005$). Sixty percent of the subjects have completed the 12-month assessments. Pre-operative HbA1c was comparable, but HbA1c at 12-month was lower in the ITx group compared to that in the control (5.6 ± 0.4 vs. $6.2 \pm 0.3\%$, $p < 0.05$). HOMA-B at 12-month recovered from nadir at 6-month in the ITx, but it was not observed in the control group, causing a marginal difference of HOMA-B between the 2 groups at 12-month (ITx vs. control: 79.3 ± 23.6 , $n = 4$ vs. $53.2 \pm 21.6\%$ from the baseline, $n = 11$, $p = 0.069$). There were 4 subjects taking vildagliptin in the control group, and the results of them were not different from those of the others in the control group.

Conclusion Even though the larger extent of pancreas resection in the ITx group, glycemic control was better with ITx compared to that with metformin and a DPP4-inhibitor. In addition, we demonstrated that ITx might recover the insulin secretion which was suppressed after partial Px.

PE9 Islet biology & insulin secretion, immunology & transplantation

Altered glucagon levels in early diabetes

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Objective Diabetes develops as a bihormonal disease. Antagonizing glucagon action represents a new avenue for intervention of diabetes. This study investigated the serum glucagon levels in Korean patients with carbohydrate metabolism abnormalities.

Methods Subjects who did not have carbohydrate metabolism abnormalities before were examined: normal subjects (CONTROL), impaired fasting glucose (IFG), impaired glucose tolerance (IGT), IFG/IGT, and type 2 diabetes of isolated fasting hyperglycemia (IFH), isolated postprandial hyperglycemia (IPH), and fasting and postprandial hyperglycemia. Plasma levels of glucose, insulin and glucagon were measured in the fasting state (GTT0), and at 30 (GTT30) and 120 (GTT120) minutes after glucose loading.

Results Patterns of insulin response in IFG and IFH were similar to CONTROL. In other groups, insulin response showed the delayed hyperinsulinemia. In patients of diabetes with increased glycated hemoglobin of more than 7.5%, even though they were newly diagnosed, insulin secretion was markedly decreased. In CONTROL, there was no change of glucagon levels before and after glucose loading. In all patients, fasting glucagon levels were higher than CONTROL except IPH. In all patients, a rise of glucagon levels was observed at GTT30. There was impairment of glucagon suppression at GTT120 except IFG and IGT. The ratios of glucagon to insulin except IGT were higher than CONTROL at GTT30, while those at GTT120 were various according to subgroups.

Conclusion According to our data, glucagon imbalance starts before diabetes is diagnosed. Further studies about different mechanisms affecting glucagon imbalance in various types of glucose intolerance are needed.

PE10 Islet biology & insulin secretion, immunology & transplantation

A case of insulin autoimmune syndrome in patient with Hashimoto's thyroiditisSang-Yoon Kim^{1*}, Sang-Jin Kim¹, Mi-Kyung Kim¹, Hye-Soon Kim¹, Won-Ki Baek², Dae-Kyu Song³, Ho-Chan Cho¹Department of Internal Medicine, Keimyung University DongSan Medical Center, Daegu, Korea¹, Department of Microbiology, Keimyung University School of Medicine², Department of Physiology, Keimyung University School of Medicine³

Insulin autoimmune syndrome is one of the rare causes of hypoglycemia, and characterized by fasting hypoglycemia, endogenous hyperinsulinemia, and the presence of autoantibodies to insulin or insulin receptor in patients never been exposed to exogenous insulin. This syndrome is occasionally accompanied by several autoimmune disorders including Graves' disease and Rheumatoid arthritis. There is no report for Insulin autoimmune syndrome presenting hypoglycemia with concomitant Hashimoto's thyroiditis in Korea. Here we report a 52-year-old female with autoimmune hypoglycemia with Hashimoto's thyroiditis. She was diagnosed with primary hypothyroidism due to Hashimoto's thyroiditis and treated with levothyroxine 0.025mg for 3 years. Recently, She experienced recurrent fasting hypoglycemic symptoms such as dizziness and cold sweating and the symptoms disappeared rapidly with a carbohydrate-rich diet. However, She had no history of diabetes, nor insulin use. Blood analysis when the symptoms exist showed hypoglycemia (glucose level, 48 mg/dL) and simultaneous serum levels of insulin and C-peptide were increased above normal to 134.4 uIU/mL (normal range 8.3~11.9 uIU/mL) and 9.0 ng/mL (normal range 1.06~3.53ng/mL) respectively. The insulin to glucose ratio was 2.4. The imaging studies including CT, MRI, EUS showed no mass lesion in the pancreas and selective calcium-stimulated venous sampling was negative result. But anti-insulin autoantibody titer was high (above 100U/mL, reference <10U/mL). Therefore, we could suspect Insulin autoimmune syndrome as the cause of endogenous hyperinsulinemic hypoglycemia with concomitant Hashimoto's thyroiditis. We should keep in mind Insulin autoimmune syndrome as one of the causes of hypoglycemia in patients with no history of diabetes, but autoimmune disorders such as Hashimoto's thyroiditis.

PE11 Islet biology & insulin secretion, immunology & transplantation

A case of autoimmune polyglandular syndrome type IIIA including type 1 diabetes with concomitant pseudohypoparathyroidismSang-Jin Kim^{1*}, Sang-Yoon Kim¹, Won-Ki Baek², Dae-Kyu Song³, Ho-Chan Cho¹Department of Internal Medicine, Keimyung University DongSan Medical Center, Daegu, Korea¹, Department of Microbiology, Keimyung University School of Medicine², Department of Physiology, Keimyung University School of Medicine³

Autoimmune Polyglandular Syndromes (APS) were initially defined as a multiple endocrine gland insufficiencies associated to an autoimmune disease of endocrine and non-endocrine system. APS-Type III is characterized by autoimmune thyroid disease associated with other autoimmune disease (excluding Addison's disease and/or hypoparathyroidism) and is classified as IIIA, IIIB, IIIC, IIID according to the new classification (Betterle 2001) and especially, APS-Type IIIA is accompanied by another autoimmune endocrine disease such as type I diabetes mellitus. Pseudohypoparathyroidism (PHP) is a rare hereditary disease caused by resistance to parathyroid hormone (PTH), and is associated with typical symptoms and signs of hypocalcemia, hyperphosphatemia and normal or increased parathyroid hormone levels with or without morphological characteristics called Albright's hereditary osteodystrophy (AHO). We report a 32-year-old female with Autoimmune Polyglandular Syndrome with concomitant PHP. She experienced recurrent seizures above three times within a month, and blood analysis showed increased postprandial glucose level (212mg/dL), increased HemoglobinA1c (7.3%), low serum calcium level (5.5mg/dL, reference 8.7-10.4), high phosphorus level (6.7mg/dL, reference 2.5-4.5) and normal immunoreactive PTH level (20.47pg/mL, reference 13-54), much prominent calcifications in both basal ganglia and thalami in Computed Tomography of brain. She had typical features of Albright's hereditary osteodystrophy including short stature, truncal obesity, round face, short neck and low intelligence (full IQ 84) and decreased memory. Insulin dependent diabetes mellitus (type 1 diabetes mellitus) developed 11 years ago and hyperglycemia was treated with insulin (36units per day) for 11 years. Recently, she starts to take medication for Hashimoto's thyroiditis. In conclusion, she had insulin deficiency and Hashimoto's thyroiditis as autoimmune disorder. Therefore, we suspected APS-Type IIIA with concomitant PHP Type Ia or Ic. After the patient had been treated with daily oral calcium (2.2g) and ergocalciferol (0.35mg), calcitriol (0.5µm), her neurological signs and symptoms as well as hypocalcemia and hyperphosphatemia were improved and seizures were not recurred. Here, we report a case of APS Type IIIA manifesting type I diabetes mellitus and Hashimoto's thyroiditis with concomitant PHP Type Ia or Ic.

PE12 Acute & chronic complication

The role of estrogen-related receptor gamma (ERRg) in the development of vascular calcificationJi-Hyun Kim^{1*}, Han-Jong Kim¹, Joon-Young Kim³, Young-Keun Choi³, Chae-Myeong Ha¹, Sun Joo Lee¹, Chang Joo Oh¹, Jeong-Kook Kim¹, Eonju Jeon², Hyun-Ae Seo², Jong Ho Kim², Yeon Kyung Choi², Keun-Gyu Park², In-Kyu Lee¹Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, South Korea¹, Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea², Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea³

Objective Vascular calcification (VC), which refers to ectopic mineralization in vascular cells occurs frequently in many diseases such as chronic kidney disease (CKD), atherosclerosis, and diabetes. VC is vastly correlated with high risk of cardiovascular morbidity and mortality, due to arterial stiffness and impaired vascular compliance. Estrogen-related receptor gamma (ERRg), a member of orphan nuclear receptor superfamily is shown to be related to bone formation. However, role of ERRg in VC has not yet been investigated. This study was undertaken to examine the role of ERRg in VC.

Methods RT-PCR, Western blot, Von kossa's staining, Promoter assay. **Results** ERRg was upregulated during inorganic phosphate (Pi)-induced calcification of vascular smooth muscle cell (VSMC), along with increased expression of bone morphogenic protein-2 (BMP2), osteocalcin and alkaline phosphatase (ALP). Transient overexpression of ERRg stimulated promoter activity of osteogenic genes such as BMP2 and osteocalcin. Adenovirus-mediated overexpression of ERRg also augmented osteogenic gene expression and exacerbates Pi-induced calcification of VSMC. Moreover, inhibition of ERRg by a selective inverse agonist attenuated both Pi-induced osteogenic gene expression and calcium deposition in cultured VSMC. Finally, ex vivo aortic tissue culture showed that the ERRg inverse agonist significantly reduced Pi-induced calcification in mouse aorta. These results demonstrate that ERRg stimulates VC by upregulating osteogenic genes.

Conclusion Our findings suggest that inhibition of ERRg may be a potential therapeutic strategy for prevention of vascular calcification.

PE13 Acute & chronic complication

Cilostazol inhibits plasminogen activator inhibitor type 1 expression in liverYun-A Jung^{1*}, Hye Soon Kim¹, Sang Yoon Kim¹, Keun Gyu Park², In Kyu Lee², Mi-Kyung Kim¹Department of Internal Medicine and Institute for Medical Science, Keimyung University School of Medicine¹, Department of Internal Medicine, Kyungpook National University School of Medicine²

Objective Accumulating evidence suggests that plasminogen activator inhibitor (PAI)-1 plays an important role in the development of hepatic fibrosis via its involvement in extracellular matrix remodeling. Cilostazol, a selective type 3 phosphodiesterase inhibitor, is a potent antiplatelet agent currently used in clinical practice to treat patients with diabetic vascular complications. Our previous study showed that cilostazol inhibits vascular PAI-1 expression through multiple mechanisms including transforming growth factor- β (TGF- β) pathway. However, the effect of cilostazol on hepatic fibrosis is unknown. Therefore, the aim of the present study was to determine whether cilostazol prevents hepatic PAI-1 expression and fibrosis.

Methods We assessed the effect of cilostazol on TGF- β -stimulated PAI-1 expression and the TGF- β /Smad3 signaling pathway in mouse hepatocyte cell line (AML-12), and human stellate cell (hTERT) using by Western blot analysis. Transient transfection study was performed to measure the effect of cilostazol on PAI-1 promoter activity in human hepatoma cell line (HepG2). To determine the molecular mechanism by which cilostazol inhibits PAI-1 expression, immunofluorescent staining and electrophoretic mobility shift assay was performed.

Results Results showed that cilostazol inhibits TGF- β -stimulated PAI-1 protein expression in the AML12 and hTERT. In addition, transient transfection of a reporter gene under the control of the PAI-1 promoter revealed that cilostazol inhibits TGF- β -stimulated, Smad3/4-mediated and ALK5-mediated PAI-1 promoter activity in the HepG2. To determine the molecular mechanism by which cilostazol inhibits PAI-1 expression, the effect of cilostazol on Smad3 activity was studied. Results showed that cilostazol inhibits TGF- β -stimulated Smad3 phosphorylation, nuclear localization and DNA-binding activity.

Conclusion In conclusion, cilostazol inhibited TGF- β -stimulated PAI-1 expression and these data suggest it could be used to prevent hepatic fibrosis.

PE14 Acute & chronic complication

Peroxisomal dysfunction exacerbated renal injury in diabetic catalase null miceInah Hwang^{1*}, Jiyoun Lee¹, Jehyun Park¹, Hi Bahl Lee², Ye-Shih Ho³, Hunjoo Ha¹Department of Bioinspired Science, Division of Life & Pharmaceutical Sciences, the Center for Cell Signaling & Drug Discovery Research, and College of Pharmacy, Ewha Womans University, Seoul, Korea¹, Kim's Clinic and Dialysis Unit, Myrang, Korea², Institute of Environmental Health Sciences, Wayne State University, Detroit, Michigan, USA³

Objective Overproduction of reactive oxygen species (ROS) under hyperglycemia plays an important role in diabetic vascular complications, including diabetic nephropathy (DN). Plasma free fatty acid (FFA) as well as glucose is increased under the diabetic milieu and peroxisome and mitochondria participates in cellular FFA oxidation; therefore, we investigated whether deficiency of catalase, a major antioxidant enzyme in peroxisome, determine accelerated diabetic renal injury through peroxisomal dysfunction and abnormal renal FFA metabolism associated with increased ROS.

Methods Experimental diabetes was induced by multiple injections of low dose streptozotocin into catalase knock-out (CKO) and wild-type (WT) C57BL/6 mice. Mesangial cells transfected with siRNA for catalase were used to further elucidate the role of endogenous catalase in peroxisomal and mitochondrial function regulating FFA oxidation.

Results At four weeks after the induction of diabetes, equivalent high plasma glucose and FFA levels were observed in diabetic WT and diabetic CKO mice. However, parameters of DN including urinary albumin excretion, glomerular hypertrophy, and accumulation of extracellular matrix (ECM) proteins along with markers of oxidative stress were much more severe in diabetic CKO mice than diabetic WT mice. Catalase deficiency in CKO mice and mesangial cells induced defects in peroxisomal and mitochondrial biogenesis and FFA oxidation leading to renal lipid accumulation. Catalase deficiency in mesangial cells also increased mitochondrial ROS.

Conclusion The present data provide unprecedented evidence that FFA-induced peroxisomal dysfunction exacerbates diabetic renal injury, and that endogenous catalase is an important antioxidant that protects the kidney through peroxisomal and mitochondrial fitness under diabetic stress.

PE15 Acute & chronic complication

Protective effect of alpha-lipoic acid on vascular calcificationChae-Myeong Ha^{1*}, Han-Jong Kim², Joon-Young Kim², Young-Keun Choi¹, Sun Joo Lee¹, Chang Joo Oh¹, Jeong-Kook Kim¹, Ji-Hyun Kim¹, Udayakumar Karunakaran¹, Ji Yun Jeong³, Eonju Jeon³, Hyun-Ae Seo³, Jong-Ho Kim³, Yeon-Kyung Choi³, Jung-Guk Kim³, Keun-Gyu Park³, In-Kyu Lee³Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, South Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea³

Objective Vascular calcification leads to increased cardiovascular morbidity and mortality and prevalent in patients with chronic kidney disease. Although several reports have implicated mitochondrial dysfunction in cardiovascular disease and chronic kidney disease, little is known about the potential role of mitochondrial dysfunction in the process of vascular calcification.

Methods The present study investigated the effect of alpha-lipoic acid (ALA), a naturally occurring antioxidant that improves mitochondrial function, on vascular calcification in vitro and in vivo. Calcifying vascular smooth muscle cells (VSMCs) treated with inorganic phosphate (Pi) exhibited mitochondrial dysfunction, as evidenced by decreased mitochondrial membrane potential and ATP production, the disruption of mitochondrial structural integrity, and concurrently increased production of reactive oxygen species.

Results Pi-induced functional and structural mitochondrial defects were accompanied by mitochondria-dependent apoptotic events, including release of cytochrome c from the mitochondria into the cytosol, subsequent activation of caspase-9 and -3, and chromosomal DNA fragmentation. ALA blocked the Pi-induced VSMC apoptosis and calcification by recovery of mitochondrial function and intracellular redox status. Moreover, ALA inhibited Pi-induced downregulation of cell survival signals through the binding of growth arrest-specific gene 6 (Gas6) to its cognate receptor Axl and subsequent Akt activation, resulting in increased survival and decreased apoptosis. ALA significantly ameliorated vitamin D3-induced aortic calcification and mitochondrial damage in mice.

Conclusion The findings suggest ALA attenuates vascular calcification by inhibiting VSMC apoptosis through two distinct mechanisms; restoration of the Gas6/Axl/Akt survival pathway and preservation of mitochondrial function via its antioxidant potential.

PE16 Acute & chronic complication

Epicardial adipose tissue thickness assessed by cardiac magnetic resonance is an independent indicator for coronary artery stenosis, but not silent myocardial ischemia in asymptomatic type 2 diabetic patientsHyun Min Kim^{1*}, Kwang Joon Kim¹, Jae Hoon Moon¹, Hye-Jeong Lee², Young Jin Kim², Eun Seok Kang¹, Bong Soo Cha¹, Hyun Chul Lee¹, Byung-Wan Lee¹Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea¹, Department of Radiology, Yonsei University College of Medicine, Seoul, Korea²

Objective We investigated the association between epicardial adipose tissue (EAT) thickness and myocardial ischemia as well as coronary artery stenosis assessed by cardiovascular magnetic resonance (CMR) in asymptomatic type 2 diabetic patients.

Methods A total of 100 type 2 diabetic subjects (51 men and 49 women; mean age: 56.4 \pm 7.6 years) were enrolled. Silent myocardial ischemia by CMR was defined as an evidence of inducible ischemia or myocardial infarction and signal reduction or stenosis of \geq 50% in the vessel diameter were used as the criteria for significant coronary artery stenosis on coronary MR angiography.

Results EAT thickness was positively correlated with BMI, waist-to-hip ratio, systolic blood pressure, postprandial glucose, fasting/postprandial triglyceride, HbA1c level, and HOMA-IR. A total of 24 patients had significant coronary artery stenosis and 14 patients had silent myocardial ischemia in CMR (3 with silent myocardial infarction, 13 with inducible ischemia, 2 with both). EAT thickness was higher in patients who had significant stenosis; however, it was not different between the subjects with silent myocardial ischemia and the subjects with no evidence of silent myocardial ischemia in CMR (13.0 \pm 2.6 mm vs. 11.5 \pm 2.1 mm, p=0.01, 12.8 \pm 2.1 vs. 11.7 \pm 2.3 mm, p=0.11, respectively). In multivariate logistic regression analysis, EAT thickness was an independent indicator for significant coronary artery stenosis after adjusting for traditional risk factors (OR 1.353, p=0.031).

Conclusion Increased EAT thickness assessed by CMR is an independent risk factor for significant coronary artery stenosis in asymptomatic type 2 diabetes; however, the thickness was not associated with silent myocardial ischemia.

PE17 Acute & chronic complication

The role of apolipoprotein B/apolipoprotein A1 ratio in predicting occult coronary atherosclerosis detected by multi-detector computed tomographyChang Hee Jung^{1*}, Jenie Yoonoo Hwang¹, Mi Seon Shin¹, Ji Hee Yu¹, Eun Hee Kim², Sung Jin Bae², Dong Hyun Yang³, Joon-Won Kang³, Joong-Yeol Park¹, Woo Je Lee¹, Hong-Kyu Kim²Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea¹, Department of Health Screening and Promotion Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea², Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea³

Objective The ratio of apolipoprotein B (apoB) and apolipoprotein A1 (apoA1) has been associated with significant coronary stenosis detected by conventional coronary angiography. However, the optimal apoB/A1 cut-off for identifying subjects with significant coronary stenosis, especially using coronary multidetector computed tomography (MDCT), has not been determined. We therefore investigated whether apoB/A1 ratio could predict occult coronary atherosclerosis detected by coronary MDCT and we determined the optimal cut-off value of apoB/A1 ratio in detecting subjects with occult coronary atherosclerosis.

Methods This cross-sectional study included 1,401 subjects (877 men and 524 women) who underwent coronary MDCT and measurements of serum apoB and apoA1 during routine health screening examinations at the Asan Medical Center, Seoul, Republic of Korea.

Results Significant coronary artery stenosis was detected in 114 subjects (8.1%), 89 men and 25 women. An increase in apoB/A1 quartiles was associated with increased percentages of subjects with significant coronary stenosis and non-calcified plaques (NCAP). After adjustment for confounding variables, each 0.1 increase in serum apoB/A1 was significantly associated with increased odds ratios [ORs] for coronary stenosis and NCAP of 1.23 (95% confidence interval [CI], 1.11-1.36) and 1.19 (95% CI, 1.10-1.29), respectively. The optimal apoB/A1 ratio cut off value for MDCT detection of significant coronary stenosis was 0.58, which had a sensitivity of 70.2% and a specificity of 48.2% (area under the curve=0.61, 95% CI=0.58-0.63, P<0.001).

Conclusion Our results indicate that apoB/A1 ratio is a good indicator of occult coronary atherosclerosis detected by coronary MDCT and that subjects with apoB/A1 ratio greater than 0.58 are good candidates for coronary MDCT.

PE18 Acute & chronic complication

The combination effect of pioglitazone and alpha lipoic acid on the peripheral nerves in experimental diabetic rats

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Objective There are many limitations to treat diabetic peripheral neuropathy (DPN) using current therapeutic strategies and so new management tools based on the pathogenesis are necessary in this field. Before development of new agents, it is worth of investigating about combination therapeutic approach using pathogenetically beneficial drugs in the diabetic peripheral neuropathy. Therefore, in present study, we have investigated the combined effect of alpha lipoic acid (ALA) and pioglitazone (PIO) on the peripheral nerves in the diabetic rats.

Methods Animals were divided into 8 groups (N=6-8) and designated as follows: Normal, Normal+ALA(100mg/kg/day), Normal+PIO(10mg/kg/day), Normal+ALA(100mg/kg/day)+PIO(10mg/kg/day), DM, DM+ALA(100mg/kg/day), DM+PIO(10mg/kg/day), DM+ALA(100mg/kg/day)+PIO(10mg/kg/day). Statistical analyses were performed about current perception threshold(CPT), mechanical allodynia using von frey filaments, oxidative stresses, intraepidermal nerve fiber density(IENFD), and axonal morphology in sciatic nerve.

Results In results, blood glucose levels were not affected, and CPT was reduced in the DM+ALA+PIO group compared with DM group. However, there was no significant differences among DM+ALA, DM+PIO, and DM+PIO+ALA groups. IENFD was less reduced significantly in the DM+ALA+PIO group than other DM groups (7.61±0.52 vs 5.62±0.96 vs 5.56±0.60 vs 7.10±0.70, P<0.05). Mean myelinated axonal area in the sciatic nerves (70.2±3.46 and 61.1±2.91, P<0.05) were higher significantly in the DM+ALA+PIO group than DM group, however there was no significant differences among DM+ALA, DM+PIO, and DM+ALA+PIO groups although mild increased pattern was observed in the DM+ALA+PIO group.

Conclusion Our results demonstrated that combination using pioglitazone and alpha lipoic acid is more beneficial than alpha lipoic acid or pioglitazone monotherapy in the respect of peripheral nerve preservation in diabetes. Moreover, pioglitazone is preferentially considered in DPN patients taking ALA and who need more intensive glucose control at the same time for additional nerve protective effect.

PE19 Acute & chronic complication

Brachial-ankle pulse wave velocity and metabolic syndrome in Korean adultsHo Chan Cho^{1*}, Sang Jin Kim¹, Won Ki Baek², Dae Kyu Song², Hyun Sook Jang³, Pil Sook Park⁴, Byung Yeol Chun⁵, Dong Hoon Shin⁶Department of Internal Medicine, Keimyung University Dongsan Medical Center, Daegu, South Korea¹, Chronic Disease Research Center, Keimyung University School of Medicine², Department of Home Economics Education, Kyungpook National University³, Department of Food and Nutrition, College of Science and Engineering, Kyungpook National University⁴, Department of Health Promotion Research Center, Kyungpook National University⁵, Department of Preventive Medicine, Keimyung University School of Medicine⁶

Objective Metabolic syndrome is a cluster of multiple cardiovascular risk factors including glucose intolerance, insulin resistance, central obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDL-C), and hypertension. The pulse wave velocity (PWV) is a novel non-invasive indicator of arterial stiffness and compliance. The aim of our study was to investigate the relationship between PWV and cardiovascular risk factors in metabolic syndrome.

Methods We recruited 1503 Korean subjects from February 2006 to December 2006. Metabolic parameters, clinical characteristics, biochemical markers, ankle-brachial pressure index (ABI), and brachial-ankle PWV (baPWV) were obtained in each subject.

Results Among 1503 subjects (Mean age 62.8±9.59), prevalence of metabolic syndrome was 635 cases (42.2%) according to the National Cholesterol Education Program Adult Treatment Panel III criteria. The baPWV levels were significantly higher in patients with metabolic syndrome compared to subjects without metabolic syndrome (Rt; 1749±445 vs. 1565±380, Lt; 1752±455 vs. 1570±382, p<0.001). The correlation between baPWV levels were significantly associated with blood pressure (BP), total cholesterol, glucose, HDL, BUN (p<0.05). The multiple regression analysis showed that the right baPWV was significantly associated with waist circumference, right ABI (p<0.05) and the left baPWV was significantly associated with systolic BP and right ABI (p<0.05).

Conclusion This study indicates that patients with metabolic syndrome may have elevated arterial stiffness, suggesting that patients with metabolic syndrome may have a higher risk of cardiovascular disease in Korean adults. This study was supported by a grant of the Korea Centers for Disease Control and Prevention (2005-E71011-00, 2006-E71009-00).

PE20 Acute & chronic complication

Association between ankle-brachial index and nerve conduction study in type 2 diabetic patients

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Objective Several reports suggest that interactions between vascular and metabolic factors are involved in the pathogenesis of diabetic neuropathy. We aimed to assess the relationship between ankle-brachial index (ABI) and nerve conduction study (NCS) in patients with type 2 diabetes mellitus.

Methods Seven hundred and thirteen type 2 diabetic patients (M: 354, F: 359) were recruited. The fasting biochemistries were measured. ABI was measured in using VP-1000 system. Motor and sensory amplitudes, conduction velocities, F responses and latencies were assessed through the measurement of peripheral nerves with an electroneuromyographic device.

Results The mean age of subjects was 61.0±12.1 years. The mean DM duration, HbA1C, and body mass index (BMI) was 12.0±7.8 years, 8.3±2.9%, and 24.7±3.5 kg/m², respectively. In motor NCS, ABI was positively associated with nerve conduction velocity of tibial nerve. In sensory NCS, there was a positive correlation between ABI and the amplitudes of superficial peroneal and sural nerve. A multiple linear regression analysis demonstrated a significant association between ABI and some parameters of NCS (nerve conduction velocity of tibial nerve, and amplitude of sural nerve).

Conclusion This study suggests that peripheral vascular property might be associated with peripheral nerve status in type 2 diabetic patients.

PE21 Acute & chronic complication

Association between plasma leptin levels and chronic complications in type 2 diabetic patients

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Objective The aim of this study was to assess the association between plasma leptin levels and the chronic complications in type 2 diabetic patients.

Methods The aim of this study was to assess the association between plasma leptin levels and the chronic complications in type 2 diabetic patients.

Results The mean age of subjects was 62.2±13.1 years. The mean DM duration, HbA1C, and body mass index (BMI) was 10.3±8.7 years, 8.6±2.3%, and 24.4±4.0 kg/m², respectively. Plasma leptin levels in female with type 2 DM were higher than in male with type 2 DM. In female, plasma leptin levels were significantly higher in subjects with cerebrovascular disease (CVD) than those without CVD. However, there were no significant differences between other micro- and macrovascular complications in female. In a multivariate analysis, there was an independent association between plasma leptin level and CVD. In male, plasma leptin levels were significantly higher in subjects with macroalbuminuria and coronary heart disease (CHD) than those without macroalbuminuria and CHD, respectively. However, there were no significant differences between other micro- and macrovascular complications in male. In a multivariate analysis, plasma leptin levels were independently associated with macroalbuminuria and CHD.

Conclusion This study suggests that plasma leptin levels may be associated with microangiopathy and macroangiopathy in type 2 diabetic patients and there may be sex differences in their relationships.

PE22 Acute & chronic complication

Hyperglycemic hyperosmolar syndrome in young diabetic patient accompanied by acute pyelonephritis and nephrogenic diabetes insipidus

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Hyperglycemic hyperosmolar syndrome (HHS) is an acute complication of diabetes characterized by profound hyperglycemia, hyperosmolarity, and dehydration. HHS usually occurs in older patients, and develops in the situation that compromises water intake. Acute pyelonephritis is characterized by acute inflammatory infiltration extended from cortex to medulla, and may be associated with polyuria and reduced capacity to concentrate urine. We describe a case of HHS in young adult precipitated by acute pyelonephritis in both kidney and nephrogenic diabetes insipidus (NDI). CASE: A 22-year-old female presented with complaints of fever, dysuria, polydipsia, and nocturia of 7 days' duration. Her past medical history was non-specific. Laboratory data showed the following: WBC 28,900/mm³, sodium 168 mEq/L, BUN 41.7 ng/dL, Cr 1.9 mg/dL, plasma glucose 1095 mg/dL, HbA1C 11.03%, calculated serum Osmol 403 mOsm/kg, urine Osmol 501 mOsm/kg, urine ketone negative, anti-GAD antibody (-), islet cell antibody (-), anti-insulin antibody(-), pH 7.343, HCO₃⁻ 18.1 mmol/L. Physical examination and abdominal imaging study showed findings compatible with pyelonephritis in both kidney. E. coli grew in blood and urine culture. A diagnosis of HHS and acute pyelonephritis was made. The patient was treated with intravenous fluids, antibiotics and insulin infusion. She showed rapid response to treatment. However, polyuria (9,000-10,000 L/day) with low urine osmolarity persisted. Water deprivation and AVP administration revealed that she had NDI. With fluid therapy, the urine osmolarity was normalized, and the patient became symptom-free.

PE23 Acute & chronic complication

Effect of sulforaphane on transforming growth factor-β/Smad in hepatic fibrosis

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Objective Sulforaphane (SFN) is a dietary isothiocyanate that exerts chemopreventive effects via NF-E2-related factor 2 (Nrf2)-mediated induction of antioxidant/Phase II enzymes, such as heme oxygenase-1 (HO-1) and NAD(P)H quinone oxidoreductase 1 (NQO1). This work was undertaken to evaluate the effects of SFN on hepatic fibrosis and pro-fibrotic transforming growth factor (TGF)-β/Smad signaling, which are closely associated with oxidative stress.

Methods RT-PCR, Immunofluorescence analysis, Immunoblot assay, ChIP assay, Promoter assay.

Results SFN suppressed TGF-β-enhanced expression of type I collagen, fibronectin, tissue inhibitor of matrix metalloproteinase (TIMP)-1, and plasminogen activator inhibitor (PAI)-1 in AML12 and HepG2 cells. SFN inhibited TGF-β-stimulated activity of a PAI-1 promoter construct and (CAGA)₉ MLP-Luc, an artificial Smad3/4-specific reporter, along with reduction in phosphorylation and nuclear translocation of Smad3. Nrf2 overexpression was sufficient to inhibit the TGF-β/Smad signaling and PAI-1 expression. Conversely, knockdown of Nrf2, but not inhibition of HO-1 or NQO1 activity, significantly abolished the inhibitory effect of SFN on (CAGA)₉ MLP-Luc activity. Reduced glutathione (GSH) also had little effect on TGF-β/Smad3 signaling. Finally, SFN treatment attenuated hepatic fibrosis induced by bile duct ligation in mice, accompanied by reduced expression of the pro-fibrogenic genes.

Conclusion Collectively, our findings reveal an anti-fibrotic effect of SFN against hepatic fibrosis in part via Nrf2-dependent but antioxidant-independent inhibition of the TGF-β/Smad signaling.

PE24 Acute & chronic complication

The prevalence and clinical implications of painful diabetic neuropathy in Korea

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Objective Painful diabetic neuropathy (PDN) has implications for patient's morbidity. However, data on the prevalence and risk factors of DPNP in Korea are limited. To determine the prevalence and risk factors and evaluate the sleep impairment and quality of life in patients with PDN among the patients with diabetic peripheral neuropathy (DN).

Methods Data from Korean Diabetes Association Neuropathy Study group, a total of 3,339 type 2 diabetic patients were evaluated. PDN was diagnosed by using visual analogue scales (VAS) and medication history. The patients were asked to answer the Brief Pain Inventory-Sort Form (BPI-SF), Medical Outcomes Study Sleep measure (MOS-Sleep), and EuroQol (EQ-5D) and VAS.

Results Among the patients with DN (n=1,338, 33.5%), 65.3% (n=874) were found to be PDN (overall 26.2% of studied patients). PDN was independently associated with duration of diabetes, and nephropathy and hypertension. All measures about pain severity and interference were higher in patients with PDN compared to those without PDN. Patients with PDN reported much impaired sleep and lower EQ-5D and VAS scores compared to those without PDN. Multivariate analysis revealed that presence of macrovascular complication and hypertension was independently associated with indices of BPI-SF, MOS-Sleep, and EQ-5D and VAS. PDN patients had far advanced diabetic complications, which associated with decreased sleep adequacy and quality of life.

Conclusion There is a clear need for further research relating to prevention and treatment of DPN including the issues of sleep and quality of life.

PE25 Acute & chronic complication

The relation of lipid profiles and carotid intima media thickness in Korean type 2 diabetic patients

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Objective Carotid intima media thickness (cIMT) is thought to be a good marker for the prediction of cardiovascular disease. Dyslipidemia is regarded as a cardiovascular risk factor. So we evaluated the relation of lipid profiles and increased carotid intima media thickness in Korean type 2 diabetic patients.

Methods We checked lipid profiles for 63 Korean type 2 diabetic patients with more than 1 mm of cIMT (43% male, mean age 61 ± 7.8 years). The patients had no history of taking any antilipidemic agents.

Results HbA1c was 7.3%. Mean DM duration was 7.9 yrs. The mean level of total cholesterol was 198.2 ± 35.2 mg/dl, triglyceride: 159.4 ± 71.6 mg/dl, LDL-C: 142.6 ± 36.6 mg/dl, HDL-C: 47.6 ± 16.7 mg/dl (male: 47.6 ± 16.7 mg/dl, female: 48.0 ± 17.1 mg/dl), nonHDL-C: 151.2 ± 35.2 mg/dl. There were 2 myocardial infarctions.

Conclusion There was no correlation between lipid profile and increased cIMT. Therefore, we recommend cardiac evaluations are needed in all type 2 diabetic patients in spite of normal range of lipid profiles.

PE26 Acute & chronic complication

The relationship between serum adipocyte fatty acid-binding protein, tumor necrosis factor- α and change of renal function in healthy adult

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Objective Adipocyte fatty acid-binding protein (FABP4) and Tumor necrosis factor- α (TNF- α) are members of adipocytokines and plasma biomarkers closely associated with obesity and metabolic syndrome. We evaluated whether serum FABP4 and TNF- α are associated with renal function measured by estimated glomerular filtration rate (eGFR).

Methods A total of 493 subjects (Men:women=325:168, 40.8 ± 6.3 years) were selected from participants in a medical check-up program at Health Promotion center at 2003. Baseline serum FABP4 and TNF- α levels were measured, and glomerular filtration rate was calculated by MDRD (modification of diet in renal disease study) equation for renal function. The subjects were followed up 4 years later.

Results Baseline levels of serum FABP4 and TNF- α were 9.95 ± 4.32 ng/mL and 3.48 ± 1.74 pg/mL, respectively. Serum FABP4 level at baseline was shown to be negatively associated with eGFR ($r = -0.293$ $p < 0.001$ in 2003, $r = -0.178$ $p < 0.001$ in 2007), and also when adjusted for sex, age, BMI, Triglyceride, LDL-cholesterol, fasting blood sugar and systolic blood pressure ($r = -0.251$ $p < 0.001$ in 2003, $\beta = -0.209$ $p < 0.001$ in 2007). On the other hand, baseline serum TNF- α level was shown to be negatively associated with eGFR only in 2003 ($r = -0.122$ $p = 0.008$ in 2003, $r = -0.044$ $p = 0.346$ in 2007), and when adjusted for same clinical factors serum TNF- α didn't have significant relationship with eGFR. Both serum FABP4 and TNF- α were not significantly related to change in eGFR during 4 years.

Conclusion It seems that serum FABP4 levels could be a related with renal function in healthy adults, although the mechanism needs to be elucidated.

PE27 Acute & chronic complication

Diagnostic value of absence of coronary artery calcification in asymptomatic patients with type 2 diabetes

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Objective A growing body of evidence has suggested that patients with absence of coronary artery calcium (CAC) are highly unlikely to have obstructive coronary artery disease (CAD) and future cardiovascular events, thereby eliminating the need for further testing. However, the clinical utility of CAC scoring to exclude obstructive CAD in asymptomatic diabetic patients is not yet well established.

Methods From May 1, 2008, to December 31, 2010, a total of 624 consecutive patients with type 2 diabetes who had undergone MDCT were enrolled from those who visited the diabetes clinic of the Asan Medical Center. Among them, patients with chest pain, known myocardial infarction, or previous coronary revascularization were excluded. The remaining 542 patients were retrospectively analyzed in this study. At least one significant coronary stenosis with $> 50\%$ luminal narrowing on MDCT was defined as obstructive CAD.

Results Of 192 patients with 0 CAC, 26 (14%) had obstructive CAD. Multivariate logistic regression analysis demonstrated that 0 CAC was significantly associated with free of $> 50\%$ stenosis, with odds ratio of 4.1 (95% confidence interval 2.5 to 6.7), independently of conventional risk factors. The sensitivity, specificity, positive and negative predictive value for positive CAC to predict obstructive CAD were 86%, 47%, 47%, and 86% respectively. Multivariate logistic regression analysis controlling conventional risk factors showed that current smoking was the only variable significantly associated with the presence of obstructive CAD in patients with 0 CAC, with odds ratio of 4.7 (95% CI 1.5 to 15.1).

Conclusion Our findings suggest that 0 CAC could not safely exclude obstructive CAD on MDCT in asymptomatic patients with type 2 diabetes, since significant coronary artery obstruction could occur in the absence of coronary calcification. Current smoking might have a critical role in the development of obstructive CAD in asymptomatic diabetic patients with the absence of calcification.

PE28 Acute & chronic complication

Exendin-4 modulates sclerostin level induced by rosiglitazone in osteocyte-like cells

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Objective Rosiglitazone, an anti-diabetic drug in the thiazolidinedione (TZDs) class, works as insulin sensitizer in type 2 diabetes by activating the nuclear receptor peroxisome proliferator-activated receptor γ (PPAR γ) in fat cells. Despite their beneficial effects on treatment of diabetes, TZDs decrease in bone mineral density (BMD) and quality and increase in bone fractures. Although impairment of osteoblast differentiation and inducing the osteoclastogenesis by TZDs provides possible mechanism, the exact cause is unknown. Glucagon-like peptide-1 (GLP-1) increases bone mineral density (BMD) through various mechanisms in normal or diabetic rats. Osteocytes are now considered central to bone homeostasis. A secreted product of osteocytes, sclerostin inhibits bone formation by blocking osteoblast differentiation.

Methods In this study, we investigated the effect of exendin-4 (Ex-4), GLP-1 receptor agonist, on modulation of SOST/sclerostin expression induced by Rosiglitazone treatment in osteocyte-like MLO-Y4 cells, by quantitative real-time RT-PCR and western blot.

Results We found that rosiglitazone increased SOST/sclerostin in MLO-Y4 osteocyte like cell line, and pretreatment with Ex-4 abolished the SOST/sclerostin induction by rosiglitazone. Also, Ex-4 decreases the expression of SOST/sclerostin through cAMP/PKA dependent pathway in osteocytes.

Conclusion In conclusion, Ex-4 might increase the osteoblast differentiation through decreasing the expression of SOST/sclerostin induced by TZDs in osteocytes. Adding GLP-1 on TZDs based treatment may play a helpful role in rosiglitazone induced bone loss as well as synergistic roles in treatment of diabetes.

PE29 Acute & chronic complication

Association of serum adipokine levels with cardiac autonomic neuropathy, in Korean type 2 diabetic patients

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Objective Cardiac autonomic neuropathy (CAN) is a common complication of diabetes associated with poor prognosis. It is thought that adipocytokines contribute to the increased risk of vascular complications in patients with type 2 diabetes mellitus (T2DM). However, literature data on the association between CAN with adipocytokines such as leptin, TNF- α , adiponectin in subjects with T2DM are limited. Therefore, in the present study, we examined the relationship between fasting serum adiponectin, leptin, and TNF- α and CAN in Korean T2DM patients.

Methods A total of 148 T2DM patients were recruited. CAN was assessed by the five tests according to the Ewing's protocol and the time and frequency domain of heart rate variability (HRV) was evaluated. Serum TNF- α and adiponectin levels were measured using enzyme-linked immunosorbent assay and serum leptin levels were measured using radioimmunoassay.

Results Although, the mean levels of leptin, TNF- α and adiponectin were not significantly different between the groups with and without CAN, the levels of leptin and adiponectin had a tendency to increase as the score of CAN increased ($p=0.049$, $p=0.005$). LF in upright position were higher in without patients with CAN than with CAN borderline significantly ($p=0.05$). Serum leptin levels showed positive correlation with HF and negative correlation with LF/HF ratio in upright position. Regarding TNF- α , significant negative correlation was observed with SDNN, RMSSD and HF in upright position. Multivariate logistic regression analysis demonstrated that the odds of CAN increased with longer duration of diabetes (1.16, [1.03-1.31]) and higher HOMA-IR (1.68, [1.07-2.63]). The relative risks for presence of CAN in the highest tertile of the adiponectin levels were 39 (39.2, [3.92-391.9]) as compared to the patients in the lowest tertile of the adiponectin levels.

Conclusion In the present study, higher serum adiponectin levels were associated with an increased risk for the presence of CAN. Also, score of CAN correlated with serum adiponectin and leptin. Serum adipocytokines such as leptin and TNF- α were significantly correlated with parameters of HRV, representative markers of CAN. Future prospective studies with larger numbers of patient are required to establish a direct relationship between plasma adipocytokine concentrations and the development or severity of CAN.

PE30 Acute & chronic complication

Relationship with serum adipokine levels and microangiopathies in Korean type 2 diabetic patients

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Objective It is thought that adipocytokines contribute to the increased risk of vascular complications in patients with T2DM. However, there is still limited information on the relationship between microvascular complications with adipocytokines such as leptin, TNF- α , adiponectin in T2DM. Therefore, we examined the relationship between fasting serum adiponectin, leptin, and TNF- α and diabetic microangiopathies in Korean T2DM patients.

Methods A total of 153 T2DM patients were recruited. We retrospectively reviewed medical records and evaluated for diabetic nephropathy, retinopathy and neuropathy. Serum TNF- α and adiponectin levels were measured using ELISA and serum leptin levels were measured using RIA. Arterial pulse wave velocity and ankle-brachial index were assessed.

Results The mean levels of leptin were significantly higher in patients with neuropathy than without neuropathy. Serum adiponectin levels were lower in patients with nephropathy than in patients without nephropathy and were significantly higher in patients with retinopathy or neuropathy than those without retinopathy or neuropathy. The mean levels of TNF- α were not different according to the presence of microangiopathies. Serum adiponectin levels showed significant negative correlations with BMI, TG, hsCRP, apoB, HOMA-IR and positive correlations with HDL-C. Regarding serum leptin levels, significant positive correlation was found with BMI, SBP, TG, hsCRP, mean PWV, HOMA-IR and negative correlation with eGFR. Serum TNF- α levels showed negative correlation with eGFR and positive correlation with age and hsCRP. Multivariate logistic regression analysis demonstrated that the odds of neuropathy decreased with higher eGFR (0.97, [0.95-0.99]). The relative risks for presence of neuropathy in the highest tertile of the adiponectin levels were 3.5 (3.5, [1.43-8.57]) as compared to the patients in the lowest tertile.

Conclusion In the present study, higher serum adiponectin levels were associated with an increased risk for the presence of neuropathy. Future prospective studies with larger numbers of patient are required to establish a direct relationship between plasma adipocytokine concentrations and the development or severity of microvascular complications.

PE31 Acute & chronic complication

Effect of intrathecally administered cholera toxin in sepsis-induced hypoglycemiaYun-Beom Sim^{1*}, Soo-Hyun Park¹, Jin-Koo Lee², Seon-Mi Kim¹, Yu-Jung Kang¹, Sung-Su Kim¹, Su-Jin Kim¹, Ji-Young Seo¹, Chea-Ha Kim¹, Su-Min Lim¹, Hong-Won Suh¹Department of Pharmacology, Institute of Natural Medicine, College of Medicine, Hallym University¹, Department of Pharmacology, College of Medicine, Translational Research Center, Institute of Bio-Science and Technology, Dankook University²

Objective The aim of this study was to investigate the effect of intrathecally (i.t.) administered cholera toxin (CTX) on the regulation of neuropeptide gene expression and blood glucose (BDG) level in experimental sepsis.

Methods In this study, we used the mice sepsis models, such as cecal ligation and puncture (CLP) and LPS/D-galactosamine (LDG) injection models. Expression of mRNA levels of neuropeptides was determined using realtime RT-PCR. BDG level was measured using glucometer (Accu-Chek Performa blood glucose monitoring system).

Results CLP and LDG-induced sepsis causes a decrease of BDG level. The mRNA levels of α CGRP, POMC, CRH, and ENK increased in hippocampus and hypothalamus of sepsis-induced mice. I.t. administered CTX dose-dependently increased BDG levels. Treatment with CTX recovered a decreased BDG level in sepsis-induced mice. In addition, i.t. administered CTX altered mRNA levels of α CGRP, POMC, CRH, and ENK in sepsis-induced mice.

Conclusion Taken together, these results suggest that the regulation of neuropeptides via signaling of CTX-sensitive G proteins can be modulate BDG levels.

PE32 Acute & chronic complication

The relationship between A1c variability and coronary angiographic finding in T2DM

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Objective The effect of glycemic control on macrovascular complication has been still discussed because there is no discrete conclusion. Traditionally, many epidemiologic studies have used A1c as the criteria of glycemic control and tool for assessing association with diabetic complications. Recent several studies suggested postprandial glucose level or glucose fluctuation including A1c variability may be more important factors for cardiovascular disease than A1c itself at certain time. We try to find out relationship between A1c variability and severity of coronary angiography finding in T2DM.

Methods We reviewed charts of type 2 diabetes that they were followed up in our hospital at least 5 years previously and performed coronary angiography. We recorded A1c levels for over 5 years and assessed A1c variability by calculating of SD of A1c levels. Coronary artery disease was defined as no vessel involved or one more vessel involved (CAD (-) or CAD(+)).

Results Total 229 patients were finally included for our study. Male were 47.6% and mean age was 63.6 ± 10.0 years old. Their mean A1c and SD of A1c values for previous 5 years were $7.46 \pm 1.20\%$ and $0.86 \pm 0.67\%$, respectively. The patients of CAD (+) group have higher SD of A1c than CAD (-) groups ($p < 0.048$). The mean A1c values and A1c value at coronary angiography were not different between 2 groups.

Conclusion Type 2 diabetes with CAD in coronary angiography showed higher SD of A1c, but not mean A1c levels and A1c values of that time. $7.46 \pm 1.20\%$

PE33 Acute & chronic complication

The relationship of thyroid stimulating hormone and free thyroxine levels with coronary angiographic finding in type 2 diabetes with normal thyroid function

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Objective It has been well known that overt thyroid dysfunctions related to cardiovascular disease. Several recent studies reported that high range of normal TSH and fT4 levels have also effect on coronary atherosclerosis and correlated to severity of CAD. The prediction of degree of involvement of coronary arteries in type 2 diabetes before angiography is still challenging. We try to find out the relationship of TSH and fT4 levels with angiographic findings of type 2 diabetes in euthyroid state.

Methods We reviewed charts of type 2 diabetes performed coronary angiography. We measured free thyroxine (fT₄) and thyroid stimulating hormone (TSH). The severity of CAD were divided by the number of significantly involved vessels, as 0,1, 2 and 3 vessel disease.

Results Total subjects were 465 and their mean age was 63.3±10.3 years old, 5.7% and 8.0% of patients were hyperthyroidism and hypothyroidism, respectively. The mean fT₄ and TSH levels of euthyroid type 2 diabetes were 1.12±0.18 and 1.67±0.97, respectively. TSH and fT₄ levels did not show any significant difference among groups divided by severity of coronary angiography.

Conclusion In our study, we could not observe that TSH and fT₄ levels related with the severity of CAD in type 2 diabetes with normal thyroid function.

PE34 Acute & chronic complication

Association of serum adipocyte-specific fatty acid binding protein (A-FABP) with fatty liver index as predictive indicator of Non-alcoholic fatty liver disease(NAFLD)

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Objective Adipocyte specific fatty acid-binding protein(A-FABP) is a cytoplasmic protein that is expressed in macrophage and adipocyte and plays a role in insulin resistance, metabolic syndrome. Recently, some experts developed the "fatty liver index (FLI)" which varies between 0 and 100 as a predictive indicator of Non alcoholic fatty liver disease(NAFLD). The aim of this study was to investigate the relationship between serum A-FABP and FLI as indicator of NAFLD in apparently healthy subjects.

Methods Total 238 apparently healthy subjects (mean age: 42.8±7.2 yr, male 66.4%) without past history of alcohol & hepatitis in a medical check-up program at a Health Promotion Center. The subjects were re-evaluated 4 years later. FLI is calculated as : $(FLI=eL/(1+eL) \times 100, L=0.953 \times \log eTriglycerides+0.139 \times BMI+0.718 \times \log eGGT+0.053 \times \text{waist circumference} - 15.745)$.

Results Baseline serum A-FABP were significantly associated with FLI 4years later after adjustment age, sex($p<0.001$). The subjects with higher A-FABP levels had higher mean FLI score (P for trend : 0.001). After adjustment age, sex, serum A-FABP at baseline were shown to be significant associated with FLI, in other word development of NAFLD by year 4 (OR, 2.680; 95% CI 1.238-5.801 for highest tertile vs. lowest tertile, $p=0.012$). Also, FLI was associated with NAFLD was based on ultrasound examination($P=0.006$).

Conclusion This study demonstrates that higher serum A-FABP levels were associated with FLI as a predictive indicator of NAFLD. In other words, high A-FABP levels were associated with the risk for development of NAFLD.

PE35 Acute & chronic complication

High glucose and fatty acid increases BMP4 expression in human endothelial cells

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Objective Bone morphogenetic protein 4 (BMP4) has been known to be pro-atherogenic molecules in the previous literatures. Here we investigate how glucolipotoxicity affects BMP4 expression in endothelial cells and how BMP4 plays a role in diabetic vascular complications.

Methods Human umbilical vein endothelial cells (HUVECs) were treated with high glucose concentration (27.5 mM) and/or palmitate (500uM) for 24 hours or 72 hours. Expression of BMP4 in HUVECs treated with high glucose and/or palmitate were examined. Effect on high glucose and/or palmitate on the expression of adhesion molecules (ICAM-1, VCAM-1, E-selectin), ROS, and monocyte binding were examined. Using siRNA for BMP4, how BMP4 affects on the expression of adhesion molecules, ROS and monocyte binding in HUVECs with high glucose and/or palmitate treatments.

Results High glucose increases BMP4 expression in dose dependent manner in HUVECs. Fatty acids (palmitate) potentiates its expression. Expression of adhesion molecules were increased by treatments with high glucose and/or palmitate. When BMP4 was knockeddown by siRNA, this expression was blunted. High glucose and/or palmitate increases ROS production in HUVECs, BMP4 knockdown ameliorated this response. In monocyte binding assay, high glucose with palmitate induced monocyte binding in HUVECs and it was prevented by BMP4 siRNA.

Conclusion This study suggests that BMP4 might play a certain role in high glucose and/or fatty acid induced atherogenesis.

PE36 Acute & chronic complication

The association between regional arterial stiffness and chronic kidney disease in type 2 diabetes

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Objective The aim of this study was to determine the pulse wave velocity (PWV) of arterial segments that is most closely associated with chronic kidney disease (CKD) in subjects with type 2 diabetes.

Methods This study consisted of 522 patients and was performed between August 2009 and December 2009. At baseline, the central PWVs including the heart-femoral (hf), heart-carotid (hc), heart-ankle (ha) and carotid-brachial (cb) segments and the peripheral PWVs including brachial-ankle (ba) and femoral-ankle (fa), and augmentation index (AI) were measured for each subject. Serum creatinine and spot urine analysis were repeated with over 3-month intervals. CKD was defined as glomerular filtration rate (GFR) less than 60 ml/min per 1.73 m² (Modification of Diet in Renal Disease equation) or presence of repeated albuminuria.

Results The group with CKD exhibited significantly higher hfPWV, haPWV and baPWV, but not hcPWV, faPWV or AI. Age, duration of diabetes, systolic and diastolic BP and pulse pressure were all positively associated with hfPWV, haPWV and baPWV. When patients were categorized into quartiles of hfPWV and multivariate logistic analyses were controlled for covariates and known risk factors of CKD, those of the fourth quartile were at a higher risk of increased CKD than other quartiles (odds ratio (OR)=2.47, (95% CI=1.27-4.82)). Conversely, all quartiles of haPWV and baPWV lost significance after adjustment for confounding factors (P for trend=0.212 and 0.129, respectively).

Conclusion We found that CKD was most closely associated with hfPWV, suggesting the most reliable index of regional arterial stiffness index in CKD.

PE37 Acute & chronic complication

LDL particle size and microvascular complications in type 2 diabetes mellitus

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Objective LDL particles with small size and high density is known as an important risk factor for cardiovascular diseases in diabetic patients as well as non-diabetics. We analyzed LDL subclass in type 2 diabetic patients with LipoPrint LDL system to investigate the LDL particle size and its role in diabetic microvascular complications.

Methods Total 150 type 2 diabetic patients (Men 80/Women 70) among 377 patients without previous medication history for dyslipidemia were analyzed. LDL subclass was determined with LipoPrint LDL system which fractionates LDL into seven parts (LDL1-7) according to size and extent of charge. From LDL3 to LDL 7 are defined as small sized LDL and we calculated "small-sized LDL proportion" from the percent of small-sized LDL over whole LDL.

Results Mean age and BMI of study population were 55.8 ± 14 years (mean \pm SD) and 24.7 ± 11 kg/m². Their average HbA1c and LDL particle size of the study population were $9.8 \pm 2\%$ and 26.3 ± 0.3 nm. Mean small-sized LDL proportion from LipoPrint LDL system was $21.6 \pm 18\%$. In partial correlation analysis, small-sized LDL proportion was positively correlated with albumin-creatinine ratio ($r=0.340$, $p<0.005$) and mean LDL particle size was negatively correlated with ACR ($r=-0.322$, $p<0.005$).

Conclusion We analyzed small-sized LDL proportion in type 2 diabetic patients and it was significantly correlated with excretion of albumin in urine after adjusting age and BMI, HbA1c. It suggests that small sized LDL might play a role in the development of diabetic nephropathy.

PE39 Clinical diabetes & therapeutics

Metabolic characteristics in Korean type 2 diabetic patients according to fatty liver and/or visceral obesityEun Young Lee^{1*}, Sena Hwang¹, Young Ju Choi², Byung Wook Huh², Byung-Wan Lee¹, Eun Seok Kang¹, Bong Soo Cha¹, Eun Jig Lee¹, Hyun Chul Lee¹, Kap Bum Huh²Department of Endocrinology and Metabolism, Yonsei University College of Medicine¹, Huh's Diabetes Center and 21st Century Diabetes and Vascular Research Institute²

Objective It is believed that both visceral fat and fatty liver are important to develop insulin resistance. To investigate metabolic characteristics of each anthropometric feature, we analyzed type 2 diabetic patients according to fatty liver (FL) and/or visceral obesity (VO).

Methods A total 5,270 (M:F 1.1:1) patients with type 2 diabetes were recruited through Huh's Diabetes Clinic from January 2003 to June 2009. We divided patients as following groups; control (n=1,407), FL (n=985), VO (n=748), and combined group who had both FL and VO (n=2,130). Insulin sensitivity was measured by a rate constant for plasma glucose disappearance (Kitt, %/min) using short insulin tolerance test (insulin resistance, Kitt < 2.5). Visceral fat thickness (VFT) and fatty changes of liver were examined by ultrasound.

Results Although patients with FL or VO did not show any difference in whole-body fat (%), their BMI was significantly higher than control group. Waist circumference (WC) and VFT increased in the following order, control, FL, VO, and combined group. Insulin resistance increased comparably in both FL and VO groups, and more prominently in combined group. BMI, WC, VFT, and systolic blood pressure increased more in VO group than FL group. However, serum triglyceride levels increased and HDL-cholesterol decreased more in FL group than VO group. On multiple regression analysis, the odds ratio for insulin resistance increased in order as follows; VO, FL, and combined group after adjusting known risk factors (OR 1.559, 1.815, and 2.338, respectively).

Conclusion Based on these results, we suggest that fatty liver may be a stronger predictor than visceral obesity of dyslipidemia and insulin-resistant states.

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PE38 Clinical diabetes & therapeutics

Association of circulating metabolic intermediates with inflammatory and oxidative stress markers and arterial stiffness in male patients with newly-diagnosed type 2 diabetesChang Young Ha^{1*}, Ji Young Kim³, Jean Kyung Paik², Oh Yoen Kim³, Eun Jig Lee⁴, Jong Ho Lee²Interdisciplinary Course of Science for Aging, Graduate School, Yonsei University¹, Research Laboratory of Clinical Nutrigenetics/Nutrigenomics, Dept. of Food & Nutrition, College of Human Ecology, Yonsei University², Yonsei University Research Institute of Science for Aging, Yonsei University³, Division of Endocrinology, Yonsei University College of Medicine⁴

Objective To determine whether circulating metabolic intermediates are associated with inflammation, oxidative stress, and arterial stiffness in men with newly-diagnosed type 2 diabetes.

Methods Men with newly-diagnosed type 2 diabetes (n=26) and age- and body mass index-matched healthy men (n=27) were included. We measured levels of inflammatory and oxidative markers, and arterial stiffness by brachial-ankle pulse wave velocity (ba-PWV). Metabolomic profiling was analyzed with ultra performance liquid chromatography and quadrupole time-of-flight mass spectrometry.

Results Diabetes patients showed higher circulating levels of glucose, triglyceride, oxidized-LDL, high sensitivity C-reactive protein, interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), homeostasis model assessment-insulin resistance, urinary 8-epi-prostaglandin F_{2a} (8-epi-PGF_{2a}), and ba-PWV than healthy men. In plasma, 19 metabolites including 3 amino acids (leucine, lysine, and phenylalanine), 8 acylcarnitines (propionyl-, octanoyl-, decanoyl-, palmityl-, heptadecanoyl-, linoleyl-, and vaccenyl-carnitines), 6 lyso-phosphatidylcholines (lysoPCs) (C14:0, C16:1, C18:1, C18:3, C20:5, and C22:6), and 2 lyso-phosphatidylethanolamines (lysoPEs) (C18:2 and C22:6) significantly increased in diabetes patients, whereas serine and lysoPE (C18:1) decreased. Decanoyl carnitine, lysoPCs (C14:0, C16:1, C18:1, and C22:6), and lysoPE (C18:1) with variable importance in the projection values >1.0 were major plasma metabolites that distinguished healthy and diabetic men. Decanoyl carnitine positively correlated with oxidized-LDL, 8-epi-PGF_{2a}, IL-6, and TNF- α , and ba-PWV. Ba-PWV correlated positively with lysoPCs C14:0 and C16:1, and negatively with lysoPE C18:1. 8-epi-PGF_{2a} correlated positively with lipoprotein-associated phospholipase A₂, ba-PWV and lysoPCs (C14:0 and C16:1).

Conclusion Metabolic analysis revealed that circulating intermediate metabolites can be closely associated with inflammation, oxidative stress, and arterial stiffness in early diabetes.

PE40 Clinical diabetes & therapeutics

Dietary calorie restriction improves RBP4 and is associated with reduced visceral fat but not with hepatic lipid in obese women with type 2 diabetesHee Jung Ahn^{1*}, Jin Young Jang¹, Hee Geum Seok¹, Jae Hyuk Lee², Gang Seo Park², Kyung Ah Han², Kyung Wan Min²Diabetes Center, Eulji Hospital¹, Department of Internal Medicine, Eulji University School of Medicine²

Objective Retinol binding protein 4 (RBP4) is a visceral adipose tissue secretory protein. Increased RBP4 serum level could be a marker of hepatic lipid content that closely associated with insulin resistance. We examined whether the dietary calorie restriction (CR) could be reversed RBP4 and related with VF and hepatic lipid in obese women with type 2 diabetes.

Methods Total 84 with type 2 diabetic were randomly assigned to CR and control group. CR group was recommended to reduce their usual energy intake by -500 kcal/d and was monitored with 3 day diet record. We examined the plasma RBP4, insulin resistance by HOMA-IR, abdominal total fat (TF), visceral fat (VF), subcutaneous fat (SF), liver attenuation (LA), which is inversely related to hepatic lipid content using computed tomography at baseline and the end of 12 week intervention.

Results The age of subjects was 55 ± 7.1 years, duration of diabetes was 4.1 ± 3.5 years and BMI was 27.2 ± 2.6 kg/m². CR group showed lower RBP4 ($-6.5 \pm 19.1\%$, $P=0.025$), body weight, HbA1c, HOMA-IR, TF, VF and SF and higher LA content compared to the C. Reduced RBP4 level was positively correlated with VF ($r=0.211$, $P=0.008$) and insulin resistance ($r=0.310$, $P<0.001$), but not SF and LA content.

Conclusion CR could be reversed RBP4 in obese women with type 2 diabetes. The decreased RBP4 is associated with VF, but not hepatic lipid, and might be associated with insulin resistance in obese women with type 2 diabetes.

PE41 Clinical diabetes & therapeutics

Aerobic exercise improves RBP4 and is associated reduced visceral fat in obese women with type 2 diabetesKyung Hwa Cha^{1*}, Hee Jung Ahn¹, Jin Young Jang¹, Hee Geum Seok¹, Jae Hyuk Lee², Gang Seo Park², Kyung Ah Han², Kyung Wan Min²Diabetes Center, Eulji Hospital¹, Department of Internal Medicine, Eulji University School of Medicine²

Objective Retinol binding protein 4 (RBP4) was shown to be predominantly secreted from visceral fat in patients with obesity and type 2 diabetes. Exercise is effective in reducing visceral fat. We examine whether the aerobic exercise could be reversed RBP4 and related with VF in obese women with type 2 diabetes.

Methods Total 60 with type 2 diabetic were randomly assigned to aerobic exercise group (AE), and Control (C) group. AE was recommended to walk briskly for 150 min/week every day, which corresponds to an energy expenditure of 500 kcal/day, was monitored with accelerometer. We examined the plasma RBP4, abdominal total fat (TF), visceral fat (VF) by computed tomography (CT), lean body mass by DXA, the aerobic exercise capacity by oxygen consumption rate at anaerobic threshold (VO2-AT) at baseline and the end of 12 week intervention.

Results The age of subjects was 54.0±7.0 years, duration of diabetes was 4.3±4.0 years and BMI was 26.7±2.4 kg/m². AE group showed higher VO2-AT (31.8±62.8%, P<0.05) and lower waist circumference (P<0.05), VF/TF (P<0.05), HbA1c (P<0.05) and RBP4 (-6.8±22.6%, P<0.05) compared to the C. However, body weight and lean body mass was significantly different between the two groups. Reduced plasma RBP4 levels was correlated with reduced VF/TF (r=0.322, P=0.009).

Conclusion Aerobic exercise induced a significant improvement in aerobic exercise capacity and reduction in visceral fat and RBP4. Reduced RBP4 is associated with visceral fat in obese women with type 2 diabetes.

PE42 Clinical diabetes & therapeutics

Low serum magnesium levels were associated with the development of type 2 diabetes In women with history of gestational diabetes mellitus: The Korean National Diabetes Program (KNDP) studySae Jeong Yang^{1*}, Tae Nyun Kim³, Sei Hyun Baik¹, Kwan Woo Lee⁴, Moon Suk Nam⁵, Yong Soo Park⁶, Jeong Taek Woo⁷, Young Seol Kim⁷, Sung-Hoon Kim²Department of Internal Medicine, Korea University College of Medicine¹, Department of Medicine, Cheil General Hospital & Women's Healthcare Center, Kwandong University College of Medicine², Department of Medicine, Haeundae Hospital, Inje University College of Medicine³, Department of Internal Medicine, Ajou University College of Medicine⁴, Department of Internal Medicine, Inha University College of Medicine⁵, Department of Internal Medicine, Hanyang University College of Medicine⁶, Department of Internal Medicine, Kyung Hee University College of Medicine⁷

Objective Gestational diabetes mellitus (GDM) is a strong predictor of postpartum prediabetes and the transition to overt type 2 diabetes (T2DM). Decreased blood and tissue levels of magnesium are related to high blood pressure, systemic inflammation, insulin resistance, and the incidence of T2DM. Although many reports indicate that low magnesium status is correlated with deteriorated glucose tolerance, serum magnesium level and the risk for T2DM in women with a GDM history has not been evaluated.

Methods We analyzed postpartum serum magnesium levels and the development of prediabetes and T2DM in women with prior GDM according to the ADA criteria using the Korean National Diabetes Program (KNDP) GDM cohort.

Results During the mean follow-up of 15.6±2.0 months after screening, 116 women were divided into three groups according to glucose tolerance status. Finally, eight patients (6.8%) were diagnosed with T2DM, 59 patients (50.9%) with prediabetes, and 49 patients (42.2%) with normal glucose tolerance (NGT) after follow-up. The T2DM group had the lowest serum magnesium level (1.30 [1.25-1.35] mEq/L) at postpartum, but the prediabetes group (1.4 [1.30-1.40] mEq/L) and the NGT group (1.4 [1.30-1.40] mEq/L) showed no significant differences (P=0.519). A multiple regression analysis showed that postpartum serum magnesium was a significant predictor for T2DM (odds ratio, 0.273×10⁻⁵, 95% confidence interval, 0.00-0.609).

Conclusion Postpartum low serum magnesium status is a potent risk factor for the development of T2DM in women with a history of GDM.

PE43 Clinical diabetes & therapeutics

Influences of different gastrointestinal tract reconstruction approaches on postoperative pancreatic β-cell function in patients with type 2 diabetes mellitus

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Objective To study influences of different gastrointestinal tract reconstruction approaches on pancreatic β-cell function in patients with type 2 diabetes mellitus (T2DM).

Methods 23 cases of gastric cancer T2DM patients were followed up, including 13 patients underwent Billroth I gastrectomy and 10 patients underwent gastrointestinal bypass surgery (Billroth II in 4 cases, Roux-en-Y anastomosis in 6 cases). The function of pancreatic β cell function was assessed evaluated by the results of OGTT. Serum insulin was measured by ECLIA and blood glucose was measured by glucose oxidase method. HOMA-IR and HOMA-β were valuated by the HOMA equation.

Results The T2DM remission rate was 90% (9/10) in the gastrointestinal bypass surgery group, and 23% (3/13) in Billroth I group (P<0.01). Glycosylated hemoglobin A1c and glycated hemoglobin HbA1 improved significantly in patients after gastrointestinal bypass surgery (P<0.05), but the difference in Billroth I group was not statistically significant (P>0.05). OGTT showed that fasting plasma glucose and post-glucose load BG at each time point was significantly lower in gastrointestinal bypass surgery group than Billroth I group. Insulin levels(30min,60min), insulin release index(30min,60min), HOMA-β and ΔI30/ΔG30, were significantly higher in gastrointestinal bypass surgery group than Billroth I group (P<0.05).

Conclusion Patients underwent gastrointestinal bypass surgery following gastrectomy resulted in significant improvement or resolution of T2DM and significant recovery of β-cells function.

PE44 Clinical diabetes & therapeutics

A case of brittle diabetes mellitus associated with circulating anti-insulin antibody

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Brittle diabetes is a term used to describe hard-to-control swings in blood glucose levels. Most cases are insulin-dependent type 1 diabetes mellitus (DM) and the causes of unstable blood glucose are obscure. A 63-year-old man (BMI 20.2 kg/m²) with an 8-year history of type 2 DM was admitted due to poor glycemic control and frequent hypoglycemia. Basal-bolus insulin therapy (detemir and aspart) had been commenced 8 months prior to the referral due to poor glycemic control (HbA1c 15.0%) and impaired renal function (Cr 2.9 mg/dL). Shortly after starting insulin, he began to have unstable blood glucose profiles, showing severe glycemic excursions at daytime and frequent fasting hypoglycemia. Various therapeutic approaches including tailored insulin doses, exercise program and consultation with dietician were ineffective in controlling his unstable blood glucose swings. His medical history was unremarkable except type 2 DM and chronic renal failure, and he had not taken medications containing sulfhydryl group. Extensive laboratory tests were in vain except anti-insulin antibody. A high titer of anti-insulin antibody [342.0 U/mL (normal range <10 U/mL)] was reported with a high level of total insulin and a low level of c-peptide. Changing the analogue insulins into the human insulins and initiation of plasmapheresis decreased the titer of anti-insulin antibody, which resulted in dramatically improvement of glycemic control with less swings of glycemic excursions. Although it is not clear whether insulin analogues triggered insulin autoimmune syndrome, this case illustrates that clinicians should be alert to the possibility of the brittle diabetes induced by anti-insulin antibody.

PE45 Clinical diabetes & therapeutics

Effect of lifestyle modification on serum chemerin concentration in overweight and obese adults with type 2 diabetes

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Objective Among the recently identified adipokines, chemerin is thought to be associated with adiposity, insulin resistance, metabolic syndrome risk factors and inflammation. In this study, we evaluated whether there was significant change in serum levels of chemerin after a 3month lifestyle modification intervention in overweight and obese adults with type 2 diabetes.

Methods 35 overweight or obese subjects with type 2 diabetes were randomized to receive intensive lifestyle modification including supervised exercise sessions (3 times per week) or usual care for 3months. Anthropometric and clinical data were collected before the intervention and after 3months.

Results 16 subjects completed the intervention both in the intervention and usual care group. There was a significant decrease in BMI, waist circumference, triglyceride, r-GTP, HbA1c, fasting glucose, 2hr postprandial glucose, HOMA-beta, visceral and subcutaneous abdominal fat area, total body fat and a significant increase in VO2 max in the intervention group compared to the usual care group. Change in serum chemerin after 3 months showed a significant decrease in the intervention group compared to the usual care group (-8.1±21.6 vs 8.2 ±15.9 ng/ml, p=0.03). Change in serum chemerin after 3 months correlated with changes with body fat change, hsCRP and lipocalin 2.

Conclusion An intensive 3 months lifestyle modification intervention was able to decrease serum chemerin level compared to usual care in overweight and obese type 2 diabetic patients. This finding should be tested in a larger population and the clinical significance needs further elucidation.

PE46 Clinical diabetes & therapeutics

The comparative study of dipeptidyl peptidase-IV inhibitor and sulfonylurea on the effect of improving glucose variability and oxidative stress in type 2 diabetic patients with inadequate glycemic control on metformin

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Objective Our study tries to compare the effect of sitagliptin on 24-hour blood glucose variability and oxidative stress marker to that of sulfonylurea such as glimepiride.

Methods A 4-week, randomized, double blind-labeled prospective design was used. We recruited total 26 patients who were treated with metformin for at least 2 months(more than 1000mg) and glycemic changes obtained by CGM and these data are averaged over all subjects.

Results The comparison of HbA1c between baseline and follow-up showed that HbA1c was significantly reduced from 7.1±0.4% to 6.8±0.3% in sitagliptin group (p=0.002) and from 7.3±0.4% to 6.9±0.4% in glimepiride group (p<0.001). Fasting glucose level showed a tendency to decrease between baseline and 4-weeks in sitagliptin group (from baseline 137.5±18.5 to 125.0±19.4 mg/dL, p=0.622) and significantly decreased in glimepiride group (from baseline 139.6±26.6 to 118.9±20.0 mg/dL, p<0.001). The sitagliptin group and the glimepiride group led to similar HbA1c levels (p=0.709) and fasting glucose level (p=0.526) after 4 weeks and there was no significant differences between two groups. The MAGE were significantly decreased in sitagliptin group (from baseline 96.6±8.0 mg/dL to 72.1±13.1 mg/dL, p=0.002), but no significant difference in glimepiride group (from baseline 103.0±27.2 mg/dL to 89.2±26.1 mg/dL, p=0.175).

Conclusion We proved that sulfonylurea can be converted into sitagliptin without problems. In addition, when sitagliptin is used in combination with metformin, the patients showed much more efficient blood glucose controlling effects.

PE47 Clinical diabetes & therapeutics

The effect of telephone counseling on glycemic control in diabetes using insulin treatment

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Objective Diabetes mellitus lowers the quality of patients by acute and chronic diabetic complications. It is important to valance among diet, exercise and medication, but we cannot mention about the treatment of diabetes without patient education. The education contains not only compliance to medication but also self-management for daily life. Above all, telephone counseling is useful for patient experiencing uncontrolled glucose state by helping insulin dose titration and diet control. The purpose of our study is to evaluate the importance of telephone counseling.

Methods We enrolled 238 diabetic patients changing to basal insulin or adding basal insulin in Dongsan Hospital from February 2008 to March 2010. They changed from other insulin to basal insulin or added basal insulin to their medication. We monitored their fasting glucose for 12 weeks by counseling insulin dose titration, diet and exercise weekly.

Results Among 238 patients, 57 patients quit the monitoring. Basal fasting glucose is 151 mg/dL, HbA1c 9.8%. After 12 weeks of monitoring, we found that fasting glucose decreased to 116mg/dL and HbA1c also improved to 7.7%. 14 patients(9.3%) were checked HbA1c below 7%, but 24 patient(19%) after 12 weeks.

Conclusion In conclusion, the effect of insulin treatment can be maximized by telephone counseling.

PE48 Clinical diabetes & therapeutics

A case of fulminant type 1 diabetes mellitus with HLA DRB1*0405/*0406-DQB1*0302/*0401

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The clinical characteristics of fulminant type 1 diabetes are a remarkably abrupt onset of disease, very short (<1 week) duration of diabetic symptoms, ketoacidosis at diagnosis, negative status of islet-related autoantibodies, virtually no C-peptide secretion (fasting plasma C-peptide<0.3 ng/ml), a near normal HbA1c level and an elevated serum pancreatic enzyme level. We experienced a case of fulminant type 1 diabetes with rapidly development of diabetic ketoacidosis. A 37-year-old woman was admitted with stuporous consciousness. This patient had suffered from epigastric pain and vomiting 4 days ago and hospitalized with diagnosis of acute pancreatitis in other hospital. At that time, her blood chemistry record showed glucose of 79 mg/dl, amylase/lipase of 271/774 U/L. 3 days later, she had dyspnea, anuria, disturbed consciousness and transferred to our hospital. The laboratory analysis showed PH 6.94, glucose 1602 mg/dL, urine ketone (+), HbA1C 5.8%, amylase/lipase 56/41 U/L. She had negative antibodies for islet-related autoantibodies. Her viral markers (included Coxsackievirus B, EBV, CMV) were all negative. HLA haplotypes were DRB1*0405-DQB1*0401, DQA1*0303-DQB1*0401, DQA1*0302-DQB1*0303, and DRB*0901 which might be a considerable risk allele for fulminant type1 diabetes. She was diagnosed with fulminant type 1 diabetes and discharged in stable condition on basal plus bolus insulin therapy. We reported a case of fulminant type 1 diabetes. The pathogenesis of this disease still remains to be clarified.

PE49 Clinical diabetes & therapeutics

HbA1c reflects dyslipidemia in older nondiabetic Korean adultsJiHye Shin^{1*}, HaeJung Lee², SangYong Kim¹, HakYeon Bae¹, JinHwa Kim¹Division of Endocrinology and Metabolism, Chosun University Hospital, Gwangju, Republic of Korea¹, Diabetes Center, Chosun University Hospital, Gwangju, Republic of Korea²

Objective Data from the National Health and Nutrition Examination Survey and the Framingham Offspring Study suggest that HbA1c levels increase with age even after adjustments for demographic and glycemic variables among nondiabetic subjects. Elevated HbA1c levels are associated with a higher incidence of microvascular and macrovascular complications in diabetes. The aim of this study is to estimate the association of HbA1c with cardiovascular disease risk factors in older nondiabetic adults.

Methods We retrospectively studied asymptomatic Korean adults of 60 years old or older who underwent voluntary regular health check-ups at the Health Promotion Center of Chosun University Hospital (Gwangju, Republic of Korea) from January 2009 to December 2010. Individuals previously diagnosed with diabetes, hypertension, or dyslipidemia and those treated with hypoglycemic agents, antihypertensive agents, and lipid lowering agents were excluded. After these exclusions, 366 individuals were included in this study.

Results HbA1c revealed a significant correlation with age ($r=0.111$, $P=0.033$), waist circumference ($r=0.104$, $P=0.047$), fasting plasma glucose ($r=0.267$, $P<0.001$), triglyceride ($r=0.139$, $P=0.008$), LDL cholesterol ($r=0.113$, $P=0.030$), and HDL cholesterol ($r=-0.116$, $P=0.027$). Multiple regression analysis showed that HbA1c had a association with fasting plasma glucose, LDL cholesterol, and HDL cholesterol.

Conclusion The HbA1c level is independently correlated with dyslipidemia other than fasting glucose level in older nondiabetic Korean adults.

PE50 Clinical diabetes & therapeutics

The effect of seasonal vitamin D supplementation on glycemic control in KoreaOhk Hyun Ryu^{*}, Juri Park, Jun Goo Kang, Sung Hoon Yu, Chul Sik Kim, Seong Jin Lee, Eun Gyoung Hong, Doo Man Kim, Sung Hee Ihm, Jae Myung Yu, Hyung Joon Yoo, Moon Gi Choi

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Objective Diabetes is associated with vitamin D deficiency. In winter, vitamin D deficiency is aggravated in Korea. But there was no intervention study to lower glucose by seasonal vitamin D supplementation in Korea. We performed randomized controlled trial to investigate the effect of seasonal vitamin D supplementation to glycemic control in winter.

Methods We enrolled female diabetic patients (50 to 70 years old) who took oral antidiabetic drugs or managed diabetes by diet or exercise. We excluded patients who took vitamin D or calcium. We also excluded participants who had chronic kidney disease. We randomly assigned participants into two groups. We provided vitamin D 1000IU+elemental calcium 500mg daily or elemental calcium 500mg for 12 weeks to intervention group and control group, respectively. We compared HbA1c, Vitamin D, mean difference of HbA1c between groups.

Results 61 participants (31 in intervention group and 30 in control group) were included in the analysis. There was no difference in baseline HbA1c (7.38 ± 0.59 vs 7.37 ± 0.71 , $P=0.949$), DM duration (8.9 ± 6.5 years vs 9.9 ± 5.6 years, $P=0.502$), and vitamin D level (12.7 ± 5.9 ng/ml vs 13.1 ± 6.9 ng/ml, $P=0.770$) in intervention group and control group, respectively. After 12 weeks of intervention, HbA1c was $7.43\pm 0.083\%$ in intervention group, HbA1c was $7.52\pm 0.88\%$ in control group ($P=0.679$). The mean difference of HbA1c before and after intervention was 0.05% and 0.18% in intervention and control group, respectively ($P=0.396$). But in the intervention group, vitamin D level after intervention is negatively correlated to mean change of HbA1c ($r=-0.377$, $P=0.048$). According to the vitamin D level for participants after the intervention (<15 ng/ml, $15-24.9$ ng/ml, ≥ 25.0 ng/ml), HbA1c was $7.57\pm 0.84\%$, $7.62\pm 0.80\%$, $7.13\pm 0.97\%$, respectively ($P=0.037$).

Conclusion There was no statistically significant effect on glycemic control in seasonal vitamin D supplementation. According to the post-interventional vitamin D levels, there was statistically significant effect on glycemic control.

PE51 Clinical diabetes & therapeutics

Achieving rate to low-density lipoprotein cholesterol goals in diabetic patients in real world clinical settingMin Jeong Kwon^{*}, Eun Ju Lee, Jung Hae Ko, Tae Kyun Kim, Soon Hee Lee, Jeong Hyun Park

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Objective It is well known that reducing low-density lipoprotein cholesterol (LDL-C) levels lowers cardiovascular mortality and morbidity in type 2 diabetic patients. The National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III recommended using statins with life style modification for lowering LDL-C less than 100 mg/dL at least for diabetic patients. We evaluated the attainment of the NCEP-ATP III LDL-C goal of less than 100 mg/dL in type 2 diabetic patients using statins in real clinical practice.

Methods A retrospective study was intended for patients prescribed statin newly at Pusanpaik Hospital from January 2008 to December 2009. Of the 2729 new users of statin therapy, 17% started on simvastatin, 23% on rosuvastatin, 49% on atorvastatin, and 11% on fluvastatin-XL. The proportion of patients who achieved the LDL-C goal of less than 100 mg/dL was assessed.

Results Patients using each statin were similar in age and sex. But baseline LDL-C was significantly lower in simvastatin group [122 ± 37 mg/dL, $P<0.05$ vs atorvastatin (142 ± 34 mg/dL), fluvastatin-XL (143 ± 39 mg/dL), and rosuvastatin (147 ± 55 mg/dL)]. The average dosage was as follows: atorvastatin (22.7 ± 13.7 mg), fluvastatin-XL (80.0 ± 0.0 mg), rosuvastatin (10.4 ± 1.9 mg) and simvastatin (22.1 ± 6.2 mg). Overall proportion of LDL-cholesterol goal attainment was 75%. The achieving rate was highest in atorvastatin group (86%) and lowest in fluvastatin-XL group (61%). But other groups had similar attainment rates (simvastatin 77%, rosuvastatin 77%).

Conclusion We found that overall 75% of patients using statins reached LDL-C goals, which is slightly higher rate than published in the several clinical trials. We guess that this higher achieving rate results from lower baseline LDL-C in our study. And it might be the result from education emphasizing the importance of lowering LDL-C.

PE52 Clinical diabetes & therapeutics

Clinical characteristics of patients admitted to emergency department with hypoglycemiaKyung Taek Park^{*}, Tae Sun Park, Ji Hyun Park, Heung Yong Jin, Kyung Ae Lee, Hea Min Yu, Hong Sun Baek

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Objective To explore the clinical characteristics of hypoglycemia patients who were admitted to the emergency department with symptoms resembling hypoglycemia.

Methods In our study, 290 hypoglycemia cases were evaluated from January 2010 to December 2010.

Results The mean age is 66.1 yrs old. The mean glucose level is 41.8mg/dL. Of 290 hypoglycemia cases, 239 (82.4%) cases are receiving treatment for diabetes mellitus (62 using insulin, 190 receiving oral anti-diabetics, and 13 using both OAD and insulin). The most common cause of hypoglycemia is loss of appetite. Among other reasons, there are malignancies (78, 26%), infection (25, 8%), chronic liver disease (15, 5%), OAD(oral anti-diabetics) use by mistake (10, 3.6%).

Conclusion Diabetes mellitus is the most common reasons for hypoglycemia in patients seen in emergency departments. Risk factors of patients admitted to emergency department with hypoglycemia are loss of appetite, malignancies, infection, chronic liver disease, OAD use by mistake. Efforts should be made as to prevent hypoglycemia through training patients on better grounds.

PE53 Clinical diabetes & therapeutics

Usefulness of one-hour plasma glucose level in diabetes diagnosis in association with A1C

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Objective Recently, it has been proposed that 1-h plasma glucose level (1hPG) during OGTT (≥ 155 mg/dl) has better predictive power to identify future diabetes than either FPG or 2hPG, and A1C $\geq 6.5\%$ was proposed as new diagnostic criteria for diabetes. The aim of this study was to evaluate the association of 1hPG with A1C and its usefulness compared with 2hPG in diabetes diagnosis.

Methods Total 82 adults (mean age 51.2 ± 11.4 years) who visited diabetic center of Pusan National University Yangsan Hospital for diabetes diagnosis were enrolled. We checked metabolic and biochemical parameters including HbA1c and performed standard 75 gram oral glucose tolerance test (75g-OGTT).

Results Among FPG, 1hPG and 2hPG, 2hPG level was most strongly correlated with HbA1c (FPG; $r=0.766$, 1hPG; $r=0.747$, 2hPG; $r=0.805$, $P < 0.001$ for all). When diabetes is defined as FPG ≥ 126 mg/dl or 1hPG ≥ 155 mg/dl, The area under the ROC curve of HbA1c for detecting diabetes was 0.835 and the most suitable cut-off value was 6.2% (Sensitivity 56.8%, Specificity 100%, in case of 6.5%; Sensitivity 41.9%, Specificity 100%). When diabetes is defined as FPG ≥ 126 mg/dl or 2hPG ≥ 200 mg/dl, the area under the ROC curve was 0.914 and the most suitable cut-off value was 6.2% (Sensitivity 74.5%, Specificity 96.3%, in case of 6.5%; Sensitivity 54.5%, Specificity 96.3%) in our data.

Conclusion These limited data showed that 2hPG, a conventional component of diabetes diagnosis, may be better correlated with A1C and still more useful than 1hPG in detecting diabetes in Korean adults. The most suitable cut-off value of HbA1c correlated with OGTT for diabetes diagnosis was 6.2% in our study.

PE55 Clinical diabetes & therapeutics

The clinical features of central obesity according to gender differences in patients with type 2 diabetes

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Objective Obesity is associated with type 2 diabetes, hypertension, dyslipidemia, insulin resistance and also an independent risk factor for cardiovascular disease. The accumulation of visceral fat was identified to important role in the development of metabolic disease and also was an increased risk of morbidity and mortality. The aim of this study was to investigate the association of visceral fat accumulation to the determination of a cardiovascular metabolic risk factor in diabetic patients by gender.

Methods A total of 363 subjects with type 2 diabetes (191 men, 172 women) were enrolled in this study. Visceral fat area was measured by single slice abdominal computed tomography scanning. Laboratory parameters such as fasting blood glucose, HbA1c, insulin resistance (HOMA-IR), and lipid profile were included and also investigated the microvascular and macrovascular complication in this study.

Results Women compared with men had increased total fat (29322.7 ± 9773.4 vs 23439.8 ± 8361.8 , $p < 0.005$), subcutaneous fat (18333.0 ± 6823.3 vs 12107.3 ± 4806.4 , $p < 0.001$), but visceral fat (10989.7 ± 4400.2 vs 11332.5 ± 4717.5 , $P=0.05$) was no significant difference. However, the ratio of visceral fat and subcutaneous fat (0.6 ± 0.2 vs 1.0 ± 0.4 , $p < 0.005$) in men was statistically significantly increased. The visceral fat in men with diabetes was correlated with age, hypertension, insulin resistance, triglycerides and Apo A. And in patients of women diabetes was correlated with hypertension, insulin resistance, triglycerides, high-density lipoprotein cholesterol.

Conclusion Men diabetic patients were relatively visceral obesity compare to women diabetes. Visceral obesity in both men and women showed a significant correlate with cardiovascular risk factors such as age, blood pressure, insulin resistance and lipid metabolism.

PE54 Clinical diabetes & therapeutics

In addition to hypertension and high HbA1c, aspirin therapy and older age are risk factors of diabetic nephropathyYu-Wen Cheng^{1*}, Shih-Liang Chang², Usman Malik¹Lee's General Hospital, Miaoli, Taiwan¹, Department of Medicinal Botanicals and Health Applications, Da-Yeh University, Changhua, Taiwan²

Objective Diabetic nephropathy is the leading cause of end-stage renal failure in many countries. Hypertension and blood glucose poor control were the important traditional risk factors. Controlling blood pressure by angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and keeping lower HbA1c were important to improve proteinuria. Aspirin is recommended to use in those patients with increased cardiovascular risk. But aspirin is one kind of NSAID, which has nephrotoxic effect. In this study, we tried to find what were the risk factors in the diabetic patients and if aspirin induced renal function impairment.

Methods Total 379 Taiwanese who were treated type 2 diabetes more than one year were analyzed in this study retrospectively.

Results There were 236 (62.3%) diabetic patients using antihypertensives in this study, and these patients had poor renal function (eGFR 64.6 vs 70.8 ml/min, $p < 0.005$). Total 154 patients were prescribed ACEI or ARB but they did not show apparent improvement of albuminuria or renal function. Only 38 (10%) patients took aspirin regularly and they had lower eGFR than those who did not take aspirin (60.4 vs 67.6 ml/min, $p < 0.05$). There were 203 (54.9%) patients with abnormal albuminuria (urine albumin-creatinine ratio (ACR) ≥ 30 mg/g), they had worse eGFR than those with normal albuminuria (65.0 vs 69.2 ml/min, $p < 0.05$) in following one year. In the 291 (82.0%) patients with HbA1c $\geq 7.0\%$, they were associated with higher prevalence of abnormal albuminuria ($p < 0.05$). After one year therapy in the normal albuminuria patients, those with older age had higher chance to become microalbuminuria ($p < 0.05$).

Conclusion Aspirin therapy, older age and hypertension were risk factors of diabetic nephropathy. Well blood glucose control could prevent worsening albuminuria. Therefore, paying more attention to those high risk patients and aggressive glucose control are the way to maintain stable renal function in those diabetic patients.

PE56 Clinical diabetes & therapeutics

The favorable effects of Kimchi on metabolic parameters in patients with type 2 diabetes mellitusSo-Yeon An^{1*}, Min Suk Lee¹, Yong Jun Choi¹, Tae Ho Kim¹, Hye-Kyung Lee¹, Won Sun Hwang¹, Sun Jung Choe¹, Seung Jin Han¹, Hae Jin Kim¹, Dae Jung Kim¹, Kwan-Woo Lee¹Department of Endocrinology and Metabolism, Ajou University School of Medicine, Suwon, Republic of Korea¹, Division of Endocrinology, Department of Internal Medicine, Kwandong University, College of Medicine, Myongji Hospital, Goyang, South Korea², Department of Food Services and Clinical Nutrition, Ajou University School of Medicine, Suwon, Republic of Korea³

Objective Kimchi is a traditional fermented Korean food that has garnered international interest due to its various beneficial effects. However, research about the effects of Kimchi to patients with type 2 diabetes mellitus (T2DM) is lacking. The aim of this study is to demonstrate the beneficial effects of Kimchi on metabolic parameters and glucose status in patients with T2DM.

Methods Twenty patients with T2DM were randomly assigned to two 4-week diet phases separated by a 2-week washout period (crossover design). During each diet phase, the subjects consumed either fresh or fermented Kimchi which were created from the same standardized recipe and ingredients. They differed in terms of fermentation. One-day-old and 10-day-old Kimchi were defined as "fresh" and "fermented" Kimchi, respectively. Diet compositions, anthropometric data, glucose, and lipid parameters were analyzed.

Results The amount of fiber intake was significantly increased after the ingestion of either Kimchi. Systolic blood pressure (mmHg) significantly decreased from 122.6 ± 11.8 to 115.9 ± 12.6 in the fresh Kimchi group and 116.5 ± 10.9 in the fermented Kimchi group. Diastolic blood pressure showed similar results. Compared to baseline data (74.1 ± 9.8), significant decreases of diastolic blood pressure were shown after intake of fresh (68.2 ± 8.7) or fermented (68.1 ± 9.5) Kimchi. Moreover, hemoglobin A1c (%) showed significant decrease in the fresh Kimchi group (6.59 ± 0.53) and fermented Kimchi group (6.62 ± 0.59) compared to the baseline hemoglobin A1c (6.80 ± 0.59).

Conclusion The intake of fresh or fermented Kimchi had positive effects on systolic/diastolic blood pressure and hemoglobin A1c in patients with T2DM.

PE57 Clinical diabetes & therapeutics

The optimal cutoff value of waist circumference based on insulin resistance and visceral fat thickness in Korean type 2 diabetes

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Objective Central obesity is an important contributor to the development of metabolic syndrome and cardiovascular diseases (CVDs). In addition, visceral fat thickness (VFT) is known to be a reliable index for detecting diabetic patients who are at high risk of CVDs. However, there was a paucity of data on the appropriate cutoff point of waist circumference (WC) associated with metabolic risk factors, mainly targeted at type 2 diabetes. The aim of this study is to investigate the optimal cutoff value of WC for visceral obesity in type 2 diabetes.

Methods We evaluated 6,579 diabetic patients (male 3,394, female 3,185, mean age 58.03±10.64 yr) who visited Huh's Diabetes Center from Jan 2003 to Jun 2009. WC was measured at the midpoint between the lower rib and the iliac crest, and insulin sensitivity was assessed by a rate constant for plasma glucose disappearance (Kitt %/min) using insulin tolerance test. The presence of visceral obesity, which was measured by ultrasonography, was defined as VFT of more than 47.6 mm and 35.5 mm in men and women, respectively, according to the criteria for diabetic patients as described by Kim et al (1). Statistic analysis was performed using ROC curve.

Results The optimal cutoff point of WC for identifying two or more metabolic components was 87cm for men and 81cm for women. Moreover, these cutoff points had a higher association with the degree of visceral obesity in subjects with insulin resistance (the lowest tertile of Kitt) than insulin sensitive subjects (the highest tertile of Kitt).

Conclusion Our results suggest that the optimal cutoff values of WC for insulin resistance and visceral obesity in Korean type 2 diabetes should be reestablished.

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PE58 Clinical diabetes & therapeutics

Urinary chiro- and myo-inositol levels as a marker for type 2 diabetes mellitus

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Objective The aim of this study was to investigate the role of the urinary chiro- and myo-inositol levels in predicting type 2 diabetes mellitus.

Methods 103 normal controls and 111 type 2 diabetic patients were enrolled in this study. The concentrations of urinary chiro- and myo-inositol were measured by high performance liquid chromatography/mass spectrometry.

Results The concentration of urinary chiro-inositol in diabetic subjects (1.86±2.64 ng/L) was significantly higher than in controls (0.44±0.42 ng/L)(p<0.001). The urinary myo-inositol level in diabetic subjects (40.59±39.09 ng/L) was also significantly higher than in controls (14.13±10.31 ng/L)(p<0.001). The urinary chiro-inositol multiplied by myo-inositol level in diabetic subjects (103.69±185.11) was significantly higher than in controls (8.26±13.26)(p<0.001). The cutoff value to predict type 2 diabetes mellitus was 0.40 ng/L (sensitivity 65.8%, specificity 65.0%) for chiro-inositol and 17.10 ng/L (sensitivity 66.0%, specificity 65.8%) for myo-inositol. The cutoff value for chiro- times myo-inositol to predict type 2 diabetes mellitus was 7.43 (sensitivity 70.0%, specificity 70.3%). The area under the receiver operating characteristic (ROC) curve (95% CI) to predict type 2 diabetic mellitus was 0.712 (0.636-0.787) for chiro-inositol and 0.690(0.611-0.769) for myo-inositol. The area under the receiver operating characteristic (ROC) curve (95% CI) for chiro-inositol multiplied by myo-inositol to predict type 2 diabetic mellitus was 0.746(0.674-0.819).

Conclusion The urinary chiro- and myo-inositol levels were increased in type 2 diabetic patients and urinary chiro-inositol multiplied by myo-inositol was sufficient marker to predict type 2 diabetes mellitus.

PE59 Clinical diabetes & therapeutics

Effects of the pravastatin on serum adiponectin levels and multimeric adiponectin in patients with type 2 diabetes mellitus and hypercholesterolemia

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Objective Adiponectin has been associated with favorable metabolic effect and increased serum level of adiponectin have been correlated with improved insulin sensitivity and glucose tolerance. In previous studies, pravastatin was known to increase serum adiponectin level in patients with hypertension or impaired glucose tolerance and coronary heart disease, although it remains an issue of controversy. This study was designed to investigate effects of the pravastatin on serum adiponectin levels and multimeric adiponectin in patients with type 2 diabetes mellitus and hypercholesterolemia.

Methods This study was placebo-controlled, multicenter, prospective, double blind, three group trial (placebo, pravastatin 20 mg/d and 40 mg/d). A total of 73 patients with type 2 diabetes and hypercholesterolemia were enrolled in this study. Serum total and high molecular weight (HMW) adiponectin, the ratio of HMW adiponectin to total adiponectin, the homeostasis model assessment of insulin resistance (HOMA IR), and lipid profile were evaluated after 16 weeks.

Results Total cholesterol and low-density lipoprotein cholesterol levels were significantly reduced after 16 weeks in pravastatin therapy group compared to placebo group (P=0.008 and P=0.004). However, pravastatin therapy with 20 mg/d and 40 mg/d did not showed significant increase of serum total and HMW adiponectin levels (P=0.348 and P=0.991). The ratio of HMW adiponectin to total adiponectin and HOMA IR also were not different between three groups (P=0.767 and P=0.777).

Conclusion A 16-week treatment with pravastatin 20mg/d and 40 mg/d does not change the serum total and HMW adiponectin levels in patients with type 2 diabetes and hypercholesterolemia. Considering type 2 diabetes as more glucose intolerant status, large-scale study with long term treatment period and more data are needed to clarify the exact effect and mechanism of pravastatin on serum adiponectin levels and multimeric adiponectin.

PE60 Clinical diabetes & therapeutics

DPP-4 inhibitor plus metformin treatment blunt glucose excursion more effectively than metformin alone or sulfonylurea plus metformin

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Objective Glycated albumin (GA) is known to be a more useful glycation index than hemoglobin A1c (A1c) for monitoring fluctuating glucose level in type 2 diabetic patients. We also previously suggested higher GA/A1c ratio might be independently correlated with plaque-forming carotid artery atherosclerosis. The aim of this study was to investigate which drug results in the greatest glycemic excursion as assessed by GA/A1c ratio.

Methods A retrospective, longitudinal study was conducted. We reviewed medical records of patients who were treated with oral hypoglycemic agents (OHA). The demographic and laboratory parameters were analyzed. We checked fasting and postprandial glucose, glycated A1c, and GA at baseline and 3 month afterward. We calculated the change (Δ , delta) based on the difference between the baseline values and values after 3 months across all variables and GA/HbA1c ratio.

Results A total of 124 patients were divided into three groups according to the OHAs classes (Group I (n=46), metformin only (M), Group II (n=25), metformin + DPP4 - inhibitor (D) g, group III (n=53), metformin + sulfonylurea (SU) group). There were no differences in fasting glucose level at 0m or 3m, Δ value and Δ HbA1c, Δ PPG, or Δ GA/A1c. There were no differences in GA or GA/A1c among the three groups at baseline. However, GA at 3 month was significantly lower than other groups. Delta GA and GA/A1c ratio of group II were lower than those of group III.

Conclusion Despite the lack of significant Δ FG, Δ PPG, Δ HbA1c, or Δ GA/A1c, differences in GA, GA/A1c across 3 groups of OHAs was observed 3 months after treatment. Based on the concept that GA and GA/A1c are indicators that can monitor glycemic excursion, DPP-4 inhibitor might results in the greatest reduction in glycemic excursion.

PE61 Clinical diabetes & therapeutics

Cathepsin K, L expression in adipocytes is upregulated by palmitate via TNF α and IL-6

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Objective Cathepsin family is lysosomal cysteine protease. It is recently reported that cathepsin K, L, S control adipogenesis and relate to acute coronary syndrome. However, it is not clear whether cathepsins expression can be affected by saturated fatty acid which has a critical role in metabolic disease. We examined the hypothesis that palmitate upregulates cathepsin K, L, S expression in obese adipose tissue and infiltrating macrophages have crucial role in this process via inflammatory cytokines.

Methods 3T3-L1 cells were fully differentiated to mature adipocytes for 8 to 10 days and treated with palmitate, lipopolysaccharide (LPS) which is ligand of TLR4 (toll-like receptor 4). Six-week-old C3H/HeN mice with normal TLR4 and C3H/HeJ mice with TLR4 gene's mutation got LPS injection (1 mg/kg) or were fed with high fat diet (60% fat of total calories) for 13 weeks and sacrifice to harvest epididymal fat.

Results Real-time PCR revealed that not cathepsin S but cathepsin K, L expression is upregulated by palmitate as dose- and time-dependent manner. But there was no additional effect when we use palmitate-treated RAW264.7 cells' media instead of direct treatment to 3T3-L1 cells. Cathepsin K, L is upregulated after treatment of TNF- α or IL-6 like palmitate. Cathepsin K, L, S expression increased in both kinds of mice fed high fat diet compared with chow diet. But we cannot find similar pattern at mice which got LPS ip injection.

Conclusion We concluded that cathepsin K, L expression in fat tissue are upregulated by saturated fatty acid via inflammatory cytokines, not TLR4, thereby might have a critical role in developing acute coronary syndrome of metabolic syndrome and there are no additional effects of infiltrating macrophages.

PE62 Clinical diabetes & therapeutics

Sarcopenic phenotype in patients with newly diagnosed type 2 diabetes

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Objective Sarcopenic phenotype is associated with the increased risk of insulin resistance and type 2 diabetes. We investigated the proportion of sarcopenia and sarcopenic obesity (SO) and their clinical characteristics in patients with newly diagnosed type 2 diabetes.

Methods We conducted a cross-sectional analysis of 133 (75 men, 58 women) patients with newly diagnosed type 2 diabetes. All patients underwent a 75 g oral glucose tolerance test. Sarcopenia was assessed by appendicular skeletal muscle mass (ASM)/weight (%) using dual-energy X-ray absorptiometry and obesity was assessed by a visceral fat area using computed tomography.

Results The mean age of the subjects was 47.14 \pm 12.14 years, the mean HbA1c level was 10.59 \pm 1.94% and the mean body mass index was 25.53 \pm 3.38 kg/m². ASM/weight (%) was inversely associated with the log-transformed homeostasis model assessment of insulin resistance (HOMA-IR) and HOMA- β . The proportion of obesity, sarcopenia and SO was 23.3%, 16.5% and 35.3%, respectively. Sarcopenic phenotype was more prevalent in women than in men (Sarcopenia 29% vs. 6.7% and, SO 44.8% vs. 28%, respectively). In comparison to normal phenotype (neither obese nor sarcopenia), SO was significantly associated with higher degree of HOMA- β and the surrogate markers of insulin resistance (HOMA-IR and insulin sensitivity index composite). Notably, SO subjects were more insulin resistant compared to obese without sarcopenia subjects, although there was no significant difference in HbA1c between two groups.

Conclusion We found the high proportion of sarcopenia and SO in patients with newly diagnosed type 2 diabetes. Among metabolic phenotype, SO was strongly associated with the degree of insulin resistance and compensated hyperinsulinemia in the early phase type 2 diabetes.

PE63 Clinical diabetes & therapeutics

The usability of 1,5-anhydroglucitol in diagnosis of diabetes

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Objective It is important to predict postprandial hyperglycemia in the early stages of glucose intolerance. Recent studies found 1,5-anhydroglucitol (1,5-AG) to generally reflect postprandial hyperglycemia, even in patients whose hemoglobin A1C levels are at or near the goal. The aim of this study was to evaluate the usability of 1,5-AG in diagnosis of diabetes.

Methods The subjects were 62 Korean who had fasting glucose levels 100-125 mg/dl, glycosylated hemoglobin 5.5-6.5% and no history of diabetes. We performed 75g oral glucose tolerance tests (OGTTs) and measured glycosylated hemoglobin and 1,5-AG simultaneously.

Results According to the results of the 75g oral glucose tolerance tests (OGTTs), there were 12 subjects (19%) with diabetes. Serum levels of 1,5-AG were significantly lower in subjects with diabetes compared with non-diabetes (11.8 \pm 6.3 vs. 20.5 \pm 8.4, P=0.001). There was a significant negative association between 1,5-AG and 2-hour post-glucose load glycaemia (γ =-0.488, P<0.001). The area under the ROC curve was 0.790, and the maximal sum of sensitivity and specificity (80% and 70%, respectively) was obtained at a 1,5-AG cutoff level of 13.0 μ g/ml.

Conclusion 1,5-anhydroglucitol may be a good predictor of diabetes in subjects with high risk of diabetes.

PE64 Clinical diabetes & therapeutics

Resolution of type 2 diabetes following IFN- α therapy for chronic hepatitis C

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We report on a patient whose type 2 diabetes resolved following interferon- α (IFN- α) therapy for hepatitis C virus (HCV). A 57-year-old man, presented with fatigue, polyuria and polydipsia. He was newly diagnosed with type 2 diabetes. During the hospital day, he was also diagnosed with chronic hepatitis. Serological studies for chronic hepatitis demonstrated presence of hepatitis C, type 2a/2c genotype. He was started on subcutaneous insulin and IFN- α . After 24 weeks of treatment of IFN- α , HCV polymerase chain reaction was negative. And diabetes resolved despite an increase in his body weight. A number of papers have described associations between IFN- α therapy and the precipitation of diabetic ketoacidosis as the presenting feature of new-onset diabetes. Our case shows a resolution of diabetes after IFN- α therapy for chronic hepatitis C. HCV mainly affects the liver, but also several tissues outside the liver have been reported to be involved, resulting in a wide spectrum of extrahepatic manifestations. It has been hypothesized that diabetes also could be one of these extrahepatic conditions attributable to HCV infection. Previous HCV infection markedly increased the prevalence of type 2 diabetes, regardless of the presence of liver cirrhosis. Non-diabetic HCV patients have insulin resistance and specific defects in the insulin-signaling pathway. The specific mechanisms by which HCV lead to type 2 diabetes are not fully understood, but it seems that an increase of insulin resistance associated with both steatosis and the overproduction of pro-inflammatory cytokine could play a crucial role. Although it is unclear whether the resolution of diabetes in this case occurred as an effect of IFN- α or as a result of becoming HCV RNA negative, it has suggested a great deal about the role of IFN- α and HCV infection in the pathogenesis of diabetes.

PE65 Clinical diabetes & therapeutics

The effect of ACEI or ARB on contrast medium induced acute kidney injury after coronary angiography in type 2 diabetes

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Objective The definition of contrast induced acute kidney injury (CIAKI) is elevation of serum creatinine level within 48-72hours after applying contrast medium. Coronary angiography is essential procedure for assessing and treatment of coronary artery disease(CAD), especially in type 2 diabetes because the prevalence of CAD is higher than general population. ACEI and ARB are one of most common medications of type 2 diabetes. The effect of medications on CIAKI has not clarified yet, therefore we tried to find out the effect of RAAS blockade on CIAKI after coronary angiography in type 2 diabetes.

Methods We reviewed charts of type 2 diabetes performed coronary angiography in our hospital. We recorded serum creatinine levels before and after coronary angiography. The criteria of CIAKI were serum creatinine elevation of more than 0,05mg/dl or more than 25% compared to baseline.

Results The groups of type 2 diabetes with RAAS blockade agent (RAAS(+)) and without (RAAS(-)) were total 254 and 323 patients, respectively. They did not show any differences in age, BMI and baseline creatinine between 2 groups. The ratio of CIAKI presence after coronary angiography was not significantly different between RAAS (+) and RAAS(-) groups.

Conclusion Using RAAS blockade agents before coronary angiography did not increase the onset of CIAKI compared to not using that medications in type 2 diabetes.

PE66 Clinical diabetes & therapeutics

Relationship between microangiopathy and brachial-ankle pulse wave velocity(baPWV) in type 2 diabetic patients

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Objective The brachial-ankle pulse wave velocity (baPWV) measurement is well established method of assessing the cardiovascular disease. We evaluated the relationship between the baPWV and microangiopathies of chronic diabetic complication in patients with type 2 diabetes.

Methods We examined 167 patients with type 2 diabetes. We checked their clinical characteristics including age, sex, BMI, duration of diabetes, and blood pressure of systolic and laboratory tests of HbA1c, Triglyceride, LDL cholesterol, and HDL cholesterol. And we assessed the diabetic complications. We measured the baPWV using VP2000 and divided them as 3 groups by baPWV levels.

Results The first group consisted of 56 patients in lowest tertile. Their mean baPWV was 1330.95±77.55 cm/s. Number of patients with documented retinopathy was 7(17.1%), nephropathy 10(18.2%), neuropathy 11(19.6%), and macroangiopathy 9(16.1%). The second group consisted of 56 patients with middle tertile of baPWV. Their mean baPWV was 1596.46±89.16 cm/s. Number of patients with documented retinopathy was 14(31.1%), nephropathy 12(23.5%), and neuropathy 14(25.5%), macroangiopathy 5(8.9%). The third group consisted of 56 patients with highest tertile. Their mean baPWV was 1953.94±207.19cm/s. Number of patients with documented retinopathy was 14(46.7%), nephropathy 26(50%), neuropathy 14(25.5%), macroangiopathy 7(12.7%). The clinical characteristics and the laboratory tests were not different significantly between the three groups except age, pulse and LDL cholesterol. The high baPWV group showed significantly great frequency of diabetic retinopathy (low vs. middle vs. high; 17.1% vs. 31.1% vs. 46.7%, p=0.027) and nephropathy (low vs. middle vs. high; 18.2% vs. 23.5% vs. 50%, p=0.001).

Conclusion The baPWV was not associated with frequency of diabetic neuropathy, but that was associated with significantly great frequency of diabetic retinopathy and nephropathy.

PE67 Clinical diabetes & therapeutics

A case of hypoglycemia with type 2 diabetes mellitus having taken metformin and vildagliptin

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Dipeptidyl peptide-4 (DPP-4) inhibitors prevent the degradation of glucagon-like peptide (GLP)-1 which increases the secretion of insulin and decreases the secretion of glucagon, thereby reducing blood sugar. DPP-4 inhibitor is clinically beneficial because it can safely be used by elderly individuals who are at increased risk of hypoglycemia. But We recently experienced a case of hypoglycemia with type 2 diabetes mellitus having taken metformin and vildagliptin. A 82-year-old man with type 2 diabetes having taken metformin 500 mg and vildagliptin 50 mg daily for 14 days was admitted with decreased mentality. At that time, blood glucose, insulin and C-peptide was each 26 mg/dL, 100 uU/mL and 25.52 ng/mL. His clinical course improved over 54 hours after infusion of dextrose solution. At improved state, insulin and C-peptide was each 11.2 uU/mL and 5.20 ng/mL. Insulin antibody was negative.

PE68 Clinical diabetes & therapeutics

Three cases of fulminant type 1 diabetes developed after drug-induced hypersensitivity syndrome

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Fulminant type 1 diabetes mellitus (T1DM) and drug hypersensitivity syndrome (DHS) are rare and life-threatening diseases. Fulminant T1DM may develop after DHS with only few previous case reports and the possible role of human herpes virus 6 (HHV-6) infection was indicated in the pathogenesis. We here presents three cases of fulminant T1DM developed shortly after the diagnosis of drug-induced hypersensitivity syndrome. The offending drugs were identified as Cefadroxil, cefuroxime and phenylbutazone respectively. All of them were treated with high dose of glucocorticoids when hyperglycemia symptoms occurred abruptly with rapid progression to ketoacidosis. In terms of immunological parameters, one patient was positive for both GADA and ZnT8A, and had haplotypes of DQA1*0601-DQB1*0301 / DQA1*0601-DQB1*0301. The second one had positive GADA and DQA1*0102-DQB1*0601 / DQA1*05-DQB1*0201 haplotypes. The third patient was negative for all autoantibodies tested and had haplotypes of DQA1*03-DQB1*0302 / DQA1*03-DQB1*0303. Although HHV-6 virus antibodies were not detected in these patients, we found herpes simplex virus type 1 IgM antibodies (HSV1 IgM) positive in one and Coxsackie virus IgM antibodies (CVB IgM) positive in another patient. Our understanding of the pathogenesis of fulminant T1DM will be improved if the relationship among DHS, glucocorticoids and virus infection can be clarified. More attention should be given to this novel and serious complication of patients with DHS.

PE69 Clinical diabetes & therapeutics

Unusual two cases diagnosed with different types of diabetes presenting similar clinical symptom

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Although c-peptide representing pancreatic beta cell function, family history, patient's age, body mass index(BMI), autoantibody, and ketosis often give the clinician a good idea of the type of diabetes, they are not very specific in distinguishing type 1 from type 2 DM. Urine ketones are often present in type 1 diabetes, but may be positive in type 2 diabetes if there is severe volume depletion. Diabetic ketoacidosis is not unique to type 1 DM. Anti-glutamic acid decarboxylase(GAD) antibodies, islet cell antibodies, and insulin autoantibodies are present in 85% of patients with type 1 DM at the time of diagnosis, but may disappear within a few years. In type 1 DM, onset often at age <35 years, but can occur in older individuals. We report two cases about differential diagnosis of diabetes type. We report two patients hospitalized with similar diabetic symptoms were diagnosed with different atypical types of diabetes, case 1: A 49-year-old man with history of polyuria, polydipsia, and weight loss referred to our hospital from local clinic for regulation of blood glucose and evaluation of type of diabetes. His BMI was 22.8 kg/m². His previous hospital laboratory data had showed ketoacidosis in initial. Although he was 49 years old, positive anti-GAD antibody, low c-peptide and no elevation of c-peptide by glucagone supported a diagnosis of type 1 DM. case 2: A 29-year-old man with history of polyuria, polydipsia, weight loss, nausea, vomit, and epigastric pain referred to our hospital from local clinic. He had been diagnosed with DM 1 year ago and taken some oral hypoglycemic agents just for 1 month at that time. Although his BMI was 25.6 kg/m², maximal BMI in his life was 28.5 kg/m². His laboratory data showed ketoacidosis, but his insulin Ab was normal, anti GAD Ab and islet cell Ab were negative. Fasting initial c-peptide was 0.89 ng/mL. So we diagnosed with ketosis prone type 2 DM.

PE70 Clinical diabetes & therapeutics

Clinical characteristics of the DPP4 inhibitors responders in Korean subjects with type 2 diabetes

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Objective Dipeptidyl peptidase-4 (DPP4) inhibitors are new class of oral antidiabetic drugs (OAD) enhancing the incretin effects. As incretin achieves glucose lowering effect mainly through pancreatic islets, beta cell reserve may be important to the action of DPP4 inhibitors. We investigated which characteristics were associated with the response to DPP4 inhibitors in Korean patients with type 2 diabetes.

Methods We reviewed medical records of type 2 diabetic patients (N=1,500) who had been prescribed DPP4 inhibitors for more than 9 months in a single center. We excluded patients who received insulin, exenatide, glucocorticoids, and immune suppressants. Patients who had a history of malignant disease and gastrointestinal surgery were also excluded. The response to DPP4 inhibitors was categorized according to HbA1c change over the 9 months: good response (GR) was defined as delta HbA1c/baseline HbA1c > 18.0%; poor response (PR) < 5.0%.

Results Total 894 patients were divided into 3 response groups. Among them, those who had changed OADs confusing the effects of DPP4 inhibitors were excluded. Finally, 138 patients were enrolled as GR, and 139 patients as PR. There were no significant differences in age, duration of diabetes, liver function, lipid profiles and concomitant prescribed OADs. Baseline FPG, HbA1c (8.5±0.9% in GR vs. 7.7±0.9% in PR, P<0.001), and c-peptide levels (2.4±1.5 in GR vs. 2.0±1.2 ng/mL in PR, P=0.019) were higher in good responders. Insulin resistance calculated by c-peptide X FPG, and serum creatinine were also higher in good responders. When correlation analysis was performed, fasting c-peptide levels were significantly correlated with DPP4 inhibitor response after adjustment.

Conclusion We can expect better response in subjects who have higher c-peptide levels. DM duration and concomitant OADs was not related with the response to DPP4 inhibitors. Further study would be required to search for other predictors such as adipokines or genetic variances.

PE71 Clinical diabetes & therapeutics

Effects of nutrition education on the dietary compliance recognition and blood glucose control in patients with type 2 diabetes mellitusMi Ja Kim^{1*}, Sun Yung Ly¹, Kyoung Hye Yu¹Dept. of Culinary Nutrition, Wgsoos University¹, Dept. of Food and Nutrition, Chungnam National University², Dept. of Food and Nutrition, Daejeon Health Science College, Daejeon, Korea³

Objective This study was intended to assess the effects of nutrition education of low glycemic index on the blood glucose and HbA1c levels and perception of diet therapy and barriers to practice diet therapy in type 2 diabetic patients.

Methods The education program was composed of 7 consecutive instructions. The subjects of this study were 48 sexmatched patients with type 2 diabetes mellitus aged 66.5±6.3 years visiting a public health center. They were divided into two groups: the control group (C group) and the highly-educated group (HE group). Fasting blood glucose, HbA1c, anthropometric indices, Hypoglycemic syndrome, dietary intake, knowledge about diabetes and barriers to practice diet therapy were measured before and after nutrition education.

Results average body weight, BMI, systolic blood pressure of HE group were reduced after education. And fasting blood glucose and HbA1c levels, and Hypoglycemic syndrome and barriers to practice diet therapy decreased significantly, the diet therapy knowledge about diabetes were significantly increased, while those of control group were not changed.

Conclusion The results of this study shown that practical education is more effective and efficient than those of informative materials in inspiring diabetic patients to practice diet therapy.

PE72 Clinical diabetes & therapeutics

Associated factors with the glycemic control in subjects with type 2 diabetes on insulin therapySoo Kyoung Kim^{1*}, Jung Tae Sik¹, Jung Jung Hwa¹, Lee Sang Min¹, Kim Ho-Su¹, Chung Hye Seo², Kwon Sam², Jeong Gui-Hwa², Cho Sung-Rae³, Jong Ryeal Hahn¹Department of Internal Medicine, School of Medicine, Gyeongsang National University¹, Division of Endocrinology and Metabolism, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine², Division of Endocrinology and Metabolism, Changwon Fatima Hospital³

Objective To investigate which factors associated with the efficacy of insulin therapy in subjects with type 2 diabetes.

Methods Fifty-four patients with type 2 diabetes enrolled (mean age, 60.5±9.4 years; body mass index, 24.8±3.4 kg/m²; median diabetic duration, 16 years (range 2-30); 27 males and 27 females). A questionnaire about clinical characteristics, self-care management behaviours was asked, and HbA1c, fasting blood glucose level, lipid profile, and status of diabetic complications were abstracted from patient's records. Poor glycemic control was defined as HbA1c ≥ 8.0%.

Results Of the total 54 patients, 44.2% had HbA1c ≥ 8.0%. Fasting serum C-peptide level, triglyceride level, and duration of diabetes (>16 years vs. ≤16 years) were different between good glycemic control and poor glycemic control groups. In the multivariate analysis, longer duration of diabetes was significantly associated with poor glycemic control (P=0.037).

Conclusion In this observation, glycemic control was poor in subjects with type 2 diabetes on insulin treatment. Longer duration of diabetes was associated with poor glycemic control.

PE73 Clinical diabetes & therapeutics

The effects of a DPP-IV inhibitor on glucose control and islet function in Korean patients with type 2 diabetes

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Objective DPP-IV inhibitors are a new approach to treat type 2 diabetes. We designed this study to evaluate the effect of DPP-IV inhibitors on glucose control and islet function in Korean patients with type 2 diabetes.

Methods 24 patients with type 2 diabetes were enrolled. Glucose, insulin and glucagon were measured during 75 g oral glucose tolerance test at baseline and after six month treatment with a DPP-IV inhibitor, sitagliptin. HbA1c was also checked.

Results 75 g oral glucose tolerance test revealed a significant improvement in glucose control after sitagliptin treatment; glucose levels were significantly decreased at 60 minutes and 90 minutes ($P < 0.05$) and insulin secretion was concurrently enhanced overall ($P < 0.05$). However, glucagon secretion showed no significant changes. Changes of HbA1c were dependent on initial HbA1c; well controlled 11 patients whose initial HbA1c were less than 7% had little change (from $6.19 \pm 0.51\%$ to $6.27 \pm 0.45\%$, $P = 0.567$) but poorly controlled 13 patients whose initial HbA1c were above 7% had significant reduction (from $8.08 \pm 1.05\%$ to $7.54 \pm 0.96\%$, $P = 0.35$).

Conclusion After six month treatment with a DPP-IV inhibitor patients with type 2 diabetes had enhanced postprandial glucose control and insulin secretion, which eventually brought improved overall glucose control. These changes were more prominent in poorly controlled patient.

PE74 Clinical diabetes & therapeutics

Current status of therapeutic target achievement according to duration of diabetes in Korean type 2 diabetic patients

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Objective Substantial evidence has shown that good glycemic, blood pressure (BP) and lipid control reduces the risk of diabetic complications. However, data regarding the proportion of individuals with diabetes who have optimal control are limited in Asian populations. We performed this study to investigate the current status of therapeutic target achievement according to duration of diabetes in Korean type 2 diabetic patients.

Methods This study was an analysis from participants of The Relationship between cardiovascular disease and Brachial-ankle Pulse Wave Velocity (baPWV) in Patients with Type 2 Diabetes (REBOUND) Study, which is a prospective multi-center cohort study in Korea. Two thousands and seventeen type 2 diabetic patients aged 30 years or more were analyzed, and patients with duration of diabetes less than 12 months were excluded. Glycemic, blood pressure, and lipid targets were defined as hemoglobin A1c less than 7%, BP less than 130/80 mm Hg, and LDL cholesterol less than 100 mg/dL, respectively.

Results Median age, BMI, and duration of diabetes were 60 years, 24.8 kg/m², and 8 years, respectively. Women were more prevalent (56%) than men. Median HbA1c was 7.1%. Prevalence of hypertension was 68.7%. Percentages reaching treatment goals of glycemic, lipid, and BP were 42.5%, 34.8%, and 38.8%, respectively. Prevalence of optimal control of all 3 parameters was 8.4%. Percentage reaching treatment goals of glycemic control decreased gradually according to duration of diabetes. But, that kind of trend didn't appear in lipid and BP control.

Conclusion In our study, each percentage reaching treatment goals of glycemic, lipid, and BP control was less than 50%. Glycemic control seems to worsen gradually according to duration of diabetes, in contrast with BP and lipid control. Strategies to improve awareness and implement evidence-based guidelines are needed to reduce the effect and burden of diabetic complications.

PE75 Clinical diabetes & therapeutics

Which oral anti-diabetic drug or combinations is more safe and effective on adding insulin glargine in chronic uncontrolled type 2 diabetic patients?

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Objective This study evaluated the optimal oral anti-diabetic drug (OAD)s combinations to add-on therapy of insulin glargine in patients with uncontrolled type 2 diabetes despite submaximal doses of metformin and sulfonylurea.

Methods Our study was a 28-week, open-label, randomized, controlled, multicenter, parallel-group clinical trial. Patients were randomly assigned to receive additional treatment for 24 weeks with insulin glargine in the morning with fixed doses of glimepiride, metformin and glimepiride plus metformin. A1C assessment in screening period and at weeks 4, 8, 16, 24 or at study discontinuation. During the treatment phase, patients had to provide daily self-measured fasting blood glucose values, and episodes of hypoglycemia were recorded in a standardized diary.

Results A1C levels improved from $8.5 \pm 0.9\%$ to $7.7 \pm 0.8\%$ with insulin glargine plus metformine, from $8.4 \pm 1.0\%$ to $7.7 \pm 1.3\%$ with insulin glargine plus glimepiride and from $8.7 \pm 0.9\%$ to $7.3 \pm 0.6\%$ with plus insulin glargine plus glimepiride plus metformine. Improvement in HbA1c was more pronounced with insulin glargine plus glimepiride plus metformine than with insulin glargine plus metformine (0.49% [CI, 0.16% to 0.82%]; $P = 0.005$) and insulin glargine plus glimepiride (0.59% [CI, 0.13% to 1.05%]; $P = 0.01$). Weight gain did not significantly differ among the treatment groups. The risk of hypoglycemia of any type was comparable and the number of patients experiencing episodes of hypoglycemia was similar among all treatment. The overall rate of hypoglycemia was low at 4.1 vs 5.8 vs 5.1 episodes per patient-year insulin glargin plus metformin versus insulin glargin plus glimepiride versus insulin glargin plus metformin plus glimepiride. Severe hypoglycemic episodes were not developed in all three treatment groups.

Conclusion The combination therapy of metformin and sulfonylurea plus glargine insulin in patients failing combination therapy with submaximal doses of metformin and sulfonylurea resulted in significant improvement in glycemic control compared with the combination therapy of metformin plus glargine insulin or sulfonylurea plus glargine.

PE76 Clinical diabetes & therapeutics

Efficacy of exenatide in clinical practice in Korean type 2 diabetic patient

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Objective Exenatide, a novel anti-diabetic agent decreases the HbA1c by 0.5-1.0%. Exenatide, a GLP-1 analogue that is resistant to degradation by DPP-IV increases insulin secretion in response to eating meals, suppresses pancreatic release of glucagon and helps slow down gastric emptying. There are few or no researches intended to analyze the exenatide's efficacy of the Koreans in the actual clinical practice, study is needed. The aim of the present study is to determine efficacy of exenatide in the real clinical practice.

Methods 76 type 2 diabetic patients who were firstly prescribed exenatide in Seoul St. Mary's hospital were included in the study. Among them, discontinuation due to improved glucose (N=2), poor control (N=2), and side effects (N=9) and loss of follow up (N=14) were excluded. Then, the following parameters of 49 patients were analyzed : changes in glucose parameters (FPG, PPG, HbA1c) and body weight at baseline and after 6 months, and side effects of exenatide.

Results The onset of significant reduction of the mean HbA1c was within 3 months in patients with exenatide. The mean HbA1c decreased from 8.6% at baseline to 7.6% at 3-month follow-up ($p < 0.05$), and to 6.9% at 6-month follow-up ($p = 0.003$). The mean fasting plasma glucose level decreased from 158.3mg/dL at baseline to 131.3mg/dL at 6-month follow-up ($p = 0.021$). Exenatide reduced the mean body weight of patients by 3.4kg at 6-month follow-up ($p < 0.05$). Nausea and vomiting occurred at a rate of 40% (10 of the 49 patients), 4 of the 10 patients with nausea and vomiting were discontinued the exenatide. And dizziness (8%), tingling sensation (4%) were reported as side effects.

Conclusion Exenatide decreased the mean HbA1c, fasting plasma glucose level and t body weight of patients at 6-month follow-up. Even if nausea and vomiting occurred at a rate of 40%, 60% of these patients maintained the exenatide and experienced the improvement of regulation of blood glucose and the weight loss at 6-month follow-up.

PE77 Clinical diabetes & therapeutics

Prevalence of type 2 diabetes mellitus and glucose intolerance among persons with chronic liver diseases in MongoliaByambatseren Jambaljav^{1*}, Tuul N², Yanjmaa S¹, Tsetsgee Dagvadorj¹Department of Endocrinology, State Central Clinical Hospital of Mongolia¹, Department of Gastroenterology, State Central Clinical Hospital of Mongolia²

Objective Background: Mongolia is known for its high endemicity for hepatitis c virus infection (20.8%, 2005), we have observed that chronic liver diseases may contribute to the development of diabetes mellitus, this relationship has not been investigated in Mongolia, and its pathogenesis remains unknown. **Objective:** to examine glucose intolerance of the patients with chronic liver diseases.

Methods Methods: we have reviewed the medical record of patients with chronic liver diseases who were hospitalized in gastroenterology and endocrinology departments of the state central clinical hospital from 2008-2010.

Results Results: total of 2600 medical records has been reviewed, median age was 42.5, m:f 52:48, 2214 patients had chronic liver diseases and 386 patients with only type 2 diabetes mellitus, only patients with glucose level of >7 mmol/l were included in the study. bmi, blood pressure, blood test, liver function test, cholesterol and glucose level, hcv and anti hbsag, liver ultrasound and clinical symptoms (extra hepatic, hepatic and mixed) were examined in 228 patients, majority of the patients had hepatic symptoms 84% and 16% had extra hepatic or mixed symptoms, 86% were hcv positive, 9.3% were anti hbsag positive and 4.7 were other etiology. 97% had glucose intolerance (averagely 7-8.5 mmol/l) and 3% type diabetes mellitus.

Conclusion Conclusion: chronic liver diseases particularly hcv infection have a significant role in the development of type 2 diabetes mellitus, in order to prevent from type 2 diabetes mellitus standard viral treatment and good control of glucose level should be considered to all patients.

PE78 Behavioral medicine & education

Performance of 7 point SMBG based on structured testing program study in clinical practice

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Objective Major clinical trials demonstrated the benefits of intensive glycemic control on diabetes complications have included SMBG as part of multifactorial interventions. SMBG can be useful in preventing hypoglycemia and adjusting medications (particularly prandial insulin doses), MNT, and physical activity. The role of SMBG on glycemic control in type 2 is not consistent. Some studies showed significant glycemic benefits with SMBG, while others have shown no significant benefits. And the optimal frequency and timing of SMBG for patients with type 2 diabetes is unclear yet. Recent one study showed structured SMBG significantly improves glycemic control in type 2 diabetes without decreasing general well being. Therefore, we tried to find out how well patients can perform structured SMBG before applying the structured testing program in clinical practice.

Methods The subjects were type 2 diabetes have checked SMBG by their own ways. We provided standardized sheet and recommend to record a 7-point SMBG profile (fasting, preprandial/2-h postprandial at each meal, bedtime) on 3 consecutive days prior to each scheduled visit.

Results Total number of subjects were 225 patients. Their mean age was 63.9 ± 10.2 years old. The percentages of male and female patients were 38.2% and 61.8% and their mean ages were 62.6 ± 11.1 and 64.7 ± 9.6 years old, respectively. The percentage of patients performed 7 point SMBG perfectly was 16.9%. 44.4% of patients performed over 4 points among 7 points and 38.7% of patients did less than 4 points. The most common reasons of not performing as recommended was because they were busy due to work and life style (50.4%). 13.3% of patients did not perform completely due to being helped by other family members in SMBG. Not understanding the way of 7 point SMBG and pain on fingers covered similar percentage of reasons. 2.7% of patients gave up 7 point checking because of stress for high glucose levels. Economic aspect was the reason in 3.5% of patients.

Conclusion The degree of performing 7 point SMBG on 3 consecutive days for structured testing program was not high in real practice. Half of them did not perform completely because they could not make the time of checking. More practical guideline for SMBG should be developed for improving glycemic control in type 2 diabetes.

PE79 Behavioral medicine & education

The relationship between health condition and health-related quality of life of adult diabetes patientsHae-Jung Lee^{1*}, So-Hui Kim¹, Hak-Yeon Ba², Sang-Yong Kim², Jin-Hwa Kim², Jong Park²Doctoral Student, Health Sciences, Chosun University¹, Department of Internal Medicine, College of Medicine, Chosun University², Department of Preventive Medicine, College of Medicine, Chosun University³

Objective Recently, as the prevalence rate of type 2 diabetes was reported 8.9% in 2001 and 9.7% in 2007, it becomes increasingly important to actively manage and value the disease to prevent it from acute and chronic complication caused by change of life style and ageing society. Since improvement of quality of life for chronic patients has increasing become important, there have been many approaches to improve the quality of life for patients. We estimated the relationship between health condition and quality of life of diabetes patients.

Methods The research selected 759 subjects whose data of health condition and quality of life exist and ages are older than 19, from the fourth Korea national health and nutrition examination survey (KNHANESVI-3).

Results As subjects' average age was 62.15 \pm 12.14, 20s and older has significantly low quality of life. As education level and monthly income point high, subjects showed tendency that EQ-5D index and 'living with spouse' points high. Most of subjects are self-managing without specific education about the disease, as 21.2% for 'never had education and any kind' and 77.4% for 'no education'. The quality of life was affected significantly by the factors: stress, health recognition and sleeping time, ($p < 0.05$) and not affected by the factors: body activity, smoking and drinking habit. Subject group smoking (48.8%), drinking (63.1%) and no-exercising (52.3%) had better health recognition. After measurement of waist, BMI, fasting blood sugar, total cholesterol and TG, there was significant relation between quality of life and fasting plasma glucose ($p < 0.05$).

Conclusion The stress, sleeping time, and fasting plasma glucose is correlated with quality of life in Korean diabetic adults. We suggest that these factors should be early identified and individual managed based on the characteristics of the population to improve quality of life in diabetic adults.

PE80 Behavioral medicine & education

Myo-inositol, glycemic index, and insulin index of Korean fruits for DM patientsJung-Eun Yim^{1*}, Jee-Hyun Ryu¹, Wan-Hee Suk¹, Young-Seol Kim¹, Cheon-Seok Park¹, Ryowon Choue²Dept. of Food and Nutrition, College of Natural Science, Changwon National University¹, Dept. of Medical Nutrition, Graduate school of East-West Medical Science, Kyung Hee University², Research Institute of Medical Nutrition, Kyung Hee University³, Dept. of Endocrine and Metabolism, College of Medicine, Kyung Hee University⁴, Dept. of Food Engineering, Kyung Hee University⁵

Objective Hyperglycemia considered as a condition with intracellular myo-inositol deficiency. Restoration of myo-inositol to normal level might be beneficial for the prevention and treatment of the complications associated with diabetes mellitus (DM). However, little information is available concerning the myo-inositol content in Korean fruits. Therefore, we analyzed the contents of myo-inositol in Korean fruits, major useful sources of myo-inositol.

Methods Frequently consumed 6 fruits (apple, water melon, tangerine, oriental melon, green and gold kiwifruits) were analyzed for their sugar contents by high-performance anion-exchange chromatography (HPAEC, Dinonex model DX-600) and electrochemical detection (ED) coupled with CarboPac MA-1 column. Myo-inositol, glucose, fructose, and sucrose in the fruits were successfully separated within 25 min using 0.612 M NaOH eluent at a flow-rate of 0.4 mL/min. Glycemic index (GI) and insulin index from 15 healthy subjects were also analyzed.

Results Contents of myo-inositol in tangerine, green kiwifruit, and water melon were 320 ± 27 , 190 ± 0.04 , and 63 ± 3 mg/100g, respectively. However, myo-inositol was not found in apple, oriental melon, and gold kiwifruit. The GIs of tangerine, green kiwi, water melon, oriental melon, and gold kiwi were 54.8 ± 6.3 , 42.7 ± 5.1 , 53.5 ± 5.0 , 51.2 ± 5.0 , 45.8 ± 5.9 , respectively. Insulin index of each fruits were 60.2 ± 10.6 , 54.8 ± 12.9 , 83.7 ± 13.5 , 147.7 ± 30.0 , 59.8 ± 12.0 , respectively.

Conclusion Fruits are high in fiber, vitamin, water and sugars, also contain various phytochemicals. Thus, intakes of fruits were emphasized for health and disease prevention. However, many patients of DM restrict intakes of fruits because of glycemic control. More investigations about Korean fruits are needed for DM patients.

PE81 Behavioral medicine & education

The effect of information provision on lifestyle changes for impaired fasting glucose persons

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Objective Many studies were shown that intensive lifestyle modification was effective to prevent DM or to delay disease progression. However, there are many limitations to implement face to face education for prediabetic persons in clinical settings. The purpose of this study is to examine the effectiveness of provision of written education material dealt overall information on prediabetes.

Methods Subjects were 100 IFG out-patients (male 57, female 43) provided a diabetes prevention book and they were not prescribed any medication. The book included the detail dietary information for prediabetes and the contents of book were as follows: the concepts of diabetes, prediabetes, metabolic syndrome, diet any approaches to prevent diabetes, dyslipidemia, hypertension and overweight and food nutrition information, exercise to prevent diabetes. Dietitians gave the books to patients and explained the importance for necessity of dietary habit modification shortly. The laboratory data related to metabolic control was collected retrospectively at baseline and at 3 months after book provision.

Results The mean age was 50.2±10.5 years and mean BMI was 24.5±2.9kg/m², FBS was 114.1±5.4mg/dl and blood pressure was 126.0±12.7/81.4±10.7mmHg. Total-cholesterol, LDL-cholesterol and triglyceride were 198.2±28.8mg/dL, 116.6±24.7mg/dL, 138.1±71.7mg/dL, FBS (baseline 114.1±5.4mg/dL, 3-month 111.7±9.7mg/dL, p<0.01) and DBP (baseline 81.0±9.8mmHg, 3-month 78.9±9.5mg/dL, p<0.05) were significantly improved 3 months after, FBS levels of 12.1% of subjects were improved below 100mg/dL. HbA1c levels of 38.5% of subjects whose HbA1c levels were higher than 6.0% were improved below <6.0%. Although they were not significant differences, SBP, total cholesterol, LDL-cholesterol, triglyceride at 3 months were improved.

Conclusion In this study, we showed the appropriate information provision without face to face education may lead a metabolic improvement in IFG persons. Further effort will be need to developed effective and well-structured education materials for prediabetes persons.

PE82 Behavioral medicine & education

Evaluation of diabetes education in patients with type 2 diabetes in Mongolia

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Objective To evaluate the diabetes education conducted among out-patients with type 2 diabetes.

Methods The study involved 109 patients with type 2 diabetes under the control of endocrinologists at State Central Clinical Hospital. The knowledge about diabetes was evaluated with the 4 package questionnaire with 16 questions before and after the education, and clinical measurements including BMI, waist circumference, blood pressure, HbA1C, Blood cholesterol and Triglyceride were tested before, 1 month and 6 month after the education. The statistical data analyzed by the SPSS12.00 software.

Results Following the inclusion criteria and obtaining an informed consent per individual, 109 participants with age ranges from 26-54 involved in the study. 7 participants were excluded from the study. Of the study participants 77% from urban and 23% from rural area and 51% was male and 49% was female. The average duration of illness is 3.8±1.6 year. A total of 5 day training was conducted per individual and group. The participants knowledge about disease was significantly correlated with fasting blood glucose, waist circumference and BMI (r=0.18, p<0.005) before and 1 and 6 month after the training. HbA1c level was improved significantly (P<0.02) after 6 month of the training.

Conclusion The individual and group diabetes education is important for patients with type 2 diabetes patients.

PE83 Behavioral medicine & education

Comparison of accuracy of SMBG and self-management according to type of diabetes

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Objective This study was done to investigate the frequency, accuracy levels, and self-management status associated with SMBG depending on the type of diabetes.

Methods Of patients seen at diabetes centers of university hospitals in Seoul during Feb and March 2011, 239 patients who measured their blood glucose at home once a week or more within the past three months were selected. The SMBG checklist (KADNE: Korean Association of Diabetes Nurse Educator, 2007), a 7-point scale measuring accuracy and self-management, separately, was used. The patients were assigned to one of three groups according to the type of diabetes: T1DM (n=14, 5.9%), T2DM (n=174, 72.8%), GDM (n=51, 21.3%).

Results The frequency of SMBG was significantly different among the three groups (T1DM: 36.1±39.0, T2DM: 6.9±8.0, GDM: 18.8±4.2 times/week, P<.001). For the T1DM group the most frequent times to do SMBG were after lunch (78.6%), and then before breakfast, after breakfast and supper (71.4%), for T2DM, before breakfast (85.7%), and for GDM, after each meal (96%), before breakfast (92.2%). Additional measurement times for T1DM were hypoglycemic state (85.7%), and after over-eating (64.3%) and for the other two groups, over-eating; T2DM (33.7%) and GDM (25.5%). Accuracy scores were significantly higher for GDM (T1DM: 5.5±1.3, T2DM: 5.6±1.1, GDM: 6.2±1.0, P=.002), scores for self-management were significantly lower for T2DM (T1DM: 5.7±1.6, T2DM: 4.2±1.7, GDM: 5.4±0.9, P<.001). The accuracy of measurement techniques for SMBG and self-management scores were significantly correlated (r=0.26, P<.001).

Conclusion Patients with T2DM had lower scores than those with T1DM or GDM in self-management. These results indicate that patients with T2DM need more intensive and repetitive education.

PE84 Behavioral medicine & education

Status on drug use patterns of diabetes mellitus in Bogra Diabetic Hospital of Bangladesh: An explorative survey among physicians and patients on knowledge and use

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Objective In Bangladesh most of the people suffer from diabetes mellitus in every times and especially aging are more considerable. The objective of this study was to determine the prevalence of diabetes mellitus in consideration of age, sex, socio-economical status, determined the present therapeutic management in diabetes mellitus, and related complication having by the patients. The survey was planned to study the drug problem in diabetes mellitus involving the first two steps of the cycle i.e. examine and diagnose by collecting data. This is to learn the exact nature of the problem and to identify the underlying causes of it.

Methods A total of hundred patient's information data were collected prospectively by a prepared questionnaire.

Results In type I diabetes mellitus; 70% patients were male, and 30% were female. In type I diabetes mellitus; 100% patients were treated with insulin, 92% with Sulfonylureas, 72% with Meglitinide, 55% with Thiazolidinedione, 99% with Cardiovascular drugs, 65% with Antiplatelet drugs, 58% with Antifibrinolytic drugs, and some more drugs were given to treat the type I diabetes mellitus. On the contrary type II diabetes mellitus; 64% patients were male and 36% were female. In type II diabetes mellitus; Sulfonylureas were given to 86% patients, Meglitinide to 85% patients, Cardiovascular drugs to 99% patients, Antifibrinolytic drugs to 68%, Antiplatelet drugs to 50% patients, Combined antihypertensive drugs to 70% patients, and 42% patients were taking Thiazolidinedione drugs. It was also observed that patients aged within 40-49 years were more seriously affected by diabetes mellitus. More than 10% of the patients had low status, 65% having medium status, and 25% having high status.

Conclusion The management of diabetes mellitus is a very important factor both global and national perspective. Introduction of an effective diabetes mellitus control and management guideline would contribute a lot of achieving health care facilities for the people.

PE85 Behavioral medicine & education

Analysis of the factors affect to dietary intake and blood sugar in diabetic patients

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Objective The purpose of this study was to identify affecting factors to blood glucose control, and by highlighting those factors in education to lead more positive results to blood glucose control.

Methods From February 2011 to July 2011, in Seoul St. Mary's Hospital, diabetes buffet education performed to 180 patients. Data were collected by questionnaire based on previous day, and for dietary evaluation, a 24-hour recall method was used. All analyses were conducted using a SAS software package version 8.2.

Results The general characteristics of subjects was male 51.1%, mean age 57.5 years, and mean BMI 24.9kg/m², 79.3% diagnosed with diabetes type 2 diabetes, gestational diabetes 2.8%, IGF & IFG 17.9%, 71.3% less than six months of receiving diagnosis, and 53.3% being prescribed hypoglycemic agents and insulin. People who doing exercise was 74.3%, 90.4% who eat a snack. The mean glycosylated hemoglobin level was 7.2%, fasting blood glucose level was 140.2mg/dl. The mean energy intake per day was 1,517kcal, protein 65.3g, fat 37.6g, carbohydrate 228.4g. The proportion of calories intake on the daily requirements in non-snack eating group statistically was lower than snack eating group(p=0.022), therefore, for in order to reduce calorie intake should pay attention to eating a snack. And calories and carbohydrate intake had no difference between exercise and non-exercise group, but glycosylated hemoglobin and fasting blood glucose level were statistically lower in exercise group(HbA1c, exercise group: 7.0%, non-exercise group: 7.6%, p= 0.021). So, even had similar calories and carbohydrate intakes, if performing exercise, better blood glucose control results were expected.

Conclusion As a result, for effective blood glucose and dietary control in diabetes patients, especially exercise and snack education need to be emphasized.

PE87 Behavioral medicine & education

Alcohol intake and insulin resistance among vitamin D deficient diabetic patients

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Objective Moderate alcohol consumption might be associated with improved insulin sensitivity in non-diabetic people with vitamin D insufficiency. We investigated whether alcohol consumption was related to insulin resistance(IR) among type 2 diabetic patients with vitamin D deficiency.

Methods Participants of study were 68 type 2 diabetic patients without renal disease. Tertiles of alcohol consumption and 25 hydroxyvitamin D level were used for predicting odds of IR after adjusting for age, gender, BMI, A1C, use of insulin sensitizers.

Results As vitamin D level rises, insulin resistance is reducing. However, among all vitamin D tertiles, there were no differences in insulin resistance between non, mild and heavy drinker.

Conclusion Alcohol consumption is not associated with insulin resistance among vitamin D deficient Korean type 2 diabetic patients.

PE86 Behavioral medicine & education

Basal characteristics and satisfaction of campers attending 2030 diabetes

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Objective Diabetes is considered to be one of the most psychologically and behaviorally demanding disease. Especially young diabetic patients of age 20-30s are usually negligent about diabetes self-management due to marriage, childbirth and busy life style. Therefore Korean Diabetes Association started hosting a diabetic camp for 20-30s called the 2030 camp. The objective of this study was to examine the basal characteristics and satisfaction of campers attending 2030 camp.

Methods During the summer of 2011, data were collected at 11th 2030 diabetes camp. The three day camp was held in Gyeonggi Province. Thirty nine young people attending 2030 diabetes camp completed the questionnaire including basal characteristics and satisfaction of 2030 diabetes camp.

Results Total 39 diabetic patients attended, 15 were female, 24 were male, and the average age for campers was 32 years. The mean length of time since diagnosis with diabetes was about 3.6 years. 23 campers (59%) had type 1 diabetes, and 16 campers (41%) had type 2 diabetes. Most of them (69%) attended the 2030 camp by recommendation of their doctors or education nurse, and 43% of campers attended the 2030 camp at least twice. Camp activities consisted of medical consultation, education of foot care and diet, activities with social welfare department, and recreation. Overall satisfaction of camp from participants was very high, about 87% of campers satisfied the program, and 93% of them wanted to attend the next camp in the future.

Conclusion The questionnaires showed that participation in 2030 camp has a positive impact on camper's lifestyle. Campers pleased with camp activities and want to return in the future, also they have learned helpful management strategies. The future direction should be the development and implementation of education methods to increase levels of life support of young diabetic patients.

PE88 Behavioral medicine & education

The correlation between patients' own assessments of their diabetes self-management and actual glycemic control

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Objective We examined correlation between patients' own assessments of their diabetes self-management and actual glycemic control status and investigated what is the key determinants of diabetes self-care.

Methods We carried a survey from patients with type 2 diabetes who had not been changed antidiabetic medications during last 6 months through questionnaires included patient's expectation of their blood glucose change and a five item scale assessing the patients' diabetes self-management (diet, exercise, blood glucose testing, foot care and medication use). We obtained their HbA1c of 2-4 months ago and that of the time of survey.

Results The patient's expectation of their blood glucose change corresponded with their actual HbA1c change ($\kappa=0.117$, $p=0.024$). They considered that diet and exercise was the most important factors to control their blood glucose. However, self-care assessment score about diet or exercise was not correlated with the HbA1c change. Self-care assessment score about medication was inversely associated with the HbA1c change ($r=-0.170$, $p=0.023$). In stepwise multivariate linear regression analysis, medication score was the only statistically significant variable for HbA1c change ($B=-0.117$, $p=0.023$). The average self-care assessment score was 3.99 ± 0.87 (7 points at maximum). The means and SDs for each self-care assessment subscale were as follows: 4.41 ± 1.32 in diet, 3.1 ± 1.86 in exercise, 1.9 ± 2.31 in blood glucose testing, 4.17 ± 1.85 in foot care, 6.59 ± 0.77 in medication.

Conclusion The patient's expectation of their blood glucose change was correlated with their actual HbA1c change. Medication was the most important factor for diabetes self-management. Effort to enhance medication adherence is warranted to improve glycemic control.

PE89 Behavioral medicine & education

The effect of hypoglycemic experience during admission period on the self management of hypoglycemia

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Objective Insulin treatment to diabetic patients is an important part of the treatment of diabetes. However, the patient fears about hypoglycemic symptoms it is the major cause of refusing insulin treatment. In former treatise, there were reports that after insulin treatment when hypoglycemia occur didn't respond despite knowing how to manage. But, it is not enough known about the effect of hypoglycemic experience on the self management of hypoglycemia. For that reason, I could find out the effect of hypoglycemic experience during admission period on the patient's self-management about hypoglycemia after discharge.

Methods From JAN, 2010 to JUN, 2011, I surveyed that the patient who didn't controlled blood glucose with OAD were treated with insulin and education of diabetes by admission, hypoglycemic experiences, hemoglobin A1c and hypoglycemic management during admission period and in 3month, 6 months after discharge.

Results Total 108 patients, hypoglycemic experienced group were 62 patients and non-experienced group were 46 patients during admission period. Diabetes education was enforced for both groups during admission period and hypoglycemic experienced group during admission period was reeducated about hypoglycemia. HbA1c of the hypoglycemic experienced group was higher than non-experienced group (HbA1C, 9.8 vs. 11.4%, $P=0.06$), in 3 months after discharge, HbA1c reduction (HbA1C reduction, 1.5 vs. 3.5%, $P=0.03$) and in 6 month, insulin dose (Insulin dose, 22 units vs. 15 units) are lower than non-experienced group. Duration of DM, sex, age and BMI were not clinically significant for both groups. Hypoglycemia occurred the most on 2nd day during admission period, and indicated high incidence rate within 3 months after discharge. According to survey of hypoglycemia management checklist after discharge, Hypoglycemic experienced group during admission than non-experienced group didn't exercise on an empty stomach, exercising a long time had a snack and didn't exercise long time at night, measured blood glucose when they feel hypoglycemic symptoms.

Conclusion Hypoglycemia was caused of refusing insulin treatment but it was developed the patient's ability to manage. When consider the frequency of hypoglycemia, it is adjudged to be effective that education for treatment and prevention of hypoglycemia is required the first day of admission, once more just before discharge and need reeducation in 3 months after discharge. Also, education for treatment and prevention of hypoglycemia need more scientific change in order that diabetes patient is provided with self management.

PE90 Behavioral medicine & education

Changes in cardiometabolic risk factors and dietary quality after web-based education program in metabolic syndrome menJi Yeon Kang^{1*}, Suk Hee Sung¹, Yoo Kyoung Park², Tae In Choi¹, Yun Mi Paek¹Radiation Health Research Institute, Korea Hydro & Nuclear Power Co., Ltd, Korea¹, Department of Medical Nutrition, Kyung Hee University, Yongin, Korea²

Objective We investigated the effects of the web-based education program on cardiometabolic risk factors and dietary quality in men with metabolic syndrome (MetS).

Methods This study comprised 244 control group and 160 education group, aged 30-59 men. The web-based program was based on a lifestyle modification, increased physical activity and nutritional education for 10 months (1 time/1 month by e-mail). To assess program effectiveness, data about anthropometric and biochemical characteristics and dietary intake were collected before and after education.

Results After program, while fasting plasma glucose (FPG), total cholesterol (TC) and low-density cholesterol (LDL) were significantly increased in control group ($P<0.05$), waist circumference (WC), high-density cholesterol (HDL) and numbers of MetS components were significantly decreased in education group ($P<0.05$). Although most nutrient of Nutrient Adequacy Ratio (NAR) were excessive, folate and calcium of NAR were assessed not adequacy in both groups. In control group, vitamin A, C and B1, folate and calcium of NAR were significantly decreased ($P<0.05$). In education group, vitamin A, folate, calcium and phosphorus of NAR were significantly decreased ($P<0.05$). The Mean Adequacy Ratio (MAR) was significantly decreased ($P<0.001$), nevertheless, MAR was excessive in both groups. The changes in WC, HDL, numbers of MetS components and possession of MetS were significantly more improved in education group than in the control group ($P<0.01$).

Conclusion This study revealed that the web-based education program for reducing risk of MetS and improving dietary quality in men with MetS. Further, this program should be evaluated in a longer term demonstration.

PE91 Behavioral medicine & education

Effectiveness of decrease of diabetes risk in male workers using web-based education programJi Yeon Kang^{1*}, Ji Young Lee¹, Yoo Kyoung Park², Tae In Choi¹, Yun Mi Paek¹Radiation Health Research Institute, Korea Hydro & Nuclear Power Co., Ltd, Korea¹, Research Institute of Clinical Nutrition, Kyung Hee University, Seoul, Korea²

Objective This study was performed to clarify which web-based education program are effective in reducing the risk of diabetes and whether the effects on subjects with impaired fasting glucose (IFG) are more effective than subjects with diabetes (DM).

Methods We conducted a controlled study in 100 IFG group (100 mg/dl \leq fasting plasma glucose (FPG) <126 mg/dl) and 100 DM group (FPG ≥ 126 mg/dl). The web-based education program consisted of 10 times of e-mail every month. Anthropometric and biochemical characteristics and dietary intake were measured in both groups at baseline and after education.

Results At baseline, waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), triglyceride (TG), FPG, insulin and HOMA-IR were significantly higher and HDL was lower in DM group than IFG group ($P<0.05$). Although most nutrient of Nutrient Adequacy Ratio (NAR) were excessive, folate and calcium of NAR were assessed not adequacy in both groups. After program, WC, SBP, FPG, TG ($P<0.01$) and Mean Adequacy Ratio (MAR) were significantly decreased ($P<0.05$), nevertheless, MAR was excessive, and HDL was significantly increased in IFG group ($P<0.05$). In DM group, WC, SBP and HOMA-IR were significantly decreased and HDL was significantly increased ($P<0.05$). The change of HDL was significantly higher in IFG group than DM group ($P<0.05$). Also, status of diabetes was significantly more improved in IFG group (46%) than DM group (27%) ($P<0.001$).

Conclusion As the result, significant differences in improving of risk of diabetes in IFG group compared with DM group. Our results suggested that subjects with diabetes are needed more intensive and continuous program to decrease risk of diabetes.

PE92 Behavioral medicine & education

Physical activity and obesity in type 2 diabetes

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Objective Physical inactivity and excessive food consumption play a major role in the etiology of obesity and type 2 diabetes mellitus (T2DM). The aim of the present study was to investigate the relationship of physical activity (PA) and eating behavior with obesity and T2DM.

Methods It was cross-sectional study including 2,472 type 2 diabetes who participated in Korean National Diabetes Program (KNDP). Three day food record was done and evaluated by Can-Pro 3.0.

Result Mean age was 54.5 years. Mean calorie intake was 1757.6 ± 423.1 kcal (men 1870.7 ± 403.5 , women 1615.6 ± 404.2 kcal) with proportion of carbohydrate, protein, and fat by 69%, 17.3% and 21.9%. Dietary fiber intake was 15.4 ± 4.8 g/1000kcal (men 14.7 ± 4.6 , women 16.4 ± 4.9 g/1000kcal). Sedentary life style (<1000 kcal/wk) is common in diabetes (52.7%). BMI and A1c were not different significantly according to the tertile of physical activity. Calcium consumption was negatively associated with total leisure time physical activity. Total calorie intake is lowest in very active patients.

Conclusion We found a strong inverse relationship between the level of PA during leisure time (including sport) and total calorie intake. Uncontrolled eating behavior was also found to have a significant effect on BMI. This study was supported by a grant of the Korean Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A050463-B50704-05N1-00040B).

PE93 Behavioral medicine & education

Development of a dietary index for Korean adults and its association with the risk of metabolic syndrome: The Korean Diet Index for Adults (KODIA)Inkyung Baik^{1*}, Nam H Cho³, Myoungsook Lee⁴, Chol Shin²

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Objective To develop a dietary index for Korean adults and assess its association with the risk of metabolic syndrome (MS) in a prospective cohort study.

Methods A prospective cohort study included 4,252 male and female Koreans aged 40 to 69 years participating in the Korean Genome Epidemiology Study. All individuals reported having no history of cardiovascular disease, cancer, diabetes mellitus, hypertension, and dyslipidemia and were found not to have 2 or more components of MS, including abdominal obesity, hypertriglyceridemia, hypo-HDL cholesterolemia, and high blood pressure and fasting glucose, at the initial health examination. They completed a food frequency questionnaire administered by trained interviewers. A dietary index (The Korean Diet Index for Adults, KODIA), which reflects a healthy dietary pattern, was constructed on the basis of dietary recommendations and data with regard to the relation to MS risk. Incident MS cases were ascertained through biennial examinations during a follow-up period from April 17, 2003 to March 12, 2009. We used pooled logistic regression models to estimate multivariate relative odds (RO) and 95% confidence interval (CI) for the association between KODIA scores and MS risk.

Results The overall mean KODIA score was 48.0 ± 10.0 with a range of 15 to 80 points. After controlling for potential confounding factors, individuals with the highest quintile of KODIA scores ranging 57 to 80 were at a 33% reduced risk of MS (95% CI: 14% to 48%) compared with those with the bottom quintile. In analysis for MS components, such beneficial effects of having high scores of KODIA were found to be driven by inverse associations with all five components.

Conclusion The proposed KODIA may be a useful tool for health care professionals to assess dietary status to predict the development of MS and to suggest a healthy eating pattern for Korean adults.

PE94 Epidemiology & genetics

A 20-week, randomized, multicenter, non-inferiority clinical trial to compare mitglinide with voglibose in a basal-plus regimen with long-acting insulin glargine in patients with type 2 diabetesJang-Won Son^{1*}, Soon-Jib Yoo¹, In-Kyu Lee², Jeong-taek Woo^{3,7}, Sei Hyun Baik⁴, Hak Chul Jang⁵, Kwan Woo Lee⁶, Bong Soo Cha⁷, Yeon-Ah Sung⁸, Tae Sun Park⁹, Kun-Ho Yoon¹⁰

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Objective This trial was conducted to compare the efficacy and safety of the combination therapy of mitglinide plus basal insulin glargine versus voglibose plus basal insulin glargine in patients with type 2 diabetes.

Methods This was a 20-week, randomized, multicenter, non-inferiority trial. Patients with HbA1c of over 7.0% were randomized to receive mitglinide (10mg tid) or voglibose (0.2mg tid) for 16 weeks concurrently, after completing the administration of basal insulin glargine for 4 weeks as monotherapy after a run-in period.

Results The intention-to-treat population included 156 patients: 79 for the mitglinide group and 77 for the voglibose group. At 20 weeks, there was no significant difference between the mitglinide group and the voglibose group in terms of mean HbA1c ($8.0 \pm 1.1\%$ and $8.4 \pm 1.3\%$, respectively) or the mean decrease in HbA1c from baseline (-1.0% and -0.8%). There was also no significant difference between two groups in terms of mean fasting plasma glucose (FPG) or the mean change in FPG from baseline. Both groups showed a significant decrease of M-value but the difference in two groups regarding the decrease of M-value was not significant. The changes in basal insulin requirements in each group were not significant. In comparison to the voglibose group, the mitglinide group showed a higher proportion of patients achieved HbA1c target goal, but there was no significant difference between two groups. Overall adverse events and the risk of hypoglycemia were not different between two groups.

Conclusion Combination therapy with mitglinide and basal insulin glargine was non-inferior to the combination of voglibose and basal insulin glargine in its effects on overall glycaemic control. Both were well tolerated, with no significant difference in the frequency of hypoglycemia or adverse events.

PE95 Epidemiology & genetics

The predictors of neonatal birth weight of Korean women with gestational diabetes mellitusHee Sook Kim^{*}, Jeong Eun Park, Sung Hoon Kim

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Objective The study was done to identify the predictor of neonatal birth weight and pregnancy outcomes in women with gestational diabetes mellitus (GDM).

Methods The methods used to be conducted in South Korea, and reviewed 901 women with GDM delivered at a Women's Healthcare Center retrospectively from May 2003 to December 2008.

Results The results observed that clinical characteristics of women with GDM were as follow; age (33.9 ± 3.8 yr), pre-pregnancy BMI (23.3 ± 4.0 kg/m²), primi-para (52.2%), GDM A1 (88.3%), GDM A2 (10.1%), and GDM B1 (1.1%). The average weight gains during pregnancy were 10.0 ± 4.3 kg. HbA1c level was $5.18 \pm 0.5\%$ at diagnosis and $5.5 \pm 2.3\%$ at delivery. Pregnancy outcomes were normal spontaneous delivery rate (51.4%), induction of labor (0.3%), primary cesarean section rate (24.2%), and delivery weeks (38.7 ± 1.5 wks) were found. Neonatal outcomes were characterized with birth weight ($3,273 \pm 493$ g), large for gestational age (26.3%), and macrosomia (6.8%). The neonatal birth weight of GDM A2 women was significantly higher than that of GDM A1 women ($3,387 \pm 538$ g vs. $3,260 \pm 485$ g, $p=0.02$) and the pre-pregnancy BMI of GDM A2 was higher than that of GDM A1 (25.8 ± 4.9 vs. 23.0 ± 3.7 kg/m², $p < 0.001$). Neonatal birth weight was strongly correlated with delivery weeks ($r=0.519$, $p < 0.001$), pre-pregnancy BMI ($r=0.183$, $p < 0.001$), and weight gains during pregnancy ($r=0.175$, $p < 0.001$). The predictor of neonatal birth weight explained 29.1% ($R=0.544$, adjusted $R^2=0.291$, $F=64.10$, $P < 0.001$).

Conclusion These findings suggested that pre-pregnancy BMI is one of the main factors for neonatal birth weight. But after GDM diagnosis, total weight gain is the important factor for neonatal birth weight also. Therefore, tight weight control is needed for women with GDM.

PE96 Epidemiology & genetics

The comparison of the insulin resistance and the prevalence of metabolic syndrome between North Korean Refugees and South KoreanJoo Hyung Kim^{1*}, Dong Seop Choi¹, Sei Hyun Baik¹, Kyung Mook Choi¹, Nan Hee Kim¹, Ji A Seo¹, Hee Young Kim¹, Hye Jin Yoo¹, Sae Jung Yang¹, Yoon Jung Kim¹, Myongjin Cho², Chae Ryung Eun¹, Hae Yoon Choi¹, Ho Chul Hong¹, Yun Jeong Lee², Sin Gon Kim¹

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Objective Currently, over 20,000 North Korean defectors are staying in South Korea and more than 2,000 subjects are coming every year. North Korean is reported to have different type of diseases or mortality compared with South Korean, because they have been lived in different environments (politically, socially, medically etc) even though having the same genetic background. In addition, health status of refugees is expected to change according to different, so called Westernized environments of South Korea.

Methods The intended sample was North Korean defectors aged 30 or more residing in NoWon area in Seoul. We interviewed them and examined their medical and psychological status. To compare the results of a total of 427 North Korean refugees (NKR) with those of South Korean (SK), we extracted data on a total of 880 SK who were age and gender matched to NKR counterpart from Korea National Health and Nutritional Examination database.

Results Most of anthropometric measures were smaller in NKR than SK, particularly among young men aged 30-39 (NKR vs SK, abdominal obesity, 5.6% vs 30.9%, $p=0.003$; BMI, 22.7 ± 2.4 vs 24.6 ± 3.4 , $p=0.0029$). In addition, the insulin resistance measured by HOMA-IR were lower in NKR compared to SK (1.55 ± 0.76 vs 2.48 ± 1.77 , $p < 0.001$ in men, 1.65 ± 0.94 vs 2.30 ± 1.11 , $p < 0.001$ in women). Nevertheless, the prevalence of metabolic syndrome has no statistically different between NKR and SK (20.8% vs 24.8%, $p=0.445$ in men, 15.3% vs 17.5%, $p=0.395$ in women). And NK refugees have significantly low insulin secretion measured by HOMA- β compared to SK.

Conclusion Even though the NK refugees have a low insulin resistance, they are so vulnerable to metabolic syndrome, and they also have a low pancreatic β -cell function. These data indicate that the prevalence of diabetes in NKR may rapidly increase in a short period.

PE97 Epidemiology & genetics

Therapeutic effects of NecroX compound on nonalcoholic steatohepatitis by suppressing mitochondrial reactive oxygen species

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Objective Nonalcoholic steatohepatitis (NASH) is associated with systemic and hepatic insulin resistance and results liver fibrosis, end-stage cirrhosis and hepatocellular carcinoma. ROS/RNS play the key roles in the development of NASH by resulting hepatocyte stress, inflammation and insulin resistance. We here show that the beneficial effects of necroX compound on NASH in leptin deficient ob/ob mice.

Methods Six week old male (N=5 per group) ob/ob mice were daily administered with necroX (LGLS Inc.) and control vehicle for 4 weeks. The effect of necroX on NASH progression was studied using biochemical, histological and molecular makers.

Results NecroX inhibited Tert-butylhydroperoxide and H₂O₂ induced cytosolic ROS/RNS and mitochondrial superoxide formation in HepG2 cells. Interestingly, necroX treated ob/ob mice revealed markedly reduced liver fat stained with oil red O (39.3±5.8% vs. 11.2±3.2, p<0.05) compare to control vehicle group. Body weights between control and treated group were not showed not statistical differences. NecroX treated mice exhibited a lower degree of infiltrated macrophage, reduced expression and secretion of proinflammatory cytokine TNF α and IL-6. Further analysis demonstrated that necroX treatment efficiently inhibited nuclear factor (NF)- κ B activation in liver and as a consequence attenuated the inflammatory response in liver.

Conclusion These results suggest that NecroX has therapeutic potentials on steatohepatitis in ob/ob mice through suppression of mitochondrial ROS and inflammatory responses.

PE98 Epidemiology & genetics

Vitamin D receptor gene polymorphisms and HLA DRB1*04 interaction in Saudi type 2 diabetes patients

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Objective The Vitamin D receptor (VDR) gene has been involved in the modulation of susceptibility to inflammatory and autoimmune conditions and could play a role in the pathogenesis of type 2 diabetes mellitus (T2DM). Susceptibility to T2DM, was very recently also suggested to associate with HLA alleles. We evaluated possible correlations between VDR polymorphisms, HLA alleles, and risk of developing T2DM. Individuals part of a well-characterized cohort followed in Riyadh, KSA (N=627: 368 T2DM patients and 259 healthy controls) were analyzed.

Methods Genomic DNA was extracted from blood and genotyped for the VDR gene single nucleotide polymorphisms (SNPs) of Fok-1, Taq-1, Apal and Bsm-I. Analyses were run by allelic discrimination real time PCR. HLA genotyping was performed as well by PCR using sequence specific primers (PCR-SSP).

Results T2DM is significantly associated with the VDR Taq1 (rs731236-AG) and Bsm-I (rs1544410-T-CT) genotypes and the VDR rs1544410-T allele. Significant interactions resulting in a robust increase of the OR were detected between Taq1 and Bsm-I VDR polymorphisms and HLA DRB1*04; finally, VDR polymorphisms correlated with metabolic parameters of susceptibility to T2DM including serum cholesterol and HDL levels.

Conclusion VDR polymorphisms are present in T2DM and correlate with HLA DRB1*04 and metabolic parameters; our results confirm an association between T2DM and HLA and add this condition to the list of diseases that are likely modulated by an HLA/VDR interaction.

PE99 Epidemiology & genetics

Type 2 diabetes risk assessment in Mongolia

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Objective To assess Type 2 diabetes risk by Finnish Diabetes Risk Score (FINDRISC) questionnaire.

Methods In this cross-sectional survey using "FINDRISC questionnaire" of Finnish Diabetes Association, we selected the participants randomly among Central Regional Electricity Transmission Grid State Owned Stock Company's employees evaluated the annual health check up at the National Central Clinical Hospital.

Results A total of 93 subjects was age between 29-56 (65% male, 35% female) Data on the FINDRISC were available from each participant. The FINDRISC risk score was Very high 2.1%, High 10.7%, Moderate 12.9%, Slightly elevated 19.3%, and Low 54.8% respectively. Among the subjects with Very high and high risk score, 5 individuals diagnosed with impaired glucose tolerance (IGT) after 2-hour plasma glucose level in oral glucose tolerance test (OGTT) or capillary blood glucose with 140-200 mg/dl; 1 individual diagnosed type 2 diabetes; and 6 were healthy. The sex and waist circumference (WC) correlation was weak (r=0.25 p<0.01). The fasting glucose (FG) were correlated to the Body Mass Index (BMI) (r=0.13, p<0.005).

Conclusion The result indicated that the FINDRISC risk score was Very high 2.1%, High 10.7%, Moderate 12.9%, Slightly elevated 19.3%, and Low 54.8% respectively. Among the subjects with Very high and high risk score, 5 individuals diagnosed with impaired glucose tolerance (IGT); 1 individual diagnosed type 2 diabetes; and 6 were healthy. 90% of people with very high and high risk score had family history and no daily physical activity at least 30 minutes at work and/or during leisure time (including normal daily activity).

PE100 Epidemiology & genetics

Long-term changes of the prevalence and control rate of hypertension among Korean adults with diagnosed diabetes: 1998-2008 Korean National Health and Nutrition Examination Survey (KNHANES)

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Objective Co-occurrence and high prevalence of diabetes and hypertension are a major health concern. The purpose of this study was to investigate long-term changes in the prevalence and control rate of hypertension among Korean adults with diagnosed diabetes.

Methods Using data from the Korea National Health and Nutrition Examination Survey (KNHANES) between 1998 and 2008, we analyzed changes in prevalence of hypertension (mean blood pressure of SBP \geq 140 mmHg, DBP \geq 90 mmHg, or use of antihypertensive medication) and control rate (the proportion with BP<130/80 mmHg) in diabetic patients. A total of 1,400 adults diagnosed with diabetes (670 men and 730 women) were enrolled and their clinical and laboratory data were analyzed.

Results Between 1998 and 2008 (n=1,400), prevalence of hypertension in diabetes changed from 52.7 to 56.7%. Mean BPs decreased from 136.7 \pm 1.2/80.7 \pm 0.7 mmHg to 124.3 \pm 1.0/76.4 \pm 0.6 mmHg (P<0.05). Awareness (39.9 to 89.7%, P<0.05), treatment (40.9 to 88.2%, P<0.05), and control rate of hypertension (25.1 to 46.4%, P<0.05) steadily increased during the last decade. Compared to men and younger population, prevalence of hypertension was higher in women (60.0 vs. 53.0%, P<0.05) and elderly population (>65 year-old) (68.0 vs. 49.9%, P<0.05) respectively in 2008, but there were no differences in control rate according to sex and age.

Conclusion Between 1998 and 2008, half of Korean adults with diabetes had hypertension. Although hypertension treatment and control rate was significantly improved, the control of elevated blood pressure is inadequate, and aggressive intervention is needed to reach target blood pressure control.

PE101 Epidemiology & genetics

Observations on the traditional phytotherapy for gestational diabetes among the inhabitants of the Narayanganj district in Bangladesh

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Objective Gestational diabetes is a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy. Gestational diabetes affects (03-10)% of pregnancies, depending on the population studied. Gestational diabetes is prevalent in Bangladesh. The population of Bangladesh mostly depends on traditional health practitioners for treatment of this disease. The traditional health practitioners rely on decoctions made from medicinal plants or plant parts to treat gestational diabetes, which decoctions can vary widely between traditional health practitioners in the various districts of the country. The objective of this present study was to conduct an ethnopharmacological survey among the traditional health practitioners of Narayanganj district, Bangladesh to learn about medicinal plants used to treat gestational diabetes.

Methods Extensive interviews were conducted of the traditional health practitioners and information collected as to medicinal plants or plant parts used and the ailments treated. Medicinal plant samples were collected and identified at the Bangladesh National Herbarium.

Results It was observed during the course of this ethnopharmacological survey that the traditional health practitioners are well-aware of gestational diabetes and treat the ailment using formulations prepared from a number of medicinal plants or plant parts. Different medicinal plants have been found to: (1) enhance insulin secretion; (2) inhibit glucose absorption; (3) enhance utilization of glucose in peripheral tissues, and (4) have mixed activity. No significant correlation was observed between the age of traditional health practitioners and the number of medicinal plants reported and the indigenous knowledge transfer was found to be similar. It was also noted in this ethnopharmacological survey that the local patients were quite satisfied with treatment by the traditional health practitioners.

Conclusion It is concluded that the ethnopharmacological information reported forms a basis for further research to identify and isolate bioactive constituents that can be developed to drugs for the management of the gestational diabetes.

PE102 Epidemiology & genetics

CA19-9 level according to fasting glucose level in general population

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Objective Serum CA19-9 is tumor marker for biliopancreatic malignancies and is well known that increase in diabetic patients. Previous studies presented diabetes is a risk factor for pancreatic cancer. In this study, to evaluate CA19-9 levels in general population according to fasting glucose levels.

Methods We retrospectively enrolled 5649 individuals who had checked the CA19-9 level for the purpose of health screening at Kosin University Hospital. The patients were classified by fasting plasma glucose levels (Group 1; <99, Group 2; 100-125, Group 3; 126-).

Results Of all, 4656 patients were Group 1, 762 were Group 2 and 231 were Group 3. The average CA19-9 level was 7.66±7.50 U/mL in Group 1, 8.23±8.30 U/mL in Group 2 and 11.64±11.65 U/mL in Group 3 (p < 0.001). Linear regression analysis showed a positive correlation fasting glucose and CA19-9 independent from age, serum CEA level (t=3.736, p < 0.001).

Conclusion CA19-9 is a tumor marker but also a marker of pancreatic tissue damage that might be caused by diabetes. This action occurs in general population according to fasting glucose levels.

PE103 Epidemiology & genetics

The effect of metabolic syndrome and smoking on arterial stiffness

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Objective Arterial stiffness assessed by pulse wave velocity has been reported to predict cardiovascular morbidity and mortality. Metabolic syndrome and smoking are associated with increased risk of cardiovascular disease each independently. Therefore, the purpose of this study is to evaluate dissociative effect of metabolic syndrome on arterial stiffness independent of smoking.

Methods We retrospectively enrolled 1583 individuals who had performed brachial-ankle pulse wave velocity (baPWV) for the purpose of health screening at Kosin University Hospital.

Results Of all, 1530 patients were men, 53 were women. We found that baPWV was positively correlated with age, BMI, waist circumference (WC), FBS, and LDL in women. Whereas baPWV was negatively correlated with BMI and WC in men who were current smoker. However in men who were never smoker BMI and WC was positively correlated with baPWV.

Conclusion Generally, the factors of metabolic syndrome and baPWV had a relationship. However, the differences were between men and women and these differences seem to be due to smoking.

PE104 Epidemiology & genetics

Association of pyruvate dehydrogenase kinase 4 gene polymorphisms with type 2 diabetes and metabolic syndrome

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Objective Pyruvate dehydrogenase kinase 4 (PDK4) plays a crucial role in glucose utilization and lipid metabolism by regulating the pyruvate dehydrogenase complex (PDC) and is an emerging therapeutic target for type 2 diabetes. To date, no study has specifically examined the relationship between PDK4 gene polymorphisms and type 2 diabetes or metabolic syndrome.

Methods The association of common single nucleotide polymorphisms (SNPs) was examined in PDK4 [-208A/G (rs10085637), IVS3+192C/T (rs3779478), IVS6+31A/G (rs2301630), IVS7+514A/G (rs12668651), IVS10+75C/T (rs10247649)] with type 2 diabetes and metabolic syndrome in 651 Korean subjects with type 2 diabetes and 350 nondiabetic Korean subjects. The association of these SNPs with clinical parameters related to metabolic syndromes including obesity, hyperglycemia, hypertension, and dyslipidemia was also examined.

Results No significant association was found between the studied SNPs and type 2 diabetes, metabolic syndrome, or clinical parameters. The PDK4 gene haplotype ACAGC showed a modest association with type 2 diabetes. However, the significance of this association was lost after considering for multiple comparisons.

Conclusion PDK4 polymorphisms may not be associated with type 2 diabetes or metabolic syndrome. Further studies utilizing a larger study population are required to confirm these results.

PE105 Epidemiology & genetics

Association analysis of the gene SNPs related to both obesity risk and physical fitness

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Objective This research attempts to find out the gene SNPs related to both obesity risk and physical fitness, then to analyze the clinical correlation between physical fitness and genotype.

Methods The study population was composed of seventy-one 10-year-old children (31 boys and 40 girls). They were divided into a low group and a high group based on cut-off scores of physical fitness level. Blood samples were obtained from each subject after a 12-hour overnight fast by evacuation from an antecubital vein into vacutainer tubes. Sixty-eight single nucleotide polymorphisms (SNPs) were screened using SNP-1™ assays with SNPstream 25K[®] System (Orchid Biosciences, Princeton, NJ, USA). The Chi-square test was used to test differences between the low group and the high group for each SNP genotype and allele. Multivariate multiple logistic regression was used to control for possible confounding by age and gender.

Results The results of the analysis showed that there were statistically significant ($p < .02$) differences in the scores of physical fitness according to the phenotypes of CNR1($p=.010$), LEP($p=.012$), HHEX($p=.009$), GC($p=.013$), LRP5($p=.014$), NPY2R($p=.003$), PPY($p=.017$), UCP2($p=.003$), CDKN2B($p=.011$) and ADIPOQ($p=.006$).

Conclusion Therefore, in the future there would have to be follow-up researches to find out the functions of the physical fitness-related genotypes: CNR1, LEP, HHEX, GC, LRP5, NPY2R, PPY, UCP2, CDKN2B and ADIPOQ - which have been identified in the present research, through observations of the changes in physical fitness according to the genotypes.

PE106 Epidemiology & genetics

Association of lipid and lipoprotein profiles with future development of type 2 diabetes in non-diabetic Korean subjects: A 4-year retrospective, longitudinal study

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Objective Traditional lipid measures are known to be associated with incident type 2 diabetes. Our objective was to assess the independent association between lipid profiles and development of type 2 diabetes in non-diabetic Korean subjects over a 4-year period.

Methods A total of 5,577 Koreans without diabetes who underwent consecutive comprehensive health check-ups annually for 5 years were enrolled. We measured concentrations of total cholesterol (TC), triglyceride (TG), apolipoprotein B (apoB), apolipoprotein A-I (apoA-I), low density lipoprotein cholesterol (LDL-C), and high density lipoprotein cholesterol (HDL-C) and calculated lipid ratios. The association between incident type 2 diabetes and initial values for lipid ratios, and other lipoprotein components was examined.

Results Over the course of 4 years, 330 subjects (5.9%) developed type 2 diabetes. TC, LDL-C, TG, Non-HDL, apoB, apoB/A-I ratio, TC/HDL ratio, TG/HDL ratio, LDL/HDL ratio and apoB/HDL ratio were associated with incident type 2 diabetes in multivariate analysis after adjustment for age and gender. Of these, the ratio of TC/HDL and apoB/HDL showed a significant association with increased risk of type 2 diabetes, compared with other lipoprotein parameters: Odds ratio (OR), 1.340, 95% CI, 1.166-1.538; and 1.338, 95% CI, 1.162-1.540, respectively. OR for development of type 2 diabetes increased significantly as the tertiles of the baseline ratio of TC/HDL and apoB/HDL increased from the first to the third tertile.

Conclusion This study suggests that lipid and lipoprotein profiles can be independently associated with later development of type 2 diabetes in non-diabetic Korean adults in a longitudinal analysis.

PE107 Epidemiology & genetics

Explosive increase in diabetes health care utilization in Korea; 1990-2008

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Objective Diabetes have become a major health care problem in Korea. We investigated changes in the health care utilization for the management of diabetes over last two decades.

Methods The Ministry of Health and Welfare of Korea conducted a series of nationwide surveys to examine the general health status of Koreans in every three years. In this study, we analyzed the data to verify the changes in medical institution utilization rate of diabetic patients and we also investigated the changes in health care utilization of diabetic patients subdivided by gender, age and hospital classifications.

Results From 1990 to 2008, the number of diabetic patients who visited outpatient clinic increased by 8.3 times. In the same period, total number of patients who visited outpatient clinic for any reason increased by 2.4 times, thus the increase in outpatients clinic visit attributable for diabetes was 3.5 fold higher than overall increase in outpatients clinic visit. At the same period, the number of hospitalized diabetic patients was increased by 2.8 times, which was comparable to 2.9 fold increase in total number of hospitalized patients for any reason. The number of health care utilization in older age group increased by 17 times, while in middle age group and younger age group, increases in health care utilization were 6.5 times and 4.5 times, respectively. The mean duration of admission increased from 15 days in the 1990s to 22.4 days in the last decade, contributable to the longer hospital stay of older diabetic patients.

Conclusion Over the last two decades, the prevalence of diabetes was not significantly changed but health care utilization by diabetic patients was explosively increased, especially in older patients. This means that public health care system for prevention and appropriate management of diabetes should be implemented in Korea.

PE108 Epidemiology & genetics

Prevalence of diabetic complication and clinical characteristics in newly diagnosed Korean type 2 diabetic patients: Korean type 2 diabetes prospective cohort study

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Objective Population based studies described that the prevalence of diabetic complication at time of diagnosis varies between 10% and 20%. About 50% of the subjects of UKPDS had substantial macro- or micro-vascular abnormalities at the time of T2DM diagnosis. The aims of this study were to describe the prevalence of diabetic complications among newly diagnosed diabetic patients who were enrolled to Korea national diabetes program (KNDP) constructing the type 2 diabetes cohort consisting of 12 university hospitals.

Methods Of 4,256 patients enrolled to the cohort, 728 newly diagnosed drug naïve patients were participated in this study. Metabolic profiles and diabetic complication status at diagnosis were investigated. In addition, data of all 198 newly diagnosed type 2 diabetics who reached 3-year follow-up periods were compared with the baseline data of metabolic profiles.

Results Mean age and HbA1c at the time of diagnosis were 51.9±11.1 years and 8.2±2.4% in 728 newly diagnosed drug naïve patients. The prevalence of metabolic syndrome at diagnosis was 50.8%. The prevalence of diabetic nephropathy, retinopathy, and neuropathy at the time of diagnosis were 21.4%, 8.4%, and 38.6% of 728 newly diagnosed drug naïve patients, respectively. Also, there were significant differences of prevalence of complication according to HbA1c values. During 3-year follow-up, lipid profile including total cholesterol, HDL-cholesterol, and LDL-cholesterol improved significantly compared with the baseline ($P < 0.001$) in 198 subjects who reached 3-year follow-up. The glycemic control was improved in all glycemic parameter; fasting plasma glucose (FPG), postprandial plasma glucose (PPG), and HbA1c.

Conclusion In summary, about 20-40% of newly diagnosed patients already have evidence of diabetic complications and potentially modifiable cardiovascular risk factors at the time of diagnosis. The introduction of intensive and systematic care into clinical practice should be necessary to prevent diabetes related chronic complication through this prospective cohort study.

PE109 Epidemiology & genetics

The association between socio-economic status and the prevalence of diabetes mellitus in the Korean population

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Objective The association between low socio-economic status (SES) and increased prevalence of diabetes mellitus has been reported in Caucasians. We compared the effect of SES on prevalence of diabetes mellitus among participants in the Korean National Health and Nutrition Examination Surveys in 1998 and 2009.

Methods In each survey, stratified, multistage, probability-sampling designs and weighting adjustments were conducted to represent the entire Korean population. The SES of participants was classified to quartile according to the familial monthly income with equivalence scale: Q1 is the highest quartile of SES and Q4 is the lowest.

Results In 2009, Q4 showed a significantly higher prevalence of diabetes compared to the others both in men and women ($P < 0.001$) after adjusting body mass index (BMI). The prevalence of diabetes mellitus is about three times higher in Q4 compared to Q1 (men: 16.7% in Q4 and 6.0% in Q1, women: 14.4% in Q4 and 5.1% in Q1). However, in 1998, only men showed the significant association between SES and the prevalence of diabetes after adjusting BMI ($P=0.013$).

Conclusion In conclusion, low SES might be one of the risk factors in the diabetes mellitus in the Korean population. In women, the effect of SES on diabetes prevalence is more prominent in 2009 compared to 1998.

PE111 Insulin action & obesity

Effects of pyruvate dehydrogenase kinase 2 (PDK2) deficiency on hepatic steatosis induced by the high fat dietYounghoon Go^{1*}, Younghoon Go¹, Nam Ho Jeoung⁴, Ji-yun Jeong³, Ae-Kyung Min², Hyeon-Ji Kang¹, Bo Yoon Park¹, Eon-Ju Jeon³, Hyun-Ae Seo³, Jong Ho Kim³, Yeon Kyung Choi³, Keun-Gyu Park³, Robert A. Harris⁵, In-Kyu Lee⁵, In-Kyu Lee¹Department of Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Departments of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea³, Department of Fundamental Medical and Pharmaceutical Sciences, Catholic University of Daegu, Daegu, Korea⁴, Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Roubidoux VA Medical Center, Indianapolis, U.S.A.⁵

Objective Regulation of the activity of the pyruvate dehydrogenase complex (PDC) is critical for disposal of excess glucose, fuel selection by tissues, and conservation of substrates for glucose synthesis. The phosphorylation of PDC by the PDK isoenzymes (1-4) inhibits the PDC activity. Relative to PDK4, less evidence has existed for an important role for PDK2 in glucose homeostasis. We examined effect of PDK2 deficiency on hepatic steatosis in diet induced obesity (DIO) model.

Methods Wild-type (WT) and PDK2^{-/-} mice fed a control diet (CD, Research diets, D12450B) or high-fat diet (HFD, Research diets, D12492) for 16 weeks. Body weights of the mice were determined weekly. Glucose tolerance test were performed with overnight-fasted mice. Glucose (1 g/kg of body weight) was given by intraperitoneal injection. All mRNA and protein level in liver were determined by real-time PCR and western blot analyses.

Results PDK2 deficiency has no effect upon fasting blood glucose levels in CD fed mice. However, in studies with HFD-fed mice, PDK2^{-/-} mice reduced body weight, lowered fasting blood glucose levels, and improved glucose tolerance compared to WT mice. The expression level of SREBP1c, ACC, and FAS were significantly reduced in the liver of PDK2^{-/-} mice compared to WT mice. The expression levels of genes involved in β -oxidation and ketogenesis were increased in liver of PDK2^{-/-} mice compare to WT mice.

Conclusion This study shows that PDK2 deficiency inhibits hepatic lipogenesis in DIO model. These results strongly suggest that PDK2 plays an important role in regulation of hepatic lipid metabolism.

PE110 Insulin action & obesity

Peroxiredoxin 3 is a key molecule regulating adipocyte oxidative stress, mitochondrial biogenesis, and adipokine expressionJoo Young Huh^{1*}, Kong-Joo Lee², Hunjoo Ha²College of Pharmacy, Division of Life & Pharmaceutical Sciences¹, Department of Bioinspired Science, Ewha Womans University, Seoul, Korea²

Objective Obesity, defined by abnormal or excessive fat accumulation, is one of the most prevalent chronic diseases worldwide. During the progression of obesity, increased oxidative stress in obese adipocytes contributes to adipokine dysregulation, inflammation, and insulin resistance. Through an advanced proteomic analysis, we found that peroxiredoxin 3 (Prx3), a thioredoxin-dependent mitochondrial peroxidase, is highly expressed in 3T3-L1 adipocytes compared to preadipocytes. Interestingly, in obese db/db mice and human subjects, adipose Prx3 levels were significantly decreased indicating its association with obesity.

Methods We therefore employed Prx3 knockout (KO) mice and transfected 3T3-L1 cells to examine the role of endogenous Prx3 in adipocyte metabolism.

Results Prx3 KO mice had increased fat mass compared to wild type due to adipocyte hypertrophy. Increased adipogenic transcription factors and lipogenic gene expression during differentiation of adipose tissue-derived stem cells from Prx3 deficient mice confirmed that these adipocytes are likely to accumulate fat. Mitochondrial protein carbonylation in Prx3 KO adipose tissue and mitochondrial superoxide level in Prx3 knockdown 3T3-L1 cells were increased showing aberrant regulation of oxidative stress. Proteomic analysis and gene expression analysis of Prx3 KO mice adipocytes also showed defect in mitochondria biogenesis along with enzymes involved in glucose/lipid metabolism and oxidative phosphorylation. In addition, expression level of adiponectin was downregulated and plasminogen activator inhibitor-1 was upregulated in Prx3 KO adipocytes. Impaired glucose tolerance and insulin resistance further implied metabolic dysregulation in Prx3 KO mice.

Conclusion These data suggest that endogenous Prx3 may play an essential role in maintaining normal characteristics of adipocytes and that defect in Prx 3 alters antioxidant system, mitochondrial function, and adipokine expression in adipocytes leading to metabolic alteration.

PE112 Insulin action & obesity

Various oscillation patterns of serum FGF21 concentrations in healthy volunteersSang Ah Lee^{1*}, Eun Hee Kim², Mi-Seon Shin², Jenie Yoonoo Hwang², Eun Hee Koh², Woo Je Lee², Joong-Yeol Park², Eunheui Jeong², Min-Seon Kim²Department of Internal Medicine, Jeju National University School of Medicine¹, Department of Internal Medicine, Asan Medical Center, University of Ulsan College of Medicine²

Objective Fibroblast growth factor 21 (FGF21) was originally identified as a PPAR- α target gene product and is known to be a hormone involved in metabolic regulation. The purpose of this study was to investigate the diurnal variation of serum FGF21 concentrations in obese and nonobese healthy volunteers.

Methods Blood samples were collected from 5 nonobese (BMI ≤ 23 kg/m²) and 5 obese (BMI ≥ 25 kg/m²) healthy young men every 30-60 min over 24 h. Serum FGF21 concentrations were determined by radioimmunoassay. Anthropometric parameters, glucose, free fatty acid, insulin, leptin, and cortisol concentrations were also measured.

Results The serum FGF21 concentrations displayed various individual oscillation patterns. The oscillation frequency ranged 6 to 12 times per day. The average duration of oscillation was 2.52 h (range, 1.9-3.0 h). The peaks and troughs of FGF21 oscillation showed no circadian rhythm. However, the oscillation frequency had a diurnal variation and was lower during the light-off than during the light-on period (2.4 vs. 7.3 times, $P < 0.001$). There was no difference in the total frequency or duration of oscillations between nonobese and obese subjects, but obese individuals had increased numbers of larger oscillations (amplitude ≥ 0.19 ng/ml).

Conclusion Various oscillation patterns in serum FGF21 concentrations were observed, and reduced oscillation frequencies were seen during sleep. The oscillation patterns of the serum FGF21 concentrations suggest that FGF21 may be secreted to the systemic circulation in a pulsatile manner. Obesity appeared to affect the amplitude of oscillations of serum FGF21.

PE113 Insulin action & obesity

PRMT1 regulates hepatic gluconeogenesis via FoxO1

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Protein arginine methyltransferase 1 (PRMT1) is an enzyme that transfers methyl groups from S-adenosyl methionine to arginine residues. It has been reported that PRMT1 methylates FoxO1 at arginine residues within a consensus motif for Akt dependent phosphorylation, and blocks apoptosis depending on PI3K-Akt signaling pathway. Therefore, we investigated whether PRMT1 is related with FoxO1-mediated gluconeogenic program in liver. Interestingly, PRMT1 knockdown in livers of mice exhibited improved glucose tolerance and decreased gluconeogenic gene expression. Also, PRMT1 knockdown led to the increased level of FoxO1 phosphorylation at Ser253 without changes in the Ser473 phosphorylation level of Akt. On the other hand, the insulin-mediated inhibition of the gluconeogenic gene expression was significantly rescued by PRMT1. These data suggest that PRMT1 directly regulates FoxO1-mediated hepatic gluconeogenesis in an Akt-independent manner. PRMT1 interacts with FoxO1 and increases the transcriptional activity of FoxO1.

PE115

WITHDRAWN

PE114 Insulin action & obesity

A crucial role for TCF4M, a short splice variant of TCF7L2, in regulation of hepatic glucose metabolism

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Common variants of the transcription factor 7-like 2 (TCF7L2) gene have been associated with Type 2 diabetes and enhanced rate of hepatic glucose production. TCF7L2 gene is subjected to alternative splicing, and generates three isoforms with structural differences; TCF4M, TCF4S, and TCF4E. In this study, we found that expression level of TCF4M, one of the short splice variants of TCF7L2, was decreased in livers of diabetic db/db, high-fat fed, and fasted mice. To assess the effects of TCF7L2 on hepatic glucose metabolism, we observed livers of TCF7L2 hetero-knockout mice and adenovirus-mediated TCF7L2 knockdown mice. Both mice exhibited elevated fasting blood glucose level and impaired glucose tolerance, which accompanied by induction of expression of gluconeogenic genes. Interestingly, hepatic TCF4M suppressed gluconeogenic gene expression by interaction with CRTC2 and FoxO1, master regulators of gluconeogenesis. Furthermore, hepatic expression of TCF4M recovered impaired gluconeogenic program in livers of TCF7L2-hetero-knockout mice. Consistently, expression of TCF4M in livers of high fat diet-fed mice alleviated impaired glucose tolerance, suppressed diet-induced expression of gluconeogenic genes, and restored impaired insulin/IR/AKT signaling pathway. Taken together, these data suggest a beneficial effect of hepatic TCF4M expression on relieving hyperglycemia in type 2 diabetes.

PE116

WITHDRAWN

PE117 Insulin action & obesity

cAMP responsive element binding protein 3-like 3 (CREB-H) decreases hepatic lipogenesisAe-Kyung Min^{2*}, Young Hoon Go³, Hyeon Ji Kang³, Bo Yoon Park³, Udayakumar Karunakaran³, Ji Yun Jeong¹, Eon Ju Jeon¹, Hyun Ae Seo¹, Keun Gyu Park¹, In-Kyu Lee¹Department of Internal Medicine, Kyungpook National University Hospital, Daegu, South Korea¹, Departments of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, South Korea², Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, Korea³

Objective Sterol regulatory element binding protein-1c (SREBP-1c) is one of the major regulators of the expression of genes involved in hepatic triglyceride synthesis. Hepatic expression of SREBP-1c is regulated by insulin-induced activation of liver X receptor (LXR) and specific protein 1 (Sp1). Endoplasmic reticulum-bound transcription factor families are shown to be involved in the control of various metabolic pathways. Here we show a novel function of ER-bound transcription factor, cAMP response element binding protein H (CREBH), in the regulation of hepatic lipogenesis.

Methods We assessed the effect of adenovirus-mediated overexpression of CREB-H on insulin or liver X receptor (LXR) agonist-stimulated SREBP-1c expression in rat hepatoma cell line (H4IIE) were determined by Northern and Western blot analysis. Transient transfection study was performed to measure the effect of CREB-H on SREBP-1c promoter activity in human hepatoma cell line (HepG2).

Results We found that fasting induced CREBH expression but feeding suppressed its expression. However, feeding did not suppress its expression when endogenous insulin was eliminated by treatment of streptozotocin. Moreover, insulin treatment decreased CREBH expression in cultured hepatocytes, suggesting that refeeding-suppressed CREBH expression is mainly mediated by insulin. Interestingly, the expression patterns of the SREBP-1c, which were upregulated by feeding, were opposite to those of CREBH, suggesting the link between CREBH and SREBP-1c expression. Indeed, adenovirus-mediated overexpression of CREBH inhibited insulin- and LXR agonist, TO901317-stimulated SREBP-1c mRNA expression in cultured hepatocytes. Moreover, adenovirus-mediated overexpression of CREBH in liver of mice by tail vein injection inhibited hepatic steatosis in animal models of hepatic steatosis through inhibition of SREBP-1c expression. Transient transfection and gel shift assays showed that CREBH inhibited the activities of LXR and Sp1, known mediators of insulin-dependent SREBP-1c expression.

Conclusion Taken together, this study suggests that CREBH could be novel negative regulator of hepatic lipogenesis.

PE118 Insulin action & obesity

Inhibitory effects of AG330 on adipocyte differentiation and obesityHyeon-Ji Kang^{1*}, Younhoon Go¹, Ae-Kyung Min², Bo-Yoon Park¹, Hyun-Ae Seo³, Ji Yun Jeong³, Eon Ju Jeon³, Keun-Gyu Park³, In-Kyu Lee³Department of Biochemistry and Cell Biology, Kyungpook National University School of Medicine, Daegu, Korea¹, Department of Research Institute of Aging and Metabolism, Kyungpook National University School of Medicine, Daegu, Korea², Department of Internal Medicine, Kyungpook National University Hospital, Daegu, Korea³

Objective Obesity related diseases such as type 2 diabetes, cardiovascular disease and metabolic syndrome. Nuclear factor E2-related factor 2 (Nrf2) is a transcription factor that is regulator of phase II detoxification has been shown to play an important role in mediating cytoprotective responses to oxidative stress and xenobiotics. Nrf2 is abundantly expressed in liver, kidney, and adipose tissue. In this study, we aimed to investigate the effect of AG330, a used Nrf2 activator on adipocyte differentiation and obesity.

Methods AG330 was treated during adipogenic process. Oil Red O staining performed on Day 8 to evaluate the accumulated lipid droplets in differentiated 3T3-L1 cells. The expression of adipocyte specific gene was determined by western blot and RT-PCR. The C57BL/6 Mice were fed either control diet (Research Diets, D12450B, 10% fat) or high fat diet (Research Diets, D12492, 60% fat) for 15 weeks. The HFD were mixed with or without AG330. The body weight was measured weekly and performed IPGTT after 13 weeks on the HFD.

Results AG330 suppresses adipocyte differentiation of 3T3-L1 preadipocyte and adipocyte specific transcription factors including C/EBP α , PPAR γ , ADD-1 and FAS. Additionally, AG330 increases protein level of Nrf2 and p21, cyclin dependent kinase inhibitor. AG330 inhibits clonal expansion through cell cycle arrest by increased Nrf2 and p21 in 3T3-L1 preadipocytes. Finally, the mice fed the HFD mixed AG330 was decreased body weight and improved glucose tolerance.

Conclusion The results suggest that AG330 regulates adipogenesis by increasing Nrf2, and therefore may have prevention effect on obesity.

PE119 Insulin action & obesity

Anti-atherogenic effect of S-adenosylmethionine through heme oxygenase-1 induction ameliorating endoplasmic reticulum stress in endothelial cellsJaechan Leem^{*}, Jung Eun Jang, Eun Hee Koh, Woo Je Lee, Min-Seon Kim, Joong-Yeol Park, Ki-Up Lee

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Objective S-adenosyl methionine (SAM) is a key intermediate in the metabolism of sulfur amino acids, and is a major methyl donor in the cell. Although low plasma SAM level was suggested to be associated with atherosclerosis, the effect of SAM administration on atherosclerosis is not established. This study was undertaken to test the possible preventive effect of SAM on atherosclerosis and its molecular mechanism.

Methods We examined effects of SAM on linoleic acid (LA)-induced endoplasmic reticulum (ER) stress and cell apoptosis in cultured human umbilical vein cells (HUVECs). Effects of SAM on atherosclerosis in high fat-fed Apo E^{-/-} mice were also examined.

Results In HUVECs, LA increased ER stress and cell apoptosis. SAM prevented LA-induced ER stress and endothelial cell apoptosis. SAM increased hemoxygenase-1 (HO-1) expression, and siRNA against HO-1 reversed SAM's effects on LA-dependent cell apoptosis and ER stress. Apo E^{-/-} mice rendered diabetic were given high fat diet to exacerbate atherosclerotic lesion. SAM treatment prevented atherosclerosis in these mice, and decreased the expression of ER stress markers in aortic tissues.

Conclusion These data demonstrate that administration of SAM prevents atherosclerosis in animal models by ameliorating endothelial ER stress. SAM treatment might be a new therapeutic strategy for atherosclerosis.

PE120 Insulin action & obesity

Effect of high glucose on IGFBP-5 expression in cardiac fibroblastSeung Eun Song^{*}, So Young Park, Yong Woon Kim, Jong Yeon Kim, Kyung Oh Doh, So Young ParkDepartment of Physiology, Yeungnam University College of Medicine¹, Aging-associated Vascular Disease Research Center, Yeungnam University College of Medicine, Daegu 705-717, Korea²

Objective The present study examined the effect of high glucose on IGFBP-5 expression and the underlying mechanisms in cardiac fibroblasts of heart.

Methods Cardiac fibroblasts were isolated from the heart of Sprague-Dawley young rats (1 to 3 day-old) and passages 2-3 were used for this experiment.

Results High glucose increased cell proliferation in a dose dependent manner at 48 h. The mRNA expression of MMP2, MMP9, collagen III was significantly increased by high glucose in a time dependent manner. Increased cell number by high glucose was significantly inhibited by ERK inhibitors (PD98059) at 48 h. The mRNA expression and protein level of IGFBP-5 was significantly increased by high glucose in a dose- and time-dependent manner in cardiac fibroblast. Increased IGFBP-5 expression by high glucose was inhibited by PD98059. In addition, miIGFBP5 increased cell proliferation in a dose- and time- dependent manner. The mRNA expression of collagen III was significantly increased by miIGFBP5 in a time dependent manner. Increased cell proliferation by miIGFBP5 was significantly inhibited by IGFBP-5 siRNA with high glucose at 48 h. In vivo study, LETO/OLETF rat is widely known as type 2 diabetic model. In comparison with LETO heart, OLETF heart increased IGFBP5 protein level.

Conclusion These results suggest that high glucose-induced cell proliferation and production of collagen III is mediated by IGFBP-5 in cardiac fibroblast.

PE121 Insulin action & obesity

WITHDRAWN

PE122 Insulin action & obesity

Association between serum free thyroxine and coronary artery calcification in healthy euthyroid subjects

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Objective Considerable evidence suggests that mild thyroid dysfunction could influence atherosclerotic vascular change. We planned this study to investigate whether thyroid function is associated with coronary artery calcification measured in healthy euthyroid subjects.

Methods A cross-sectional analysis was performed among subjects who visited our hospital for a health checkup. Among 1,849 subjects, 669 (mean age 55.3 ± 8.8 years; 392 men) with normal free thyroxine (FT4) and thyroid-stimulating hormone (TSH) range were included after excluding those with diabetes, history of current smoking and cardiovascular disease (CVD) or use of hypertensive, antithyroid drug and thyroid hormone. Coronary artery calcium score (CACS) was measured by multi-detector computed tomography.

Results Subjects with CACS >100 had lower FT4 levels than those with lower CACS ($P=0.017$) whereas no difference was shown in TSH levels among CACS categories. FT4 levels had an odd ratio of 0.06 for high CACS [95% confidence interval=0.01-0.74; $P=0.0028$] after adjustment for CVD risk factors. In multivariate regression analysis, CACS was negatively correlated with FT4 levels ($\beta=-0.823$, $P=0.032$) and the inverse association between FT4 and CACS remained significant only in men ($P=0.028$) by gender stratification.

Conclusion FT4 levels were inversely associated with coronary artery calcification in the euthyroid healthy subjects, especially in men independently of conventional CVD risk factors. Further studies are needed to validate that subject with decreased FT4 levels within normal reference range are at high CVD risk and have poor cardiovascular outcome.

PE123 Insulin action & obesity

The effect of fenofibrate on the morphology of the mitochondria of liver in obese (OLETF) ratsSu Kyung Park^{1*}, Hye-Jeong Lee², Mi-Kyoung Park¹, Duk Kyu Kim¹Department of Internal medicine, College of Medicine, Dong-A University¹, Department of Pharmacology, College of Medicine, Dong-A University²

Objective The deterioration of the mitochondrial function is understood the important pathogenesis of obesity and diabetes. The fenofibrate induces the proliferation of the peroxisomes and enhances the fatty acid oxidation. We exam this study to know how this drugs act on the mitochondria in the obesity and diabetes.

Methods We used the OLETF rats(O) as the obese model ($n=10$) and the LETO rats(L) as the control ($n=10$). All the groups were fed liberally to 16 weeks of age. Since 17 weeks, Each group was divided into the fenofibrated treated group(F) which was fed a standard chow and fenofibrate(30mg/kg/day) and the control(C) group which was fed a standard chow only. After 10 weeks, all of rats were sacrificed and the liver were gained and fixed. We examined the hepatic mitochondria by transmission electron microscope and measure the body weight and the plasma level of lipid.

Results Basal body weights and the plasma level of total cholesterol were not different between the groups. In the O and L group, the final plasma level of triglyceride in F subgroup is significantly higher than that in C subgroup but it is not significant (93 ± 30.8 mg/dL [O-C group] vs. 105 ± 19.6 mg/dL [O-F group], $P=0.54$, 40 ± 4.7 mg/dL [L-C group] vs. 43 ± 4.5 mg/dL [L-F group], $P=0.63$). The hepatic mitochondria of O group showed the destruction of spherical shape, swelling and inhomogeneity compared with L group. And the structure of cristae was disappeared. After 10 weeks of fenofibrate treatment, the hepatic mitochondria of F subgroup in O group were denser and compacter compared with C subgroup but the inhomogeneity was remained. Also the peroxisomes of F subgroup in O and L group were increased after fenofibrate therapy compared with C subgroup.

Conclusion In the obese model, the structure of hepatic mitochondria is deteriorated. The fenofibrate can reverse this change but not completely.

PE124 Insulin action & obesity

The increases in hepcidin and fat accumulation in pancreas of the high fat/iron overloaded mice

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Objective The pathogenesis of type 2 diabetes is characterized by insulin resistance and β -cell dysfunction. The iron accumulation in the pancreas may contribute to the development of insulin resistance and β -cell dysfunction. We investigated that the effect of feeding high fat and iron overloaded diet on the histological features of pancreatic tissue, the serum glycemic profiles, and the synthesis and secretion of insulin along with the change of hepcidin expression in a mouse model.

Methods The male C57BL/6J mice received LF diet (10% energy from fat) or HF diet (45% energy from fat) containing with or without carbonyl iron (2% of diet weight) for 7 weeks. We measured insulin resistance index and iron status indices in the plasma and the pancreas.

Results HF diet significantly increased the insulin resistance and glucose intolerance and plasma inflammatory cytokine levels. Iron overload made those effects worse. The plasma levels of iron and ferritin were significantly increased with iron overload but not significantly affected by HF diet. The deposition of iron and fat as well as the expression of ferritin and hepcidin in the pancreatic tissue was greater in the HF diet group and much greater in HF with high iron diet group. These changes induced less expression of pancreatic insulin but increase of islet circumference possibly maintained higher plasma insulin levels to compensate for the insulin resistance.

Conclusion High fat/Iron overload is associated with impaired glucose tolerance and insulin resistance through the deposition of pancreatic fat and iron. The increased expression of hepcidin in β -cells suggests that pancreatic β -cells may be involved in iron metabolism in addition to insulin resistance regulation.

PE125 Insulin action & obesity

Role of AMP-activated protein kinase in biosynthesis of S-Adenosyl-L-methionine in liverHye-Jeong Lee^{1*}, Eunhui Seo¹, Ae-wha Seo¹, So-Young Park¹, Sang-Oh Choi¹, Soo-Kyoung Park², Mi-Kyoung Park², Duk Kyu Kim²Department of Pharmacology, Dong-A University College of Medicine^{1,2}, Department of Internal Medicine, Dong-A University College of Medicine²

Objective S-Adenosyl-L-methionine (SAM) is a methyl donor to a key metabolite that regulates hepatocyte growth, death, and differentiation. Biosynthesis of SAM occurs in all mammalian cells as the first step in methionine catabolism in a reaction catalyzed by methionine adenosyltransferase (MAT). Decreased hepatic SAM biosynthesis is a consequence of all forms of chronic liver injury. In an animal model of chronic liver SAM deficiency, the liver is predisposed to further injury and develops spontaneous steatohepatitis and hepatocellular carcinoma. SAM treatment in experimental animal models of liver injury shows hepatoprotective properties. Recent data show that exogenous SAM can regulate hepatocyte growth and death, independent of its role as a methyl donor. This raises the question of its mechanism of action. In addition, we questioned what signaling pathway may be associated with the hepatoprotective properties of SAM.

Methods In the present study, we explored whether AMP-activated protein kinase (AMPK) affects on the synthesis of SAM. Adenoviral-mediated AMPK gene transfer employed for overexpression of AMPK in mice. For cell culture experiment, we used Chang liver cells known as human normal hepatocytes and CCL9.1 cells as murine normal hepatocytes.

Results Overexpression of AMPK by adenoviral transfer showed increased expression of MAT in murine liver. Treatment of AICAR as activator of AMPK also increased expression of MAT in both Chang liver cells and CCL9.1 cells. Treatment of Compound C as inhibitor of AMPK did not increase the expression of MAT in both cells.

Conclusion These results suggest that hepatoprotective role of AMPK may depend on the biosynthesis of SAM via expression of MAT.

PE126 Insulin action & obesity

Ectopic expression of olfactory receptor in human endothelial cell

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Objective Olfactory receptors (ORs) are the largest gene family in the human genome. Although they are expected to be expressed specifically in olfactory tissue, about 10% of ORs have ectopic expression. However, the function of ectopic ORs is not well explored except their chemotactic function on sperm and testis. The present study explores the expression of one of the representative OR- OR1D2- in a human endothelial cell and assesses the potential functional implication of such ectopic expression.

Methods We performed western analysis using OR1D2 antibody to identify transcript of OR from human endothelial cell. Chemical odorants including bourgeonal, octanal were treated and also alpha-lipoic acid, linoleic acid, and DHEA were given to elicit function of OR1D2 in endothelium. Using siRNA to silence OR1D2 expression in culture human endothelial cells, functional change of endothelial cells was explored by caspase-3 assay and Tunnel staining.

Results Among odorants, only bourgeonal, which is known to stimulate OR1D2 on sperm and testis cells, elicited a decrease of OR1D2 by western blotting. By using siRNA, expression of OR1D2 was down-regulated and apoptosis of human endothelial cells 24hr p.i. in dose dependent manner.

Conclusion Although the mechanism is not well known, OR1D2 may have crucial role in apoptosis of human endothelium. And alpha-lipoic acid, which is known to protect endothelial cells from apoptosis, may reverse apoptosis provoked by inhibiting expression of OR1D2. THuhs, OR1D2 may be a new target of endothelial dysfunction.

PE127 Insulin action & obesity

Effects of acetyl-L-carnitine on fatty acid metabolism and insulin resistance in high fat diet-fed mice

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Objective Carnitine is studied extensively in part because of the important role it plays in fatty acid oxidation and energy production and because it is a well-tolerated and generally safe therapeutic agent. However, it is still unknown whether acetyl-L-carnitine (ALC) is beneficial in metabolic syndrome and if so, the mechanisms. The aim of the present study was to evaluate the effects of acetyl-L-carnitine on fatty acid oxidation, energy production and insulin sensitivity in C57BL/6J mice fed on a High-fat(HF) diet.

Methods Male C57BL/6J mice were fed an HF (60% lipids) diet with or without intraperitoneal injections of (4.9, 9.8 and 49.2 mM kg-1day-1) ALC for 8 weeks. Morphometry, immunostaining, ELISA, Western blot analysis and electron microscopy were used.

Results The HF diet yielded overweight phenotype, glucose intolerance, hyperinsulinaemia, and hypertrophied islets and reduced liver peroxisome-proliferator activated receptor alpha (PPAR-alpha) concomitant with enhanced sterol-regulatory element binding protein-1 (SREBP-1) expression. Conversely, ALC treatments resulted in significant weight loss, a reversal of insulin resistance and islet hypertrophy, and alleviated hepatic steatosis. The treated mice also showed higher expressions of the genes related to mitochondrial energy metabolism (PGC-1 α) consistent with the increased mitochondrial biogenesis and energy expenditure in a dose-dependent manner.

Conclusion In conclusion, our data suggest that ALC may play an important role in improvement of insulin resistance through the fatty acid oxidation and energy production.

PE128 Insulin action & obesity

Association between metabolic risk factors and dietary intakes by the obesity level in male workers

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Objective We investigated the relationships of metabolic risk factors, Shift Work, stress and dietary intakes in male workers.

Methods A cross-sectional study was performed. We selected 6,199 male subjects(mean age 42.52 \pm 7.35 years) who received a regular health check-up in 2010 KHNP Study. Body mass index was calculated from height and weight measured. Normal, obesity classes I and II were defined as a body mass index of 24.9, 25.0 to 29.9 and \geq 30.0 kg/m². Male subjects were Normal(4,044), obesity I(2,027) and obesity II(128). Dietary information collected from food-frequency questionnaires (FFQs). Anthropometric and biochemical parameters were measured.

Results There were significant differences in the anthropometric and biochemical parameters among three groups(p<0.05, respectively). The obesity II group had the higher rate of drinking (p=0.000), smoking (p=0.000) and exercise(p<0.05). The prevalence of metabolic syndrome by the obesity level were 21.08%(Normal 12.58%, Obesity I 34.96% and Obesity II 73.27%) in 2010(p=0.000). A high blood pressure was the most frequent finding in total followed by high triglyceride, high glucose, low HDL cholesterol and high waist circumference. Nutrient intakes were that energy, carotene, sodium, zinc, cholesterol, SFA, MUFA and PUFA in obesity II group was higher than normal and obesity I group(p<0.05). The mean ratio of carbohydrate: protein: fat were 63.20 : 16.61 : 20.19. The intake of Folate and calcium were lower than the % KDRI in among three groups. Multiple linear regression analysis showed that bmi was associated with a WC and high energy consumption in male workers.

Conclusion The subjects had more number of lifestyle disease. Therefore, diet diversity is closely connected with lifestyle disease. Further study of the food intakes on obesity level using longitudinal study designs is warranted.

PE129 Insulin action & obesity

Exendin-4 increased canonical wnt/ β -catenin signaling pathway, resulting in decrease of SREBP and PPAR γ in hepatocytesJinmi Lee^{1*}, Seok-Woo Hong¹, Ji-Hun Choi², Se-Eun Park², Eun-Jung Rhee², Cheol-Young Park², Ki-Won Oh², Sung-Woo Park², Sun-Woo Kim², Won-Young Lee²Institute of Medical Research, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea¹, Department of Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea²

Objective Exendin-4, as a GLP-1 receptor (GLP-1R) agonist, reduces liver steatosis via suppression of lipogenesis in mouse and rat. Wnts are a family of secreted proteins that act through paracrine and autocrine mechanisms to regulate many aspects of cell fate and development. Recently, it is reported that wnt signaling pathway inhibits adipogenesis via expression of wnt/ β -catenin target genes-reduced adipogenic genes. Therefore, we investigated the effects of exendin-4 mediating wnt signaling in palmitic acid-induced hepatosteatosis.

Methods HepG2 cells, a human hepatocyte, adding 0.4mM palmitic acid (PA) were untreated or treated with 100nM exendin-4 for 24h. Decreased expression of β -catenin performed by β -catenin siRNA for 24h. RT-PCR and western blot were performed to observe the expression of wnt signaling pathway and lipogenesis-associated genes in hepatocyte.

Results PA increased intracellular lipid content and expression of lipogenic genes such as SREBP, SCD1, FAS, ACC, C/EBP and LXR α in HepG2 cells, whereas exendin-4 treatment decreased PA-induced intracellular lipid content and expression of FAS, ACC and LXR α mRNA. No change on expression of non-canonical wnt signaling factors was obtained between in the PA and PA + exendin-4-treated groups. However, exendin-4 treatment increased expression of β -catenin and its target genes, including TCF4 and C-myc. In addition, inhibition of β -catenin by β -catenin siRNA induced increase of PPAR γ and SREBP.

Conclusion Exendin-4 treatment improves PA-induced hepatosteatosis through inhibition of lipogenesis by canonical wnt/ β -catenin signaling.

PE130 Insulin action & obesity

Visfatin induces sickness responses in the brainByong Seo Park^{*}, Sung Ho Jin, Byung Ju Lee

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Objective Visfatin, also known as nicotinamide phosphoribosyltransferase or pre-B cell colony enhancing factor, is a pro-inflammatory cytokine whose serum level is increased in sepsis and cancer as well as in obesity. Here we report a pro-inflammatory role of visfatin in the brain, to mediate sickness responses including anorexia, hyperthermia and hypoactivity.

Methods Rats were intracerebroventricularly (ICV) injected with visfatin, and changes in food intake, body weight, body temperature and locomotor activity were monitored. Real-time PCR was applied to determine the expressions of proinflammatory cytokines, proopiomelanocortin (POMC) and prostaglandin-synthesizing enzymes in their brain. To determine the roles of cyclooxygenase (COX) and melanocortin in the visfatin action, rats were ICV-injected with visfatin with or without SHU9119, a melanocortin receptor antagonist, or indomethacin, a COX inhibitor, and their sickness behaviors were evaluated.

Results Administration of visfatin decreased food intake, body weight and locomotor activity and increased body temperature. Visfatin evoked significant increases in the levels of pro-inflammatory cytokines, prostaglandin synthesizing enzymes and POMC, an anorexigenic neuropeptide. Indomethacin attenuated the effects of visfatin on hyperthermia and hypoactivity, but not anorexia. Further, SHU9119 blocked visfatin-induced anorexia but did not affect hyperthermia or hypoactivity.

Conclusion Visfatin induced sickness responses via regulation of COX and the melanocortin pathway in the brain.

PE131 Insulin action & obesity

The increase of microRNA-96 induced by mitochondrial dysfunction causes insulin resistance in hepatocytes through the translational repression of IRS-1Hyo Jin Jeong^{*}, Wan Lee

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Objective Mitochondrial dysfunction induces insulin resistance in myocytes and hepatocytes through the reduction of IRS-1. Although endogenous non-coding microRNAs (miRNAs) have been implicated in the pathogenesis of various diseases, the role and identity of miRNAs in insulin resistance remain mostly unknown. Recently, we have shown that miRNAs targeting IRS-1 3' untranslated regions (3'UTR) are increased in mitochondrial dysfunction. In this study, we demonstrated how miR-96, one of miRNAs targeting IRS-1, are actively involved in the development of insulin resistance.

Methods We used Affimatrix miRNA Array to characterize the differential expression of miRNAs in mitochondrial DNA-depleted hepatocytes. We also used qRT-PCR to confirm cellular levels of selected miRNAs that are thought to target IRS-1 3'UTR. Targeting site as well as its binding of miR-96 in the 3'UTR of IRS-1 was analyzed by reporter gene assay. Using overexpression of miR-96, we investigated whether IRS-1-targeting miRNA causes insulin resistance in hepatocytes.

Results Mitochondrial dysfunction resulting from genetic (mitochondrial DNA depletion) or metabolic inhibition (Rotenone or Antimycin A) induced insulin resistance in hepatocytes via a reduction of IRS-1 protein. In addition, we observed a significant up-regulation of several miRNAs, such as miR-96, in hepatocytes with mitochondrial dysfunction. Using reporter gene assay we confirmed that miR-96 directly targeted to IRS-1 3'UTR. Furthermore, the overexpression of miR-96 in hepatocytes caused a substantial reduction in IRS-1 protein expression, and a consequent impairment in insulin signaling.

Conclusion We demonstrated that miR-96 was actively involved in the development of insulin resistance induced by mitochondrial dysfunction. These data provide novel insights into the molecular basis of insulin resistance, and implicate miRNA in the development of metabolic disease.

PE132 Insulin action & obesity

Hypothalamic vaspin/SERPIN12 mediates the anorexigenic action of leptinGil Myoung Kang^{1*}, Byung Soo Youn³, Ju Young Lee¹, Hyun Kyong Kim¹, Ji Hee Yu¹, Mi-Seon Shin², So Young Gil¹, Joong-Yeol Park², Ki-Up Lee², Min seon Kim²Asan Institute for Life Sciences¹, Department of Internal Medicine, University of Ulsan College of Medicine², Adipogen Inc., Incheon 406-840, Korea

Vaspin/SERPIN12 has been identified as a visceral adipose tissue-derived adipokine having glucose-lowering and insulin-sensitizing effects. Here we report that vaspin is also expressed in the hypothalamic nuclei, which are involved in body weight homeostasis. In addition, vaspin has potent weight-reducing effects when administered intracerebroventricularly in normal C57BL6 mice. These effects were mediated through a reduction in food intake and an enhancement in energy expenditure. Interestingly, leptin deficient ob/ob mice have reduced hypothalamic vaspin expression whereas leptin administration increased hypothalamic vaspin expression. Moreover, like leptin, vaspin activates hypothalamic Stat3 signaling pathways and regulates expression of appetite regulating neuropeptides, proopiomelanocortin, neuropeptide Y and agouti related protein. Conversely, reduced hypothalamic vaspin expression using small inhibitory RNA inhibited hypothalamic leptin signaling and its anorexigenic action, suggesting that vaspin is an anorexigenic molecule that constitutes hypothalamic leptin signaling pathway. Further investigation of the molecular mechanism of vaspin actions revealed that NMDA receptor-mediated calcium influx induced by vaspin activated Stat3 signaling cascades. Importantly, the central metabolic effects of vaspin were much reduced when serpin domain was mutated, indicating that serpin activity is important for central vaspin actions. In summary, we firstly describe vaspin as a novel anorexigenic peptide that conveys hypothalamic leptin actions.

PE133 Insulin action & obesity

The effects of growth hormone treatment on leptin, adiponectin and interleukin 1 β (IL1 β) changes in hypopituitarism patients

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Yonsei University Hospital

Objective Growth hormone deficiency (GHD) in adult life has been associated with increased central adiposity, decreased insulin sensitivity, dyslipidemia and increased risk of cardiovascular disease. GH therapy is associated with a reduction in fat mass and increase in lean mass in subjects with GH deficiency. The mechanisms of this action are unclear. To evaluate the effects of growth hormone replacement on adipocytokine levels and insulin resistance and changes in body fat content in adult-onset GHD patients.

Methods Fourteen patients (mean age 34.4 \pm 8.2 years) with adult-onset GHD received recombinant human GH for 12 weeks. Body composition with whole-body dual energy X-ray absorptiometry (Lunar Delphi, Hologic) and fasting serum and abdominal subcutaneous adipose tissue analyses were assessed at baseline and at the end of the study.

Results GH replacement did not affect body weight (60.9 \pm 3.0, 60.3 \pm 3.2 kg, P=.30) and BMI (23.1 \pm 1.0, 22.9 \pm 1.0 kg/m², P=.51), body fat mass (19.3 \pm 1.6, 18.4 \pm 1.8 kg, P=.21), and HOMA-IR (1.6 \pm 0.3, 1.9 \pm 0.4, P=.42). Yet, serum leptin concentration was distinctly reduced after GH (8.69 \pm 1.1, 6.46 \pm 1.0 ng/mL, P=.002). Also, GH changed the concentration of serum insulin-like growth factor -1 (IGF-1) (171.5 \pm 26.3, 350.3 \pm 37.4 ug/L, P=.0001), LDL-cholesterol (151.1 \pm 10.0, 119.2 \pm 6.1 mg/dL, P=.004), and adiponectin (6.81 \pm 1.2, 5.51 \pm 0.8 mg/L, P=.047). Moreover, abdominal subcutaneous adipose tissue interleukin 1 β (IL1 β) gene expressions changed (0.73 \pm 0.14, 2.37 \pm 0.70 ug/L, P=.022).

Conclusion This data indicate that short-term replacement of low-dose rhGH decreases the serum leptin and adiponectin concentration even without affecting body weight in adult-onset GHD patients. Conclusively, we can speculate that GH may improve body composition through interleukin 1 β (IL1 β) changes in human adipose tissues.

PE134 Insulin action & obesity

Exendin-4 directly ameliorates steatohepatitis by improvement of fat metabolism and insulin signalingIn-Kyung Jeong^{1*}, Sung Jig Lim², You-Cheol Hwang¹, Kyu Jeung Ahn¹, Ho Yeon Chung¹, Min-Kyung Chae³, Hyung-Joon Yoo⁴, Seung-Hyun Koh⁵, Myung-Joon Kim⁵, Suk Chon¹, Seungjoon Oh¹, Jeong-taek Woo¹, Sung Woon Kim¹, Jin-Woo Kim¹, Young Seol Kim¹

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Objective Nonalcoholic steatohepatitis is associated with insulin resistance. Exendin-4(Ex-4) is a GLP-1 analogue which stimulates insulin secretion and decreases insulin resistance. But the effect of Ex-4 on the insulin resistance is not clear. The aim of this study is to investigate the direct effect of Ex-4 on the insulin sensitivity of liver.

Methods HEP3B cell was treated with palmitate and oleate with or without Ex-4. Insulin signaling was measured by western blot. 16 week-old male OLETF rats and LETO rats were treated with daily I.P. injection of Ex-4 for 4 weeks and then retreated with Ex-4 for 3 weeks having a high fat diet. We measured food intake, body weight, plasma glucose, and insulin and performed IPGTT, ITT, histology, PCR and microarray of liver tissue in control(vehicle), Ex-4 group, and pair feeding group at 7 weeks after start of Ex-4 treatment.

Results GLP-1 receptor was expressed in HEP3B cell. Phosphorylation of Akt and Erk was blunted by palmitate and oleate, which was reversed by Ex-4. Food intake was significantly lower in Ex-4 group. Body weight was significantly lower in Ex-4 group than control and pair-feeding group. On IPGTT, plasma glucose level was not significantly different between three groups. But ITT showed that KITT(%/min) of Ex-4 group was significantly higher in both OLETF(control vs Ex-4=3.25 vs 3.83) and LETO (3.48 vs 4.82) rats than that of control. The glucose infusion rate(mg/kg/min) of Ex-4 group was significantly higher than that of control(146.4 vs 189.5). Steatohepatitis was improved in the Ex-4 group on the histology section. Microarray data showed that Stearoyl-Coenzyme A desaturase 1, hormone sensitive-lipase, alpha-methylacyl-CoA racemase was significantly down regulated in Ex-4 group.

Conclusion In conclusion, Ex-4 directly improved insulin sensitivity HEP3B cell line and steatohepatitis in obese diabetic rat model, Ex-4 directly ameliorates insulin resistance in liver.

PE135 Epidemiology & genetics

The usefulness of fat mass index to diagnose the metabolically un-healthy obese people

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Objective The body mass index (BMI) is the most popular tool for the evaluation of obesity, due to its simplicity and low cost. However, there were discrepancies in measurements of real adiposity and BMI. In this paper, we investigated the usefulness of the body fat mass/Ht² to predict the metabolic syndrome(Mets) in the overweight and obese people.

Methods We used The Fourth Korea National Health and Nutrition Examination Surveys (KNHANES IV) data (1368 men and 1922 women; over 19 years). Body fat mass were measured by DXA methods. We make Fat mass index (body fat mass/ body weight²; FMI) classification ranges along with corresponding BMI ranges for comparison.

Results Mets incidences were differed in BMI group. In overweight group (23 \leq BMI<25), Mets were 12% of men and 16% of women. And in obese group (BMI \geq 25), Mets were 42.4% of men and 50.2% of women. When FMI cut-off defined as FMI \geq 5 in men and FMI \geq 8 in women; Mets risks in overweight group were increased 3.181(CI: 3.159-3.203; p<0.001) in men and 3.557(CI: 3.528-3.586; p<0.001) in women and those in obesity group (BMI \geq 25) were increased 1.783(CI: 1.769-1.796; p<0.001) in men and 3.258(CI: 3.237-3.279; p<0.001) in women.

Conclusion In this study, Fat mass index were useful define the metabolic un-healthy population in overweight population (BMI>23) in Korea.

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