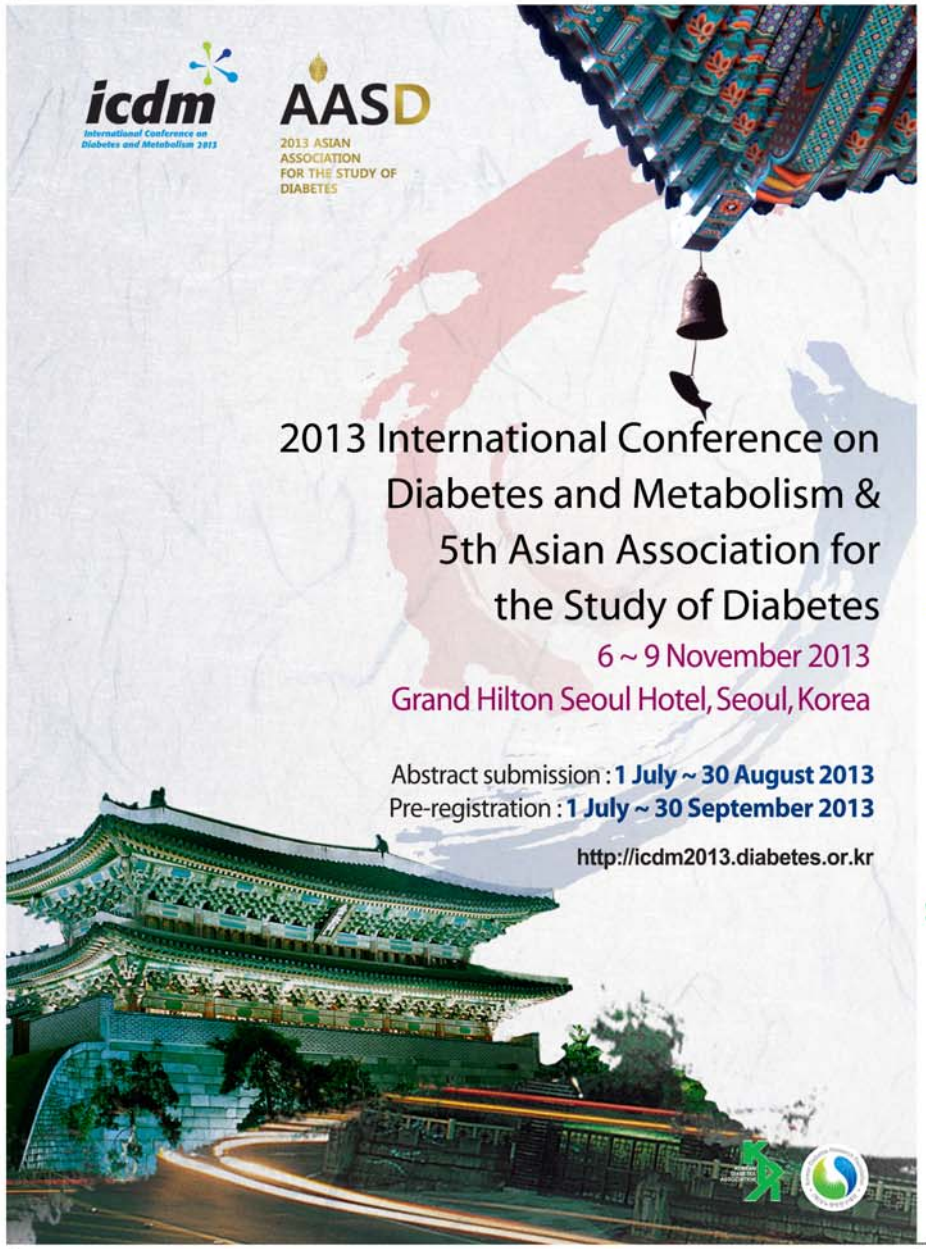

2012 International Conference on Diabetes and Metabolism

Korean Diabetes Association

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Abstract Book

icdm 2012

2012 International Conference on Diabetes and Metabolism

8~10 November 2012
Grand Hilton Seoul Hotel, Seoul, Korea

Plenary lectures

Symposia

icdm
International Conference on Diabetes and Metabolism 2012

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2012 International Conference on Diabetes and Metabolism

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Plenary lectures

Metabolically healthy obesity: role of mitochondrial function in adipocytes

Ki-Up Lee *(University of Ulsan, Korea)*

Autophagy and mitochondrial dysfunction in diabetic cardiomyopathy

E. Dale Abel *(University of Utah, USA)*

Symposia

S1 Diabetes education
S2 Clinical diabetes & therapeutics
S3 Obesity
S4 Islet biology & insulin secretion
S5 Self care
S6 Nutrition
S7 Epidemiology
S8 Insulin resistance
S9 Diabetic microvascular complications
S10 Current guidelines for diabetes management
S11 Genetics
S12 Physical activity
S13 Diabetic macrovascular complications
Professional section interest group
Again ADA 2012

Korean Diabetes Research Foundation

KOREAN DIABETES ASSOCIATION

Invitation

To diabetes researchers across the world

As representatives of Korean Diabetes Association, it is our pleasure to have the opportunity inviting you to the 2nd International Conference on Diabetes and Metabolism (ICDM), which will take place in Grand Hilton Seoul Hotel, Seoul, Korea, from November 8th to 10th, 2012.

ICDM 2011 was the first international academic symposia with Korean Diabetes Association as the main host. Approximately 1,400 participants across 20 countries have joined the conference.

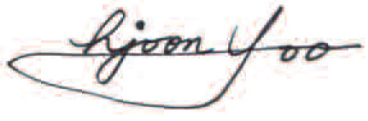
The ICDM 2012 will focus on a wide range of dynamic topics and controversial issues concerning insulin secretion & biology, insulin action & obesity, clinical diabetes & therapeutics, epidemiology & genetics, acute & chronic complication, and behavioral medicine & education.

This year, we are preparing the "Again ADA 2012" session, which will select several especially outstanding presentations from this year's ADA scientific session. This session is expected to leave big impact on much of the audience.

Once again, we would like to express our warmest welcome to you for joining the ICDM 2012. We hope you to experience and enjoy the unique and wonderful cultural attraction during your stay in Seoul.

We look forward to welcoming you to Seoul where you will have the opportunity to enjoy the beautiful scientific sessions in the wonderful cultural attentions.

Yours sincerely,



Hyung Joon Yoo, M.D., Ph.D
President
Korean Diabetes Association

Bong Yun Cha, M.D., Ph.D
Chairman, Board of Directors
Korean Diabetes Association

Timetable

	Emerald Hall, 3F	Convention Hall A, 4F	Convention Hall B, 4F	Convention Hall C, 4F	Diamond Hall, 3F
1st day (Thursday, 8 November 2012)					
14:00~16:00	Korean diabetes pregnancy study group	Diabetic vascular cell biology research meeting	New strategy for beta-cell replacement therapy	Korean Diabetes Association interest group on genetics	Current findings about metabolic syndrome and related disorders
16:00~16:30	Coffee break				
16:30~17:00	Sulwon lecture				
17:00~18:00	Satellite symposium 1, 2				
18:00~					Welcome reception
2nd day (Friday, 9 November 2012)					
07:30~08:30		Breakfast symposium 1	Breakfast symposium 2		
09:00~11:00	S1 Diabetes education (Korean)	S2 Clinical diabetes & therapeutics	S3 Obesity	S4 Islet biology & insulin secretion	
11:00~11:20	Coffee break				
11:20~11:30		Opening address			
11:30~12:20		Plenary lecture 1			
12:20~13:40	Luncheon symposium 4	Luncheon symposium 1	Luncheon symposium 2	Luncheon symposium 3	
13:40~14:40	S5 Self care (Korean)	Oral presentation 1	Oral presentation 2	Oral presentation 3	Again ADA 2012(1)
14:40~15:40		Oral presentation 4	Oral presentation 5	Oral presentation 6	
15:40~16:00	Coffee break				
16:00~18:00	S6 Nutrition (Korean)	S7 Epidemiology	S8 Insulin resistance	S9 Diabetic microvascular complications	Again ADA 2012(2)
18:00~	Dinner & art performance (Grand ballroom, Hotel 2F)				
3rd day (Saturday, 10 November 2012)					
07:30~08:30		Breakfast symposium 3	Breakfast symposium 4		
09:00~11:00	S10 Current guidelines for diabetes management (Korean)	S11 Genetics	S12 Physical activity	S13 Diabetic macrovascular complications	Again ADA 2012(3)
11:00~11:30	Coffee break				
11:30~12:20		Plenary lecture 2			
12:20~13:30		Luncheon symposium 5	Luncheon symposium 6	Luncheon symposium 7	
13:30~15:00	Oral presentation 7	Oral presentation 8	Oral presentation 9	Oral presentation 10	Again ADA 2012(4)

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Chair : Yong Soo Park, Soon Jib Yoo

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Friday 9 Nov. 14:40~15:40 / Convention Hall B, 4F

Oral Presentation 5
Chair : In Kyu Lee, Minho Shong

Insulin resistance & obesity I / 204

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Poster exhibition

Friday 9 Nov. 09:00~Saturday 10 Nov. 15:00 / Convention Center 3F & 4F Lobby

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PLENARY LECTURES

Ki-Up Lee

University of Ulsan, Korea
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➤Educational background & professional experience

1976-1980	College of Medicine, Seoul National University	M.D.
1984-1986	Graduate School, Seoul National University (Medical Science)	Ph.D.
1981-1984	Internal Medicine, Seoul National University Hospital	Resident
1984-1986	Endocrinology and Metabolism, Seoul National University Hospital	Clinical fellow
1986-1988	University of Calgary, Calgary, Canada	Research fellow
1989-present	Asan Medical Center, University of Ulsan College of Medicine	Instructor - professor

➤Research interests

Pathogenesis of diabetes and metabolic syndrome

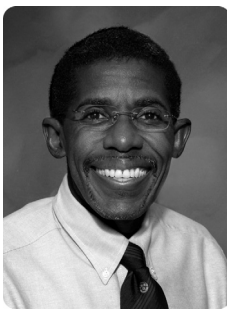
➤Brief list of publications

1. Koh EH, Lee WJ, Lee SA, Kim EH, Cho EH, Jeong E, Kim DW, Kim MS, Park JY, Park KG, Lee HJ, Lee IK, Lim S, Jang HC, Lee KH, Lee KU. Effects of alpha-lipoic acid on body weight in obese subjects. Am J Med. 2011 124(1):85.e1-8.
2. 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(2):290-7.
3. Koh EH, Kim M, Ranjan KC, Kim HS, 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 298(4):E846-53.
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. 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.
6. 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.
7. Lee KU, Lee IK, Han J, Song DK, Kim YM, Song HS, Kim HS, Lee WJ, Koh EH, Song KH, Han SM, Kim MS, Park IS, Park JY: Effects of Recombinant Adenovirus-Mediated Uncoupling Protein 2 Overexpression on Endothelial Function and Apoptosis. Circ Res. 2005; 96:1200-1207.
8. Lee WJ, Lee IK, Kim HS, Kim YM, Koh EH, Won JC, Han SM, Kim MS, Jo I, Oh GT, Park IS, Youn JH, Park SW, Lee KU, Park JY: Alpha-lipoic acid prevents endothelial dysfunction in obese rats via activation of AMP-activated protein kinase. Arterioscler Thromb Vasc Biol 2005 25:2488-94.
9. Kim MS, Park JY, Namkoong C, Jang PG, Ryu JW, Song HS, Yun JY, Namgoong IS, Ha J, Park IS, Lee IK, Viollet B, Youn JH, Lee HK, Lee KU. Anti-obesity effects of alpha-lipoic acid mediated by suppression of hypothalamic AMP-activated protein kinase. Nat Med. 2004;10(7):727-33.
10. Koh EH, Kim MS, Park JY, Kim HS, Youn JY, Park HS, Youn JH, Lee KU. Peroxisome proliferator-activated receptor (PPAR)-alpha activation prevents diabetes in OLETF rats: comparison with PPAR-gamma activation. Diabetes. 2003 Sep;52(9):2331-7.

Metabolically healthy obesity: role of mitochondrial function in adipocytes

Ki-Up Lee
University of Ulsan, Korea

Obesity is the most important risk factor for metabolic and cardiovascular disorders. The majority of individuals with obesity develop insulin resistance, type 2 diabetes, dyslipidemia, fatty liver, hypertension and cardiovascular disease. However, approximately 10-30% of obese individuals are considered metabolically healthy, even though there is no consensus regarding the diagnostic criteria of "metabolically healthy obesity". Possible causes of the difference between unhealthy and healthy obesity include fat distribution (visceral vs. subcutaneous), ectopic fat accumulation, inflammatory response in adipose tissue, and alteration in free fatty acid trafficking. Adiponectin is one of the proteins secreted by adipocytes. Plasma adiponectin levels are paradoxically reduced in obese subjects, but high plasma adiponectin levels are associated with metabolically healthy obese phenotype. Recently, we have conducted a series of studies regarding why plasma adiponectin levels are reduced in obese subjects. We found that mitochondrial function is crucial for adiponectin synthesis in adipocytes, and that mitochondrial dysfunction in adipose tissue can explain decreased plasma adiponectin levels in obesity. Adipocytes undergo maturation by two steps: differentiation and hypertrophy. During the early stage of maturation (diffe rentiation), adipocytes have high levels of metabolic activities and increased fuel consumption. These young, healthy adipocytes are relatively small in size and produce much adiponectin. Adiponectin is the most abundant protein in adipocytes, and adiponectin synthesis could be a major energy-consuming process in adipocytes. Thus increased mitochondrial function is critically required to match increased energy demand for adiponectin synthesis. By contrast, mitochondrial dysfunction leads to decreased fatty acid oxidation and increased triglyceride accumulation, making inactive, large (hypertrophied) adipocytes that cannot produce much adiponectin. Instead, these unhealthy adipocytes produce various inflammatory adipocytokines to promote systemic inflammation. I will present our recent data on the role of mitochondrial function in adiponectin synthesis and its implications in the genesis of metabolically healthy or unhealthy obesity.



E. Dale Abel

University of Utah, USA
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➤Educational background & professional experience

1985	Faculty of Medical Sciences, University of the West Indies, Kingston, Jamaica	MB. BS
1991	Clinical Medicine Faculty, University of Oxford. Oxford United Kingdom	D. Phil
Present	University of Utah , USA	Chief of the division of endocrinology, Metabolism and diabetes

➤Research interests

1. Pathophysiology of cardiovascular complications of diabetes.
2. Role of mitochondrial dysfunction in the pathophysiology of insulin resistance and obesity

➤Brief list of publications

1. Boudina S, Sena S, Sloan C, Tebbi A, Han YH, O'Neill BT, Cooksey RC, Jones D, McClain DA, Abel ED. Early Mitochondrial Adaptations in Skeletal Muscle to Diet-Induced Obesity are Strain Dependent and Determine Oxidative Stress and Energy Expenditure but not Insulin Sensitivity. Endocrinology. 2012: In Press.
2. Zhang QJ, Holland WL, Wilson L, Tanner JM, Kearns D, Cahoon JM, Dix P, Losee J, Duncan B, Gale D, Kowalski CA, Deeter N, Nichols A, Michole Deesing M, Arrant C, Ruan T, Boehme C, McCamey DR, Rou J, Ambal K, Narra KK, Summers SA, Abel ED, Symons JD. Ceramide mediates vascular dysfunction in diet-induced obesity by PP2A-mediated dephosphorylation of the eNOS-Akt complex. Diabetes. 2012. In Press.
3. Bugger H, Riehle C, Jaishy B, Wende AR, Tuinei J, Chen D, Soto J, Pires KM, Boudina S, Theobald HA, Luptak I, Wayment B, Wang X, Sheldon E. Litwin SE, Weimer BC, Abel ED. Genetic Loss of Insulin Receptors Worsens Cardiac Efficiency in Diabetes. J Mol Cell Cardiol. 2012: 52:1019-26.
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6. Shimizu I, Minamino T, Toko H, Okada S, Ikeda H, Yasuda N, Tateno K, Moriya J, Yokoyama M 1, Nojima A, Koh GY, Akazawa H, Shiojima I, Kahn CR, Abel ED, Komuro I. Excessive cardiac insulin signaling exacerbates systolic dysfunction induced by pressure overload. J. Clin Invest. 2010: 120:1506-14.
7. Bugger H, Chen D, Riehle C, Soto J, Theobald HA, Hu XX, Ganesan B, Weimer BC, Abel ED. Tissue-Specific Remodeling of the Mitochondrial Proteome in Type 1 Diabetic Akita Mice. Diabetes. 2009 58:1986-97.
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10. Boudina S, Bugger H, Sena S, O'Neill B T, Zaha VG, Ilkun O, Wright JJ, Mazumder PK, Palfreyman E, Tidwell TJ, Theobald HA, Khalimonchuk O, Wayment B, Sheng X, Rodnick KJ, Centini R, Chen D, Litwin SE, Weimer BC, Abel ED. Contribution of impaired insulin signaling to mitochondrial dysfunction and oxidative stress in the heart. Circulation 2009: 119:1272-1283.

Autophagy and mitochondrial dysfunction in diabetic cardiomyopathy

E. Dale Abel
University of Utah, USA

Diabetes increases the risk for heart failure, via mechanisms that are incompletely understood. We have examined temporal changes in myocardial insulin signaling in the heart in the various rodent models of diabetes. Insulin signaling is an important regulator of myocardial autophagy. The presentation will review recent findings describing specific mechanisms by which insulin signaling regulates autophagy in cardiac muscle, and describe the implications of these changes in the pathophysiology of diabetic cardiomyopathy. The presentation will also review novel mechanisms by which increased myocardial lipid uptake impairs autophagosome turnover. The presentation will review the implication of these phenomena in the pathogenesis of mitochondria dysfunction that contributes to the pathogenesis of diabetic cardiomyopathy.

SYMPOSIA

Hyung Joon Yoo

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➤Educational background & professional experience

1977	Graduated from College of Medicine, Seoul National University	
1977-1981	Division of Endocrine & Metabolism, Department of Internal Medicine, Seoul National Univ. Hospital	Internship & residency
1985	Seoul National University	Ph. D.
1985-1986	Hagedorn Diabetes Research Center, Copenhagen, Denmark	Research fellow
1995-1996	Department of Geriatrics, Faculty of Medicine, Tokyo University, Japan	Research professor
2002-2004	Elderly Diabetes Investigation Team, KDA	Leader
2007-2009	The Korean Geriatrics Society	Chairman
2008-2010	The Korean Geriatrics Association (Foundation)	Chairman
2008-2010	The Federation of Korean Gerontological Societies	President
2010-present	Geriatric syndrome Research Committee	Leader
2011-present	The Organizing Committee for The 20th IAGG Congress of Gerontology and Geriatrics Seoul 2013 Korean Diabetes Association	Vice chairman, Chairman of, scientific committee president

➤Research interests

Elderly diabetes mellitus, vascular aging in diabetes

➤Brief list of publications

1. Yoo HJ: Appropriate public action plan for elderly diabetic patients in Korea. Proceedings of 8th IDFWPR Congress p. 92, Busan Bexco, 2010.10.17-20. (WPR-Symposium)
2. Kim CS, Park SY, Kang JG, Lee SJ, Ihm SH, Choi MG, Yoo HJ : Insulin dose titration system in diabetes patients using a short messaging service automatically produced by a knowledge matrix. Diabetes Technol Ther. 2010 Aug;12(8):663-9.
3. Noh J-H, Cho YJ, Nam HW, Kim JH, Kim DJ, Yoo HS, Kwon YW, Woo MH, Cho JW, Hong MH, Yoo JH, Gu MJ, Kim SA, An KE, Jang SM, Kim EK, Yoo HJ: Web-based Comprehensive Information System for Self-management of Diabetes Mellitus. Diabetes Technology & Therapeutics 2010;12(5): 333-337.
4. Yoo HJ: Ethnogeriatrics - introduction. The J of Nutrition, Health & Aging (JNHA) 13 (Suuppl. 1):S117, 19th IAGG, Paris, 2009(SB8-210-1).
5. Lee SJ, Kang JG, Ryu OH, Kim CS, Ihm SH, Choi MG, Yoo HJ, Kim DS, Kim TW: Effects of alpha-lipoic acid on transforming growth factor beta1-p38 mitogen-activated protein kinase-fibronectin pathway in diabetic nephropathy. Metabolism. 2009 May;58(5):616-23.
6. H. S. Park, C. Y. Park, S. W. Oh and H. J. Yoo: National Prevalence of Obesity Prevalence of obesity and metabolic syndrome in Korean adults. Obesity reviews (2008) 9, 104–107.
7. Cho GY, Jeong IK, Kim SH, Park WJ, Oh DJ, Yoo HJ: Effect of growth hormone on cardiac contractility in patients with adult onset growth hormone deficiency. Am J Cardiol 2007 Sep 15;100(6):1035-9.
8. Lee BW, Ihm S-H, Choi MG, Yoo HJ: The comparison of cystatin C and creatinine as an accurate serum marker in the prediction of type 2 diabetic nephropathy. DRCP 78(2007):428-434.
9. Lee SY, Park HS, Kim DJ, Han JH, Kim MS, Cho GJ, Kim DY, Kwon HS, Kim SR, Lee CB, Oh SJ, Park CY, Yoo HJ: Appropriate waist circumference cutoff points for central obesity as main component of the new International Diabetes Federation definition in Korean adults. Diabetes Research and Clinical Practice 75:72-80, 2007.
10. Noh JH, Kim SK, Cho YJ, Nam HU, Kim IJ, Jeong IK, Choi MG, Yoo HJ, Ahn YH, Bae HY, Jang HC: Current status of diabetes management in elderly Koreans with diabetes. Diabetes Res Clin Pract. 77:71-75, 2007.

Geriatric secrets

Hyung Joon Yoo
Hallym University, Korea

The body changes in aging, and many organs and organ systems become to carry out intended functions. However, clinically pathologic problems generally result from disease, not normal aging. Geriatric disease can be treated or managed.

Physiologic changes in most organ systems contributed to the diminished reserve observed in the elderly. And so older people have limited physiologic reserve and they often tolerate illness or stimuli to homeostasis poorly.

Geriatric patients have multiple chronic diseases, along with all the sequelae and treatments that chronic conditions cause. In geriatrics there is rarely one diagnosis; the average is four. Multiple chronic diseases interact, adding ambiguity and complications. As a result, geriatric clinical situations are almost always challenging.

Geriatric patients are frail and often have social problems in addition to complex pathology. Geriatrics is inherently interdisciplinary to provide comprehensive care. The hallmarks of a well-functioning cooperative team are flexibility, mutual respect, and the ability to accomplish the goals of geriatric care.

Geriatric Syndromes are groups of specific signs and symptoms that occur more often in the elderly and can impact patient morbidity and mortality. Normal aging changes, multiple co-morbidities, and adverse effects of therapeutic interventions contribute to the development of geriatric syndromes. With an enhanced knowledge of geriatric syndromes, assessment, care, and management of elderly patients can be improved and age-specific complications may be decreased. There was a strong pathophysiological reason to believe that diabetics might be at greater risk for the syndrome. Care of the elderly person with diabetes cannot be restricted to the management of hyperglycemia, associated risk factors, and specific diabetic complications. An integrated approach must assess and manage the presence of geriatric syndromes.

Geriatrics is a family-oriented specialty. The geriatrician relies on an older person's family to implement the treatment or management in many ways to function as a member of the team. While a geriatrician's interactions with family members are complex, four dimensions seem universal: emotional support, decision making, provision of care, and education. Family members interact with geriatricians in two other ways: as surrogate decision makers and as potential patients. Education is fundamental in the interaction. The best geriatric care can be accomplished through open communication between the family and geriatric team.

Hak Chul Jang

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➤Educational background & professional experience

1977-1983	Seoul National University College of Medicine	M.D.
1983-1984	Seoul National University Hospital	Intern
1987-1990	Seoul National University Hospital, Internal Medicine	Resident
1989-1991	Seoul National University	M.S.
1991-1994	Seoul National University	Ph.D.
1997-2003	Sungkyunkwan University	Assistant professor
2003-present	Seoul National University	Professor

➤Research interests

Clinical epidemiological study of elderly diabetes / gestational diabetes mellitus
Insulin resistance and beta cell function in high risk population
Sarcopenia and sarcopenic obesity

➤Brief list of publications

1. Kim KE, Jang SN, Lim S, Park YJ, Paik NJ, Kim KW, Jang HC, Lim JY. Relationship between muscle mass and physical performance: is it the same in older adults with weak muscle strength? Age Ageing. 2012 Aug 21.
2. Kim JH, Choi SH, Lim S, Lim JY, Kim KW, Park KS, Shin CS, Jang HC. Thigh muscle attenuation measured by computed tomography was associated with the risk of low bone density in community-dwelling elderly population. Clin Endocrinol (Oxf). 2012 Aug 18.
3. Lee Y, Shin H, Vassy JL, Kim JT, Cho SI, Kang SM, Choi SH, Kim KW, Park KS, Jang HC, Lim S. Comparison of regional body composition and its relation with cardiometabolic risk between BMI-matched young and old subjects. Atherosclerosis. 2012 Jul 16.
4. Kwak SH, Kim SH, Cho YM, Go MJ, Cho YS, Choi SH, Moon MK, Jung HS, Shin HD, Kang HM, Cho NH, Lee IK, Kim SY, Han BG, Jang HC, Park KS. A Genome-Wide Association Study of Gestational Diabetes Mellitus in Korean Women. Diabetes. 2012 Feb;61(2):531-41.
5. Lim S, Shin H, Kim MJ, Ahn HY, Kang SM, Yoon JW, Choi SH, Kim KW, Song JH, Choi SI, Chun EJ, Shin CS, Park KS, Jang HC. Vitamin D inadequacy is associated with significant coronary artery stenosis in a community-based elderly cohort: the Korean Longitudinal Study on Health and Aging. J Clin Endocrinol Metab. 2012 Jan;97(1):169-78.
6. Lim S, Kim JH, Yoon JW, Kang SM, Choi SH, Park YJ, Kim KW, Cho NH, Shin H, Park KS, Jang HC. Optimal cut points of waist circumference (WC) and visceral fat area (VFA) predicting for metabolic syndrome (MetS) in elderly population in the Korean Longitudinal Study on Health and Aging (KLoSHA). Arch Gerontol Geriatr. 2012 Mar;54(2):e29-34.

Geriatric syndrome and elderly diabetes

Hak Chul Jang
Seoul National University, Korea

"Geriatric syndrome" refers to clinical conditions commonly seen in older adults that do not fit into discrete disease categories. Many of the common conditions cared for by geriatricians, including delirium, falls, frailty, dizziness, syncope and urinary incontinence, are classified as geriatric syndromes. However, the concept of the geriatric syndrome is still poorly defined.

Geriatric syndromes share many common features. They are highly prevalent in older adults, especially frail people. Their effect on quality of life and disability is substantial. Multiple underlying factors, involving multiple organ systems, tend to contribute to geriatric syndromes.

Diabetes is common in older adults and the prevalence is estimated at least 20% of population aged over 65 years old in Korea. Diabetes is considered to accelerate ageing, functional decline, and atherosclerotic disease compared to non-diabetic adults. In addition, the development of micro- and macro-vascular complications, dependent on the duration of diabetes are common in older adults with diabetes. So the older adults with diabetes have increased risk of functional disability and frailty. The geriatric syndrome may lead older adults with diabetes to more frail state, loss of independence and poor quality of life. Importantly, this geriatric syndrome might be main barriers in the diabetes treatment and care of older adults.

Comprehensive assessment for geriatric syndrome should be performed as an initial examination of older adults with diabetes. Assessment of family or social support, living accommodation and surrounding is also critical. Because of multifactorial and shared risk factors in geriatric syndrome, diabetic patients with geriatric syndrome should be treated with a multidisciplinary concentric strategy including supervised exercise therapy, psychological support, social support, and good glycemic control without hypoglycemia. A unified approach to prevention of this syndrome is also important.

Hong Woo Nam

National Medical Center, Korea
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➤Educational background & professional experience

1988	Diploma in Medical College, Chonnam National University 1988	M.D.
1992	Board of Internal Medicine	
Present	National Medical Center	Director of endocrinology

➤Research interests

Diabetes in the elderly
Diabetes education

➤Brief list of publications

1. Boudina S, Sena S, Sloan C, Tebbi A, Han YH, O'Neill BT, Cooksey RC, Jones D, McClain DA, Abel ED. Early Mitochondrial Adaptations in Skeletal Muscle to Diet-Induced Obesity are Strain Dependent and Determine Oxidative Stress and Energy Expenditure but not Insulin Sensitivity. Endocrinology. 2012: In Press.
2. Zhang QJ, Holland WL, Wilson L, Tanner JM, Kearns D, Cahoon JM, Dix P, Losee J, Duncan B, Gale D, Kowalski CA, Deeter N, Nichols A, Michole Deesing M, Arrant C, Ruan T, Boehme C, McCamey DR, Rou J, Ambal K, Narra KK, Summers SA, Abel ED, Symons JD. Ceramide mediates vascular dysfunction in diet-induced obesity by PP2A-mediated dephosphorylation of the eNOS-Akt complex. Diabetes. 2012. In Press.
3. Bugger H, Riehle C, Jaishy B, Wende AR, Tuinei J, Chen D, Soto J, Pires KM, Boudina S, Theobald HA, Luptak I, Wayment B, Wang X, Sheldon E. Litwin SE, Weimer BC, Abel ED. Genetic Loss of Insulin Receptors Worsens Cardiac Efficiency in Diabetes. J Mol Cell Cardiol. 2012: 52:1019-26.
4. Riehle C, Wende AR, Zaha VG, Pires KM, Wayment B, Olsen C, Bugger H, Buchanan J, Wang X, Moura AB, Doenst T, Medina-Gomez G, Litwin SE, Lelliott CJ, Vidal-Puig A, Abel ED. PGC-1β Deficiency Accelerates the Transition to Heart Failure in Pressure Overload Hypertrophy. Circulation Research. 2011: 109:783-93.
5. Sloan C, Tuinei J, Nemetz K, Frandsen J, Soto J, Wride N, Sempokuya T, Alegria L, Bugger H, Abel ED. Central leptin signaling is required to normalize myocardial fatty acid oxidation rates in caloric restricted ob/ob mice. Diabetes. 2011: 60:1424-34.
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Diabetes in old age

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Age is the single most important influencing the prevalence of diabetes. Glucose disposal is progressively impaired with age. Postprandial plasma glucose levels increased 15mg/dL per decade and fasting plasma glucose levels increased 1-2mg/dL per decade. There seems to be a disproportionate increase over the age of 30 year. Diabetes is already common in elderly Koreans. The prevalence of diabetes is approximately 30%.

The most common type of diabetes in the elderly is type 2. There are some difference in type 2 diabetes presenting. A lean elderly diabetic patient predominantly exhibits deficits in insulin secretion; the obese elderly diabetic patient often has insulin resistance.

The classic symptoms of type 2 diabetes may not be present in an elderly persons. Presentation may be with nonspecific symptoms, complications such as myocardial infarction, cerebrovascular accident, or hyperosmolar non-ketotic state or coma. Elderly patients with diabetes are more likely to have other comorbidity conditions, cognitive impairment and depression. Compared with younger subjects the elderly are also more likely to be dependent, socially isolated and taking multiple medications. Hypoglycemia is the most common therapeutic complication of diabetes mellitus and especially in elderly diabetes patient with diminished cardiac and cerebral circulation can cause serious tissue damage. The risk of severe hypoglycemia increases with age, due to multiple factors, e.g. impaired secretion of glucagon, autonomic response, hypoglycemia awareness. These factors should be born in mind, and efforts made to reduce the risk of hypoglycemia, when selecting therapeutic agents for diabetic patients in old age.

It is important in elderly diabetic patient that treatment goals be clearly defined. The quality of life must be taken into consideration. Age, with its physiologic deterioration and change in nutritional status, makes the elderly diabetic patient different to manage.

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➤Educational background & professional experience

1987	Collage of nursing, Kyung hee University	Nursing
2005	Graduate School of Public Administration Kyung hee University	Public administration
2004-present	Head Nurse in Department of Internal Medicine, Inje university seoul paik hospital	
2003-present	Cyber Education Instructor, Korean Nurse Association	
2010	Senior Advisor in Korean Association of Diabetes Nurse Educators	
2011-present	Member of research committee in Korea Institute for Healthcare Accreditation	
2012-present	Member of Education committee in Korea Diabetes Association	

➤Research interests

Education

➤Brief list of publications

1. A Study of Knowledge and Diffusion of Knowledge for Nursing Care of Diabetes Mellitus among Clinical Nurses.2009.
2. A Study on the Behavior of Insulin Injection in Diabetic Patients.2009.
3. A Study on Effects and Their Continuity of the Self Regulation Education Program in Patients with Type 2 Diabetes.2009.
4. A Study on the condition of the diabetic patient' s taking medications.2007.
5. A Study of diabetic patient's Sexual Dysfunction in Korean adults males.2005.

Education of older persons with diabetes

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In the early 1900s, Joslin had argued the importance of education on diabetes patients for a thorough control of the disease; the WHO states "diabetes education is the groundwork for curing diabetes and is crucial for patients' smooth social lives."

Education on diabetes is to make the patient aware correctly about the disease so that he or she could utilize the knowledge, and ultimately put the knowledge into practice.

The risk of cognitive and physical impairment increases with age, these changes may interfere with diabetes management if not assessed and addressed.

People of older adults with diabetes needs to have an accurate diagnosis and a diabetes treatment plan tailored to their specific situation that include DSME.

DSME for older persons with diabetes should consider the individual's life expectancy, functional status, and the presence of cognitive changes as well as the individual's preferred learning style, language, literacy, and health literacy. DSME for older persons needs to be individualized, simplified, and conducted in a stepwise manner.

In 2009 AADE suggested "The AADE7TM Self-Care Behaviors" that should be necessarily considered in educating and caring for older person with diabetes. It's Healthy Eating, Being Active, Monitoring, Taking Medication, Problem Solving, Reducing Risks, Healthy Coping.

The AADE7TM Self-Care Behaviors need to be considered when developing DSME treatment plans and goals to address clinical, educational, and psychosocial needs. The AADE7TM Self-Care Behaviors providers a framework for developing DSME that is relevant for older adults.

The diabetes educator helps older persons with diabetes set appropriate goals, learn skills, and acquire knowledge about their disease. It is important to strengthen the self-therapy methods to meet the older adults needs. And diabetic educators also educate care providers, homecare aides, and institution staff about the AADE7TM Self-Care Behaviors and their relevance to older persons with diabetes.

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➤Educational background & professional experience

1984-1990	Kyung Hee University, Seoul, Korea	M.D.
1995-2001	Kyung Hee University, Seoul, Korea	Ph.D.
1998-2001	Kyung Hee Univ. Hospital, Seoul, Korea	Fellow
2001-2003	Department of Pharmaceutics, Univ. of Utah	Research fellow
2003-2007	Kyung Hee Univ. Hospital, Seoul, Korea	Assistant professor
2007-2012	Kyung Hee Univ. Hospital, Seoul, Korea	Associate professor
2012-present	Kyung Hee Univ. Hospital, Seoul, Korea	Professor

➤Research interests

Therapeutics for diabetes, GLP-1

➤Brief list of publications

1. Yun Jung Lee, Heeyeon Lee, Sun Ha Jee, Seong Su Lee, Sung Rae Kim, Seon Mee Kim, Myung Won Lee, Chang Beom Lee, Seungjoon Oh. Serum osteocalcin is inversely associated with adipocyte specific fatty acid binding protein in the Korean metabolic syndrome research initiatives. Diabetes Care e90, 2010.
2. The ORIGIN Trial Investigators. Rationale, design, and baseline characteristics for a large international trial of cardiovascular disease prevention in people with dysglycemia: The ORIGIN Trial (Outcome Reduction with an Initial Glargine Intervention). Am Heart J 155:26-32, 2008.
3. Sharma SK, Al-Mustafa M, Oh SJ, Azar ST, Shestakova M, Guler S, Vaz JA. Biphasic insulin aspart 30 treatment in patients with type 2 diabetes poorly controlled on prior diabetes treatment: results from the PRESENT study. Current Medical Research and Opinion 24:645-52, 2008.
4. Choi Y-R, Chae SY, Ahn C-H, Lee M, Oh S, Byun Y, Rhee BD, Ko KS. Development of polymeric gene delivery carriers: PEGylated copolymers of L-lysine and L-phenylalanine. J Drug Tageting 15(6):391-8, 2007.
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• S2-1 •

Glucagon receptor antagonists

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Glucagon is composed of 29 amino acids and processed from proglucagon by PC2 in pancreatic α -cells. Through its effect on hepatic glucose production, glucagon plays a crucial role in the regulation of glucose homeostasis. In patients with type 2 diabetes, abnormal regulation of glucagon secretion has been implicated in the development of fasting and postprandial hyperglycemia. Glucagon excess is an important pathogenesis in diabetes, thus glucagon antagonist is a new therapeutic candidate for diabetes.

Approaches to inhibit glucagon action include peptide antagonists, non-peptidyl orally active antagonists and monoclonal antibodies to glucagon or the glucagon receptor (GCGR). Among the therapeutic candidate of GCGR, only a few have been tested in humans. Considering the critical role of glucagon in glucose homeostasis, effective and safe GCGR blockade opens a new way to treat diabetes. However, GCGR blockade may predispose hypoglycemia and may interfere with recovery from hypoglycemia by blocking glucagon. In this lecture, I will review focuses on the mechanism of action, safety, and effect of glucagon antagonists in the treatment of type 2 diabetes.

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➤Educational background & professional experience

1982-1988	Yonsei University College of Medicine	M.D., M.S.
1992-1995	Yonsei University College of Medicine, Graduate School	B.S.
1995-1998	Yonsei University College of Medicine, Graduate School	Ph.D.
1998-2000	University of California San Diego, VA Hospital	Post-doc
2000-present	Yonsei University College of Medicine	Professor

➤Research interests

Insulin resistance, pathogenesis of type 2 diabetes
Energy homeostasis, lipid metabolism
PPAR related topics

➤Brief list of publications

1. 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. Int J Neuropsychopharm.
2. Up-regulation of hepatic low-density lipoprotein receptor-related protein 1: A possible novel mechanism of anti-atherogenic activity of HMG-CoA reductase inhibitor. Metabolism 60:930-940, 2011.
3. Fat redistribution preferentially reflects the anti-inflammatory benefits of pioglitazone treatment. Metabolism 60: 165-172, 2011.
4. Retinol-binding protein-4 is associated with endothelial dysfunction in adults with newly diagnosed type 2 diabetes mellitus. Atherosclerosis 204:23-5, 2009.
5. Rosiglitazone and fenofibrate improve insulin sensitivity of pre-diabetic OLETF rats reducing malonyl-CoA levels in the liver and skeletal muscle. Life Science 84:688-695, 2009 (as co-corresponding author).
6. Effect of ABCA1 variant on atherogenic dyslipidemia in patients with type 2 diabetes treated with rosiglitazone. Diabetic Med 26:577-581, 2009.

• S2-2 •

Peroxisome proliferator-activated receptor α/γ (PPAR-α/γ) dual agonists

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Type 2 diabetes is characterized by a failure on the part of the pancreatic β-cell to compensate sufficiently for the defect in insulin action in insulin-resistant individuals. Insulin resistance is a major determinant for various conditions such as type 2 diabetes, obesity, metabolic syndrome, atherosclerotic diseases, and etc. With lifestyle modification, therapeutic intervention should be done to improve insulin sensitivity in most insulin resistant person.

Thiazolidinediones (TZDs) are oral antihyperglycemic agents that reduce insulin resistance in peripheral tissues and decrease hepatic glucose production. TZDs are potent, synthetic ligands for peroxisome proliferator-activated receptor gamma (PPAR-γ), which mediates physiologic responses by altering the transcription of genes that regulate glucose and lipid metabolism. TZDs provide many benefits to patients with type 2 diabetes by improving glycemic control and insulin sensitivity, thereby having the potential to decrease the risk of cardiovascular disease associated with insulin resistance. TZDs are known to increase HDL-C concentrations, LDL particle size, and LDL cholesterol resistance to oxidation. In addition, TZDs decrease intima-media thickness and prevent restenosis after coronary stent implantations. However, some studies have reported the unwanted effects of TZDs on the levels of total cholesterol and LDL-C concentrations and also on body weight. Recently, pure PPAR-γ agonist such as rosiglitazone was withdrawn from the market due to several reasons. Another TZD such as pioglitazone is known to have additional effect of PPAR-α agonist and have additional benefit for atherosclerotic dyslipidemia. Several years ago, muraglitazar, a newly developed PPAR-α/γ co-agonist was also withdrawn due to serious side effects. Recently, another new PPAR-α/γ co-agonist, aliglitazar is under clinical inverstigation.

Until recently, TZDs are the unique class of drugs to improve insulin resistance and have long-term results. Unfortunately, long-term safety issues are under debate now. Clinically, PPAR-γ activation for insulin-resistant individuals is still very important. In the near future, we hope that new/safe PPAR modulator or PPAR-α/γ co-agonists are available to treat type 2 diabetes.

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➤Educational background & professional experience

1996	Toyama Medical & Pharmaceutical University	M.D.
2000-2004	In Biological Information Science, Shiga University of Medical Science	Ph.D.
1996	Shiga University of Medical Science, Internal Medicine	Resident
1997	Otsu Red Cross Hospital, Internal Medicine	Resident
1999	Shiga Social Insurance Hospital, Endocrinology, etabolism and Nephrology	Staff physician
2004	Juntendo University, Nephrology and Hypertension	An assistant professor
2004	Nagahama city Hospital, Endocrinology, Metabolism and Nephrology	Physician in chief
2006	Kanazawa Medical University, Endocrinology and Metabolism	An assistant professor
2008-2010	Harvard university, Joslin Diabetes Center (Dr. King Lab.)	Research fellow
2010-present	Kanazawa Medical University, Diabetology and Endocrinology	Senior assistant professor

➤Research interests

SIRT1 as the therapeutic target for type2 diabetes
The molecular mechanisms of diabetic nephropathy

➤Brief list of publications

1. Mima A, Kitada M, Geraldes P, Li Q, Matsumoto M, Mizutani K, Qi W, Li C, Leitges M, Rask-Madsen C, King GL. Glomerular VEGF resistance induced by PKCδ/SHP-1 activation and contribution to diabetic nephropathy. FASEB J. 2012 Apr 12.
2. Tanaka Y, Kume S, Kitada M, Kanasaki K, Uzu T, Maegawa H, and Koya D: Autophagy as a Therapeutic Target in Diabetic Nephropathy. Exp Diabetes Res, 2012, 2012;628978.
3. Kanasaki M, Nagai T, Kitada M, Koya D, Kanasaki K: Elevation of the antifibrotic peptide N-acetyl-seryl-aspartyl-lysyl-proline: a blood pressure-independent beneficial effect of angiotensin I-converting enzyme inhibitors. Fibrogenesis Tissure Repair.2011, 30; 4-25.
4. Kitada M, Takeda A, Nagai T, Ito H, Kanasaki K, and Koya D: Dietary restriction ameliorates diabetic nephropathy through anti-inflammatory effects and regulation of the autophagy via restoration of Sirt1 in Diabetic Wistar fatty (fa/fa) rats, a model of type 2 diabetes. Exp Diabetes Res 2011, 2011;908185.
5. Atsumi H, Kitada M, Kanasaki K, Koya D: Reversal of redox-dependent inhibition of diacylglycerol kinase by antioxidants in mesangial cells exposed to high glucose. Molecular Medicine Reports 2011, 4: 923-927.
6. Kitada M, Kume S, Imaizumi N, Koya D: Resveratrol improves oxidative stress and protects against diabetic nephropathy through normalization of Mn-SOD dysfunction in AMPK/SIRT1-independent pathway. Diabetes 2011, 60(2):634-643.
7. Mima A, Ohshiro Y, Kitada M, Matsumoto M, Geraldes P, Li C, Li Q, White GS, Cahill C, Rask-Madsen C et al: Glomerular-specific protein kinase C-beta-induced insulin receptor substrate-1 dysfunction and insulin resistance in rat models of diabetes and obesity. Kidney Int 2011.
8. Kitada M, Zhang Z, Mima A, King GL. Molecular mechanisms of diabetic vascular complications. J Diabetes Invest. 2010; 1:77-89.
9. Koya D, Hayashi K, Kitada M, Kashiwagi A, Kikkawa R, Haneda M. Effects of antioxidants in diabetes-induced oxidative stress in the glomeruli of diabetic rats.J Am Soc Nephrol. 2003 Aug; 14(8 Suppl 3):S250-3.
10. Kitada M, Koya D, Sugimoto T, Isono M, Araki S, Kashiwagi A, Haneda M. Translocation of glomerular p47phox and p67phox by protein kinase C-beta activation is required for oxidative stress in diabetic nephropathy. Diabetes. 2003 Oct; 52(10):2603-14.

SIRT1 as a therapeutic target for type 2 diabetes

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The rising incidence of diabetes and metabolic syndrome is now a major public health problem in industrialized countries. New therapeutic strategies to prevent these diseases are urgently needed worldwide. It is well known that calorie restriction (CR) can retard the aging process in organisms ranging from yeast to rodents, and delay the onset of numerous age-related diseases including diabetes. Molecules that mimic CR metabolically may be therefore potentially new therapeutic targets for age-related diseases including diabetes. Sirtuin 1 (SIRT1), the mammalian homolog of SIR2, is originally identified as a NAD-dependent histone deacetylase and its activity is closely associated with lifespan elongation under CR. Growing evidence suggests that SIRT1 regulates glucose or lipid metabolism through its deacetylase activity for over two dozen known substrates, and has a positive role in the metabolic pathway through its direct or indirect involvement in insulin signalingin insulin-sensitive organs including adipose tissues, liver and skeletal muscle. In addition, SIRT1 regulates adiponectin secretion, inflammatory responses, gluconeogenesis, and levels of reactive oxygen species, which together contribute to the development of insulin resistance. Moreover, overexpression of SIRT1 and several SIRT1 activators including resveratrol have beneficial effects on glucose homeostasis and insulin sensitivity in obese mice models. Therefore, SIRT1 may be a new therapeutic target for the prevention of disease related to insulin resistance, such as metabolic syndrome and diabetes, although direct evidence from clinical studies in humans is needed to prove this possibility. In this time, we summarize current understanding of the biological functions of SIRT1, and show some clinical data using resveratrol in humans and discuss its potential ability as a therapeutic promise of SIRT1 in type 2 diabetes.

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➤Educational background & professional experience

1991-2002	Merck and Company	Research fellow, Sr. Research fellow, Director, Senior director
2002-2004	ExSAR Corporation	Chief science officer
2004-2007	The Scripps Research Institute-Florida	Professor of biochemistry
2004-present	The Scripps Research Institute-Florida	Director, translational research institute
2007-present	The Scripps Research Institute-Florida	Professor and chair, molecular therapeutics

➤Research interests

Nuclear receptor signaling, chemical biology, GPCRs, proteomics, hydrogen deuterium exchange, protein conformational dynamics, metabolic disorders.

➤Brief list of publications

1. Molecular Mimicry Regulates ABA Signaling by SnRK2 Kinases and PP2C Phosphatases, Soon FF, Ng LM, Zhou XE, West GM, Kovach A, Tan MH, Suino-Powell KM, He Y, Xu Y, Chalmers MJ, Brunzelle JS, Zhang H, Yang H, Jiang H, Li J, Yong EL, Cutler S, Zhu JK, Griffin PR, Melcher K, and Xu HE., Science, 2011, 335, 85-8. PMCID:PMCID in process.
2. Anti-Diabetic Actions of a Non-Agonist PPARγ Ligand Blocking Cdk5-Mediated Phosphorylation, Choi JH, Banks AS, Kamenecka TM, Busby SA, Chalmers MJ, Kumar N, Kuruvilla DS, Shin Y, He Y, Bruning JB, Marciano DP, Cameron MD, Laznik D, Jurczak MJ, Schürer SC, Vidović D, Shulman GI, Spiegelman BM, and Griffin PR, Nature, 2011, 477, 477-81. PMCID:PMCID in process (NIHMS313556).
3. Inhibition of TH17 Differentiation and Suppression of Autoimmunity by a Selective Synthetic ROR Ligand, Solt LA, Kumar N, Nuhant P, Wang Y, Lauer JL, Liu J, Istrate M, Kamenecka TM, Roush WR, Vidović D, Schürer SC, Xu J, Wagoner G, Drew PD, Griffin PR, and Burris TP, Nature, 2011, 472, 491-4. PMCID:PMC3148894.
4. Antidiabetic Effects of a Novel Agonist Ligand for the Nuclear Receptor LRH-1, Lee JM, Lee YK, Mamrosh KL, Busby SA, Griffin PR, Pathak MC, Ortlund EA and Moore DD, Nature, 2011, 447, 506-10. PMCID: PMC3150801.
5. DNA binding alters coactivator interaction surfaces of the intact VDR–RXR complex, Zhang J, Chalmers MJ, Stayrook KR, Burris LL, Wang Y, Busby SA, Pascal BD, Garcia-Ordonez RD, Bruning JB, Istrate MA, Kojetin DJ, Dodge JA, Burris TP and Griffin PR, Nat Struct Mol Biol, 2011, 18, 556-63. PMCID: PMC3049237.
6. Disorder-to-order transition underlies the structural basis for the assembly of a transcriptionally active PGC-1α/ERRγ complex, Devarakonda S, Gupta K, Chalmers MJ, Hunt JF, Griffin PR, Van Duyne GD, Spiegelman BM., Proc Natl Acad Sci U S A., 2011, 108, 18678-83. PMCID:PMCID in process.
7. Ligand-dependent perturbation of the conformational ensemble for the GPCR β2 adrenergic receptor revealed by HDX., West GM, Chien EY, Katritch V, Gatchalian J, Chalmers MJ, Stevens RC, and Griffin PR. Structure, 2011, 19, 1424-32. PMCID:PMC3196059.
8. Anti-diabetic drugs inhibit obesity-linked phosphorylation of PPARg by cdk5. Choi JH, Banks AS, Estall JL, Kajimura S, Laznik D, Chalmers MJ, Kamenecka TM, Griffin PR, and Spiegelman BM, Nature, 2010, 466, 451-6. PMCID:PMC2987584.
9. The Benzenesulfoamide T0901317 is a Novel RORα/γ Inverse Agonist. Kumar N, Solt LA, Conkright JJ, Wang Y, Istrate MA, Busby SA, Garcia-Ordonez RD, Burris TP, and Griffin PR, Mol Pharm, 2010, 77, 228-36. PMCID:PMC2812071.
10. Unique Ligand Binding Patterns Between Estrogen Receptor α and β Revealed by Hydrogen/Deuterium Exchange. Dai SY, Burris TP, Dodge JA, Montrose-Rafizadeh C, Wang Y, Pascal BD, Chalmers MJ, and Griffin PR, Biochemistry, 2009, 48, 9668-76. PMCID: PMC2782520.

• S2-4 •

Mechanism of action of novel insulin sensitizers

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The nuclear receptor peroxisome proliferator-activated receptor gamma (PPARG) is the pharmacological target of the antidiabetic thiazolidinedione (TZD) class of drugs. TZDs are extremely effective as insulin sensitizers and have reported efficacy for several other disorders, including cardiovascular disease in non-diabetics and cancer. Unfortunately, concerns over adverse effects have reduced their clinical utility and created a need for development of the next generation therapeutics. Recently our lab demonstrated that the efficacy of TZDs correlates with their ability to block the obesity-induced phosphorylation of PPARG, while adverse effects are mostly a result of receptor activation. Based on these findings we developed SR1664, termed a 'non-agonist' as it lacks the ability to drive AF-2-dependent receptor activation, but this compound blocks phosphorylation of the receptor at S273. More importantly we demonstrated that this compound (as well as several analogs) is efficacious at insulin sensitization with minimal adverse effects in vivo. Here we report the co-crystal structure of PPARG in complex with SR1664 and we propose a mechanism by which these novel PPARG modulators avoid receptor activation. Additionally, we present preliminary data suggesting SR1664 represses inflammatory gene expression, the mechanism of action thought to drive efficacy in non-diabetic cardiovascular disease patients.

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➤Educational background & professional experience

1984-1990	Seoul National University College of Medicine	M.D.
1993-1995	Graduate School, Seoul National University	M.S.
1995-2000	Graduate School, Seoul National University	Ph.D.
1996-2000	Endocrine Unit Hammersmith Hospital Imperial College School of Medicine	Research fellow
2000-2001	Division of Endocrinology and Metabolism, Department of Internal Medicine, Seoul National University Hospital	Fellow
2002-2008	Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Ulsan College of Medicine	Assistant professor
2008-present	Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Ulsan College of Medicine	Associate professor

➤Research interests

Obesity, diabetes mellitus

➤Brief list of publications

1. Role of Hypothalamic Proopiomelanocortin Neuron Autophagy in the Control of Appetite and Leptin Response. Quan W, Kim HK, Moon EY, Kim SS, Choi CS, Komatsu M, Jeong YT, Lee MK, Kim KW, Kim MS (co-corresponsing author), Lee MS. Endocrinology. 2012 Feb 14. [Epub ahead of print] Endocrinology. 2012 Apr;153(4):1817-26.
2. Kim HK, Shin MS, Youn BS, Namkoong C, Gil SY, Kang GM, Yu JH, Kim MS. Involvement of Progranulin in Hypothalamic Glucose Sensing and Feeding Regulation. Endocrinology. 2011 Sep 20. [Epub ahead of print] 2011 Dec;152(12):4672-82.
3. Hypothalamic Angptl4/Fiaf is a Novel Regulator of Food Intake and Body Weight. Kim HK, Youn BS, Shin MS, Namkoong C, Park KH, Baik JH, Kim JB, Park JY, Lee KU, Kim YB, Kim MS. Diabetes. 2010 Nov;59(11):2772-80.
4. 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-κB activation in hypothalamic POMC neurons is essential in illness- and leptin-induced anorexia. J Biol Chem. 2010 Mar 26;285(13):9706-15.
5. Won JC, Jang PG, Namkoong C, Koh EH, Kim SK, Park JY, Lee KU, Kim MS. Central Administration of an Endoplasmic Reticulum Stress Inducer Inhibits the Anorexigenic Effects of Leptin and Insulin. Obesity (Silver Spring). 2009 Jun 18. Obesity 17(10):1861-5.
6. 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 body weight. Nature Neuroscience 2006 Jul;9(7):901-6.
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9. Kim MS, Yoon CY, Jang PG, Park YJ, Shin CS, Park HS, Ryu JW, Pak YK, Park JY, Lee KU, Kim SY, Lee HK, Kim YB, Park KS. The mitogenic and anti-apoptotic actions of ghrelin in 3T3-L1 adipocytes. Mol Endocrinol. 2004 Sep;18(9):2291-301.
10. Kim MS, Park JY, Namkoong C, Jang PG, Ryu JW, Song HS, Yun JY, Namgoong IS, Ha JH, Park IS, Lee IK, Viollet B, Youn JH, Lee HK, Lee KU. Anti-obesity effects of alpha-lipoic acid mediated by suppression of hypothalamic AMP-activated protein kinase. Nature Med. 2004 Jul;10(7):727-33.

Hypothalamic neuron cilia and energy metabolism

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Ciliary dysfunction in human genetic disorders such as Bardet-Biedel Syndrome (BBS) and Alström syndrome is associated with the development of obesity. Consistent with human disease, BBS-2,4,6 null mice developed leptin resistance and obesity. Defective ciliogenesis in hypothalamic neurons (i.e. POMC-specific KIF3a null mice) also impaired central leptin signaling and led to hyperphagia and obesity.

In the present study, we conversely investigated if obesity may alter ciliogenesis of hypothalamic neurons. We found that the average lengths of neuron cilia were significantly decreased in the arcuate nucleus and ventromedial nucleus of the hypothalamus in high fat diet-induced obese (DIO) mice. Moreover, cilia lengths were remarkably shortened in the hypothalamus from the *ob/ob* and *db/db* mice. In contrast, obesity did not affect cilia lengths in the hippocampus of DIO, *ob/ob* and *db/db* mice, suggesting that impaired neuronal ciliogenesis in obese animals was hypothalamus-specific.

Interestingly, leptin replacement in ob/ob mice and leptin treatment in hypothalamus neuron cells elongated the cilia. Investigation of the mechanisms underlying these effects revealed that leptin treatment induced a serial phosphorylation of PI3K (activation), PDK (inhibition) and GSK-3β (inhibition) in hypothalamic neurons. Overexpression of PDK and GSK-3β gene or treatment of PI3K inhibitors blocked leptin-induced ciliogenesis, suggesting that leptin promoted ciliogenesis via the pathways dependent on PI3K, PDK and GSK-3β. We also found that a transcription factor RFX1 was negatively regulated by GSK-3β. GSK-3β expression inhibited the stimulatory effects of RFX-1 on the transcriptional activities of ciliary proteins such as KIF3a, IFT-88 and IFT-20. Finally, we demonstrated that leptin-induced anorexia and STAT3 activation were significantly attenuated in mice injected with the small inhibitory RNAs specific to IFT88 and KIF3a into the hypothalamus. Thus, a transient and acquired impairment in hypothalamic ciliogenesis can induce central leptin resistance.

Overall, our findings demonstrate that hypothalamic neuron ciliogenesis is dynamically regulate by metabolic regulators and dysregulation of hypothalamic neuron ciliogenesis in turn leads to impaired central leptin signaling.

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➤Educational background & professional experience

2005-2006	University of Texas	Research fellow
2009-present	Korea University	Professor

➤Research interests

Adipokines, vascular inflammation, metabolic syndrome

➤Brief list of publications

1. Choi KM, Han KA, Ahn HJ, Hwang SY, Hong HC, Choi HY, Yang SJ, Yoo HJ, Baik SH, Choi DS, Min KW. Effects of exercise on sRAGE levels and cardiometabolic risk factors in patients with type 2 diabetes: A randomized controlled trial. J Clin Endocrinol Metab 2012, In press.
2. Choi KM, Hwang SY, Hong HC, Yang SJ, Choi HY, Yoo HJ, Lee KW, Nam MS, Park YS, Woo JT, Kim YS, Choi DS, Youn BS, Baik SH. C1q/TNF-related Protein-3 (CTRP-3) and Pigment Epithelium-Derived Factor (PEDF) Concentrations in Patients with Type 2 Diabetes and Metabolic Syndrome. Diabetes 2012, In press.
3. 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-FDG PET. Int J Cardiol 2012, In press.
4. Yang SJ, Kim SE, Hwang SY, Kim TN, Choi HY, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Association between sRAGE, esRAGE Levels and Vascular Inflammation: Analysis with 18F-FDG PET. Atherosclerosis 2012 Feb;220(2):402-6.
5. 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 Aug;96(8):E1325-9.
6. Kim NH, Cho HJ, Kim YJ, Cho MJ, Choi HY, Eun CR, Kim JH, Yang SJ, Yoo HJ, Kim HY, Seo JA, Kim SG, Baik SH, Choi DS, Choi KM. Combined Effect of High-normal Blood Pressure and Low HDL Cholesterol on Mortality in Elderly Korean Population: The South-West-Seoul (SWS) Study. Am J Hypertens 2011 Aug;24(8):918-23.
7. Choi HY, Kim S, Yang SJ, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Association between adiponectin, resistin and vascular inflammation: Analysis with 18F-FDG PET. Arterioscler Thromb Vasc Biol 2011 Apr;31(4):944-9.
8. Yoo HJ, Kim SE, Park MS, Choi HY, Yang SJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Serum Adipocyte fatty acid-binding protein is associated independently with vascular inflammation: Analysis with 18F-FDG PET. J Clin Endocrinol Metab 2011 Mar;96(3):E488-92.
9. Choi KM, Yannakoulia, Park MS, Gho GJ, Kim JH, Lee SH, Hwang TG, Yang SJ, Kim TN, Yoo HJ, Baik SH, Kim SM, Mantzoros CS. Serum adipocyte-fatty acid binding protein, retinol binding protein 4, and adiponectin levels in relation to the development of metabolic syndrome in Korean children: A 3-year long prospective cohort study. Am J Clin Nutr 2011 Jan;93(1):19-26.
10. Kim TN, Park MS, Yang SJ, Yoo HJ, Kang HJ, Song W, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Prevalence and determinant factors of sarcopenia in patients with type 2 diabetes: the Korean Sarcopenic Obesity Study (KSOS). Diabetes Care; 2010 Jul; 33(7):1497-1499.

Novel adipokines and hepatokines

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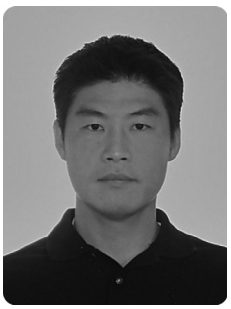
Obesity is a strong risk factor for metabolic syndrome, type 2 diabetes, and cardiovascular diseases. Adipose tissue releases a large number of bioactive mediators (adipokines) that signal to organs such as brain, liver, skeletal muscle, and the immune system, which lead to modulate lipid and glucose metabolism, inflammation, and atherosclerosis. Dysregulated production of adipokines has been found to participate in the development of metabolic and vascular diseases related to obesity. Moreover, dysregulation of adipokine production by excess adipose tissue promotes a state of low-grade systemic inflammation, implicated in the development of both atherosclerosis and subsequently cardiovascular diseases.

Fetuin-A is a 64-kDa glycoprotein produced exclusively by the liver and secreted into serum in relatively high concentrations in humans. Fetuin-A has been known as an inhibitor of ectopic calcium deposition, while it is also an important promoter of insulin resistance. Fetuin-A binds and inhibits the insulin receptor tyrosine kinase in skeletal muscle and hepatocytes, resulting in insulin resistance in these target tissues. Fetuin-A null mice are insulin sensitive and are resistant to weight gain when challenged with a high-fat diet. In humans, higher fetuin-A levels were associated with obesity and insulin resistance in the general population. A recent study has shown that fetuin-A levels are associated with future risk of diabetes. In addition, higher fetuin-A levels associate with increased body mass index (BMI) and hypertriglyceridemia. Treatment with pioglitazone induced a decline in fetuin-A levels and an increase in adiponectin levels. Interestingly, higher fetuin-A levels also associated with fat accumulation in the liver in humans. Therefore, higher fetuin-A and lower adiponectin may provoke obesity-induced insulin resistance and development of NAFLD in humans.

In this presentation, I would like to summarize previous studies about several novel hepatokines and their relationship with adipokines as well as metabolic disorders including diabetes and NAFLD.



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➤Educational background & professional experience

1990-1994	Yonsei University, Biology	B.S.
1994-1996	Yonsei University, Biology	M.S.
1999-2006	University of Texas Southwestern Medical Center	Ph.D.
2007-2008	University of Texas Southwestern Medical Center	Postdoctoral fellow
2009-present	Salk Institute	Postdoctoral fellow

➤Research interests

Adipose tissue development and function
Nuclear receptor physiology
Metabolism and disease

➤Brief list of publications

1. Jonker, J.W., Suh J.M., Atkins, A.R., Ahmadian, M., Li, P., Whyte, J., He, M.X., Juguilon, H., Yin, Y., Phillips, C.T., Yu, R.T., Olefsky, J.M., Henry, R.R., Downes, M., and Evans, R.M. (2012) A PPARγ-FGF1 axis is required for adaptive adipose remodeling and metabolic homeostasis. Nature, 485, 391-394.
2. Zeve, D., Seo, J., Suh, J.M., Stenesen, D., Tang, W., Berglund, E.D., Wan, Y., Williams, L.J., Lim, A., Martinez, M.J., McKay, R.M., Millay, D.P., Olson, E.N., Graff, J.M. (2012) Wnt signaling controls an insulin-independent mechanism to regulate glucose uptake. Cell Metab, 15, 492-504.
3. Wei, W., Zeve, D., Suh, J.M., Wang, X., Du, Y., Zerwekh, J.E., Dechow, P.C., Graff, J.M., Wan, Y. (2011) Biphasic and dosage-dependent regulation of osteoclastogenesis by β-catenin. Mol Cell Biol, 31, 470619.
4. Fang, S., Suh, J.M., Atkins, A.R., Hong, S.H., Leblanc, M., Nofsinger, R.R., Yu, R.T., Downes, M., Evans, R.M. (2011) Corepressor SMRT promotes oxidative phosphorylation in adipose tissue and protects against diet-induced obesity and insulin resistance. Proc Natl Acad Sci USA, 108, 3412-7.
5. Seo, J., Fortuno, E.S., Suh, J.M., Stenesen, D., Tang, W., Parks, E.J., Adams, C.M., Townes, T., Graff, J.M. (2009) Atf4 Regulates obesity, glucose Homeostasis, and energy expenditure. Diabetes, 58, 2565-73.
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7. Suh, J.M., Stenesen, D., Peters, J.M., Inoue, A., Cade, A., and Graff, J.M. (2008). An RGS-containing sorting nexin controls Drosophila lifespan. PLoS ONE, 3, e2152.
8. McKay, R.M., McKay, J.P., Suh, J.M., Avery, L., and Graff, J.M. (2007). Tripeptidyl peptidase 2 promotes fat formation in a cell-autonomous and conserved fashion. EMBO Rep 8, 1183-9.
9. Suh, J.M., Zeve, D., McKay, R., Seo, J., Salo, Z., Li, R., Wang, M., and Graff, J. M. (2007). Adipose is a conserved dosage-sensitive anti-obesity gene. Cell Metab 6, 195-207.
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A new NR-FGF1 axis: regulation of feast and famine

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While feast and famine cycles illustrate that adipose tissue remodelling in response to fluctuations in nutrient availability is essential for maintaining metabolic homeostasis, the underlying mechanisms remain poorly understood. We identify FGF1 as a critical transducer in this process and link its regulation to the nuclear receptor PPARγ, the adipocyte master regulator and target of the thiazolidinedione (TZD) class of insulin sensitizing drugs. We show that FGF1 is highly induced in adipose tissue in response to high-fat diet (HFD) and that mice lacking FGF1 develop an aggressive diabetic phenotype coupled to aberrant adipose expansion when challenged with HFD. Further analysis of adipose depots revealed multiple histopathologies in the vasculature network, inflammatory immune compartments and adipocyte size distribution. Upon HFD withdrawal, this inflamed adipose tissue fails to properly resolve as evidenced by extensive fat necrosis. Mechanistically, we show that adipose induction of FGF1 is regulated by a promoter proximal PPAR response element, and that this PPARγ-FGF1 axis is evolutionarily conserved in mammals. Finally, in diabetic patients FGF1 expression in adipocytes is induced by pharmacological activation of PPARγ and this induction correlates with the efficacy of TZDs to lower fasting glucose levels. This work describes the first phenotype of the FGF1 knockout mouse and establishes FGF1 as a new member of the NR-FGF axis critical for maintaining metabolic homeostasis and insulin sensitization.

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➤Educational background & professional experience

1965	Hokkaido University, Faculty of Science	B.Sc.
1970	Osaka University, Graduate School of Science	Ph.D.
1974	Ehime University, School of Medicine	Associate professor
1989	Hokkaido University, School of Veterinary Medicine	Professor
2006-present	Tenshi College, Department of Nutrition	Professor

➤Research interests

Regulation mechanisms of energy metabolism, with special references to brown adipose tissue and obesity

➤Brief list of publications

1. Nonpungent capsaicin analogs (capsinoids) increase energy expenditure through the activation of brown adipose tissue in humans. Yoneshiro T, Aita S, Kawai Y, Iwanaga T, Saito M. Am J Clin Nutr 95: 845-850, 2012
2. Deficient of a clock gene, brain and muscle arnt-like protein-1 (BMAL1), induces dyslipidemia and ectopic fat formation. Shimba S, Ogawa T, Hitosugi S, Ichihashi Y, Nakadaira Y, Kobayashi M, Tezuka M, Kosuge Y, Ishige K, Ito Y, Komiyama K, Okamatsu-Ogura Y, Kimura K, Saito M. PloS One 6: e25231(1-10), 2011.
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5. High incidence of metabolically active brown adipose tissue in healthy adult humans: Effects of cold exposure and adiposity. Saito M, Okamatsu-Ogura Y, Matsushita M, Watanabe K, Yoneshiro T, Nio-Kobayashi J, Iwanaga T, Miyagawa M, Kameya T, Nakada K, Kawai Y, Tsujisaki M. Diabetes 58: 1526-1531, 2009.
6. FSP27 contributes to efficient energy storage in murine white adipocytes by promoting the formation of unilocular lipid droplets. Nishino N, Tamori Y, Tateya S, Kawaguchi T, Shibakusa T, Mizunoya W, Inoue K, Kitazawa R, Kitazawa S, Matsuki Y, Hiramatsu R, Masubuchi S, Omachi A, Kimura K, Saito M, Amo T, Ohta S, Yamaguchi T, Osumi T, Cheng J, Fujimoto T, Nakao H, Nakao K, Aiba A, Okamura H, Fushiki T, Kasuga M. J Clin Invest. 118 (8): 2808-2821, 2008.
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Brown adipose tissue as a regulator of body fat in humans

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Brown adipose tissue (BAT) is the major site for non-shivering thermogenesis during cold exposure and overfeeding, at least small rodents. Current studies using fluorodeoxyglucose (FDG) - positron emission tomography (PET) have demonstrated the existence of BAT in adult humans. During the last 5 years, we have examined the metabolic activity of BAT by FDG-PET in more than 200 healthy volunteer subjects. When PET scan was performed after exposing the subjects to cold at 19°C with light clothing for 2 hours, apparent uptake of FDG was found at the supraclavicular and paraspinal regions in about one-half of the younger subjects but in less than 10% of the fifties and sixties. The FDG uptake disappeared when they were kept at 28°C. These results indicate that a large number of adult humans have significant amounts of cold-activated BAT.

To test whether BAT contributes significantly to whole-body energy expenditure (EE), we estimated EE by measuring oxygen consumption in the BAT-positive and -negative subject groups. EE at the basal level (28°C) was almost same in the two groups, but after cold exposure it increased by 20% in the BAT-positive group, while by only 3% in the BAT-negative group. The adiposity-related parameters such as BMI, body fat content and visceral fat were significantly lower in the BAT-positive group. It was also found that the parameters increased with age in the BAT-negative group, while they remained unchanged from the twenties to forties in the BAT-positive group. All these results suggest that BAT contributes to the regulation of EE and adiposity in humans, and thereby plays a protective role against aging-related accumulation of body fat. The stimulatory effect of some food ingredients including capsaicin on BAT will also be discussed in context with the management of obesity.

Peter Proks

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➤Educational background & professional experience

1982-1987	Comenius University, Bratislava	Undergraduate
1988-1990	Institute of Molecular Physiology and Genetics, Bratislava	Postgraduate scholarship
1991-1992	University of Oxford	Visiting student
1992-1995	University of Oxford	D.Phil. in physiology
1996-present	University of Oxford	Research scientist

➤Research interests

K_{ATP} channel, biophysics of ion channels, neonatal diabetes

➤Brief list of publications

1. Proks P, de Wet H, Ashcroft FM. (2010) Activation of the KATP channel by Mg-nucleotide interaction with SUR1. J Gen Physiol 136:389-405.
2. Clark R, Proks P (2010) ATP-Sensitive Potassium Channels in Health and Disease. Adv Exp Med Biol 654:165-192.
3. Proks P, Ashcroft FM (2009) Modeling KATP channel gating and its regulation. Prog Biophys Mol Biol. 99: 7-19.
4. Craig TJ, Ashcroft FM, Proks P. (2008) How ATP inhibits the open KATP channel. J Gen Physiol 132: 131-144.
5. Proks P, Shimomura K, Craig TJ, Girard CA, Ashcroft FM. (2007) Mechanism of action of a sulphonylurea receptor SUR1 mutation (F132L) that causes DEND syndrome. Hum Mol Genet 16: 2011-2019.
6. Proks P, Girard C, Haider S, Gloyn AL, Hattersley AT, Sansom MSP, Ashcroft FM (2005) A gating mutation at the internal mouth of the Kir6.2 pore is associated with DEND syndrome. EMBO Rep 6: 470-475.
7. Proks P, Antcliff JF, Lippiat J, Gloyn AL, Hattersley AT, Ashcroft FM (2004) Molecular basis of Kir6.2 mutations associated with neonatal diabetes or neonatal diabetes plus neurological features. Proc Natl Acad Sci 101: 17539-17544.

Modulation of sulphonylurea block of K_{ATP} channels by adenosine nucleotides

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Introduction:

Sulphonylureas stimulate insulin secretion from pancreatic β-cells by closing ATP-sensitive potassium (K_{ATP}) channels in the β-cell plasma membrane. Their primary, clinically relevant effect is mediated via a high-affinity binding site on the regulatory subunit of the K_{ATP} channel, the sulphonylurea receptor (SUR1). KATP channel activity is also regulated by intracellular adenosine nucleotides, with ATP having an inhibitory effect and Mg-nucleotides (MgATP or MgADP) a stimulatory effect. Previous studies have demonstrated that sulphonylurea block of K_{ATP} channels is substantially altered in the presence of Mg-nucleotides.

Objectives:

The aim of this study was to characterize the molecular mechanism underlying adenosine nucleotide modulation of sulphonylurea block of K_{ATP} channels using the sulphonylurea gliclazide and electrophysiological techniques.

Results:

Gliclazide dramatically increased the values of EC_{50} for channel activation by MgADP and MgATP and substantially impaired the mechanism by which nucleotide binding is communicated to channel gate. This suggests gliclazide impairs activation mediated via nucleotide binding domain 2 (NBD2) of SUR1. Gliclazide also enhanced the inhibitory effect of ATP (but not ADP) on wild-type K_{ATP} channels both in the absence and presence of Mg^{2+}. This effect required both NBD1 and NBD2 to be intact and was abolished by many mutations that impair ATP binding to Kir6.2 subunit of the channel. Mg-nucleotides significantly increased the IC_{50} for gliclazide block of K_{ATP} channels, consistent with the idea that nucleotide binding to NBD2 has a negative effect on sulphonylurea binding to SUR1.

Conclusions:

Our results indicate that in the presence of adenosine nucleotides, high-affinity sulphonylurea block of K_{ATP} channels is altered in a complex way that involves all three types of nucleotide-binding sites on the K_{ATP} channel (Kir6.2, NBD1 and NBD2 of SUR1).

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➤Educational background & professional experience

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	Chiba University School of Medicine, Chiba, Japan	Professor
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 Graduate School of Medicine, Kobe, Japan	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 Cell signaling in insulin secretion: the molecular targets of ATP, cAMP and sulfonylurea. Diabetologia 55: 2096-2108, 2012.
2. Matsubara T et al. PGRN is a key adipokine mediating high fat diet-induced insulin resistance and obesity through IL-6 in adipose tissue. Cell Metab. 15: 38-50, 2012.
3. Seino S et al. Dynamics of insulin secretion and the clinical imiplications for obesity and diabetes. J Clin Invest. 121: 2118-2125, 2011.
4. Yasuda T et al. Rim2 alpha determines docking and priming states in insulin granule exocytosis. Cell Metab. 12: 117-129, 2010.
5. Zhang CL et al. The cAMP sensor Epac2 is a direct target of anti-diabetic sulfonylurea drugs Science. 325: 607-610, 2009.
6. Shibasaki et al. Essential role of Epac2/Rap1 signaling in regulation of insulin granule dynamics by cAMP. Proc Natl Acad Sci USA. 104: 19333-19338, 2007.
7. Seino S and Shibasaki T PKA-dependent and PKA-independent pathways for cAMP-regulated exocytosis. Physiol Rev. 85: 1303-1342, 2005.
8. Ozaki N et al. cAMP-GEFII is a target of cAMP in regulated exocytosis. Nat Cell Biol. 2: 805-811, 2000.
9. Seino S ATP-sensitive potassium channels: a model of heteromultimeric potassium channel/receptor Assemblies. Annu Rev Physiol. 61: 337-362, 1999.
10. Inagaki N et al. Reconstitution of IKATP: An inward rectifier subunit plus the sulfonylurea receptor. Science. 270: 1166-1170, 1995.

• S4-2 •

Elucidation of the mechanisms of insulin secretion by metabolomics

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Insulin secretion from pancreatic β-cells plays a central role in glucose homeostasis and impaired insulin secretion contributes to the development of diabetes. Metabolic signals in β-cells are crucial in regulation of insulin secretion. For example, ATP generated by glucose metabolism is a key signal in glucose-induced insulin secretion (GIIS), which is the most important mechanism of insulin secretion. In addition to GIIS, potentiation of GIIS also is required for normal regulation of insulin secretion. cAMP is a well-known second messenger in β-cells that potentiates insulin secretion in a glucose-dependent manner. Utilizing this effect, incretin (gut hormones that increase cAMP in the β-cells)-related anti-diabetic drugs have been developed recently. However, the mechanism of the glucose-dependency of cAMP action in insulin secretion remains unknown. Using metabolome-based analysis, we find that glutamate the malate-aspartate (MA) shuttle, an NADH shuttle linked to glycolysis, is essential for potentiation of insulin secretion by incretin/cAMP signaling. We are currently identifying a novel metabolic signal in cAMP-induced insulin secretion. Metabolomics is a powerful approach to identification of novel metabolic signals and potential therapeutic targets in insulin secretion.

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➤Educational background & professional experience

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

Pathophysiology of diabtes mellitus, incretin hormone, GLP-1, islet biology and islet transplantation

➤Brief list of publications

1. Kim JY, Lim DM, Park HS, Moon CI, Choi KJ, Lee SK, Baik HW, Park KY, Kim BJ.Exendin-4 Protects Against Sulfonylurea-Induced β-Cell Apoptosis. J Pharmacol Sci. 118(1):65-74, 2012.
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. 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. Ca2+-induced Ca2+ Release from Internal Stores in INS-1 Rat Insulinoma Cells. Korean J Physiol Pharmacol. 15(1):53-9. 2011.
5. 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 β-Cell Apoptosis through Reduced JNK and GSK3β Activity. J Korean Med Sci 25: 1626-1632. 2010.
6. 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.
7. Kim W, Shin YK, Kim BJ, Egan JM. Notch signaling in pancreatic endocrine cell and diabetes Biochem Biophys Res Commun. 392:247-251. 2010.
8. Byung-Joon Kim. Stimulation of Glucagon Like Peptide-1 Secretion in Enteroendocrine L cells. . Korean Diabetes J 33:458-463, 2009.
9. Byung-Joon Kim. Beta Cells Preservation in Diabetes using GLP-1 and Its Analog. Hanyang Med Rev 29:140-147, 2009.
10. Ju-Young Kim, Seong-Kyu Lee, Haing-Woon Baik, Ki-Ho Lee, Hyun-Jin Kim, Kang-Seo Park, Byung-Joon Kim. Protective Effects of Glucagon Like Peptide-1 on HIT-T15 beta Cell Apoptosis via ER Stress Induced by 2-deoxy-D-glucose. Korean Diabetes J 32(6):477-487, 2008.

• S4-3 •

Long acting GLP-1 analog by using transferrin fusion technology

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Glucagon-like peptide-1 (GLP-1) is a 30/31-amino acid peptide secreted from intestinal enteroendocrine L cells. GLP-1 treatment to type2 diabetes had an insulinotropic effect with a glucose-dependent manner and improves total insulin secretion. Also, GLP-1 exerts multiple actions throughout the body, including a neuro-protective action in the brain, an increase in cardiac output, reduction of appetite and body weight, and inhibition of gastric emptying. One pharmacokinetic impediment, however, to the creation of GLP-1-based agents has been its short circulatory half-life ($t_{1/2}$) of approximately 1 to 2 min. Making a long acting GLP-1 analogue has become an important pharmaceutical approach for treating type 2 diabetes.

Fusion proteins made up of GLP-1 fused to a non-glycosylated form of human transferrin (GLP-1-Tf) were produced and evaluated. GLP-1-Tf activated the GLP-1 receptor, was resistant to inactivation by dipeptidyl peptidases, and had a half-life of approximately 2 days, compared with 1 to 2 min for native GLP-1 or 2 to 3 hour for Exendin-4. GLP-1-Tf retained the acute, glucose-dependent insulin-secretory properties of native GLP-1 in diabetic animals and had a profound effect on proliferation of pancreatic beta-cells. In addition, Tf and the fusion proteins did not cross the blood-brain-barrier but still reduced food intake after peripheral administration. EX-4-Tf proved to be as effective as EX-4 but had longer lived effects on blood glucose and food intake. This novel transferrin fusion technology could another method for making the long acting analogue of GLP-1 or Exendin-4.

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➤Educational background & professional experience

1988-1992	Kyungpook National University	Biochemistry / B.S.
1993-1995	Kyungpook National University	Biochemistry / M.S.
1999-2002	Yonsei University	Medical science / Ph.D.
1997-2002	Yonsei University	Research assistant
2002-2003	Yonsei University	Research instructor
2003-2007	University of Texas Southwestern Medical Center	Postdoctoral researcher
2007-2011	Gachon University	Assistant professor
2011-present	Gachon University	Associate professor

➤Research interests

Metabolism, transcriptional regulation, diabetes, fatty liver

➤Brief list of publications

1. Kim EH, Bae JS, Hahm KB, Cha JY. Endogenously synthesized n-3 polyunsaturated fatty acids in fat-1 mice ameliorate high-fat diet-induced non-alcoholic fatty liver disease. Biochemical Pharmacology. 2012; doi:10.1016/j.bcp.2012.08.029.
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Role of LXR in beta-cell function and glucose homeostasis

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The endocrine pancreas produces insulin and thus serves as a master regulator of glucose homeostasis. The synthesis and secretion of insulin by specialized beta-cells in pancreatic islets are tightly regulated by metabolite intermediates to maintain proper blood glucose levels. Dysfunction of this important endocrine system is responsible for diabetes mellitus. Over the last several years, research has suggested that liver X receptors (LXRs) may play an important role in the maintenance of glucose homeostasis and islet function.

LXRβ, and to a lesser extent LXRα, are present in the beta-cell of islets. Exposing isolated mouse islets to the synthetic LXR agonist T1317 results in increased glucose-stimulated insulin secretion (GSIS). Incubation of islets from *lxr*-null mice with this ligand has no effect on GSIS thus suggesting the T1317 effects is mediated by LXRs. In addition, oral administration of T1317 to wild type, but not *lxr*-null mice, altered islet GSIS *in vivo* and promoted efficient glucose clearance. These results suggest that activation of LXR in islet cells can modify islet function and help to control serum glucose levels.

Although several studies suggest the beneficial effects of LXR activation on beta-cell function, chronic activation of LXR increases lipogenesis, leading to the accumulation of excess lipid in pancreatic beta-cells and eventually to beta-cell death. These different effects on LXRs on beta-cell growth and function may result from different levels and durations of LXR activation. To determine the role of beta-cell specific activation of LXR on islet function, transgenic mice which express constitutively active LXR specifically in beta-cells were developed and analyzed. In this symposium, we will discuss detailed analytical results on beta-cell function and glucose homeostasis in *lxr*-null and *lxr*-transgenic mice. In addition, potential mechanisms involved in beta-cell dysfunction by chronic LXR activation will be discussed.

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➤Educational background & professional experience

1997-2001	Ewha Womans University	Business administration / B.B.A.
1997-2001	Ewha Womans University	Statistics / B. S.
2002-2005	Ewha Womans University	Business administration / M.A.
2005-2008	Samsung Medical Center, Samsung Health Care Management Research Institute	Researcher / Seoul, Korea
2006-2008	Korea University	Public Health(Health Policy and Hospital Management) / Ph.D.
2009-2010	Eulji University, Department of Hospital Management	Full-time Instructor / Seongnam, Korea
2010-2011	United Way of Central Maryland	Practicum / Maryland, USA
2010-2011	Jhpiego - an affiliate of Johns Hopkins University	Internal Internships / Maryland, USA
2011-2011	WHO (World Health Organization), WHO European Centre for Environment and Health	Intern / Bonn, Germany
2010-2011	Johns Hopkins University, Carey Business School	Business(Healthcare mnagement) / M.B.A
2010-2011	Johns Hopkins University, Bloomberg School of Public Health	Public health(Health fnance and Management) / M. P. H
2011-2012	Rare Genomic Institute (RGI)	Business consultant / Maryland, USA
2012-present	Eulji University, Department of Hospital Management	Instructor

➤Research interests

Healthcare financing, hospital accounting, healthcare behavior and science

➤Brief list of publications

1. Cigarette smoking, alcohol use and depressive symptoms in Koreans: The Korean Longitudinal Study of Aging / 5025.0, "Global issues in mental health" poster presenter for the 140th APHA Annual Meeting (October 27 - October 31, 2012) in San Francisco, CA
2. Reproductive health services in Malawi: An evaluation of a quality improvement intervention / Oct 2011 / Midwifery (2011), doi:10.1016/j.midw.2011.10.005
3. A comparison of risk and protective factors in general population and incarcerated population for substance use / Oct 2011 / Abstract Author - 139th APHA Annual Meeting / Submitted for the Alcohol, Tobacco, and Other Drugs program of the 139th APHA Annual Meeting (October 29 - November 2, 2011) to be held in Washington, DC.
4. Implications of WHO global plan on worker's health related to asbestos / Sep 2011 / theHealth 2011; 2(3): 74 / Guest Editorial
5. 'Management Principles for Health Professionals' 5th E. / Jan 2011 / Gratto-Liebler, Joan and McConnell, Charles R., Jones & Bartlett Learning / Co- Translator of the Korean version of the book
6. Internal and external environmental factors affecting the outputs of hospital-based home nursing care / International Nursing Review Issue 58(2) / June 2010
7. Measures of Hospital Market Competition by the Herfindal Hirschman Index / Dec 2007 / Health Service Management Review 2007;1(1):13-22.
   - Developed an index measuring the size of the hospitals in relationship to the industry and an indicator of the amount of competition among them
   - The first to index the competition of hospitals at the country level in Korea

• S5-1 •

How to apply cost-effectiveness analysis to diabetes education

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Background:

Diabetes mellitus is a chronic ailment needing continuous treatment and self-management. To bring successful long-term treatment, diabetes education is a critical element. In the state of limited resources meeting medical demands and needs, priority setting in resource consumption is inevitable. Diabetic patients expect better health status and life style and less health care cost by diabetes education. Questions were raised regarding market economic value of diabetes education among many alternatives in allotting health care resources. Economic evaluation is a means of indicating the direction efficient resource allocation.

Objective:

In order to evaluate the effectiveness of the current diabetes education program conducted by certified diabetes educators, this course introduces methodology of measuring the education program costs and direct/indirect effectiveness of the result of the program. We truly believe that when the diabetic patients' quality and span of life are considered, the entire benefit of the society as a whole will exceed the cost of the diabetes education program which has targets following;

1. Sustain the life of diabetic patients and remove symptoms of the disease.
2. Support patients to have the best possible normal social life.
3. Establish and maintain favorable metabolic state.
4. Avoid the complications of diabetes.

(WHO, 1985)

Method:

Cost-effectiveness, as useful economics analysis instrument, shows relative spending and results of multiple factors of action. Grasping the cost/comparative effectiveness derives better outcomes for decreased medical and healthcare expenditure.

Result:

Correlated DSME/T with reduced and saved cost, cost-effectiveness or plus return on spending clearly showed on more than half (18) of the 26 papers of reported literature review. Profits of people with diabetes which connected with education on self-management and lifestyle change are positive and surpass the prices connected with the treatment. (Boren et al, TDE, Jan 2009)

Conclusion:

Long-term health of people with diabetes can be enhanced and medical care costs as a whole can be saved when education effects patients to learn about their disease and become active participants in managing their health.

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➤Educational background & professional experience

1993-1999	Seoul National University Hospital	OBGY nurse
2008-present	College of Nursing, Seoul National University	Clinical instructor
2011	College of Nursing, Yonsei University	Women health nursing / Ph.D.
2011-present	Korean Association of Diabetes Nurse Educations	Member of research committee
2011-present	Korean Diabetes Association : Gestational diabetes mellitus interest group	Member
2012-present	The Academic Society of Parent-Child Health	Editorial board member

➤Research interests

Gestational diabetes mellitus, diabetes education, blended e- learning, women health
Pregnancy outcome of diabetes in pregnancy

➤Brief list of publications

1. Doctoral dissertation: Effects of an Integrated Self-Management Program on Self-Management, Glycemic Control, and Maternal Identity in Women with Gestational Diabetes Mellitus, 2011.
2. Sue Kim, HeeSook Kim, HaYoon Cheong. Effects of a Coaching-based Childbirth Program on Anxiety and Childbirth Self-Efficacy among Primigravida Women. Korean Journal of Women Health Nursing 2011;17(4):369-377.
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4. ChaeWeon Chung, HeeSook Kim, YoungSook Park. Effects of High-Fidelity Simulation-Based Education on Maternity Nursing. Perspectives in Nursing Science 2011;8(2):86-96.
5. SoonBok Chang, HeeSook Kim,, YunHee Ko, ChoonHee Bae, SungEun An. Effects of Abdominal Breathing on Anxiety, Blood Pressure, Peripheral Skin Temperature and Saturation Oxygen of Pregnant Women in Preterm Labor. Korean Journal of Women Health Nursing 2009;15(1):32-42.
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• S5-2 •

Health outcomes and measurement methods of diabetes care

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Outcomes research aimed at assessing the quality and effectiveness of health care as measured by the attainment of a specified end result or outcome. Measures include parameters such as improved health, lowered morbidity or mortality, and improvement of abnormal states. Outcomes research seeks to understand the end results of particular health care practices and interventions.

Important outcome measures for diabetes health education include morbidity and mortality rates, incidence and progression of diabetic complications, and improvements in patient empowerment and quality of life. There are also a number of qualitative measures that can indicate the value and effectiveness of health education interventions. Outcome measures reflect the different stages of the disease in which the specialist nurse are involved. Primary outcomes are HbA1c, BP, and quality of life. Secondary outcomes are BMI; lipid levels, short-term and long-term diabetic complications, total and specific mortality rates, acute hospital admissions, attitude scales, patient satisfaction scores (patient empowerment and self efficacy), adverse effects, knowledge of disease, and health economics analysis.

Specialist diabetes nurses provide education and support services to people with diabetes in many health care systems. A key goal is to help enable people to self-manage their diabetes. Patients in contact with specialist nurses are generally satisfied with the level of care that they receive and it is thought that patients often contact the specialist nurses in preference to their general practices. The impression is that this is because the specialist nurses can provide better information and advice than general practice staff. However, measurement of outcomes of receiving care from specialist nurses have not been reviewed. Thus, evidence of the benefits and effectiveness of the nurse specialist is required.

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➤Educational background & professional experience

1994	Gachon University of Medicine and Science Major in Nursing Science
2000	Diabetes educater license
2008-present	Work for Gwang Myung Sung Ae Hospital, Diabetes Educator

• S5-3 •

AADE7 self-care behaviors

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Diabetes is currently impossible to cure. The objective of the treatment for diabetes is to prevent or delay acute or chronic diabetes and its complications. In order to manage these acute and chronic complications, the patient must use medications as well as practice self-care through behavior change. To have effective self-care, education from diabetes specialists is important, and this education is now becoming part of the treatment.

Recently, the importance of education has been recognized. Thus, it has been legalized that the effects after education should be evaluated. However, in Korea there is no tool for this type of evaluation. In this paper we introduce the AADE 7 self-Care Behaviors framework, which was developed by the American Association of Diabetes Nurse Educator in order to measure the effects of education.

The AADE 7 self-Care Behaviors framework consists of 7 behaviors: healthy eating, being active, monitoring, taking medication, problem solving, reducing risks, and healthy coping. The framework includes a description of each behavior for patients and healthcare professionals. With each behavior there is information on knowledge and skills and help for individuals to cope with the disease by identifying barriers that hinder self-care management. After education, the measurement of effectiveness is done at baseline, 3 months, 6 months, and 12 months. Measurements are of immediate outcome, intermediate outcome, post-intermediate outcome, and long-term outcome in order to improve the health status of patients through behavior change.

The AADE 7 self-Care Behaviors framework has been developed through a systematic literature review of evidenced-based medicine. With this tool, educators provide education based on evidence and evaluate outcomes immediately after education.

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➤Educational background & professional experience

1995	Gyeongsang National University	Department of nursing / B.A.
2003	Ewha Womans University	Department of nursing science / Master
2011	Ewha Womans University	Department of nursing science / Ph.D.
1995-2003	Seoul National University Hospital	Nurse
2003-present	Seoul National University Bundang Hospital	Diabetes nurse educator
2012	Korean Association Diabetes Nurse Educator	Director of research

➤Research interests

Alcohol consumption and smoking behaviors in men with diabetes mellitus

➤Brief list of publications

1. Jung JH, Kim OS. Alcohol consumption and cigarette smoking in men with Diabetes Mellitus. Journal of Korean Academy of Adult Nursing 2005;17(1):68-76.
2. Kim OS, Kim JH, Jung JH. Stress and cigarette smoking in Korean men with Diabetes. Addictive Behaviors 2006;31(5):901-6.

• S5-4 •

Evaluation of the effectiveness of diabetes education

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Diabetes education is a cornerstone of diabetes care. Evaluation of diabetes education is an essential component of the curriculum.

Diabetes education is the ongoing process of facilitating the knowledge, skill, and ability necessary for diabetes self-care. The objectives of diabetes education are to support self-care behaviors and to improve clinical outcomes, health status, and quality of life. Self-care behaviors and quality of life are the key outcomes of the diabetes education and should be measured and monitored as a part of care.

The diabetes education must be measured attainment of patient-defined goals and patient outcomes at regular intervals using appropriate measurement to evaluate the effectiveness of the education intervention. The AADE7 self-care behaviors provide a useful framework for assessment and evaluation. Behavioral change is the unique outcome measurement for diabetes education.

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➤Educational background & professional experience

1989-1993	Kyung-Won University	Food and nutrition / B.S.
1994-1996	Korea University	Food technology / M.S.
2004-2007	Korea University	Food biotechnology / Ph.D.
2007-2012	Korea University	Research professor
2012-present	Agency for Korea National Food Cluster	Manager

➤Research interests

Diabetes and diabetic complication, advanced glycation end products (AGE), skin, bone growth

➤Brief list of publications

1. Silk protein hydrolysate increases glucose up take through up-regulation of GLUT4 and reduces the expression of leptin in 3T3-L1 adipocyte, Nutrition Research, 31, 937-943 (2011).
2. Novel tripeptides with a-glucosidase inhibitory activity isolated from silk cocoon hydrolysate, J. of Agricultural and Food Chemistry, 59, 11522-11525 (2011).
3. Inhibitory effects of Terminalia chebula extract on glycation and endothelial cell adhesion, Planta Medica, 77, 1060-1067.
4. Monocyte-endothelium-smooth muscle cell interaction in co-culture: Proliferation and cytokine productions in response to advanced glycation end products, Biochemica et Biophysica Acta, 1810, 907-912 (2011).
5. Stimulation of osteoblastic differentiation and mineralization in MC3T3-E1 cells by yeast hydrolysate, Phytotherapy Research, 25, 716-723 (2011).
6. Glucose tolerance and anti-oxidant activity of spent brewer's yeast hydrolysate with a high content of cyclo-his-pro (CHP), Journal of Food Science, 76 272-278 (2011).
7. Feeding silk protein hydrolysates to C57BL/KsJ-db/db mice improved blood glucose and lipid profiles, Nutrition Research, 30, 783-790 (2010).
8. Preventive effects of chebulic acid isolated from Terminalia chebula on advanced glycation endproduct-induced endothelial cell dysfunction, Journal of Ethnopharmacology, 131, 657-574 (2010).
9. Isolation of caffeic acid from Perilla frutescens and its role in enhancing gamma-glutamylcysteine synthetase activity and glutathione level, Food chemistry, 119, 724-730 (2010).
10. Acute and subacute toxicity of yeast hydrolysate from Saccharomyces cerevisiae, Food and Chemical Toxicology, 48, 1677-1681 (2010).

• S6-1 •

Advanced glycation endproducts (AGEs) and nutrition in people with type 2 diabetes

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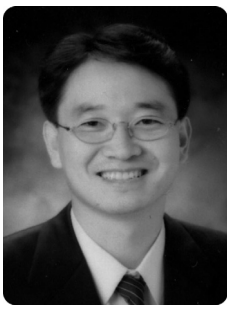
Advanced glycoxidation end products (AGEs) constitute a group of heterogeneous moieties produced endogenously from the nonenzymatic glycation of proteins, lipids, and nucleic acids. This reaction is also known as the Maillard or browning reaction. AGEs have been associated with numerous diabetic complication and renal complications as well as with Alzheimer's disease. Aminoguanidine (AG), the prototype AGEs inhibitor, has been effective in retarding the full range of diabetic complications, such as nephropathy, neuropathy, retinopathy, and vasculopathy. Extract of *Terminalia chebula* show the inhibitory activity of AGE formation in vitro and the prevention effects of diabetic complication *in vivo.* Previous researchers reported a 33% decrease in glycated albumin after 3 months with 1 g/day of ascorbate and an 18% reduction in glycated hemoglobin. The antioxidant and anti-AGE agent in the supplement have the glycation lowering effect in our body. In addition to AGEs that form within the body, AGEs also exist in foods. Because it had previously been assumed that dietary AGEs (dAGEs) are poorly absorbed, their potential role in human health and disease was largely ignored. However, recent studies that dAGEs are absorbed and contribute significantly to the body's AGE pool. Consumption of AGE-rich diets by experimental animals is associated with elevated circulating and tissue AGEs and conditions such as atherosclerosis and kidney disease. On the other hand, restriction of dAGEs prevents vascular and kidney dysfunction, diabetes type 1 or type 2, improves insulin sensitivity, and accelerates wound healing. AGEs are naturally present in uncooked animal-derived foods, and cooking results in the formation of new AGEs within these foods. Therefore, the limitation of dAGEs may be especially important for people with diabetes.



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➤Educational background & professional experience

1988-1994	College of Medicine, Chonbuk national university	Medicine / M.D.
1999-2001	Master course of medical science, Graduate school, Chonbuk national university	Internal medicine / Master
2002-2007	Ph.D. course of medical science, Graduate school, Chonbuk national university, Majored in diabetology	Endocrinology & metabolism / Ph.D.
1998-2002	Resident, Internal medicine, Medical college of Chonbuk national university hospital	
2002-2003	Fellowship, Endocrinology & Metabolism, Medical college of Chonbuk national university hospital	
2003-present	Division of endocrinology and metabolism, Sejong general hospital	

➤Research interests

Majored in diabetology & diabetic neuropathy

➤Brief list of publications

1. Prevalence and clinical characteristics of diabetic peripheral neuropathy in hospital patients with type 2 diabetes in Korea. Diabet Med. 2012 Sep;29(9):e290-e296.
2. Autoimmune Hypoglycemia in a Type 2 Diabetic Patient With Anti-Insulin and Insulin Receptor Antibodies. Diabetes Care 27: 288-289,2005.
3. 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.
4. A case of a ruptured pheochromocytoma with an intratumoral aneurysm managed by coil embolization. Endocr J. 2003 Dec;50(6):653-6.

Clinical importance and meta-analysis of study of sodium in diabetic patients

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In patients with type 2 diabetes, hypertension is associated with a range of adverse outcomes including cardiovascular disease (CVD) and premature mortality. Consequently, clinical guidelines recommend that patients with type 2 diabetes undertake measures to maintain a blood pressure at or below target levels. Among the interventions advocated to assist in achieving these targets, most guidelines recommend a reduced intake of sodium, as dietary sodium intake is positively correlated with blood pressure levels in the general population. Moreover, in patients with type 2 diabetes,salt restriction confers a modest reduction in blood pressure, and salt supplementation reduces the antihypertensive efficacy of blood pressure–lowering agents in the short term. However, the precise relationship between salt intake and mortality in patients with type 2 diabetes has not been previously explored. It is widely assumed that any blood pressure lowering associated with reduced dietary salt intake may be translated into protection from end-organ damage in the context of diabetes. However, there is also evidence that reduced sodium intake is associated with activation of metabolic and neurohormonal pathways, including the sympathetic nervous system and the renin-angiotensinaldosterone system (RAAS), as well as increases in total and LDL cholesterol and reduced peripheral insulin sensitivity.

In the context of type 2 diabetes, each of these factors may offset or even outweigh gains achieved from blood pressure lowering.

Hence, in this talk I discuss with Clinical importance and meta-analysis of study of sodium intake in diabetic patients

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3. Ekinci EI, Thomas G, MacIsaac RJ, et al. Salt supplementation blunts the blood pressure response to telmisartan with or without hydrochlorothiazide in hypertensive patients with type 2 diabetes. Diabetologia 2010;53:1295–1303
4. Graudal NA, Gall ø e AM, Garred P. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride: ameta-analysis. JAMA 1998;279:1383–1391
5. Petrie JR,Morris AD,Minamisawa K, et al. Dietary sodium restriction impairs insulin sensitivity in noninsulin -dependent diabetes mellitus. J Clin Endocrinol Metab 1998;83:1552–1557

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➤Educational background & professional experience

1990	Sangmyung Women's University Graduation	Home economics education / B.D.
1996	Graduate School of Sangmyung University Graduation	Food and nutrition / M.D.
2001	Graduate School of Sangmyung University Graduation	Food and nutrition / Ph.D.
2002-2005	Korea Food and Nutrition Foundation	Researcher
2001-2012	Sangmyung Univ., Konkuk Univ., Seokyeong Univ., Ansan Univ., Namseoul Univ., Yongin Univ., etc	Part-time lecturer
2007-2011	Cancer Epidemiology Branch, Research Institute, National Cancer Center	Visiting researcher
2009-present	FANSA(food and nutrition statistical analysis)	Director

➤Research interests

A study on the perception and practice levels of dietary life in children
A studies using KNHANES data: Relationship between disease and dietary life, food, nutrient intake, etc

➤Brief list of publications

1. Park J. Lee JS. Jang YA, Chung HR, Kim J. A comparison of food and nutrient intake between instant noodle consumers and non-instant noodle consumers in Korean adults. Nutr Res Pract 5(5):443-449, 2011.
2. Lee JS, Kim HYP, Choi YS, Kwak TK, Chung HR, Kwon S, Choi YJ, Lee SK, Kang MH. Comparison of perception and practice levels of dietary life in elementary school children according to gender and obesity Status. Korean J Nutr 44(6) : 527-536, 2011.
3. Kim J, Kang M, Lee JS, Inoue M, Sasazuki S, Tsugane S. Fermented and non-fermented soy food consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies. Cancer Sci 102(1) : 231-244, 2011.
4. Lee JS, Park J, Kim J. Dietary factors related to hypertension risk in Korean adults-data from the Korean national health and nutrition examination survey III. Nutr Res Pract 5(1):60-65, 2011.
5. Hong H, Lee JS. The Relationship between Food and Nutrient Intakes, Glycemic Index, Glycemic Load, and Body Mass Index among High School Girls in Seoul . Korean J Nutr 43(5):500-512, 2010.
6. Park J, Lee JS, Kim J. Relationship between dietary sodium, potassium, and calcium, anthropometric indexes, and blood pressure in young and middle aged Korean adults. Nutr Res Pract 4(2):155-162, 2010.
7. Kim J, Lee JS, Shin A, Kang MH, DS Shin, Chung HR, Kim WK. Sociodemographic and Lifestyle Factors are Associated with the Use of Dietary Supplements in a Korean Population. J Epidemio 20(3) : 197-203, 2010.
8. Kim HJ, Lim SY, Lee JS, Park S, Shin A, Choi BY, Shimazu T, Inoue M, Tsugane S, Kim J. Fresh and pickled vegetable consumption and gastric cancer in Japanese and Korean populations: A meta-analysis of observational studies. Cancer Sci 101(2) : 508-516, 2010.
9. Lee JS, Kim J. Factors Affecting the Use of Dietary Supplements by Korean Adults: Data from the Korean National Health and Nutrition Examination Survey III. J Am Diet Assoc. 109:1599-1605, 2009.
10. Kim J, Shin A, Lee JS, Youn S, Yoo KY. Dietary Factors and Breast Cancer in Korea: An Ecological Study. Breast J Nov-Dec;15(6):683-6, 2009.

• S6-3 •

How to measure of sodium intake & use of KNHANES data in people with diabetes mellitus

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Diabetes mellitus is not only influenced by various environmental factors but also dietary factors. In addition, it has been reported that the prevalence of hypertension or cardiovascular diseases is increased as the duration of diabetes increases. Recently, the government has been emphasizing the reduction of sodium intake to prevent hypertension or cardiovascular diseases. Although various types of studies have been conducted to find out the relationship between sodium intake and hypertension and various diseases, it is impossible for individual researchers to perform a large-scale study for the whole population. Thus, KNHANHES data can be considered as a tool for individual researchers to conduct a nation-level study to understand the relationship between disease and dietary intake. The KNHANES survey has been conducted since 1995, and its content has been supplemented every year. To measure dietary intakes of diabetic patients using KNHANES data, one can use health examination data and dietary survey data. That is, the presence of diabetes can be identified through health examination data, and then the nutrient intake including sodium can be figured out using 24-hour dietary survey data, and the intake per food can also be checked. However in KNHANES data, because samples are extracted using stratified sampling method, the analysis using general statistical methods is not appropriate and thus should use statistical packages for stratified sample analysis of SAS, SPSS, and STATA or use SUDAAN, a statistical program for stratified sampling data analysis.

In domestic and foreign presentations related to diabetes using KNHANES data, most of them are about the tendency of diabetes prevalence and the quality of life, and studies related to dietary factors are few. Among studies on diabetes and dietary factors, a study on the relationship between glycemic index, glycemic load and carbohydrate intake and diabetes prevalence rate showed that dietary glycemic index and dietary glycemic load did not affect the diabetes incidence in men but the risk for diabetes incidence was 2.34 times (Crude OR, 95% CI : 1.34-04.06) increased when the dietary glycemic load was over 260.5 in women. There is no study on the relationship between sodium intake and diabetes incidence using KNHANES data. Since diabetes related studies using KNHANES data has not been sufficiently conducted currently, it is hoped that various studies on the relationship between diabetes and dietary factors and the risk for the incidence of other diseases can be conducted by many investigators in the future.

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➤Educational background & professional experience

2000	Seoul National University, Seoul, Korea	Food and nutrition / Bachelor's degree
2005	Harvard University, Boston, MA	Epidemiology / Master of science
2005	Harvard University	Nutrition and epidemiology / Doctor of science
2003-2005	Harvard School of Public, Health, Boston, MA	Nutritional epidemiology/Graduate research assistant
2005-2007	Harvard School of Public, Health	Nutritional epidemiology/Research fellow
2007-2009	Brigham and Women's Hospital, and Harvard Medical School, Boston, MA	Nutritional epidemiology/Research fellow
2009-2010	Brigham and Women's Hospital	Nutritional epidemiology/Associate epidemiologist
2009-2010	Harvard Medical School	Nutritional epidemiology/Instructor
2010-present	Sookmyung Women's University, Seoul, Korea	Nutritional epidemiology/Assistant professor

➤Research interests

Dietary and biochemical factors associated with chronic disease incidence and survival
Nutrigenomic factors associated with chronic disease incidence and survival
Nutritional epidemiology methodology
Community-based nutritional status monitoring
Dietary interventions

➤Brief list of publications

1. Lee JE, Wei EK, Fuchs CS, Hunter DJ, Lee I-M, Selhub J, Stampfer MJ, Willett WC, Ma J, Giovannucci E. Plasma folate, methylenetetrahydrofolate reductase (MTHFR), and colorectal cancer risk in three large nested case-control studies. Lee JE and Wei EK contributed equally. Cancer Causes Control. 2012;23:537-45.
2. Kim HI, Kim K, Lee JE. Evaluating adherence to recommended diets among cancer patients. Support Care Cancer. 2012;20:2041-52.
3. Song DY, Song S, Song Y, Lee JE. Alcohol intake and renal cell cancer risk: a meta-analysis. Br J Cancer. 2012;106:1881-90.
4. Lee JE, Chan AT. Fruit, vegetables, and folate: cultivating the evidence for cancer prevention. Gastroenterology 2011;141:16-20.
5. Park JE, Lee JE. Cardiovascular disease risk factors and depression in Korean women: Results from the fourth Korean National Health and Nutrition Examination Survey. Psychiatry Res. 2011;190:232-9.
6. Lee JE, Baba Y, Ng K, Giovannucci E, Fuchs C, Ogino S, Chan AT. Statin use and colorectal cancer risk according to molecular subtypes in two large prospective cohort studies. Cancer Prev Res (Phila). 2011;11:1808-15.
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10. Lee JE, Hunter DJ, Spiegelman D, Adami H-O, Albanes D, Bernstein L, van den Brandt PA, Buring JE, Cho E, Folsom AR, Freudenheim JL, Giovannucci E, Graham S, Horn-Ross PL, Leitzmann MF, McCullough ML, Miller AB, Parker AS, Rodriguez C, Rohan TE, Schatzkin A, Schouten LJ, Virtanen M, Willett WC, Wolk A, Zhang SM, Smith-Warner SA. Alcohol Intake and Renal Cell Cancer in a Pooled Analysis of 12 Prospective Studies. J Natl Cancer Inst. 2007;99:801-10.

• S6-4 •

Plan of research on sodium intake in diabetic patients in Korea

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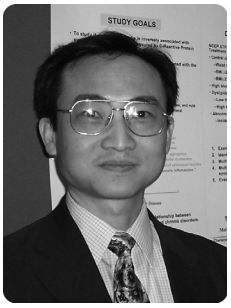
Sodium intake has been suggested to increase risk of hypertension, cardiovascular disease, and overall mortality. Because high blood pressure and unfavorable lipid profile are risk factors for complications among diabetic patients, blood pressure control is essential to minimize risk of progression of diabetes-related complications. Given more than 2 times higher intake of sodium, on average, than the current recommended daily intake in Korean adults, understanding of the effect of sodium intake on mortality and morbidity among diabetic patients is of considerable significance. However, the Dietary Approach to Stop Hypertension (DASH) trial which included participants with or without hypertension has been the basis for sodium intake guidelines for diabetic patients and there remains little evidence about the effect of sodium intake among diabetic patients. Therefore, further prospective and intervention studies in Korea should be actively conducted to provide health professionals and patients with Korean-specific evidence-based guidelines. Strengths and limitations of prospective and intervention studies and meta-analysis will be discussed and the relevant existing studies will be presented. Also, issues to consider in epidemiologic studies involving dietary measurement or dietary intervention, including complexity of diet, bias and interaction, and a possible strategy for reducing errors and bias will be discussed. Especially, when investigators conduct intervention studies in the clinical setting, appropriate selection of study design, study participants, study duration, exposures and outcomes may allow for the success of intervention study. Also, interaction with treatment, genes, and other disease condition, compliance and drop-out should be considered and examined in intervention studies. In summary, emphasis should be placed on research on sodium intake among patients with metabolic diseases in the clinical nutrition and well-designed Korean prospective and intervention studies on sodium intake are warranted.



Ka He

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➤Educational background & professional experience

2006-2009	Northwestern University	Assistant professor
2009-2012	University of North Carolina at Chapel Hill	Associate professor
2012-present	Indiana University at Bloomington	Professor and dept. chair

➤Research interests

My primary research interests lie in nutritional epidemiology, specifically, diet and nutrients in relation to cardiovascular disease, diabetes, obesity and cancer.

➤Brief list of publications

1. Xun P, Liu K, Cao W, Sidney S, Williams OD and He K: Fasting insulin level is positively associated with incidence of hypertension among American young adults: a 20-year follow-up study. Diabetes Care. 2012.
2. Xun P and He K: Fish consumption and incidence of diabetes: a meta-analysis of data from 438,000 individuals in 12 independent prospective cohorts with an average 11 years of follow-up. Diabetes Care. 35 (4): 930 – 938, 2012.
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4. Dong JY, Xun P, He K, and Qin LQ: Magnesium intake and risk of type 2 diabetes: meta-analysis of prospective cohort studies. Diabetes Care. 34 (9): 2116 – 2122, 2011.
5. Kim D, Xun P, Liu K, Loria C, Yokota K, Jacobs DR and He K: Magnesium intake in relation to systemic inflammation, insulin resistance and the incidence of diabetes. Diabetes Care. 33 (12): 2604 – 2610. 2010.
6. He K, Liu K, Daviglus ML, Morris SJ, Loria CM, Van Horn L, Jacobs DR Jr., and Savage PJ: Magnesium intake and incidence of metabolic syndrome among young adults. Circulation. 113: 1675-1682, 2006.
7. Song Y, He K, Levitan EB, Manson JE, and Liu S: Effects of oral magnesium supplementation on glycemic control in type 2 diabetes mellitus – a meta-analysis of controlled clinical trials. Diabetic Medicine. 23: 1050-1056, 2006.
8. He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, and Greenland P: Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. Circulation. 109: 2705-2711, 2004.
9. He K, Merchant AT, Rimm EB, Rosner BA, Stampfer M, Willett WC, and Ascherio A: Dietary fat intake and risk of stroke in male US health professionals – a 14-year prospective cohort study. British Medical Journal (BMJ), 7418: 777-782, 2003.
10. He K, Rimm EB, Merchant AT, Rosner BA, Stampfer M, Willett WC, and Ascherio A: Fish consumption and risk of stroke in men. Journal of American Medical Association (JAMA), 288 (24): 3130-3136, 2002.

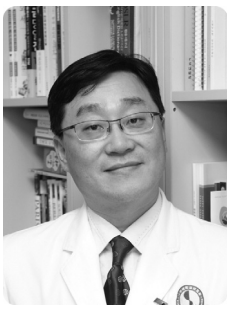
• S7-1 •

Magnesium intake and risk of diabetes and metabolic syndrome

Ka He

Indiana University, USA

A body of literature indicates a pivotal role of magnesium in glucose homeostasis and insulin secretion and action. Studies also suggest that higher intake of magnesium may decrease blood triglycerides and increase high-density lipoprotein cholesterol levels. We prospectively examined the relations between magnesium intake and incident diabetes and metabolic syndrome in approximately 5000 Americans, aged 18 to 30 years, who were free from metabolic syndrome and diabetes at baseline. Diabetes cases were diagnosed based on plasma glucose, OGTT, A1C, and anti-diabetes medications. Metabolic syndrome was determined according to the National Cholesterol Education Program/Adult Treatment Panel III definition. Diet was assessed by an interviewer-administered quantitative food frequency questionnaire, and magnesium intake was derived from the nutrient database developed by the Minnesota Nutrition Coordinating Center. After adjustment for major lifestyle variables and other potential confounders, magnesium intake was inversely associated with incident diabetes and metabolic syndrome. Compared the highest magnesium intake group to the lowest, multivariable-adjusted hazard ratio (95% confidence interval) were 0.69 (0.52 to 0.91, *P* for trend 〈 0.01) and 0.53 (0.32 to 0.86, *P* for trend 〈 0.01) for metabolic syndrome and diabetes, respectively. In conclusion, our findings suggest that young adults with higher magnesium intake have lower risk of development of diabetes and metabolic syndrome.



Dae Jung Kim

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➤Educational background & professional experience

1987-1993	Yonsei University College of Medicine	Medicine / M.D.
1999-2002	Yonsei University Graduate School of Medicine	Medicine / M.Sc.
1997-2001	Internal Medicine, Severance Hospital	Resident
2001-2002	Internal Medicine, Yonsei University College of Medicine	Clinical fellow
2002-2003	Endocrinology, NHIC Hospital	Doctor
2003-2007	Endocrinology, Ajou University School of Medicine	Assistant professor
2007-present	Endocrinology, Ajou University School of Medicine	Associate professor

➤Research interests

Epidemiology of diabetes, obesity and metabolic syndrome

➤Brief list of publications

1. Lee YH, Bang H, Kim HC, Kim HM, Park SW, Kim DJ. A Simple Screening Score for Diabetes for the Korean Population: Development, validation, and comparison with other scores. Diabetes Care. 2012 Aug;35(8):1723-30.
2. Choi YJ, Lee MS, An SY, Kim TH, Han SJ, Kim HJ, Chung YS, Lee KW, Kim DJ. The relationship between diabetes mellitus and health-related quality of life in Korean adults: The fourth Korea National Health and Nutrition Examination Survey (2007-2009). Diabetes Metab J 2011 Dec;35(6):587-594.
3. Kim DJ. The Epidemiology of Diabetes in Korea. Diabetes Metab J. 2011 Aug;35(4):303-308.
4. Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR Jr, He K. Magnesium Intake in Relation to Systemic Inflammation, Insulin Resistance, and the Incidence of Diabetes. Diabetes Care. 2010 Dec;33(12):2604-2610.
5. Choi YJ, Kim HC, Kim HM, Park SW, Kim J, Kim DJ. Prevalence and Management of Diabetes Mellitus in Korean Adults: Korea National Health and Nutrition Examination Surveys 1998-2005. Diabetes Care. 2009 Nov;32(11):2016-2020.

• S7-2 •

A simple screening score for diabetes for the Korean population

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We developed and validated a self-assessment score for diabetes risk in Korean adults. The Korea National Health and Nutrition Examination Survey (KNHANES) 2001 and 2005 data were used to develop a diabetes screening score. After excluding patients with known diabetes, 9,602 participants aged ≥ 20 years were selected. Undiagnosed diabetes was defined as a fasting plasma glucose ≥ 126 mg/dL and/or non-fasting plasma glucose ≥ 200 mg/dL. The SAS Survey Logistic Regression analysis was used to determine predictors of undiagnosed diabetes (n = 341). We validated our model and compared it with other existing methods using the KNHANES 2007~2008 data (n = 8,391).

Age, family history of diabetes, hypertension, waist circumference, smoking, and alcohol intake were independently associated with undiagnosed diabetes. We calculated a diabetes screening score (range 0~11), and a cut point of$5 defined 47% of adults as being at high risk for diabetes and yielded a sensitivity of 81%, specificity of 54%, positive predictive value of 6%, and positive likelihood ratio of 1.8 (area under the curve [AUC] = 0.73). Comparable results were obtained in validation datasets (sensitivity 80%, specificity 53%, and AUC = 0.73), showing better performance than other non-Asian models from the U.S. or European population.

This self-assessment score may be useful for identifying Korean adults at high risk for diabetes. Additional studies are needed to evaluate the utility and feasibility of this score in various settings.

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➤Educational background & professional experience

2005	Department of Medicine and Therapeutics, Chinese University of Hong Kong (CUHK)	Professor of medicine and therapeutics
2005	Faculty of Medicine, CUHK	Assistant dean
2005	Hong Kong Institute of Diabetes and Obesity, CUHK	Director
2007	Asia Diabetes Foundation	Chief executive officer

➤Research interests

Epidemiology, genetics, clinical trials and care models of diabetes with particular reference to young onset diabetes, kidney disease, cancer and depression

➤Brief list of publications

1. Yang XL, So WY, Ma RCW, Kong APS, Xu G, Chan JCN. Diabetes and cancer: the mechanistic Implications of epidemiological analyses from the Hong Kong Diabetes Registry. Diabetes Metab Res Rev 2012:10.1002/dmrr.2287.
2. Chan JC, So WY, Ma RCW, Tong P, Wong R, Yang XL. The complexity of both vascular and non-vascular complications of diabetes: The Hong Kong Diabetes Registry. Curr Cardiovasc Risk Rep 2011;5:230-9.
3. So WY, Raboca J, Sobrepena L, et al. Comprehensive risk assessments of diabetic patients from seven Asian countries: The Joint Asia Diabetes Evaluation (JADE) program. J Diabetes 2011;3:109-18.
4. Ko GT, So WY, Tong PC, et al. From design to implementation--the Joint Asia Diabetes Evaluation (JADE) program: a descriptive report of an electronic web-based diabetes management program. BMC Med Inform Decis Mak 2010;10:26.
5. Chan JC, Malik V, Jia W, et al. Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 2009;301:2129-40.
6. Chan JCN, So WY, Ko G, et al. The Joint Asia Diabetes Evaluation (JADE) Program: A Web-based Program To Translate Evidence To Clinical Practice in Type 2 Diabetes. Diabetic Med 2009;26:693-9.
7. Chan JCN, So WY, Yeung CY, et al. The SURE Study: Effects of Structured versus Usual care on Renal Endpoint in Type 2 diabetes: A randomized multi-centre translational study Diabetes Care 2009;32:977-82.
8. Wu JY, Leung WY, Chang S, et al. Effectiveness of telephone counselling by a pharmacist in reducing mortality in patients receiving polypharmacy: randomised controlled trial. BMJ 2006;333:522.

Quality diabetes care - from research to practice

Juliana C.N. Chan

Chinese University of Hong Kong, Chinese Hong Kong

Diabetes is a complex disease characterized by chronic hyperglycemia and multiple phenotypes. In 1995, we used a doctor-nurse-clerk team and structured protocol to establish the Hong Kong Diabetes Registry in a quality improvement program. The detailed phenotypes at enrollment and follow-up medications have allowed us to develop a series of risk equations to predict multiple endpoints with high sensitivity and specificity. Using this registry, we were able to validate findings from clinical trials in real practice, confirm close links between cardiovascular and renal disease, and demonstrate the emerging importance of cancer as a leading cause of death. Inspired by the extremely low clinical endpoints in clinical trial settings, we systematically proven the marked benefits of protocol-guided team-based care. In 2007, we incorporated these risk equations, care protocols and decision support into the web-based Joint Asia Diabetes Evaluation (JADE) Program to enable doctors to establish their own clinic registries and to promote shared and informed decision between doctors and patients. More than 35,000 patients from Asia have been enrolled in this ongoing registry and patients who underwent repeat assessments had significant improvement in risk factor control suggesting that systemic collection and communication of information have reduced clinical inertia and improved self care. These research findings highlight the importance of using an integrated approach including change of practice environment and use of team and protocol to translate evidence to practice with ongoing evaluation.

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➤Educational background & professional experience

1985-1991	Catholic University College of Medicine	Medicine / M.D.
1991-1996	Kangnam St. Mary's Hospital	Int. Medicine/ Intern, residency
1996-1999	Army	Physician/Lieutenant
1999-2001	St. Mary;s Hospital	Clinical instructor
2006-2012	ungkyunkwan University, Kangbuk Samsung Hospital	Assistant & Associate Prof. / Ph.D.
2012-present	Sungkyunkwan University, Kangbuk Samsung Hospital	

➤Research interests

Insulin resistance, obesity and beta cell physiology

➤Brief list of publications

1. Lee J, Hong SW, Chae SW, et al. Exendin-4 improves steatohepatitis by increasing Sirt1 expression in high-fat-diet-induced obese C57BL/6J mice. PLOS one 2012:7(2):e31394.
2. Hong SW, Lee J, Park SE, et al. Repression of sterol regulatory element-binding protein 1-c is involved in the protective effects of exendin-4 in pancreatic β-cell line. Mol Cell Endocrinol 2012;362(1-2):242-52.
3. Bae JC, Rhee EJ, Lee WY, et al. Combined Effect of Nonalcoholic Fatty Liver Disease and Impaired Fasting Glucose on the Development of Type 2 Diabetes: A 4-year retrospective longitudinal study. Diabetes Care 2011: 34(3):727-9.
4. Seo MH, Bae JC, Park SE, et al. Association of lipid and lipoprotein profiles with future development of type 2 diabetes in nondiabetic korean subjects: a 4-year retrospective, longitudinal study. J Clin Endocrinol Metab. 2011;96(12):E2050-4.
5. Bae JC, Rhee EJ, Lee WY, et al. Optimal range of HbA1c for the prediction of future diabetes: A 4-year longitudinal study. Diabetes Res Clin Pract. 2011:93(2):255-9.
6. Rhee EJ, Lee WY, et al. A multicenter, randomized, placebo-controlled, double-blind phase II trial evaluating the optimal dose, efficacy and safety of LC 15-0444 in patients with type 2 diabetes. Diabetes Obes Metab 2010:12(12):1113-9.
7. Bae JC, Cho YK, Lee WY, et al. Impact of Nonalcoholic Fatty Liver Disease on Insulin Resistance in Relation to HbA1c Levels in Nondiabetic Subjects. Am J Gastroenterol. 2010:105(11):2389-95.

Lipid, lipoprotein and risk for type 2 diabetes

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Recent data suggest that changes in HDL and LDL could also influence beta cell function and mass, implying a role for lipoprotein particles in the pathogenesis of type 2 diabetes mellitus (T2DM).

It was reported that ABCA1 deletion provokes cholesterol accumulation in the beta cell membrane and subsequently inhibits insulin secretion. It was also suggested that HDLs can inhibit beta cell apoptosis.

HDLs are reported to enhance cellular glucose uptake in cultures of primary human skeletal muscle cells isolated from patients with T2DM. Thus, basic experimental studies display that HDLs have improve glucose homeostasis by both preserving beta cell function and by enhancing skeletal muscle glucose uptake.

Recent clinical data also suggest that lipid and lipoprotein profiles can be independently associated with development of T2DM both in cross-sectional and longitudinal studies. I would present the data on the relation between lipoproteins and glucose metabolism.

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➤Educational background & professional experience

1996-2000	Department of Internal Medicine, Kyunghee University Medical Center	Resident
1997-1999	Internal Medicine, Kyunghee University School of Medicine	M.S.
2000-2002	Endocrinology, Internal Medicine, Kyunghee University School of Medicine	Ph.D.
2000-2003	Department of Endocrinology and Metabolism, Kyunghee University Medical Center	Clinical instructor
2003-2008	Endocrinology and Metabolism, Department of Internal Medicine, Hallym Sacred Heart Hospital	Assistant professor
2005-2009	Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan university	Assistant professor
2009-present	Endocrinology and Metabolism, Department of Internal Medicine, Kangbuk Samsung Hospital, Sungkyunkwan university	Assistant professor

➤Research interests

Diabetes, obesity and metabolism

➤Brief list of publications

1. Kim WJ, Park CY, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW, Kim SW, Song SJ. The association between regional arterial stiffness and diabetic retinopathy in type 2 diabetes. Atherosclerosis 2012 Sep 13 Epub ahead of print].
2. Kim WJ, Park CY. 1,5-anhydroglucitol in diabetes mellitus. Endocrine. 2012 Jul 31. [Epub ahead of print]
3. Koo DH, Park CY, Lee ES, Ro JS, Oh SW. Progranulin as a Prognostic Biomarker for Breast Cancer Recurrence in Patients Who Had Hormone Receptor-Positive Tumors: A Cohort Study. PLoS One. 2012;7(6):e39880.
4. Won JC, Park CY, Oh SW, Park SW. Increased plasma levels of retinol-binding protein 4 with visceral obesity is associated with cardiovascular risk factors. Journal of Diabetes Investigation 2012.
5. Park CY, Park SW. Role of peroxisome proliferator-activated receptor gamma agonist in improving hepatic steatosis: Possible molecular mechanism. Journal of Diabetes Investigation 2012; 3(2):93-95.
6. Kim WJ, Park CY, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW, Kim SW, Park HS, Kim YJ, Song SJ, Ahn HY. Serum 1,5-Anhydroglucitol is associated with diabetic retinopathy in type 2 diabetes. 2012 Sep;29(9):1184-90.
7. Kim WJ, Park CY, Lee KB, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW. Serum 1,5-Anhydroglucitol Concentrations Are a Reliable Index of Glycemic Control in Type 2 Diabetes With Mild or Moderate Renal Dysfunction. Diabetes Care. 2012 Feb;35(2):281-6. Epub 2011 Dec 30.
8. Yang SJ, Choi JM, Chae SW, Kim WJ, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW, Kim SW, Park CY. Activation of Peroxisome Proliferator-Activated Receptor Gamma by Rosiglitazone Increases Sirt6 Expression and Ameliorates Hepatic Steatosis in Rats. PLoS ONE 2011 Feb 23;6(2):e17057.
9. Yang SJ, Choi JM, Kim L, Kim BJ, Sohn JH, Kim WJ, Park SE, Rhee EJ, Lee WY, Oh KW, Park SW, Kim SW, Park CY. 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. Biochem Biophys Res Commun. 2011 Apr 1.;407(1):153-7, Epub 2011 Mar 1.
10. Kang JG, Park CY, Ihm SH, Yoo HJ, Park H, Rhee EJ, Won JC, Lee WY, Oh KW, Park SW, Kim SW. Mechanisms of Adipose Tissue Redistribution with Rosiglitazone Treatment in Various Adipose Depots. Metabolism 59, 46-53, 2010.

• S8-1 •

Two NAD donors differently regulate the NAD-sirtuin pathway in terms of glucose control and hepatic steatosis

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Sirtuins is a family of proteins with NAD^+-dependent deacetylase and ADP-ribosyltransferase activities. It have been suggested as metabolic regulators and potential therapeutic targets for metabolic syndrome. Nicotinic acid (NA) and nicotinamide (NAM) are major forms of niacin and exert their physiological functions as nicotinamide adenine dinucleotide (NAD). We investigate the effects of two NAD donors, NA and NAM on glucose control and hepatic NAD-sirtuin pathway. The effects were investigated in AML12 hepatocyte cell line and OLETF rat, a rodent model of obesity and type 2 diabetes. With HF condition, NAM improved serum fasting glucose and area under the curve of oral glucose tolerance test, serum adiponectin, and serum triglyceride. With regard to NAD-sirtuin pathway, intracellular nicotinamide phosphoribosyltransferase (iNampt), NAD, NAD/NADH ratio, mRNA expression of Sirt1 and Sirt1 activity were increased in livers of NAM-treated condition. NA treatment did not exert evident effects as shown with the treatment of NAM. These results demonstrate that two NAD donors, NA and NAM differently regulate the NAD-sirtuin pathway in treatment- and dose-specific ways, suggesting complexity in the NAD-sirtuin pathway.

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➤Educational background & professional experience

1982	Kyungpook National University, Daegu, Korea	M.D.
1988	Kyungpook National University, Daegu, Korea	Ph.D.
1994-1995	Harvard Medical School, Boston	Research fellow
1998-2005	Dept. of Int. Medicine Keimyung University Medical School, Daegu	Professor
2005-present	Dept. of Int. Med., Kyungpook National Univ. Med. School, Daegu	Professor
2008-present	World Class Univ. Project, Kyungpook National University	Principal investigator
2009-present	Res. Inst. of Aging & Metabolism, Kyungpook National University	Director
2011-present	Mid-Career researcher:National Research Lab program, Kyungpook National University	Principal investigator
2011-present	Leading-edge Research Center for Drug Discovery and Development for Diabetes and Metabolic Diseases, Kyungpook National University Hospital, Daegu	Vice director
2012-present	Bio-Medical Research Institute, Kyungpook National University Hospital, Daegu	Director

➤Research interests

Diabetes and diabetic complications
Fatty liver (liver steatosis) and liver fibrosis
Pancreatic b-cell function (ER stress)

➤Brief list of publications

1. Lee KM, Seo YJ, Kim MK, Seo HA, Jeong JY, Choi HS, Lee IK, Park KG. Mediation of glucolipotoxicity in INS-1 rat insulinoma cells by small heterodimer partner interacting leucine zipper protein (SMILE). Biochem Biophys Res Commun. 2012 Mar 23;419(4):768-73.
2. Oh CJ, Kim JY, Min AK, Park KG, Harris RA, Kim HJ, Lee IK. Sulforaphane attenuates hepatic fibrosis via NF-E2-related factor 2-mediated inhibition of transforming growth factor-β/Smad signaling. Free Radic Biol Med. 2012 Feb 1;52(3):671-82.
3. 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. 2012 Feb:16(2):273-286.
4. Jung GS, Kim MK, Jung YA, Kim HS, Park IS, Min BH, Lee KU, Kim JG, Park KG, Lee IK. Clusterin Attenuates the Development of Renal Fibrosis. J Am Soc Nephrol. 2012 Jan:23(1):73-85
5. 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.
6. 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..
7. Kim HJ, Yoo EK, Kim JY, Choi YK, Lee HJ, Kim JK, Jeoung NH, Lee KU, Park IS, Min BH, Park KG, Lee CH, Aronow BJ, Sata M, Lee IK. Protective role of clusterin/apolipoprotein J against neointimal hyperplasia via antiproliferative effect on vascular smooth muscle cells and cytoprotective effect on endothelial cells. Arterioscler Thromb Vasc Biol. 2009 Oct 29(10):1558-1564.

Differential regulation of of PDK isotype and PDH flux in non-alcoholic fatty liver disease (NAFLD)

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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 Four isoforms of PDK (PDK1-4) have been identified in mammals and are expressed in in a tissue-specific manner. The expression level of PDK4 is increased in peripheral tissues of starved and diabetic human and rodents. Previously we had reported that PDK4 deficiency in mice ameliorates the hyperglycemia induced by high saturated fat diet compared to wild type mice due to reduce the plasma levels of gluconeogenic substrates(pyruvate, lactate and alanine). Reduction of plasma gluconeogenic substrate in PDK4 knockout (PDK4-/-) mice is caused by increase of pyruvate oxidation in skeletal muscle due to increase the PDC activity. However, we observed that the PDK4 deletion did not affect hepatic PDC activity. In addition, the expression level of PDK4 is decreased in livers of high saturated fat diet mice. These results suggest that PDK4 may not play an important role in regulation of PDC activity in the liver especially in high fat diet induced obesity. We and other group have reported that PDK2, a constitutively expressed in all tissues, is also up-regulated in several tissues including liver by high fat diet induced obesity animals. Based on these observations, we hypothesized that PDK2 presumably plays a pivotal role in regulation of PDC activity, leading to orchestrate the hepatic glucose and lipid metabolism.

However, how much PDK2 play on the regulation of PDC activity in the liver as well as PDK2 could play an important role on the abnormality of glucose-fatty acid metabolism in diet induced non-alcoholic fatty liver disease still remains unclear. In order to answer these questions, we used the PDK2 knockout (PDK2-/-) mice under condition of a high fat diet. Here, we report that PDK2 deficiency in high fat diet fed mice increase the hepatic fatty acid oxidation and ketogenesis, and decrease hepatic fatty acid synthesis, thereby leading to the protective effect of progressing hepatic steatosis along with the improvement of the hepatic insulin resistance. We also observe that hepatic anapleotic influx from pyruvate and TCA cycle intermediates are increased by high fat diet, which leads to induce the non-alcoholic fatty liver disease in wild type mice while those are normalized in PDK2-/- mice. The data of this study suggest that PDK2 plays an important role in progression of diet induced non-alcoholic fatty liver disease and hepatic insulin resistance, indicating that PDK2 is a potential therapeutic target to prevent obesity and NAFLD.

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➤Educational background & professional experience

1987-1993	Kobe University School of Medicine, Kobe, Japan, Awarded the degree of M.D.	M.D.
1996-2001	Kobe University Graduate School of Medicine, working on molecular mechanism of insulin resistance. Awarded the degree of Ph.D. (Supervised by Prof. Masato Kasuga)	Ph.D.
1996-2003	Division of Diabetes, Digestive and Kidney Diseases, Department of Clinical Molecular Medicine, Kobe University Graduate School of Medicine	Research associate
1993-1994	Department of Internal Medicine, Kobe University School of Medicine	Resident
1994-1996	Internal Medicine, Nishiwaki City Hospital	Resident
2003-2007	Diabetes and Endocrinology Research Center at Columbia University, New York, NY (Supervised by Prof. Domenico Accili)	Post doctoral research / Scientist
2007-2008	Division of Diabetes, Metabolism and Endocrinology, Department of Internal Medicine, Kobe, Japan	Research associate
2008-2010	Department of Clinical Pharmacology, Research Institute, International Medical Center of Japan, Tokyo, Japan	Director
2010-present	Department of Molecular Metabolic Regulation, Diabetes Research Center, Research Institute, National Center for Global Health and Medicine, Tokyo, Japan	Director

➤Research interests

Our research interests are the molecular mechanism of insulin action, the transcriptional control of energy metabolism and the pathogenesis of diabetes.

➤Brief list of publications

1. CITED2 links hormonal signaling to PGC-1α acetylation in regulation of gluconeogenesis. Sakai M, Matsumoto M, Tujimura T, Cao Yongheng, Noguchi T, Inagaki K, Inoue H, Hosooka T, Takazawa K, Kido Y, Yasuda K, Hiramatsu R, Matsuki Y, Kasuga M. Nat Med. 18(4): 612-7, 2012.
2. Overexpression of KLF15 in adipocytes of mice results in down-regulation of SCD1 expression in adipocytes and consequent enhancement of glucose-induced insulin secretion. Nagare T, Sakaue H, Matsumoto M, Cao Y, Inagaki K, Sakai M, Takashima Y, Nakamura K, Mori T, Okada Y, Matsuki Y, Watanabe E, Ikeda K, Taguchi R, Kamimura N, Ohta S, Hiramatsu R, Kasuga M. J Biol Chem. 286(43): 37458-69, 2011.
3. The obesity susceptibility gene Cpe links FoxO1 signaling in hypothalamic pro-opiomelanocortin neurons with regulation of food intake. Plum L, Lin HV, Dutia R, Tanaka J, Aizawa KS, Matsumoto M, Kim AJ, Cawley NX, Paik JH, Loh YP, DePinho RA, Wardlaw SL, Accili D. Nat Med. 15(10): 1195-201, 2009.
4. Impaired regulation of hepatic glucose production in mice lacking the forkhead transcription factor Foxo1 in liver. Matsumoto M, Pocai A, Rossetti L, Depinho RA, Accili D. Cell Metab. 6(3): 208-16, 2007.
5. Dual role of transcription factor FoxO1 in controlling hepatic insulin sensitivity and lipid metabolism. Matsumoto M, Han S, Kitamura T, Accili D. J Clin Invest. 116(9): 2464-72, 2006.
6. Role of STAT-3 in regulation of hepatic gluconeogenic genes and carbohydrate metabolism in vivo. 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. Nat Med. 10(2): 168-74, 2004.
7. PKClambda in liver mediates insulin-induced SREBP-1c expression and determines both hepatic lipid content and overall insulin sensitivity. Matsumoto M, Ogawa W, Akimoto K, Inoue H, Miyake K, Furukawa K, Hayashi Y, Iguchi H, Matsuki Y, Hiramatsu R, Shimano H, Yamada N, Ohno S, Kasuga M, Noda T. J Clin Invest. 112(6): 935-44, 2003.
8. Role of the insulin receptor substrate 1 and phosphatidylinositol 3-kinase signaling pathway in insulin-induced expression of sterol regulatory element binding protein 1c and glucokinase genes in rat hepatocytes. Matsumoto M, Ogawa W, Teshigawara K, Inoue H, Miyake K, Sakaue H, Kasuga M. Diabetes 51(6): 1672-80, 2002.
9. Hyperinsulinemia, glucose intolerance, and dyslipidemia induced by acute inhibition of phosphoinositide 3-kinase signaling in the liver. Miyake K, Ogawa W, Matsumoto M, Nakamura T, Sakaue H, Kasuga M. J Clin Invest. 110(10): 1483-91, 2002.
10. Inhibition of insulin-induced activation of Akt by a kinase-deficient mutant of the epsilon isozyme of protein kinase C. Matsumoto M, Ogawa W, Hino Y, Furukawa K, Ono Y, Takahashi M, Ohba M, Kuroki T, Kasuga M. J Biol Chem. 276(17): 14400-6, 2001.

CITED2: a new player in hormonal regulation of hepatic gluconeogenesis

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In mammals deprived of food, induction of hepatic gluconeogenesis is important to ensure energy homeostasis in response to the energy demand. However, such induction is dysregulated in type 2 diabetes, resulting in the development of fasting hyperglycemia. Hormonal and nutrient regulation of metabolic adaptation during fasting is mediated predominantly by the transcriptional coactivator PGC-1α (peroxisome proliferator-activated receptor gamma-coactivator-1α) in concert with various other transcriptional regulators including the transcription factors FoxO1, HNF-4α and CREB as well as the histone acetyltransferse CBP. Although CITED2 (CBP/p300-interacting transactivator with glutamic acid- and aspartic acid–rich COOH-terminal domain 2) interacts with many of these molecules, the role of this protein in regulation of hepatic gluconeogenesis has been unknown. We investigated the role of CITED2 in hepatic gluconeogenesis by using gain- and loss-of-function approaches in vitro and in vivo. The abundance of CITED2 was found to be increased in the liver of mice by fasting as well as in cultured hepatocytes by glucagon and cAMP signaling. CITED2 inhibited the acetylation of gluconeogenic transcriptional coactivator PGC-1α by blocking its interaction with GCN5, a key acetyltransferase for PGC-1α. The consequent reduction in the level of PGC-1α acetylation resulted in an increase in its transcriptional coactivation activity and up-regulation of the expression of gluconeogenic genes. In addition, the interaction of CITED2 with GCN5 was found to be disrupted by insulin in a manner dependent on phosphoinositide 3-kinase (PI3K) signaling. These results thus reveal that CITED2 functions as a transducer of glucagon and insulin signaling in the regulation of PGC-1α activity associated with the transcriptional control of gluconeogenesis, and that this function is mediated through modulation of GCN5-dependent acetylation of PGC-1α.

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➤Educational background & professional experience

1997	School of Medicine, Kanazawa University	M.D.
2003	Endocrinology and Metabolism, Graduate School of Medical Science, Kanazawa University	Ph.D.
2005	Columbia University College of Physicians and Surgeons	Postdoctoral research scientist
2008	Frontier Science Organization, Kanazawa University (tenure-track)	Assistant professor
2012-present	Department of Cell Metabolism and Nutrition, Brain/Liver Interface Medicine Research Center, Kanazawa University (tenure granted)	Associate professor

➤Research interests

Diabetes and immune system, lipoprotein metabolism and NAFLD

➤Brief list of publications

1. Kitade H, Sawamoto K, Nagashimada M, Inoue H, Yamamoto Y, Sai Y, Takamura T, Yamamoto H, Miyamoto K, Ginsberg HN, Mukaida N, Kaneko S, Ota T: CCR5 plays a critical role in obesity- induced adipose tissue inflammation and insulin resistance by regulating both macrophage recruitment and M1/M2 status. Diabetes IN PRESS doi:10.2337/db11-1506.
2. Kimura K, Yamada T, Matsumoto M, Kido Y, Hosooka T, Asahara S, Matsuda T, Ota T, Watanabe H, Sai Y, Miyamoto K, Kaneko S, Kasuga M, Inoue H: Endoplasmic reticulum stress inhibits STAT3-dependent suppression of hepatic gluconeogenesis via dephosphorylation and deacetylation. Diabetes 61:61-73, 2012.
3. Caviglia JM, Gayet C, Ota T, Hernandez-Ono A, Conlon DM, Jiang H, Fisher EA, Ginsberg HN: Different fatty acids inhibit apolipoprotein B100 secretion by different pathways: Unique roles for endoplasmic reticulum stress, ceramide, and autophagy. J Lipid Res 52:1636-1651, 2011.
4. 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, 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 12:483-495, 2010.
5. Uno M, Kurita S, Misu H, Ando H, Ota T, Matsuzawa-Nagata N, Kita Y, Nabemoto S, Akahori H, Zen Y, Nakanuma Y, Kaneko S, Takamura T: Tranilast, an antifibrogenic agent, ameliorates a dietary rat model of nonalcoholic steatohepatitis. Hepatology 48:109-118, 2008.
6. Ota T, Gayet C, Ginsberg HN: Inhibition of apolipoprotein B100 secretion by lipid-induced hepatic endoplasmic reticulum stress in rodents. J Clin Invest 118:316-332, 2008.
7. Ota T, Takamura T, Kurita S, Matsuzawa N, Kita Y, Uno M, Akahori H, Misu H, Sakurai M, Zen Y, Nakanuma Y, Kaneko S: Insulin resistance accelerates a dietary rat model of nonalcoholic steatohepatitis. Gastroenterology 132:282-293, 2007.
8. Ota T, Takamura T, Kaneko S: Pioglitazone in nonalcoholic steatohepatitis. N Engl J Med 356: 1068-1069, 2007.
9. Matsuzawa N, Takamura T, Kurita S, Misu H, Ota T, Ando H, Yokoyama M, Honda M, Zen Y, Nakanuma Y, Miyamoto K, Kaneko S: Lipid-induced oxidative stress causes steatohepatitis in mice fed an atherogenic diet. Hepatology 46:1392-1403, 2007.
10. Ota T, Takamura T, Ando H, Nohara E, Yamashita H, Kobayashi K: Preventive effect of cerivastatin on diabetic nephropathy through suppression of glomerular macrophage recruitment in a rat model. Diabetologia 46:843-851, 2003.

Chemokine systems: a potential link between obesity and insulin resistance

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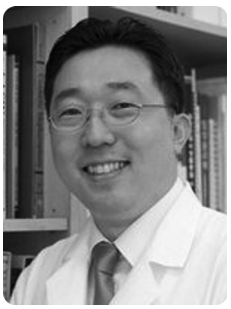
Obesity involves a state of chronic low-grade systemic inflammation. This inflammation causes insulin resistance and metabolic disorders including type 2 diabetes and metabolic syndrome. Although the factors that initiate this inflammatory response remain to be fully identified, increasing evidence supports the conclusion that obesity-induced inflammation is mediated primarily by immune cells such as the macrophages and T lymphocytes in metabolic tissues. In particular, a significant advance in our understanding of obesity-associated inflammation and insulin resistance has been recognition of the critical role of adipose tissue macrophages (ATMs).

ATM accumulation through C-C motif chemokine receptor 2 (CCR2) and its ligand monocyte chemoattractant protein-1 (MCP-1) is considered pivotal in the development of insulin resistance. However, chemokine systems appear to exhibit a high degree of functional redundancy. To-date, more than 50 chemokines exhibiting various physiological and pathological properties have been discovered. In addition, all chemokines signal via seven-transmembrane G-protein-coupled receptors and chemokine receptors have overlapping ligand specificities. Therefore, additional, unidentified chemokine/chemokine receptor pathways that may play significant roles in ATM recruitment and insulin sensitivity remain to be fully identified.

Our new study has shown that CCR5, a different CC chemokine receptor, plays an important role in the inflammatory response of adipose tissue to obesity by regulating both macrophage recruitment and M1/M2 status. We found that $CCR5^+$ ATMs accumulate in white adipose tissue of obese mice. Furthermore, CCR5 ablation in mice prevents insulin resistance, diabetes, and fatty liver induced by high-fat feeding. Importantly, the beneficial effects of CCR5 deficiency are due to both the decrease in ATM recruitment and the M2-dominant shift in ATM polarization. Taken together, these data indicate that CCR5 is a novel link between obesity, adipose tissue inflammation, and insulin resistance. Finally, I will discuss how CCR5 and MCP-1-CCR2 as well as other chemokine systems, connect obesity, inflammation, and insulin resistance.



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➤Educational background & professional experience

1992-1998	Seoul National University College of Medicine, Seoul, Korea	M.D.
2001-2006	Postgraduate School, Seoul National University, Seoul, Korea	Ophthalmology / Ph.D.
1998-1999	Internship, Seoul National University Hospital, Seoul, Korea	
1999-2003	Residency in Dept. of Ophthalmology, Seoul National University Hospital, Seoul, Korea	Ophthalmology
2003-2006	Public Health Doctor, Gyonggi Province 2nd Office, Euijeongbu-si, Gyonggi Province, Korea	
2006-2007	Clinical Instructor in Dept. of Ophthalmology, Seoul National University Hospital, Seoul, Korea	
2007-present	Clinical Professor in Dept. of Ophthalmology, Seoul National University Hospital, Seoul, Korea	
2010-present	Assistant Professor, Seoul National University College of Medicine, Seoul, Korea	

➤Research interests

1. Blood-retinal barrier: regulatory mechanism to form and maintain blood-retinal barrier at the interface of neurogenesis, gliogenesis and angiogenesis
2. Retinal vascular diseases following blood-retinal barrier: Retinopathy of prematurity, diabetic retinopathy, age-related macular degeneration
3. Tumor angiogenesis in retinoblastoma
4. Normal eye development

➤Brief list of publications

1. Lim Y, Jo DH, Kim JH, Ahn JH, Hwang YK, Kang DK, Chang SI, Yu YS, Yoon Y, Kim JH. Human Apolipoprotein(a) Kringle V Inhibits Ischemia-Induced Retinal Neovascularization via Suppression of Fibronectin-Mediated Angiogenesis. Diabetes. 2012 Jun;61(6):1599-608. Epub 2012 Mar 16. PubMed PMID: 22427380.
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3. Heo JW, Kim JH, Cho CS, Jun HO, Kim DH, Yu YS, Kim JH. Inhibitory activity of bevacizumab to differentiation of retinoblastoma cells. PLoS One. 2012;7(3):e33456. Epub 2012 Mar 22. PubMed PMID: 22457763; PubMed Central PMCID: PMC3310877.
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5. Jo DH, Kim JH, Yu YS, Lee TG, Kim JH. Antiangiogenic Effect of Silicate Nanoparticle on Retinal Neovascularization Induced by Vascular Endothelial Growth Factor. Nanomedicine. 2011 Sep 21. [Epub ahead of print].
6. Kim JH, Yu YS, Kim KW, Kim JH. Investigation of barrier characteristics in the hyaloid-retinal vessel of zebrafish. J Neurosci Res. 2011 Jun;89(6):921-8. doi: 10.1002/jnr.22607. Epub 2011 Mar 15. PubMed PMID: 21412815.
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8. Kim JH, Kim JH, Yu YS, Mun JY, Kim KW. Autophagy-induced regression of hyaloid vessels in early ocular development. Autophagy. 2010 Oct 1;6(7):922-8. Epub 2010 Oct 11. PubMed PMID: 20818164.
9. Kim JH, Yu YS, Kim KW, Kim JH. Impaired retinal vascular development in anencephalic human fetus. Histochem Cell Biol. 2010 Sep;134(3):277-84. Epub 2010 Jul 27. PubMed PMID: 20661586.
10. Kim JH, Kim JH, Jun HO, Yu YS, Kim KW. Inhibition of Protein Kinase C {delta} Attenuates Blood-Retinal Barrier Breakdown in Diabetic Retinopathy. Am J Pathol. 2010 Mar;176(3):1517-24. Epub 2010 Jan 28. PubMed PMID: 20110406.

• S9-1 •

Strategy targeting to VEGF-mediated blood retinal barrier breakdown in diabetic retinopathy

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The blood-retinal barrier (BRB) is essential for the normal structural and functional integrity of the retina. As the BRB serves critical functions in the eye, the BRB breakdown followed by retinal or choroidal neovascularization could therefore result in the serious vision loss. In the retina, hypoxic-ischemic stress appears to be an important cause of BRB breakdown. In particular, retinal ischemia leads to inner BRB breakdown, which is characterized by vascular leakage due to increased vascular permeability. Vascular endothelial growth factor (VEGF), the best known pro-angiogenic factor, is originally isolated as a vascular permeability factor to increase the vascular permeability of microvessels *via* uncoupling of junctional molecules in endothelial cells. It has been known that VEGF, sufficient to induce vascular abnormalities including vascular leakage, microangiopathy, and neovascularization plays a major role in the initiation and development of variable retinopathies. That is, VEGF-mediated alteration of tight junction proteins leads to BRB breakdown which result in retinal neovascularization. Actually, with recent development of anti-VEGF therapy using anti-VEGF antibody, the visual outcome in patients with retinal and choroidal vascular diseases has been revolutionarily improved.

Based on my recent results, I'd like to suggest that targeting to VEGF-mediated BRB breakdown could be a therapeutic strategy to diabetic retinopathy.

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➤Educational background & professional experience

1977-1981	Ewha Womans University, Seoul, Korea	Pharmacy, B.S.
1981-1987	University of Minnesota, Mpls., MN, U.S.A.	Pharmacology, Ph.D.
1990-2000	Yonsei University College of Medicine / Pharmacology	Associate professor
1990-1991	Tokyo University Faculty of Medicine, Tokyo, Japan	Pharmacology, visiting scholar
1994-1995	University of California College of Medicine, Irvine, CA, USA	Nephrology, visiting scholar
2000-2003	Hyonam Kidney Laboratory, Soon Chun Hyang University	Pharmacology, associate professor
2003-present	Ewha Woman University College of Pharmacy	Pharmacology, professor

➤Research interests

Pathogenesis of diabetic kidney injury
Mechanism of reactive oxygen species-induced tissue injury

➤Brief list of publications

1. Huh JY, Son D, Lee Y, Lee J, Kim B, Lee HM, Jo H, Choi S, Ha H, Chung M-H: 8-hydroxy-2-deoxyguanosine prevents plaque formation and inhibits vascular smooth muscle cell activation through Rac1 inactivation. Free Rad Biol Med 53(1):109-121, 2012.
2. Hwang I, Lee J, Huh JY, Park J, Lee HB, Ho Y-S, Ha H: Catalase deficiency accelerates diabetic renal injury through peroxisomal dysfunction. Diabetes 61 (3):728-738, 2012.
3. Huh JY, Kim Y, Jeong J, Park J, Kim I, Huh KH, Kim YS, Woo HA, Rhee SG, Lee K-J, HaH: Peroxiredoxin 3 is a key molecule regulating adipocyte oxidative stress, mitochondrial biogenesis, and adipokine expression. Antioxid Redox Sign 16 (3): 229-243, 2012.
4. Lee E, Seo E, Kwon Y, Ha H: A Rapid and reliable measurement for evaluating directly the reactivity of N-acetylcysteine with glucose degradation products in peritoneal dialysis fluids. Anal Chem 83:1518-1522, 2011.
5. Noh H, Ha H: ROS and oxidative stress in Diabetes & the Kidney, Contrib Nephrol 170:102-112, 2011.
6. Noh H, Oh EY, Yu MR, Kim OK, Ha H, Lee HB: Histone deacetylase 2 is a key regulator of diabetes and TGF-β1-induced renal injury. Am J Phsyiol 297(3):F729-F739. 2009.
7. Ha H, Oh E, Lee HB: The role of plasminogen activator inhibitor-1 in renal and cardiovascular diseases. Nat Rev Nephrol 5: 203-211, 2009.
8. Noh H, Kim JS, Han KH, Lee GT, Song JS, Chung SH, Jeon JS, Ha H, Lee HB: Oxidative stress during peritoneal dialysis: implications in functional and structural changes in the membrane. Kidney Int 69(11):2022-2028, 2006.
9. Rhyu DY, Yang Y, Lee GT, Song JS, Uh ST, Lee HB, Ha H: Role of reactive oxygen species in TGF-β1-induced MAPK activation and epithelial- mesenchymal transition in renal tubular epithelial cells. J Am Soc Nephrol 16:667-675, 2005.

• S9-2 •

Role of peroxisome in diabetic kidney injury

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Reactive oxygen species (ROS) plays a critical role in the development and progression of diabetic vascular complications including nephropathy. Among many pathways, nicotinamide adenosine dinucleotide phosphate (NADPH) oxidase and mitochondrial dysfunction have been recognized as two major sources of ROS generation in diabetic kidneys. Considering that plasma free fatty acids (FFAs) as well as glucose are increased in diabetes and that peroxisomes and mitochondria participate in FFA oxidation in an interconnected fashion, we have investigated whether deficiency of catalase, a major peroxisomal antioxidant, accelerates diabetic kidney injury through peroxisomal dysfunction and abnormal renal FFA metabolism. Despite equivalent hyperglycemia, parameters of diabetic kidney injury along with markers of oxidative stress were accelerated in diabetic catalase knock-out mice than diabetic wild-type mice up to 10 weeks of diabetes. Catalase deficient mice and mesangial cells showed impaired peroxisomal/mitochondrial biogenesis and FFAs oxidation. Catalase deficiency increased mitochondrial ROS in response to FFAs, which were effectively restored by catalase overexpression or N-acetylcysteine. Our recent data provide unprecedented evidence that FFA-induced peroxisomal dysfunction exacerbates diabetic kidney injury and that endogenous catalase plays an important role in protecting the kidney from diabetic stress through maintaining peroxisomal and mitochondrial fitness.

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➤Educational background & professional experience

1989	Yonsei University College of Medicine	M.D.
1993	Yonsei University Medical Center	Residency, internal medicine
1998	Yonsei University College of Medicine	
1999	Yonsei University Medical Center	Fellowship, cardiology
2002	Caritas St. Elizabeth's Medical Center, Tufts Univ	Post-doc fellow
2003-2007	Tufts University School of Medicine	Assistant professor, associate professor
2008-present	Emory University School of Medicine	Associate professor

➤Research interests

My research focuses on vascular and cardiac regeneration with stem and progenitor cells. We also have made a major effort to restore diabetic neurovascular complications with a cell-based approach.

➤Brief list of publications

1. Jeong JO, Han JW, Kim JM, Cho HJ, Park CW, Lee NH, Kim DW, Yoon YS. Malignant Tumor Formation After Transplantation of Short-Term Cultured Bone Marrow Mesenchymal Stem Cells in Experimental Myocardial Infarction and Diabetic Neuropathy. Circ Res 2011;108(11):1340-7. PMC3109741.
2. Lee JY, Park C, Cho YP, Lee E, Kim H, Kim P, Yun SH, Yoon YS. Podoplanin-expressing cells derived from bone marrow play a crucial role in postnatal lymphatic neovascularization. Circulation. 2010;122:1413-1425 PMCID: PMC2989430.
3. Kim SW, Kim HB, Cho HJ, Lee JU, Levit R, Yoon YS. Human peripheral blood-derived CD31+ cells have robust angiogenic and vasculogenic properties and are effective for treating ischemic vascular disease. J Am Coll Cardiol 2010;56(7):593-607 (with an editorial comment), PMCID: PMC2917842.
4. Kim HB, Cho HJ, Kim SW, Liu B, Cho YJ, Lee JY, Sohn YD, Schlauch K, Lee MY, Houge M, Yoon YS. CD31+ cells represent highly angiogenic and vasculogenic cells in bone marrow: novel role of non-endothelial CD31+ cells in neovascularization and their therapeutic effects on ischemic vascular disease. Circ Res 2010;107(5):602-14 PMCID: PMC2938961.
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6. Cho HJ, Lee NH, Wecker A, Gavin M, Kusano K, Qin GJ, Yoon YS. Role of host tissues for sustained humoral effects following endothelial progenitor cell transplantation in the ischemic heart. J Exp Med 2007;204:3257-69 PMCID: PMC2150988.
7. Yoon YS, Uchida S, Masuo O, Cejna M, Park JS, Gwon HC, Kirchmair R, Bahlman F, Walter D, Curry C, Hanley A, Isner JM, Losordo DW. Progressive attenuation of myocardial vascular endothelial growth factor expression is a seminal event in diabetic cardiomyopathy: restoration of microvascular homeostasis and recovery of cardiac function in diabetic cardiomyopathy after replenishment of local vascular endothelial growth factor. Circulation 2005;111:2073-85 PMID15851615.
8. Yoon YS, Wecker A, Heyd L, Park JS, Tkebuchava T, Kusano K, Hanley A, Scadova H, Asahara T, Losordo DW. A Clonally expanded novel population of multipotent stem cells derived from human bone marrow regenerates myocardium after myocardial infarction. J Clin Invest 2005;115;326-338 PMCID: 546424.
9. Yoon YS, Park JS, Tkebuchava T, Luederman C, Losordo DW. Unexpected calcification in infarcted myocardium transplanted with bone marrow cells. Circulation 2004;109:3154-7 PMID15197139.
10. Yoon YS, Murayama T, Gravereuax E, Tkebuchava T, Silver M, Curry C, Wecker A, Kirchmair R, Hu CS, Kearney M, Ashare A, Jackson DG, Kubo H, Isner JM, Losordo DW. VEGF-C gene therapy augments postnatal lymphangiogenesis and ameliorates secondary lymphedema. J Clin Invest 2003;111:717-725 PMID 12618526.

• S9-3 •

Cell therapy for diabetic neurovascular complications

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Diabetic neuropathy (DN), the most common complication of diabetes, frequently leads to foot ulcers and may progress into amputation of limbs. Despite continuous increase in incidence, no clinical therapy could effectively treat DN. Pathogenetically, DN is characterized by reduced vascularity in peripheral nerves and deficiency in angiogenic and neurotrophic factors. To reverse this process, studies have attempted delivery of neurotrophic or angiogenic factors for treatment as a protein or in the form of gene therapy; however, the effects turned out to be ineffective or very modest. We will briefly review the pathogenetic mechanism of DN and will address effects of cell therapies for DN and the mechanisms underlying these effects. Recent studies have demonstrated that bone marrow (BM)-derived cells such as mononuclear cells, endothelial progenitor cells (EPCs) or mesenchymal stem cells can effectively treat various cardiovascular diseases through their paracrine effects. As BM-derived cells include multiple beneficial angiogenic and neurotrophic cytokines, these cells were used for treating experimental DN and found to be effective for reversing manifestations of DN. Particularly, EPCs were shown to exert favorable therapeutic effects through enhanced neural neovascularization and neuro-protective effects. Cell therapy is a novel therapeutic modality for DN although further clinical study is required to clearly determine the therapeutic effects and potential adverse effects.

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➤Educational background & professional experience

1997-1999	Tohoku University School of Medicine	The Japan society for the promotion of Science (JSPS) research associate
1999-2000	Kanazawa University School of Medicine	Instructor
2001-2006	Kanazawa University Graduate School of Medical Science	Assistant professor
2006-2009	Joslin Diabetes Center and Harvard Medical School	Visiting fellow
2009-present	Kanazawa University Graduate School of Medical Sciences	Associate professor

➤Research interests

Innate immune system and diabetic complications

➤Brief list of publications

1. Saito H, Yamamoto Y, Yamamolto H. Diabetes alters the subsets of mouse endothelial progenitor cells that reside in blood, bone marrow and spleen. Am J Physiol Cell Physiol 2012; 302(6): C892-901.
2. He M, Kubo H, Morimoto K, Fujino N, Suzuki T, Takahashi T, Yamada M, Yamaya M, Yamamoto Y, Yamamoto H. RAGE binds phophatidylserine and mediates clearance of apoptotic cells. EMBO Rep 2011; 12(4): 358-364.
3. Yamamoto Y, Harashima A, Saito H, Tsuneyama K, Munesue S, Han D, Watanabe T, Asano M, Takasawa S, Okamoto H, Shimura S, Karasawa T, Yonekura H, Yamamoto H. Septic shock is associated with receptor for advanced glycation endproducts (RAGE) ligation of LPS. J Immunol 2011; 186 (5): 3248-3257.
4. Li J, Qu X, Yao J, Caruana G, Ricardo SD, Yamamoto Y, Yamamoto H, Bertram JF. Blockade of endothelial-mesenchymal-transition by a Smad3 inhibitor delays the early development of streptozotocin-induced diabetic nephropathy. Diabetes 2010; 59 (10): 2612-2624.
5. Myint KM, Yamamoto Y, Doi T, Kato I, Harashima A, Yonekura H, Watanabe T, Shinohara H, Takeuchi M, Hashimoto N, Asano M, Takasawa S, Okamoto H, Yamamoto H. RAGE control of diabetic nephropathy in a mouse model: effects of RAGE gene disruption and administration of low molecular weight heparin. Diabetes 2006; 55(9):2510-22.
6. Inagi R, Yamamoto Y, Nangaku M, Usuda M, Okamato H, Kurokawa K, Charles van Ypersele de Strihou, Yamamoto H, Miyata T. A severe diabetic nephropathy model with early development of nodule-like lesions induced by megsin overexpression in the RAGE/ iNOS transgenic mice. Diabetes 2006; 55:356-66.
7. Abeyama K, Stern MD, Ito Y, Kawahara K, Yoshimoto Y, Tanaka M, Uchimura T, Ida N, Yamazaki Y, Yamada S, Yamamoto Y, Yamamoto H, Iino S, Taniguchi N, Murayama I. The N-terminal domain of thrombomodulin sequesters high-mobility group-B1 protein, a novel antiinflammatory mechanism. J Clin Invest 2005; 115(5):1267-74.
8. Ohashi S, Abe H, Takahashi T, Yamamoto Y, Takeuchi M, Arai H, Nagata K, Kita T, Okamoto H, Yamamoto H, Doi T. Advanced glycation end products increase collagen-specific chaperone protein in mouse diabetic nephropathy. J Biol Chem 2004; 279:19816-23.
9. Yonekura H, Yamamoto Y, Sakurai S, Watanabe T, Petrova RG, Abedin MdJ, Li H, Yasui K, Takasawa S, Okamoto H, Yamamoto H. Novel splice variants of the receptor for advanced glycation endproducts (RAGE) expressed in human vascular endothelial cells and pericytes, and their putative roles in diabetes-induced vascular injury. Biochem J 2003; 370:1097-109.
10. Yamamoto Y, Kato I, Doi T, Yonekura H, Ohashi S, Takeuchi M, Watanabe T, Yamagishi S, Sakurai S, Takasawa S, Okamoto H, Yamamoto H. Development and prevention of advanced diabetic nephropathy in RAGE-overexpressing mice. J Clin Invest 2001; 108(2):261-8.

• S9-4 •

RAGE, diabetes and its vascular complications

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abetes is a life-threatening disease which is ascribed to its devastating vascular complications such as cardiovascular disease, stroke, and microvascular diseases. Extensive intracellular and extracellular formation of advanced glycation end-products (AGE) is a pathogenic factor in sustained hyperglycemia-induced vascular injuries in diabetes. AGE-induced cellular dysfunction and tissue damage are arising from both receptor-dependent and -independent mechanisms. The receptor for AGE (RAGE), originally an AGE-binding receptor, is now recognized as a member of pattern-recognition receptors (PRRs) and a pro-inflammatory molecular devise mediating danger signals to the body. RAGE-induced diabetic vascular injuries have been demonstrated in animal studies. Prophylactic and therapeutic strategies focusing on RAGE and its ligand axis will be of great importance in conquering diabetic vascular complications.

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➤Educational background & professional experience

1992	College of Medicine, Ewha Womens University	B.S.
2000	Ajou University, College of Medicine	Internal medicine / M.S.
2003	Ajou University, College of Medicine	Preventive medicine / Ph.D.
1992-1997	Hallym University, Kangnam Sacred Heart Hospital	Internship & residency
1997-1998	Department of Internal Medicine, Sejong Hospital	Faculty
1998-2000	Ajou University School of Medicine	Clinical research fellow
2000-2002	Pochon CHA University, College of Medicine	Full-time lecturer
2002-present	Hallym University, Kangnam Sacred Heart Hospital	Associate professor

➤Research interests

Molecular signal pathway and metabolic changes in diabetic heart disease
Association between inflammatory or anti-inflammatory cytokines and insulin sensitivity

➤Brief list of publications

1. Ko SH, Kim SR, Kim DJ, Oh SJ, Lee HJ, Shim KH, Woo MH, Kim JY, Kim NH, Kim JT, Kim CH, Kim HJ, Jeong IK, Hong EG, Cho JH, Mok JO, Yoon KH: 2011 Clinical Practice Guidelines for Type 2 Diabetes in Korea. diabetes and Metab J 5:431-436, 2011.
2. KimJH, Oh SJ, Lee JM, Hong EG, Yu JM, Han KA, Min KW, Son HS, ChangSA: The Effect of an Angiotensin Receptor Blocker on Arterial Stiffness in Type 2 Diabetes Mellitus Patients with Hypertension. Diabetes and Metab J 3:236-242, 2011.
3. Hong EG: Drug Therapy of Elderly Diabetic Patients. Korean Int Med 6:635-642, 2011.
4. Yew NS, Zhao H, Hong EG, Wu IH, Przybylska M, Siegel C, Shayman JA, Arbeeny CM, Kim JK, Jiang C, Cheng SH: Increased hepatic insulin action in diet-induced obese mice following inhibition of glucosylceramide synthase. PLoS One 5(6): e11239, 2010.
5. Lee JM, Kim JH, Son HS, Hong EG, Yu JM, Han KA, Min KW, Chang SA: Valsartan increases circulating adiponectin levels without changing HOMA-IR in patients with type 2 diabetes mellitus and hypertension. J Int Med Res 38(1): 234-41, 2010.
6. Kim CS, Park SY, Yu SH, Kang JG, Ryu OH, Lee SJ, Hong EG, Kim HK, Kim DM, Yoo JM, Ihm SH, Choi MG, Yoo HJ: Is A1C Variability an Independent Predictor for the Progression of Atherosclerosis in Type 2 Diabetic Patients? Korean Diabetes J 34(3): 174-81, 2010.
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10. Hong EG, Ko HJ, Cho YR, Kim HJ, Ma Z, Yu TY, Friedline RH, Kurt-Jones E, Finberg R, Fischer MA, Granger EL, Norbury CC, Hauschka SD, Philbrick WM, Lee CG, Elias JA, Kim JK: Interleukin-10 Prevents Diet-Induced Insulin Resistance by Attenuating Macrophage and Cytokine Response in Skeletal Muscle. Diabetes. 2009 58(11): 2525-35.

New EASD guideline for the management of diabetic patients

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The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) convened a joint task force to examine the evidence and develop recommendations for anti-hyperglycemic therapy in type 2 diabetes. Several guideline documents have been developed by members of these two organizations and by other societies and federations. These new recommendations are less prescriptive than and not as algorithmic as prior guidelines. The intent of this recommendation is to encourage an appreciation of the variable and progressive nature of type 2 diabetes, the specific role of each drug, the patient and disease factors that drive clinical decision-making and the constraints imposed by age and co-morbidity.

Glycemic targets of anti-hyperglycemic therapy were designed to reduce the incidence of microvascular complications. HbA1c is targeted to 〈 7.0% achieved with a mean plasma glucose of ~150-160 mg/dL; ideally, fasting and pre-meal glucose maintained at 〈 130 mg/dL and the postprandial glucose at 〈 180 mg/dL. However, individualized target is key point of these recommendations according to the degree of disease duration, life expectancy, important comorbidities, established vascular complications, patient support system, and hypoglycemia or other adverse effects of treatment.

Lifestyle interventions are critical parts of type 2 diabetes management and designed to impact an individual's physical activity levels and food intake. Metformin, if not contraindicated and if tolerated, is the preferred and most cost-effective first agent. If metformin cannot be used, another oral agent could be chosen, such as a sulfonylurea/glinide, pioglitazone, or a DPP-4 inhibitor; in occasional cases where weight loss is seen as an essential aspect of therapy, initial treatment with a GLP-1 receptor agonist might be useful. And monotherapy alone does not achieve/maintain an HbA1c target over ~3 months, the next step would be to add a second oral agent, a GLP-1 receptor agonist or basal insulin. Notably, the higher the HbA1c, the more likely insulin will be required. Triple combination therapy of anti-hyperglycemic agents can be tried in patient without achieving the glycemic targets, but these patients should be monitored closely, with the approach promptly reconsidered if it proves to be unsuccessful. The degree of hyperglycaemia (e.g. ≥ 8.5%) makes it unlikely that another drug will be of sufficient benefit, and prompt change to insulin should be considered.

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➤Educational background & professional experience

1986-1992	Korea University Medical School	M.D.
1994-1996	Korea University Medical School	M.Sc.
1997-1999	Korea University Medical School	Ph.D.
1997-2000	Korea University Hospital	fellow
2000-2005	Korea University Ansan Hospital	Assistant professor
2005-2011	Korea University Ansan Hospital	Associate professor
2006-2008	NIDDK, NIH, USA	Research fellow
2011-present	Korea University Ansan Hospital	Professor

➤Research interests

Diabetic epidemiology, nephropathy

➤Brief list of publications

1. Kim NH, Mason CC, Nelson RG, Afton SE, Essader AS, Medlin JE, Levine KE, Hoppin JA, Knowler WC, Sadnler DP. Arsenic Exposure and Incidence of Type 2 Diabetes in Southwestern American Indians. Am J Epidemiol (in press).
2. Ahn JH, Hong HC, Cho MJ, Kim YJ, Choi HY, Eun CR, Yang SJ, Yoo HJ, Kim HY, Seo JA, Kim SG, Choi KM, Baik SH, Choi DS, Kim NH. Effect of eplerenone, a selective aldosterone blocker, on the development of diabetic nephropathy in type 2 diabetic rats. Diabetes Metab J. 2012 Apr;36(2):128-35. Epub 2012 Apr 17.
3. Seo JA, Kim NH. Fibroblast growth factor 21: a novel metabolic regulator. Diabetes Metab J. 2012 Feb;36(1):26-8. Epub 2012 Feb 17.
4. Seo JA, Cho H, Eun CR, Yoo HJ, Kim SG, Choi KM, Baik SH, Choi DS, Park MH, Han C, Kim NH. Association between visceral obesity and sarcopenia and vitamin d deficiency in older koreans: the ansan geriatric study. J Am Geriatr Soc. 2012 Apr;60(4):700-6.
5. NH Kim, HS Kim, CR Eun, JA Seo, HJ Cho, SG Kim, KM Choi, SH Baik, DS Choi, MH Park, C Han, NH Kim. Depression is associated with sarcopenia, not central obesity in elderly Korean men. J Am Geriatr Soci. 2011 Nov;59(11):2062-8.
6. NH Kim, HJ Cho, YJ Kim, MJ Cho, HY Choi, CR Eun, JH Kim, SJ Yang, HJ Yoo, HY Kim, JA Seo, SG Kim, SH Baik, DS Choi, KM Choi. Combined Effect of High-normal Blood Pressure and Low HDL Cholesterol on Mortality in Elderly Korean Population: The South-West-Seoul (SWS) Study. Am J Hypertens 2011 Aug;24(8):918-23.
7. Kim NH, Pavkov ME, Knowler WC, Hanson RL, Weil EJ, Curtis JM, Bennett PH, Nelson RG. Predictive value of albuminuria in American Indian youth with or without type 2 diabetes. Pediatrics. 2010 Apr;125(4).
8. Kim BJ, Kim NH*, Kim SG, Roh H, Park HR, Park MH, Park KW, Cho SC, So YT (*Co-primary author). Utility of the cutaneous silent period in patients with diabetes mellitus. J Neurol Sci. 2010 Jun 15;293(1-2):1-5.
9. Kim NH, Pavkov ME, Nelson RG, Hanson RL, Bennett PH, Curtis JM, Sievers ML, Knowler WC. The separate and joint effects of prolonged QT interval and heart rate on mortality. Atherosclerosis. 2010 Apr;2009(2):539-44.
10. Seo JA, Kim BG, Cho H, Kim HS, Park J, Baik SH, Choi DS, Park MH, Jo SA, Koh YH, Han C, Kim NH. The cutoff values of visceral fat area and waist circumference for identifying subjects at risk for metabolic syndrome in elderly Korean: Ansan Geriatric (AGE) cohort study. BMC Public Health. 2009 Dec 2;9:443.

Review of guidelines for management of dyslipidemia in diabetic patients

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The National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) has provided education and guidance for decades on the management of dyslipidemia. Its third report (ATP III) was published 10 years ago. The new ATP IV guidelines are expected to be released this summer. The major focus of this version will be as follows. 1) Definition of the very high and high risk patients 2) LDL target goal in secondary prevention 3) LDL treatment goal in patients with diabetes 4) Treatment for triglyceride and HDL-cholesterol 5) Clinical usefulness of non-conventional CV risk markers such as CRP, Lp(a) and carotid IMT.

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➤Educational background & professional experience

1984-1990	Seoul National University College of Medicine	Bachelor
2005-2006	Division of Epidemiology Department of Family Medicine and Preventive Medicine, University of California San Diego	Post-doctoral fellowship
1999-2002	Inje University College of Medicine	Instructor
2003-2006	Inje University College of Medicine	Assistant professor
2006-2012	Inje University College of Medicine	Associated professor
2012-present	Inje University College of Medicine	Professor

➤Research interests

Diabetes epidemiology and complications

➤Brief list of publications

1. Hye Mi Kang, Dong-Jun Kim. Total energy intake may be more associated with glycemic control compared to each proportion of macronutrients in Korean population with diabetes. Diabetes Metab J.2012;36: 300-306.
2. Hye Mi Kang, Dong-Jun Kim. Body mass index and waist circumference according to glucose tolerance status in Korea: The 2005 Korean Health and Nutrition Examination Survey. J Korean Med Sci. 2012;27:518-24.
3. Hye Mi Kang, Dong-Jun Kim. Metabolic syndrome vs. Framingham risk score for association of self-reported coronary heart disease: The 2005 Korean Health and Nutrition Examination Survey. Diabetes Metab J.2012;36: 237-244.
4. Kim DJ, Bergstrom J, Barrett-Conner E, Laughlin GA. Visceral adiposity and subclinical artery disease in elderly adults: Rancho Bernardo study. Obesity 2008;16(4): 853-858.
5. Kim DJ, Barrett-Conner E. Association of serum proinsulin with hormone replacement therapy in nondiabetic older women: the Rancho Bernardo Study. Diabetes Care. 2006;29(3):618-24.
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7. Noh JH, Kim DJ, et al. Depressive symptoms of type 2 diabetics treated with insulin compared to diabetics taking oral anti-diabetic drugs: A Korean study. Diabetes Research and Clinical Practice 2005;69:243-248.
8. Dong-Jun Kim, et al. The cutoff value of fasting plasma glucose to differentiate frequencies of cardiovascular risk factors in a Korean population. Diabetes Care 2003;26(12): 3354-3356.
9. Kim DJ, Lee MS, Kim KW, Lee MK. Insulin secretory dysfunction and insulin resistance in the pathogenesis of korean type 2 diabetes mellitus. Metabolism. 2001;50(5):590-3.

Review of guidelines for management of hypertension in diabetic patients

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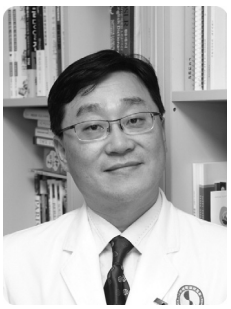
Current guidelines and position statements show a remarkable consistency in setting a target blood pressure level in diabetic patients at 130/80 mmHg (JNC 7, AHA and ACC, ESC and ESH, CHEP, and ADA). The main conclusion that can be drawn from the ACCORD BP trial is that a systolic blood pressure target of 120 mmHg cannot be recommended for the majority of patients with type 2 diabetes. Although the optimal BP target remains uncertain, results from ACCORD BP and recent meta-analyses (The Bangalore et al., and the Reboldi et al.) do not provide compelling evidence to alter the present recommendation (〈 130/80 mmHg). This was mainly supported by the association between SBP 〈 130 mmHg and reduction of stroke on one hand, and the increased risk of adverse events with lower SBP targets on the other hand, with the majority of adverse effects associated with SBP 〈 120 mmHg.

In my talk, I will review several guidelines for management of hypertension in diabetic patients (including JNC 8 guideline), in terms of similarity and difference.



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➤Educational background & professional experience

1987-1993	Yonsei University College of Medicine	Medicine / M.D.
1999-2002	Yonsei University Graduate School of Medicine	Medicine / M.Sc.
1997-2001	Internal Medicine, Severance Hospital	Resident
2001-2002	Internal Medicine, Yonsei University College of Medicine	Clinical fellow
2002-2003	Endocrinology, NHIC Hospital	Doctor
2003-2007	Endocrinology, Ajou University School of Medicine	Assistant professor
2007-present	Endocrinology, Ajou University School of Medicine	Associate professor

➤Research interests

Epidemiology of diabetes, obesity and metabolic syndrome

➤Brief list of publications

1. Lee YH, Bang H, Kim HC, Kim HM, Park SW, Kim DJ. A Simple Screening Score for Diabetes for the Korean Population: Development, validation, and comparison with other scores. Diabetes Care. 2012 Aug;35(8):1723-30.
2. Choi YJ, Lee MS, An SY, Kim TH, Han SJ, Kim HJ, Chung YS, Lee KW, Kim DJ. The relationship between diabetes mellitus and health-related quality of life in Korean adults: The fourth Korea National Health and Nutrition Examination Survey (2007-2009). Diabetes Metab J 2011 Dec;35(6):587-594.
3. Kim DJ. The Epidemiology of Diabetes in Korea. Diabetes Metab J. 2011 Aug;35(4):303-308.
4. Kim DJ, Xun P, Liu K, Loria C, Yokota K, Jacobs DR Jr, He K. Magnesium Intake in Relation to Systemic Inflammation, Insulin Resistance, and the Incidence of Diabetes. Diabetes Care. 2010 Dec;33(12):2604-2610.
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Epidemiology & current management status of diabetes mellitus in Korea

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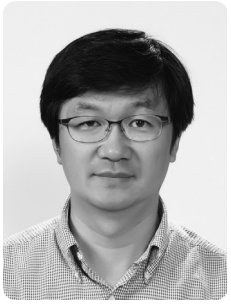
Diabetes is an increasing global health problem worldwide. Diabetes and its complications have become a major cause of morbidity and mortality in Korea. The prevalence of diabetes in Korea has increased six- to seven-fold from 1.5% to 9.9% in the past 40 years. The prevalence of diabetes among adults aged ≥ 30 years in 1998, 2001, 2005, and 2007-2009 was 11.1%, 8.9%, 9.1%, and 9.9%, respectively. The proportion of known cases of diabetes drastically increased from 23.2% in 1998 to 41.2% in 2001, 68.0% in 2005 and 72.3% in 2007-2009. The prevalence of IFG also increased from 17.4% in 2005 to 20.4% in 2007-2009. The International Diabetes Federation has estimated that the prevalence of diabetes will rise to 11.4% in 2030. When an A1C level of < 7.0% was used as a criterion, adequate glucose control was achieved in 43.5% of those with known cases of diabetes in 2005, whereas only 22.9% achieved adequate glucose control based on an A1C level of < 6.5%. Possible risk factors for diabetes in Korea are age, male gender, obesity, prediabetes, gestational diabetes, smoking, decreased physical activity, and short sleep duration. With increasing obesity, especially in childhood, and improved longevity, the prevalence of diabetes is expected to dramatically increase more than previously estimated.



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➤Educational background & professional experience

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1986	Department of Statistics, Seoul National University, Korea	Statistics / M.S.
1990	Department of Biostatistics, University of Michigan, USA	Biostatistics / B.S.
1990-1991	Department of Preventive Medicine, University of Iowa, USA	Visiting research scientist
1991-1992	National Institute of Child Health and Human Development, National Institutes of Health, USA	Visiting fellow
1992-1999	Department of Statistics, Hankuk University of Foreign Studies, Korea	Associate professor
1999-2001	Department of Statistics, Seoul National University, Korea	Associate professor
2001-present	Department of Statistics, Seoul National University, Korea	Professor
2005-2008	Interdisciplinary Program in Bioinformatics, Seoul National University, Korea	Head
2005-2010	National Research Laboratory of Bioinformatics and Biostatistics, Seoul National University, Korea	Director
2007-2009	Department of Statistics, Seoul National University, Korea	Chair
2009-2010	Department of Biotatistics, University of Washington, USA	Visiting professor
2012-present	Creative Research Initiative of Bioinformatics and Biostatistics	Director

➤Research interests

DNA Microarray data analysis, genetic network
Statistical genetics, gene-gene interaction analysis
Missing data analysis, repeated measures data and longitudinal data analysis

➤Brief list of publications

1. Nam, S. and Park, T. Pathway-based evaluation in early onset colorectal cancer suggests focal adhesion and immunosuppression along with epithelial-mesenchymal transition, PLoS ONE, 2012.
2. Young Jin Kim, et al. New multiple genetic loci for metabolic traits identified from large scale East Asian genome-wide association studies, Nature Genetics, 2011 Sep 11. doi: 10.1038/ng.939.
3. Teslovich, T. M. et al., Biological, Clinical, and Population Relevance of 95 Loci Mapped for Serum lipid Concentrations, Nature, 2010 Aug 5;466(7307):707-13.
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5. Kim, Y., Bekiranov, S., Lee, J. K., and Park, T. Double Error Shrinkage Method for Identifying Protein Binding Sites Observed by Tiling Arrays with Limited Replication. Bioinformatics, 2009 1;25(19):2486-91.
6. Namkung, J., Kim., K., Yi, S., Chung, W., Kwon, M.-S., and Park, T. New Evaluation Measures for Multifactor Dimensionality Reduction Classifiers in Gene-Gene Interaction Analysis. Bioinformatics, 2009 25(3):338-345.
7. Cho, Yoon Shin, et al. A large scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits, Nature Genetics , 2009 41(5): 527-34.
8. Chung, Y., Lee, SY, Elston, RC, and Park , T. Odds ratio based multifactor-dimensionality reduction method for detecting gene-gene interactions, Bioinformatics, 2007 23: 71-76.
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10. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, Baehner FL, Walker MG, Watson D, Park T, Hiller W, Fisher ER, Wickerham DL, Bryant J, Wolmark N. A Multigene Assay to Predict Recurrence of Tamoxifen-Treated, Node-Negative Breast Cancer. N Engl J Med. 2004 Dec 10.

• S11-1 •

Improving statistical powers in large scale genetic association studies for type 2 diabetes

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In recent years, a large scale genetic association studies such as genome-wide association (GWA) studies have successfully led to many discoveries of genetic variants affecting common complex traits, including type 2 diabetes (T2D). Although these genetic studies have made much progress in finding single nucleotide polymorphisms (SNPs) associated with many complex traits, such SNPs have been shown to explain only a very small proportion of the underlying genetic variance of complex traits. This is partly due to that fact that most current genetic studies have relied on single-marker approaches that identify single genetic factors individually and have limitations in considering the joint effects of multiple genetic factors on complex traits. In order to improve power in genetic studies, we first consider the joint identification of multiple genetic factors and then consider multivariate analysis considering multiple correlated phenotypes. Joint identification of multiple genetic factors would be more powerful and provide a better prediction of complex traits, since it utilizes combined information across variants. Recently, a new statistical method for joint identification of genetic variants for common complex traits via the elastic-net regularization method was proposed. In this study, we applied this joint identification approach and multivariate approach to a large-scale GWA dataset (i.e., 8842 samples and 327,872 SNPs) in order to identify genetic variants of T2D phenotypes for the Korean population.

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➤Educational background & professional experience

1998-1999	Korean Army / Medical Officer	
1999-2003	Severance Hospital, Seoul, Korea	Resident
2003-2005	Severance Hospital, Seoul, Korea	Clinical fellow
2005-2006	Yonsei University College of Medicine, Seoul, Korea	Instructor
2006-2010	Yonsei University College of Medicine, Seoul, Korea	Assistant prof.
2010–Present	Yonsei University College of Medicine, Seoul, Korea	Associate prof.
2009-2011	Harvard Medical School, Beth Israel Deaconess Medical Center, Boston MA	Visiting professor

➤Research interests

Posttransplantation diabetes (new onset diabetes after transplantation)
Pancreatic zinc transporter
Pharmacogenetics
Type 2 diabetes genetics

➤Brief list of publications

1. Variants of the Adiponectin and Adiponectin Receptor 1 Genes and Posttransplantation Diabetes Mellitus in Renal Allograft Recipients. JCEM 97:E129-E135, 2012.
2. Low-risk ZnT-8 allele (W325) for PTDM is protective against cyclosporin A-induced impairment of Beta-cell insulin secretion capacity. Pharmacogenomics J 11:191-198, 2011.
3. Circulating vaspin and visfatin are not affected by acute or chronic energy deficiency or leptin administration in human subjects. Eur J Endo 164:911-917, 2011.
4. Leptin replacement improves postprandial glycemia and insulin sensitivity in HIV-infected lipoatrophic men treated with pioglitazone: a pilot study. Metabolism 60:1045-1049, 2011.
5. Effects of Leptin and Adiponectin on Pancreatic Beta Cell Function. Metabolism 60:1664-1672, 2011.
6. Association of Common type 2 Diabetes Risk Gene Variants and PTDM in Renal Allograft Recipients in Korea. Transplantation 88:693-698, 2009.
7. Effect of ABCA1 Variant on Atherogenic Dyslipidemia in Patients with Type 2 Diabetes Treated with Rosiglitazone. Diabetic Med 26:577-581, 2009.
8. The C609T variant NQO1 is associated with carotid artery plaques in patients with type 2 diabetes. Molecular Genetics & Metabolism 97:85-90, 2009.
9. A Variant of the TCF7L2 Gene and the Risk of PTDM in Renal Allograft Recipients. Diabetes Care 31:63-68, 2008.
10. Lithospermic Acid B Ameliorates the Development of Diabetic Nephropathy in Type 2 Diabetic Rats. Eur J Pharma 579:418-425, 2008.
11. A Polymorphism in the Zinc Transporter Gene, SLC30A8, Confers Resistance against PTDM in Renal Allograft Recipients. Diabetes 57:1043-1047, 2008 .
12. Modification of the NFκB p65 subunit with O-linked N-acetylglucosamine Decreases its Binding to IκB and Increases its Transcriptional Activation. PNAS 105:17345-17350, 2008.

Genetic risk factors of PTDM

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Posttransplantation Diabetes Mellitus (PTDM) or New-onset diabetes mellitus after kidney transplantation (NODAT) is a major clinical challenge in the field of solid organ transplantation. The improving rate of long-term kidney transplant attrition has resulted in an accumulation of medical conditions, such as PTDM. PTDM may reflect a genetic predisposition to diabetes influ-enced by multiple environmental factors. Genetic risk factors of PTDM share in much part with garden variety of type 2 diabetes. Some studies have shown a significant association between PTDM and genetic polymorphisms. These polymorphisms were associated with genes involving insulin secretion (*KCNJ11, HNF4A, NFATc4, ENPP1/PC-1, CCL5, VDR*), insulin resistance (*ACDC, ADIPOR1, PAI-1*), and oxidative stress (SOD). We have studied several genetic markers of PTDM and found that TCF7L2 rs7903146, SLC30A8 rs13266634, *HHEX* rs1111875, *HHEX* rs7923837, *HHEX* rs5015480, *CDKAL1* rs10946398, *CDKN2A/B* rs10811661, *KCNQ1* rs2237892, and *ADIPOQ* rs1501299. Among them R325W (rs13266634) in *SLC30A8* is a non-synonymous poly¬morphism in the islet-specific zinc transporter protein and may be associated with a defect in insulin secretion. We investigated the functional aspect of the zinc transporter gene, based on the hypothesis that the polymorphic residue at position 325 of ZnT-8 might determine susceptibility to cyclosporine A (CsA) suppression of insulin secretion. INS1E cells expressing the W325 variant showed enhanced glucose stimulated insulin secretion (GSIS) and were less sensitive to CsA suppression of GSIS. A reduced number of insulin granule fusion events accompanied the decrease in insulin secretion in CsA-treated cells expressing ZnT-8 R325; however, ZnT-8 W325-expressing cells exhibited resistance to the dampening of insulin granule fusion by CsA and transported zinc ions into insulin vesicles more efficiently. Both tacrolimus and rapamycin caused similar suppression of GSIS in cells expressing ZnT-8 R325. However, cells expressing ZnT-8 W325 were resistant to tacrolimus, but not to rapamycin. Overexpression of the DSCR1, an endogenous calcineurin inhibitor, and subsequent calcineurin inhibition significantly reduced GSIS in cells expressing the R325 but not the W325 variant, suggesting that differing sus-ceptibility to CsA may be due to different interactions with calcineurin. These data suggest that the ZnT-8 W325 variant is protective against CsA-induced suppression of insulin secretion may contribute to the protective action on the development of PTDM in renal allograft recipients.

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➤Educational background & professional experience

1979-1985	Shiga University of Medical Science (SUMS)	M.D.
1986-1990	Postgraduate course of SUMS	Ph.D.
1993-1996	Department of Pathology, University of Michigan	Research fellow
1990-2000	Third department of Medicine, SUMS	Instructor
2001-2008	RIKEN SNP Research Center	Laboratory head
2008-present	RIKEN Center for Genomic Medicine	Laboratory head
2008-present	Juntendo University Graduate School of Medicine	Visiting professor
2012-present	St. Marianna University School of Medicine	Visiting professor

➤Research interests

Genetics of type 2 diabetes and diabetic nephropathy

➤Brief list of publications

1. Imamura M, Maeda S, Yamauchi T, Hara K, Yasuda K, Morizono T, Takahashi A, Horikosi M, Nakamura M, Fujita H, Tsunoda T, Kubo M, Watada H, Maegawa H, Okada-Iwabu M, Iwabu M, Shojima N, Ohshige T, Omori S, Iwata M, Hirose H, Kaku K, Ito C, Tanaka Y, Tobe K, Kashiwagi A, Kawamori R, Kasuga M, Kamatani N, DIAGRAM consortium, Nakamura Y, Kadowaki T. A single nucleotide polymorphism in ANK1 is associated with susceptibility to type 2 diabetes in Japanese populations. Hum Mol Genet 21: 3042-3049, 2012.
2. Wen W, Cho YS, Zheng W, Dorajoo R, Kato N, Qi L, Chen C-H, Delahanty RJ, Okada Y, Tabara Y, Gu D, Zhu D, Haiman CA, Mo Z, Gao Y-T, Saw SM, Go MJ, Takeuchi F, Chang L-C, Kokubo Y, Liang J, Hao M, Marchand LL, Zhang Y, Hu Y, Wong TY, Long J, Han B-G, Kubo M, Yamamoto K, Su M-H, Miki T, Henderson BE, Song H, Tan A, He J, Ng DPK, Cai Q, Tsunoda T, Tsai F-J, Iwai N, Chen GK, Shi J, Xu J, Sim X, Xiang Y-B, Maeda S, Ong RTH, Li C, Nakamura Y, Aung T, Kamatani N, Liu JJ, LuW, Yokota M, Seielstad M, Fann CSJ, The GIANT Consortium, Wu J-Y, Lee J-Y, Hu FB, Tanaka T, Tai ES, Shu XO Meta-analysis identifies common variants associated with body mass index in East Asians, Nature Genetics 44: 307-311, 2012.
3. Okada Y, Kubo M, Ohmiya H, Takahashi A, Kumasaka N, Hosono N, Maeda S, Wen W, Dorajoo R, Go MJ, Zheng W, Kato N, Wu J-Y, Lu Q, the GIANT consortium, Tsunoda T, Yamamoto K, Nakamura Y, Kamatani N, Tanaka T Common variants at CDKAL1 and KLF9 are associated with body mass index in East Asian populations. Nature Genetics 44: 302-306, 2012.
4. Cho YS, Chen C-H, Hu C, Long J, Ong RTH, Sim X, Takeuchi F, Wu Y, Go MJ, Yamauchi T, Chang Y-C, Kwak SH, Ma RCW, Yamamoto K, Adair LS, Aung T, Cai Q, Chang L-C, Chen Y-T, Gao Y, Hu FB, Kim H-L, Kim S, Kim YJ, Lee JJ-M, Lee NR, Li Y, Liu JJ, Lu W, Nakamura J, Nakashima E, Ng DPK, Tay WT, Tsai F-J, Wong TY, Yokota M, Zheng W, Zhang R, Wang C, So WY, Ohnaka K, Ikegami H, Hara K, Cho YM, Cho NH, Chang TJ, Bao Y, Hedman ÅK, Morris AP, McCarthy MI, DIAGRAM consortium, MuTHER consortium, Takayanagi R, Park KS, Jia W, Chuang L-M, Chan JCN, Maeda S, Kadowaki T, Lee J-Y, Wu J-Y, Teo YY, Tai ES, Shu XO, Mohlke KL, Kato N, Han B-G, Seielstad M. Meta-analysis of genome-wide association studies identifies 8 new loci for type 2 diabetes in East Asians. Nature Genetics 44: 67-72, 2012.
5. Okamoto K, Tokunaga K, Doi K, Fujita T, Suzuki H, Katoh T, Watanabe T, Nishida N, Mabuchi A, Takahashi A, Kubo M, Maeda S, Nakamura Y, Noiri E. Common variation in GPC5 is associated with acquired nephrotic syndrome. Nat Genet 43: 459-463, 2011.
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• S11-3 •

Genome-wide association study for type 2 diabetes in Japan

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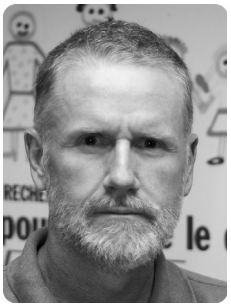
Genome-wide association studies (GWAS) have identified over 60 confirmed loci for type 2 diabetes, mostly performed in populations of European descent. Some of them have been shown to confer similar susceptibility to type 2 diabetes in non-European populations. However, most of the genetic factors for type 2 diabetes still remain to be identified, especially in non-European populations. Cumulative evidence suggests that Asians may be more genetically susceptible to type 2 diabetes than populations of European ancestry. Also, there are significant interethnic differences in the risk allele frequency or in effect sizes at several loci, which may affect the power to detect associations in these populations. Therefore, it is considered to be relevant to perform GWAS for type 2 diabetes using non-European populations as well as European populations to uncover the missing heritability of type 2 diabetes. In 2008, two GWAS conducted in Japanese populations have identified *KCNQ1* as a novel susceptibility locus for type 2 diabetes. We further performed an independent GWAS for 459,359 SNPs in 7,541 Japanese individuals (4,470 type 2 diabetes and 3,071 controls), and identified two new loci *UBE2E2* and *C2CD4A-C2CD4B*. Subsequent extended analyses for 2,229,890 imputed SNPs additionally identified *ANK1* locus as a new locus for type 2 diabetes. Furthermore, in an effort of Asian Genetic Epidemiology Network (AGEN), 8 new loci were identified by a meta-analysis of East Asian GWAS. The associations of *KCNQ1*, *C2CD4A-C2CD4B* and *ANK1* with type 2 diabetes were consistently observed among European populations, underlining the importance of examining non-European populations through GWAS. Further efforts for increasing sample size by scale-upped non-European GWAS will help us identify not only ethnicity-specific loci, but also common-susceptibility loci among different ethnic groups, although new approaches other than GWAS, such as exome sequencing, will be required to elucidate a heritability of type 2 diabetes more precisely.



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➤Educational background & professional experience

1965-1968	University of Calgary, Calgary, Canada	B.Sc. in zoology
1968-1971	University of Calgary, Calgary, Canada	M.Sc. in biology
1971-1977	University of California, San Francisco	Ph.D. in biochemistry
1977-1981	University of California, San Francisco	Adjunct assistant professor, department of Biochemistry and biophysics
1981-1986	Chiron Corporation, Emeryville, CA	Senior scientist
1986-1990	University of Chicago	Associate professor, department of biochemistry and molecular biology
1990-present	University of Chicago	Professor of medicine and human genetics
2005-present	University of Chicago	Director, University of Chicago Diabetes Research and Training Center

➤Research interests

Genetics of diabetes

➤Brief list of publications

1. Johansson S, Irgens H, Chudasama KK, Molnes J, Aerts J, Roque FS, Jonassen I, Levy S, Lima K, Knappskog PM, Bell GI, Molven A, Njølstad PR. Exome Sequencing and Genetic Testing for MODY. PLoS One. 2012;7(5):e38050. Epub 2012 May 25.
2. Greeley SA, Naylor RN, Philipson LH, Bell GI. Neonatal diabetes: an expanding list of genes allows for improved diagnosis and treatment. Curr Diab Rep. 2011 Dec;11(6):519-32.
3. Fajans SS, Bell GI. MODY: history, genetics, pathophysiology, and clinical decision making. Diabetes Care. 2011 Aug;34(8):1878-84.
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6. Fajans SS, Bell GI, Paz VP, Below JE, Cox NJ, Martin C, Thomas IH, Chen M. Obesity and hyperinsulinemia in a family with pancreatic agenesis and MODY caused by the IPF1 mutation Pro63fsX60. Transl Res. 2010 Jul;156(1):7-14. Epub 2010 Apr 23.
7. Greeley SA, Tucker SE, Naylor RN, Bell GI, Philipson LH. Neonatal diabetes mellitus: a model for personalized medicine. Trends Endocrinol Metab. 2010 Aug;21(8):464-72. Epub 2010 Apr 29.
8. Støy J, Edghill EL, Flanagan SE, Ye H, Paz VP, Pluzhnikov A, Below JE, Hayes MG, Cox NJ, Lipkind GM, Lipton RB, Greeley SA, Patch AM, Ellard S, Steiner DF, Hattersley AT, Philipson LH, Bell GI; Neonatal Diabetes International Collaborative Group. Insulin gene mutations as a cause of permanent neonatal diabetes. Proc Natl Acad Sci U S A. 2007 Sep 18;104(38):15040-4. Epub 2007 Sep 12.

• S11-4 •

Diabetes mellitus - a model for personalized genetic medicine

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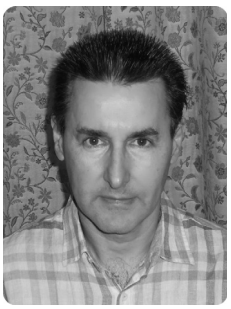
Diabetes mellitus is a clinically heterogeneous group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The American Diabetes Association and other organizations recognize four "etiologic types": type 1, type 2, other specific types, and gestational diabetes. Genetic studies (primarily genome-wide association studies) have found that genetic variation in at least 40 loci affects risk of type 1 diabetes and more than 70 loci are implicated in the development of type 2 diabetes. Fifty-percent of the genetic risk for type 1 diabetes is conferred by a single locus, the HLA region on chromosome 6. By contrast, the various type 2 diabetes susceptibility genes have only a modest effect on risk. Many of the genes associated with type 2 diabetes are also associated with gestational diabetes. Studies of "other specific types" of diabetes such as permanent neonatal diabetes mellitus and maturity-onset diabetes of the young have highlighted the role of specific genes in the development of diabetes. They have also shown how a genetic diagnosis can impact treatment as illustrated by the transition of infants with mutations in *KCNJ11* and *ABCC8*, which encode protein subunits of the ATP-sensitive potassium channel, from insulin to sulfonylurea pills. Monogenic forms of diabetes were once thought to be very rare. We now know that they are quite common accounting for 2% or more of all cases and usually misdiagnosed as type 1 diabetes or more commonly type 2 diabetes. Mutations in three genes (*GCK, HNF1A, HNF4A*) account for more than 50% of all cases of genetic forms of diabetes and for each, a genetic diagnosis leads to a specific recommendation for treatment. In this presentation, I will review the genetics of diabetes and discuss the use of genetic testing in diagnosis and treatment – personalized genetic medicine.



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➤Educational background & professional experience

1981	Dept of Biochemistry, University of Bucharest	Bachelor of science
1992	Dept of Clinical Chemistry, Karolinska Institute, Stockholm	Doctor of medical sciences
1999-2003	Centre for Integrated Systems Biology and Medicine, University of Nottingham	Senior research fellow
2003-2011	Centre for Integrated Systems Biology and Medicine, University of Nottingham	Principal research fellow
2012-present	MRC/Arthritis Research UK Centre for Musculoskeletal Ageing Research, University of Nottingham	Principal research fellow

➤Research interests

My research interest can be viewed as an integration of in vivo functional measurements in human and animal models with molecular signalling pathways in skeletal muscle. More specifically, I am interested in:

- Skeletal and cardiac muscle energy metabolism in health, disease and during contraction.
- The integration of fat and carbohydrates metabolism and interaction diet-gene expression at rest and during muscle contraction.
- Molecular signalling pathway that controls the surgery-, sepsis- and immobilisation-mediated insulin resistance state and the latter's association with muscle atrophy. The roles for testosterone, dichloroacetate, pre-operative administration of CHO load or exercise in counter acting these effects.

➤Brief list of publications

1. Constantin-Teodosiu D, Constantin D, Stephens F, Laithwaite D, Greenhaff PL. The role of FOXO and PPAR transcription factors in diet-mediated inhibition of PDC activation and carbohydrate oxidation during exercise in humans and the role of pharmacological activation of PDC in overriding these changes. Diabetes, 61(5), 1017-24, 2012.
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3. Formenti F, Constantin-Teodosiu D, Emmanuel Y, Cheeseman J, Dorrington KL, Edwards LM, Humphreys SM, Lappin TR, McMullin MF, McNamara CJ, Mills W, Murphy JA, O'Connor DF, Percy MJ, Ratcliffe PJ, Smith G, Treacy M, Frayn KN, Greenhaff PL, Karpe F, Clarke K and Robbins PA. Regulation of human metabolism by hypoxia-inducible factor. PNAS 107(28), 12722-7, 2010.
4. Awad S, Constantin-Teodosiu D, Constantin D, Rowlands BJ, Brian J, Fearon KCH, Macdonald IA and Dileep LN. Cellular mechanisms underlying the protective effects of preoperative feeding: a randomized study investigating muscle and liver glycogen content, mitochondrial function, gene and protein expression. Annals of surgery, 252(2), 247-53, 2010.
5. Mallinson JE, D Constantin-Teodosiu, J Sidaway, F. Russell Westwood, PL Greenhaff. Blunted Akt/FOXO Signalling and Activation of Genes Controlling Atrophy and Fuel Use in Statin Myopathy. J Physiol 587(1), 219-230 2009.
6. Constantin-Teodosiu D, DJ Baker, D Constantin and PL Greenhaff. PPARδ agonism inhibits skeletal muscle PDC activity, mitochondrial ATP production and force generation during prolonged contraction. J Physiol 587(1), 231-239, 2009.
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8. Tsintzas K, K Chokkalingam, K Jewell, L Norton, IA Macdonald, D Constantin-Teodosiu. Elevated Free Fatty Acids Attenuate the Insulin-Induced Suppression of PDK4 Gene Expression in Human Skeletal Muscle: Potential Role of Intramuscular Long-Chain Acyl-Coenzyme A. J Clin Endocrinol Metab 92, 3967-72, 2007.
9. Constantin D, D Constantin-Teodosiu, R Layfield, K Tsintzas, AJ Bennett, Greenhaff, PL PPARδ agonism induces a change in fuel metabolism and activation of an atrophy programme, but does not impair mitochondrial function in rat skeletal muscle. J Physiol 583, 381-390, 2007.

• S12-1 •

Can activation of muscle PDC overcome type 2 diabetes?

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High-fat diet (HFD) inhibits the mitochondrial pyruvate dehydrogenase complex (PDC)-controlled carbohydrate (CHO) oxidation, contributing to muscle insulin resistance, which is an underlying cause of chronic elevation in blood glucose concentration and metabolic inflexability in type 2 diabetes. Conversely, muscle contraction increases simultaneously CHO-derived pyruvate generation and pyruvate oxidation by enhancing glycogenolysis and leg glucose uptake and by increasing the amount of active mitochondrial PDC, respectively. The activation of muscle PDC during muscle contraction is achieved by the accumulation of mitochondrial calcium and pyruvate. They function by activating two phosphatases (PDP1 and 2) and inhibiting two kinases (PDK2 and 4 - the most prevalent isoforms in muscle), respectively, and jointly appear to be able to fully activate PDC at exercise intensities of 75% maximal oxygen consumption and above. Nevertheless, when exercise at this workload is preceded by several days of HFD intake, calcium and pyruvate seem unable to activate PDC to the same extent as in the control condition resulting in reduced CHO oxidation compared to control at exercise intensities where muscle glycogen is an important contributor to energy production. We have recently revealed molecular (i.e. FOXO1) and biochemical changes underpinning this process in human quadriceps muscle biopsies samples collected at rest and during different models of exercise (electrically evoked maximal intermittent isometric contraction and sub-maximal intensity cycling at 75% of VO2 max) following three days of HFD. We also showed in humans that activation of PDC using dichloroacetate, which is a more potent pharmacological inhibitor of PDK2 and 4 proteins than pyruvate, overrides these diet-induced changes and restores the HFD-mediated inhibition of CHO oxidation during exercise.

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➤Educational background & professional experience

1992-1996	Department of Leisure and Recreation, Ewha Womans University, Seoul, Korea B.Sc., 1996 / Physical Education, Leisure studies
1998-2000	Faculty of Kinesiology and Recreation Management, University of Manitoba, Winnipeg, MB, Canada / M.Sc., 2001 / Exercise Physiology, Cardiac Rehabilitation, Mentor: Elizabeth Ready, Ph.D.
2001-2004	School of Kinesiology and Health Studies, Queen's University, Kingston, ON, Canada / Ph.D., 2005 / Obesity, Insulin Resistance and Exercise in Obesity and T2DM / Mentor: Robert Ross, Ph.D.
2005-2007	Division of Weight Management and Wellness, Department of Pediatrics, Children's Hospital of Pittsburgh University of Pittsburgh School of Medicine / Post-Doctoral Research Associate/Mentor: Silva/Arslanian, M.D.
2007-Present	Division of Weight Management and Wellness, Department of Pediatrics, Children's Hospital of Pittsburgh, University of Pittsburgh School of Medicine / Assistant Professor of Pediatrics

➤Research interests

physical activity, obesity, body fat distribution, skeletal muscle, insulin resistance, metabolic syndrome

➤Brief list of publications

1. Lee S, Bacha F, Hannon T, Kuk JL, Boesch C, Arslanian S. Effects of aerobic versus resistance exercise without calorie restriction on abdominal fat, intrahepatic lipid and insulin sensitivity in obese adolescent boys: A randomized controlled trial. Diabetes. 2012 Jun 29. [Epub ahead of print].
2. Lee S, Boesch C, Kuk J, Arslanian S. Effects of an overnight intravenous lipid infusion on intramyocellular lipid content and insulin sensitivity in African-American versus Caucasian adolescents. Metabolism. 2012 In press.
3. Lee S, Guerra N, Arslanian S. Skeletal muscle lipid content and insulin sensitivity in black versus white obese adolescents: Is there a race differential?. J Clin Endocrinol Metab. 2010 May;95(5):2426-32.
4. Lee S, Arslanian SA. Fat oxidation in black and white youth: Is it a metabolic phenotype predisposing black girls to obesity? J Clin Endocrinol Metab. 2008 Nov;93(11):4547-51.
5. Lee S, Gungor N, Bacha F, Arslanian SA. Insulin resistance: link to the components of the metabolic syndrome and biomarkers of endothelial dysfunction in youth. Diabetes Care. 2007 Aug;30(8):2091-7.
6. Lee S, Bacha F, Gungor N, Arslanian SA. Waist circumference is an independent predictor of insulin resistance in African-American and White youth. J Pediatr. 2006 Feb;148(2):188-94.
7. Lee S, Bacha F, Gungor N, Arslanian SA. Racial differences in adiponectin in youth: Relationship to visceral fat and insulin sensitivity. Diabetes Care. 2006 Jan;29(1):51-6.
8. Lee S, Hudson R, Kilpatrick K, Graham TE, Ross R. Caffeine ingestion is associated with reductions in glucose uptake independent of obesity and type 2 diabetes before and after exercise training. Diabetes Care. 2005 Mar;28(3):566-72.
9. Lee S, Kuk JL, Davidson LE, Hudson R, Kilpatrick K, Graham TE, Ross R. Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without type 2 diabetes. J Appl Physiol. 2005 Sep;99(3):1220-5.
10. Lee S, Kuk JL, Katzmarzyk PT, Blair SN, Church TS, Ross R. Cardiorespiratory fitness attenuates metabolic risk independent of abdominal subcutaneous and visceral fat in men. Diabetes Care. 2005 Apr;28(4):895-901.

• S12-2 •

Does exercise alone reduce obesity related co-morbidities?

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The epidemic rate of obesity in adults and adolescents is a major public health concern because it is triggering long-term comorbid conditions such as nonalcoholic fatty liver disease, insulin resistance, type 2 diabetes mellitus and cardiovascular diseases. It is suggested that abdominal obesity, in particular visceral fat, is an important culprit for many obesity related co-morbidities. Previous studies have shown that individuals with low fitness are more likely to have increased visceral adiposity, hypertension, dyslipidemia and type 2 diabetes compared with individuals with higher fitness for similar BMI categories. Furthermore, intervention studies report that regular exercise alone is beneficial to reduce abdominal fat, fatty liver and insulin resistance in the absence of calorie restriction or weight loss. In this symposium we will discuss the role of regular physical activity alone as a treatment strategy to reduce abdominal obesity and risk factors for type 2 diabetes in both adults and adolescents.

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➤Educational background & professional experience

2005-2009	Deakin University, Australia	Bachelor of biomedical science (honors)
2009-present	St Vincent's Institute of Medical Research, Australia	Summer student
2009-present	Melbourne University, Australia	Ph.D. candidate

➤Research interests

Obesity, type 2 diabetes, insulin resistance, exercise, whole-body and skeletal muscle metabolism
Interplay between nutrients and disease

➤Brief list of publications

1. Jorgensen, S.B., O'Neill, H.M., Sylow, L; Honeyman, J; Hewitt, K; Palanivel, R, Fullerton, M.D.; Oberg, L; Balendran, A; Galic, S; van der Poel, C; Trounce, I; Lynch, G; Schertzer, J.D.; Steinberg, G.R. Deletion of skeletal muscle SOCS3 prevents insulin resistance in obesity. Diabetes. Accepted June 2012.
2. O'Neill, H.M., Holloway, G.P. and Steinberg, G.R.. AMPK regulation of fatty acid metabolism and mitochondrial biogenesis: implications for obesity. MEC. Accepted June 2012.
3. O'Neill, H.M., Maarbjerg, S, Crane, J.D., Jeppensen, J., Jorgensen, S.B., Schertzer, J.D., Shyroka, O., Kiens, B., van Denderen, B.J., Tarnopolsky., M.A., Kemp, B.E., Richter, E.A. and Steinberg, G.R.. AMPK muscle null mice reveal an essential role for AMPK in maintaining mitochondrial content and glucose uptake during exercise. PNAS, 2011 Aug 108(38): 16092-16097.
4. Steinberg, G.R.., O'Neill, H.M., Dzamko, N.L., Galic, S., Naim, T., Koopman. R., J ø rgensen, S.B., Honeyman, J., Hewitt, K., Chen, Z.P., Schertzer, J.D., Scott, J.W., Koentgen, F., Lynch, G.S., Watt, M.J., van Denderen, B.J., Campbell, D.J., Kemp, B.E. Whole body deletion of AMP-activated protein kinase $\beta 2$ reduces muscle AMPK activity and exercise capacity. JBC, 2010 Nov 26;285(48):37198-209.
5. Beck Jorgensen, S., O'Neill, H.M., Hewitt, K, Kemp, B.E. and Steinberg, G.R.. Reduced AMP-activated protein kinase activity in mouse skeletal muscle does not exacerbate the development of insulin resistance with obesity. Diabetologia, 2009 Nov; 25(11):2395-404.

Role of skeletal muscle AMPK in regulating metabolism at rest and during exercise

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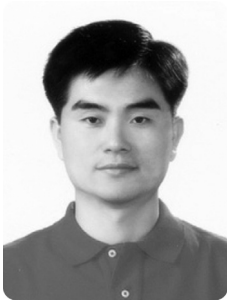
AMP-activated protein kinase (AMPK) is an evolutionary conserved serine/ threonine stress sensing kinase that once activated, by low energy status (exercise), restores energy balance by switching off ATP consuming pathways (fatty acid synthesis) and switching on ATP generating pathways (fatty acid oxidation, glucose uptake, mitochondrial biogenesis). Acetyl-CoA carboxylase (ACC 1 and 2) was one of the first identified substrates of AMPK, and phosphorylation of ACC1 at S79 (equivalent S212 site on ACC2) inhibits enzyme activity and enhances fatty acid oxidation in liver, where ACC1 is predominantly expressed. No studies have assessed the contribution of S212 phosphorylation on ACC2; predominant isoform in skeletal muscle. Skeletal muscle is a major contributor to whole-body energy expenditure and is responsible for ~80% of insulin-stimulated glucose disposal; therefore, metabolic alterations in this tissue could influence whole-body insulin sensitivity and substrate utilization. Pharmacological activation of AMPK with aminoimidazole-4-carboxamide-1-β-D-ribonucleoside (AICAR) enhances fatty acid oxidation, glucose uptake, insulin sensitivity and mitochondrial biogenesis in skeletal muscle; however, AMPK deficient mouse models where a single subunit has been mutated or deleted show a relatively minor role for AMPK in regulating these processes at rest and during exercise. An important caveat of these studies is that AMPK activity is partially suppressed due to presence of the alternative subunit isoform. Therefore, to assess the contribution of AMPK and ACC2 in regulating substrate utilization at rest and during exercise, we generated muscle-specific AMPKβ1 β2 null (MKO) and whole-body ACC2 S212A knockin (KI) mice. Under resting conditions, all mice had similar body and tissue weights, oxygen consumption, substrate utilization and activity levels compared to wild-type (WT) littermates. AMPK β1β2 MKO mice had normal insulin sensitivity despite reduced mitochondria content and impaired exercise tolerance and glucose uptake during exercise/ muscle contraction. ACC2 S212A KI mice reveal that AMPK-independent pathways regulate fatty acid oxidation during exercise.



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➤Educational background & professional experience

1994	Seoul National University	Physical education / B.Ed.
1996	Seoul National University	Exercise physiology / M.S.
2004	Texas A&M University	Exercise physiology / M.S.
2007	Texas A&M University	Exercise physiology / Ph.D.
2008-2010	East Carolina University	Postdoctoral fellow
2010-2011	East Carolina University School of Medicine	Research assistant professor
2012-present	Inha University	Assistant professor

➤Research interests

Effects of obesity, aging, and exercise on mitochondrial function, ROS, insulin resistance, and apoptosis in skeletal muscle and heart

➤Brief list of publications

1. Kwak HB, Thalacker-Mercer A, Anderson EJ, Lin CT, Kane DA, Lee NS, Cortright RN, Bamman MM, and Neufer PD. Simvastatin impairs ADP-stimulated respiration and increase mitochondrial oxidative stress in primary human skeletal myotubes. Free Radic Biol Med 52: 198-207, 2012.
2. Lawler JM, Kwak HB, Kim JH, Lee Y, Hord JM, and Martinez DA. Biphasic stress response in the soleus during reloading following hindlimb unloading. Med Sci Sports Exerc 44: 600-609, 2012.
3. Kane DA, Lin CT, Anderson EJ, Kwak HB, Cox JH, Brophy P, Hickner RC, Neufer PD, and Cortright RN. Progesterone increases skeletal muscle mitochondrial H2O2 emission in non-menopausal women. Am J Physiol Endocrinol Metab 300: E528-535, 2011.
4. Kwak HB, Kim JH, Joshi K, Yeh A, Martinez DA, and Lawler JM. Exercise training reduces fibrosis and matrix metalloproteinase dysregulation in the aging rat heart. FASEB J 25: 1106-1117, 2011.
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6. Lawler JM and Kwak HB. Potential exercise mitigation and regulation of age-induced apoptosis and remodeling in the heart. In: Modern Insights into Disease from Molecules to Man: Apoptosis. V. R. Preedy (Ed.). Enfield, NH: Science Publishers, p. 389-403, 2010.
7. Song W, Kwak HB, Kim JH, and Lawler JM. Exercise training modulates the nitric oxide synthase profile in skeletal muscle from old rats. J Gerontol A Biol Sci Med Sci 64: 540-549, 2009.
8. Lawler JM, Kwak HB, Kim JH, and Suk MH. Exercise training inducibility of MnSOD protein expression and activity is retained while reducing pro-oxidant signaling in the heart of senescent rats. Am J Physiol Regul Integr Comp Physiol 296: R1496-R1502, 2009.

Exercise and obesity-induced insulin resistance in skeletal muscle

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The development of insulin resistance (IR), particularly in skeletal muscle, is closely associated with obesity and type II diabetes. Obesity-induced IR in skeletal muscle is a multifactorial process. So far, it is not clear what specific mechanism(s) are responsible for obesity-related IR. However, a number of contributing factors have been suggested. We will highlight some potential mechanisms of obesity-induced IR in skeletal muscle in terms of mitochondrial role in the cells; 1) mitochondrial-independent mechanisms including accumulations of intramyocellular lipid (IMCL) and lipid intermediates (e.g., FA-CoA, DAG, and ceramide) and 2) mitochondrial-dependent mechanisms including mitochondrial overload-related incomplete fatty acid oxidation and mitochondrial oxidative stress. Mitochondrial dysfunction is central to the pathogenesis of multiple diseases such as obesity, diabetes, aging, and cancer. Mitochondrial reactive oxygen species (ROS), a byproduct of mitochondrial oxidative phosphorylation, has been also implicated in insulin resistance in skeletal muscle. We recently found that high fat diet (HFD)-induced mitochondrial H_2O_2 emission was a primary factor linking excess fat intake to the development of IR in skeletal muscle. Mitigating HFD-induced H_2O_2 emission by high energy demand (e.g., exercise) may be a potential strategy to treat and/or prevent IR in obesity. We determined whether a daily mild increase in energy expenditure by exercise is sufficient to prevent the increase in skeletal muscle mitochondrial H_2O_2 emitting potential, and the decrease in insulin sensitivity induced by HFD in rodents. Young male Sprague-Dawley rats (3groups, n = 10/ group) were fed a standard chow or HFD (60% of total calorie from fat) for seven weeks. The animals given HFD were also administered by low intensity treadmill exercise (15 m/min, 0grade, 2 h/d, 7 d/wk, 7 wks). Insulin resistance by oral glucose tolerance test (2 g/kg) was elevated in HFD-fed rats. However, exercise preserved whole body insulin sensitivity. Exercise attenuated HFD-induced mitochondrial H_2O_2 emitting potential challenged by succinate (complex II substrate) and multiple substrates in permeabilized skeletal muscle fibers. These data demonstrate that a daily mild increase in energy expenditure induced by aerobic exercise training prevents the increase of mitochondrial H_2O_2 production in skeletal muscle and development of insulin resistance by HFD, supporting the concept that the governance of mitochondrial H_2O_2 emitting potential is a primary factor regulating insulin sensitivity in skeletal muscle.

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➤Educational background & professional experience

1985	University of California, Berkeley (Chemistry)	B.S.
1990	University of California, San Francisco (Medicine)	M.D.
2002-2007	University of Washington	Assistant professor in medicine
2007-present	University of Washington	Associate professor in medicine
2008-present	University of Washington	Endowed professorship in preventive cardiology

➤Research interests

Endothelial nitric oxide signaling and vascular inflammation
The role of insulin resistance and obesity in the development of vascular disease

➤Brief list of publications

1. Cheng AM, Handa P, Tateya S, Schwartz J, Tang C, Mitra P, Oram JF, Chait A, Kim F. Apolipoprotein A-I attenuates palmitate-mediated NF-kB activation by reducing Toll-like receptor-4 recruitment into lipid rafts. PLoS One. 2012:7(3):e33917.
2. Iwata NG, Pham M, Rizzo NO, Cheng AM, Maloney E, Kim F. Trans fatty acids induce vascular inflammation and reduce vascular nitric oxide production in endothelial cells. PLoS One. 2011:6(12):e29600.
3. Tateya S, Rizzo NO, Handa P, Cheng A, Morgan V, Daum G, Clowes AW, Schwartz MW, Kim F. Endothelial Nitric Oxide/cGMP/Vasodilator-stimulated Phosphoprotein Signaling Attenuates Kupffer Cell activation and hepatic insulin resistance induced by High Fat Feeding. Diabetes 2011;60(11):2792-801.
4. Handa P, Tateya S, Rizzo NO, Cheng AM, Morgan-Stevenson V, Han CY, Clowes AW, Daum G, O'Brien KO, Schwartz MW, Chait A, Kim F. Reduced vascular nitric oxide/cGMP signaling contributes to adipose tissue inflammation during high fat feeding. Arteriosclerosis, Thrombosis, and Vascular Biology. 2011;31:2827-2835.
5. Rizzo NO, Maloney E, Pham M, Luttrell I, Wessells H, Tateya S, Daum G, Handa P, Schwartz MW, Kim F. Reduced Nitric Oxide/cGMP Signaling Contributes to Vascular Inflammation and Insulin Resistance Induced by High Fat Feeding. Arteriosclerosis, Thrombosis, and Vascular Biology. 2010; 30:758-765.
6. Maloney E, Sweet IR, Hockenbery DM, Pham M, Rizzo NO, Tateya S, Schwartz MW, Kim F. Activation of NF-kB by Palmitate in Endothelial Cells: A Key Role for NADPH oxidase-derived Superoxide in response to TLR4 Activation. Arteriosclerosis, Thrombosis, and Vascular Biology. 2009;29:1370-5.
7. Kim F, Pham M, Maloney E, Rizzo NO, Morton GJ, Wisse BE, Kirk EA, Chait A, Schwartz MW. Vascular Inflammation, Insulin Resistance and Reduced Nitric Oxide Production Precede the Onset of Peripheral Insulin Resistance. Arteriosclerosis, Thrombosis, and Vascular Biology. 2008;28:1982-1988.
8. Kim F, Pham M, Luttrell I, Bannerman DD, Tupper J, Thaler J, Hawn TR, Raines EW, Schwartz MW. Toll Like Receptor-4 Mediated Vascular Inflammation and Insulin Resistance in Diet-Induced Obesity. Circulation Research. 2007;100:1589-1596.
9. Kim F, Tyselling K, Rice J, Haji L, Gallis B, Baas A, Paramsothy P, Giachelli CM, Corson M, Raines EW. Free Fatty Acid Impairment of Nitric Oxide Production in Endothelial Cells is Mediated by IKKb Arteriosclerosis, Thrombosis, and Vascular Biology. 2005;25 989-994.
10. Sweet IR, Gilbert M, Maloney E, Hockenbery D, Schwartz MW, Kim F. Endothelial Inflammation induced by excess glucose is associated with cytosolic glucose 6-phosphate but increased mitochondrial respiration. Diabetologia 2009;52:921-31.

The effect of VASP signaling on vascular inflammation

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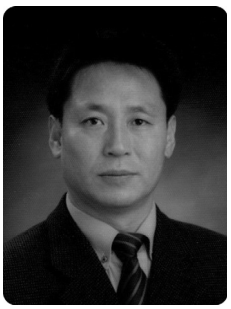
Activation of vascular inflammatory pathways is an important early step in vascular insulin resistance and in the development of atherosclerosis. Vasodilatory-stimulated phosphoprotein (VASP) was discovered as an important phosphorylated protein in platelets in response to agents that elevate cGMP and cAMP levels. In target cells, NO activates a complex cascade of events. First, NO activates soluble guanylate cyclase leading to cGMP synthesis. cGMP exerts its main biologic activation by activating the cGMP-dependent protein kinase (PKG). Down regulation of sGC and PKG impairs NO function and leads to increased proliferation and vascular constriction. Since NO has well known anti-inflammatory effects, we hypothesized that VASP may mediate NO-dependent inhibition of NF-kB activation.

To determine the effects of VASP signaling on endothelial NF-kB and insulin signaling, we overexpressed VASP protein and empty vector constructs in bovine aortic endothelial cells (BAECs). In empty vector-transduced BAEC, palmitate increased NF-kB and attenuated insulin-mediated activation of phospho-Akt and phospho-eNOS, whereas VASP overexpression attenuated palmitate-mediated NF-kB activation and restored insulin signaling in transduced BAEC. These results, suggest that overexpression of VASP is sufficient to reverse the inflammatory effects of palmitate and restore endothelial insulin signaling.

We next assessed VASP signaling *in vivo* in a diet-induced obesity model of insulin resistance. Thoracic aortic lysates were analyzed by western blot for PKG, VASP, and VASP serine 239 phosphorylation (a marker of VASP activity). HF-feeding reduced phospho-VASP levels, without significant changes in total PKG or total VASP levels. Finally, in chow fed VASP-/- mice and litter-mate control mice, we found evidence for increased vascular inflammation and impaired insulin mediated activation of Akt and eNOS in the thoracic aorta in the VASP-/- mice. These findings suggest that, the absence of VASP signaling is sufficient to cause vascular insulin resistance.

These data demonstrate that vascular VASP signaling plays an important role in regulating vascular inflammation.



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➤Educational background & professional experience

1990-1993	Seoul National University	Department of veterinary medicine / Ph.D.
1995-1997	University of North Carolina (Chapell Hill, NC)	Department of pathology/Research associate fellow
1988-2004	Korea Research Institute of Bioscience & Biotechnology(KRIBB)	Senior research scientist, principal research scientist
2010-2011	Harvard Medical School	Devision of vascular medicine/Visiting professor
2010-2012	National Research Foundation of Korea	Review board
2007-2012	National Research Laboratory Program(NRL), National Research Foundation of Korea	Haed
2012-present	National Creative Research Center for Immune and Vascular cell Network, National Research Foundation of Korea	Director
2004-present	Ewha Womans University	Division of molecular life sciences/Professor, associate professor

➤Research interests

Molecular medcine; cardiovascular disease
Developmental genetics; transgenic animal model

➤Brief list of publications

1. In-Hyuk Jung, You-Han Lee, Ji-Young Yoo, Se-Jin Jeong, Seong Keun Sonn, Jong-Gil Park, Keun Ho Ryu, Bong Yong Lee, Hye Young Han, So Young Lee, Dae-Yong Kim, Hang Lee, Goo Taeg Oh. Ginkgo bilobaExtract(GbE) Enhances the Anti-atherogenic Effect of Cilostazol by Inhibiting ROS Generation. Exp Mol Med. 2012 May 31;44(5):311-318.
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3. Jong-Gil Park, Ji-Young Yoo, Se-Jin Jeong, Jae-Hoon Choi, Mi-Ran Lee, Mi-Ni Lee, Jeong Hwa Lee, Hyoung Chin Kim, Hanjoong Jo, Dae-Yeul Yu, Sang Won Kang, Sue Goo Rhee, Mun-Han Lee, Goo Taeg Oh. Peroxiredoxin 2 deficiency exacerbates atherosclerosis in apolipoprotein E-deficient mice. Circulation Research 2011 Sep 16;109(7):739-749.
4. Jong Gil Park, Goo Taeg Oh. The role of peroxidases in the pathogenesis of atherosclerosis. BMB Reports. 2011 Aug;44(8):497-505.
5. Jae-Hoon Choi, Jong-Gil Park, Hyung Jun Jeon, Mi-Sun Kim, Mi-Ran Lee, Mi-Ni Lee, Seong Keun Sonn, Jae-Hong Kim, Mun Han Lee, Myung-Sook Choi, Yong Bok Park, Oh-Seung Kwon, Tae-Sook Jeong, Woo Song Lee, Hyun Bo Shim, Dong Hae Shin, Goo Taeg Oh. 5-(4-Hydroxy-2,3,5-trimethylbenzylidene) thiazolidine-2,4-dione attenuates atherosclerosis possibly by reducing monocyte recruitment to the lesion. Exp Mol Med. 2011 Aug 31;43(8):471-478.
6. Jae-Hoon Chio, Hyung Jun Jeon, Jong-Gil Park, Seong Keun Sonn, Mi-Ran Lee, Mi-Ni Lee, Hye Jin You, Geun-Young Kim, Jae-Hong Kim, Mun Han Lee, Oh-Seung Kwon, Ki-Hoan Nam, Hyoung-Chin Kim, Tae-Sook Jeong, Woo Song Lee, Goo Taeg Oh. Anti-atherogenic effect of BHB-TZD having inhibitory activities on cyclooxygenase and 5-lipoxygenase in hyperlipidemic mice. Atherosclerosis 2010 Sep;212(1):146-152.

Resistin-like molecule-α ameliorates hypercholesterolemia and atherosclerosis via enhancement of cholesterol metabolism.

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Hyperlipidemia is a well-recognized risk factor of atherosclerosis, and can be induced by abnormal production of adipokines. Resistin-like molecule (Relm) α, one of adipokines, is induced under the diet/energy intake. However, direct relationship between Relm-α and circulating lipids is unclear. Here we report that the induction of Relm-α maintains cholesterol homeostasis by regulating bile acid production under hyperlipidemic conditions. Relm-α-overexpressing mice display reduction of the serum cholesterol level under high-fat diet feeding conditions. Gene expression analysis based on whole-genome microarray profiling demonstrates that Relm-α induces expressions of cholesterol 7alpha-hydroxylase (Cyp7a1) and sterol 12 alpha-hydroxylase (Cyp8b1), hepatic key enzymes that affect whole-body cholesterol balance through degradation of cholesterol into bile acid, suggesting that these genes are molecular targets to account for the cholesterol-lowering effect of Relm-α. Furthermore, induction of Cyp7a1 and Cyp8b1 by Relm-α leads to the enhancement of hepatic cholesterol catabolism, which is accompanied by leading to increase of hepatic bile acid production and fecal bile acid excretion. Finally, these effects by Relm-α protect against atherosclerosis in diet-induced hyperlipidemic LDL receptor-deficient mice. Taken together, these results indicate that Relm-α is an anti-atherosclerotic adipokine that may offer novel therapeutic strategies to combat hypercholesterolemia and atherosclerosis.

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➤Educational background & professional experience

1986	Seoul National U, College of Medicine	B.A.
1990	Seoul National U, College of Medicine	S
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1990	Seoul National U Hospital	Resident
1995	Seoul National U Hospital	Fellow
present	Seoul National U Hospital	Professor

➤Research interests

Type 1 diabetes immunogenetics, diabetes complication, islet biology

➤Brief list of publications

1. Min D, Park Y, et al. Amelioration of diabetic neuropathy by TAT-mediated enhanced delivery of metallothionein and SOD. Endocrinology 153(1):81-91, 2012.
2. Park Y, Hong SM, Park LJ, Woo JT, Paik SH, Nam MS, Lee KW, Kim YS, and the KNDP. LADA prevalence estimation and insulin dependency during follow-up. Diab Metab Res Rev 27(8):975-9. 2011.
3. Kim EM, Park Y, et al. The mouse small ubiquitin-like modifier-2 (SUMO-2) inhibits interleukin-12 (IL-12) production in mature dendritic cells by blocking the translocation of the p65 subunit of NFkB into the nucleus. Mol Immunol 48: 2189-2197, 2011.
4. Park L, Min D, Kim H, Park J, Choi S, Park Y. The combination of metallothionein and superoxide dismutase protects pancreatic β cells from oxidative damage. Diab Metab Res Rev 27(8):802-8, 2011.
5. Hwang KW, Won TJ, Kim H, Chun HJ, Chun T, Park Y. Characterization of regulating mechanism of the small ubiquitin-like modifier protein (SUMO). Diab Metab Res Rev 27(8):854-61, 2011.
6. Park LJ, Min DS, Kim HO, Chung HY, Lee CH, Park IS, Kim YH, Park Y. TAT-enhanced delivery of metallothionein can partially prevent the development of diabetes. Free Radic Biol Med 51(9):1666-74, 2011.
7. Chun MY, Hwang HS, Cho HY, Chun HJ, Woo JT, Lee KW, Nam MS, Baik SH, Kim YS, Park Y. Association of vascular endothelial growth factor polymorphisms with non-proliferative and proliferative diabetic retinopathy. J Clin Endocrinol Metab 95(7):3547-51, 2010.
8. Park Y: Functional evaluation of the type 1 diabetes susceptibility candidate genes. Diabetes Res Clin Pract 77: S110-S115, 2007.
9. Park Y: Why is type 1 diabetes uncommon in Asia? Ann NY Acad Sci 1079:31-40, 2006.
10. Park Y, Park S, Kang J, Yang S, Kim D: Assessing the validity of the association between the SUMO4 M55V variant and risk of type 1 diabetes. Nat Genet 37:112, 2005.

Amelioration of diabetic micro- and macrovascular complications by TAT-mediated delivery of metallothionein and SOD

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Diabetes mellitus and diabetic micro- and macrovascular complications (DCx) might be resulted from oxidative stress in various tissues including pancreatic islets and antioxidant treatment may improve underlying conditions. To circumvent their limited access into the biologic membrane, we made Tat-MT and Tat-SOD constructs applying cell penetrating peptide technologies, delivered to cardinal primary cultured cells of diabetes and diabetic complication development or their surrogate cell lines and studied cell viability in different injury conditions of high glucose, hypoxia and AGE treatment. The protective effect of Tat-MT and Tat-SOD in combination against the development of diabetes and complications development were also studied in OLETF rats. Tat-MT and Tat-SOD were successfully delivered to various cultured cells, and the intracellular activities of MT and SOD increased in line with the amount of protein delivered. These agents inhibited three different oxidative injuries as well as angiotensin II-mediated injuries and altered the expression of the downstream signaling molecules. In OLETF rats, a single intraperitoneal injection of Tat-MT and Tat-SOD resulted in delivery of these antioxidants to the various organs. Continuous treatment decreased the expression of ROS and downstream signaling molecules in various tissues and delayed the clinical development of diabetes and diabetic complications. The ameliorative effects of these agents against the development of micro- and macrovascular complications in vivo may be related to inhibition of ROS itself and downstream signaling pathways. We conclude that effective delivery of a combination antioxidant treatment may prevent and treat the pathophysiology in patients with diabetes and its complications.

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➤Educational background & professional experience

1977-1983	Chonbuk National University Medical School	M.D.
1983-1990	Chonbuk National University Medical School	Ph.D.
1983-1987	Chonbuk National University Medical School	Research assistant
1987-1990	Flight Surgeon, Korean Air Force Academy (Military duty)	
1990-1991	Department of Physiology, Cornell University Medical College	Research fellow
1992-1994	Indiana University, Krannert Institute of Cardiology	Research fellow and associate
1995-2001	Department of Physiology, Chonbuk National University Medical School	Assistant professor/Associate professor
2001-2003	Pohang University of Science and Technology (POSTECH)	Associate professor, department of life sciences
2003-2010	Professor	
2011-present	Graduate School of Medical Science and Engineering Korea Advanced Institute of Science and Technology (KAIST)	Distinguished professor

➤Research interests

Cardiac Regeneration, Angiogenesis, lymphangiogenesis, Adipogenesis, Stem Cells

➤Brief list of publications

1. ROCK suppression promotes differentiation and expansion of endothelial cells from embryonic stem cells-derived Flk1+ mesodermal precursor cells. Blood, 2012 Aug 14. [Epub ahead of print] PMID: 22896004.
2. Regulation and implications of inflammatory lymphangiogenesis. Trends in Immunology 33:350-356, 2012.
3. Angiopoietin-1 promotes endothelial differentiation from embryonic stem cells and induced pluripotent stem cells. Blood 118:2094-2104, 2011.
4. The spatiotemporal development of adipose tissue. Development 138:5027-5037, 2011.
5. Stromal Vascular Fraction From Adipose Tissue Forms Profound Vascular Network Through the Dynamic Reassembly of Blood Endothelial Cells. Arterioscler. Thromb. Vasc. Biol. 31:1141-50, 2011.
6. Double anti-angiogenic and anti-inflammatory protein, Valpha, targeting VEGF-A and TNF-α in retinopathy and psoriasis. J. Biol. Chem. 286:14410-14418, 2011.
7. T Lymphocytes Negatively Regulate Lymph Node Lymphatic Vessels Through Interferon-Gamma. Immunity 34:96-107, 2011.
8. Regulation of chemo-resistant melanoma cell metastasis by a lymphatic metastatic niche: a key role of CXCR4 signaling. Cancer Research 70:10411-10421, 2010.
9. Double anti-angiogenic protein, DAAP, targeting VEGF-A and angiopoietins in tumor angiogenesis, metastasis, and vascular leakage. Cancer Cell 18:171-184, 2010.

Beneficial effects of angiopoietin-1 in diabetic complications: insights from preclinical animal studies

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Microvascular dysfunction and accompanied inflammation are the major causes of impaired wound healing, nephropathy, cardiopathy, retinopathy, erectile dysfunction and neuropathy seen in patients with chronic diabetes. Therefore, re-establishment of structural and functional microvasculature could alleviate diabetes-induced complications. Angiopoietin-1 (Ang1) is a secreted protein that acts as a ligand for Tie2, which is mainly expressed in growing vascular endothelial cells (ECs). Indeed, systemic or topical supplementation of Ang1 leads to accelerated wound closure and epidermal/dermal regeneration by enhanced angiogenesis, lymphangiogenesis and blood flow in the wound region of *db/db* diabetic mice. In *db/db* mice, systemic supplementation of Ang1 does not merely a dramatic increase in smooth muscle coverage on the vasculature of myocardial ischemia, but it also causes delay the fibrotic changes in the renal glomeruli through its anti-inflammatory effects. Intravitreal Ang1 supplementation induced organized retinal angiogenesis with a fair amount of pericyte coverage in the ischemic retina of a proliferative diabetic retinopathy mouse model, leading to reduction of avascular regions, hypoxia, leakage, and neuronal injury in the retina. Moreover, intracavernous delivery of Ang1 restores erectile dysfunction not only by promotion of cavernous neovascularization, eNOS phosphorylation, and cGMP production but also by reduction of cavernous vascular permeability via restoration of EC junction proteins in *db/db* and streptozotocin-induced diabetic mice. Furthermore, Ang1 recovers the molecular biomarkers of neuropathy, promotes angiogenesis in endoneural microvessels, and suppresses inflammation in the sciatic nerves of *ob/ob* diabetic mice. Taken together, Ang1 exerts an anti-diabetic role and delays diabetic complications mainly via the restoration of microvascular function.

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➤Educational background & professional experience

1993	College of Medicine, the Catholic University of Korea, Seoul, Korea	M.D. degree
1993-1994	Kangnam St. Mary's Hospital, Seoul, Korea	Internship
1994-1998	Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea	Residency
1997	College of Medicine, the Catholic University of Korea, Seoul, Korea	Master degree
2001-2003	Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea	Clinical instructor
2003-2005	Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea	Instructor
2005	College of Medicine, the Catholic University of Korea, Seoul, Korea	Ph.D. degree
2005-	Division of Endocrinology and Metabolism, Assistant Professor Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea	
2007-2008	Division of Cardiology, Emory University, GA, USA	Visiting scholar
2009-present	Division of Endocrinology and Metabolism, Department of Internal Medicine, The Catholic University of Korea, Seoul, Korea	Associate professor

➤Research interests

Pathogenesis and risk factors of diabetic vascular complications
Pathogenesis and risk factors of the metabolic syndrome and diabetes mellitus

➤Brief list of publications

1. Usefulness of Albuminuria as Predictor for Coronary Artery Stenosis, Regardless of Estimated Glomerular Filtration Rate, in Patients With Type 2 Diabetes Mellitus. Am J Cardiol. 2012 Aug 1. [Epub ahead of print].
2. Influence of Visceral Adiposity on Cardiovascular Autonomic Neuropathy in Patients with Type 2 Diabetes Mellitus. Diabetes Metab J 2012;36:285-292.
3. Serum BMP-4 levels in relation to arterial stiffness and carotid atherosclerosis in patients with Type 2 diabetes. Biomark Med. 2011 Dec;5(6):827-35.
4. Identifying metabolically obese but normal-weight (MONW) individuals in a nondiabetic Korean population: the Chungju Metabolic disease Cohort (CMC) study. Clin Endocrinol (Oxf). 2011 Oct;75(4):475-81.
5. Association of serum bone morphogenetic protein 4 levels with obesity and metabolic syndrome in non-diabetic individuals. Endocr J. 2011 Jan 30:58(1):39-46.
6. Diabetic retinopathy is associated with subclinical atherosclerosis in newly diagnosed type 2 diabetes mellitus. Diabetes Res Clin Pract. 2011 Feb 91(2):253-259.
7. Insulin resistance and inflammation may have an additional role in the link between cystatin C and cardiovascular disease in type 2 diabetes mellitus patients. Metabolism. 59(2):241-246, 2010.
8. Clinical Implications of Serum Biomarkers in Diabetic Cardiovascular Complications. Korean Diabetes J. 33(5):363-372, 2009.
9. Cystatin C is a Valuable Marker for Predicting Future Cardiovascular Diseases in Type 2 Diabetic Patients. Korean Diabetes J. 32(6):488-497, 2008.
10. The prevalence and clinical characteristics of the metabolic syndrome in middle-aged Korean adults. Korean J Med. 68(4):359-368, 2005.

How to assess glycemic control in GDM during pregnancy?

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Fasting plasma glucose usually decreases in early normal pregnancy, but mean and postprandial glucose levels slightly increase during the second and third trimesters of normal pregnancy. In non-diabetic pregnant women, suggested normal reference ranges for capillary fasting, overnight, and pre-meal glucose are 50~99 mg/dL, with post-meal peak values 60-70 min after meals of 81~129 mg/dL. Regular glucose self-monitoring by patients is the central part of the management of diabetes during pregnancy. Frequent sampling is needed during pregnancy because of the high possibility of rapid-onset hypoglycemia without food or after exercise. Exaggerated hyperglycemic response to food intake, emotional stress are also commonly observed in pregnancy. However, the optimal timing and frequency of glucose monitoring during pregnancy are still controversial. One study reported that lower frequencies of perinatal complications with the treatment targeting on post-meal glucose. Another study supported these data that revealed postprandial glucose levels as the best predictor of fetal macrosomia. However, other studies reported that perinatal complications are more closely related to fasting glucose levels than to post-challenge glucose levels measured at the time of diagnosis of GDM.

Studies with continuous glucose monitoring system (CGMS) in diabetic pregnant women showed the mean peak postprandial glucose to average 90 min after beginning the meal, with patient-to-patient or day-to-day variabilities. Some experts suggest that teaching patients to measure at 1 hour after finishing the meal might approximate these peaks. However, delayed gastric emptying, meals with high fat content prolong the postprandial peak glucose excursion. The greater carbohydrate content in the meal cause higher postprandial glucose level. Processed foods containing sugars can elevate the glucose level quickly with usual peak at 1 hour after ingestion.

In the absence of definitive evidence, it has become common practice to ask patients to measure capillary glucose levels before breakfast and 1~2 hours after breakfast, lunch and dinner. Commonly recommended targets are fasting plasma glucose levels $\leq$ 95 mg/dL, 1 hour post-meal glucose levels $\leq$ 140 mg/dL and 2 hour post-meal glucose levels 120 mg/dL.

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➤Educational background & professional experience

1991-1995	Seoul National University College of Medicine	M.D.
2001-2003	Seoul National University College of Medicine	OBGYN / M.S.
2003-2012	Seoul National University College of Medicine	OBGYN / Ph.D.
1995-1996	Seoul National University Hospital	Internship
1996-1999	Military Surgeon	As a compulsary
1999-2003	Dept. of OBGYN, Seoul National University Hospital	Resident ship
2003-2004	Dept. of OBGYN, Seoul National University Hospital	Clinical fellow
2004-2005	Perinatal Research Branch of NIH, USA	Research fellow
2005-2005	Dept. of OBGYN, Seoul National University Bundang Hospital	Clinical fellow
2005-2012	Dept. of OBGYN, Seoul National University Bundang Hospital	Assistant professor
2010-2011	Wayne State University, USA	Visiting scholar
2012-present	Dept. of OBGYN, Seoul National University Bundang Hospital	Associate professor

➤Research interests

Intrauterine fetal growth, gestational diabetes

➤Brief list of publications

1. Hong JS, Choi CW, Park KU, Kim SN, Lee HJ, Lee HR, Choi EH, Park KH, Suh CS, Kim BI, Choi ST, Kim SS. Genital group B Streptococcus carrier rate and serotype distribution in Korean pregnant women: implications for group B streptococcal disease in Korean neonates. J Perinat Med. 2010 Jul;38(4):373-7.
2. Hong JS, Park KH, Noh JH, Suh YH. Cervical length and the risk of microbial invasion of the amniotic cavity in women with preterm premature rupture of membranes. J Korean Med Sci. 2007 Aug;22(4):713-7.
3. Hong JS, Choi JY, Zhu L, Lee JH, Lim IS, Chung YS, Choi CW, Park KH, Suh CS, Han ES. Echocardiographic Assessment of Left Ventricular Diastolic Function in Transitional Circulation Period. Korean Circ J. 2006 Sep;36(9):652-660.
4. Hong JS, Park KH, Kim HJ, Han SH, Jeon YT, Kim YB, Suh CS. Effect of oligohydramnios and intrauterine infection on fetal blood vessels and umbilical artery blood flows in patients with preterm premature rupture of membranes. Korean J Obstet Gynecol. 2006 Jun;49(6):1219-1229.
5. Hong JS, Santolaya-Forgas J, Romero R, Espinoza J, Gonçalves LF, Kim YM, Edwin S, Yoon BH, Nien JK, Hassan S, Mazor M. Maternal plasma osteoprotegerin concentration in normal pregnancy. Am J Obstet Gynecol. 2005 Sep;193(3 Pt 2):1011-5.
6. Hong JS, Yoon BH. Pregnancy outcome, intra-amniotic inflammation and the value of repeated fetal fibronectin test in patients with a positive cervical fetal fibronectin. Korean J Obstet Gynecol. 2005 Mar;48(3):563-574.

Is early screening of diabetes necessary in Korean women?

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Pre-pregnancy diabetes (overt diabetes) first noted during pregnancy is important for several reasons: an increased risk of congenital anomalies of fetus; high risk of end organ diabetes complications requiring treatment during pregnancy; need for rapid treatment and close follow-up during pregnancy to ensure prompt restoration of normal glycemia and need to ensure appropriate treatment of diabetes after pregnancy. To identify women with overt diabetes in pregnancy properly, the International Association of Diabetes and Pregnancy Study Group (IADPSG) recommends screening pregnant women at the initial visit for prenatal care with use of fasting plasma glucose, glycosylated hemoglobin, or random plasma glucose. There are several issues that should be considered. Decision to perform universal early testing or to limit testing to only women with characteristics indicating a high risk for diabetes should be made on the basis of the background population prevalence of diabetes in young women. Attending the first prenatal visit in the fasting state is impractical in usual setting. Furthermore, the clinical value and cost-effectiveness of this early testing in pregnancy to detect overt diabetes is uncertain. These issues in Korean women will be discussed.

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➤Educational background & professional experience

1991-1997	Inje University, College of Medicine	Medical science / Bachelor/M.D.
1997-1998	University of Michigan, USA	Medical science / Visiting scholar
2001-2003	Inje University, Graduate school	Internal medicine / Master
2003-2005	Ulsan University, Graduate school	Internal medicine / Ph.D.
1999-2003	Inje University Sanggye Paik Hospital	Internal medicine / Residency
2003-2005	Asan Medical Center, Endocrinology & Metabolism	Clinical/Research fellow
2005-2007	Korean Organ Donation Center, Internal Medicine	Advisory board
2007-present	MizMedi Hospital, Endocrinology & Metabolism	Clinical staff

➤Research interests

Major: gestational diabetes mellitus

➤Brief list of publications

1. Lee WJ, Kim SW, Kim GH, Han SM, Won JC, Jung CH, Park HS, Choi do S, Lee KU, Park JY. Alpha-lipoic acid activates dimethylarginine dimethylaminohydrolase in cultured endothelial cells. Biochem Biophys Res Commun. 2010 Aug 6;398(4):653-8. Epub 2010 Jul 11. Erratum in: Biochem Biophys Res Commun. 2010 Oct 22;401(3):491.
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3. Han SM, Namkoong C, Jang PG, Park IS, Hong SW, Katakami H, Chun S, Kim SW, Park JY, Lee KU, Kim MS. Hypothalamic AMP-activated protein kinase mediates counter-regulatory responses to hypoglycaemia in rats. Diabetologia. 2005 Oct;48(10):2170-8.
4. Lee WJ, Lee IK, Kim HS, Kim YM, Koh EH, Won JC, Han SM, Kim MS, Jo I, Oh GT, Park IS, Youn JH, Park SW, Lee KU, Park JY. Alpha-lipoic acid prevents endothelial dysfunction in obese rats via activation of AMP-activated protein kinase. Arterioscler Thromb Vasc Biol. 2005 Dec;25(12):2488-94.
5. Lee KU, Lee IK, Han J, Song DK, Kim YM, Song HS, Kim HS, Lee WJ, Koh EH, Song KH, Han SM, Kim MS, Park IS, Park JY. Effects of recombinant adenovirus-mediated uncoupling protein 2 overexpression on endothelial function and apoptosis. Circ Res. 2005 Jun 10;96(11):1200-7.
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7. Han SM, Kim ES, Kim YI, Song KH, Kim MS, Kim WB, Park JY, Lee KU. Prevalence and clinical characteristics of metabolic syndrome in a rural population of South Korea. Diabet Med. 2004 Oct;21(10):1141-3.
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The current status of using oral antidiabetic agent in GDM

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Gestational diabetes mellitus (GDM) complicates substantial number (2~10%) of pregnancies. The incidence is increasing as the rates of obesity increase. The prevalence will significantly increase if the new IADPSG recommendations are more widely adopted, although there are controversies surrounding the widespread application of them.

Numerous studies have shown the direct relationship between the maternal hyperglycemia and perinatal outcomes. Therefore, the treatment during pregnancy emphasizes intensification of metabolic management by combination of medical nutrition therapy and medication. To achieve specific goals of glycemic control, between 20% to 50% of women with GDM will require pharmacologic therapy.

Traditionally, insulin therapy has been considered the gold standard for the management of GDM, because of its efficacy in achieving target glucose level and the fact that it dose not cross the placenta. But, difficulty in administration with multiple daily injections, potential hypoglycemia, and increase in weight make this therapeutic option sometimes cumbersome. Since both GDM and T2DM are based on the insulin resistance and relatively decreased insulin secretion to overcome, the oral antidiabetic agents that target these defects can be alternatives to insulin therapy. Much of the concern over the use of oral agents is the lack of convincing data regarding the extent to which they cross placenta and the potentials of fetal risk. As such, the use of these medications remain issue of debate and ongoing research.

Among several available oral antidiabetic agents in pregnancy, glyburide (glibenclamide) and metformin are the two most commonly used agents in the world. In this presentation, the objectives are to review available data on efficacy and adverse effects of these medications and discuss the currents gaps between research and clinical practice.

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➤Educational background & professional experience

1977-1983	Seoul National University College of Medicine	M.D.
1983-1984	Seoul National University Hospital	Intern
1987-1990	Seoul National University Hospital, Internal Medicine	Resident
1989-1991	Seoul National University	M.S.
1991-1994	Seoul National University	Ph.D.
1997-2003	Sungkyunkwan University	Assistant professor
2003-present	Seoul National University	Professor

➤Research interests

Clinical epidemiological study of elderly diabetes / gestational diabetes mellitus
Insulin resistance and beta cell function in high risk population
Sarcopenia and sarcopenic obesity

➤Brief list of publications

1. Kim KE, Jang SN, Lim S, Park YJ, Paik NJ, Kim KW, Jang HC, Lim JY. Relationship between muscle mass and physical performance: is it the same in older adults with weak muscle strength? Age Ageing. 2012 Aug 21. [Epub ahead of print].
2. Kim JH, Choi SH, Lim S, Lim JY, Kim KW, Park KS, Shin CS, Jang HC. Thigh muscle attenuation measured by computed tomography was associated with the risk of low bone density in community-dwelling elderly population. Clin Endocrinol (Oxf). 2012 Aug 18.
3. Lee Y, Shin H, Vassy JL, Kim JT, Cho SI, Kang SM, Choi SH, Kim KW, Park KS, Jang HC, Lim S. Comparison of regional body composition and its relation with cardiometabolic risk between BMI-matched young and old subjects. Atherosclerosis. 2012 Jul 16.
4. Kwak SH, Kim SH, Cho YM, Go MJ, Cho YS, Choi SH, Moon MK, Jung HS, Shin HD, Kang HM, Cho NH, Lee IK, Kim SY, Han BG, Jang HC, Park KS. A Genome-Wide Association Study of Gestational Diabetes Mellitus in Korean Women. Diabetes. 2012 Feb;61(2):531-41.
5. Lim S, Shin H, Kim MJ, Ahn HY, Kang SM, Yoon JW, Choi SH, Kim KW, Song JH, Choi SI, Chun EJ, Shin CS, Park KS, Jang HC. Vitamin D inadequacy is associated with significant coronary artery stenosis in a community-based elderly cohort: the Korean Longitudinal Study on Health and Aging. J Clin Endocrinol Metab. 2012 Jan;97(1):169-78.
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Gestational diabetes mellitus in Korea: now and future

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Gestational diabetes mellitus (GDM) is defined as glucose intolerance of variable severity with onset or first recognition during pregnancy. It is well known that GDM is associated with adverse pregnancy outcomes including preeclampsia, Cesarean delivery, macrosomia, and perinatal morbidities. In addition, women with GDM are at an increased risk for type 2 diabetes mellitus (type 2 DM) later in life. The first criteria for the diagnosis of GDM were established more than 40 years ago, and it was derived from identifying women at high risk for diabetes after pregnancy, not to identify pregnant women with increased risk for adverse pregnancy outcome.

Recently the International Association of Diabetes and Pregnancy Study Groups (IADPSG) IADPSG introduced the new diagnostic criteria for gestational diabetes based on the results of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. HAPO study was an observational study to clarify the association between maternal glucose levels and adverse pregnancy outcome in multinational, ethnically diverse cohort of 25,000 women. However, the incidence of GDM using the new criteria was 17.8% in HAPO cohort.

In Korea, 2 to 5% of all pregnant women were previously reported to have GDM. Considering the recent trend of pregnant women is getting older and obese, the incidence of GDM in Korean women is expected to increase. The cumulative incidence of diabetes in Korean women with previous GDM was reported as 40% within 5 years postpartum. Although the BMI of Korean women with previous GDM was much lower than that of women living in U.S., the incidence of diabetes after delivery was similar. Genetic or constitutional factors might play a role in the development of diabetes on Korean women, but further studies are needed. In addition, the strategy for detecting GDM suitable in Korean women should be developed.

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➤Educational background & professional experience

1996	Kyoto University Medical School	M.D.
2003	Kyoto University Graduate School of Medicine	Ph.D.
2003-2007	RIKEN Center for Developmental Biology	Research scientist
2007-2009	Kobe City Medical Center General Hospital	Assistant head physician
2009-present	Kobe University Graduate School of Medicine	Assistant professor

➤Research interests

My clinical experience as an ophthalmologist motivated me to investigate molecular mechanisms underlying macular edema and deregulated angiogenesis in diabetic retinopathy. By utilizing mouse retinal angiogenesis as a model system, I am currently focusing on two topics: endothelial integrity in the absence of pericytes, and angiogenic directionality in ischemic retinas. By combining pharmacological and genetic manipulations in the mouse eye, I am evaluating potential of endothelial-specific signaling molecules as drug targets to treat diabetic retinopathy.

➤Brief list of publications

1. Felcht M, Luck R, Schering A, Seidel P, Srivastava K, Hu J, Bartol A, Kienast Y, Vettel C, Loos EK, Kutschera S, Bartels S, Appak S, Besemfelder E, Terhardt D, Chavakis E, Wieland T, Klein C, Thomas M, Uemura A, Goerdt S, Augustin HG. Angiopoietin-2 differentially regulates angiogenesis through Tie2 and integrin signaling. J Clin Invest. 122:1991-2005, 2012.
2. Kurogane Y, Miyata M, Kubo Y, Nagamatsu Y, Kundu RK, Uemura A, Ishida T, Quertermous T, Hirata K, Rikitake Y. FGD5 mediates pro-angiogenic action of vascular endothelial growth factor in human vascular endothelial cells. Arterioscler Thromb Vasc Biol. 32:988-996, 2012.
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4. Fukuhara S, Simmons S, Kawamura S, Inoue A, Orba Y, Tokudome T, Sunden Y, Arai Y, Moriwaki K, Ishida J, Uemura A, Kiyonari H, Abe T, Fukamizu A, Hirashima M, Sawa H, Aoki J, Ishii M, Mochizuki N. The sphingosine-1-phosphate transporter Spns2 expressed on endothelial cells regulates lymphocyte trafficking in mice. J Clin Invest. 122:1416-1426, 2012.
5. Fukushima Y, Okada M, Kataoka H, Hirashima M, Yoshida Y, Mann F, Gomi F, Nishida K, Nishikawa S, Uemura A. Sema3E-PlexinD1 signaling selectively suppresses disoriented angiogenesis in ischemic retinopathy in mice. J Clin Invest. 121:1974-1985, 2011.
6. Moriya J, Minamino T, Tateno K, Okada S, Uemura A, Shimizu I, Yokoyama M, Nojima A, Okada M, Koga H, Komuro I. Inhibition of semaphorin as a novel strategy for therapeutic angiogenesis. Circ Res. 106:391-398, 2010.
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8. Uemura A, Kusuhara S, Wiegand SJ, Yu RT, Nishikawa S. Tlx acts as a pro-angiogenic switch by regulating extracellular assembly of fibronectin matrices in retinal astrocytes. J Clin Invest. 116:369-377, 2006.
9. Uemura A, Kusuhara S, Katsuta H, Nishikawa S. Angiogenesis in the mouse retina: a model system for experimental manipulation. Exp Cell Res. 312:676-683, 2006.
10. Uemura A, Ogawa M, Hirashima M, Fujiwara T, Koyama S, Takagi H, Honda Y, Wiegand SJ, Yancopoulos GD, Nishikawa S. Recombinant angiopoietin-1 restores higher-order architecture of growing blood vessels in mice in the absence of mural cells. J Clin Invest. 110:1619-1628, 2002.

Mouse retinal angiogenesis as a model system of diabetic retinopathy

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Vision impairment in diabetic retinopathy is attributable to elevated vascular permeability and deregulated angiogenesis. Since vascular endothelial growth factor (VEGF) exacerbates vascular leakage and neo-angiogenesis, anti-VEGF drugs are intraocularly administered worldwide in the treatment of diabetic macular edema and proliferative diabetic retinopathy. However, because of insufficient efficacy and adverse effects of anti-VEGF therapy, alternative modalities which can fundamentally restore the retinal vascular abnormality are desired. Given the infeasibility of recapitulating diabetic retinopathy in animals with high blood glucose, we have utilized postnatal mouse retina as a model system to represent human retinopathy. While pericyte dropout is an initial pathological change in diabetic retinopathy, administration of anti-PDGF beta receptor antibody to neonatal mice enabled us to evaluate the deteriorated integrity of retinal vascular walls devoid of pericytes. Furthermore, the oxygen-induced retinopathy (OIR) model has given invaluable insights into the molecular mechanisms underlying disoriented angiogenesis, which is responsible for vitreous hemorrhage and retinal detachment. By combining these experimental models with pharmacological and genetic manipulations, we have shown potential of new modalities which normalize the vascular architecture in the absence of pericytes and in ischemic retinas. In this meeting, I will introduce mouse retinal angiogenesis as a model system for mimicking human diabetic retinopathy, and its usefulness for the identification of novel drug targets to treat retinal vascular disorders.

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➤Educational background & professional experience

1990-1997	College of Veterinary Medicine, CNU, Korea	DVM / Ph.D.
1994-2000	Laboratory Animal Center, KRIBB, Korea	Researcher
2000-2006	Laboratory Animal Center, KRIBB, Korea	Senior researcher
2002-2004	The Jackson Laboratory, USA	Visiting investigator
2005-present	University of Science and Technology (UST), Korea	Professor
2005-present	Laboratory Animal Center, KRIBB, Korea	Principal researcher

➤Research interests

Metabolic diseases / animal models

➤Brief list of publications

1. Kim YD, Kim YH, Tadi S, Yu JH, Yim YH, Jeoung NH, Shong M, Hennighausen L, Harris RA, Lee IK, Lee CH, Choi HS. Metformin Inhibits Growth Hormone-Mediated Hepatic Pyruvate Dehydrogenase Kinase 4 Gene Expression Through Induction of Orphan Nuclear Receptor Small Heterodimer Partner. Diabetes (In press).
2. Kim DK, Ryu D, Koh M, Lee MW, Lim D, Kim MJ, Kim YH, Cho WJ, Lee CH, Park SB, Koo SH, Choi HS. Orphan Nuclear Receptor Estrogen-Related Receptor γ (ERRγ) Is Key Regulator of Hepatic Gluconeogenesis. J Biol Chem, 287(26): 21628-21639, 2012.
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5. Kim YH, Hwang JH, Noh JR, Gang GT, Kim do H, 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, 91(3): 519-527, 2011.
6. Yuk JM, Shin DM, Lee HM, Kim JJ, Kim SW, Jin HS, Yang CS, Park KA, Chanda D, Kim DK, Huang SM, Lee SK, Lee CH, Kim JM, Song CH, Lee SY, Hur GM, Moore DD, Choi HS, Jo EK. The orphan nuclear receptor SHP acts as a negative regulator in inflammatory signaling triggered by Toll-like receptors. Nat Immunol, 12(8): 742-751, 2011.
7. Yoon YS, Lee MW, Ryu D, Kim JH, Ma H, Seo WY, Kim YN, Kim SS, Lee CH, Hunter T, Choi CS, Montminy MR, Koo SH. Suppressor of MEK null (SMEK)/protein phosphatase 4 catalytic subunit (PP4C) is a key regulator of hepatic gluconeogenesis. Proc Natl Acad Sci (USA), 107(41): 17704-17709, 2010.
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9. Chanda D, Lee CH, Kim YH, Noh JR, Kim DK, Park JH, Hwang JH, Lee MR, Jeong KH, Lee IK, Kweon GR, Shong M, Oh GT, Chiang JY, Choi HS. Fenofibrate differentially regulates PAI-1 gene expression via AMPK-dependent induction of orphan nuclear receptor SHP. Hepatology, 50(3): 880-892. 2009.
10. Yang CS, Shin DM, Kim KH, Lee ZW, Lee CH, Park SG, Bae YS, Jo EK. NADPH oxidase 2 interaction with TLR2 is required for efficient innate immune responses to mycobacteria via cathelicidin expression. J Immunol, 182(6): 3696-3705. 2009.

Activation of NAD(P)H:quinone oxidoreductase-1 improves blood pressure via enhancement of eNOS coupling following by increase of aortic GTP cyclohydrolase-1.

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NAD(P)H:quinone oxidoreductase-1 (NQO1) is a homodimeric enzyme that catalyzes the oxidation of NAD(P)H to $NAD(P)^+$ by various quinones. β-lapachone (βL), a well-known substrate of NQO1, increases the cellular NAD(P)+/NAD(P)H ratio via the activation of NQO1. GTP cyclohydrolase-1 (GTPCH-1) is rate-limiting enzyme in *de novo* synthesis of tetrahydrobiopterin, an essential cofactor for endothelial nitric oxide (NO) synthase (eNOS) coupling. AMP-activated protein kinase (AMPK) is crucial for GTPCH-1 preservation, and LKB1, an upstream kinase of AMPK, is activated by SIRT1-mediated deacetylation. Recent studies have reported that βL increases AMPK phosphorylation via activation of NQO1, resulting in beneficial effects such as prevention of arterial restenosis and anti-obesity. In this study, we have evaluated whether βL-induced activation of NQO1 modulates BP through preservation of GTPCH-1 in an animal model of hypertension. Spontaneously hypertensive rats (SHR), primary aortic endothelial cell and endothelial cell line were used to investigate hypotensive effect of βL and its action mechanism, respectively. βL treatment dramatically lowered BP and vascular tension in SHR and induced eNOS activation in endothelial cells. Consistent with these effects, βL supply also elevated the levels of both aortic cGMP and plasma NO in SHR. Meanwhile, βL-treated SHR showed significantly increased levels of aortic NAD^+, LKB1 deacetylation, AMPK Thr^{172} phosphorylation, and GTPCH-1 protein expression. Enhanced LKB1 deacetylation and AMPK activation was also elicited by βL in endothelial cells. However, inhibition of LKB1 deacetylation by blocking of NQO1 or SIRT1 blunted AMPK activation by βL. Moreover, AMPK inhibition by overexpression of dominant-negative AMPK almost abolished GTPCH-1 protein conservation. In conclusion, this study is the first to demonstrate that activation of NQO1 relieves spontaneous hypertension through eNOS coupling regulation via increase of aortic GTPCH-1 following LKB1/AMPK activation. These findings provide strong evidence to suggest that NQO1 might be a new therapeutic target for hypertension.

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➤Educational background & professional experience

1994	Kynng-Hee University, College of Medicine, Seou1, Korea	M.D.
1999	Department of Endocrino1ogy, Department of Internal Medicine, Graduate School of Medical Science, Kynng-Hee University, Seou1, Korea	Ph.D.
1999-2002	Samsung Medical Center, Seoul, Korea	Clinical research fellow
2004-2006	Division of Endocrinology & Metabolism, Department of Internal Medicine Hangang Sacred Heart Hospital, The Hallym University College of Medicine, Seoul, Korea	Assistant professor
2006-2010	Center of Endocrinology and Metabolism, East-West Neo Medical Center, Kyung-Hee University College of Medicine, Seoul, Korea	Assistant professor
2008-2009	Harvard University Joslin Diabetes Center-	Visiting researcher
2010-present	Department of Endocrino1ogy and Metabo1ism, Kynng-Hee University Hospital	Associate professor

➤Research interests

Vascular biology, beta-cell biology, hepatic insulin resistance

➤Brief list of publications

1. Hwang YC, Jee JH, Jeong IK, Ahn KJ, Chung HY, Lee MK. Circulating Osteocalcin Level Is Not Associated With Incident Type 2 Diabetes in Middle-Aged Male Subjects: Mean 8.4-year retrospective follow-up study. Diabetes Care. 2012 Jul 6. [Epub ahead of print].
2. Jeong IK.The role of cortisol in the pathogenesis of the metabolic syndrome.Diabetes Metab J. 2012 Jun;36(3):207-10. Epub 2012 Jun 14.
3. Kim KS, Jeong IK, Lee SH, Song R, Yang HI, Kim JY.Musculoskeletal manifestation in the joints of the diabetic animal model Otsuka Long-Evans Tokushima Fatty rat: A histological study. Mol Med Report. 2012 Mar;5(3):779-82.
4. Kim HS, Lee TY, Kim EY, Choi JH, Kim SY, Hwang YC, Kang JH, Ahn KJ, Chung HY, Jeong IK. Fulminant type 1 diabetes in a pregnant woman as an initial manifestation of the insulin autoimmune syndrome. Diabet Med. 2012 Feb 22. doi: 10.1111/j.1464-5491.2012.03623.x. [Epub].
5. 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. 2012 Apr;23(4):1337-42. Epub 2011 Jun 9.
6. Jeong IK, Oh da H, Park SJ, Kang JH, Kim S, Lee MS, Kim MJ, Hwang YC, Ahn KJ, Chung HY, Chae MK, Yoo HJ. Inhibition of NF-κB prevents high glucose-induced proliferation and plasminogen activator inhibitor-1 expression in vascular smooth muscle cells Exp Mol Med. 2011 Dec 31;43(12):684-92.
7. Ko SH, Kim SR, Kim DJ, Oh SJ, Lee HJ, Shim KH, Woo MH, Kim JY, Kim NH, Kim JT, Kim CH, Kim HJ, Jeong IK, Hong EK, Cho JH, Mok JO, Yoon KH; Committee of Clinical Practice Guidelines, Korean Diabetes Association.2011 clinical practice guidelines for type 2 diabetes in Korea. Diabetes Metab J. 2011 Oct;35(5):431-6. Epub 2011 Oct 31.
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.

The new perspectives on diabetic vascular complications: the balance between endogenous protective factors and harmful factors induced by hyperglycemia

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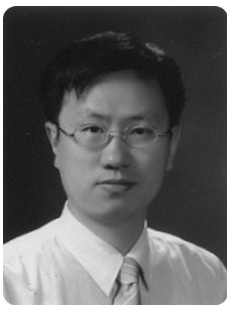
The diabetic vascular complications are leading causes of morbidity and mortality in diabetic patients. In past, many studies have focused on the mechanisms of hyperglycemia - induced chronic vascular complication via the formation of toxic metabolites such as oxidative stress, advanced glycosylated end products, persistent activation of protein kinase C, and increased sorbitol concentration. However, the vascular complications result from the imbalance between increase of systemic toxic metabolites such as hyperglycemia, dyslipidemia and the loss of endogenous protective factors such as platelet derived growth factor (PDGF), vascular endothelial growth factor (VEGF), and Insulin. PDGF-B or PDGF receptor-β knockout mice exhibited pericyte apoptosis and retinal microvascular abnormalities similar to the early stages of diabetic retinopathy, indicating that PDGF-B is a very important survival factor for retinal pericytes. However, the level of PDGF-B expression was observed to be elevated in diabetic state compared with non-diabetic animal. Recently Geraldes P et al clearly demonstrated that hyperglycemia induced a persistent activation of PKC-δ which leads to inhibition of PDGF -related survival actions to cause pericyte apoptosis in diabetic retinopathy. Another survival factor is vascular endothelial growth factor (VEGF) which is one of the most important endogenous angiogenic polypeptide that responds to hypoxia in normal physiological conditions. However, the expression of VEGF is increased in the retina to cause diabetic proliferative retinopathy. VEGF is also produced by renal podocyte. receptors for VEGF (VEGFR-1 and VEGFR-2) were expressed by glomerular endothelial cells. podocyte specific, heterozygous, conditional knock out of VEGF-A mice showed the loss of endothelial cell fenestrations, endothelial cell necrosis. Podocyte-derived VEGF, an angiogenic factor whose expression is increased in animal models of diabetic kidney disease. However, recently Eremia et al reported proteinuria, hypertension and renal failure in several patients treated with anti-VEGF agent, bevacizumab. In contrast with diabetic microvascular complication, VEGF expression is reduced in diabetic heart and macrovasculature. impaired insulin signaling has decreased VEGF expression and aggravated ischemic injury. Insulin is another important survival factor for vascular endothelial cell. Insulin has been shown to possess both antiatherosclerotic and proatherosclerotic actions in vascular cells. In diabetes, hyperglycemia can selectively inhibit insulin's anti-atherosclerotic actions while hyperinsulinemia, as observed in insulin-resistant type 2 diabetes, can enhance insulin's proatherosclerotic effects to accelerate the prevalence of atherosclerotic diseases. Rask-Madsen C et al recently reported that loss of insulin signaling in the endothelial cells accelerated atherosclerosis in apolipoprotein E null mice. Also, insulin therapy increased number of endothelial progenitor cells in diabetic animal model through direct and indirect action. Insulin released scaffold improved angiogenesis in Hindlimb ischemia model through activation of p-AKT signaling and increase of VEGF expression. In conclusion, new therapeutic approaches for the diabetic vascular complication need to increase and restore the action of protective factors.



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➤Educational background & professional experience

1992	Chung-Ang University, College of Medicine	M.D.
1997	Korean Board of Internal Medicine	
2002	Chung-Ang University, College of Medicine	Ph.D.
2006-2011	Department of Internal Medicine, Chung-Ang University, College of Medicine	Associate professor
2006-2008	Visiting Scholar, University of Utah, USA	
2011-present	Department of Internal Medicine, Chung-Ang University, College of Medicine	Professor

➤Research interests

Diabetic complications

➤Brief list of publications

1. Receptor activator of nuclear factor-κB ligand (RANKL) is a novel inducer of myocardial inflammation. CARDIOVASCULAR RESEARCH 94(1):105-114, 2012.
2. Conditional deletion of insulin receptor in thyrocytes does not affect thyroid structure and function. ENDOCRINE JOURNAL 58(11):1013-1019, 2011.
3. Mechanisms for increased myocardial fatty acid utilization following short-term high-fat feeding. CARDIOVASCULAR RESEARCH 82(2):351-360, 2009.
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Akt isoforms in the cardiovascular system

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In the cardiovascular system, IGF-1/insulin-phosphoinositol -3 kinase (PI3K)-Akt signaling plays an important role in the regulation of cardiac growth and metabolism. Although Akt signaling in cardiac growth has been widely studied, the role of Akt in the coordinate regulation of cardiac growth and contractile function is partially understood. There are three distinct Akt isoforms (Akt1, 2, and 3) that are the products of distinct genes but are highly related proteins. While deletion of Akt1 results in smaller heart size and $Akt2^{-/-}$ mice are mildly insulin resistant, $Akt1^{-/-}/Akt2^{-/-}$ mice exhibit perinatal lethality, indicating a large degree of functional overlap between the isoforms of Akt. The presentation will review recent evidence for the cooperative contribution of Akt1 and Akt2 on structure and contractile function in adult hearts.

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➤Educational background & professional experience

1984	Seoul national University	Chem Eng / B.S.
1986	KAIST	Chem Eng / M.S.
1994	University of Utah	Pharmaceutics / Ph.D.
1994-1996	University of Michigan	Pharmaceutics / Post-doc
1996-2005	GIST	Mater. Sci & Eng / Assi/Asso professor
2005-present	Seoul National Univeristy	Pharmacy/ Professor

➤Research interests

Drug delivery System, cell transplantation

➤Brief list of publications

1. Functional enhancement of beta cells in transplanted pancreatic islets by secretion signal peptide-linked exendin-4 gene transduction, Journal of Controlled Release, vol.159(3),pp 368–375(2012).
2. Surface modification of pancreatic islets using heparin-DOPA conjugate and anti-CD154 mAb for the prolonged survival of intrahepatic transplanted islets in a xenograft model, Biomaterials, vol.33(1), pp295-303 (2012).
3. Surface Camouflage of Pancreatic Islets Using 6-arm-PEG-catechol in Combined Therapy with Tacrolimus and Anti-CD154 monoclonal Antibody for Xenotransplantaion, Biomaterials, vol.32(31),pp7961-70 (2011).
4. Pharmacokinetic evaluation of an oral tablet form of low-molecularweight heparin and deoxycholic acid conjugate as a novel oral anticoagulant, Thrombosis and Haemostasis, vol. 105(6), pp1060-71 (2011).
5. High antiangiogenic and low anticoagulant efficacy of orally active low molecular weight heparin derivatives, Journal of Controlled Release, vol.148(3), pp317-26 (2010).
6. Diabetes Correction in Pancreatectomized Canines by Orally Absorbable Insulin-Deoxycholate Complex, Molecular Pharmaceutics, vol.7, pp708-17 (2010).
7. Antiangiogenic activity of orally absorbable heparin derivative in different types of cancer cells, Pharmaceutical Research, Vol.26, pp2667-76 (2009).
8. Polyproline-type helical-structured low-molecular weight heparin (LMWH)-taurocholate conjugate as a new angiogenesis inhibitor, International Journal of Cancer, Vol.124, pp2755-65 (2009).
9. Antimetastatic Effect of an OrallyActive Heparin Derivative on Experimentally Induced Metastasis, Clinical Cancer Research, Vol.14, pp2841-2849 (2008).
10. Optimal aggregation of dissociated islet cells for functional islet-like cluster, Journal of Biomaterials Science-Polymer Edition, Vol.19, pp441-452 (2008).

Molecular shielding of pancreatic Islets for xenotransplantation

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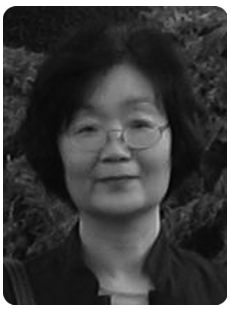
Pancreatic islet transplantation is a possible cell therapy for treating type 1 insulin-dependent diabetes mellitus. After islet transplantation, however, several kinds of immunosuppressant therapies, such as Edmonton protocol, should be continuously followed to inhibit immune rejection. Since immunosuppressants are known to induce complications, this reminds us that the final goal of islet transplantation remains the elimination of chronic recipient immunosuppression. In this study, we evaluated the clinical potential of a new combinatorial therapy based on PEGylation, immunosuppressant administration and gene therapy to reduce immune reaction and to enhance the islet functionality. The long-functioning PEGylated islets firmly expressed insulin, glucagon and somatostatin hormone. When CoCl2 and CsA were coadministered to recipients of PEGylated islet transplantation, all islets survived for more than 100 days. When PEGylated islets that had survived for 100 days were evaluated with immunohistological analysis, islets were properly protected against immune cells, and anti-insulin immunostained islets were well presented in transplantation sites. Interestingly, the long-surviving PEGylated islets were strongly stained by anti-HO-1 antibody although the $CoCl_2$ treatment was terminated on 5 days after transplantation. The successful cell therapy using islet transplantation for the treatment of diabetes mellitus may be achievable using a combined PEGylation and low dose of immunosuppressive drugs with HO-1 induction. This finding is of significant importance from the viewpoint of avoiding the adverse effects of the immunosuppressive drugs. Therefore, this study describes a potentially highly effective alternative approach, which is conceptually based on a combination of PEGylation and cytoprotection.



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➤Educational background & professional experience

1984	Seoul National University College of Medicine	Medicine / M.D.
1988	Seoul National University College of Medicine	Internal medicine / M.Sc.
1990	University of Calgary School of Medicine, AB, Canada	Microbiology / Ph.D.
1984-1985	Seoul National University Hospital	Internship
1985-1988	Dept of Internal Medicine, Seoul National University Hospital	Residency
1988-1988	Division of Endocrinology & Metabolism, Seoul National University Hospital	Fellowship
1988-1990	Julia-McFarlane Diabetes Research Centre, University of Calgary School of Medicine	Research fellowship
2002-2004	Diabetes Institute for Immunology & Transplantation, Department of Surgery, University of Minnesota, MN, USA	PostDoc. associate
1991-present	Department of Internal Medicine, Hallym University College of Medicine	Faculty / Currently professor

➤Research interests

Pancreatic islet cytoprotection, islet transplantation, pathogenic mechanism of beta-cell failure in diabetes

➤Brief list of publications

1. Chae HY, Kang JG, Kim CS, Lee SJ, Lee M, Kang DC, Jun HS, Ihm SH: Effect of glucagon-like peptide-1 gene expression on graft function in mouse islet transplantation. Transplant Int. 2012;25(2):242-249.
2. Lee BW, Lee M, Chae HY, Lee SH, Kang JG, Kim CS, Lee SJ, Yoo HJ, Ihm SH: Effect of hypoxia-inducible VEGF gene expression on revascularization and graft function in mouse islet transplantation. Transplant Int. 2011;24(3):307-314.
3. Lee BW, Chae HY, Kwon SJ, Park SY, Ihm J, Ihm SH: RAGE ligands induce apoptotic cell death of pancreatic β-cells via oxidative stress. Int J Mol Med. 2010;26:813-818.
4. Lee S, Kim HA, Park JH, Lee SH, Lee BW, Ihm SH, Kim TI, Kim SW, KoKS, Lee M: Enhanced protection of Ins-1 cells from apoptosis under hypoxia by delivery of DNA encoding secretion signal peptide-linked exendin-4. J Drug Target. 2009;17(3):242-248.
5. Lee BW, Chae HY, Tuyen TTN, Kang D, Kim HA, Lee M, Ihm SH: A comparison of non-viral vectors for gene delivery to pancreatic β-cells: Delivering a hypoxia-inducible vascular endothelial growth factor gene to rat islets. Int J Mol Med. 2009;23(6):757-762.
6. Lee BW, Kwon SJ, Chae HY, Kang JG, Kim CS, Lee SJ, Yoo HJ, Kim JH, Park KS, Ihm SH: Dose-related cytoprotective effect of alpha-lipoic acid on hydrogen peroxide-induced oxidative stress to pancreatic beta cells. Free Rad Res. 2009;43(1):68-77.
7. Ihm SH, Matsumoto I, Zhang HJ, Ansite JD, Hering BJ: Effect of short-term culture on functional and stress-related parameters in isolated human islets. Transpl Int. 2009; 22(2):207-216.
8. Kim HA, Lee BW, Kang D, Kim JH, Ihm SH,Lee M: Delivery of hypoxia-inducible VEGF gene to rat islets using polyethylenimine. J Drug Target. 2009;17(1):1-9.
9. Bellin MD, Kandaswamy R, Parkey J, Zhang HJ, Liu B, Ihm SH, Ansite JD, Witson J, Bansal-Pakala P, Balamurugan AN, Papas K, Sutherland DE, Moran A, Hering BJ: Prolonged insulin independence after islet allotransplants in recipients with type 1 diabetes. Am J Transplant. 2008;8(11):2463-2470.
10. Ihm SH, Matsumoto I, Sawada T, Nakano M, Zhang HJ, Ansite JD, Sutherland DE, Hering BJ: Effect of donor age on function of isolated human islets. Diabetes. 2006;55(5):1361-1368.
11. Hering BJ, Kandaswamy R, Ansite JD, Eckman PM, Nakano M, Sawada T, Matsumoto I, Ihm SH, Zhang HJ, Parkey J, Hunter DW, Sutherland DE: Single-donor, marginal-dose islet transplantation in patients with type 1 diabetes. JAMA. 2005;293(7):830-835.

Islet cytoprotection for islet transplantation

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Given the limited supply of donor pancreatic islets, considerable efforts have been made to prevent the loss of islet mass in the post-TPL period. Islets may be manipulated in vitro prior to TPL, providing opportunities for therapeutic strategies aiming at conferring cytoprotection to maximize their engraftment and survival. Since the substantial early post-TPL graft loss is mainly due to apoptosis from hypoxic and inflammatory insults, intervention of these cell death pathways may substantially enhance preservation of islet mass following TPL. Utilization of additives in the culture media (antioxidants, growth factors, etc.) may result in reduced islet cell death and better function, representing a simple strategy toward the optimization of islet engraftment. The possibility to modify islets by gene therapy utilizing viral and non-viral vectors represents an appealing approach for the cytoprotection of islet cells.

For gene transfer strategies to improve islet engraftment, vascular endothelial growth factor (VEGF) expression should be regulated in a way that matches the transient nature of revascularization with simultaneously avoiding undesirable effects of overexpression. In our study, the hypoxia-inducible VEGF gene transfer using the RTP801 promoter to mouse islets induced VEGF expression specifically under hypoxia in vitro, and enhanced islet vascular engraftment and preserved islet function overtime in syngeneic transplants. Because glucagon-like peptide-1 (GLP-1) was shown to stimulate beta-cell proliferation and have anti-apoptotic effects on beta cells, we examined whether adenovirus-mediated gene transfer of GLP-1 would result in cytoprotection of mouse islets in syngeneic TPL setting. Our results indicated that the local overexpression of GLP-1 in islets improved islet survival and function in transplants.

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➤Educational background & professional experience

1981	Dept. of Zoology, College of Natural Sciences, Seoul National University	B.S.
1983	Dept. of Zoology, Graduate School, Seoul National University	M.S.
1986	Dept. of Zoology, Graduate School, Seoul National University	Ph.D.
1987-1988	Experimental Embryology & Teratology Unit, MRC, England	Post-Doc
1988-1991	Dept. of Population Dynamics, Johns Hopkins University, USA	Post-Doc
1991-present	Dept. of Biotechnology, Seoul Women's University	Professor
2011-present	Korean Society for Reproductive Medicine	President

➤Research interests

Stem cell biology

➤Brief list of publications

1. Kim et al. (2012) Human Insulin Secreted From Insulinogenic Xenograft Restores Normoglycemia in Type I Diabetic Mice without Immunosuppression. Cell Transplant. 2012 Apr [Epub ahead of print].
2. Kang et al. (2011) Insulin-like growth factor 2 enhances insulinogenic differentiation of human eyelid adipose stem cells via the insulin receptor. Cell Prolif. June 44(3):254-263.
3. Kang et al. (2009) Insulin-secreting cells from human eyelid-derived stem cells alleviate type I diabetes in immunocompetent mice. Stem Cells, Aug; 27(8): 1999-2008.
4. Han et al. (2008) Human amnion-derived mesenchymal stem cells are a potential source for uterine stem cell therapy. Cell Prolif, Sep; 41(5):709-725.
5. Moon et al. (2008) Successful vitrification of human amnion-derived mesenchymal stem cells. Hum. Reprod. Aug; 23(8): 1760-1770.
6. Kim et al. (2007) Ex vivo characteristics of human amniotic membrane-derived stem cells. Cloning and Stem Cells, Dec; 9(4): 581-594.
7. Kang et al. (2007) Estrogen stimulates the neuronal differentiation of human umbilical cord blood mesenchymal stem cells (CD34-). Neuroreport, Jan 8;18(1):35-38.
8. Kim et al. (2007) Human amniotic fluid-derived stem cells have characteristics of multipotent stem cells. Cell Prolif, Feb; 40(1):75-90.

Cell therapeutics for the insulin-dependent diabetes mellitus

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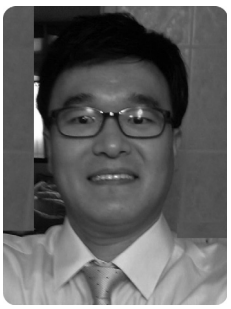
Human adult stem cells have been examined as therapeutic cells for the treatment of insulin-dependent diabetes. Studies using diabetic mice model have shown that undifferentiated stem cells, mid-differentiated cells expressing PDX1, as well as differentiated cells producing c-peptide are effective in reducing blood glucose level. However, it has not been clarified how these cells act to restore the normoglycemia in vivo. We isolated stem cells from the human eyelid adipose tissues and amniotic membrane. After the differentiation culture in an appropriate condition, both cell types expressed β-cell-related genes and proteins, and secreted insulin and c-peptide in a glucose-dependent manner. When these differentiated cells were transplanted into kidneys of streptozotocin-treated, immunocompetent mice, about half of recipient mice showed normoglycemia as long as one and half year. Only human insulin and c-peptide, neither the mouse insulin nor c-peptide, were detected in the normoglycemic mice. Removal of the kidneys transplanted with cells after 2 months resulted in a sharp increase of blood glucose level. The kidney tissues also showed diminished or null expression of some human immune-related genes. By contrast, mice transplanted with undifferentiated stem cells never showed any recovery from hyperglycemia and eventually died within 2 months. In conclusion, human insulin-secreting cells could restore the normoglycemia of diabetic mice by providing human insulin.



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➤Educational background & professional experience

1998-2000	Korea University	Creative research initiative (CRI) center for dell death / Senior research scientist
2000-2001	Mount Sinai School of Medicine	Cancer center / Post-Doc.
2001-2003	Korea University	Life Sciences and Biotechnology / research professor
2003-present	Konkuk University	Department of animal biotechnology/ professor
2006-present	Konkuk University	BK21 / IDASI (Incurable disease animal model and Stem cell research institute)/ Director
2011-present	Institut Pasteur Korea	Bioimaging / visiting scientist

➤Research interests

Stem cell / iPS cell / diabetes / beta-cell differentiation / apoptosis / kinase signaling

➤Brief list of publications

1. Jeon KS, Lim HJ, Kim JH, Han DW, Lee ER, Yang GM, Song MK, Kim JH, Cho SG. (2012) Bax Inhibitor-1 Enhances Survival and Neuronal Differentiation of Embryonic Stem Cells via Differential Regulation of Mitogen-Activated Protein Kinases Activities. BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR CELL RESEARCH In press.
2. Jeon KS, Lim HJ, Kim JH, Thuan NV, Park SH, Lim YM, Choi HY, Lee ER, Kim JH, Lee MS, Cho SG. (2012) Differentiation and transplantation of functional pancreatic beta cells generated from induced pluripotent stem cells derived from a type 1 diabetes mouse model. Stem Cells and Development. In press.
3. Jeon KS, Oh HJ, Lim HJ, Kim JH, Lee DH, Lee ER, Park BH, Cho SG (2012) Self-renewal of embryonic stem cells through culture on nanopattern polydimethylsiloxane substrate. Biomaterials. 33(21):5206-5220.
4. Cho JH, Lee MK, Yoon KW, Lee JR, Cho SG, Choi EJ (2012) Arginene methylation-dependent regulation of ASK1 signaling by PRMT1. CELL DEATH DIFFER. 19(5): 859-870.
5. Kim JH, Lee ER, Jeon KS, Choi HY, Lim HJ, Kim SJ, Chae HJ, Park SH, Kim SU, Seo YR, Kim JH, Cho SG. (2012) Role of BI-1 (TEGT)-mediated ERK1/2 activation in mitochondria-mediated apoptosis and splenomegaly in BI-1 transgenic mice. BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR CELL RESEARCH. 1823(4):876-888.
6. Song MJ, Paul S, Lim HJ, Dayem AA, Cho SG. (2012) Induced pluripotent stem cell research: A revolutionary approach to face the challenges in drug screening. Arch. Pharm. Res. 35(2):245-260.
7. Hwang HS, Hwang SG, Cho JH, Chae JS, Yoon KW, Cho SG, Choi EJ. (2011) CIIA functions as a molecular switch for the Rac1-specific GEF activity of SOS1. J CELL BIOL. 195(3):377-386.
8. Lee CH, Kim JH, Lee HJ, Jeon KS, Lim HJ, Choi HY, Lee ER, Park SH, Park JY, Hong SH, Kim SH, Cho SG. (2011) The generation of iPS cells using non-viral magnetic nanoparticlebased transfection. Biomaterials. 32(28):6683-6691.
9. Park MR, Lee AR, Bui HT, Park CK, Park KK, Cho SG, Song H, Kim JH, Thuan NV, Kim JH. (2011). CHROMOSOME REMODELING AND DIFFERENTIATION OF TETRAPLOID EMBRYOS DURING PREIMPLANTATION DEVELOPMENT. Dev. Dyn. 240(7): 1660-1669.
10. Jeong HS, Choi HY, Lee ER, Kim JH, Jeon KS, Lee HJ, Cho SG. (2011) Involvement of caspase-9 in autophagy-mediated cell survival pathway. BIOCHIMICA ET BIOPHYSICA ACTA-MOLECULAR CELL RESEARCH. 1813 (2011) 80-90.

Differentiation and transplantation of functional pancreatic beta cells generated from induced pluripotent stem cells derived from a type 1 diabetes mouse model

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Discovery of induced pluripotent stem (iPS) cells gave a new directional path to knock the disease world with new resource for cell transplantation and drug screening. Further progress and advances in iPS cell generation technology, from viral to non-viral system and from integrating to non-integrating approach of foreign gene into host genome, kept adding feathers to the technology making it more feasible for clinical application. iPS cell technology will enable autologous transplantation and more efficient drug discovery. For application into drug discovery, iPS cells which were generated from animal model or patient-derived somatic cells, are tried to differentiate into specific cells to express specific phenotypes and can be used as disease model. This disease model iPS cells are helpful for understanding the disease progression mechanism as well as for application into cell-based efficient drug screening.

The non-obese diabetic (NOD) mouse is a classical animal model for autoimmune type 1 diabetes (T1D), closely mimicking features of human T1D. Thus, the NOD mouse presents an opportunity to test the effectiveness of induced pluripotent stem cells (iPSCs) as a therapeutic modality for T1D. Here, we demonstrate a proof of concept for cellular therapy using NOD mouse-derived iPSCs (NOD-iPSCs). We generated iPSCs from NOD mouse embryonic fibroblasts (NMs) or NOD mouse pancreas-derived epithelial cells (NPEs), and applied directed differentiation protocols to differentiate the NOD-iPSCs toward functional pancreatic beta cells. Finally, we investigated whether the NPE-iPSC-derived insulin-producing cells could normalize hyperglycemia in transplanted diabetic mice. The NOD-iPSCs showed typical embryonic stem cell (ESC)-like characteristics such as expression of markers for pluripotency, in vitro differentiation, teratoma formation, and generation of chimeric mice. We developed a method for stepwise differentiation of NOD-iPSCs into insulin producing cells, and found that NPE-iPSCs differentiate more readily into insulin-producing cells. The differentiated NPE-iPSCs expressed diverse pancreatic beta cell markers and secreted insulin in response to glucose and KCl stimulation. Transplantation of the differentiated NPE-iPSCs into diabetic mice resulted in kidney engraftment. The engrafted cells responded to glucose by secreting insulin, thereby normalizing blood glucose levels.

We propose that NOD-iPSCs will provide a useful tool for investigating genetic susceptibility to autoimmune diseases and generating a cellular interaction model of T1D, paving the way for the potential application of patient-derived iPSCs in autologous beta cell transplantation for treating diabetes.

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➤Educational background & professional experience

1990-1994	Aberdeen University	Biochemistry / B.Sc.
1994-1997	MRC Centre, Cambridge, UK,	Bioinformatics / Ph.D.
1998-1999	Harvard University, USA	
1999-2001	EBI (European Bioinformatics Institute), Cambridge, UK	
2001-2003	MRC Centre, Cambridge, UK	
2003-2005	KAIST, South Korea	
2005-2009	KOBIC (Korean Bioinformation Center), South Korea	
2009-present	Genome Research Foundation, South Korea	

➤Research interests

Gerontology, bioinformaics, genomics

➤Brief list of publications

1. KGP: Korean Genome Project: http://koreangenome.org.
2. Cancer genome analyses.
3. The first Korean Human Genome analysis.
4. Wild Soybean genome analysis.
5. Pan Asian SNP analysis / The first tiger genome analysis.
6. RNA-seq of Horses: 24 horse transcriptome sample project.

Genome analysis using NGS (next generation sequencers)

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The most important technology in biology is sequencing. Sequencing and subsequent genomic data enabled humans to decipher the network of instructions built over billions of years of evolution. The future of biology lies in the ability to associate genomic data with phenotype data. Hence, genome sequencing should be cheaper and faster than ever. The simple conclusion of any biology is to utilized sequencing as much as possible to medical applications such as diagnosis, treatment, disease control, and reducing the cost of healthcare.

The latest sequencing technology is called NGS (next generation sequencer). NGS is a machine that is equivalent to a whole factory in terms of the sequencing capacity and speed. NGS applications are growing and personalized medicine is perhaps the most important. The core of personal medicine is personal genomics. Personal genomics has two meanings. One is it is research on many people's genomes. The other is it is done by non-academic researchers such as doctors, hospitals, and companies. The core of personal genomics is analyzing genomes using computers. Information technology is the key in biology. Fast and efficient pipelines for genome sequences are critical. Large international projects such as PGP (personal genome project) and PAPGI (pan asia population genomics) are introduced. De novo sequencing is a technology used to map genomes of species that do not have already available reference genomes. Preliminary de novo genome analyses of animal genomes are also presented.

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➤Educational background & professional experience

2000-2004	Duk-Sung Women's University	Statistics / B.S.
2004-2006	Yonsei University	Biostatistics / M.S.
2009-	Yonsei University	Biostatistics / Ph.D.
2006-2009	Korean National Institute of Health, KCDC	Associate researcher
2009-present	Korean National Institute of Health, KCDC	Senior researcher

➤Research interests

My major research interest is the identification of genetic bases for complex disease (such as T2D) and complex traits (such as fasting plasma glucose). I am currently conducting genome-wide association (GWA) studies and GWA meta-analyses and trans-ethnic fine mapping.

➤Brief list of publications

1. Meta-analysis identifies multiple loci associated with kidney function-related traits in East Asian population. Okada Y, Sim X, Go MJ, Wu JY, Gu D, Takeuchi F, Takahashi A, Maeda S, Tsunoda T …., Yamamoto K, Kubo M, Nakamura Y, Kamatani N, Kato N, He J, Chen YT, Cho YS, Tai ES, Tanaka T.
2. A Common Variant in SLC8A1 Is Associated with the Duration of the Electrocardiographic QT interval. Kim JW, Hong KW, Go MJ, Kim SS, Tabara Y, Kita Y, Tanigawa T, Cho YS, Han BG, Oh B. Am J Hum Genet. 2012 Jul 13;91(1):180-4.
3. Common variants at CDKAL1 and KLF9 are associated with body mass index in East Asian populations. Okada Y, Kubo M, Ohmiya H, Takahashi A, Kumasaka N, Hosono N, Maeda S, Wen W, Dorajoo R, Go MJ, Zheng W, Kato N, …., Yamamoto K, Nakamura Y, Kamatani N, Tanaka T. Nat Genet. 2012 Feb 19;44(3):302-6. doi: 10.1038/ng.1086.
4. Meta-analysis identifies common variants associated with body mass index in east Asians. Wen W, Cho YS, Zheng W, Dorajoo R, Kato N, Qi L, Chen CH, Delahanty RJ, Okada Y, Tabara Y, Gu D, Zhu D, Haiman CA, Mo Z, Gao YT, Saw SM, Go MJ, Takeuchi F, ……, Wu JY, Lee JY, Hu FB, Tanaka T, Tai ES, Shu XO. Nat Genet. 2012 Feb 19;44(3):307-11. doi: 10.1038/ng.1087.
5. A genome-wide association study of gestational diabetes mellitus in Korean women. Kwak SH, Kim SH, Cho YM, Go MJ, Cho YS, Choi SH, Moon MK, Jung HS, Shin HD, Kang HM, Cho NH, Lee IK, Kim SY, Han BG, Jang HC, Park KS. Diabetes. 2012 Feb;61(2):531-41. Epub 2012 Jan 10.
6. Meta-analysis of genome-wide association studies identifies eight new loci for type 2 diabetes in east Asians. Cho YS, Chen CH, Hu C, Long J, Ong RT, Sim X, Takeuchi F, Wu Y, Go MJ, Yamauchi T, Chang YC, Kwak SH, Ma RC, Yamamoto K, Adair LS, Aung T, Cai Q, Chang LC, Chen YT, Gao Y, Hu FB, Kim HL, Kim S, Kim YJ, …., Maeda S, Kadowaki T, Lee JY, Wu JY, Teo YY, Tai ES, Shu XO, Mohlke KL, Kato N, Han BG, Seielstad M. Nat Genet. 2011 Dec 11;44(1):67-72. doi: 10.1038/ng.1019.
7. Large-scale genome-wide association studies in east Asians identify new genetic loci influencing metabolic traits. Kim YJ, Go MJ, Hu C, Hong CB, Kim YK, Lee JY, Hwang JY, Oh JH, Kim DJ, Kim NH, Kim S, Hong EJ, Kim JH, Min H, Kim Y, Zhang R, Jia W…., Kang D, Shin C, Cho NH, Kim HL, Han BG, Lee JY, Cho YS.

New susceptibility loci associated with one-hour plasma glucose as predisposing risk factors for type 2 diabetes risk

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Most recently, one-hour hyperglycemia has been recognized as a further risk factor for type 2 diabetes (T2D). To date, previous genome-wide association studies (GWAS) for glycemic traits have a limited impact on the fasting state and 2-h plasma glucose level in an oral glucose challenge. To identify genetic susceptibility in different stages of glucose tolerance, we performed a meta-analysis for glycemic traits including 1-h plasma glucose (1-hPG) from 14,232 non-diabetic individuals in the Korean population. Newly implicated variants were found to be significantly associated with 1-hPG. We also demonstrated associations with gestational diabetes mellitus (GDM). Our results could provide additional insight into the genetic variation in the clinical range of glycemia.

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➤Educational background & professional experience

1986-1990	Korea University	Chemistry / B.S.
1990-1992	Korea University	Physical chemistry / M.S.
1994-1999	California Institute of Technology	Physical chemistry / Ph.D.
2000-2002	Pacific Northwest National Laboratory	Postdoc / Ph.D.
2002-present	Korea University	Physical chemistry/Professor / Ph.D.

➤Research interests

1. Development of high-performance mass spectrometry and high-resolution separation techniques for proteomics researches
2. Development of data management and analysis system for MS based proteomics
3. Discovery and validation of cancer biomarkers by using MS based proteomic approach
4. Development of proteome enrichment techniques by nano-structures
5. Applications of high throughput, highly informative proteomics techniques

➤Brief list of publications

1. Downregulation of RNase E activity by an internal site that uncompetitively interferes with RNA binding. Go, H.; Moore, C. J.; Lee, M.; Shin, E.; Jeon, C. O.; Cha, C.-J.; Han, S. H.; Kim, S.-J.; Lee, S.-W.; Lee, Y.; Ha, N.-C.; Kim, Y.-H.; Cohen, S. N.; Lee, K. RNA Biol. 2011, 8(6), 1022-1034.
2. A Serum Protein Profile Predicative of the Resistance to Neoadjuvant Chemotherapy in Advanced Breast Cancers. Hyung, S.-W.; Lee, M. Y.; Yu, J.-H.; Shin, B.; Jung, H.-J.; Park, J.-M.; Han, W.; Zhang, H.; Aebersold, R.; Hwang, D.; Lee, S.-W.; Yu, M.-H.; Noh, D.-Y. Mol. Cell. Proteomics 2011 10:M111.011023.
3. Effects and Potentials of Controlled Temperature Elevation of Separation Column of Ultra-high Pressure Microcapillary Liquid Chromatography/Tandem Mass Spectrometry on Proteomic Analysis. Hyung, S.-W.; Kim, M.-S.; Mun, D.-G.; Lee, H.; Lee, S.-W. Analyst 2011, 136 (10), 2100-2105.
4. Shot-gun Proteomic Analysis of Mitochondrial D-loop DNA Binding Proteins: Identification of Mitochondrial Histones" Choi, Y.-S.; Jeong, J. H.; Min, H.-K.; Jung, H.-J.; Hwang, D.; Lee, S.-W.; Kim-Pak, Y. Mol. Biosyst. 2011, 7, 1523-1536.
5. Pressurized Pepsin Digestion in Proteomics: An Automatable Alternative to Trypsin for Integrated Top-down Bottom-up Proteomics. Lopez-Ferrer, D.; Petritis, K.; Robinson, E. W.; Hixson, K. K.; Tian, Z.; Lee, J. H.; Lee, S.-W.; Tolic, N.; Weitz, K. K.; Belov, M. E.; Smith, R. D.; Pasa-Tolic, L. Mol. Cell. Proteomics 2011 10:M110.001420.
6. Integrated Post-Experiment Monoisotopic Mass Refinement: An integrated approach to accurately assign monoisotopic precursor masses to tandem mass spectrometric data. Jung, H.-J.; Purvine, S. O.; Kim, H.; Petyuk, V. A.; Hyung, S.-W.; Monroe, M. E.; Mun, D. G.; Kim, K. C.; Park, J.-M.; Kim, S.-J.; Tolic, N.; Slysz, G. W.; Moore, R. J.; Zhao, R.; Adkins, J. N.; Anderson, G. A.; Lee, H.; Camp, D. G. II; Yu, M.-H.; Smith, R. D.; Lee, S.-W. Anal. Chem. 2010, 82, 8510-8518.
7. Trypsin coatings on electrospun and alcohol-dispersed polymer nanofibers for trypsin digestion column. Jun, S.-H.; Chang, M. S.; Kim, B. C.; An, H. J.; Lopez-Ferrer, D.; Zhao, R.; Smith, R. D.; Lee, S.-W.; Kim, J. Anal. Chem. 2010, 82, 7828-7834.
8. Mitochondrial oxidative phosphorylation system is recruited to detergent-resistant lipid rafts during myogenesis Kim, B.-W.; Lee, J.-W.; Choo, H.-J.; Lee, C. S.; Jung, S.-Y.; Yi, J.-S.; Ham, Y.-M.; Lee, J.-H.; Hong, J.; Kang, M.-J.; Chi, S.-G.; Hyung, S.-W.; Lee, S.-W.; Kim, H. M.; Cho, B. R.; Min, D.-S.; Yoon, G.; Ko, Y.-G. Proteomics 2010, 10, 2498-2515.
9. Effect of a peroxisome proliferator-activated receptor γ smoylation mutant on neointimal formation after balloon injury in rats. Lim, S.; Ahn, B. Y.; Chung, S. S.; Park, H. S.; Cho, B. J.; Kim, M.; Choi, S. H.; Lee, I. K.; Lee, S.-W.; Choi, S. J.; Chung, C. H.; Cho, Y. M.; Lee, H. K.; Park, K. S. Atherosclerosis 2009, 206, 411-417.

Master AMT database approach for label-free quantitation (MAD4QUAN): application to uncover biomarkers for T2DM

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Advances in proteomics technologies are providing increasingly powerful new approaches for understanding cellular function and discovering biological marker molecules for specific diseases. The ability to quantitatively determine changes in protein abundances, including protein PTMs in cells, tissues and biofluids, is essential for elucidating cellular processes and signaling pathways as well as for discovering useful candidate protein biomarkers. One of the most pressing needs for (quantitative) proteomics relates to the dynamic range of measurements or the ability to measure low abundance proteins within proteomic samples. Important classes of proteins and modified proteins are generally present at very low abundances, and the dynamic range of interest for mammalian proteomics is at least 106, and potentially 〉1010 for biofluids.

Here we present the development of a label-free proteome quantitation method that is based on master accurate mass and time tag (AMT) databases. Current method, coined as MAD4QUAN, employs advanced data analysis tools such as integrated Post-Experimental Monoisotopic Mass Refinement (iPE-MMR), a neural network LC elution time normalization, and experimental Xcorr (E-Xcorr) calculation. The current method was applied to quantitatively analyze proteomes from adipose tissues of diabetic patients against those of non-diabetic individuals. We compiled a total of 25,733 unique peptides (from 4,611 proteins or 2373 genes) in the master adipose proteome database and the MAD4QUAN analysis identified 408 differentially expresses genes. Network analysis on the observed DEGs led to discover novel protein candidates to be further validated and used for diagnosis of diabetes mellitus type 2.

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➤Educational background & professional experience

1983-1987	Korea Univ. College of Medicine	Nursing / BSN
1987-1989	Seoul Nat'l Univ. School of Public Health	Epidemiology / MPH
2000-2005	The Johns Hopkins Univ. Bloomberg School of Public Health	Genetic epidemiology / Ph.D.
1990-1992	US Army Medical Research Center	Epidemiologist
2005-2006	The Johns Hopkins Univ. Bloomberg School of Public Health	Post-doctoral fellow/Instructor
2006-2007	Seoul Nat'l University, Interdisciplinary Program in Bioinformatics	Instructor
2006-2009	Samsung Biomedical Research Center /Sungkyunkwan Univ. School of Medicine	Senior scientist/Research professor
2009-present	Hallym Univ. College of Medicine, Dept. Medical Genetics	Assistant professor

➤Research interests

Medical Genetics/ Genetic epidemiology
Disease gene identification (Aging traits, Birth defects)
Disease risk prediction

➤Brief list of publications

1. Seo YJ, Park JW, Kim YH, Baek SH. Differences in Initial Growth Pattern of Cleft Children Before Alveolar Bone Graft Stage According to Cleft Type: Unilateral Cleft Lip and Alveolus, Unilateral Cleft Lip and Palate, and Cleft Palate. Angle Orthod. 2011;81(6):1103-10.
2. Yoon D, Park SK, Kang D, Park T, Park JW. Meta-analysis of homogeneous sub-groups reveals association between PDE4D gene variants and ischemic stroke. Neuroepidemiology. 2011;36(4):213-222.
3. Jee SH, Sull JW, Lee JE, Shin C, Park J, Kimm H, Cho EY, Shin ES, YUN JE, Park JW, Kim SY, Lee SJ, Jee EJ, Baik I, Kao L, Yoon SK, Jang Y, Beaty TH. Adiponectin concentrations: a genome-wide association study. Am J Hum Genet. 2010;87(4):545-52.
4. Park JW, Ji YI, Choi YH, Kang MY, Jung E, Cho SY, Cho HY, Kang BK, Joung YS, Kim DH, Park SC, Park J. Candidate Gene Polymorphisms for Diabetes Mellitus, Cardiovascular Disease and Cancer are Associated with Longevity in Koreans. Exp Mol Med. 2009:41(11):772-81.
5. Cho YS, Go MJ, Kim YJ, Heo JY, Oh JH, Ban HJ, Yoon D, Lee MH, Kim DJ, Park M, Cha SH, Kim JW, Han BG, Min H, Ahn Y, Park MS, Han HR, Jang HY, Cho EY, Lee JE, Cho NH, Shin C, Park T, Park JW, Lee JK, Cardon L, Clarke G, McCarthy MI, Lee JY, Lee JK, Oh B, Kim HL. A large-scale genome-wide association study of Asian populations uncovers genetic factors influencing eight quantitative traits. Nat Genet. 2009;41(5):527-34.
6. Park JW, Yun JE, Park T, Cho E, Jee SH, Yang Y, Beaty TH, Samet JM. Family history of diabetes and risk of atherosclerotic cardiovascular disease in Korean men and women. Atherosclerosis. 2008;197(1):224-31.
7. Park JW, Lee SY, Kim SY, Choe H, Jee SH. BMI and stroke risk in Korean women. Obesity. 2008;16(2):396-401.
8. Park JW, McIntosh I, Hetmanski JB, Jabs EW, Vander Kolk CA, Wu-Chou YH, Chen PK, Chong SS, Yeow V, Jee SH, Park BY, Fallin MD, Ingersoll R, Scott AF, Beaty TH. Association between IRF6 and nonsyndromic cleft lip with or without cleft palate in 4 populations. Genet in Med. 2007;9(4):219-227.
9. Park JW, Cai J, McIntosh I, Jabs EW, Fallin MD, Ingersoll R, Hetmanski JB, Vekemans M, Attie-Bitach T, Lovett M, Scott AF, Beaty TH. High throughput SNP and expression analyses of candidate genes for nonsyndromic oral clefts. J Med Genet. 2006;43(7):598-608.
10. Park JW, Beaty TH, Boyce P, Scott AF, McIntosh I. Comparing whole genome amplification methods and sources of biological sample for single-nucleotide polymorphism genotyping. Clin Chem. 2005;51:1520-1523.

Intermediate trait loci that predict the risk of type 2 diabetes

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Common complex diseases such as type 2 diabetes mellitus (T2DM) result from the complex interplay of multiple genes and environmental factors. Since an intermediate phenotype can be on the pathway to a disease, the presence of deleterious genotypes of the intermediate phenotype may be a surrogate indicator of the disease. Recent GWAS have identified tens of T2DM loci; however, the presence of inter-individual variation in intermediate biomarker's response to stress (e.g. blood pressure and BMI) may affect an individual's susceptibility to related diseases such as T2DM. Here, we evaluated the utility of SNPs that were validated to be associated with T2DM-related traits such as hypertension, obesity, and chronic kidney disease in the risk prediction of T2DM. Firstly, we identified susceptibility SNPs for intermediate phenotypes in age-gender specific groups with multiple covariates adjustment under three genetic models. Initially, analysis was performed using data obtained from large scale Korean prospective cohort studies (Ansung and Ansan) composed of 8,842 participants. The SNPs passed the genome-wide level of significance were further evaluated for replication under the identical model in the Health Examinee cohort composed of 3,703 participants. Secondly, we evaluated the pleiotropic effects of the replicated SNPs to the risk of T2DM. Finally, we evaluate the improved prediction ability of the model that incorporates the genetic effects of intermediate phenotypes for T2DM. In this talk, I will discuss the validity of risk models considering the combining effect of non-genetic and genetic factors in predicting risk of T2DM.

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➤Educational background & professional experience

1990-1996	Chosun University medical school	
1998-2000	Chosun University Graduate school	Internal medicine / Master degree
2003-2005	Chosun University Graduate school	Internal medicine / Ph.D.
2004-2005	Samsung Seoul Hospital, Division of Endocrinology	Clinical fellow
2005-2007	Chosun University, College of Medicine	Full-time instructor
2007-2011	Chosun University, College of Medicine	Assistant P.
2010-2012	Harvard Beth Israel Deaconess Medical Center	Visiting P.
2011-present	Chosun University, College of Medicine	Associate P.

➤Research interests

1. role of adipose tissue hormone in glucose metabolism
2. early detection of diabetes in high risk patients and metabolic syndrome

➤Brief list of publications

1. Discordance between HbA1C and fasting plasma glucose criteria for diabetes screening is associated with obesity and old age in Korean individuals. Diabetes Res Clin Pract. 2011;94(2):27-9.
2. Leptin in human physiology and pathophysiology. Am J Physiol Endocrinol Metab. 2011;301(4):567-84.
3. Protein phosphatase 5 is necessary for ATP-mediated DNA repair. Biochem Biophysic Reserch 2011;404(4):476-481.
4. Inhibitory effects of olmesartan on catecholamine secretion from the perfused rat adrenal medulla. Korean J Physio Pharmacol 2010;14(4):241-248.
5. Association of hemoglobin A1C with cardiovascular disease risk factors and metabolic syndrome in non-diabetic adults. Journal of Korean Diabetes Association 2008;32(5):435~445.
6. Evaluation of fasting plasma glucose as a screening for diabetes mellitus in middle-aged adults in Naju country. Journal of Korean Diabetes Association 2008;32(4):328~338.
7. Clinical correlation of vimentin, cyclin-D, and thyroglobulin with prognosis in papillary thyroid cancer. J Korean Surg 2006;70(6):425-429.
8. Effects of caloric restriction on the expression of PGC-1 and PPARs mRNA in liver of OLETF rats. Journal of Korean Diabetes Association 2006;30(3):161~170.
9. Insulin secretory defect plays a major role in the development of diabetes in patients with distal pancreatectomy. Metabolism 2006;55:135-141.
10. Heterogeneity of early onset and ketosis resistant diabetes in Korean subjects- is it possible to determine cut-off age of early-onset type 2 diabetes? Diabetes Res Clin Pract. 2005;70(1):38~45.

Aberrant platelet activation in metabolic syndrome

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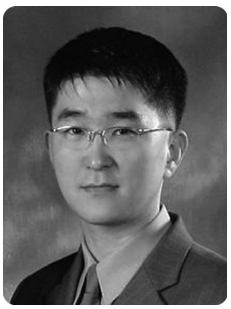
Metabolic syndrome, defined on the basis of a combination of central obesity, impaired glucose metabolism, dyslipidemia and hypertension, is a powerful predictor of cardiovascular events. It is also well documented that metabolic syndrome is characterized by the presence of a prothrombotic state, resulting from a combination of increased thrombin generation, platelet hyperactivity and decreased fibrinolysis. Among them, aberrant platelet activation plays a central role to accelerate atherothrombosis and is the result of the interaction among the features clustering in metabolic syndrome.

Many factors associate with platelet hyperactivity in metabolic syndrome such as insulin resistance, inflammation, oxidative stress and endotherial dysfunction. Insulin resistance couples vascular and metabolic pathophysiology by triggering a series of mechanisms, including inflammation, endothelial dysfunction and vasoconstriction, predisposing insulin resistant individuals to accelerated atherosclerosis and thrombosis. The finding that human platelets have insulin receptors that modulate platelet function led to the hypothesis that platelets were sites of insulin resistance, thus causing the lack of the physiological action exerted by insulin on platelet function.

Despite the availability of multiple interventions including appropriate diet, regular exercise, weight control, anti-diabetic drugs, and antiplatelet agents, relative failure to control the incidence of metabolic syndrome and its vascular complications reflects both the scarce compliance of patients to established strategies and the multifactorial nature of the disease. Additional explanations possibly date back to the pathophysiology of metabolic syndrome, as for the relative failure of low-dose aspirin in the prevention of atherothrombosis in this setting. Platelet activation is a candidate common soil, downstream event and in-depth understanding of the mechanisms triggering and sustaining platelet hyper-reactivity might help suggesting ways to overcome this phenomenon.

This presentation will address the complex interactions between platelets and the pathogenic events occurring in metabolic syndrome in order to establish novel strategies in the prevention/treatment of atherothrombosis.



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➤Educational background & professional experience

2007	Seoul National University	Animal biotechnology / Ph.D.
2007-2008	National Institute of Alcohol Abuse and Alcoholism (NIAAA) /National Institute of Health (NIH)	Post-doctoral fellow
2008-2011	Beth Israel Deaconess Medical Center/Harvard Medical School	Research fellow
2010-present	Enocrinology Section/Boston VA Health Care System /Harvard Medical School	Lab manager
2011-present	Medicine/Beth Israel Deaconess Medical Center /Harvard Medical School	Instructor

➤Research interests

Endocrinology, obesity-related cancers

➤Brief list of publications

1. Moon HS, Liu X, Nagel MJ, Chamberland JP, Diakopoulos KN, Hatziapostolou M, Brinkoetter MT, Wu Y, Robson SC, Iliopoulos D, Mantzoros CS. Salutary effects of adiponectin on colon cancer: in vivo and in vitro studies in mice. GUT (in press).
2. Moon HS, Matarese G, Brennan AM, Chamberland JP, Liu X, Fiorenza CG, Mylvaganam GH, Abanni L, Carbone F, Williams CJ, De Paoli AM, Schneider BE, Mantzoros CS. Efficacy of Metreleptin in Obese Type II Diabetics: Cellular and Molecular Pathways underlying Leptin Tolerance. Diabetes 2011;60:1647-1656.
3. Moon HS, Chamberland JP, Diakopoulos KN, Mantzoros CS. Amylin directly activates leptin-mediated modulation of signaling pathways in mouse GT1-7 hypothalamic, C2C12 muscle, and AML-12 liver cell lines. Diabetologia 2012;55:215-225.
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5. Moon HS, Chamberland JP, Aronis K, Tseleni-Balafouta S, Mantzoros CS. Direct role of adiponectin and adiponectin receptors in endometrial cancer: in vitro and ex vivo studies in humans. Molecular Cancer Therapeutics 2011;10:2234-2243.
6. Mitsiades N, Pazaitou-Panayiotou K, Aronis K, Moon HS, Liu X, Chamberland JP, Panagiotou V, Mylvaganam G, Tseleni-Balafouta S, Mantzoros CS. Circulating adiponectin is inversely associated with risk of 1 thyroid cancer: in vivo and in vitro studies. Journal of Clinical Endocrinology Metabolism (Highlighted Paper) 2011;96:E2023-E2028.
7. Kim HY, Moon HS, Cao D, Lee JR, Kevala K, Jun SB, Lovinger D, Akbar M, Huang BX. N-Docosahexaenoylethanolamide promotes development of hippocampal neurons. Biochemical Journal 2011; 435:327-336.
8. Moon HS, Guo DD, Lee HG, Choi YG, Kang JS, Jo K, Eom JM, Yun CH, Cho CS. Alpha-eleostearic acid suppresses proliferation of MCF-7 breast cancer cells via activation of PPARγ and inhibition of ERK $\frac{1}{2}$. Cancer Science 2010;101:396-402.
9. Moon HS, Lee HG, Seo JH, Kim IY, Kim TG, Chung CS, Choi YJ, Cho CS. Anti-obesity effect of PEGylated conjugated linoleic acid on C57BL/6J (ob/ob) mice: attenuation of insulin resistance and enhancement of antioxidant defenses. Journal of Nutritional Biochemistry 2009;3:187-194.
10. Moon HS, Lee HG, Seo JH, Guo DD, Kim IY, Seo SJ, Chung CS, Kim TG, Choi YJ, Cho CS. Lipolysis is stimulated by PEGylated conjugated linoleic acid through the cyclic adenosine monophosphate-independent signaling pathway in 3T3-L1 cells: activation of MEK/ERK MAPK signaling pathway and hyper-secretion of adipo-cytokines. Journal of Cellular Physiology 2008;214:282-294.

Role of adiponectin in colon cancer development

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Objective

Obesity and high-fat-diet are associated with risk and progression of colon cancer. Low adiponectin levels may play an important role against the development of colon and other obesity-related malignancies. No prior studies have directly investigated mechanistic effects of adiponectin on colon cancer in the settings of obesity, high-fat diet and/or adiponectin deficiency.

Design

To investigate the effects of adiponectin on the growth of colorectal cancer in adiponectin-deficient or wild-type-C57BL/6 mice fed low-fat or high-fat diet.

Results

Mice on high-fat-diet gained more weight and had larger tumors, compared to mice fed on a low-fat-diet. Adiponectin administration suppressed implanted tumor growth, causing larger central necrotic areas. Adiponectin treatment also suppressed angiogenesis assessed by CD31 staining and VEGF-B and VEGF-D mRNA expression in tumors obtained from mice fed a high-fat-diet and from adiponectin-deficient mice. Adiponectin treatment decreased serum-insulin levels in high-fat-diet mice and increased serum-IL-12 levels in adiponectin-deficient mice. *In vitro*, we noted that adiponectin directly controls malignant potential (cell proliferation, adhesion, invasion and colony formation) and regulates metabolic (AMPK/S6), inflammatory (STAT3/VEGF) and cell cycle (p21/p27/p53/cyclins) signaling pathways in both mouse MCA38 and human HT29, HCT116, and LoVo colon cancer cell lines in a *LKB1*-dependent way.

Conclusion

Our novel mechanistic and pathophysiology studies provide evidence for an imporant role of adiponectin in colon cancer. Our data indicate that adiponectin or analogues might be useful agents in the management or chemoprevention of colon cancer.

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➤Educational background & professional experience

1991-1997	Ewha Women's University School of Medicine	Medicine
2003-2005	Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine	Endocrinology and metabolism / Fellowship
2004-2007	The Catholic University School of Medicine	Internal medicine / Doctor of philosophy
2010-2011	Cardiovascular Division, Brigham and Women's Hospital, Harvard University, Boston, MA, USA	Visiting professor
2011-present	Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine	Associate professor
2012-present	Assistant administrator of Committee of Research, Korean Diabetes Association	
2012-present	Vice-secretary of Korean Society of Lipidology and Atherosclerosis	

➤Research interests

Endocrinology and metabolism
Vascular complications of diabetes

➤Brief list of publications

1. Kwon CH, Rhee EJ, Song JU, Kim JT, Sung KC. Reduced lung function is independently associated with increased risk of type 2 diabetes in Korean men. Cardiovasc Diabetol. 2012 Apr 24;11(1):38.
2. Rhee EJ, Nallamshetty S, Plutzky J. Retinoid metabolism and its effects on the vasculature. Biochim Biophys Acta. 2011 Jul 23.
3. Rhee EJ, Sung KC. The reply. Am J Med. 2011 Sep;124(9):e15.
4. Choi JH, Rhee EJ, Kim KH, Woo HY, Lee WY, Sung K. Plasma omentin-1 levels are reduced in non-obese women with normal glucose tolerance and polycystic ovary syndrome. Eur J Endocrinol. 2011 Aug 24.
5. Lim SY, Rhee EJ, Sung KC. Metabolic syndrome, insulin resistance and systemic inflammation as risk factors for reduced lung function in Korean nonsmoking males. J Korean Med Sci. 2010 Oct;25(10):1480-6.
6. Rhee EJ, Lee WY, Yoon KH, Yoo SJ, Lee IK, Baik SH, Kim YK, Lee MK, Park KS, Park JY, Cha BS, Lee HW, Min KW, Bae HY, Kim MJ, Kim JA, Kim DK, Kim SW. A multicenter, randomized, placebo-controlled, double-blind phase II trial evaluating the optimal dose, efficacy and safety of LC 15-0444 in patients with type 2 diabetes. Diabetes Obes Metab. 2010 Dec;12(12):1113-9.
7. Jung CH, Rhee EJ, Choi JH, Bae JC, Yoo SH, Kim WJ, Park CY, Mok JO, Kim CH, Lee WY, Oh KW, Park SW, Kim SW. The relationship of adiponectin/leptin ratio with homeostasis model assessment insulin resistance index and metabolic syndrome in apparently healthy korean male adults. Korean Diabetes J. 2010 Aug;34(4):237-43.
8. Lim SY, Rhee EJ, Sung KC. Metabolic syndrome, insulin resistance and systemic inflammation as risk factors for reduced lung function in Korean nonsmoking males. J Korean Med Sci. 2010 Oct;25(10):1480-6.
9. Rhee EJ, Lee WY, Yoon KH, Yoo SJ, Lee IK, Baik SH, Kim YK, Lee MK, Park KS, Park JY, Cha BS, Lee HW, Min KW, Bae HY, Kim MJ, Kim JA, Kim DK, Kim SW. A multicenter, randomized, placebo-controlled, double-blind phase II trial evaluating the optimal dose, efficacy and safety of LC 15-0444 in patients with type 2 diabetes. Diabetes Obes Metab. 2010 Dec;12(12):1113-9.
10. Choi ES, Rhee EJ, Choi JH, Bae JC, Yoo SH, Kim WJ, Park SE, Park CY, Lee WY, Cho YK, Oh KW, Park SW, Kim SW. The association of brachial-ankle pulse wave velocity with 30-minute post-challenge plasma glucose levels in korean adults with no history of type 2 diabetes. Korean Diabetes J. 2010 Oct;34(5):287-93.

Comparison of metabolic disease development according to metabolic health and obesity

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Obesity is one of the mostly serious health problem worldwide. This is caused by sedentary life style, high caloric diet and stressful life. In the last decade, the worldwide prevalence of obesity has increased considerably, and so has the incidence of type 2 diabetes and cardiovascular disease (CVD). Several studies have shown that the obese phenotype may be present without metabolic abnormalities. This clinical condition, termed benign obesity or metabolically healthy obesity (MHO), is restricted to a unique subset of the obese population which, despite excessive body mass index (BMI) or body fat, are insulin sensitive and have a normal blood pressure, lipid, inflammation and hormonal profile. There are no unified criteria for the definition of MHO yet. Also, there is not much data regarding the true impact of MHO on metabolic diseases, such as type 2 diabetes and CVD. In this talk, I will discuss the current knowledge about MHO and will review the data on the association between MHO and the development of various metabolic diseases.

Soo Lim

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➤Educational background & professional experience

1990-1996	Seoul National University College of Medicine	M.D.
2002-2004	Postgraduate School, Seoul National University School of Public Health	Master of public health
2004-2006	Postgraduate School, Seoul National University College of Medicine	Ph.D.
2011-2012	Visiting Scholar, Massachusetts General Hospital /Harvard Medical School, Boston, MA, USA	

➤Research interests

Diabetes, metabolic syndrome, and obesity.

➤Brief list of publications

1. Lim S, et al. Subclinical atherosclerosis in a community-based elderly cohort: The Korean Longitudinal Study on Health and Aging. International Journal of Cardiology. 2012 Feb 23;155(1):126-33.
2. Lim S, et al. Vitamin D inadequacy is associated with significant coronary artery stenosis in a community-based elderly cohort: the korean longitudinal study on health and aging. Journal of Clinical Endocrinology and Metabolism. 2012 Jan;97(1):169-78.
3. Lim S, et al. Effect of S-adenosylmethionine on neointimal formation after balloon injury in obese diabetic rats. Cardiovascular Research. 2011 May 1;90(2):383-93.
4. Lim S, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean national health and nutrition examination survey for 1998-2007. Diabetes Care. 2011 Jun;34:1323-1328.

Changes in metabolic syndrome in American and Korean youth, 1997-2008

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Seoul National University, Korea

Background:

Metabolic syndrome (MetSyn) in children and adolescence is increasing worldwide, however, its pattern may be different between Caucasians and Asians. This study compares the prevalence and patterns of MetSyn between American and Korean children and adolescents between roughly 1998 and 2007.

Methods:

Data from the American and Korean versions of the National Health and Nutrition Examination Survey (NHANES and KNHANES) were used for this study.

The main outcome is prevalence and pattern of MetSyn among participants separately in each country. In each survey, stratified multistage probability sampling designs and weighting adjustments were conducted to represent the entire population. The revised National Cholesterol Education Program criteria were used to define MetSyn.

Results:

Totals of 934, 1781, and 1690 Americans aged 12-19 participated in NHANES 1988-1994, NHANES 1999-2002, and NHANES 2003-2006, respectively; and 1225, 976, 705, and 456 Koreans aged 12-19 have participated in KNHANES 1998, 2001, 2005, and 2007. The age-adjusted prevalence of MetSyn in American NHANES decreased from 7.3% to 6.7% and 6.5% while in Korean NHANES there was an increase from 4.0% to 5.9%, 6.6%, and 7.8% in each countries respective studies. Increases in dyslipidemia and abdominal obesity contributed to the increased prevalence in Korea, while in the U.S., decreases in low HDL-cholesterolemia and high blood pressure contributed to a decreased prevalence.

Conclusions:

Considering different phenotype changes, different approaches should be conducted at the national level to reduce the burden and consequences of MetSyn between Korea and the U.S.

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➤Educational background & professional experience

1983	University of Chicago Pritzker School of Medicine; Chicago, IL (USA)	Medical school
1983-1985	Stanford University Medical Center; Palo Alto, CA (USA)	Residency, internal medicine
1985-1987	Harbor UCLA Medical Center, Torrance, CA (USA)	Residency, internal medicine
1986-1988	Cedars-Sinai Medical Center, Los Angeles, CA (USA)	Fellowship; endocrinology
1989, 2010	Endocrine Subspecialty Board	Diplomat
2000-Present	Keck School of Medicine of USC	Professor
1992-1996	Comprehensive Diabetes Outpatient Program, Cedars-Sinai Medical Center, Los Angeles CA	Director
2010-Present	ADA/EASD Writing Group; 2012 Treatment Guidelines for Type 2 Diabetes Mellitus	Member
2011-Present	American Diabetes Association National Board	Member

➤Research interests

Dr. Peters has been a principal investigator on multiple clinical trials focusing on diabetes and diabetes prevention. She established the Community Diabetes Initiatives Research Center in collaboration with Childrens' Hospital Los Angeles with funding from the Keck Foundation, the JDRF, ADA, California Nutrition Network and Helmsley Trust. Dr. Peters is a Principal Investigator for the NIH Look AHEAD Study and the UCLA/USC NIH P50 program project, "Family and Neighborhood Interventions to Reduce Heart Disease Risk in East L.A."

➤Brief list of publications

1. Romley JA, Goldman DP, Solomon M, McFadden D, Peters AL. Exenatide Therapy and the Risk of Pancreatitis and Pancreatic Cancer in a Privately Insured Population. Diabetes Technology and Therapeutics 14:on-line, 2012.
2. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR. Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach: Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 35:1364-1379, 2012.; Diabetologia 55:1577-1596, 2012.
3. Langellier BA, Garza JR, Glik D, Prelip ML, Brookmeyer R, Roberts CK, Peters A, Ortega AN. Immigration Disparities in Cardiovascular Risk Factor Awareness. J Immigrant Minority Health. Published on-line January 2012.
4. Schwartz AV, Hodges M, Johnson KC, Kahn SE, Nevitt M, Peters AL, Williams C, Bray G. Effect of One Year of Intentional Weight Loss on Bone Mineral Density in Type 2 Diabetes: Results from Look AHEAD. JBMR 27:619-627, 2012.
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6. Wing R, Lang W, Wadden TA, Safford M, Knowler WC, Bertoni AG, Hill JO, Brancati FL, Peters A, Wagenknecht L for the Look AHEAD Research Group. Benefits of Modest Weight Loss in Improving Cardiovascular Risk Factors in Overweight/Obese Individuals with Type 2 Diabetes. Diabetes Care, 34, 2011.
7. Look AHEAD Research Group, Pi-Sunyer X, Blackburn G, Brancati FL, Bray GA,, Peters A,.Wing RR, Yanovski SZ. Long term effects of lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes: Four year results of the Look AHEAD trial. Archives of Internal Medicine 170:1566–1575, 2010.
8. Ruelas V, Roybal GM, Lu Y, Goldman D, Peters A. Clinical and Behavioral Correlates of Achieving and Maintaining Glycemic Targets in an Underserved Population with Type 2 Diabetes. Diabetes Care, 32:54-56, 2009.
9. Look AHEAD Research Group, Pi-Sunyer X, Blackburn G, Brancati FL, Bray GA, Bright R, Clark JM, Curtis JM, Espeland MA, Foreyt JP, Graves K, Haffner SM, Harrison B, Hill JO, Horton ES, Jakicic J, Jeffery RW, Johnson KC, Kahn S, Kelley DE, Kitabchi AE, Knowler WC, Lewis CE, Maschak-Carey BJ, Montgomery B, Nathan DM, Patricio J, Peters A, Redmon JB, Reeves RS, Ryan DH, Safford M, Van Dorsten B, Wadden TA, Wagenknecht L, Wesche-Thobaben J, Wing RR, Yanovski SZ. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes Care. 2007 30:1374-83.

New ADA / EASD algorithm for management of hyperglycemia

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Type 2 diabetes (T2DM) is a costly disease that accounts for a large proportion of global health care budgets, and costs will rise disproportionally once a patient develops diabetes-related complications. Therefore, in addition to lifestyle measures and treatment of hypertension and dyslipidemia, early and aggressive treatment of hyperglycemia in T2DM, which has been shown to prevent micro- and macrovascular disease, is warranted. Over the last several years, evidence has accumulated from randomized controlled trials (RCTs) showing efficacy of several novel agents that may have added value in the treatment of T2DM. However, other, mainly observational studies, have raised safety concerns with respect to some of the available, some of the novel treatment options. Within this turbulent climate, healthcare providers need guidance how to best treat their patients and therefore, continuous update of evidence-based guidelines and recommendations by experts and diabetes societies, reflecting current state-of-the-art, are needed. Thus, the recently published position statement of the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) on the Management of Hyperglycemia in T2DM, in contrast to previous versions of the guideline, have attempted to be less prescriptive and advocate a more individualized patient-centered approach.

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➤Educational background & professional experience

1983	University of Chicago Pritzker School of Medicine; Chicago, IL (USA)	Medical school
1983-1985	Stanford University Medical Center; Palo Alto, CA (USA)	Residency, internal medicine
1985-1987	Harbor UCLA Medical Center, Torrance, CA (USA)	Residency, internal medicine
1986-1988	Cedars-Sinai Medical Center, Los Angeles, CA (USA)	Fellowship; endocrinology
1989, 2010	Endocrine Subspecialty Board	Diplomat
2000-Present	Keck School of Medicine of USC	Professor
1992-1996	Comprehensive Diabetes Outpatient Program, Cedars-Sinai Medical Center, Los Angeles CA	Director
2010-Present	ADA/EASD Writing Group; 2012 Treatment Guidelines for Type 2 Diabetes Mellitus	Member
2011-Present	American Diabetes Association National Board	Member

➤Research interests

Dr. Peters has been a principal investigator on multiple clinical trials focusing on diabetes and diabetes prevention. She established the Community Diabetes Initiatives Research Center in collaboration with Childrens' Hospital Los Angeles with funding from the Keck Foundation, the JDRF, ADA, California Nutrition Network and Helmsley Trust. Dr. Peters is a Principal Investigator for the NIH Look AHEAD Study and the UCLA/USC NIH P50 program project, "Family and Neighborhood Interventions to Reduce Heart Disease Risk in East L.A."

➤Brief list of publications

1. Romley JA, Goldman DP, Solomon M, McFadden D, Peters AL. Exenatide Therapy and the Risk of Pancreatitis and Pancreatic Cancer in a Privately Insured Population. Diabetes Technology and Therapeutics 14:on-line, 2012.
2. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR. Management of Hyperglycemia in Type 2 Diabetes: A Patient-Centered Approach: Position Statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care 35:1364-1379, 2012.; Diabetologia 55:1577-1596, 2012.
3. Langellier BA, Garza JR, Glik D, Prelip ML, Brookmeyer R, Roberts CK, Peters A, Ortega AN. Immigration Disparities in Cardiovascular Risk Factor Awareness. J Immigrant Minority Health. Published on-line January 2012.
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Women, diabetes, and cardiovascular disease: the perfect storm?

Anne Peters
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The challenge of cardiovascular disease (CVD) in women is a global problem. Recent data document the scope of this issue: heart disease is the leading cause of death in women in every major developed country and most emerging economies. And given the worldwide health and economic implications of CVD in women, there is strong rationale to sustain efforts to control major CVD risk factors and to apply evidence-based therapies in women.

For example, up to 72% of women in the United States have a major form of CVD, with hypertension being the most common, followed by other heart disease conditions, coronary heart disease, myocardial infarction, angina pectoris, and stroke, with the prevalence increasing with age. Of note, women have higher mortality after MI than men with diabetes. Since 1984, the number of deaths for women has exceeded those for men; in 2005, women represented 52.6% of deaths from coronary heart disease.

For women with diabetes, the age-adjusted prevalence of major CVD is twice as high versus women without the disease. In addition, the prevalence of CVD in women with diabetes was higher in non-Hispanic blacks than it was in non-Hispanic whites or in Hispanics. Although CVD mortality rates are declining for men and women without diabetes, as well as for men with diabetes, the CVD mortality rates for women with diabetes are not declining. It is not surprising, therefore, that mortality rates are doubled for women with diabetes versus those without diabetes. But does the confluence of these three factors produce a "perfect storm" of increased risk? Why does cardiovascular disease disparately affect women with diabetes? And what are the implications for cardiovascular disease prevention and treatment in women with diabetes?

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➤Educational background & professional experience

2000	University of Pretoria, South Africa	MBChB
2003	Royal College of Physicians, UK	MRCP
2011	Royal College of Pathologists, UK	FRCPath
2011	University of Glasgow, UK	Ph.D.

➤Research interests

My particular interests are clinical trials of lipid-modifying agents and glucose-lowering agents, meta-analyses of important clinical events in these large trials, the relationship between glycaemia and cardiovascular disease, and also familial hypercholesterolaemia.

➤Brief list of publications

1. Preiss D, Tikkanen MJ, Welsh P, Ford I, Lovato LC, Elam MB, LaRosa JC, DeMicco DA, Colhoun HM, Goldenberg I, Murphy MJ, MacDonald TM, Pedersen TR, Keech AC, Ridker PM, Kjekshus J, Sattar N, McMurray JJ. Lipid-modifying therapies and risk of pancreatitis: a meta-analysis. JAMA. 2012 Aug 22;308(8):804-11.
2. Preiss D, Seshasai SR, Welsh P, Murphy SA, Ho JE, Waters DD, DeMicco DA, Barter P, Cannon CP, Sabatine MS, Braunwald E, Kastelein JJ, de Lemos JA, Blazing MA, Pedersen TR, Tikkanen MJ, Sattar N, Ray KK. Risk of incident diabetes with intensive-dose compared with moderate-dose statin therapy: a meta-analysis. JAMA. 2011 Jun 22;305(24):2556-64.
3. Preiss D, Sattar N, McMurray JJ. A systematic review of event rates in clinical trials in diabetes mellitus: the importance of quantifying baseline cardiovascular disease history and proteinuria and implications for clinical trial design. Am Heart J. 2011 Jan;161(1):210-219.
4. Preiss D, Welsh P, Murray HM, Shepherd J, Packard C, Macfarlane P, Cobbe S, Ford I, Sattar N. Fasting plasma glucose in non-diabetic participants and the risk for incident cardiovascular events, diabetes, and mortality: results from WOSCOPS 15-year follow-up. Eur Heart J. 2010 May;31(10):1230-6.
5. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, Seshasai SR, McMurray JJ, Freeman DJ, Jukema JW, Macfarlane PW, Packard CJ, Stott DJ, Westendorp RG, Shepherd J, Davis BR, Pressel SL, Marchioli R, Marfisi RM, Maggioni AP, Tavazzi L, Tognoni G, Kjekshus J, Pedersen TR, Cook TJ, Gotto AM, Clearfield MB, Downs JR, Nakamura H, Ohashi Y, Mizuno K, Ray KK, Ford I. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. Lancet. 2010 Feb 27;375(9716):735-42.
6. Ray KK, Seshasai SR, Wijesuriya S, Sivakumaran R, Nethercott S, Preiss D, Erqou S, Sattar N. Effect of intensive control of glucose on cardiovascular outcomes and death in patients with diabetes mellitus: a meta-analysis of randomised controlled trials. Lancet. 2009 May 23;373(9677):1765-72.

Do statins cause diabetes?

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Following the publication of the Scandinavian Simvastatin Survival Study in 1994, numerous large trials have confirmed the ability of statin therapy to reduce the risk of cardiovascular events. Pooled analyses of these trials suggest 20-25% reductions in major cardiovascular events, like stroke and myocardial infarction, per 1mmol/L lower LDL-cholesterol. Then, in 2008, the JUPITER trial provided surprising evidence of a 25% increased risk of new-onset diabetes compared to placebo in a prespecified analysis. This was followed by a comprehensive meta-analysis of published and unpublished data from 13 placebo- and standard care-controlled trials in 2010, with 〉 90,000 participants, which confirmed a 9% higher risk of new-onset diabetes on statin therapy. Subsequent research has also confirmed the presence of a dose-dependent effect between statins and new-onset diabetes. Data from all five large statin trials, comparing intensive-dose statin therapy to moderate-dose therapy, demonstrated a further 12% increase in risk on intensive-dose therapy. HbA1c levels in those with and without diabetes have also been shown to worsen on statins compared to control therapy, though only slightly. The mechanism underlying these observations remains unknown but studies in animal models suggest that statin therapy may affect peripheral insulin signaling. The cardiovascular benefits of statins are clear, and risk/benefit considerations remain firmly in favour of statin therapy especially for secondary prevention and moderate to high risk primary prevention. However, screening for diabetes in those on statins should be considered.

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➤Educational background & professional experience

2000	University of Pretoria, South Africa	MBChB
2003	Royal College of Physicians, UK	MRCP
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2011	University of Glasgow, UK	Ph.D.

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Cardiovascular impact of incretin-based therapies

David Preiss
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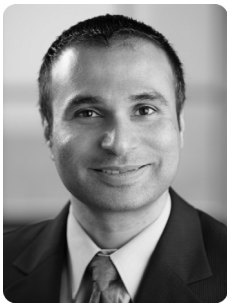
Glucagon-like peptide-1 (GLP-1) is a gut hormone secreted by the intestine in response to food intake. It has numerous effects including increased pancreatic insulin release, reduced glucagon secretion, reduced hepatic gluconeogenesis, increased satiety and regulation of gastric emptying. GLP-1 receptors have been localised not only in the pancreas and other organs, but also in cardiac tissue and arterial walls. Two groups of incretin-based therapies exist that exploit this pathway: GLP-1 receptor agonists (incretin mimetics) and dipeptidyl peptidase (DPP)-4 inhibitors (incretin enhancers). Both are recommended as add-on therapy with metformin for treatment of type 2 diabetes mellitus. As with other new diabetes agents, large trials are underway to attempt to demonstrate the cardiovascular safety of incretin-based therapies. At present, 70,000 patients are participating in at least seven large cardiovascular outcome trials. Encouraging data from small randomized trials using surrogate markers of cardiovascular disease (blood pressure, endothelial function, weight, total cholesterol, left ventricular function), and meta-analyses of cardiovascular events in short trials primarily designed to assess effect on glucose control, suggest that incretin-based therapies may prove to be effective in reducing cardiovascular events.



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➤Educational background & professional experience

1994-1995	St. Johns Hospital, Bangalore, India	Rotating internship
1996	Nair Hospital Internal Medicine, Topiwala National Medical College, Bombay, India	Senior house officer
1997-2000	St. Barnabas Hospital Internal Medicine, Bronx, New York	Residency
2000-2002	Tulane University, Endocrinology, Diabetes and Metabolism, New Orleans, Louisiana	Fellowship
2012-present	University of Nebraska Medical Center, Department of Internal Medicine, Division of Diabetes, Endocrinology & Metabolism, Omaha, Nebraska	Professor
2011-present	University of Nebraska Medical Center, Department of Internal Medicine, Chief, Division of Diabetes, Endocrinology & Metabolism, Omaha, Nebraska	Chief
2010-present	VA Nebraska Western Iowa Healthcare System, Director, Diabetes and Obesity Program, Medicine Department (111), Omaha, Nebraska	Director
2010-2011	University of Nebraska Medical Center, Department of Internal Medicine, Director, Fellowship Program, Division of Diabetes, Endocrinology & Metabolism, Omaha, Nebraska	Director
2002-present	VA Nebraska Western Iowa Healthcare System, Staff Physician - Endocrinology, Medicine Department (111), Omaha, Nebraska	Staff physician

➤Research interests

Cardiovascular disease in diabetes
Endothelial dysfunction in diabetes
Mental health and apathy in diabetes
Inflammation and insulin resistance

➤Brief list of publications

1. Padala PR, Padala KP, Sullivan DH, Reynolds DW, Desouza CV, Potter JF, Burke WJ. Improvement of glycemic control using methylphenidate treatment of apathy: A preliminary report. J Am Geriatr Soc 2012 Jul;60(7):1383-4.
2. Desouza C. Delay insulin therapy. Dialogues in Diabetes 2011 Dec;1(1):12-14.
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4. Desouza CV, Hamel FG, Bidasee K, O'Connel K.. Role of inflammation and Insulin resistance in Endothelial Progenitor Cell dysfunction. Diabetes 2011 Apr;60(4):1286-94 Feb 23 2011 Epub 2011 Feb 23.
5. Desouza C., Rentschler L., Haynatzki G. Effect of group clinics on diabetes outcomes. Primary Care. Diabetes 2010 Oct Epub.
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8. Desouza C., Fonseca V. Therapeutic Targets to Reduce Cardiovascular Disease in Type 2 Diabetes. Nature Reviews May 2009.
9. Desouza C., Gerety M., Hamel FG. Long-term effects of a PPAR-gamma agonist, pioglitazone, on neointimal hyperplasia and endothelial regrowth in insulin resistant rats. Vascular Pharmacology 46(2007)188-194.
10. Fonseca V., Desouza C., Asnani S., Jialal I. Non-Traditional risk factors for cardiovascular disease in diabetes. Endocrine Reviews Feb 2004 25(1)153-175.

The insulin-cancer connection

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The incidence of cancer is associated with diabetes as well as certain diabetes risk factors and diabetes treatments based upon epidemiologic evidence. Potential mechanisms include hyperglycemia, chronic inflammation, or hyperinsulinemia, whether endogenous (due to insulin resistance) or exogenous (due to administered insulin or insulin secretogogues). If there is an increase in exogenous or endogenous insulin, is there a risk of cancer? Concerns about the risk of cancer from insulin first arose in 2009 based upon retrospective analysis of a large German health-insurance database, which showed a positive association between the two. But what have we learned since this 2009 report? Results of three retrospective analyses and one prospective study were presented at the 72nd Scientific Session of the American Diabetes Association addressed this concern.

The Northern European Database Study compared insulin glargine with other non-glargine insulin; an analysis from Kaiser Permanente (Oakland, California USA) examined prevalent users of NPH insulin who switched to insulin glargine as well as new users of insulin glargine; Inovalon, Inc reviewed a registry of new users of insulin glargine versus those patients initiating treatment with NPH insulin; and, the Outcome Reduction with Initial Glargine Intervention (ORIGIN) study randomized people at high risk for, or in the early stages of, type 2 diabetes to either one daily injection of glargine insulin or standard care (no insulin), and evaluated various endpoints, including cancer.

This presentation will address the association between diabetes and cancer incidence or prognosis, list risk factors that are common to both diabetes and cancer, identify possible biologic links between diabetes and cancer risk, and elaborate on results of clinical research that investigated the use of insulin glargine and the risk of different types of cancers.

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➤Educational background & professional experience

1999-2001	Massachusetts General Hospital	Clinical and research fellow
2001-2003	University of Chicago	Instructor of medicine
2003-2010	University of Chicago	Assistant professor of medicine
2010-present	University of Chicago	Associate professor of medicine
2010-2011	Office of the Assistant Secretary for Planning and Evaluation, Department of Health and Human Services	Senior advisor to the deputy assistant secretary for health policy

➤Research interests

Dr. Huang's main research focus is in the area of medical decision making for elderly patients with type 2 diabetes where uncertainty exists regarding how to best individualize diabetes treatments based on clinical parameters and patient preferences. Over the past decade, Dr. Huang has established one of the most active research programs in geriatric diabetes in the country. Dr. Huang is principal investigator with Dr. Andrew Karter from Kaiser Permanente of the NIH-sponsored Diabetes and Aging Study. Apart from his work in geriatric diabetes, Dr. Huang has also performed other seminal translational diabetes research in the area of cost-effectiveness analysis.

➤Brief list of publications

1. Laiteerapong N, Karter AJ, Liu JY, Moffet HH, Sudore R, Schillinger D, John PM, Huang ES. Correlates of Quality of Life in Older Adults with Diabetes: The Diabetes & Aging Study. Diabetes Care. 2011; 34(8):1749-53.
2. Huang ES, Liu JY, Moffet HH, John PM, Karter AJ. Glycemic Control, Complications, and Death in Older Diabetic Patients: The Diabetes & Aging Study. Diabetes Care. 2011; 34(6):1329-1336.
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4. Huang ES, Basu A, O'Grady M, Capretta J. Projecting the future diabetes population size and related costs for the United States. Diabetes Care. 2009; 32: 2225-2229.
5. Huang ES, Gandra N, Zhang Q, Chin MH, Meltzer DO. The effect of functional status and comorbid illness on the expected benefits of intensive glucose control in older people with type 2 diabetes: a decision analysis. Ann Intern Med. 2008; 149(1): 11-19.
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10. Huang ES, Meigs JB, Singer DE. The effect of interventions to prevent cardiovascular disease in type 2 diabetes mellitus. Am J Med. 2001; 111:633-642.

Diabetes and dementia

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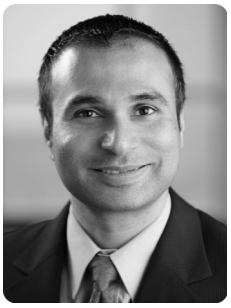
Dementia affects the way the brain normally functions, and the onset of the condition can adversely affect an individual's memory, speech and ability to successfully complete daily activities. The burden of chronic disease management disproportionately affects those with diabetes. In a disease which relies so heavily on self-management, dementia and its manifestations is a significant barrier to achieving positive outcomes.

Dementia strikes individuals with poorly controlled diabetes, high blood pressure, high cholesterol and heart disease to a greater degree, as these conditions increase the risk for a condition called vascular dementia. The most common form of dementia in the elderly is Alzheimer's disease, but other factors, too. Caused by a series of small strokes that damage or destroy brain tissue and prevent oxygen from reaching the brain, vascular dementia is a serious health concern for older adults with diabetes.

Screening patients for dementia and discerning the difference between dementia and depression are critical in treating patients with diabetes. This lecture will discuss the impact of diabetes on the development of dementia, the rudiments of dementia assessment, and review the basic skills necessary to effectively manage these patients.



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➤Educational background & professional experience

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1996	Nair Hospital Internal Medicine, Topiwala National Medical College, Bombay, India	Senior house officer
1997-2000	St. Barnabas Hospital Internal Medicine, Bronx, New York	Residency
2000-2002	Tulane University, Endocrinology, Diabetes and Metabolism, New Orleans, Louisiana	Fellowship
2012-present	University of Nebraska Medical Center, Department of Internal Medicine, Division of Diabetes, Endocrinology & Metabolism, Omaha, Nebraska	Professor
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2002-present	VA Nebraska Western Iowa Healthcare System, Staff Physician - Endocrinology, Medicine Department (111), Omaha, Nebraska	Staff physician

➤Research interests

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The ORIGIN trial - final results

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Type 2 diabetes has been shown to significantly increase the risk for cardiovascular disease (CVD) and all-cause mortality. A study by Haffner et al showed individuals with type 2 diabetes without prior myocardial infarction (MI) and people with a prior MI but without diabetes have a similar level risk of survival. Therefore, diabetes is considered as a CVD equivalent. However, the results of clinical trials that studied the effects of intensive glucose-lowering treatment in patients with type 2 diabetes have not been convincing in terms of lowering short-term CVD risk and survival.

Insulin resistance can result in impairment of the entire vasculature irrespective of vessel size, resulting in diabetes-induced vascular complications. Macrovascular and microvascular dysfunction are important not only in the development of obesity-related target organ damage, but also in the development of CV risk factors, including hypertension and insulin resistance. It would seem logical that interrupting these negative associations at an earlier stage of the disease process, would provide benefit. For individuals with type 2 diabetes, initial therapeutic approach emphasizes management of blood glucose levels with lifestyle intervention as well as pharmacologic therapies, including insulin, where indicated. But does blood glucose lowering with insulin reduce CV morbidity and/or mortality?

The Outcome Reduction with an Initial Glargine Intervention (ORIGIN) Trial sought to answer two questions: (1) whether insulin glargine-mediated normoglycemia can reduce CV morbidity and/or mortality in people at high risk for vascular disease with either impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or early type 2 diabetes; and, (2) determine whether omega-3 fatty acids can reduce cardiovascular mortality in people with IFG, IGT or early type 2 diabetes. This discussion will review the final results of the ORIGIN Trial.

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➤Educational background & professional experience

1999-2001	Massachusetts General Hospital	Clinical and research fellow
2001-2003	University of Chicago	Instructor of medicine
2003-2010	University of Chicago	Assistant professor of medicine
2010-present	University of Chicago	Associate professor of medicine
2010-2011	Office of the Assistant Secretary for Planning and Evaluation, Department of Health and Human Services	Senior advisor to the deputy assistant secretary for health policy

➤Research interests

Dr. Huang's main research focus is in the area of medical decision making for elderly patients with type 2 diabetes where uncertainty exists regarding how to best individualize diabetes treatments based on clinical parameters and patient preferences. Over the past decade, Dr. Huang has established one of the most active research programs in geriatric diabetes in the country. Dr. Huang is principal investigator with Dr. Andrew Karter from Kaiser Permanente of the NIH-sponsored Diabetes and Aging Study. Apart from his work in geriatric diabetes, Dr. Huang has also performed other seminal translational diabetes research in the area of cost-effectiveness analysis.

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Hypoglycemia unawareness

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Clinical studies have shown that tight blood glucose control slows and may prevent development of long-term microvascular complications of diabetes. In these studies, however, hypoglycemia was a side effect, which was increased three-fold with intensive therapy.

Iatrogenic hypoglycemia is a problem, especially for people with type 1 diabetes, and can cause recurrent morbidity, and sometimes death, as well as a vicious cycle of recurrent hypoglycemia. This is due to increasing duration of diabetes and a loss of sympatho-adrenal activation due to repeated hypoglycemia. Some patients lose all or most of their warning signs, such as tremor, sweating, and/or palpitations, and are then at major risk of sudden, dangerous severe periods of coma. When hypoglycemia occurs in the absence of these warning signs/symptoms, it is called "hypoglycemic unawareness". But there may be a reason why patients are unaware of their hypoglycemia. In the Diabetes Control and Complications Trial (DCCT), more than half of the hypoglycemic events occurred during sleeping hours. But hypoglycemia is also seen in patients with type 2 diabetes. In the UKPDS, 2.3% of patients with type 2 diabetes receiving insulin therapy experienced a major hypoglycemic event; one patient died from complications of hypoglycemia.

It is possible to restore some hypoglycemic warning symptoms if patients are prepared to work with clinicians to avoid all hypoglycemic episodes. The most effective techniques involve simply teaching patients the skills of insulin self-management. However some are resistant to altering their glycemic targets and continue to be a danger to both themselves and their families.

CORPORATE SYMPOSIA

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➤Educational background & professional experience

1981-1987	Kyung Hee University College of Medicine	Medicine / M.D.
1991-1993	Kyung Hee University, Graduate School	Internal medicine/ Master degree
1994-1997	Kyung Hee University, Graduate School	Internal medicine / Ph.D. degree
1991-1995	Kyung Hee University Hospital	Residency in internal medicine
1995-1998	Samsung Seoul Hospital	Fellowship in endocrinology
1998-1999	Kwandong University, College of Medicine	Assistanst professor
1999-2006	Eulji University Hospital	Associate professor
2006-present	Kyung Hee University, College of Medicine	Professor

➤Research interests

Pathophysiology in diabetes

➤Brief list of publications

1. 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, 2012, 23, 1337-42.
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Going beyond A1c drop with vildagliptin: smoothing out glycemic excursions

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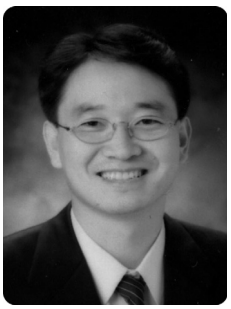
The dysglycemia of diabetes includes two components; sustained chronic hyperglycemia and acute glucose fluctuations. Glucose fluctuations exhibited a more specific triggering effect on oxidative stress than chronic sustained hyperglycemia. Increased oxidative stress has a primary role in the pathogenesis of diabetic complications. We recommend that any strategy aimed at controlling the glycaemic disorders associated with type 2 diabetes should target the 'glucose tetrad', which comprises the following components: HbA1c, fasting and postprandial plasma glucose, and markers of glycaemic variability. Therefore, dipeptidyl peptidase IV inhibition therapy should target not only reducing HbA1c but also flattening acute glucose fluctuations. In a previous study, we found that the effects on glucose fluctuations over a day, as estimated from MAGE indexes, were more pronounced in the vildagliptin than in the sitagliptin group.

Also, an ideal add-on treatment should have a complementary mechanism of action and provide additional glycaemic control without adding a significant burden in terms of safety or AEs such as body weight increase and risk of hypoglycaemia. We investigated the efficacy and safety of early combination of vildagliptin and metformin in patients with Korean T2DM who are inadequately controlled with prior metformin monotherapy in comparison to uptitrating metformin dose. We first present the result of this study.



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➤Educational background & professional experience

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1999-2001	Master course of medical science, Graduate school, Chonbuk national university	Internal medicine / Master
2002-2007	Ph.D. course of medical science, Graduate school, Chonbuk national university, Majored in diabetology	Endocrinology & metabolism / Ph.D.
1998-2002	Resident, Internal medicine, Medical college of Chonbuk national university hospital	
2002-2003	Fellowship, Endocrinology & Metabolism, Medical college of Chonbuk national university hospital	
2003-present	Division of endocrinology and metabolism, Sejong general hospital	

➤Research interests

Majored in diabetology & diabetic neuropathy

➤Brief list of publications

1. Prevalence and clinical characteristics of diabetic peripheral neuropathy in hospital patients with Type 2 diabetes in Korea. Diabet Med. 2012 Sep;29(9):e290-e296.
2. Autoimmune Hypoglycemia in a Type 2 Diabetic Patient With Anti-Insulin and Insulin Receptor Antibodies. Diabetes Care 27: 288-289,2005.
3. 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.
4. A case of a ruptured pheochromocytoma with an intratumoral aneurysm managed by coil embolization. Endocr J. 2003 Dec;50(6):653-6.

Recent advances in the management of diabetic peripheral neuropathy: where are we now and where to go?

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Diabetic peripheral neuropathy (DPN) is very common, affecting approximately 50% of both type 1 and type 2 diabetic patients. It has major detrimental effects sufferers, as it confers much morbidity and is associated with increased mortality. DPN is not a single entity, but encompasses several neuropathic syndromes.

Studies in experimental diabetes examining the pathogenesis of DPN have identified a number of metabolic abnormalities including polyol pathway hyperactivity, increased advanced glycation end-point formation, alterations in the protein kinase C beta pathway through diacylglycerol and oxidative stress. There is now strong evidence implicating nerve ischemia as the cause of DPN. Studies in human and animal models have shown reduced nerve perfusion and endoneurial hypoxia. These endoneurial microvascular changes strongly correlate with clinical severity and the degree of nerve-fiber pathology. Unfortunately, many compounds that have been effective in animal models of neuropathy have not been successful in human diabetic neuropathy. The only compounds found to be efficacious in human diabetic neuropathy, and are in clinical use, are the anti-oxidant, a-lipoic acid and the aldose reductase inhibitor, epalrestat. Overall, the evidence emphasizes the importance of vascular dysfunction, driven by metabolic change, in the etiology of DPN, and highlights potential therapeutic approaches. Epidemiological data on diabetic painful neuropathic pain (DPNP) are limited. In one population-based study, the prevalence of DPNP, as assessed by a structured questionnaire and examination, was estimated at 33%. It was notable that, of these patients, 12.6% patients knew they had DPN and 32% had never received treatment for their pain. Thus, despite being common, DPNP continues to be underdiagnosed and undertreated. Pharmacological treatment of DPNP include tricyclic compounds, serotonin noradrenalin reuptake inhibitors, the anti-oxidant a-lipoic acid, anticonvulsants, opiates, membrane stabilizers, topical capsaicin and so on. Management of the patient with DPNP must be tailored to individual requirements and will depend on

the presence of other comorbidities.

I'll discuss recent management of diabetic peripheral neuropathy: Where are we

now and where to go?

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1991-1997	Yonsei University College of Medicine	M.D.
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2004-2007	Seoul National University	Medical instructor
2006	Yonsei University College of Medicine	Ph.D.
2007-2011	Seoul National University	Assistant professor
2009-2011	Columbia University, NYC, USA	Visiting scholar
2012-present	Seoul National University & Bundang Seoul National University Hospital	Associate professor

➤Research interests

Adipocytokine, cardiometabolic risk, T2DM

➤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 22(9):353-363.
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How can we optimize the management for residual risks of atherosclerosis in patients with diabetes?

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It is well know that insulin resistance causes dyslipidemia, typically elevated triacylglyceride, lower HDL-cholesterol, and high small dense-LDL cholesterol in patients with obesity, diabetes, and cardiovascular disease, we called dyslipidemic triad. From many statin trials, we did see that significant reduction in CV mortality by targeting LDL-cholesterol lowering around 20-30%, however, there still has been residual risks exist explaining up to 65-90% of CV events. Recent ACCORD lipid trial showed that initial combination therapy had no beneficial effect on primary macrovascular outcome (CV death, non-fatal MI, non-fatal stroke). In this lecture, I want to discuss about the method for effective reduction of residual risks of atherosclerosis and who will be the proper target for the combination therapy in treating dyslipidemia.

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➤Educational background & professional experience

1996	Niels Bohr Institute, Denmark	B.Sc. Biophysics
2003	University of Copenhagen, Denmark	M.D. Medicine
2009	Copenhagen Business School, Denmark	E.M.B.A
2005-2010	Novo Nordisk, Victoza Medical department	Medical director
2011	Novo Nordisk, Degludec medical department	Vice president

➤Research interests

Diabetes drug development

➤Brief list of publications

Insulin development - past, present and future

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Insulin therapy has undergone tremendous development since its discovery 90 years ago.

Development has moved from early advances in extraction and purification over recombinant genetic advances to todays modern insulins with specific protein designs to meet clinical needs.

One of the latest developments is the ultra-long-acting insulin degludec designed to overcome specific clinical challenges.

Development considerations for this and other new insulin in development will be discussed.

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➤Educational background & professional experience

1983-1989	Kyunghee University, School of Medicine	
1989-1990	Kyunghee University Hospital	Medical intern
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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

Pathophysiology of diabtes mellitus, incretin hormone, GLP-1, islet biology and islet transplantation

➤Brief list of publications

1. Kim JY, Lim DM, Park HS, Moon CI, Choi KJ, Lee SK, Baik HW, Park KY, Kim BJ.Exendin-4 Protects Against Sulfonylurea-Induced β-Cell Apoptosis. J Pharmacol Sci. 118(1):65-74, 2012.
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.
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8. Byung-Joon Kim. Stimulation of Glucagon Like Peptide-1 Secretion in Enteroendocrine L cells. . Korean Diabetes J 33:458-463, 2009.
9. Byung-Joon Kim. Beta Cells Preservation in Diabetes using GLP-1 and Its Analog. Hanyang Med Rev 29:140-147, 2009.
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A new opportunity for patient-centric treatment

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The prevalence and overall burden of diabetes is high and increasing, largely due to the growing prevalence of type 2 diabetes, which accounts for 85 to 95% of all cases of diabetes in many countries[1]. Maintaining glycemic control in patients with type 2 diabetes can be challenging due to the natural progression of the disease[2]. The natural progression of type 2 diabetes may require multiple agents with comprehensive mechanisms of actions[2]. ADA/EASD 2012 recommends on combination therapy if monotherapy alone does not achieve/maintain an HbA1c target over ~3 months and all treatment decisions, where possible, should be made in conjunction with the patient, focusing on his/her preferences, needs and values.3 However, combination therapy often comes with the trade-offs of less convenient twice-daily dosing or tolerability concerns. Given the chronic nature of diabetes, patient's adherence to therapy is very important in preventing complications of the disease. Less complex treatment regimens with fewer pills and once-daily dosing are associated with higher rates of adherence[4]. Kombiglyze XR (Saxagliptin + Metformin XR combination) is the first and only once-a-day DPP-4 inhibitor with metformin XR combination. In multicenter, randomized, double blind, placebo-controlled trial saxagliptin plus metformin XR combination was reported to improve plasma glucose concentrations through the 24-h dosing interval[5]. In another multicenter, randomized, double blind, active-controlled Phase-III trial saxagliptin + metformin were compared with saxagliptin or metformin monotherapy in patients with treatment naive T2DM.6 Patients achieving HbA1c 〈 7% was 60.3% with saxagliptin 5 mg + metformin at 24 weeks of treatment[6].

Kombiglyze XR provides once-a-day combination control across 3 key glycemic measures with tolerability similar to metformin alone. This can lead to increased compliance, improved glycemic control and hence decreased risk of the associated complications.

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4. Nau DP, Am J Manag Care 2012 Apr; 18(3 Suppl):S49-54
5. Stenlöf K et al. Curr Med Res Opin. 2010;26(10):2355-2363
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➤Educational background & professional experience

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

➤Research interests

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.
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What is next after metformin?

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This year, position statement of American diabetes association (ADA) and European Association for the Study of Diabetes (EASD) showed that, unless there are prevalent contraindications, metformin is the optimal first-line drug. However after metformin, there are limited data to guide us. Combination therapy with an additional 1-2 oral or injectable agents is reasonable, aiming to minimize side effects where possible.

Pioglitazone is an oral antidiabetic agent that reduces insulin resistance in adipocyte, liver and muscle. This valuable action is intermediated by its link to a nuclear receptor called peroxisome proliferator-activated receptor-γ. Beyond the beneficial effects on glucose metabolism, pioglitazone has many positive effects on lipid metabolism, blood pressure, endothelial function, and inflammatory markers. Pioglitazone is already approved for the treatment of type 2 DM in combination with metformin, sulfonylurea, DPP-IV inhibitors, and insulin. The combination of pioglitazone with another antidiabetic drug should be based on the pathophysiological basis and risk profiles of an individual patient. The goal of any therapeutic options should include better glucose control, minimizing the risk of hypoglycemia, preserving beta-cell number and function, and improving the cardiovascular outcome in patients with type 2 DM.

Tight glucose control in type 2 DM was shown to have positive effects on microvascular complications, while the effect of tight glucose control on the macrovascular complications in type 2 DM was found to be controversial. Therefore, the strategies in the treatment of type 2 DM should aim to decrease the individual cardiovascular risk in an individual patient instead of solely concentrating on the lowering glucose effects. Treatment of type 2 DM patients by addressing not only glucose control but also implying the pathophysiology of diabetes, can help to improve their prognosis, especially with regard to the vascular complications. In the view of this point, pioglitazone is next choice after considering metformin.

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➤Educational background & professional experience

1997	Faculty of Medicine, the University of Tokyo	M.D.
2003	Graduate School of Medicine, the University of Tokyo	Ph.D.
2005-2011	University of Texas Southwestern Medical Center at Dallas	Postdoctoral fellow
2011-present	Graduate School of Medicine, the University of Tokyo	Project associate professor

➤Research interests

Diabetes and atherosclerosis: with special interests on neutral lipids, lipase and lipid signaling.

➤Brief list of publications

1. Okazaki H, Goldstein, JL, Brown, MS, Guosheng L: LXR-SREBP-1c-Phospholipid Transfer Protein Axis Controls Very Low Density Lipoprotein (VLDL) Particle Size. J Biol Chem 285:6801-10, 2010.
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5. Okazaki H, Igarashi M et al. Identification of neutral cholesterol ester hydrolase, a key enzyme removing cholesterol from macrophages. J Biol Chem 283:33357-33364, 2008.
6. Okazaki H, Tazoe F et al. Increased cholesterol biosynthesis and hypercholesterolemia in mice overexpressing squalene synthase in the liver. J Lipid Res 47:1950-1958, 2006.
7. Okazaki H et al. Identification of a novel member of the carboxylesterase family that hydrolyzes triacylglycerol: a potential role in adipocyte lipolysis. Diabetes 55:2091-2097, 2006.
8. Sekiya M, Osuga JI, Okazaki H et al. Absence of hormone-sensitive lipase inhibits obesity and adipogenesis in Lep ob/ob mice. J Biol Chem 279:15084-15090, 2004.
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10. Okazaki H et al. Lipolysis in the absence of hormone-sensitive lipase: evidence for a common mechanism regulating distinct lipases. Diabetes 51:3368-3375, 2002.

Diabetic dyslipidemia - statins & beyond statins

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A large body of evidence has established the safety and efficacy of statins for the prevention of cardiovascular disease (CVD). Statins are effective in diabetic patients as well; however, being a high-risk group of CVD, diabetics have a substantial residual risk. New therapeutic modalities are awaited.

Epidemiological studies in diabetics have unraveled multiple CVD risks other than LDL-cholesterol, such as high triglycerides (TG), low HDL-cholesterol, high blood pressure, and hyperglycemia. Treating each of these risks is expected to reduce CVD event in diabetics. Among these risks, high TG + low HDL-cholesterol, so-called "diabetic dyslipidemia" is the least treated, but its importance in atherogenesis has been recognized.

High TG + low HDL-cholesterol are often associated with an increase in small, dense LDL, a well-known class of atherogenic lipoproteins, and these three features are collectively called "atherogenic lipid triads". Treating atherogenic lipid triads may reduce CVD risk, as implied by a number of fibrate trials. However, safety concerns remain on the combination of statins and fibrates, necessitating the identification of a new drug target. For that, the mechanisms of diabetic dyslipidemia should be clarified.

The classical view underscores the importance of the plasma lipoprotein lipase (secreted from muscle/adipose tissue and clearing TG-rich lipoproteins) and adipocyte TG lipases (releasing FFA and promoting VLDL-TG secretion) in the pathogenesis of diabetic dyslipidemia. In addition to these lipolytic pathways in peripheral tissues, the role of liver, another insulin-sensitive organ, has emerged. Liver normally secretes small-size VLDL (VLDL2); but in diabetic liver, production of TG-rich large VLDL (VLDL1) is enhanced, contributing to high plasma TG. The basic research studies by us and others suggest that this pathway might be an attractive target for the treatment of diabetic dyslipidemia.

Statin therapy is the gold standard for CVD prevention; but for diabetics, additional drug targets awaited.

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2005-2006	University of Texas	Research fellow
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➤Research interests

Adipokines, vascular inflammation, metabolic syndrome

➤Brief list of publications

1. Choi KM, Han KA, Ahn HJ, Hwang SY, Hong HC, Choi HY, Yang SJ, Yoo HJ, Baik SH, Choi DS, Min KW. Effects of exercise on sRAGE levels and cardiometabolic risk factors in patients with type 2 diabetes: A randomized controlled trial. J Clin Endocrinol Metab 2012, In press.
2. Choi KM, Hwang SY, Hong HC, Yang SJ, Choi HY, Yoo HJ, Lee KW, Nam MS, Park YS, Woo JT, Kim YS, Choi DS, Youn BS, Baik SH. C1q/TNF-related Protein-3 (CTRP-3) and Pigment Epithelium-Derived Factor (PEDF) Concentrations in Patients with Type 2 Diabetes and Metabolic Syndrome. Diabetes 2012, In press.
3. 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-FDG PET. Int J Cardiol 2012, In press.
4. Yang SJ, Kim SE, Hwang SY, Kim TN, Choi HY, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Association between sRAGE, esRAGE Levels and Vascular Inflammation: Analysis with 18F-FDG PET. Atherosclerosis 2012 Feb;220(2):402-6.
5. 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 Aug;96(8):E1325-9.
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7. Choi HY, Kim S, Yang SJ, Yoo HJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Association between adiponectin, resistin and vascular inflammation: Analysis with 18F-FDG PET. Arterioscler Thromb Vasc Biol 2011 Apr;31(4):944-9.
8. Yoo HJ, Kim SE, Park MS, Choi HY, Yang SJ, Seo JA, Kim SG, Kim NH, Baik SH, Choi DS, Choi KM. Serum Adipocyte fatty acid-binding protein is associated independently with vascular inflammation: Analysis with 18F-FDG PET. J Clin Endocrinol Metab 2011 Mar;96(3):E488-92.
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Advantages of incretin therapy for type 2 diabetes mellitus including Korean patients

Kyung Mook Choi
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The increasing burden of type 2 diabetes mellitus (T2DM) has led to a request for novel therapeutic options for T2DM. Achieving optimal blood glucose levels is crucial in preventing or delaying the progression of complications related to T2DM.

Since the discovery of incretins, therapy using dipeptidylpeptidase-4 (DPP-4) inhibitors has become an essential strategy in combating T2DM. The role of DPP-4 inhibitors in the therapeutic guidelines is continuously evolving, as their potential strengths and weakness become better defined. Sitagliptin is a well-tolerated, efficacious, weight-neutral oral antidiabetic agent, with a very low risk of hypoglycemia. Animal experiments suggest a protective effect of sitagliptin on the pancreatic β-cells, thus preventing the progression of the disease. Unresolved future issues may include the durability of glucose control in humans, resulting from β-cell protection effect, beneficial impact on cardiovascular disease and long-term safety data.

This lecture will include an updated review, providing an analysis of both the similarities and the differences between DPP-4 inhibitors. Furthermore, the positioning and perspective of sitagliptin in the management of T2DM will be discussed.

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➤Educational background & professional experience

1992	College of Medicine, Ewha Womens University	B.S.
2000	Ajou University, College of Medicine	Internal medicine / M.S.
2003	Ajou University, College of Medicine	Preventive medicine / Ph.D.
1992-1997	Hallym University, Kangnam Sacred Heart Hospital	Internship & residency
1997-1998	Department of Internal Medicine, Sejong Hospital	Faculty
1998-2000	Ajou University School of Medicine	Clinical research fellow
2000-2002	Pochon CHA University, College of Medicine	Full-time lecturer
2002-present	Hallym University, Kangnam Sacred Heart Hospital	Associate professor

➤Research interests

Molecular signal pathway and metabolic changes in diabetic heart disease
Association between inflammatory or anti-inflammatory cytokines and insulin sensitivity

➤Brief list of publications

1. Ko SH, Kim SR, Kim DJ, Oh SJ, Lee HJ, Shim KH, Woo MH, Kim JY, Kim NH, Kim JT, Kim CH, Kim HJ, Jeong IK, Hong EG, Cho JH, Mok JO, Yoon KH: 2011 Clinical Practice Guidelines for Type 2 Diabetes in Korea. diabetes and Metab J 5:431-436, 2011.
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10. Hong EG, Ko HJ, Cho YR, Kim HJ, Ma Z, Yu TY, Friedline RH, Kurt-Jones E, Finberg R, Fischer MA, Granger EL, Norbury CC, Hauschka SD, Philbrick WM, Lee CG, Elias JA, Kim JK: Interleukin-10 Prevents Diet-Induced Insulin Resistance by Attenuating Macrophage and Cytokine Response in Skeletal Muscle. Diabetes. 2009 58(11): 2525-35.

Evidence for vildagliptin as a therapeutic option for type 2 diabetes: efficacy considerations

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Defective insulin secretion and inappropriate glucagon suppression are key abnormalities in the pathophysiology of type 2 diabetes[1]. The incretin effect is major determinant of both insulin and glucagon secretion and is largely mediated through the intestinally derived peptide hormone, glucagon like peptide 1 (GLP-1), which increases alpha and beta cell glucose sensitivity producing glucose dependent effects on both glucagon and insulin secretion. The incretin effect is reduced in type 2 diabetes, inhibition of the enzyme DPP-4 increases active forms of plasma GLP-1 level, thereby utilising the therapeutic potential of the incretin effect to produce reductions in blood glucose, with a low risk of hypoglycaemia.

There are a variety of currently available DPP-4 inhibitors, which can be broadly categorised as either substrate or competitive inhibitors. Subtle, but significant pharmacological differences exist between currently available agents[2] which can potentially translate into differences in the therapeutic profiles of the agents. Vildagliptin is a potent DPP-4 substrate inhibitor, which has been shown to produce greater inter-prandial GLP-1 levels and glucagon suppression compared with Sitagliptin[3]. Clinical studies have demonstrated the efficacy and safety of vildagliptin in a wide range of patient populations including the very elderly and those with mild, moderate and severe renal impairment[4,5]. Results from indirect comparative analyses suggests that there may be differences between the available DPP-4 inhibitors with respect to their clinical effects and although there is a relative lack of direct comparative clinical trial data, in a recent study in Japanese patients vildagliptin resulted in greater reduction in HbA1c compared with sitagliptin[6].

Thus while there are many available DPP-4 inhibitors there is a growing body of data to suggest that not all DPP-4 inhibitors are the same.

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6. Signorovitch JE et al. Clin Drug Investig. 2011;31(9):665-74

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➤Educational background & professional experience

1990-1992	Premedical Course, Seoul National University College of Natural Science	
1992-1996	Seoul National University College of Medicine	M.D.
1998-2004	Graduate School, Seoul National University	M.S., Ph.D.
1996-2003	Department of Internal Medicine, Seoul National University Hospital	Intern, resident, fellow
2009-2010	Department of Cellular and Physiological Sciences, University of British Columbia, Vancouver, B.C., Canada	Visiting professor
2003-present	Department of Internal Medicine, Seoul National University College of Medicine	Professor

➤Research interests

Gut hormones, insulin therapy, treatment model for diabetes mellitus

➤Brief list of publications

1. Cho YM, Merchant CE, Kieffer TJ. Targeting the Glucagon Receptor Family for Diabetes and Obesity Therapy. Pharmacol Ther 2012 (in press).
2. Speck M, Cho YM (co-first author), Asadi A, Rubino F, Kieffer TJ. Duodenal-jejunal bypass protects GK rats from {beta}-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. Cho YM, Kieffer TJ. K-cells and glucose-dependent insulinotropic polypeptide in health and disease. Vitam Horm. 2010;84:111-50.
5. Cho YM, Kim JH, Kim M, Park SJ, Koh SH, Ahn HS, Kang GH, Lee JB, Park KS, Lee HK. Mesenchymal Stem Cells Transfer Mitochondria to the Cells with Virtually No Mitochondrial Function but Not with Pathogenic mtDNA Mutations. PLoS ONE 2012;7(3):e32778.
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8. 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.

DPP-4 inhibitors: beyond glycemic control in diabetes treatment

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Good glycemic control from the onset of type 2 diabetes mellitus (T2DM) is critical in preventing the development of its microvascular or macrovascular complications. Recently, vast interest is being generated in incretin-based therapies (glucagon-like peptide-1 [GLP-1] receptor agonists and dipeptidyl peptidase-4 inhibitors [DPP-4i]) based on an increasing body of evidence that suggests incretin hormones may have additional effects beyond their blood glucose lowering actions.

In preclinical studies, both incretin hormones - LP-1 and glucose-dependent insulinotropic polypeptide (GIP) - have β-cell protective effects, and enhancement of endogenous incretin levels by DPP-4 inhibition leads to improvements in β-cell mass and function. Changes in β-cell functional mass have not yet been demonstrated in humans, but DPP-4 inhibitors have been associated with beneficial effects on β-cell function in clinical studies. Receptors for GLP-1 are present in cardiac and vascular tissues, and preclinical studies suggest that GLP-1 possesses cardioprotective properties. Treating with exogenous GLP-1 and DPP-4 inhibitors has both been shown to be capable of increasing left ventricular function (LVF) in clinical studies. GLP-1 has vasodilatory property and improves endothelial dysfunction in both healthy subjects and patients with T2DM. Rodent studies have indicated that both incretin hormones may have anti-atherosclerotic actions, with reduced atherosclerotic lesions being observed following treatment with the exogenous GLP-1 or with DPP-4 inhibitors.

In rodents, neuroprotective effects of DPP4 inhibitor via elevated GLP-1 have been demonstrated, and studies in male Sprague-Dawley diabetic rats have suggested that the raised endogenous GLP-1 concentrations obtained by DPP-4 inhibition may reduce peripheral nerve degeneration.

Recently, renoprotective action through DPP4 inhibition with Linagliptin has been demonstrated in mouse model, this effect may be due to the inhibition of podocyte damage and myofibroblast transformation. In a separate post-hoc analysis to investigate the clinical effect of linagliptin 5 mg qd versus placebo on albuminuria has shown that Linagliptin treatment significantly lower albuminuria in patients with diabetic nephropathy.

Together, the evidence suggests the possibility that DPP-4 inhibitors may have potential non-glycemic benefits in addition to their glucose-lowering action, but this needs to be demonstrated in dedicated clinical studies.

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➤Educational background & professional experience

1983	Kyung Hee University School of Medicine	M.D.
1993	Kyung Hee University School of Medicine	Ph.D.
2007	Kyung Hee University School of Medicine	Professor
2005-present	Department of Endocrinology and Metabolism, Kyung Hee University Hospital	Chief

➤Research interests

Insulin therapy, betacell function

➤Brief list of publications

1. Kim TH, Chun KH, Kim HJ, Han SJ, Kim DJ, Kwak J, Kim YS, Woo JT, Park Y, Nam M, Baik SH, Ahn KJ, Lee KW. Direct medical costs for patients with type 2 diabetes and related complications: a prospective cohort study based on the Korean National Diabetes Program. J Korean Med Sci. 2012;27(8):876-82.
2. Kwang Sik Suh, Seungjoon Oh, Jeong-Taek Woo, Sung-Woon Kim, Jin-Woo Kim, Young Seol Kim and Suk Chon Apigenin Attenuates 2-Deoxy-D-ribose-Induced Oxidative Cell Damage in HIT-T15 Pancreatic β-Cells. Biol Pharm Bull. 2012;35(1):121-6.
3. S. Y. Rhee, Y.-C. Hwang, H. Y. Chung, J.-T. Woo. Vitamin D and diabetes in Koreans: analyses based on the Fourth Korea National Health and Nutrition Examination Survey (KNHANES), 2008–2009 Diabet Med. 2012;29(8):1003-10.
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9. Hae Jin Kim, Ki Hong Chun, Dae Jung Kim, Seung Jin Han, Young Seol Kimc, Jeong Taek Woo,Yongsoo Park, Moon Suk Nam, Sei Hyun Baik, Kyu Jeung Ahn, Kwan Woo Lee. 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;93(1):115-22.
10. Sang Youl Rhee and Jeong-Taek Woo. The Prediabetic Period: Review of Clinical Aspects. Diabetes Metab J. 2011; 35(2): 107–116.

ORIGIN - What can we learn from this landmark trial?

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ORIGIN (Outcome Reduction with Initial Glargine Intervention) is the world's longest and largest worldwide trial in dysglycemic individuals with high CV risk and either pre-diabetes or early type 2 diabetes, and has provided valuable new data on the use of Glargine in this previously under-investigated population.

The study demonstrated that there was no positive nor negative effect of Glargine on CV outcomes in the users of insulin Glargine. The study also confirmed the efficacy and established profile of Glargine. This landmark trial also demonstrated a new outcome whereby Glargine significantly reduced progression from pre-diabetes to diabetes by 28% compared with standard care treatment. Hypoglycemic events were infrequent; over the 6 years of the trial 58% of patients never experienced confirmed non-severe symptomatic hypoglycemia. This is a real breakthrough in our understanding of early diabetes, and constitutes a robust answer to a highly clinically relevant question.

ORIGIN is the only study in which a specific insulin has been tested against standard care treatment for a long period of time, so the safety data obtained are unmatched by any other glucose-lowering agent; including oral anti-diabetic agents and injectable medications.

ORIGIN will be extended by an additional two years. The extension of ORIGIN will be called ORIGINALE. These data will build on the extensive Glargine safety and efficacy evidence in more than 47 million real-life patient-years and over 10 years of clinical experience involving 80,000 participants in clinical development programs.

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➤Educational background & professional experience

1991-1997	Ewha Women's University School of Medicine	Medicine
2003-2005	Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine Fellowship	Endocrinology and metabolism
2004-2007	The Catholic University School of Medicine	Internal Medicine / Doctor of philosophy
2010-2011	Cardiovascular Division, Brigham and Women's Hospital, Harvard University, Boston, MA, USA	Visiting professor
2011-present	Endocrinology and Metabolism, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine	Associate professor
2012-present	Assistant administrator of Committee of Research, Korean Diabetes Association	
2012-present	Vice-secretary of Korean Society of Lipidology and Atherosclerosis	

➤Research interests

Endocrinology and metabolism
Vascular complications of diabetes

➤Brief list of publications

1. Kwon CH, Rhee EJ, Song JU, Kim JT, Sung KC. Reduced lung function is independently associated with increased risk of type 2 diabetes in Korean men. Cardiovasc Diabetol. 2012 Apr 24;11(1):38.
2. Rhee EJ, Nallamshetty S, Plutzky J. Retinoid metabolism and its effects on the vasculature. Biochim Biophys Acta. 2011 Jul 23.
3. Rhee EJ, Sung KC. The reply. Am J Med. 2011 Sep;124(9):e15.
4. Choi JH, Rhee EJ, Kim KH, Woo HY, Lee WY, Sung K. Plasma omentin-1 levels are reduced in non-obese women with normal glucose tolerance and polycystic ovary syndrome. Eur J Endocrinol. 2011 Aug 24.
5. Lim SY, Rhee EJ, Sung KC. Metabolic syndrome, insulin resistance and systemic inflammation as risk factors for reduced lung function in Korean nonsmoking males. J Korean Med Sci. 2010 Oct;25(10):1480-6.
6. Rhee EJ, Lee WY, Yoon KH, Yoo SJ, Lee IK, Baik SH, Kim YK, Lee MK, Park KS, Park JY, Cha BS, Lee HW, Min KW, Bae HY, Kim MJ, Kim JA, Kim DK, Kim SW. A multicenter, randomized, placebo-controlled, double-blind phase II trial evaluating the optimal dose, efficacy and safety of LC 15-0444 in patients with type 2 diabetes. Diabetes Obes Metab. 2010 Dec;12(12):1113-9.
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Targeting post-prandial glucose control: metabolic and clinical implications

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Strict glucose control is important for the prevention of cardiovascular complications of diabetes. Many studies have been performed to clarify which glucose control, between fasting and postprandial, is more important for the prevention of complications. In the DECODE (Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe) study, subjects with impaired glucose tolerance with high postprandial glucose showed higher risk for cardiovascular diseases compared with subjects with impaired fasting glucose with high fasting glucose. Postprandial hyperglycemia causes increased oxidative stress in our body and repetitive oxidative stress leads to impaired endothelial dysfunction. In this talk, I will discuss the importance of postprandial glucose control and review various studies regarding the impact of postprandial glucose control.

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➤Educational background & professional experience

1990-1996	Seoul National University College of Medicine	M.D.
2002-2004	Postgraduate School, Seoul National University School of Public Health	Master of public health
2004-2006	Postgraduate School, Seoul National University College of Medicine	Ph.D.
2011-2012	Visiting Scholar, Massachusetts General Hospital /Harvard Medical School, Boston, MA, USA	

➤Research interests

Diabetes, metabolic syndrome, and obesity.

➤Brief list of publications

1. Lim S, et al. Subclinical atherosclerosis in a community-based elderly cohort: The Korean Longitudinal Study on Health and Aging. International Journal of Cardiology. 2012 Feb 23;155(1):126-33.
2. Lim S, et al. Vitamin D inadequacy is associated with significant coronary artery stenosis in a community-based elderly cohort: the korean longitudinal study on health and aging. Journal of Clinical Endocrinology and Metabolism. 2012 Jan;97(1):169-78.
3. Lim S, et al. Effect of S-adenosylmethionine on neointimal formation after balloon injury in obese diabetic rats. Cardiovascular Research. 2011 May 1;90(2):383-93.
4. Lim S, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean national health and nutrition examination survey for 1998-2007. Diabetes Care. 2011 Jun;34:1323-1328.

Factors predicting therapeutic efficacy of combination treatment with sitagliptin and metformin in type 2 diabetic patients: the COSMETIC study

Soo Lim

Seoul National University, Korea

It has been well established that inhibition of dipeptidyl peptidase-4 (DPP-4) reduces blood glucose levels in both fasting and postprandial states, and preserves pancreatic β-cell function in patients with type 2 diabetes. The response to DPP-4 inhibitors and metformin combination therapy may be different in individuals according to their pancreatic function and insulin resistance status. We assessed the predictive parameters for therapeutic efficacy of initial combination therapy with sitagliptin and metformin in drug-naïve type 2 diabetic patients. In this 52-week treatment study, 150 patients (mean age, 54.9 ± 12.5 years) with type 2 diabetes and HbA1c of 7.0~10% were treated with sitagliptin 100 mg once and metformin 500 mg twice daily. To assess the predictive parameters for therapeutic efficacy, a multivariate regression analysis was performed with baseline fasting glucose, insulin, C-peptide and glucagon levels, homeostasis model assessment-insulin resistance (HOMA-IR) and β-cell function (HOMA-B), insulinogenic index (IGI, defined as 30-0 min insulin/30-0 min glucose), and area under the curve for glucose, insulin and C-peptide obtained after 75 gram oral glucose tolerance test.

After 52 weeks, mean HbA1c levels, and fasting and postload 2-h glucose were significantly decreased from 8.7 ± 1.4 to 7.2 ± 1.3%, 9.2 ± 3.0 to 7.2 ± 1.8 mmol/L, and 17.5 ± 5.1 to 10.9 ± 3.6 mmol/L, respectively ($P < 0.01$). HOMA-B and IGI increased significantly from 50.3 ± 33.5 to 75.1 ± 32.8 and from 11.3 ± 1.3 to 35.0 ± 6.3 at 52 weeks, respectively ($P < 0.01$). Multivariate regression analysis indicated that the reduction in HbA1c was significantly associated with high baseline HbA1c, low IGI, and short duration of diabetes after adjusting for age, sex, BMI, blood pressure, triglycerides, creatinine, hsCRP, glucagon, c-peptide, HOMA-B and HOMA-IR. No severe adverse events were observed.

These results suggest that drug-naïve type 2 diabetic patients with low β-cell function would benefit the most from early initial combination therapy of sitagliptin and metformin (Clinical trial number: NCT00969566).

ORAL PRESENTATIONS

Oral Presentation 1. Epidemiology
[OP-1-1~OP-1-5] 9 Nov. 13:40~14:40 / Convention Hall A, 4F

Oral Presentation 2. Clinical diabetes & therapeutics
[OP-2-1~OP-2-5] 9 Nov. 13:40~14:40 / Convention Hall B, 4F

Oral Presentation 3. Islet biology & insulin secretion
[OP-3-1~OP-3-5] 9 Nov. 13:40~14:40 / Convention Hall C, 4F

Oral Presentation 4. Islet biology & insulin secretion and immunity
[OP-4-1~OP-4-5] 9 Nov. 14:40~15:40 / Convention Hall A, 4F

Oral Presentation 5. Insulin resistance & obesity I
[OP-5-1~OP-5-5] 9 Nov. 14:40~15:40 / Convention Hall B, 4F

Oral Presentation 6. Chronic complications of diabetes I
[OP-6-1~OP-6-5] 9 Nov. 14:40~15:40 / Convention Hall C, 4F

Oral Presentation 7. Behavioral medicine & education
[OP-7-1~OP-7-5] 10 Nov. 13:30~14:30 / Emerald Hall, 3F

Oral Presentation 8. Epidemiology & genetics
[OP-8-1~OP-8-5] 10 Nov. 13:30~14:30 / Convention Hall A, 4F

Oral Presentation 9. Insulin resistance & obesity II
[OP-9-1~OP-9-5] 10 Nov. 13:30~14:30 / Convention Hall B, 4F

Oral Presentation 10. Chronic complications of diabetes II
[OP-10-1~OP-10-5] 10 Nov. 13:30~14:30 / Convention Hall C, 4F

OP1-1 Epidemiology

Long sleep duration is associated with metabolic Syndrome in young Korean women

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Objective Sleep duration may contribute to metabolic risks. U-shaped pattern have been observed in the relationships between sleep duration and mortality, cardiovascular disease, diabetes and hypertension. The aim of this study was to investigate the association between sleep duration and metabolic syndrome (MS) in young Korean women.

Methods We recruited 2,950 young women (15~39yrs). Detailed questionnaire including demographic information, lifestyle habits and sleep duration were completed. Anthropometric measurements and metabolic parameters were determined. Subjects were classified into 3 groups according to their sleep duration: short (〈 6hr, n = 234), normal (6-8hr, n = 1,639) and long sleeper (〉 8hr, n = 1,077).

Results Short sleepers were younger and more obese than normal or long sleepers. In long sleepers, post loading 2hr glucose, fasting insulin, triglycerides levels were higher and insulin sensitivity index, HDL cholesterol were lower than normal sleepers (P 〈 0.05). Long sleepers were significantly associated with metabolic syndrome (OR = 1.706, 95% CI: 1.105-2.632) after adjusting for age and BMI, but not in short sleepers (OR 1.201, 95% CI:0.586-2.463). The prevalence of MS (7.3, 4.3 and 7.0% in short, normal and long sleepers), central obesity (26.9, 16.9 and 19.8%), high triglycerides (5.6, 3.9, 6.9%) and low HDL cholesterol (47.6, 46.9 and 53.4%) was significantly different among these 3 groups (P 〈 0.05).

Conclusion In young Korean women, long sleep duration was significantly associated with MS and also high triglycerides and low HDL cholesterol levels.

OP1-2 Epidemiology

The change of glycated hemoglobin and fasting glucose according to the age in healthy overweight and obese Korean. KHNANES 2008-2010

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Objective With increasing age. The incidence of obesity and diabetes are increasing. As the early or pre-diabetes has no symptoms, the timing of the screening test is very important. Although postprandial hyperglycemia is common in Korean, the fasting plasma glucose and glycosylated hemoglobin are different. It is not known that the usual serum blood glucose and glycated hemoglobin in overweight and obese Korean.

Methods Data were from three rounds of nationally representative cross-sectional surveys for Korean men and women adult (7178 in 2008, 7893 in 2009, and 6740 in 2010). A stratified multistage probability sampling design and weighting adjustments were made to obtain a representative Korean population.

We calculate the mean value of HbA1c and fasting glucose level according to the age.

Results A healthy percentage of the population is 20s 39.0%, 30s 50.3%, 40s 56.9%, 50s 57.4%, 60s 54.2%, and 70s above 37.3%.

Glycated hemoglobin(HbA1c) are 20s 6.167%, 30s 7.494%, 40s 7.780%, 50s 7.200%, 60s 6.881%, and 70s above 6.892%. (P 〈 0.000)

Fasting glucose level are 20s 89.683 mg/dL 30s 94.007 mg/dL 40s 98.404 mg/dL 50s 97.784 mg/dL 60s 97.784 mg/dL and 70s above 103.054 mg/dL. (P 〈 0.000)

Fasting serum triglyceride are 20s 129.674 mg/dL, 30s 154.733 mg/dL, 40s 161.562 mg/dL, 50s 161.591 mg/dL, 60s 153.709 mg/dL and 70s above 154.966 mg/dl. (P 〈 0.000)

Conclusion Fasting glucose and TG levels are within normal range, depending on the age. Glycosylated hemoglobin level was increased sharply from the age of 30s. The reason of the mismatch may occur as the postprandial hyperglycemia is common. Further research for the effective diabetes screening test in overweight and obese Korean is needed.

OP1-3 Epidemiology

Explosive increase in diabetes health care utilization in Korea

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Objective Diabetes is a major health care problem in Korea. However, the influence of diabetes on public health is underestimated with its suboptimal management and control. We investigated changes in the health care utilization for the management of diabetes over the 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 in outpatients clinic and hospital admissions. 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, which is consistent with 7.4 fold increase in the number of daily outpatient clinic visits per 100,000 persons. In the same period, total number of patients who visited outpatient clinic for any reason increased by 2.4 times, thus the increase in out patients clinic visit attributable for diabetes was 3.5 fold higher than overall increase in out patients clinic visit. At the same period of time from 1990 to 2008, 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. This means the most part of the health care utilization increase by diabetic patients was from outpatient clinic visits. Gender difference in health care utilization increase was not obvious. The number of health care utilization in older age group (older than 65 years old) increased by 17 times, while in middle age group (45 to 64 years old) and younger age group (15 to 44 years old), increases in health care utilization were 6.5 times and 4.5 times, respectively. A notable increase of hospitalization rate by older diabetic patients was also observed in the same period. 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. In 2008, two thirds of diabetic patients were managed in the private clinic instead of general hospital and this difference was intensified over last decade.

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.

OP1-4 Epidemiology

Adherence to the antidiabetic medication improves cardiovascular outcome in patients with type 2 diabetes

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Objective Type 2 diabetes (T2D) is associated with an high rate of mortality and morbidity. Evidences abound that the most important predictor of reduction of morbidity and mortality due to diabetes complication is the level of glycemic control achieved. We estimated the effects of medication adherence with hypoglycemics on reducing the macrovascular complications in T2D patients recruited from a prospective cohort study (the KNDP database (2005-2010)).

Methods We exploited the hospitalization data from the Korean Health Insurance Review and Assessment Service (HIRA) database as an independent source of data linked the KNDP cohort data to compensate for the incompleteness of prospective follow-up of the cardiovascular events. Adherence to diabetes medication was assessed by calculating the rates of prescription refills from the HIRA database for a uniform period of 1 year over a maximum of 5.9 years of follow-up.

Results Of 3842 eligible patients, 261 (6.8%) experienced cardiovascular events during the follow-up period. Adherence of diabetic medication in both gender had independent effect on developing new cardiovascular events in multivariate models. Based on a model of covariate adjustment, age (P 〈 0.001), duration of diabetes (P 〈 0.001), hypertension (P = 0.008) and the compliance of diabetic medication (P 〈 0.001) predicted the cardiovascular disease. The highest adherence of diabetes medication reduced 75% (95% CI = 0.17-0.36) of the cardiovascular disease risk and the middle third reduced 59% (95% CI = 0.30-0.57) of the cardiovascular disease risk than the lowest adherence of diabetes medication, indicating a significant benefit of medication adherence with hypoglycemics on the reduction of macrovascular complications.

Conclusion Unlike to the prior clinical trial results, but consistent with the conventional belief, the study estimated that higher medication adherence may result in reduced risk of macrovascular complications among patients with T2D. Medical plans and policy makers should consider implementing interventions targeted to improve antidiabetic medication adherence, which may translate to better outcomes.

OP1-5 Epidemiology

Mortality and cause of death of patients with type 2 Diabetes Mellitus in Korea : A prospective cohort study based on the Korea National Diabetes Program

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Objective There are only limited data about the mortality of type 2 diabetes mellitus in Korea. We evaluated the mortality and cause of death in type 2 diabetes mellitus with prospective cohort of Korean type 2 Diabetes Mellitus.

Methods Korea National Diabetes Prorgram (KNDP) is a multicenter large-scale prospective cohort study which began in 2005 and currently ongoing. This study analyzed the mortality, cause of death and risk factors of death using clinical data of patients whom were registered in KNDP cohort and cohort's public health data(mortality data of the Statistics Korea (KOSTAT) and claim data of the Health Insurance review and Assessment Service(HIRA)of Korea (2006~2010)). We analyzed 4516 patients whose data is fully collected.

Results The mean age of the patients was 58.3 ± 10.5 years and BMI was 25.2 ± 3.2 kg/m^2. Mean glycosylated hemoglobin level was 7.9 %, the mean duration of diabetes was 6.1 years. The follow up duration of cohort was 3.2 ± 1 years. The all-cause mortality rate (death per 1000 person-year) was 5.35 and the cardiovascular disease (CVD) mortality rate was 1.53, cancer mortality rate was 2.01. In patients without baseline cardiovascular disease or cancer, total mortality rate was 3.96, CVD mortality was 0.7, cancer mortality was 1.5. In the univariate analysis of the risk factors which was associated with the total mortality of patients without cardiovascular disease or cancer, age, diabetes duration, the use of insulin, and hypertension were shown to be significant, and in the multivariate analysis, age and use of insulin were the significant risk factor.

Conclusion This study shows the first mortality data of Korean type 2 diabetes mellitus. Supported by further studies, we suggest that the strategy of the management of Korean type 2 diabetes mellitus might need some modification.

OP2-1 Clinical diabetes & therapeutics

Differences in the glucose-lowering efficacy of dipeptidyl peptidase-4 inhibitors between Asians and non-Asians: A systematic review and meta-analysis

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Objective To compare the glucose-lowering efficacy of DPP-4 inhibitors between Asian and non-Asian patients with type 2 diabetes.

Methods We searched MEDLINE, EMBASE, LILACS, CENTRAL, ClinicalTrials.gov, and conference proceedings. Studies were eligible if they were randomised controlled trials with a treatment duration of at least 12 weeks, compared a DPP-4 inhibitor with a placebo as either monotherapy or combination therapy, had information on ethnicity and HbA1c values, and were published or described in English. A systematic review and meta-analysis with a meta -regression analysis was conducted.

Results Among 809 potentially relevant studies, 58 trials were included. A meta-analysis revealed that DPP-4 inhibitors lowered HbA1c greater in studies with ≥ 50% Asian participants (weighted mean difference [WMD] -0.92%; 95% CI, -1.02% to -0.82%) than in studies with 〈 50% Asian participants (WMD -0.64%; 95% CI, -0.68% to -0.60%). The between-group difference was -0.27% (95% CI, -0.37% to -0.18%, P 〈 0.001). The baseline BMI significantly correlated with the HbA1c-lowering efficacy of DPP-4 inhibitors. The RR of achieving the goal of HbA1c 〈 7.0% was higher in studies with ≥ 50% Asian participants (3.4 [95% CI, 2.6-4.7] vs. 1.9 [95% CI, 1.8-2.0]). The fasting plasma glucose-lowering efficacy was higher with monotherapy in the Asian-dominant studies, but the postprandial glucose -lowering efficacy and changes in body weight were comparable between the two groups.

Conclusion DPP-4 inhibitors exhibit a better glucose-lowering efficacy in Asians than in other ethnic groups, which requires further investigation to understand the underlying mechanism.

OP2-2 Clinical diabetes & therapeutics

Serum irisin levels in new-onset type 2 diabetes

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Objective Irisin has been identified as a novel myokine that drives brown-fat-like conversion of white adipose tissue. In this cross-sectional study, we investigated whether serum irisin levels are decreased in patients with type 2 diabetes (T2D) compared to control subjects with normal glucose tolerance (NGT), and assessed the association between serum irisin levels and various metabolic parameters.

Methods This population-based study included 104 subjects with NGT and 104 subjects with new-onset T2D. Serum irisin and adiponectin levels and metabolic parameters were measured. Multivariate logistic regression analysis was performed to assess the association between irisin levels and the development of T2D.

Results Serum irisin levels were significantly decreased in the new-onset T2D group compared with the NGT control group (P =0.003). Multiple regression analysis showed that 2h OGTT glucose was an independent variable influencing serum irisin levels (P = 0.004). Furthermore, in a multivariable model adjusted for various metabolic parameters, increased irisin levels were associated with reduced odds (OR 0.636, 95% CI 0.465–0.871, P = 0.005) of T2D incidence.

Conclusion In the present study, we found that serum irisin levels were decreased in T2D patients and inversely associated with the development of T2D, suggesting that irisin may play a crucial role in glucose intolerance and T2D.

OP2-3 Clinical diabetes & therapeutics

Effect of mild physical activity on glycemic control, Physical fitness and quality of life in elderly obese women with uncontrolled type 2 diabetes in a southeast Asian-indian population

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Objective Diabetes rates has been constantly increasing in the South East Asian population because of lack of structural physical activity beyond household work and lack of exposure to an exercise culture. Our study aimed to demonstrate the effectiveness of a simple physical activity regimen in improving glycemic control, physical fitness and overall quality of life in elderly obese women with type 2 DM.

Methods Study consisted of two matched, randomized groups of elderly-obese women with uncontrolled type 2 diabetes. After physical exam, complete laboratory work-up was done. Level of physical fitness was assessed by a 6-minute walk test and quality of life (QOL) was assessed by EQ5D VAS questionnaire. Control group received standard care of treatment. Cases group, in addition was put on a regular simple exercise regimen. They were instructed to walk for 5 minutes every hour (apart from their regular household activities) for a minimum of 35 minutes/day and were given a diary to document the same. They were regularly contacted through phone for monitoring and motivation. Duration of study was 6 months with intermediate follow-ups every two months during which the diaries (from cases) were reviewed and labs repeated At the end the study complete labs repeated and all participants repeated 6-minute walk test and filled up EQ5D QOL questionnaire.

Results At the end of the study there was a drop in HbA1c from mean value of 9.06 ± 1.27 to 7.60 ± 0.64 (P = 0.008) in cases, when compared to a rise in mean HbA1c value from 8.34 ± 0.81 to 9.34 ± 1.71 (P = 0.07) in controls. Cases group also had an improvement in exercise tolerance (P = 0.008) demonstrated by increase in mean distance covered in 6-minute walk test and significant improvement in QOL (P = 0.01) assessed by EQ5Dquestionnaire.

Conclusion Our results indicate that a simple physical activity regimen with motivational interviewing could cause a significant improvement in glycemic control, physical fitness and quality of life in elderly obese women with uncontrolled type 2 diabetes.

OP2-4 Clinical diabetes & therapeutics

The relationships between brown adipose tissue detected by FDG-PET/CT and thyroid function, insulin resistance, inflammation, and visceral obesity: A prospective matched case-control study

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Objective Recent studies have shown that adult humans possess brown adipose tissue (BAT), which may play an active role in regulating energy expenditure and adiposity. This prospective matched case-control study evaluated whether the presence of BAT is associated with thyroid function, insulin resistance, inflammation or visceral obesity in adult humans.

Methods Forty BAT-positive and 40 BAT-negative subjects were enrolled and matched in age, gender, use of levothyroxine or β-blocker medication and season/year of ^{18}F-FDG positron emission tomography/computed tomography (FDG-PET/CT). All follow-up measurements were performed after a median 23.0 (16.0, 31.0) months.

Results Among the 6,877 consecutive FDG-PET/CT scans in 4,736 subjects, 146 subjects (3.1%) had a positive BAT scan. The BAT-detected group and the matched undetected group did not differ significantly in waist circumference (P = 0.205) and other components of metabolic syndrome (all P 〉 0.05). Visceral fat area (VFA) and subcutaneous fat area measured using abdominal CT were not significantly different (P = 0.985 and P = 0.544, respectively). When stratified by VFA tertile, BAT detection rate was not different among VFA tertile groups (P = 0.964). Furthermore, free T4 (P = 0.852), TSH (P = 0.895), homeostasis model assessment of insulin resistance (HOMA-IR) (P = 0.172) and high-sensitivity C-reactive protein (hsCRP) levels (P = 0.693) were not significantly different between groups.

Conclusion The present study does not support the hypothesis that the presence of BAT detected by FDG-PET/CT in thermoneutral conditions is associated with thyroid function, insulin resistance, inflammation or visceral obesity in adult Asian women.

OP2-5 Clinical diabetes & therapeutics

Compare the effects of different visfatin concentration on cardiovascular risk factors, adiponectin and insulin resistance in patients with T2DM

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Objective The discovery of new adipokine, visfatin can significantly enhance our knowledge of insulin resistance and diabetes mellitus. We explored the relation of visfatin concentrations to cardiovascular risk factors, adiponectin and insulin resistance criteria in patients with type 2 diabetes mellitus (T2DM).

Methods Fifty-eight patients with T2DM were recruited from the out patients clinic of Shariati Hospital. Laboratory and anthropometric measurements include FBG, OGTT, HbA1c, fasting serum visfatin, insulin and adiponectin, HOMA-IR and hsCRP, weight, height, BMI and WHR were performed in all participants. All of the statistical data were analyzed using the SPSS15 software.

Results The log10-transformed (log) plasma visfatin concentration was in significant positive correlation with age (r = 0.286, P = 0.033). Patients were divided in two groups by median log visfatin (0.85 ng/mL): group I had low values and group II had high values. In group I the log visfatin was in significant positive correlation with age (r = 0.436, P = 0.018) and in group II log visfatin was in significant negative correlation with FPG and HbA1c (r 〉 0.4, P 〈 0.05).

Conclusion In conclusion high circulating levels of visfatin could be in healthy relations with cardiovascular risk factors, insulin resistance status and adiponectin in diabetic patients.

OP3-1 Islet biology & insulin secretion

The incretin effect measured by the isoglycemic intravenous glucose infusion in Korean subjects with normal glucose tolerance or type 2 diabetes

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Objective The incretin effect is known to be decreased in type 2 diabetes (T2D). However, no study has directly measured the incretin effect in non-Caucasian subjects. Because Asian patients with T2D are characterized by decreased insulin secretion, this study set out to examine the incretin effect in Korean subjects with normal glucose tolerance (NGT) or T2D.

Methods We performed 75 g OGTTs and corresponding isoglycemic intravenous glucose infusion (IIGI) studies in subjects with NGT (n = 14) or T2D (n = 16). The incretin effect was calculated based on the incremental area under the curves (iAUCs) of insulin, C-peptide, or insulin secretion rate (ISR). The plasma levels of total glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) were measured by ELISA.

Results The incretin effect was not different between the subjects with NGT and T2D (43 ± 6% vs. 47 ± 4%, P = 0.575 by insulin; 29 ± 7% vs. 38 ± 4%, P = 0.253 by C-peptide; 28 ± 7% vs. 35 ± 5%, P = 0.372 by ISR, respectively). However, the gastrointestinally mediated glucose disposal (GIGD) was decreased in T2D (28.5 ± 4.2% vs. 59.0 ± 4.3%, P 〈 0.001). The plasma levels of the total GLP-1 and GIP during the OGTTs were comparable between the two groups.

Conclusion In Koreans, the secretion of GLP-1 or GIP during OGTTs and the incretin effect were comparable between subjects with NGT and T2D, whereas the GIGD was significantly decreased in patients with T2D.

OP3-2 Islet biology & insulin secretion

Metformin protects INS-1 cells from glucotoxicity via suppression of fatty acid translocase/ cluster determinant 36 (CD36)

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Objective Although metformin regulates blood glucose level primarily by improving insulin sensitivity, there is evidence that it also preserve insulin secretion of pancreatic β-cells from glucotoxicity or lipotoxicity directly. However, the exact mechanism is not clarified yet. Previously we showed that inhibition of CD36, a fatty acid transporter, prevents glucotoxicity and ameliorate high level of glucose induced β- cell dysfunction. The aims of this study are to investigate the beneficial effect of metformin on β-cell function and whether if this effect is associated with change of CD36.

Methods We compare insulin expression, glucose stimulated insulin secretion (GSIS), ROS and change of CD36 expression under high glucose (HG, 30 mM) condition with normal glucose (NG, 5.6 mM) in INS-1 cells. We also assessed aforementioned factors in condition with metformin for evaluation of glucotoxicity prevention effect.

Results CD36 expression was increased with 12-hour HG exposure in INS-1 cells, which was suppressed by metformin. Insulin and PDX-1 mRNA expression were decreased and GSIS was completely disappeared by 3-day of HG, which was restored partly by metformin. Also Metformin partially recovered elevated ROS by 3-day HG.

Conclusion Metformin suppresses the CD36 expression elevated by HG, which may be associated with glucotoxicity. These results suggest that metformin prevents CD36 related glucotoxicity in INS-1 cells and further in vivo studies are needed.

OP3-3 Islet biology & insulin secretion

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.

OP3-4 Islet biology & insulin secretion

Effects of early exercise and administration of dipeptidyl peptidase-4 inhibitor MK-0626 on structure and function of islets in kkay mice

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Objective To study the changes of islet beta-cell morphology and function after lifestyle intervention and administration of dpp-4 inhibitor (MK0626) in HFD induced kkay mice.

Methods 1. Establish models of prediabetes-hyperinsulinism by administrating HFD in kkay mice. 2. 5 weeks old male HFD induced kkay mice were divided randomly into: kkay normal diet(KN) group, kkay high fat diet(KH) group, kkay exercise(KE) group, kkay DPP-4I(KD) group and C57BL/6J served as normal control(CN) group. During 8 weeks intervention, general features were collected weekly, FINS measurement, OGTT and IPITT were performed at 7w and 15w respectively. 2. Analyzed morphology, proliferation and apoptosis in islet beta-cell ; 3.Evaluated the expression of PDX-1 and MafA.

Results 1. 5 week-old kkay mice will be proper models for the study after 2 weeks of HFD. At 15 weeks old, general conditions, glucose tolerance, insulin sensitivity and Islet morphology were improved in KE group and KD group. 2. Propotion of ki67 positive cells in intervention groups were higher than other groups ($P < 0.01$). Apoptosis were no significant differences among these groups. 3. Expression of MafA were increased in intervention groups. There were no significant difference in the expression of PDX-1.

Conclusion 1. it is a proper kkay mice model of prediabetes-hyperinsulinism by early administrating HFD; 2. early intervention of life style and administration of MK0626 could delay the onset of diabetes. 3. There were no obvious changes in the expression of PDX-1 at early stage of diabetes in kkay mice. MafA may play a crucial role in the development of diabetes in this model.

OP3-5 Islet biology & insulin secretion

Beta-cell surrogates for the cure of type I diabetes mellitus from neonatal pig liver-derived hepatocytes via viral transduction of PDX-1/VP16, BETA2/NeuroD and MafA and chemically defined medium

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Objective Generation of beta-cell surrogate from non-beta cells is urgently needed to treat diabetes mellitus because current therapies, organ or islet cell transplantation, have some limitations such as shortage of donors, immune suppression. Liver-derived cells could be attractive source for generating beta cell surrogates because of their differentiating and proliferating capacity. Also, liver and pancreas share common characteristics such as glucose sensing ability. Therefore, liver-derived cells can be attractive source having advantages for beta cell surrogates over other stem cells source. In this study, we focused on neonatal pig liver because of their differentiation and proliferation capacity.

Methods Neonatal pig liver-derived cells were induced transdifferentiation into insulin-producing cells via sequential transduction of key transcription factors in endocrine development such as Ad-PDX-1/VP-16, BETA2/NeuroD and MafA and chemically defined medium. We induced aggregation of transduced cells to make islet like clusters.

Results We note that cells highly expressed GLUT-2 and insulin as well as other endocrine related markers. Then, we quantified insulin positive cells in induced hepatocytes. Also, we evaluate the function of glucose-responsiveness in transduced cells. As a result, they could not only secrete insulin and c-peptide by glucose stimulation in vitro but also improve hyperglycemia in diabetic nude mice after renal capsular transplantation. At six weeks after transplantation, glucose tolerance test were statistical significantly improved by transplantation. Engrafted cells highly expressed insulin and c-peptide in the kidney graft.

Conclusion In conclusion, we generated functional insulin-producing cells from neonatal pig derived hepatocytes via sequential transduction of Ad-PDX-1/VP-16, BETA2/NeuroD and MafA. These results suggest that neonatal pig derived hepatocytes could be useful source for the beta cell surrogates and could provide the basis of generating for transplantable beta cell source for the treatment of diabetes mellitus.

OP4-1 Islet biology & insulin secretion and immunity

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

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Objective Metformin was reported to increase 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 PPARα agonist, fenofibrate, exhibits an additive or synergistic effect on glucose metabolism independent of its lipid-lowering action, when added to metformin.

Methods Non-obese diabetic Goto-Kakizaki (GK) rats were divided into 4 groups and treated with metformin, fenofibrate, metformin plus fenofibrate, or vehicle (n = 6 for each group). Body weights, random blood glucose levels and food intake for 24 hours were monitored. We performed oral glucose tolerance tests (OGTTs) and intraperitoneal glucose tolerance tests (IPGTTs) with GLP-1 analogue injection after 4 weeks treatment.

Results Blood glucose levels, body weights, food intake, and serum lipid profiles were not significantly different among groups. After 4 weeks, metformin, but not fenofibrate, markedly reduced blood glucose levels during OGTTs, which was attenuated by adding fenofibrate. Metformin increased the expression of the GLP-1 receptor in pancreatic islets. In IPGTTs with a GLP-1 analogue injection, metformin did not improve the insulin response, while fenofibrate alone or combination treatment decreased it.

Conclusion In conclusion, fenofibrate did not add any beneficial effect on glucose homeostasis but deteriorate metformin's glucose-lowering action in GK rats, which discourages the addition of fenofibrate to metformin in order to improve glycemic control.

OP4-2 Islet biology & insulin secretion and immunity

Effects of vildagliptin on the pancreatic β cell in β cell-specific Atg7 knockout mice

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Objective Pancreatic β cell-specific autophagy-deficient (*Atg7*(-/-)) mice showed β cell mass reduction and β cell dysfunction, causing insulin deficiency and mild hyperglycemia. Glucagon-like peptide (GLP-1) has been reported to regenerate islet cells and to inhibit apoptosis of β cell in some rodent models. The aim of this study is to investigate effects of vildagliptin, a DPP4-inhibitor, on the *Atg7*(-/-) mice.

Methods When the *Atg7*(-/-) mice were 8 weeks of age, vildagliptin was administrated through drinking water (0.3 mg/mL of vildagliptin) for 12 weeks. Water without vildagliptin was supplied to control *Atg7*(-/-) mice. Blood glucose and insulin levels were monitored, pancreata were harvested for morphologic examination and islets were isolated to evaluate glucose -stimulated insulin secretion (GSIS).

Results Vildagliptin administration to the *Atg7*(-/-) mice did not alter body weight and random blood glucose levels, but significantly lowered blood glucose levels after intraperitoneal glucose loading. Fasting serum insulin levels were comparable between the vildagliptin group and the control, but ex vivo GSIS with isolated islets demonstrated increased stimulated index in the vildagliptin group. Morphologic exam revealed increased β cell area estimated by point counting, with decreased ubiquitin aggregation in the islets of the vildagliptin group.

Conclusion Our results suggest that vildagliptin improved glucose tolerance and glucose-stimulated insulin secretion in the *Atg7*(-/-) mice. It could result from reduced ubiquitin accumulation, which induced increased β cell mass and function. Whether vildagliptin affects autophagic activity or not is under investigation.

OP4-3 Islet biology & insulin secretion and immunity

Repression of sterol regulatory element-binding protein 1-c is involved in the protective effects of exendin-4 in pancreatic β-cell lines

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Objective Exendin-4 (Ex-4), a long-acting agonist of glucagon-like peptide–1 receptor, is a novel anti-diabetic drug that prevents β-cells against various toxicities. However, the mechanism and molecules mediating the protection procession of Ex-4 are not fully understood. We investigated the protective effect of Ex-4 against lipotoxicity, mediated by a repression of sterol regulatory element-binding protein (SREBP) -1c, a regulator of genes expression involved in fat and cholesterol synthesis.

Methods To observe the effect of Ex-4, we evaluated insulin secretion and apoptosis in the MIN6 pancreatic β-cell line, which were cultured in DMEM medium containing 500 μM palmitate, with or without 10 nM Ex-4. We also examined the roles of SREBP-1c in lipotoxicity model by knockdown with si-RNA.

Results We found that Ex-4 improved insulin secretion and survival as well as reduced SREBP-1c expression and activity in palmitate-treated MIN6 cells. This improvement was accompanied with an upregulation of PI3K/Akt signaling pathway, and LY294,002, a specific inhibitor of PI3 kinase, abrogated effects of Ex-4 on insulin secretion. Moreover, SREBP-1c in nuclei was increased by the inhibition of PI3 kinase. Lipotoxic effects of palmitate in the insulin secretion and apoptosis were significantly prevented by SREBP-1 knockdown.

Conclusion In conclusion, Ex-4 protects β-cell against palmitate-induced β -cell dysfunction and apoptosis, by inhibiting SREBP-1c expression and activity through the PI3K/Akt signaling pathway.

OP4-4 Islet biology & insulin secretion and immunity

Protective effect of sirt3 on lipotoxicity-induced β cell dysfunction

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Objective SIRT3 is a NAD^+-dependent protein deacetylase localized on mitochondria and deacetylates mitochondrial proteins. Free fatty acids (FFAs) can lead to insulin resistance and pancreatic β cell dysfunction. In this study, we investigated whether overexpression of sirt3 protects free fatty acid induced-β cell dysfunction.

Methods To investigate role of sirt3 in lipotoxicity-induced β cell dysfunction, expression of sirt3 was induced by using adenovirus in pancreatic β cell line, NIT-1. To generate lipotoxicity, palmitic acid was added to the media. ATP and cell viability were measured to determine the effect of sirt3 on mitochondria dysfunction. To examine effect of sirt3 on palmitate-induced p44/42 MAPK activation, Western blot analysis was performed. To elucidate the effect of sirt3 on fatty acid oxidation, fatty acid oxidation rate was measured using ^{14}C-palmiate.

Results When cell were treated with palmitate, cell viability was reduced and this cytotoxic effect was attenuated by overexpression of sirt3. While treatment of palmitate significantly reduced ATP level in NIT-1 cells, intracellular ATP level was not decreased in the presence of palmitate when sirt3 was overexpressed. Overexprssion of sirt3 suppressed palmitate-induced phosphorylation of p44/42 MAPK and p38. In addition, fatty acid oxidation was increased by sirt3 overexpression.

Conclusion Overexpression of sirt3 protects free fatty acid induced-β cell dysfunction.

OP4-5 Islet biology & insulin secretion and immunity

Preadipocyte factor-1/Dlk1 promotes human ductal cell transdifferentiation into β-cells

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Objective Preadipocyte factor-1/Dlk1 (Pref-1/Dlk1) is involved in the proliferation and differentiation of various precursor cells; however, the detailed signaling mechanisms controlling these processes have not been well defined, particularly in the pancreas.

Methods To extend our understanding for the role of Pref-1/Dlk1, we analyzed the mechanism of pancreatic ductal cells after Pref-1/Dlk1 treatment

Results Treatment of human pancreatic duct cells with purified soluble Pref-1/Dlk1 protein increased Akt, ERK1/2, and FOXO1 phosphorylation. Pref-1/Dlk1-induced FOXO1 phosphorylation was specifically blocked by inhibition of ERK1/2 phosphorylation. Pref-1/Dlk1 treatment increased PDX1 protein level, decreased FOXO1 protein synthesis, and simultaneously induced the cytosolic to nuclear translocation of PDX1 and the nuclear to cytosolic translocation of FOXO1. Pref-1/Dlk1 also induced insulin gene expression and protein synthesis through ERK1/2 phosphorylation. Furthermore, we found the Rab GTPase-activating protein, to be a target of Akt signaling through the use of two-dimensional electrophoresis (2-DE) and matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF). In turn, the phosphorylation of Rab GTPase-activating protein also increased the synthesis of vesicular proteins, including synaptophysin and secretogranin, and promoted glucose-stimulated insulin secretion. Treatment of cells with Pref-1/Dlk1 increased cellular insulin content and induced glucose-stimulated insulin secretion through the independent phosphorylation of ERK1/2 and Akt.

Conclusion Here, we demonstrate a novel role for Pref-1/Dlk1 in regulating pancreatic duct cell transdifferentiation into β-cells.

OP5-1 Insulin resistance & obesity I

Micro-environmental alteration with stage-specific signaling modulation Favors pancreatic specification during in vitro differentiation

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Objective Insulin-producing β cells derived from human pluripotent stem cells including hESCs and iPSCs could not only be one of the prominent therapy of type 1 diabetes but also suggest in vitro disease model of genetic disease. In this regard, human embryonic stem cells are differentiated into pancreatic endocrine cells through defined spatiotemporal regulation.

Methods 1) Q-RT PCR; 2) Immunofluorescence analysis

Results 1) For definitive endoderm stage induction, both Activin/Nodal signaling and WNT signaling are activated. Human embryonic stem cells were differentiated more efficiently and rapidly when WNT signaling was activated with Activin/Nodal signaling compared to Actin/Nodal signaling activation alone. 2) Single cell dissociation and replating after definitive endoderm stage reduced hepatic differentiation process significantly. This mechanical modulation in the replating condition increased the expression of mesenchymal cell type markers such as N-Cadherin, Fibronectin in more homogeneous manner. However, epithelial cell type marker gene expression was not changed after replating.

Conclusion 1) The first stage of in vitro differentiation from hESCs is definitive endoderm. To induce the appropriate definitive endoderm state for pancreatic specification, WNT signaling was activated with Activn/Nodal signaling showing more rapid differentiation. This indicates the critical point of the state of definitive endoderm stage for pancreatic cell fate specification. 2) After definitive endoderm stage, single cell dissociation and replating process significantly decreased the expression of AFP, one of the hepatic cell type markers. In addition, the expression of mesenchymal cell markers such as N-Cadherin, Fibronectin, Vimentin was homogeneously increased after replating. This phenomenon indicates micro-environmental alteration enhances EMT during pancreatic specification by recapitulating in vivo development. As a result, not only could the spontaneous hepatic cell fate differentiation be inhibited but also pancreatic specification could be more efficiently regulated. 3) For more efficient endocrine differentiation and insulin-producing β cell maturation, defined signaling modulation is required after pancreatic cell fate specification.

OP5-2 Insulin resistance & obesity I

C1q/TNF-related Protein-3 (CTRP-3) and Pigment Epithelium-Derived Factor (PEDF) concentrations in patients with type 2 diabetes and metabolic syndrome

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Objective Recent studies have suggested that a novel adipokine, C1q/TNF -related protein-3 (CTRP-3), a paralog of adiponectin, may play an important role in the regulation of glucose metabolism and innate immunity. Pigment epithelium-derived factor (PEDF), a multifunctional protein with anti-oxidant and anti-inflammatory properties, is associated with insulin resistance and metabolic syndrome. In this study, we examined the circulating CTRP-3 and PEDF concentrations in patients with diverse glucose tolerance statuses. Furthermore, we evaluated the influence of CTRP-3 and PEDF on cardiometabolic risk factors such as insulin resistance, inflammation, estimated glomerular filtration rate (eGFR), and brachial-ankle pulse wave velocity (baPWV).

Methods We examined circulating CTRP-3 and PEDF concentrations in 345 subjects with diverse glucose tolerance statuses. Furthermore, we evaluated the involvement of CTRP-3 and PEDF with cardiometabolic risk factors including insulin resistance, high-sensitivity C-reactive protein (hsCRP), estimated glomerular filtration rate (eGFR) and brachial-ankle pulse wave velocity (baPWV).

Results CTRP-3 concentrations were significantly higher in patients with type 2 diabetes or prediabetes than normal glucose tolerance group, whereas PEDF levels were not different. Subjects with metabolic syndrome showed significantly higher levels of both CTRP-3 and PEDF compared to subjects without metabolic syndrome. Both CTRP-3 and PEDF were significantly associated with cardiometabolic parameters, including waist-to-hip ratio, triglyceride, HDL-cholesterol, alanine aminotransferase, eGFR, hsCRP, and baPWV.

Conclusion In conclusion, circulating CTRP-3 concentrations were elevated in patients with glucose metabolism dysregulation. Both CTRP-3 and PEDF concentrations were increased in subjects with metabolic syndrome and were associated with various cardiometabolic risk factors (ClinicalTrials.gov: NCT01034826, NCT01212198).

OP5-3 Insulin resistance & obesity I

OxPhos dysfunction in macrophages causes inflammation and insulin resistance

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Objective Insulin resistance is closely related to chronic low-grade inflammation in adipose tissue, liver and muscle with following activation of macrophage proinflammatory pathways and cytokine secretion. At the molecular level, insulin resistance is promoted by a transition in macrophage polarization from an M2 (alternatively activated macrophages) state controlled by STAT6 and PPARs to a M1 (classically activatedmacrophages) state driven by NF-κB, and other signal transcription factors. However, key factors of function and polarization in macrophage in metabolism are unclear.

Methods To determine the role of mitochondria of macrophages in IR, we have generated macrophage specific OxPhos complex-deficient ($LysM^{cre}$ $CRIF1^{flox/flox}$) mice, because CRIF1 plays a critical role in the integration of OxPhos polypeptides into the mitochondrial membrane in mammals. $CRIF1^{flox/flox}$ strain was intercrossed with $LysM^{cre}$ strain to generate $LysM^{cre}$ $CRIF1^{flox/flox}$. Macrophages were stimulated with cytokines or LPS for 30 minutes or 18 hours, and western blot analysis, Q-PCR and ELISA were performed. For animal study, body weight, GTT and ITT of mice were monitored after 10 weeks on HFD.

Results The proinflammatory cytokines, reactive oxygen species (ROS) were significantly increased in bone marrow-derived macrophages (BMDMs) from $LysM^{cre}$ $CRIF1^{flox/flox}$ mice compared with control. Moreover, LPS and Interferon (IFN)-γ stimulation of BMDM from $LysM^{cre}$ $CRIF1^{flox/flox}$ mice caused a marked potentiation of TNFα, IL-6 and iNOS response, it is direct evidence that OXPHOS complex dysfunction promotes and amplifies M1-like phenotype. However, M2-like activation was impaired in IL-4 stimulated BMDM from $LysM^{cre}$ $CRIF1^{flox/flox}$ mice. In addition to, insulin-stimulated phosphorylation of AKT was markedly decreased in BMDM from $LysM^{cre}$ $CRIF1^{flox/flox}$ mice. In animal study, Body weights were similar in both groups, but $LysM^{cre}$ $CRIF1^{flox/flox}$ mice were significantly more glucose intolerant after a 10 week HFD challenge.

Conclusion Taken together, these date demonstrate that OxPhos complex has a critical role in macrophage M1 and M2-like polarization and regulates metabolic homeostasis.

OP5-4 Insulin resistance & obesity I

Body size phenotypes and sarcopenia: The Korean sarcopenic obesity study (KSOS)

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Objective Recently, unique subsets of body size phenotypes have been described. These subsets seem to be more prone or more resistant to the development of obesity-associated metabolic disorders, although the underlying mechanism is not yet clearly understood. We investigated the prevalence and risk of sarcopenia in subjects who are classified as either metabolically healthy normal weight (MHNW), metabolically abnormal but normal weight (MANW), metabolically healthy obese (MHO), or metabolically abnormal obese (MAO). Subjects were classified based on body mass index and presence of metabolic syndrome.

Methods Thigh muscle cross-sectional area (tmCSA) was evaluated using computed tomography as an index of sarcopenia in 492 apparently healthy adults enrolled in the Korean Sarcopenic Obesity Study (KSOS), an ongoing prospective observational cohort study. Sarcopenia was defined as tmCSA divided by weight (%) of 〈 1 SD below the mean values of young adults in both sexes.

Results The prevalence rates of sarcopenia in MHNW, MANW, MHO, and MAO subjects were 6.2%, 17.8%, 23.2%, and 33.7%, respectively. In a multiple logistic regression analysis adjusted for confounding factors, men with the MANW phenotype showed a remarkably increased risk of sarcopenia (odds ratio (OR) = 9.62, 95% confidence interval (CI): 1.43–64.58) compared to those with MHNW but not in women (OR = 2.07, 95% CI: 0.62 –.85). Furthermore, in both men and women, MHO or MAO subjects had higher ORs of sarcopenia compared to MHNW subjects

Conclusion The present study suggests that sarcopenia may be associated with different metabolic consequences according to body size phenotype.

OP5-5 Insulin resistance & obesity I

Effect of Helicobacter pylori infection on endothelial function in metabolic syndrome

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Objective Metabolic Syndrome (MetS) is associated with impaired endothelial function and increased cardiovascular risk and type 2 diabetes mellitus. On the other hand, a lot of studies have been carried out on *Helicobacter pylori (H. pylori)* infection and found a possible causal relationship through releasing some of biochemical factors, which result in endothelial dysfunction. We aimed to evaluate the effect of H. pylori on endothelial function in MetS patients.

Methods Eighty subjects (21 men and 59 women, mean age: 48.9 ± 10.0 years) with MetS were studied according to IDF criteria (waist circumference ≥ 80/94 cm (female/male) plus any two of others altered factors). Exposure to H. pylori was detected by plasma IgG test. Also, plasma endothelin-1 (ET-1), inter-cellular adhesion molecule 1(ICAM-1), E-selectin, nitrite and nitrate concentrations were measured, as endothelial function parameters.

Results Overall prevalence of *H. pylori* infection was 62.5% (50/80). Plasma ET-1 level in *H. pylori(+)* subjects was higher than *H. pylori(-)* group (2.93 ± 2.33 vs. 1.90 ± 1.40 pg/mL, P = 0.037). Also, the levels of nitrite and nitrate were significantly higher in seropositive subjects to *H. pylori* than in seronegative subjects to *H. pylori*, respectively (nitrite: 19.46 ± 7.11 vs. 15.46 ± 4.56 μM, P = 0.003; nitrate: 20.8 ± 10.53 vs.16.85 ± 6.03 μM, P = 0.036). But, there was no significant difference between ICAM-1 and E-selectin in *H.pylori(+)* and *H.pylori(-)* subjects, respectively. (ICAM-1: 39.21 ± 14.55vs. 37.74 ± 18.57 ng/mL; P = 0.695 and E-selectin: 10.66 ± 4.37 vs. 10.34 ± 5.25 ng/mL; P = 0.770).

Conclusion Chronic infection with H. pylori may be involved in the development of the MetS via endothelial dysfunction. The evidence for this hypothesis include that the levels of ET-1, nitrite and nitrate increased in *H. pylori(+)*compared to *H. pylori(-)*patients . Association of ET-1, nitrite and nitrate with H. pylori suggests the role of chronic infection in the severity of MetS, via endothelial dysfunction.

OP6-1 Chronic complications of diabetes I

Usefulness of albuminuria as predictor for coronary artery stenosis, regardless of estimated glomerular filtration rate, in patients with type 2 diabetes mellitus

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Objective The aim of this study was to evaluate independent predictors for coronary artery stenosis in patients with type 2 diabetes mellitus (DM) and subclinical atherosclerosis.

Methods A total of 232 patients with type 2 DM and subclinical atherosclerosis underwent multi-slice computed tomography coronary angiography (MSCTA). Subclinical atherosclerosis was determined by carotid intima-media thickness (IMT) or carotid plaque.

Results MSCTA revealed significant coronary stenosis (〉50% in diameter) in 71 subjects (31%). The subjects who had significant coronary stenosis were much older and had a longer duration of DM. In particular, the log-transformed albumin:creatinine ratio (ACR) was higher in the subjects with significant coronary stenosis when compared with the subjects without significant coronary stenosis. The age- and sex-adjusted odds ratio for significant coronary stenosis increased in proportion to albuminuria with a given estimated glomerular filtration rate. The ACR as a continuous variable (odds ratio 4.167, 95% CI = 1.497–11.599) or a categorical variable (ACR 〉 30 mg/mg, odds ratio 4.619, 95% CI = 1.562–13.659) was associated with increased risk of significant coronary stenosis, independent of conventional cardiovascular risk factors. In ROC analysis, ACR had an additive effect with carotid IMT for predicting significant coronary stenosis (AUC 0.625 with carotid IMT; AUC 0.710 with carotid IMT plus ACR, P = 0.0144).

Conclusion In conclusion, the presence of albuminuria is an independent predictor for significant coronary stenosis in patients with type 2 DM and subclinical atherosclerosis.

OP6-2 Chronic complications of diabetes I

Serum glycated albumin level has negative correlation with ankle-brachial index in Korean diabetes patients

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Objective Ankle-brachial pressure index (ABI) is a noninvasive method to assess the patency of the lower extremity arteries. Low ABI has predicted pending various cardiovascular events. This study aimed to examine the relationship between ABI and glycemic indices such as HbA1c, glycated albumin (GA), GA/A1c ratio in type 2 diabetic patients.

Methods In this retrospective, cross-sectional study, we recruited diabetic patients who had been taken ABI and serum glycemic indices simultaneously. Our attentions were focused on the correlation between ABI and glycemic indices by examining correlation coefficient, and multivariable regression analysis.

Results A total of 436 patients (249 men and 187 women) with a mean age of 63.1 ± 9.32 were finally enrolled. Mean and SD of ABI and HbA1c were 1.12 ± 0.10 and 7.06 ± 1.08 %, respectively. Of the glycemic indices, ABI was significantly associated with GA (β = -0.0110, P = 0.022) but not with HbA1c and GA/A1c ratio. Multivariable linear regression analysis revealed that GA had a significant correlation with ABI after adjusting age, BMI, systolic blood pressure, lipids (standardized β = -0.107, P = 0.28), which was not seen in HbA1c.

Conclusion Not HbA1c but GA is significantly correlated with ABI. We suggest that high level of GA might reflect the artherosclerosis.

OP6-3 Chronic complications of diabetes I

High urinary ACE2 concentrations are associated with severity of glucose intolerance and microalbuminuria

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Objective Angiotensin-converting enzyme2 (ACE2) plays a role in glucose metabolism and renal function. We investigated whether urinary ACE2 levels are associated with abnormal glucose homeostasis and microalbuminuria.

Methods For the measurement of urinary ACE2 concentrations, we developed an enzyme-linked immunosorbent assay (ELISA). Using this assay, we assessed urinary ACE2 levels in 621 subjects with normal glucose tolerance (NGT; n = 77); impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) (n = 132); and type 2 diabetes mellitus (T2DM, n = 412). Urinary albumin-to-creatinine ratio (ACR) was used as a measure of urinary albumin excretion.

Results Urinary ACE2 levels were significantly higher in subjects with IFG or IGT and T2DM than in the NGT group (P 〈 0.001). Urinary ACE2 concentrations appeared to correlate with fasting blood glucose, triglyceride, homeostasis model assessment for insulin resistance (HOMA-IR), high sensitivity C-reactive protein (hsCRP), serum creatinine, urinary ACR and estimated glomerular filtration rate, and systolic blood pressure (all P 〈 0.05). Subjects in the higher urinary ACE2 tertiles also exhibited higher values for systolic blood pressure, fasting blood glucose, HbA1c, triglyceride, HOMA-IR, hsCRP, serum creatinine, and urinary ACR levels. Urinary ACE2 concentration was associated with a higher risk for both T2DM and microalbuminuria after adjusting for clinical risk factors (OR 1.80, 95% CI 1.05-3.08, P = 0.02 for T2DM; OR 2.68, 95% CI 1.55-4.64, P 〈 0.001 for microalbuminuria).

Conclusion Our data suggest that the urinary ACE2 level is closely associated with T2DM and is an independent risk factor for microalbuminuria.

OP6-4 Chronic complications of diabetes I

Diurnal fluctuation of real-time heart rate variability in normal volunteers

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Objective HRV has been used as a marker of cardiac autonomic nervous function. Although an imbalance of cardiac autonomic function is widely known to be a direct cause of cardiovascular diseases, methods for HRV monitoring have not been devised in detail. Therefore, we observed the diurnal fluctuations of HRV in real time by monitoring in an attempt to determine the pattern of HRV changes during everyday life.

Methods The volunteers were fitted with a long-term R-R interval (RRI) recorder MOCA (Monitor and Care; Taewoong Medical, Korea). Data were analyzed at 5-min intervals, generating a total of 288-data points. Sixty-one young healthy clerical workers(aged 22–45 years), with no history of any disease or medication, were recruited as volunteers and were asked to wear the continuous HRV monitor for 24–48h.

Results In these healthy subjects, the HR and LF/HF ratio showed a similar pattern, with a minimum value during nocturnal sleep, a sharp increase on waking in the morning, and a maximum value during the afternoon(working time). HR in the afternoon increased by 24.3% compared to that at nighttime, whereas the LF/HF ratio increased by 77%. Interestingly, a sharp increase in HR and the LF/HF ratio was observed at approximately 6:00am, which was the wake-up time. SDNN started to increase during nighttime, reaching a peak level early in the morning, and then decreased to a minimum at approximately 3:00pm.

Conclusion We believe that, by quantifying the diurnal patterns of HRV, this real-time monitoring system could provide information relevant to various kinds of chronic diseases. Investigating how diurnal fluctuations in HRV can aggravate a patient's condition could help determine new solutions for the more effective management of these diseases and their complications. Ultimately, we hope to effectively manage chronic disease by using biofeedback programs that affect HRV directly, thereby improving the quality of patient care at a national level.

OP6-5 Chronic complications of diabetes I

Glycated albumin is associated with diabetic retinopathy in diabetic patients

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Objective Recently, the role of glycated albumin as a glycemic control marker was reported in many studies. Glycated albumin level is known to reflect the glycemic change over a 2 weeks period. The aims of this study was to investigate whether there is a association between serum glycated albumin as a marker of glycemic control marker and prevalence of diabetic retinopathy in diabetic patients.

Methods Glycated albumin was measured in 490 patients with type 2 diabetes using enzymatic assay. Retinal examinations after pupil dilation were performed in all patients. We evaluated the relationship between serum glycated albumin levels and presence of diabetic retinopathy.

Results Both serum glycated albumin levels and glycated hemoglobin levels were higher in patients with diabetic retinopathy group compared non-diabetic retinopathy group (Glycated albumin: 16.42% vs. 19.74%, P < 0.001). Glycated albumin levels were correlated with fasting plasma glucose, post-prandial glucose, BMI, waist circumference, urinary microalbumin level. After adjusting age, sex and BMI, glycated albumin was significantly associated with fasting plasma glucose, post-prandial glucose, urinary microalbumin levels (all P < 0.001). When patients were categorized into tertiles of serum glycated albumin, the presence of diabetic retinopathy was significantly increased (P for trend < 0.001). Serum glycated albumin levels were significantly associated with diabetic retinopathy after adjusting age, sex, fasting insulin , CRP, total cholesterol, BMI, waist circumference, SBP, urinary microalbumin levels (OR 8.376, 95% CI 4.033-17.397 for highest tertile vs. lowest tertile, P < 0.001).

Conclusion Glycated albumin levels are significantly associated with diabetic retinopathy. This results suggest that glycated albumin levels might be a important marker for diabetic microvascular complication.

OP7-1 Behavioral medicine & education

Study for the pre-occupied conception on the insulin use in type 2 diabetic patients with multiple oral hypoglycemic agents

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Objective Recent clinical studies including UKPDS scientifically showed the inevitable progression of type 2 diabetes mellitus due to the deterioration of insulin secreting pancreatic beta cell function. At now, it is clear that many type 2 diabetic patients should eventually receive insulin treatment for the appropriate metabolic control. But starting insulin treatment for the insulin naïve type 2 diabetic patients in clinical practice is very difficult, due to the low acceptance of the patients. This study was designed to analyze the pre-occupied conception on the insulin treatment of the type 2 diabetic patients with poor glycemic control on multiple oral hypoglycemic agents.

Methods Total two hundred type 2 diabetic patients with multiple oral hypoglycemic agents were included. Known diabetes duration, HbA1c, other metabolic parameters including lipid profile, the status of micro- and macro-angiopathic complications were recorded. A questionnaire survey consisting of 10 questions on the pre-occupied conception on the insulin and insulin injection were done. The results of the questionnaire were analyzed according to the status of multiple laboratory and clinical parameters.

Results The most of the type 2 diabetic patients knew well about the necessity of insulin treatment for the sound metabolic control, but they did not know the exact pharmacological characteristics of the insulin. The main reason of the reluctance for the initiating insulin treatment was the fear for the long-term safety. The degrees of fear and anxiety were highest in the patients with poor metabolic control despite of multiple oral hypoglycemic agents.

Conclusion These results suggest that the detailed education in the nature and the characteristics of the insulin, and the long-term benefit and the safety is mandatory to improve the compliance of the diabetic patients before starting insulin treatment. Further studies would be necessary.

OP7-2 Behavioral medicine & education

The effectiveness of physical activities and diet reduction on total cholesterol and HDL in healthy overweight and obese Korean

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Objective Overweight and obesity have become an increasing. The exercise and dietary reduction has been recommended. However, it is not known the real effectiveness of exercise and dietary reduction in Korea.

Methods Data were from three rounds of nationally representative cross-sectional surveys for Korean men and women adult (7178 in 2008, 7893 in 2009, and 6740 in 2010). We calculate the mean of total cholesterol and HDL according the exercise and dietary reduction in healthy overweight and obese in Korea.

Results Overweight and obese people without any diagnosed disease accounted for 49.3% of the healthy population, didn't exercise (EX) 44.9%, walking (WLK) 34.3%, high intense exercises (HIE) 7.1%, walking exercise and high intensity exercises 12.5%.

Dietary reduction group (DRG) usually intake 2016 Calories, while non dietary control group intake 2212 Calories. In non-dietary control group, the average of total cholesterol (TC) was 191.86 mg/dL in none-Ex, 191.98 mg/dL in WLK, 193.14 mg/dL in HIE, 189.98 in WLK and HIE (P < 0.05).

In DRG, the average of TC was 191.9 mg/dL among people who didn't EX, 192.8 mg/dL in WLK, 199.2 mg/dL in HIE, 182.5 mg/dL in WLK and HIE (P < 0.05).

In non-DR, the average of HDL was 48.6 mg/dL in none-EX, 49.7 mg/dL in WLK, 50.3 mg/dL in HIE, 50.0 mg/dL in WLK and HIE.

While in DRG, 49.0 mg/dL, 49.5 mg/dL, 51.0 mg/dL, 52.3 mg/dL values were checked (P < 0.05) Whether people did dietary reduction or not, the higher Calories intake (average 2301Calories) with WLK and HIE, followed by HIE (average 2148Calories), and WLK (average 2067Calories) (P < 0.05).

Conclusion The mean amount of dietary reduction is 196 Calories. The high intense exercise without dietary reduction raises total cholesterol because of increasing food intake. Statistically significant, but there is no clinically significant differences.

However, HDL increases in proportion to the intensity of exercise, and is more in diet reduction group than opposite.

OP7-3 Behavioral medicine & education

Comparison of the food and nutrient intakes in Korean adult and elderly people with type 2 diabetes mellitus: The Fourth and Fifth Korea National Health and Nutrition Examination Survey (2007-2010)

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Objective South Korea has undergone a rapid economic development, and diet and lifestyle transition during the past three decades. This led to an explosive 5-fold increase in the prevalence of type 2 diabetes mellitus (T2DM) to the current level of 10.0% of adults 〉 30 years of age. Though classified as the same T2DM patients, clinical and nutritional characteristics can be different by age group because each group had undergone nutrition transition during different stage of the life cycle. The objective of this study was to compare food and nutrient intake patterns of two age groups (adults: 30-49 years vs. elderly: 60-79 years) with T2DM, using the Korea National Health and Nutrition Examination Survey (KNHANES IV and V, 2007-2010) data.

Methods From a total of 14,605 subjects with all available variables, 190 adult and 1125 elderly subjects had T2DM. Significant differences were observed in the mean BMI, and the distribution of gender, family income and residential area between two age groups and also between control and T2DM within the same age group.

Results The consumption of total food and proportions of animal food, and intake of total energy and proportions of macronutrients were significantly different; elderly subjects consumed more energy from carbohydrates and less from proteins and fats. Further analysis by a generalized linear model showed that the elderly were found to consume more cereals and cereal products, less animal food, and consume a diet with lower nutrient density after adjusting for confounding factors (BMI, residential area, income, alcohol/cigarette smoking and log-transformed energy intake).

Conclusion Our results show that the food and nutrient intake pattern of Korean diabetes is indeed different by age group. The results of our study suggest that different dietary strategies and meal plans targeted toward specific age groups may be needed to help T2DM patients improve glycemic and metabolic control.

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OP7-4 Behavioral medicine & education

The different neural activation in response to pictures of high-carbohydrate foods in diabetic patients

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Objective Hyperphagia is one of the classical symptoms of diabetes mellitus. Our preliminary study revealed that diabetic patients had higher food cravings, especially high-carbohydrate foods, than the healthy controls. However, it is still unclear whether diabetic patients regulate their desire for foods differently compared to non-diabetic individuals. Thus, we investigated the brain responses to pictures of foods in diabetic and non-diabetic subjects using functional MRI (fMRI).

Methods Participants were 20 subjects with type 2 diabetes mellitus (T2DM) (9 male, 11 female) and 20 age- and sex-matched non-diabetic controls. They performed fMRI in fasting state in the morning. Picture stimuli for fMRI consisted of high-carbohydrate foods, high-fat foods, and non-food neutral pictures.

Results For visual stimulation of high-carbohydrate foods, the diabetic group showed significant neural activation in the left caudate nucleus compared to the control group. In contrast, there was no difference in neural activation for stimulation of high-fat foods or non-foods between groups. Within-group contrasts revealed that pictures of high-carbohydrate foods activated the superior frontal cortex, cuadate and cerebellum in non-diabetic subjects, whereas it deactivated the lingual gyrus and cuneus in diabetic patients. For the contrast of high-fat vs. non-foods, the diabetic patients exhibited the deactivation in cuneus, lingual gyrus, fusiform gyrus and left middle temporal gyrus and middle occipital gyrus, while the control group showed the deactivation only in the right middle occipital gyrus.

Conclusion Diabetic patients showed the different neural activation in response to visual cues of foods, especially high-carbohydrate foods, suggesting that they might regulate their desire for foods differently compared to healthy individuals.

OP7-5 Behavioral medicine & education

The effect of buffet-style nutrition education on the glycemic control in T2DM patients

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Objective Recently the importance of practical nutrition education has been emphasized. The buffet-style nutrition education is one of the nutrition education methods for DM patients in Korean hospitals. We examined the effect of buffet-style nutrition education on the glycemic control in T2DM patients.

Methods Subjects were 408 T2DM patients taken medical treatment at Kangbuk Samsung Hospital. We compared data from 188 T2DM patients who experienced buffet-style nutrition education (BNE group) and 220 T2DM patients who had no experience in BNE (control group). To BNE group, clinical dietitians gave simple information on meal planning, and then made the subjects to choose foods for themselves, and checked & adjusted the foods chosen (kinds, amount etc). After then subjects ate those foods and discussed with clinical dietitians on diabetic diet freely. We collected glycemic data at baseline, 3-month, 6-month, 12-month, & 24-month.

Results There were no significant differences in the gender distribution, BMI, & HbA1c. HbA1c at 3-month was significantly decreased compared to baseline level in both groups. In BME group, HbA1C levels at 6-month, 12-months & 24-month were significantly improved compared to baseline level (baseline 6.8%, 6-month 6.6%, 12-month 6.7%, 24-month 6.6%, P 〈 0.05). However in control group, there were no significant improvements after 6-month compared to in HbA1C level and 24-month HbA1C was higher than baseline (baseline 6.9%, 24-month 7.1%, P 〈 0.05). Also the improvement of HbA1C was shown in BNE subjects who taken no nutrition education except BNE.

Conclusion These results showed that buffet-style nutrition education might be very helpful approach for self DM management. It was thought that dietary skill practice & experience did important role. It will be recommended that practical nutrition education including BNE is provide to diabetic patients actively. Also further studies on the effect of practical nutrition education & trials to develop effective nutrition education program will be needed.

OP8-1 Epidemiology & genetics

Genome-wide association analysis identifies variants associated with non-alcoholic fatty liver disease in Koreans

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Objective Nonalcoholic fatty liver disease (NAFLD) is one of the most frequent causes of abnormal liver function, but most of its genetic studies were candidate gene approach. This study aimed to identify genetic variants associated with NAFLD by genome wide association study (GWAS) in Korean population.

Methods In 2,269 samples from Korean population-based cohort established as part of the Korean Genome Epidemiology Study, SNP markers with call rate (〈 95%), low MAF (〈 0.01) and significant deviation from Hardy-Weinberg equilibrium (P 〈 1×10^{-6}) were excluded, leaving a total of 316,078 markers to be examined. Using unenhanced CT, the liver attenuation index (LAI), the difference between the mean hepatic and splenic attenuation, was calculated. NAFLD was defined by LAI 〈 5 HU. We tested the association between SNPs and LAI or NAFLD by using multivariate regression analysis.

Results SNPs in *PNPLA3-SAMM50* gene (rs12483959, rs2076211, rs2281135, rs2073081, rs1883350, rs2143571, rs2281298, rs16991236) in chromosome 22, and in *NRBF2-JMJD1c* gene (rs12416113, rs9414780, rs9629895, rs907, rs10761745) in chromosome 10 were significantly associated with LAI after adjusting for age, sex, and body mass index (BMI) (P-vlaue $3*10^{-6}$ ~ $7.8*10^{-15}$). Most SNPs in these genes were not associated with BMI, fasting glucose, HOMA-IR, visceral fat amount, and lipid levels. Only rs12483959 and rs2281135 in PNPLA3 gene were associated with serum AST and ALT levels.

In the haplotype analysis, the combination of haplotypes associated with lower LAI in PNPLA3 gene showed 53.7% increased OR for NAFLD compared to those with higher LAI (OR=1.54, 95% CI=1.30-1.81, $p=2.9*10^{-7}$). It was still observed after adjusting for age, sex, visceral fat area, HOMA-IR, triglycerides, AST, ALT and hsCRP. This relationship was not different according to the obesity status.

Conclusion We identified several genetic variants in *PNPLA3-SAMM50*, *NRBF2-JMJD1c* genes associated with NAFLD in GWAS. These findings suggest that several genetic variants may confer increased susceptibility to NAFLD regardless of obesity in Koreans.

OP8-2 Epidemiology & genetics

Exercise, anti-hyperglycemic agents and HbA1c in South Korean, 2008-2010

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Objective Obesity and diabetes worldwide is increasing. Exercise, as well as insulin and oral hypoglycemic agents, is very important in the treatment of diabetes. Demonstrated in experimental studies the effects of exercise, but exercise in large-scale surveys of national status and maintain blood sugar is a lack of data on the effects.

Methods Data were from three rounds of nationally representative cross-sectional surveys for Korean men and women adult (7178 in 2008, 7893 in 2009, and 6740 in 2010). A stratified multistage probability sampling design and weighting adjustments were made to obtain a representative Korean population. We compared HbA1c according to the exercise and medication.

Results 57.5% of the population uses oral hypoglycemic agents (OHA), insulin(insulin only or insulin and OHA) 6.6% and the untreated group was 9.3%. According to the type of exercise, vigorous physical activities is 14.6%, moderate physical activities 7.7%, walking 30.3%, none was 46.5%. In oral hypoglycemic agents group, vigorous physical activities had 7.353 of HbA1c, moderate physical activities 7.169, walking 7.512 and the group does not exercise 7.684. In insulin group, vigorous physical activities had 8.626 of HbA1c, moderate physical activities 9.106, walking 8.227 and the group does not exercise 8.871, respectively. The differences between each group were statistically significant. ($P < 0.05$)

Conclusion Oral anti-hyperglycemic agent group was the lowest HbA1c in moderate physical activity, but, walking was the lowest HbA1c in insulin group.

OP8-3 Epidemiology & genetics

Withdrawn

OP8-4 Epidemiology & genetics

Quantitative recovery of IRS-1 with RXRα targeting medication in mitochondria dysfunction associated insulin resistance

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Objective Mitochondrion is a well-known organelle generating energy via metabolic pathway of our main nutrients, glucose and lipid. Thus, its malfunction accompanies with many pathophysiological problems: especially, insulin resistance in insulin-responsive tissues. Our previous study discovered that retinoid X receptor α (RXRα) is associated with mitochondria dysfunction in mtDNA A3243G mutation-the most frequent mutation causing diabetes mellitus-cell line we established. Based on this, we hereinafter have made headway into finding adequate RXRα activating medication to recover insulin sensitivity.

Methods To investigate the association between the protein level of RXRα and of IRS-1 in mitochondria dysfunction-induced tissues and cell line, we performed western blot analysis. Likewise, real-time PCR analysis was carried out to compare the RNA level of the sample above. To induce mitochondria dysfunction, we provided mice with high fat diet and C2C12 skeletal muscle cells with ETC complex inhibitors, respectively. Three RXR specific ligands were tested for quantitative recovery of IRS-1. To measure mitochondrial function, ATP bioluminescent assay was performed.

Results Compared to the normal chow diet mice, high fat diet mice showed quantitative decrease of RXRα and of IRS-1, especially in their skeletal muscle. Likewise, we confirmed the quantitative decrease of IRS-1 and of RXRα in mitochondria dysfunction-induced skeletal muscle cell while we also observed the decrease of IRS-1 in RXRα-knockdown cells. To the cells where mitochondria dysfunction was induced, RXR specific ligands were treated and these medication improved insulin signaling with the quantitative recovery of IRS-1.

Conclusion Quantitative recovery of IRS-1 is achieved by RXRα targeting medication in mitochondria dysfunction associated insulin resistant condition.

OP8-5 Epidemiology & genetics

Predicting cardiovascular outcomes by intima-medial thickness (IMT)

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Objective Type 2 diabetes (T2D) is a major cause of cardiovascular disease. Carotid intima-media thickness (IMT) or presence of plaques in common carotid artery has been shown to have a strong relationship with cardiovascular accidents (CVA). However, only few studies have evaluated the usefulness of IMT or presence of plaques in predicting future development of CVA in Asian T2D patients.

Methods Using a total of 1489 patients with T2D (M:F=839:650, mean age: 55.1 yr at baseline) recruited from the Korea National Diabetes Program (KNDP), a prospective natural history study of T2D, we examined the influence of the progression of IMT on predicting the development of CVA in a Korean T2D cohort. B-mode carotid ultrasonographic measurements (the mean IMT, the maximum IMT and the presence of plaques) were performed and repeated annually for a mean of 3.1 years of follow-up. Development of CVAs was evaluated prospectively for 3.1 years, and anthropometrics and biochemical parameters were measured annually.

Results During the follow-up, 74 patients (5%) developed CVAs and the annual progression of mean IMT was 0.0580 ± 0.1423 mm. Development of CVAs was associated with abnormal mean IMT (> 0.08 cm) [OR (95% confidence interval); 1.29 (1.01-1.66)] and the presence of plaques [OR (95% confidence interval); 1.34 (1.06-1.68)]. After adjusting for anthropometrics and biochemical parameters with logistic regression, the presence of plaques were clearly associated with the development of CVAs [OR (95% confidence interval); 1.65 (1.02-1.79)], but the association with abnormal mean IMT decreased due to interaction with age [OR (95% confidence interval); 1.09 (1.06-1.12)], duration of diabetes [OR (95% confidence interval); 1.04 (1.01-1.08)], and HDL cholesterol [OR (95% confidence interval); 0.98 (0.96-1.00)].

Conclusion Although the presence of plaques and elevation of IMT were all found to be associated with cardiovascular outcomes, only the presence of plaques predicted cardiovascular outcomes independent from conventional cardiovascular risk factors in Asian T2D patients during short-term follow-up.

OP9-1 Insulin resistance & obesity II

The role of skeletal muscle mass in fatty liver disease: Fatty liver index is correlated not only visceral fat but also skeletal muscle

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Objective Fatty liver disease is known to be correlated with insulin resistance. Recently, fatty liver index (FLI) has been proposed and validated for predicting the presence of fatty liver. A relationship of between visceral fat and fatty liver disease (FLD) has been established; but it is not clear whether skeletal muscle plays a role as a risk factor of FLD. The purpose of this study is to elucidate the association of skeletal muscle and visceral fat in development of fatty liver disease.

Methods Among 11,116 (male 6,242) health check-up subjects at Yeungnam University Medical Center in 2009-2011, patients with abnormal liver enzyme (upper normal limit 〉 2.5 times) and serologic positive finding for hepatitis B or C were excluded. Finally, 9,565 (male 5,293) individuals were included. We categorized into low (〈 20), intermediate (20~59) and high (≥ 60) FLI group and determined high FLI group as a fatty liver disease. We measured the skeletal muscle mass and visceral fat area by bioelectric impedance analysis (BIA) and examined how they influence in development of fatty liver disease.

Results Low FLI group showed higher skeletal muscle and lower VFA than high group. `Skeletal muscle to Visceral fat Ratio (SVR, g/cm$^2$)` and `Skeletal Muscle Index (SMI, %)` had an inverse correlation with FLI adjusted for age and gender. Comparing quartiles according to SVR, the highest quartile group had the lowest risk of fatty liver disease adjusted for age, gender, lipid profile, DM, HTN and hsCRP (OR=0.037, 95% CI 0.029-0.049).

Conclusion Fatty liver disease is associated with not only visceral fat but also skeletal muscle. These results suggest that the body composition including skeletal muscle is more important rather than simple obesity in developing fatty liver disease, and concerns about preventing sarcopenia are needed.

OP9-2 Insulin resistance & obesity II

Salsalate and adiponectin improve palmitate-induced steatosis and impairment of lipid metabolism via inhibition of fetuin-A through the AMPK-NFκB pathway

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Objective Fetuin-A was recently identified as a novel hepatokine which is associated with obesity, insulin resistance and non-alcoholic fatty liver disease. Salsalate, a prodrug of salicylate with an anti-inflammatory effect and lower side effect profile, significantly lowers glucose and triglyceride levels, and increased adiponectin concentrations in randomized clinical trials.

Methods In this study, we examined the effects and regulatory mechanisms of salsalate and full length-adiponectin (fAd) on fetuin-A expression,steatosis and lipid metabolism in palmitate-treated HepG2 cells.

Results Incubation of hepatocytes with palmitate significantly increased fetuin-A and SREBP-1c expression which lead to steatosis and knock-down of fetuin-A by siRNA restored these changes. Salsalate significantly down-regulated palmitate-induced fetuin-A mRNA expression and secretion in a dose- and time-dependent manner. Inhibition of palmitate-induced fetuin-A by salsalate was mediated by AMPK-mediated reduction of NFκB activity, which was blocked by AMPK siRNA or an inhibitor of AMPK. Salsalate attenuated the excessive steatosis by palmitate through SREBP-1c regulation in hepatocytes. Furthermore, fAd also showed suppression of palmitate-induced fetuin-A through the AMPK pathway and improvement of steatosis accompanied by restoration of SREBP-1c, PAPR-α and CD36. In preliminary in vivo experiments, salsalate treatment inhibited high fat diet (HFD)-induced steatosis as well as fetuin-A mRNA and protein expression in SD rats.

Conclusion In conclusion, salsalate and fAd improved palmitate-induced steatosis and impairment of lipid metabolism in hepatocytes via fetuin-A inhibition through the AMPK-NFκB pathway.

OP9-3 Insulin resistance & obesity II

cAMP response element binding protein H mediates fenofibrate-induced suppression of hepatic lipogenesis by inhibition of sterol regulatory binding protein-1c expression

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Objective Fenofibrate is a drug used to treat hyperlipidemia and works by inhibiting hepatic triglyceride synthesis. Sterol regulatory element binding protein-1c (SREBP-1c) is a major regulator of the expression of genes involved in hepatic triglyceride synthesis. In addition, endoplasmic reticulum-bound transcription factor families are involved in the control of various metabolic pathways. Here, we show a novel function for an ER-bound transcription factor, cAMP response element binding protein H (CREBH), in fenofibrate-mediated inhibition of hepatic lipogenesis.

Methods The effects of fenofibrate and adenovirus-mediated CREBH overexpression (Ad-CREBH) on hepatic SREBP-1c expression and lipogenesis in vitro and in vivo were investigated. We also examined whether down-regulation of endogenous hepatic CREBH by small interfering RNAs (siRNA) restores the fenofibrate effect on hepatic lipogenesis and SREBP-1c expression. Finally, we examined the mechanism by which CREBH inhibits hepatic SREBP-1c expression.

Results Fasting and fenofibrate treatment induced CREBH expression and decreased SREBP-1c levels. Indeed, Ad-CREBH inhibited insulin- and liver X receptor agonist TO901317-induced SREBP-1c mRNA expression in cultured hepatocytes. Moreover, overexpression of CREBH in the livers of mice following tail vein injection of Ad-CREBH inhibited high fat diet-induced hepatic steatosis through inhibition of SREBP-1c expression. The inhibition of endogenous CREBH expression by siRNA restored fenofibrate-induced suppression of SREBP-1c expression and hepatic lipid accumulation both in vitro and in vivo.

Conclusion These results show that fenofibrate decreases hepatic lipid synthesis through induction of CREBH. This study suggests CREBH as a novel negative regulator of SREBP-1c expression and hepatic lipogenesis.

OP9-4 Insulin resistance & obesity II

Adipose inflammation and systemic insulin resistance in adipose-specific CRIF1-deficient mice

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Objective Adipose tissues play an important role in maintaining whole body energy homeostasis. Adipocyte dysfunction is strongly linked with adipose inflammation which may causes insulin resistance and systemic glucose intolerance. In this study, we attempted to investigate the role of mitochondrial OXPHOS dysfunction in adipocytes in the maintenance of whole body energy metabolism.

Methods To develop the model of adipose-specific mitochondrial OXPHOS dysfunction, we generated adipose-specific CRIF1-deficient mice (CRIF1$^{f/f,\ adipoq\text{-}Cre}$) by crossing CRIF1-floxed mice with Adiponectin-Cre recombinase transgenic mice. The metabolic phenotypes of CRIF1$^{f/f,\ adipoq\text{-}Cre}$ and control mice (CRIF1$^{+/+,\ adipoq\text{-}Cre}$) including adipose pathology were analysed.

Results Adipose-specific CRIF1-deficient mice (CRIF1$^{f/f,\ adipoq\text{-}Cre}$) showed mitochondrial dysfunction in adipose tissue with decreased expression of OXPHOS complexes. The body weight between Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice and control mice was similar, but fat weight was reduced by 2-fold in Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice than control mice on normal chow diet. Interestingly, Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice showed accumulated macrophages in adipose tissue compared to control mice, accompanied with increased pro-inflammatory cytokine secretion. Infiltrated macrophages in adipose tissue from Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice exhibited higher expression of CD11c than control mouse. And adipose tissue in Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice showed enhanced expression of TNFa which was known to induce systemic insulin resistance. Crif1$^{f/f,\ adipoq\text{-}Cre}$ mice showed marked insulin resistance phenotype by insulin tolerance test.

Conclusion Collectively, adipocyte specific mitochondrial dysfunction mice results inflammatory phenotypes characterized with infiltration of macrophages in adipose tissues and it is also linked with systemic insulin resistance.

OP9-5 Clinical diabetes & therapeutics

Association between low SIRT1 expression in visceral and subcutaneous adipose tissues and metabolic abnormalities in women with obesity and type 2 diabetes

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Objective Sirtuin 1 (SIRT1), an NAD^+-dependent protein deacetylase, is a principal modulator of pathways that operate downstream of caloric restriction. SIRT1 appears to play a role in the regulation of energy metabolism and glucose homeostasis in rodents. However, there are few studies examining the connection between SIRT1 expression in insulin-sensitive tissues and metabolic regulation in humans. The present study assessed the importance of adipose tissue SIRT1 in the regulation of whole-body metabolism in humans with obesity and type 2 diabetes by examining the association between SIRT1 expression in adipose tissues and metabolic parameters.

Methods In total, 19 non-diabetic obese women, 19 type 2 diabetic women undergoing gastric bypass surgery, and 27 normal-weight women undergoing gynecological surgery (total 65 women) were enrolled. Their anthropometric variables, abdominal fat distribution and metabolic parameters, serum adiponectin concentrations, and SIRT1 mRNA and protein and adiponectin mRNA expressions in visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) were measured.

Results SIRT1 mRNA levels in VAT and SAT were similar and these levels were suppressed in obese and type 2 diabetic women compared to normal weight subjects. These decreases in SIRT1 expression were observed in both adipocytes and non-fat cells. There was a strong association between adipose tissue SIRT1 mRNA and protein levels. Adipose SIRT1 expression correlated inversely with HOMA-IR and other insulin resistance-related parameters. Adipose SIRT1 and adiponectin mRNA expression correlated very strongly and positively. SIRT1 mRNA level in VAT correlated inversely with visceral obesity whereas its expression in SAT correlated negatively with body mass index.

Conclusion Adipose tissue SIRT1 may play a key role in the regulation of whole body metabolic homeostasis in humans. Downregulation of SIRT1 in VAT may contribute to the metabolic abnormalities that are associated with visceral obesity.

OP10-1 Chronic complications of diabetes II

S-adenosylmethionine prevents atherosclerosis by inducing heme oxygenase-1 and ameliorating endoplasmic reticulum stress in vascular endothelial cells

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Objective S-adenosylmethionine (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 investigate the possible preventive effect of SAM on atherosclerosis and its molecular mechanism.

Methods Eight-week-old male Sprague-Dawley (SD) rats were given normal rat chow or a high fat diet (HFD) with or without 30 mg/kg/day of SAM. In addition, eight-week-old male $ApoE^{-/-}$ mice on the C57BL/6 background received an intraperitoneal injection of 4-mg/kg of streptozotocin for 5 consecutive days. Both STZ-administered and control $ApoE^{-/-}$ mice were maintained on regular chow until 4 weeks after starting the STZ administration, when they were switched to HFD for 16 weeks with or without 30 mg/kg/day SAM.

Results SAM treatment prevented endothelial dysfunction in HFD-fed rats, and prevented atherosclerosis in diabetic Apo E-/- mice given HFD. In cultured human aortic endothelial cells, SAM prevented linoleic acid (LA)-induced cell apoptosis and endoplasmic reticulum (ER) stress. SAM increased heme oxygenase-1 (HO-1) expression in an NF-E2-related factor 2-dependent manner. siRNA against HO-1 reversed SAM's effects on cell apoptosis.

Conclusion These data demonstrate that SAM prevents vascular dysfunction and atherosclerosis in HFD-fed animals. In cultured endothelial cells, SAM induced HO-1, ameliorated ER stress and prevented cell apoptosis. SAM treatment may be a new therapeutic strategy for atherosclerosis.

OP10-2 Chronic complications of diabetes II

The roles of the Mig-6 gene on vascular smooth muscle cell

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Objective Mitogen Inducible Gene 6, *Mig-6* is identified as a negative feedback inhibitor of epidermal growth factor receptor (EGFR) signal. The Molecular targets of neointima formation still have not been fully addressed. We investigated the effect of *Mig-6* gene ablation in vascular smooth muscle cell (VSMC) and its role in intimal hyperplasia.

Methods Conditional ablated *Mig-6* in the VSMC was generated using the Tagln-Cre mouse model ($Tagln^{Cre/+}$*Mig-6*$^{f/f}$; *Mig-6*$^{d/d}$). To investigate the neointima formation, we used balloon injury mouse model. Primary cultured VSMCs were obtained from 10-week-old *Mig-6*$^{f/f}$ and *Mig-6*$^{d/d}$ male mice for immunoblotting, proliferation and migration assays.

Results The neointima formation of injured artery was significantly enhanced in the *Mig-6*$^{d/d}$ mice compared to *Mig-6*$^{f/f}$ after balloon injury. Primary cultured *Mig-6*$^{d/d}$ VSMC caused a significant increase in the proliferative and migratory capability of the cells compared to *Mig-6*$^{f/f}$. EGF, Angiogensin II and SDF1 stimulation in the primary cultured *Mig-6*$^{d/d}$ VSMC increased growth and motility. Furthermore, angiotensin II receptor blocker and inhibitors of EGFR, PI3K and MAPK reversed these enhanced proliferation and migration of primary cultured *Mig-6*$^{d/d}$ VSMC. On western blotting, the increased phosphorylation of EGFR was observed in primary cultured *Mig-6*$^{d/d}$ VSMC compared to *Mig-6*$^{f/f}$.

Conclusion We found that neointima formation was augmented in the VSMC specific *Mig-6*$^{d/d}$ mice. *Mig-6* plays an important role in determining growth and motility of VSMC. Therefore, we suggest that *Mig-6* may provide a new insight into development of more effective ways for the treatment and prevention of neointima formation.

OP10-3 Chronic complications of diabetes II

Clusterin attenuates angiotensin II-induced renal fibrosis

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Objective The blockade of angiotensin II (Ang II) is a main therapeutic target of diabetic nephropathy. Here, we examined whether clusterin prevents Ang II-induced renal fibrosis.

Methods The effects of clusterin on renal fibrosis in clusterin knockout (KO) and wild type mice were assessed using Ang II-induced renal fibrosis model with osmotic mini pump. Histological analyses were performed to see the effect of clusterin on Ang II-induced renal fibrosis. The effects of adenovirus mediated overexpression of clusterin on PAI-1, type 1 collagen and fibronectin expression in cultured renal cells were measured by real time RT PCR and western blot analysis. Transient transfection study with reporter constructs of PAI-1 promoter was performed to measure the effect of clusterin on PAI-1 promoter activity.

Results Histological examinations showed that loss of clusterin increased renal fibrosis and the expression of PAI-1, type 1 collagen and fibronectin was increased compared with the kidney of control mice. Infusion of Ang II using osmotic mini pump accelerated these expressions in clusterin KO mice compared with those of wild type mice. In addition, we found that adenovirus-mediated overexpression of clusterin inhibited Ang II-stimulated PAI-1, type I collagen, and fibronectin expression in cultured renal tubular epithelial cells. Transient transfection study showed that clusterin inhibited Ang II-stimulated PAI-1 promoter activity. Moreover, up-regulation of clusterin expression in the kidney by adenovirus expressing clusterin attenuated Ang II-induced renal fibrotic gene and protein expression.

Conclusion In conclusion, clusterin attenuated Ang II-induced renal fibrosis. The present study raises the possibility that clusterin can be a therapeutic target for renal fibrosis.

OP10-4 Chronic complications of diabetes II

Vaspin increases nitric oxide bioavailability through the reduction of asymmetric dimethylarginine in vascular endothelial cells

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Objective Vaspin is an adipocytokine recently identified in the visceral adipose tissue of diabetic rats and having anti-diabetic effects. We have recently shown that vaspin has anti-atherogenic effect through Akt-mediated inhibition of endothelial cell apoptosis. Decreased activity of endothelial nitric oxide synthase (eNOS) plays an important role in the pathogenesis of atherosclerosis. Asymmetric dimethylarginine (ADMA) is a well-known endogenous competitive inhibitor of eNOS and risk factor of cardiovascular diseases. The aim of this study was to examine whether vaspin might protect against atherosclerosis through its beneficial effects on the ADMA-eNOS system.

Methods We used human aortic endothelial cells (HAECs). We measured the level of ADMA and NO in culture media using ELISA kit. Western blotting analysis was used to measure the change of eNOS phosphorylation. The change of DDAH II by vaspin treatment was determined using real time PCR and reporter gene assay. Electrophoretic mobility shift assay (EMSA) was performed to determine the DNA-binding activity of STAT3, a nuclear transcription factor having binding sites at DDAH II promoter region.

Results Treatment of vaspin significantly increased NO secretion from endothelial cells. For the mechanism of vaspin-induced NO biosynthesis, vaspin activated the STAT3 signaling pathway and stimulated eNOS phosphorylation (Ser 1177), a marker of eNOS activation, through STAT3-dependent mechanism. Furthermore, vaspin treatment increased the expression of dimethylarginine dimethylaminohydrolase (DDAH) II, the responsible enzyme for the degradation of ADMA, leading to a reduction in ADMA levels. Vaspin-induced increase in DDAH II gene expression was through STAT3-mediated stimulation of DDAH II promoter activity. These results suggest that vaspin increases eNOS activity by reducing ADMA level through STAT3-mediated regulation of DDAH II expression.

Conclusion We identified vaspin as a new transcriptional modulator of DDAH II and an activator of endothelial STAT3. These results provide a novel molecular mechanism underlying vaspin's antiatherogenic function in endothelial cells.

OP10-5 Chronic complications of diabetes II

Chrysanthemum zawadski extracts attenuate the highly reducing sugar-induced oxidative cell damage in pancreatic beta cells and vascular endothelial cells

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Objective *Chrysanthemum zawadski* have traditionally been used in folk medicine, known as "Gujeolcho" in Korea for the treatment of various diseases. In the present study, Extracts of *Chrysanthemum zawadski* (CZE) was investigated to determine whether it could influence the highly reducing sugar, 2-deoxy-d-ribose (dRib)-induced oxidative damage and cellular dysfunction in pancreatic beta cells and vascular endothelial cells.

Methods Cells were treated with highly reducing sugar, dRib in the presence or absence of CZE. Cell viability, apoptosis, and ROS production were subsequently examined. In addition, inflammation-related genes and antioxidant enzyme genes were measured by real time PCR.

Results It was observed that dRib reduced cell survival, while it markedly increased intracellular levels of ROS and apoptosis. However, pretreatment of cells with CZE attenuated all the dRib-induced effects on the pancreatic beta cells and vascular endothelial cells. The anti-oxidants, N-acetyl-L-cysteine (NAC) also prevented dRib–induced oxidative cell damage. CZE upregulated the gene expression of antioxidant enzymes, superoxide dismutase 2 (SOD2), SOD3 and glutathione peroxidase 4 (GPX4) in vascular endothelial cells, which were inhibited by Rib, while there were no effects on pancreatic beta cells. We also found that CZE inhibited dRib-induced increased expression of COX-2 gene in vascular endothelial cells.

Conclusion Taken together, these results suggest that CZE attenuates dRib-induced cell damage in pancreatic beta cells and vascular endothelial cells and may be useful for the treatment of diabetes-related complications.

POSTER EXIBITIONS

- Date & Time: Friday 9 ~ Saturday 10 November 2012
- Place: Convention center 4F Lobby (PE001~PE076, PE121)
  3F Lobby (PE077~PE120)

[PE001~PE021,PE121]	Epidemiology & genetics
[PE022~PE055]	Clinical diabetes & therapeutics
[PE056~PE076]	Insulin action & obesity
[PE077~PE082]	Islet biology & insulin secretion, immunology & transplantation
[PE083~PE102]	Acute & chronic complications
[PE103~PE120]	Behavioral medicine & education

PE001 Epidemiology & genetics

A model for studying effects of misfolding proinsulin on cellular function

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Objective Mutations in the preproinsulin protein that affect processing of preproinsulin to proinsulin or folding of proinsulin are a common cause of permanent neonatal diabetes. The mutant proteins accumulate in the endoplasmic reticulum and induce the unfolded protein response (UPR). The UPR is unable to resolve the cellular stress resulting from the accumulation of the protein, eventually leading to beta-cell death.

Methods We expressed wild-type and diabetes-causing C96Y human preproinsulin (INS^{WT} and INS^{C96Y}, respectively) in the Drosophila eye using the UAS-GAL4 system.

Results The expression of INS^{C96Y} but not INS^{WT} caused severe degeneration of the eye in addition to ommatidial disorganization. The effect of INS^{C96Y} on eye degeneration was modified by sex, temperature and genetic background. We also carried out expression profiling studies in imaginal discs of 3rd instar larva to identify transcriptional alterations due to expression of the mutant proinsulin protein. We found increased expression of UPR-associated genes as well as those involved, in protein modification and folding, endoplasmic reticulum associated degradation (ERAD), protein transport and oxidoreductase/ mitochondrial proteins. This model system may be useful for identifying proteins and pathways that modify (suppress or enhance) the effect of misfolded insulin on ER homeostasis. Such proteins and pathways could then be examined in mammalian systems including cultured insulinoma cell lines and mouse models

Conclusion Together, these studies may lead to new approaches for preserving beta-cell function in patients with diabetes due to expression of a misfolded proinsulin as well as in those with type 2 diabetes where high levels of expression of proinsulin induces cellular stress.

PE002 Epidemiology & genetics

Good predictor of type 2 diabetes risk in Koreans

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Objective The aim of study was to evaluate the risk of obesity and body fat distribution to incidence of type 2 diabetes in Korea.

Methods We analysed the anthropometric and laboratory data of 66,510 non-diabetic Korean adults (40,160 men and 26,350 women). Diabetes was defined as fasting glucose≥ 7.0 mmol/l and HbA1c≥ 6.5% and pre-diabetic condition defined as fasting glucose ≥ 5.6mmol/L or 5.7% ≤ HbA1c ≤ 6.4%.

Results of the 66510 adults, 1500 subjects (2.26%) detected diabetes and 14787 subjects (22.23%) detected pre-diabetic condition. The general obesity (BMI, fat mass, percent body fat) and central obesity(waist circumference) were risk factor of type 2 diabetes. Logistic regression models for detecting undiagnosed type 2 diabetes; men: Ln (probability / [1-Probability]) = -29.416 + 0.036(age(years)) + 0.102(percent body fat(%)) + 0.25(Waist circumference(cm)) + 0.190(Fasting glucose(mg/dL)) women: Ln (probability / [1-Probability]) = -30.506 + 0.116(age(years)) + 0.411(fat mass) + 0.007 (Waist circumference(cm)) + 0.199(Fasting glucose(mg/dL)) + 0.102 (hs-CRP).

Conclusion Age, fat mass and waist circumference were good predictor of type 2 diabetes risk in Koreans.

PE003 Epidemiology & genetics

Circulating osteocalcin level is not associated with the development of cardiovascular disease: mean 8.4-year retrospective follow-up study

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Objective In addition to the association with glucose tolerance, recent studies suggested that serum osteocalcin is associated with the cardiovascular risk factors. However, little is known about the causality of serum osteocalcin on the development of cardiovascular disease (CVD). Therefore, the aim of this study was to determine whether serum total osteocalcin level is independently associated with the development of CVD.

Methods A retrospective cohort study was performed of 2,077 subjects (1,404 men and 673 women), aged 20-78 years, who were recruited from the Health Promotion Center, Samsung Medical Center, between January 1997 and December 1997. They were followed regularly at the center on an out-patient basis and during hospitalization for a mean of 8.4 years, and the development of CVD (coronary heart disease [CHD] and stroke) was determined.

Results In the baseline analysis, body fat percentage, fasting glucose, and prevalence of diabetes or metabolic syndrome were decreased as the osteocalcin tertiles increased, and age and subjects with current smoking were increased. However, no differences were observed in blood pressure, HOMA-IR value, and lipid parameters across the osteocalcin tertiles. Incident CVD occurred in 106 (5.1%) of the study subjects (38 CHD and 71 stroke). In Cox proportional hazards models, however, no statistical differences in the development of CVD across the osteocalcin tertiles were observed after adjustment of other risk factors for CVD including age, sex, body mass index, body fat percentage, current smoking, systolic blood pressure, LDL-cholesterol, HbA1c, and presence of diabetes, hypertension, or metabolic syndrome.

Conclusion Despite baseline inverse associations with cardiovascular risk factors, serum total osteocalcin level was not associated with the development of CVD.

PE004 Epidemiology & genetics

Association of Inflammatory markers with cardiovascular risk factors and metabolic syndrome in an apparently healthy general population

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Objective Metabolic syndrome is associated with the presence of a low grade sub-clinical inflammatory process. Highly sensitive C-reactive protein (hs-CRP), fibrinogen, and homocysteine have been suggested as inflammatory markers, insulin resistance or cardiovascular disease risk predictors. The aim of this study is to estimate the association of inflammatory markers with cardiovascular disease risk factors and metabolic syndrome in an apparently healthy general population.

Methods We retrospectively studied 1,862 asymptomatic Korean adults of 20 years old or older who underwent voluntary regular health check-ups at the Health Promotion Center of Chosun University Hospital from January 2008 to June 2010. Individuals previously diagnosed with diabetes, hypertension, or dyslipidemia and those treated with hypoglycemic agents, antihypertensive agents, and lipid lowering agents were excluded.

Results Pearson's correlation analysis and multiple linear regression analyses showed that hs-CRP was significantly associated with glucose and HbA1c. Fibrinogen was significantly associated with BMI, HbA1c, waist circumference, and HDL cholesterol. Homocysteing was significantly associated with LDL cholesterol, Triglyceride, systolic blood pressure, and HDL cholesterol.

Conclusion hs-CRP, fibrinogen, and homocysteine were significantly associated with cardiovascular risk factors and metabolic syndrome in an apparently healthy general population. Fibrinogen is a better marker that predicts the development of metablic syndrome or cardiovascular disease.

PE005 Epidemiology & genetics

Association of metabolic syndrom and benign prostate enlargement in Korean male workers

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Objective This study was conducted to evaluate the association between metabolic syndrome(MS) and benign prostatic enlargement in Korean male workers. Also, we investigated the relationship between metabolic syndrome componants and prostate-related factors.

Methods Total 1,643 healthy male workers without prostate related disease were included. We divided the subjects into two groups, 484 the MS group and 1,159 non-MS (NMS) group. The subjects completed a questionnaire including the International Prostate Symptom Score (IPSS), and were measured hematological characteristics and prostate volume (PV) via lower abdominal ultrasonography.

Results There were no significantly difference of the PV, IPSS and PSA between in the MS group and in the NMS group. In NMS group, total testosterone was significantly higher than that in MS group after adjustment age ($P < 0.001$). PV was significantly positive correlation with body mass index (BMI) ($P < 0.05$) and negative correlation with triglyceride (TG) ($P < 0.01$). PSA was significantly positive correlation with diastolic blood pressure ($P < 0.05$). Total testosterone was significantly positive correlation with high density lipoprotein ($P < 0.001$) and negative correlations with BMI, waist circumference and TG ($P < 0.01$).

Conclusion In conclusion, there were significant correlations between each MS factors and the PV. This study suggested that management of MS is important way for decrease risk of benign prostate enlargement, moreover cardiovascular disease.

PE006 Epidemiology & genetics

Association of heavy metals with diabetes in the Korean population

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Objective Despite increasing concern regarding health problems due to environmental pollutants, no association of toxic heavy metals with diabetes has been demonstrated in the general population. We investigated the association of heavy metals, including lead, mercury, and cadmium, with diabetes in the Korean population.

Methods This cross-sectional study is based on data from the fourth and fifth Korea National Health and Nutritional Examination Surveys (KNHNES), which were conducted in 2009 and 2010 among members of the Korean population. Participants included 1588 males and 1596 females 30 years of age or older, who were selected from all of the 16 administrative districts of South Korea. Measurements of blood lead, mercury, and cadmium levels were performed. Homeostatic model assessment of insulin resistance (HOMA-IR) and homeostatic model assessment of β-cell function (HOMA-β) were calculated in participants without diabetes.

Results Blood concentration of lead, mercury, and cadmium were slightly higher, but non-significantly, in participants with diabetes, compared to those without. After adjustment for age, sex, region, smoking, alcohol consumption, and regular exercise, the prevalence of diabetes did not differ among quartiles of blood heavy metal concentrations. Correlation analysis of heavy metals with HOMA-IR and HOMA-β did not indicate a significant relationship. The relationship of sum of heavy metal mixture with prevalent diabetes was also not significant.

Conclusion Lead, mercury, and cadmium have no significant relationship with diabetes in the Korean population. Below toxic level, these heavy metals may not have a direct effect on incidence of diabetes.

PE007 Epidemiology & genetics

Age is a major determinant for metabolic abnormalities in women with polycystic ovary syndrome

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Objective Polycystic ovary syndrome (PCOS) is a heterogenous condition and phenotype varies widely depending on life stage. PCOS usually begins at adolescence with reproductive manifestations, proceeding to metabolic complications over time. In this study, we aimed to evaluate the effect of aging on hormonal and metabolic features in young women with PCOS.

Methods We recruited 494 women with PCOS (16~39 yrs) and 962 regular cycling heatlhy women as control (16~39 yrs). Anthropometric measurements were obtained and metabolic and hormonal parameters were determined. Glucose tolerance status was assessed by 75 g OGTT. Women with PCOS and controls were divided into 3 groups by age; < 20, 20~29 and 30~39 yrs old.

Results In the total PCOS group, age correlated positively with BMI ($r = 0.097$, $P < 0.05$), waist ($r = 0.140$, $P < 0.01$), fasting glucose ($r = 0.143$, $P < 0.01$) and post-load 2 hr glucose levels ($r = 0.231$, $P < 0.001$), but there was no significant correlation with total and free androgen levels. In total control group, age was negatively correlated with free testosterone levels ($r = -0.139$, $P < 0.001$) and positively correlated with waist ($r = 0.071$, $P < 0.05$). Based on age groups, the prevalence of IFG or IGT (9.8, 10.9, 17.2%, P for trend < 0.05), DM (1.1, 2.7, 15.6%, P for trend < 0.05) and metabolic syndrome (16.3, 15.1, 45.3%, P for trend < 0.05) were significantly higher in age over 30 years old compared to the other 2 groups in women with PCOS, but not in controls.

Conclusion Metabolic abnormalities worsen during reproductive life in women with PCOS and this may be attributable to the increase in obesity.

PE008 Epidemiology & genetics

Effects of high fat diet on phenotypes of liver-specific knock-out mice of Mitogen-Inducible Gene 6 (Mig-6)

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Objective Mitogen inducible gene 6 (Mig-6) is a nonkinase adaptor protein, which is an immediate-early feedback inhibitor of EGFR signaling pathway. Therefore, deletion of Mig-6 gene leads to activation of EGFR signaling pathway. It was reported that liver-specific deletion of the gene resulted in hepatomegaly and increased plasma concentration of cholesterol with decreased bile acid excretion, indicating important roles of the gene in the metabolic syndrome. In this study, it was evaluated the effect of high fat diet on the phenotypes of liver specific K.O. mice of the Mig-6 gene.

Methods The high fat diet (40% of total weight) had been supplemented to the wild (Mig-$6^{f/f}$) and the K.O. ($Alb^{cre/+}$Mig-$6^{f/f}$, Mig-$6^{d/d}$) mice for 20 weeks from 5-week-of-age. The body weight change, the glucose tolerance, the insulin resistance, the concentrations of some plasma biochemical parameters and the weights of organs were measured and compared to animals fed with normal chow

Results The Mig-$6^{d/d}$ mice were revealed lower body weight than the Mig-$6^{f/f}$ mice with reduced fat weight. The fasting plasma cholesterol and glucose concentration were higher in the K.O. mice than the wild mice, but the K.O. mice had the improved glucose tolerance and insulin resistance. The high fat diet showed same effects on Mig-$6^{f/f}$ and Mig-$6^{d/d}$ mice but more significant in male than in female.

Conclusion These results suggest that the liver specific knock out of Mig-6 can sufficiently affect the metabolic phenotypes of the animals and Mig-6 should have important roles in controlling both fasting plasma glucose concentration and insulin resistance.

PE009 Epidemiology & genetics

Variants of the adiponectin gene and diabetic microvascular complications in patients with type 2 diabetes

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Objective The aim of this study was to examine the association between common polymorphisms of the adiponectin gene (*ADIPOQ*) and microvascular complications in patients with type 2 diabetes mellitus (T2DM).

Methods Rs2241766 and rs1501299 of *ADIPOQ* were genotyped in 708 patients with T2DM. Fundus photography, nerve conducting velocity, and urine analysis were performed to check for the presence of microvascular complications including diabetic nephropathy, retinopathy and neuropathy.

Results The prevalence of diabetic nephropathy tended to be different according to rs2241766 genotype (P = 0.057) and the GG genotype of rs2241766 was associated with diabetic nephropathy [urine albumin/creatinine ratio (UACR) greater than 30 mg/g] after adjusting for age, sex, body mass index, duration of diabetes, HDL-cholesterol, smoking status, and blood pressure (odds ratio = 1.98; 95% confidence interval = 1.01-3.87). Also, the G allele of rs2241766 demonstrated a trend to be associated with an increase in UACR (P = 0.087). Rs2241766 genotype was not associated with diabetic retinopathy (P = 0.955) and neuropathy (P = 0.104) or any diabetic microvascular complications (P = 0.104). There was no significant association between the rs1501299 genotype of *ADIPOQ* and the prevalence of diabetic retinopathy and neuropathy or any diabetic microvascular complications even after adjustment.

Conclusion These data suggest that the GG genotype at rs2241766 is independently associated with risk for diabetic nephropathy defined as UACR greater than 30 mg/day in patients with T2DM.

PE010 Epidemiology & genetics

Association of extraverted personality and abnormal glucose regulation in young women

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Objective Depression and psychological distress are known to be associated with diabetes development as well as the disease progression including glycemic control and chronic complication. However, the relationship of personality trait and diabetes is not studied yet.

We examined whether the personality trait and the presence of abnormal glucose regulation (AGR, diabetes and pre-diabetes) is associated in young women.

Methods Personality trait was assessed by self-reported questionnaire using Five-Factor Model (Extraversion, Neuroticism, Agreeableness, Conscientiousness, and Openness) consisting of five-point scale ranging from 'strongly disagreeable' to 'strongly agreeable'.

A total of 1,702 young women aged 16 to 39 years without previously diagnosed diabetes were participated voluntarily. Glucose tolerance status was assessed by standard 75-g oral glucose tolerance test.

Results One-hundred sixteen women were newly diagnosed with AGR (6.8%). Among 5 factors, only 'Extraversion' trait was significantly associated with AGR. Multiple linear regression analysis showed the significant negative association with 2 hr post-load glucose after adjustment for age, BMI, systolic blood pressure, triglycerides, HDL cholesterol, and family history of diabetes (b = -0.17, P = 0.0065). Multiple logistic regression showed that the 'Extraversion' trait was significantly associated with the presence of AGR after adjustment for the same covariates (OR 0.98, 95% CI 0.96-0.99, P = 0.038). The frequency of AGR was significantly increased according to the decrease of 'Extraversion' trait score (P for trend with exact test = 0.047).

Conclusion In conclusion, extraverted personality might be associated with decreased prevalence of AGR in young women.

PE011 Epidemiology & genetics

Transcription factor 7-like 2 (TCF7L2) gene polymorphism and diabetic complications

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Objective TCF7L2 polymorphisms have been consistently associated with susceptibility of type 2 diabetes mellitus. Furthermore, several studies have reported that TCF7L2 polymorphisms are associated with diabetic complications such as retinopathy, nephropathy, neuropathy and coronary artery disease. This study aimed to explore the effect of TCF7L2 polymorphism on diabetic complications and diabetes related factors in Korean diabetic subjects.

Methods We genotyped TCF7L2 variant rs7903146 in 810 Korean diabetic subjects. The effect of the TCF7L2 variant on diabetic complication and diabetes related factors was investigated.

Results The TCF7L2 variant was rare among 810 Korean diabetic subjects; 63 (7.8%) subjects harboring CT genotype and 2 (0.2%) subjects harboring TT genotype. Prevalence of diabetic complications was not significantly different between subjects without the TCF7L2 variant T (CC genotype) and subjects with the TCF7L2 variant T (CT genotype or TT genotype); 9.4% vs. 13.8%, 12.5% vs. 13.8%, 37.8% vs. 33.9%, 9.8% vs. 9.2% and 37.9% vs. 38.5%; stroke, coronary artery disease, retinopathy, nephropathy and neuropathy, respectively. The proportion of patients on anti-hypertensive medication and anti-dyslipidemic medication was not significantly different between these two groups. There was no significant difference in height, weight, BMI, diabetes duration, onset of diabetes, HbA1c, fasting blood glucose, serum C-peptide, serum insulin, serum Cr, serum total cholesterol, serum triglyceride, serum HDL cholesterol, serum LDL cholesterol, serum SGOT and serum SGPT. Interestingly, the frequency of the TCF7L2 variant in Korean diabetic subjects was considerably lower than that of Caucasians diabetic subjects (minor allele frequency 4.1% vs. 37~44%).

Conclusion These results suggest that the TCF7L2 variant rs7903146 does not confer the risk of developing diabetic complications in Korean diabetic subjects. This lack of association may be attributed to the low frequency of the TCF7L2 variant found among Korean subjects in contrast to the high frequency found among Caucasians.

PE012 Epidemiology & genetics

Diabetes, hypertension, and colorectal adenoma

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Objective Diabetes and hypertension have been suggested to increase colorectal neoplasia. We examined the association between history or presence of diabetes and hypertension and the prevalence of colorectal adenoma in Korean adults.

Methods Study participants were Korean men and women aged 39-73 who underwent colonoscopy at the health examination center at Daegu Catholic University Medical Center. A total of 689 participants (263 men and 426 women) were included and classified into the colorectal adenoma group (n = 201) or the control group without adenoma (n = 488). We analyzed the associations of systolic blood pressure (SBP), diastolic blood pressure (DBP), history or presence of hypertension, fasting blood sugar (FBS), history or presence of diabetes in relation to the prevalence of colorectal adenoma. We calculated odds ratios (ORs) and 95% confidence intervals (CIs) using the multivariate logistic regression model.

Results We found that participants with adenoma tended to have higher DBP levels compared to those without adenoma; OR (95% CI) was 1.56 (0.94-2.61, P for trend = 0.03) in the age-sex adjusted model. In the multivariate analysis where we adjusted for age, sex, smoking status, pack years of smoking, alcohol intake and BMI; OR (95% CI) was 1.50 (0.88-2.56, P for trend = 0.05). However, we did not observe statistically significant associations or trends for history or presence of diabetes, history of hypertension or fasting blood sugar levels.

Conclusion There was suggestion that DBP levels were associated with high prevalence of colorectal adenoma.

PE013 Epidemiology & genetics

The effects of meal calorie variation on metabolic syndrome, hypertension, and diabetes mellitus

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Objective There are few studies about association between meal calorie variation and metabolic syndrome, hypertension, diabetes mellitus in healthy populations. This study was done to assess the association of meal calorie variation and metabolic syndrome, hypertension, diabetes mellitus.

Methods A total of 4,512 subjects were selected. The diagnosis of metabolic syndrome was made according to the criteria of NCEP-ATP III established in 2001 with Asia-Pacific waist circumference.

We defined meal calorie variation as the standard deviation of four meal's calorie (breakfast, lunch, dinner, snacks). To examine the association between the metabolic syndrome components and meal calorie variation, we used the method of multiple linear regression analysis. To examine the association between the metabolic syndrome, hypertension, diabetes mellitus and meal calorie variation, we used the method of multiple logistic regression analysis.

Results The prevalence of the metabolic syndrome, hypertension, and diabetes mellitus in our subjects was 30.6%, 26.5%, 8.7%. Increased meal calorie variation was not associated with the components of metabolic syndrome. The only significant finding was that HDL-cholesterol was associated negatively with increased meal calorie variation in men. (β = -4.73, P value = 0.003) Unfortunately, meal calorie variation was not associated with the prevalence of metabolic syndrome, hypertension, diabetes mellitus.

Conclusion After statistical adjustment for age, body mass index, smoking, total calorie intake, physical activity, regular exercise, total alcohol intake, total carbohydrate, fat, protein intake, monthly income, the meal calorie variation was not associated with the metabolic syndrome, hypertension, diabetes mellitus.

PE014 Epidemiology & genetics

A study on the identification of single nucleotide polymorphisms related to type 2 diabetes throuh Genom-Wide Association Studies (GWAS)

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Objective This study aimed to excavate dielectric materials related to Type 2 Diabetes in Korea people through GWAS.

Methods This study used health examination and questionnaire data from a total of 5,657 individuals: 4,914 healthy individuals and 743 patients with Type 2 Diabetes. It also conducted a linkage analysis using genotype information according to GWAS-study.

Results SNPs from a total of sixteen genes related to the occurrence of diabetes were found. Of which, 8 SNPs such as SNP(SNP_A-1923579, SNP_A-2269207, SNP_A-2192706, SNP_A-4276472, SNP_A-2203798, SNP_A-2105831, SNP_A-1795635, and SNP_A-1874661) increased the growth risk of type 2 diabetes, whereas the remaining 8 SNPs such as SNP(SNP_A-2018557, SNP_A-4251277, SNP_A-2288944, SNP_A-1895643, SNP_A-2093582, SNP_A-2264360, SNP_A-4269412, and SNP_A-2090981 suppressed the growth risk of type 2 diabetes. The more the number of risk allele, the higher the growth risk of diabetes.

Conclusion From this research, SNPs from a total of sixteen genes affecting the occurrence of diabetes could be found.

PE015 Epidemiology & genetics

Elevated serum arylhydrocarbon receptor mediated transcriptional activity in patients with type 2 diabetes mellitus

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Objective Persistent organic pollutants (POPs) are stable lipophilic chemicals which include dioxin and dioxin-like substances. Serum concentrations of POPs were found to be positively associated with insulin resistance and metabolic syndrome in several epidemiologic studies. Dioxin-like substances bind to aryl hydrocarbon receptor (AhR), leading to the transcriptional activation of multiple genes. We aimed to investigate the association between serum concentrations of dioxin-like substances and type 2 diabetes mellitus (T2DM) and its related metabolic phenotypes.

Methods We collected sera from 83 patients with T2DM, 130 subjects with impaired glucose tolerance (IGT) and 83 normal glucose tolerant (NGT) subjects. Cell-based AhR ligand assay was developed to determine the AhR-mediated transcriptional (AHRT) activities which reflect the concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). The AHRT activities (TCDD equivalent or TCDDeq) were measured in our study subjects.

Results There were significant difference of serum TCDDeq among NGT, IGT, and T2DM groups and the T2DM group had the highest TCDDeq levels (median [interquartile range] 53.3 [46.1-63.7] pM in NGT vs. 60.2 [45.8-75.1] pM in IGT vs. 68.1 [53.1-81.5] pM in T2DM, P = 0.003). In the NGT or IGT groups, serum TCDDeq level showed significant positive correlation with fasting glucose, fasting insulin, and HOMA-IR and a significant negative correlation with adiponectin concentration. Multivariate logistic regression analysis revealed that serum TCDDeq is an independent risk factor of T2DM after adjusting for age, sex, and body mass index.

Conclusion In conclusion, serum TCDDeq level was significantly higher in the T2DM group and was significantly associated with metabolic parameters of fasting glucose, fasting insulin, and adiponectin. These results suggest that serum POPs may play an important role in the pathogenesis of T2DM.

PE016 Epidemiology & genetics

The relationship between insulin therapy and cancer incidence in patients with diabetes : follow up study in Korea

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Objective The vast body of epidemiological literature has suggested the risk of cancer in people with diabetes. As several mechanisms of cancer incidence, such as insulin resistance, hyperinsulinemia, increased insulin-like growth factor have been proposed, there have been growing concerns about the long-term effect of insulin on the risk of several types of cancer.

The aim of this study was to investigate the relationship between insulin therapy and cancer incidence in patients with diabetes in Korea.

Methods We analyzed the database of 4,537 DM patients who registered in the Korean National diabetes Program (KNDP) from April 1st, 2006 to March 31st, 2011. We included those who had been diagnosed with any type of cancer since one year after the cohort registration. Overall, 3,445 patients were included in the analysis. We classified insulin users according to the types of insulin used. Data were analyzed by Cox's proportional hazard models adjusting for, but not limited to, demographic factors, insulin use, and metformin use. Cumulative cancer incidence was calculated by Kaplan-Meier method.

Results All insulin users had longer diabetes duration, worse glucose control, were less obese, and involved to microvascular diabetic complications more. We observed 142 incident cancers (4.1 %, 12.2 per 1000 person years). The most frequent site of cancer in the diabetic cohort was the prostate, followed by colon in men and the thyroid, followed by liver in women. There was no difference in the total number of cancer incidence between any types of insulin users and non-insulin users.

Any type of insulin use was not associated with cancer incidence after adjusting for sex, age, metformin use, diabetes duration, glucose control, and body mass index (BMI).

Conclusion The association between insulin therapy and cancer incidence was not observed in the Korean diabetes patient cohort. Longer-term large studies are needed.

PE017 Epidemiology & genetics

Effect of insulin resistance and body mass index on the risk of diabetes incidence: The Chungju metabolic disease cohort (CMC) study

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Objective To investigate associations between combinations of insulin resistance (IR) and body mass index (BMI) categories and the risk of diabetes mellitus in a rural population of Korea.

Methods This CMC study is an ongoing community-based prospective cohort study. A total of 4,948 subjects age 40 and older, free of T2DM, and had complete data at baseline were included in the present study. According to IR/BMI status, they were classified as normal weight (BMI 〈 23 kg/m^2) without IR (homeostasis model assessment-IR in the highest quartile, n = 1,578), normal weight with IR (n = 215), overweight (BMI 23– 〈 25 kg/m^2) without IR (n = 959), overweight with IR (n = 267), obese (BMI ≥ 25 kg/m^2) without IR (n = 1,173), and obese with IR (n = 756). We investigated the associations between BMI/IR categories at baseline and diabetes incidence.

Results Four hundred and ninety-six incident cases of diabetes for average of 4.5 years were identified. Multiple logistic regression analysis showed that increased risks for diabetes incidence were observed in the normal weight with IR (odds ratio [95% confidence intervals], 1.88 [1.14-3.07]), overweight without IR (1.71 [1.25-2.32]), overweight with IR (2.41 [1.58-3.69]), obese without IR (1.59 [1.17-2.16]), and obese with IR (4.17 [3.10-6.61]) groups compared with the normal weight without IR group.

Conclusion Subjects with combined effect of IR and BMI were at increased risk for diabetes and each factor independently predicted increased diabetes risk. To decrease risk of diabetes, it is necessary that identification of subjects with overweight, obese and/or IR, and an appropriate intervention for each group in the community.

PE018 Epidemiology & genetics

A case of MODY5 without genitourinary abnormalities: The P159L-HNF-1β mutation

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Contents Mutations in the hepatocyte nuclear factor-1β (HNF-1β) gene cause maturity-onset diabetes of the young type 5 (MODY5), usually with other various phenotypes as renal abnormalities, genital malformation. We report a case of HNF-1β mutation which presents only as insulin-dependent diabetes mellitus. The patient is 27-year-old woman who was diagnosed as diabetes mellitus by routine examination at the age of 14 years. Her father and grandmother were affected by diabetes, and she had one brother with normoglycemia. Blood tests and the ultrasonography revealed she had not any problems in kidney and genitalia. Insulin therapy had to be maintained for glycemic control, but autoantibodies for pancreatic β cell were not detected. The HNF-1β gene was screened by direct sequencing, resulting in the detection of a point mutation. We found a heterozygous P159L (CCT to CTT at the codon 159 in exon 2) mutation in the patient and her father, not in her mother and the brother. Now we are on functional study of this HNF-1β gene mutation.

PE019 Epidemiology & genetics

Withdrawn

PE020 Epidemiology & genetics

The association of serum vitamin D level and metabolic syndrome in Korean men

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Objective Vitamin D status, as indicated by 25-hydroxyvitamin D [25-(OH)D], is inversely associated with glucose homeostasis, lipid profiles, and blood pressure. Evidence on the association of vitamin D with metabolic syndrome (MS), however, is very limited. Therefore we investigated the relationship of serum 25-(OH)D levels and MS in Korean men.

Methods This study was a cross sectional study including 2,582 Korean adults who visited a health promotion center in a university hospital from January 2010 to May 2011. MS was defined according to the AHA/NHLBI criteria and the Korean Society for the Study of Obesity. MS and its individual components were assessed as well as serum 25-(OH)D levels with multiple logistic regression analysis.

Results The overall prevalence of the MS in participants of this study was 17.2%. Compared with the highest quantile serum 25-(OH)D level group (21.6-58.3 ng/mL), the odds ratio for MS in the lowest level group (4.0-12.3 ng/mL) was 1.55 (95% CI = 1.07-2.25), in the lower level group (12.4-16.7 ng/mL) was 1.21 (95% CI = 0.85-1.74), and in the intermediate level group (16.8-21.5 ng/mL) was 0.90 (95% CI = 0.62-1.29). Among the components of metabolic syndrome, the odds ratios for abdominal obesity, impaired fasting glucose, elevated blood pressure, low HDL cholesterol level, and high triglyceride level in the lowest serum 25-(OH)D level group were 0.98 (0.59-1.62), 0.89 (0.97-0.70), 0.84 (0.65-1.10), 0.90 (0.65-1.23), and 1.76 (1.33-2.28), respectively.

Conclusion We found that a low serum 25-(OH)D level is significantly associated with a high risk of MS and some metabolic components, especially the high triglyceride level in Korean men.

PE021 Epidemiology & genetics

The prevalence of diabetes mellitus in Korean women aged 30 59 years have decreased for recent 10 years: Results from the Korean national health and nutrition examination surveys, 1998-2010

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Objective During the recent 30 years, the prevalence of diabetes in South Korea has increased about 3 folds: It reached about 9~10% in Korean adults aged ≥ 30 years. However, it has maintained stable in 2000's although Korean population is aging. We investigated the change of prevalence of diabetes according to age-group in recent 10 years.

Methods We analyzed with Korean National Health and Nutrition Examination Surveys from 1998 through 2010. The surveys were conducted with stratified, multistage, probability-sampling designs and weighting adjustments to represent the entire Korean population. Age-adjustment was done with the Korean population 30 years or older in 2010 as a standard population. Definition of metabolic abnormalities was based on the revised National Cholesterol Education Program criteria.

Results The age-adjusted prevalence of diabetes mellitus did not change among entire study population with age 30 years or more: 12.6 (standard error, 0.7)% in men and 10.2 (0.6)% in women in 1998 and 11.8 (0.7) % in men and 9.1 (0.6)% in women in 2010. However, it showed a decreasing tendency in women aged 30~59 for about 10 years (figure 1) and time series analysis confirmed the statistical significance of the change: about 40% reduction from 1998 to 2010 (95% confidential interval, 17~57%, P = 0.001). The prevalence of each metabolic abnormality such as abdominal obesity, low HDL cholesterolemia and hypertension as well as that of metabolic syndrome in women aged 30-59 have also decreased significantly during that period.

Conclusion Although the prevalence of diabetes in the Korean adult aged 30 years or more did not changed significantly, that of women aged 30~59 years decreased significantly for recent 10 years along with decreasing prevalence of other metabolic abnormalities.

PE022 Clinical diabetes & therapeutics

A case of recurrent insulin autoimmune syndrome by alpha-lipoic acid in Type 2 diabetes

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Contents Insulin autoimmune syndrome (IAS) is characterized by spontaneous hypoglycemia caused by autoantibodies to insulin in individuals without exogenous insulin administration. Drugs containing sulfhydryl groups are known to play an important role in pathogenesis of IAS. A 67-year-old woman with a 5 year diabetes history visited in outpatient department because of paresthesia of both feet by diabetic peripheral polyneuropathy. She was prescribed alpha-lipoic acid (ALA). 2 weeks later, she complained hypoglycemic symptoms in late postprandial period. A high level of insulin and high titers of insulin autoantibodies were detected. ALA contains two sulfur atoms. Her HLA genotype contained DRB1*0406 allele, which confers a high level of susceptibility to IAS. She was recovered by prednisolone treatment. After this episode, she experienced hypoglycemic events twice more after taking ALA for diabetic neuropathy in other hospitals. As ALA is used widely for treating diabetic peripheral polyneuropathy, physician should consider the possibility of IAS due to ALA in diabetic patients suffering from spontaneous hypoglycemia without previous insulin use.

PE023 Clinical diabetes & therapeutics

A case of fulminant type 1 diabetes with Graves' disease

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Contents We describe herein an unusual case of simultaneous presentation of a fulminant type 1 diabetes and a Graves' disease. A 67-year old male was admitted to the hospital with nausea, vomiting, and abdominal discomfort. He had a palpitation, hand tremor and mild weight loss during last month and his conditions aggravated acutely with nausea and vomiting, prior 3 days before admission.

Laboratory findings included: glucosuria(+++), ketonuria(+++), serum glucose 677 mg/dL, HbA1c 6.5%, insulin 0.614 uU/mL, c-peptide 0.223 ng/mL, amylase 100 IU/L, lipase 259 U/L, GAD antibody 0.74 [0-0.9] U/mL, IA-2 antibody 〈 0.4 [0-0.4] U/mL, insulin antibody 5.4 [0-7]%, free T4 3.33 [0.93-1.7] ng/dL, TSH 0.007[0.27-4.2] uIU/mL, TSH receptor antibody 4.83 [~1.75] IU/L. An abdominal CT scan was showed normal pancreas, and a Tc-99m pertechnetate thyroid scan revealed homogeneously increased activity in the thyroid gland (20 minute Tc-pertechnetate uptake = 52.5).

The clinical characteristics of the patient were remarkably abrupt onset diabetes, very short duration of diabetic symptoms, acidosis at the time of diagnosis, negative findings for islet-related autoantibodies and no c-peptide secretion. His diagnosis was compatible with fulminant type 1 diabetes. And, thyroid function test with autoantibody and thyroid scan results were suggestive Graves' hyperthyroidism.

We often observed classic type 1A diabetes associated with autoimmune thyroid disease. This case was unique in that fulminant type 1 diabetes developed simultaneously with Graves' hyperthyroidism

PE024 Clinical diabetes & therapeutics

The favorable effects of Kimchi on metabolic parameters in patients with prediabetes

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Objective Kimchi is a traditional Korean food. Kimchi, especially in its fermented form, is found to reduce body weight and improve metabolic parameters in overweight and obese patients. However, research about the effects of Kimchi in patients who show abnormality in glucose metabolism is lacking. The aim of this study is to investigate the beneficial effects of Kimchi on glucose metabolism in patients with prediabetes.

Methods Nineteen patients, diagnosed with prediabetes according to the criteria of the American Diabetes Association (100 ≤ fasting glucose 〈 126 mg/dL or 140 ≤ 2-hour post-load glucose 〈 200 mg/dL), were enrolled. They were randomly assigned to an 8-week diet phase. During the diet phase, the subjects consumed either fresh or fermented Kimchi which were created from the same standardized recipe and ingredients. The Kimchi differed in terms of fermentation. One-day-old and 10-day-old Kimchi were defined a "fresh" and "fermented", respectively. A percentage of patients who showed an improved glucose metabolic status were analyzed.

Results In the fresh Kimchi group, 2 of 8 (25%) showed improved glucose metabolism status. Of the two patients with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), one of them showed improved IFG and the other showed improved IGT after ingestion of fresh Kimchi for 8 weeks. In the fermented Kimchi group, 7 of 11 (63.6%) represented improved glucose metabolism status. Among the 7 patients who showed improvement, 5 patients with IFG and/or IGT showed normal glucose tolerance (NGT) after ingestion of fermented Kimchi for 8 weeks.

Conclusion After ingestion of fresh or fermented Kimchi for 8 weeks in prediabetes patients, 25% and 63.6% showed improved glucose metabolism status, respectively.

PE025 Clinical diabetes & therapeutics

Recipient age predicts improved glucose homeostasis in new-onset diabetes after liver transplantation

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Objective New-onset diabetes mellitus after transplantation (NODAT) is a major predisposing factor for cardiovascular disease and its complications. Identifying patients at high risk of NODAT will help researchers design clinical prevention trials. Most of studies have been from Western countries. So we studied to determine pretransplant risk factors associated with NODAT in Korean populations who were not diabetic prior to transplantation, and to compare this cohort with improved NOADT patients.

Methods From August 2005 to January 2011, a total of 51 LTs were performed in adults at the Chonbuk National University hosipital, Korea. Patient demographic information and important medical history before and after LT were investigated, including age, sex, race, body mass index (BMI), hypertension, etiology of liver disease, Model for End-stage Liver Disease (MELD) score, dyslipidemia, HgA1c, preoperative fasting glucose, the type of immunosuppressive agents, the type of anti-diabetic agents that were used NOADT groups, and donor type. Continuous variables were described using mean, standard deviation, and quantitative descriptive variables were analyzed by an independent sample Student's t-test or the Mann-Whitney test. Logistic regressions were used to determine the relation between independent variables and the development of NODAT.

Results After 51 LT cases, 4 (7.8%) recipients were normal glucose, 20 (39.2%) recipients were NOADT, 13 (25.5%) recipients were sustained prediabetes, and 9 (17.6%) recipients were pre-LT diabetes. On multivariate analysis, the mean level of pre-LT FBG level was significantly higher in the sustained NOADT group versus the normal group (148.3 ± 29.6mg/dL vs. 83.0 ± 6.6 mg/dL; P = 0.009). Potential risk factors- recipient age, pre-LT HTN, pre-LT dyslipidemia, body weight, MELD score, the type of donor (living vs. decessed) were not different significantly.

Among NOADT group, 13 (61.9%) recipients showed improved pattern of glucose level after liver transplantation, so they could stop anti-diabetic agents. Among prediabetes group, 9 (69.2%) recipients decreased fasting blood glucose (FBG) level (mean: 47.6 ± 24.6 mg/dL, 4-76 mg/dL) after LT. Among pre-LT diabetes group, 2 (22.2%) recipients also showed improved pattern of blood glucose level, so they could stop anti-diabetic agents. Lower recipient age was related with improved NOADT group compared with sustained NOADT group (46.4 ± 9.2 & 55.0 ± 6.5, P = 0.040).

Conclusion In summary, NOADT develops in 39.2%, and additional 25.5% of patients develop impaired fasting glucose or impaired glucose tolerance. Pretransplant risk factor for development of NOADT in Asian peoples include higher pre-LT fasting blood glucose level. Among impaired glucose homeostasis groups, 25 (59.5%) recipients showed improved pattern of glucose level after liver transplantation. Pretransplant predictive factor for improvement of impaired glucose homeostasis include pre-LT recipient age. Given the implication of abnormal glucose homeostasis on long-term allograft and patient survival in LT recipients, further studies to risk stratify patients and conduct preventive strategies are necessary in this field.

PE026 Clinical diabetes & therapeutics

Clinical usefulness of the measurement of serum fructosamine in the management of childhood diabetes

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Objective HbA1c can usually be used as an indicator of glucose control and correlated with the development of long-term diabetic complications. But it usually reflects the mean glucose levels of 2~3 months and can be variable in the situation of hemoglobinopathy or the conditions of altered RBC lifespan. In contrast, serum fructosamine levels reflect the mean glucose levels of 2~3 weeks. This study was designed to see the clinical usefulness of the measurement of serum fructosamine in the management of childhood diabetes and the correlation between the HbA1c and fructosamine levels.

Methods Clinical data were evaluated from the sixty Korean diabetic patients in the department of Pediatrics, Dankook University Hospital. Fructosamine and HbA1c levels were also reviewed on the basis of clinical information and analyzed using IBM SPSS Statistics version 20.

Results HbA1c levels showed strong association with the fructosamine levels ($P < 0.001$). Fructosamine levels better indicated the average glucose concentration over the previous 2~3 weeks than HbA1c levels. Fructosamine levels were useful for the evaluation of the recent therapeutic efficacy after the change of the therapeutic modality as well as for the estimation of the disease onset such as fulminant diabetes.

Conclusion The measurement of fructosamine levels is useful in the management of childhood diabetes especially, if there is some discrepancy between the clinical information and HbA1 levels. It is useful for the short-term evaluation about the recent glucose control after the change of the treatment modality of diabetes.

PE027 Clinical diabetes & therapeutics

Recovery of pancreatic beta cell function in type 2 diabetes by insulin pump therapy for six years

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Objective Type 2 diabetes is characterized with impaired beta cell function and reduced beta cell mass, which deteriorates over time. To see if beta cell function can be improved in type 2 diabetic patients through long-term continuous insulin infusion (CSII) therapy, we examined changes in serum C-peptide levels during six years of the treatment.

Methods We discontinued oral antidiabetic drugs (OADs) and applied CSII therapy to subjects with type 2 diabetes who had failed to control hyperglycemia with OADs and/or insulin injections (number, 754 with 58.6 % of male; age, 58.9 ± 11.0 years; duration, 10.9 ± 7.6 years; HbA1c 9.0 ± 2.2 %). Blood samplings were performed yearly for 6 years at 12-h overnight fasting and 120 minutes after ingestion of a standard mixed meal (500 kcal; carbohydrate 52.9%, lipid 30.4%, protein 16.7%) with at least 9-h cessation of CSII.

Results During the 6 year-CSII treatment, the mean HbA1c significantly decreased from 9.0 ± 2.2 % to 6.99 ± 0.90 % ($P < 0.001$) and the mean serum C-peptide level at 120 minutes after meal ingestion (PC 2-h) significantly increased from 4.30 ± 2.47 to 5.70 ± 2.22 ng/mL ($P < 0.001$) after 6 years. The higher PC 2-h C-peptide levels were significantly associated with lower HbA1c, shorter disease duration, and higher BMI at baseline. A low BMI at baseline increased towards normal range and a high BMI at baseline decreased towards normal range during the CSII therapy.

Conclusion The resolution of glucotoxicity and maintenance of euglycemia through long-term CSII therapy may contribute to the restoration of β-cell function in terms of serum C-peptide level after meal in type 2 diabetic patients. For preservation of beta cell function and prevention of diabetic complications, the early initiation of CSII therapy is mandatory.

PE028 Clinical diabetes & therapeutics

Unsuccessful switch from insulin to sulfonylurea therapy in permanent neonatal diabetes mellitus due to an R201H mutation in the KCNJ11 gene: a case report

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Contents Permanent neonatal diabetes mellitus (PNDM) is a rare disease characterized by hyperglycemia within the first three months of life. It is permanent and requires lifelong insulin treatment. Common causes of PNDM are activating mutations in the KCNJ11 gene, which encodes the Kir6.2 subunit of the K_{ATP}-sensitive channel in pancreatic β-cells. In the previous report, all 18 patients carrying an R201H mutation in the KCNJ11 gene showed successful switches from insulin to sulfonylurea. Our patient was an 18-year-old male with an R201H mutation in the KCNJ11 gene and no DEND syndrome. At that time, he was on an insulin dose of 1.6 U/kg/day. The latest HbA1c level was 15.3% and lifestyle modification was poor. The initial glibenclamide dose was 0.2 mg/kg/day and the dose was increased up to 2.2 mg/kg/day for 4 weeks. However, there was no rapid sulfonylurea response, even though decreased insulin demand and increasing fasting C-peptide levels. Glibenclamide produced no side effects. There was a marked reduction in HbA1C from 15.3% to 10.8 % and the demand for insulin decreased from 1.6 U/kg/day to 0.91 U/kg/day. Fasting C-peptide levels increased to 0.73 ng/mL after treatment with glibenclamide at a maximal dose. We stopped glibenclamide therapy because there was no insulin independence after treatment with the maximal dose of glibenclamide for 4 weeks and because of concerns over future side effects of glibenclamide. The patient was switched back to multiple insulin therapy (insulin glargine at bedtime and insulin lispro three times a day).

Here, we report an unsuccessful switch in an 18-year-old patient carrying the common R201H mutation in the KCNJ11 gene.

PE029 Clinical diabetes & therapeutics

A case of severe hypernatremic myopathy by primary hypodipsia, hyperglycemic hypertonic state in a 17-year old patient with mental retardation

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Contents Severe hypernatremia, values above 180 mEq, is associated with a high mortality rate, particularly in adults. There are few reports about severe hypernatremia in patients with diabetic ketoacidosis (DKA). Hypernatremic myopathy have been reported with severe dehydration, acute kidney injury and rhabdomyolysis. In diabetic patient with mental retardation, dehydration can be caused by osmotic diuresis and exacerbated by hypodipsia. Therefore, intense education of regular oral hydration seems to be important. We report a 17-year-old patient with reversible severe hypernatremia (serum corrected sodium 180 mEq/L) with primary hypodipsia and without DKA. The patient visit emergency room due to agitation and weaknesses on both lower extremities. He had mental retardation, dysgenesis of corpus callosum, complete cleft palate. He showed 46XY normal karyotype in chromosomal study. Initial laboratory findings included that hyperglycemia (serum glucose 695 mg/dL), acute kidney injury (serum creatinine 1.86 mg/dL, estimated GFR 50.54 ml/min), acute hepatitis (serum AST 61 IU/L, ALT 117 IU/L), myopathy (serum CK 762 IU/L), high serum and high urine osmolarity (serum 420 mOs/kg, urine 899 mOs/kg). After hydration with quarter-isotonic saline and intensified insulin therapy, his symptoms and abnormal laboratory findings improved completely. And both leg weaknesses were also recovered.

PE030 Clinical diabetes & therapeutics

Efficacy and safety of combined insulin-sitagliptin treatment in type 2 diabetes

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Objective In recent years, the DPP-4 inhibitor sitagliptin has emerged as a new treatment for diabetes.

The combined sitagliptin–insulin therapy has been available in Japan for type 2 diabetes since November, 2011. To investigate the relationship between the effects of this new treatment and patient background, we used the conventional insulin treatment regimens supplemented with sitagliptin (50 mg).

Methods We categorized 44 type 2 diabetes cases (age, 65.6 ± 11 years; sex ratio, 29–15; BMI, 24.5 ± 4.3; HbA1c, 8.1% ± 1%, total insulin per day, 30.2 ± 17.2 units) into four groups according to the therapy regimen used: the basal-supported group, premixed insulin group, basal-bolus group, and the bolus-supported group. Then, the HbA1c levels were examined after three and six months.

Results In all the groups, HbA1c levels improved; we registered a decrease of 0.7% (to 7.3% ± 0.9%) after three months of insulin–sitagliptin treatment.

Although HbA1c has improved compared with the time of a start to 7.5 ± 0.9% also in six months, compared with the three-month back, it was getting worse +0.1%.

(All insulin groups had no predominance differences of their character.)

On the basis of our results, we also classified the patients into three categories: the responder, rebound, and non-responder group. The rebound group had higher BMI than the other groups, and the total insulin levels were low. The non-responder group consisted of older patients with a long disease history.

However, not all differences between these groups were statistically significant. Finally there were most 6.5~7.0% of HbA1c value groups, and then there was much 7.0~7.5%.

Conclusion The combined insulin–sitagliptin treatment may improve HbA1c levels in patients not responding well to the conventional insulin treatment.

PE031 Clinical diabetes & therapeutics

The association of cardiovascular events with non-albuminuric renal impairment of type 2 DM in Korean adults

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Objective Diabetes is known to increase more than three times the incidence of coronary artery disease. Microalbuminuria in patients with diabetes has been reported as an important predictor of cardiovascular disease, including coronary artery disease, and death. But, it has been reported that reduced glomerular filtration rate (GFR) may occur in some non-albuminuric diabetic patients. The aim of this study is to evaluate whether reduced GFR without albuminuria is to predict cardiovascular complications in Korean type 2 DM patients.

Methods Between November 2008 and April 2012, we analyzed 1,013 patients with type 2 diabetes who visited Diabetes Center in Pusan National University Yangsan Hospital. Patients were divided into 4 groups according to initial eGFR and urine albumin excretion rate. Group 1 was non-albuminuric renal impairment (eGFR 〈 60/mL/min, albuminuria 〈 30 ug/mL), group 2 was albuminuric renal impairment (eGFR 〈 60/mL/min, albuminuria 〉 30 ug/mL), group 3 was albuminuria only (eGFR 〉 60/mL/min, albuminuria 〉 30 ug/mL) and group 4 was normal range (eGFR 〉 60/mL/min, albuminuria 〈 30 ug/mL).

Results Of the 1,013 people from 14% of patients with type 2 diabetes who had eGFR 〈 60 mL/min, 49% of patients had non-albuminuric ranges. Non-albuminuric renal impairment group was 46 patients (4.5%), albuminuric renal impairment group was 96 patients (9.5%), albuminuria only group was 421 patients (41.6%), and normal range group was 450 patients (44.4%). Compared to the normal range group by Non-albuminuric renal impairment group had a significant correlation with increased triglyceride (P = 0.019) and decreased HDL cholesterol (P = 0.001). There was no correlation with total cholesterol, LDL cholesterol, apo B, and homocysteine.

Conclusion This preliminary data showed possibility which may evaluate the correlation of non-albuminuric renal impairment and cardiovascular disease and marker in Korean type 2 DM patients.

PE032 Clinical diabetes & therapeutics

Protective effect of a novel selective 11β-HSD1 inhibitor against glucose tolerance, adipogenesis and osteoporosis

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Objective 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) is an important regulator for maintaining local glucocorticoid levels. Selective inhibitors of 11β-HSD1 have the considerable potential for treating patients with osteoporosis as well as type 2 diabetes and metabolic syndrome. In the present study, we investigated the anti-diabetic, anti-adipogenic and anti-osteoporotic effects of KR-67500, as a novel selective 11β-HSD1 inhibitor; we also investigated the underlying molecular mechanisms in the cortisone-induced 3T3-L1 adipogenesis, the bone morphogenetic protein (BMP)-2-induced C2C12 osteogenesis model system and RANKL induced osteoclast differentiation model.

Methods To assay cellular 11β-HSD1 activity, we examined by the HTRF method. For OGTT and ITT, KR-67500 (50 mg/kg BW) was administrated by oral gavage daily for 28 days in the DIO-C57BL/6J mice. The effect of KR-67500 on lipid accumulation was determined by Oil Red O Staining. For evaluating anti-osteoporotic activity of KR-67500, BMP-2 induced C2C12 differentiation and RANKL induced osteoclast differentiation model systems were used.

Results The administration of KR-67500 (50 mg/kg/day, orally for 28 days) improved the glucose tolerance and insulin sensitivity in DIO-C57BL/6J mice. In cortisone-induced adipogenesis in 3T3-L1 cells, KR-67500 suppressed adipocytes differentiation with the suppression of the adipogenesis related genes expression and 11β-HSD1 enzyme activity. In in vitro osteoporosis model, KR-67500 enhanced the BMP-2-induced osteoblast differentiation in C2C12 cells and inhibited the RANKL-mediated osteoclast differentiation in bone marrow macrophages. Anti-osteoporotic activity of KR-67500 was also supported by the increased expression of ALP and various BMP mRNAs in the osteoblast differentiation model and the suppressed expressions of c-Fos, NEATc1, TRAP, DC-STAMP and cathepsin K in the osteoclast differentiation model.

Conclusion It is suggested that a selective 11β-HSD1 inhibitor, KR-67500, may provide a new therapeutic window in the prevention and/or treatment of type 2 diabetes with obesity and osteoporosis.

PE033 Clinical diabetes & therapeutics

Asymptomatic pancreatitis associated with DPP-IV inhibitor

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Contents DPP-IV inhibitors had been considered to be associated with acute pancreatitis. Acute pancreatitis is usually evaluated at patients showing symptoms. Hence subclinical or chronic inflammation of pancreas related with DPP-IV inhibitors is susceptible to an underdetection. We report a case of asymptomatic pancreatitis subsequent to sitagliptin treatment at therapeutic doses for blood glucose control. Patients taking DPP-IV inhibitors require more careful observation of the pancreas inflammation. A 43-year-old Korean man, on regular follow up for a management of type 2 diabetes mellitus, presented to the out-patient department with results of a routine health screening. Serum levels of amylase and lipase were 250 IU/L (reference range 54~168 IU/L) and 230 IU/L (reference range 7~60 U/L), respectively. He had no history of alcohol abuse. On presentation he had no abdominal pain and denied any symptom of pancreatitis. A contrast CT scan of the pancreas was performed that showed mild swelling of pancreas gland without peripancretic fluid collection. He had no history of pancreatitis or other known risk factors that would have caused the abnormal laboratory results. He has been treated with the combination drug of sitagliptin and metformin for 3 years to manage his diabetes mellitus. We had no data of his baseline serum amylase and lipase levels before initiation of taking sitagliptin. We ordered to stop taking the drug. On follow up evaluation approximately 6 months after discontinuation of sitagliptin, serum amylase and lipase return to normal. There has been no recurrence of asymptomatic pancreatitis.

PE034 Clinical diabetes & therapeutics

Clinical factors that influence the efficacy of liraglutide in patients with type 2 diabetes

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Objective The aim of the present study is to assess the long-term efficacy of liraglutide.

Methods Subjects consisted of 43 Japanese patients with type 2 diabetes who received liraglutide.

Results After 12 weeks, the administration of liraglutide led to significant reductions of the average HbA1c level (7.7 ± 1.7%) relative to baseline (9.1 ± 1.8%) (P 〈 0.01).

Patients who received the administration of liraglutide more than 12 weeks were classified in the long term administration group. Patients who discontinued the administration of liraglutide due to ineffectiveness within 12 weeks were classified in the short term administration group.

There was no significant difference between two groups in clinical factors such as the level of HbA1c, serum-CPR at base line, BMI and duration of diabetes. However, mean age of the short term administration group is significantly higher than that of the long term administration group (70.6 ± 12.7 vs 57.5 ± 11.3, P 〈 0.01).

Among all patients, the level of HbA1c at the base line was correlated with the improvement rate of HbA1c after 12 weeks and 24 weeks (r = 0.681, P 〈 0.01 and r = 0.817, P 〈 0.01).

Among the patients who switched from insulin to liraglutide, the insulin dose was inversely correlated with the improvement rate of HbA1c after 24 weeks (r = 0.443, P 〈 0.05).

Conclusion It is possible that liraglutide is more effective with young patients than with elderly patients. Moreover, liraglutide is likely to be effective with patients whose levels of HbA1c at the base line are high and with patients who receive fewer doses of insulin.

PE035 Clinical diabetes & therapeutics

Pregnancy outcomes in women with type 1 and type 2 diabetes

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Objective Pregestational diabetes mellitus (PGDM) has known to be associated adverse perinatal outcomes. The purpose of this observational study was to assess and to compare glycemic control, maternal and neonatal outcomes in women with T1DM and T2DM.

Methods We performed a retrospective survey of 163 pregnancies in women with PGDM from 2003 to 2010 in Cheil General Hospital, Korea. Subjects were grouped into 11 women with T1DM and 152 with T2DM. We compared the glycemic control as well as maternal and neonatal outcomes between two groups.

Results Compared to T1DM, women with T2DM were significantly heavier (pregnancy BMI 25.4 ± 4.9 vs. 19.5 ± 2.8 kg/m^2, P 〈 0.001). Women with T2DM had more family history of DM than women with T1DM (75.7 women vs. 18.2%, P 〈 0.001). T2DM had glycemic control in the 1st trimester as measured by HbA1c (7.0 ± 1.4 vs. 6.2% ± 1.1, P = 0.106). We observed a decrease of HbA1c level in both groups in the 2nd trimester (5.7 ± 0.9 vs. 5.9% ± 1.0, P = 0.542) and 3rd trimester (6.2 ± 0.8 vs. 5.8% ± 0.4, P = 0.295). The differences in HbA1c were not significant. The cesarean section (36.8 vs. 45.5%), birth weight (3,378.1 ± 537.1 vs 3,371.3g ± 669.0), perinatal mortality (0 vs. 0%), and the rate of major congenital malformations (4.9 vs. 9.1%) were similar in both groups. However, women with T1DM had higher PIH (8.1 vs. 45.5%, p = 0.002) and preterm labor (6.6 vs. 27.3%, P = 0.046) than those with T2DM.

Conclusion In this study we found similar pregnancy outcomes and neonatal outcomes in women with T1DM and T2DM except PIH and preterm labor.

PE036 Clinical diabetes & therapeutics

Comparison of LDL cholesterol concentrations by friedewald calculation and direct measurement for evaluation of Plasma LDL-cholesterol in patients with type 2 diabetes

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Objective In most clinical practice, low density lipoprotein (LDL) cholesterol is usually estimated indirectly with the Friedewald equation (LDL-C = TC − (HDL-C 1 triacylglycerols / 5)) or directly. But it remains unclear how direct measurement compares with the Friedewald calculation in evaluating hypercholesterolemia. The aim of this study was to compare LDL-cholesterol values obtained by both methods on the diagnosis of hypercholesterolemia.

Methods We examined 2640 patients with type 2 diabetes enrolled in REBOUND study being conducting by multi center endocrinologists of one city. We checked their clinical characteristics including age, sex, and BMI and laboratory tests of total cholesterol, Triglyceride, LDL cholesterol, and HDL cholesterol. LDL-cholesterol was also estimated indirectly with the Friedewald equation. And we compared LDL-cholesterol values obtained by both methods. In this study, we excluded patients whose triglyceride levels exceeded 400 mg/dL (n = 74).

Results They had the fellowing characteristics: age 59.30 ± 10.94 years, M/F 44.7 : 55.3. The mean direct LDL-C was 95.12 +/- 41.76 mg/dL and the mean Friedewald LDL-C was 95.63 +/- 46.79 mg/dL. The LDL-cholesterol values obtained by both methods was not different (P = 0.541, by paired t-test). Direct LDL-C showed a significantly positive correlation with Friedewald LDL-C (R = 0.551, P 〈 0.0001). Also, the frequency of study subjects diagnosed with hypercholesterolemia, defined as LDL-C 〉 or = 100 mg/dL, was not different.(38.23% in the direct measurement, 37.33% in the Friedewald calculation).

Conclusion We demonstrated that the direct measurement showed similar rate of hypercholesterolemia prevalence with the Friedewald calculation. This result suggests that we can use indirect method measuring LDL-C in the clinical diagnosis and management decisions of hypercholesterolemia.

PE037 Clinical diabetes & therapeutics

The effect of aerobic and resistance exercise on left ventricular function in diabetic heart

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Objective Type 2 Diabetes mellitus (T2DM) is related to left ventricular (LV) structural and functional abnormality, indicating concentric LV geometry. Although exercise effectively treats in diabetic heart, the mechanism leading to exercise-induced improvement is unclear. In this study, we investigate the effects of aerobic and resistance exercise on cardiac function in diabetic rats.

Methods At the age of 25 weeks, Otsuka Long-Evans Tokushima fatty (OLEFT) rats were divided into aerobic exercise (EXA, n = 7), resistance exercise (EXR, n = 7), sedentary control (SED, n = 7) and Long-Evans Tokushima Otsuka (LETO, n = 7) groups as normal control. EXA groups were treated for 30~60 minutes at 10~20 m/min on the treadmill and EXR groups climbed ladder inclined at 85 degrees with weights attached to their tails. Both of exercise was performed 5 days/week for 12 weeks. After exercise, intraperitoneal glucose tolerance tests, lipid metabolism studies and echocardiography were done and LV mass index (LVMI) and relative wall thickness (RWT) were analyzed.

Results We observed significantly decreased glucose uptake, lipid metabolism in SED rats compared to LETO rats. SED rats indicated increased RWT and decreased LVMI, indicating concentric remodeling compared to LETO rats. Both of exercise improved glucose tolerance and lipid metabolism. EXA and EXR rats significantly reduced wall thickness (intraventicular septum, posterior wall) and increased LV chamber size (LVIDd, EDV) in diabetes. LVMI and RWT were reduced in EXA and EXR rats compared with SED rats.

Conclusion Our results suggested that T2DM shows thickened wall and diminished LV chamber, indicating as concentric remodeling and exercise training confers recovery against diabetes-induced morphological heart change. Further studies will be required to reveal the molecular mechanism of aerobic and resistance exercise-induced protection or recovery from cardiac damages in diabetes.

PE038 Clinical diabetes & therapeutics

The effects of 1,2month subcutaneous administration of exendin-4 on body composition in obese type 2 diabetes mellitus

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Objective The majority of patients with T2DM are obese and suffer from eating disorders. Drug therapies with insulin, glitazone and sulfonylurea actually result in weight gain worsening these problems. The weight control for the T2DM management should aim to redue lipocytes and to maintain muscle strength. Therefore, the authors aim to examine the effects of Exendin-4 on the body composition of obese T2DM.

Methods 5 ug of Exendin-4 was initially administered to T2DM whose BMI was above 25 kg/m^2 twice a day for a month and the dosage was increased to 10ug afterwards. The patients' height, weight, BMI, body fat mass and muscle mass were measured with an inbody prior to the experiment after a month and after the two months.

Results The weight, the BMI, the % body fat, the muscle mass and the body fat mass measured after a month were 87.90 ± 13.44 vs 85.92 ± 13.28 (P = 0.001), 33.32 ± 4.46 vs 32.96 ± 4.32 (P = 0.003), 40.27 ± 6.95 vs 38.46 ± 7.57 (P = 0.064), 28.89 ± 6.09 vs 29.23 ± 6.31 (P = 0.824) and 35.18 ± 7.95 vs 33.13 ± 8.40 (P = 0.003) respectively. Of 21 subjects, only 9 patients were treated with the medication for two months. The differences after months were recorded as 88.06 ± 13.23 vs 84.67 ± 15.03 (P = 0.008), 35.18 ± 5.07 vs 33.80 ± 5.53 (P = 0.008), 43.28 ± 7.22 vs 42.95 ± 7.33 (P = 0.063), 27.51 ± 5.96 vs 26.84 ± 6.59 (P = 0.128) and 38.13 ± 8.62 vs 36.90 ± 9.28 (P = 0.017) respectively.

Conclusion The short-term use of Exendin-4 in obese T2DM reduced BMI and body fat mass without losing muscle mass.

PE039 Clinical diabetes & therapeutics

Adipose tissue inflammation and OXPHOS function according to body mass index

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Objective The aim of this study is to determine the role of inflammation and OXPHOS function of visceral adipose tissue in insulin resistance related to obesity.

Methods A total 58 women undergoing obstetric operation were recruited after informed consent. Oral glucose tolerance test was performed and omental adipose tissue samples were obtained in all subjects. Serum levels of hsCRP, adiponectin, resistin, leptin, MCP-1, TNF-α, IL-1β were measured using multiplex cytokine/chemokine array. OXPHOS expression was quantified using quantitative PCR and western blotting.

Results Mean body mass index (BMI) was 23.74 ± 2.83 (Kg/m^2) and mean fasting glucose was 101.98 ± 23.69 (mg/dL) and mean HbA1c was 5.57 ± 1.06 (%), which mean subjects were relatively non-obese and non-severe hyperglycemic. Leptin concentration was higher and adiponectin was lower in obese group (BMI ≥ 25) than lean group (BMI 〈 25). However serum hsCRP, IL-1β, MCP-1, TNF-α, CD68 mRNA expression were not different between two groups. CRIF-1 protein expression was decreased in obese group. ND1, NDUFA9, COX4, ATP5A1 pretein expression were not different between two groups, however, ND1, NDUFA9, COX4, ATP5A1 mRNA expression were increased in obese group.

Conclusion In this sample of relatively non-obese Korean, circulating biomarkers of inflammation, adipose tissue Macrophage and OXPHOS complex protein expression were not different according to BMI. Some other factors should be evaluated for insulin resistance and glucose intolerance according to BMI in non-obese Korean.

PE040 Clinical diabetes & therapeutics

Restoration of the first-phase insulin secretion and a decline in fat mass are predictors for achieving long-term glycemic control after early intensive insulin therapy in patients with newly diagnosed type 2 diabetes

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Objective Recently, early intensive insulin therapy was reported to improve b-cell function and induce long-term remission in patients with newly diagnosed type 2 diabetes. However, the possible mechanisms responsible for this disease-modifying effect are still unclear. We retrospectively evaluated clinical characteristics of patients with newly diagnosed type 2 diabetes, who achieved a long-term glycemic control after early intensive insulin therapy.

Methods A total of 59 subjects with newly diagnosed diabetes participated in a 12 week course of intensive insulin therapy and followed up for 1year. The patients underwent a 75 g oral glucose tolerance test (OGTT) and an assessment of body composition using computed tomography and dual-energy X-ray absorptiometry before and after intensive insulin therapy.

Results According to post-insulin therapy OGTT, patients were categorized diabetes group (n = 31) and non-diabetes group n = 28). At 1 year follow up, all patients with diabetes group was received either insulin or oral hypoglycemic agents. Among patients with non-diabetes group, excluding 2 patients lost to follow up, 11 patients achieved long-term glycemic control without pharmacologic therapy, but remaining 15 patients were maintained pharmacologic therapy at 1 year follow up. There is no significant difference in clinical characteristics at baseline between patients with or without maintaining pharmacologic therapy. Compared to a total of 46 patients with maintaining pharmacologic therapy, b-cell function as identified by the insulinogenic index (P 〈 0.001) was improved significantly after intensive insulin therapy in those patients with achieving long-term glycemic control without pharmacologic therapy. In addition, the increment of the insulinogenic index (P 〈 0.001) and a loss of fat mass (P = 0.018) were significant before and after intensive insulin therapy in this subgroup.

Conclusion These findings suggest that the improvement of early-phase insulin secretion could be an important mechanism for the maintaining long-term glycemic control without anti-diabetic medication after early intensive insulin therapy in patients with newly diagnosed type2 diabetes.

PE041 Clinical diabetes & therapeutics

The clinical usefulness of cystatin C in patients with type 2 diabetes mellitus

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Objective Diabetic nephropathy is a risk factor for atherosclerotic cardiovascular disease, heart failure, and their mortality. Although microalbuminuria is used as a marker of early diabetic nephropathy, it has low accuracy. Recently, Cystatin C has been shown as a surrogate marker of renal dysfunction and it is more sensitive to detect mild decrease of GFR than serum creatinine. The present study was aimed to investigate the usefulness of Cystatin C detecting renal insufficiency and as a cardiovascular risk factor in patients with type 2 diabetes mellitus (T2DM).

Methods We conducted a retrospective observational study of total 666 (M:F = 341:324, mean age : 63.0 ± 10.2) subjects with T2DM who visited Yeungnam University Hospital in 2011 and 2012. Urinary albumin excretion rate (UAER) and Cystatin C levels were analyzed according to estimated GFR (eGFR). Additional subgroup analysis was performed in subjects who were examined brachial artery pulse wave velocity (BaPWV), ankle-brachial index (ABI) and echocardiography.

Results Cystatin C was more closely associated with eGFR than UAER ($P < 0.05$). In subjects without albuminuria (UAER < 30 mg/dL), Cystatin C based GFR was significantly associated with BaPWV negatively and with ABI positively ($P < 0.05$). And it had significant negative association with left ventricular mass index and E/E' estimated by echocardiography ($P < 0.05$).

Conclusion Serum Cystatin C may be a more useful surrogate marker of renal insufficiency than UAER in patients with T2DM. In addition, Cystatin C based GFR may be helpful in predicting risk of atherosclerosis, left ventricular hypertrophy and diastolic cardiac dysfunction in type 2 diabetics without albuminuria. To confirm these results, prospective large multicenter trials are needed.

PE042 Clinical diabetes & therapeutics

The effect of high-dose vitamin D supplementation on glycemic control and arterial stiffness

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Objective Vitamin D deficiency is very common in Korea. It is well established that vitamin D affects bone health via calcium homeostasis. Recent epidemiologic studies showed the striking inverse relationship among vitamin D level, cardiovascular disease, and insulin resistance/glucose intolerance. But there are few interventional studies that evaluate the causal relationship among vitamin D, glycemic control, and vascular function.

We investigated the role of high-dose vitamin D on glycemic control and arterial stiffness in type 2 diabetic patients.

Methods We enrolled type 2 diabetic patients who took antidiabetic agents or managed diabetes by lifestyle modification. We excluded patients who took vitamin D or calcium. We also excluded chronic kidney disease patients (in men: Cr > 1.5 mg/dL, in women: Cr > 1.4 mg/dL) and heavy alcoholics. We randomized participants into 2 groups: intervention group (Vitamin D 2000 IU/day + Calcium 200 mg/day) or placebo group (Calcium 200 mg/day). We compared HbA1c, brachial-ankle pulse wave velocity (baPWV) for the study period.

Results We randomized 81 participants into placebo (n = 41) and intervention (n = 40) group. There was no difference in glycemic control (HbA1c 7.54 ± 0.50% vs 7.50 ± 0.49% in placebo and intervention group, respectively), diabetes duration, oral antidiabetic agents, body mass index, and baPWV between groups. 62 participants completed the 24-week study. In the end of study, HbA1c was 7.49 ± 0.62% in placebo group and 7.63 ± 0.69% in intervention group (P = 0.417). There was no difference in adjusted means of baPWV (Rt baPWV 1498 ± 46 cm/sec vs 1549 ± 42 cm/sec, Lt baPWV 1478 ± 49 vs 1542 ± 44 cm/sec) after controlling for age, sex, diabetes duration, and pulse pressure.

Conclusion Daily 2000 IU vitamin D supplementation in short-term period may be inefffective in lowering blood glucose and ameliorating peripheral arterial stiffness.

PE043 Clinical diabetes & therapeutics

Prevention on alloxan-induced diabetes by ribes diacanthum pall methanolic extract in mice

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Objective The objective of this study was investigate the hypoglycemic and preventive effects of Ribes Diacanthum Pall (RDP) extract in animal models of diabetes mellitus (DM).

Methods Antihyperglycemic activity of different doses of Ribes Diacanthum Pall methanolic extract (MRDP) was evaluated by oral administration of MRDP in alloxan-induced diabetic mice. Hyperglycemia was induced by intraperitoneal administration of alloxan (50 mg/kg). The body weight, liver and kidney weight changes and blood levels of glucose, cholesterol and triglyceride were measured.

The mice treated with MRDP at a different doses of 50, 100 mg/kg b.w/day for 2 weeks, respectively.

The antihyperglycemic activity of a daily oral dose of MRDP for 14 days was evaluated by measuring the fasting blood glucose and peak of blood glucose level within 120 min of oral glucose tolerance test (OGTT) in diabetic mice.

Results The MRDP extract significantly reduced the blood glucose level in experimentally diabetic mice while no significant was shown on normal mice.

The levels of glucose, urea nitrogen, AST, ALT, HDL and TG were significantly ($P < 0.05$) increased in plasma of alloxan-induced diabetic mice with the control group. The single doses for the methanol extract (50, 100 mg/kg) significantly decreased in serum triglycerides levels. The liver and kidney weight /100 g B.W. in diabetic group were greater than those of normal group but after treatment group, liver and kidney weight were decreased significantly.

Conclusion RDP had been shown to have a hypoglycemic effect in diabetes this is the first demonstration of a preventive effect of RDP on alloxan-induced diabetes.

PE044 Clinical diabetes & therapeutics

Possible evidence of a novel mutation from the first case of Werner syndrome in Korea

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Objective Werner syndrome (WS) is an autosomal recessive genetic disease that causes adult-onset progeria. It has been found to be associated with a *WRN* (RecQ protein-like 2) gene mutation in > 90% of patients with WS. We recently identified a patient with clinically relevant WS for the first time in Korea and performed experiments to elucidate the pathogenesis in this patient.

Methods The patient was a 54-year-old male with a medical history and clinical manifestations consistent with the textbook definition of WS. We performed a sequencing analysis of genomic DNA to identify the *WRN* mutation. In addition, we estimated telomere length and hSIRT1 expression to molecularly validate the patient's age.

Results Despite clinical consistency, no mutations were found in 34 exons or any exon-intron boundaries within the *WRN* gene of the patient. In addition, no mutations were found in the splicing junction of the coding region and exon-intron boundary within the *WRN* gene. However, the telomere length of the patient was significantly shorter and hSIRT1 expression was significantly lower than control subjects.

Conclusion Based on the clinical manifestations and present experiments, we definitively diagnosed this patient with WS. However, the results also suggested that a novel mutation involving a gene other than *WRN* may have played an important role in the pathogenesis of this patient.

PE045 Clinical diabetes & therapeutics

Frequency of metabolic syndrome according to increasing fasting blood glucose level in healthy elderly in Korea

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Objective High levels of fasting glucose is one of the components of metabolic syndrome. In previous our data, increasing fasting glucose within normal range is associated with metabolic syndrome in all ages. So, we investigated the relations in case of elderly, separately.

Methods Data was obtained from 24603 individuals who underwent health examination in Eulji medical center from January 2006 to June 2007. We selected nondiabetic patients aged 65 and over. Fasting glucose, Waist circumference, blood pressure and lipid profile of 707 individuals were obtained. After dividing the participants into 4 groups according to quartile of fasting glucose level, each groups were compared with the frequency of metabolic syndrome and metabolic parameter, respectively.

Results The total number of people who had normal fasting glucose was 624 and 10.4 %(76 individuals) had metabolic syndrome. The prevalence of metabolic syndrome of men was higher than women (77.6% vs. 22.4%, $P < 0.01$). Fasting glucose levels ranged from 58 mg/dL to 99 mg/dL. As increasing fasting glucose levels, the frequency of metabolic syndrome was increasing without statistically significance. However, fasting glucose levels were significantly related with metabolic parameter in metabolic syndrome ($P < 0.05$).

Conclusion In non-diabetic elderly with normal glucose level, fasting glucose level within normal range was not correlated with the frequency of metabolic syndrome but associated with metabolic parameters in metabolic syndrome, significantly. Although this results is differed from a previous our data that was obtained from a survey in all ages, it suggest that increasing fasting glucose level also is key marker of metabolic derangement, not metabolic syndrome in healthy elderly.

PE046 Clinical diabetes & therapeutics

Comparison of serum markers for assessment of short-term changes of glycemic variability in type 1 diabetes

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Objective Patients with type 1 diabetes have been reported that show more severe glycemic variability than patients with type 2 diabetes. Glycemic variability is closely correlated with poor glycemic control and cardiovascular complications. The aim of this study was to establish which serum glycemic markers are appropriate for assessment of short-term changes of glycemic variability in type 1 diabetes.

Methods Seventeen patients with type 1 diabetes treated with multiple insulin injections or continuous subcutaneous insulin infusion were enrolled. For evaluation of changes of glycemic variability, continuous glucose monitoring system was applied twice to each subject with two weeks interval. The changes of HbA1c, glycated albumin and 1,5-anhydroglucitol (1,5-AG) were also evaluated.

Results The change of glycated albumin showed correlation with the change of mean amplitude of glucose excursion (MAGE) ($r = 0.517$). The change of 1,5-AG strongly correlated with the changes of most variability indicators, such as MAGE ($r = -0.613$), lability index ($r = -0.600$), mean postmeal maximum glucose ($r = -0.630$), and area under the curve for glucose above 180 mg/dL ($r = -0.500$). However, the change of HbA1c did not correlate with the changes of any variability indicators.

Conclusion For assessment of short-term changes of glycemic variability in type 1 diabetes, glycated albumin and especially 1,5-AG could be a valuable marker.

PE047 Clinical diabetes & therapeutics

Beta cell function evaluated by HOMA as a predictor of long term hypoglycemic effect of pioglitazone

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Objective The glycemic response to TZD is variable among individuals, and several studies indicate that patients with greater insulin resistance or lower HDL levels display better glycemic response to TZD, however, the treatment periods were relatively short. Thus, we investigated the patient factors associated with long-term hypoglycemic effect of pioglitazone in routine clinical practice.

Methods This was a retrospective analysis of type 2 diabetic patients who were newly initiated on pioglitazone in 2006, and maintained for more than 48 months without dose-up of another medication. Baseline plasma lipid concentration, pancreatic β-cell function, and insulin resistance levels using the homeostasis model assessment (HOMA) were checked. HbA1c concentrations were measured every 6 months after pioglitazone treatment.

Results A total of 158 patients (M:F = 76:82, mean age: 59.1 ± 9.3 years) were enrolled. The mean HbA1c was 7.7 ± 1.4% at baseline, 6.8 ± 0.9 % after 6 months, and 6.6 ± 0.6 % after 48 months of pioglitazone treatment. When stratified according to tertile of baseline HOMA-IR, although the baseline HbA1c was higher in the 3rd tertile, the degrees of glycemic control were comparable. However, regarding baseline HOMA-B, HbA1c level after 48 months were lower in the highest HOMA-B group (6.79 ± 0.60 % vs. 6.78 ± 0.66 % vs. 6.41 ± 0.53 %, $P = 0.002$) as well as the proportion of patients who achieved a target HbA1c of ≤ 7%, were higher (69.8% vs. 66.0% vs. 88.5%, $P = 0.029$). Moreover, in multiple logistic regression analysis, HOMA-B retained their significance as the independent predictors for long term glycemic control (C.I. 1.005-1.037, $P = 0.009$).

Conclusion These results suggest that better hypoglycemic effect of pioglitazone treatment is expected in the patients with reserved beta cell function after long term treatment.

PE048 Clinical diabetes & therapeutics

Effects of a 6-month exenatide therapy on HBA1c and weight in Korean diabetic patients with insulin therapy

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Objective This study was designed to analyze the effects of exenatide on blood glucose level and body weight in Korean diabetic patients with insulin therapy.

Methods We reviewed the records of the patients with diabetes who visited Seoul St. Mary's Hospital and for whom exenatide was prescribed from June 2009 to October 2011. After excluding the subjects for race/ethnicity, medical history, loss to follow-up, or stopping of the exenatide therapy within 6 months, 24 subjects were included in the final analysis.

Results The mean glycated hemoglobin (HbA1c) level and weight were remarkably decreased from 8.5 ± 1.6% to 7.6 ± 1.2% ($P = 0.015$) and from 75.9 ± 13.5 kg to 72.8 ± 13.8 kg ($P < 0.001$), respectively. The reduction in HbA1c level was significantly associated with higher baseline HbA1c level ($P < 0.001$) whereas weight loss had no significant correlation with other factors.

Conclusion These results suggest that the 6-month exenatide injection therapy significantly improved the HbA1c levels and body weights without causing serious adverse effects in the Korean diabetic patients with insulin therapy.

PE049 Clinical diabetes & therapeutics

Therapeutic effects of NecroX-7 on nonalcoholic steatohepatitis by suppressing mitochondrial ROS/RNS and inflammatory responses

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Objective Nonalcoholic steatohepatitis (NASH) is associated with systemic and hepatic insulin resistance and induces liver fibrosis, end-stage cirrhosis, and hepatocellular carcinoma. ROS/RNS play the key roles in the development of NASH through hepatocyte stress, chronic inflammation, and insulin resistance. However, the therapeutic molecular target of NASH has not been fully addressed. We here show that the beneficial effects of NecroX-7 (novel ROS scavengers) on NASH in leptin deficient ob/ob mice.

Methods Six weeks old male (N = 10 per group) ob/ob mice were daily administered with NecroX-7 (LGLS Inc.) and control vehicle for 12 weeks. The effect of NecroX-7 on NASH progression was evaluated using biochemical, histological, and molecular makers

Results NecroX-7 inhibited *Tert*-butylhydroperoxide and H_2O_2 induced cytosolic ROS/RNS and mitochondrial superoxide formation in primary hepatocytes. NecroX-7 treated ob/ob mice revealed markedly decrease of serum AST/ALT and fasting blood glucose compared to control group. Interestingly, hepatic macro- and micro-vesicular steatosis, and lipid peroxidation significantly improved compared to control group. Body weights between control and treated group did not show statistical differences. Furthermore, NecroX-7 treated mice exhibited a lower degree of kupffer cell activation, reduced expression and secretion of TNF-α in the liver.

Conclusion NecroX-7 improved steatosis of liver in ob/ob mice through suppression of mitochondrial ROS/RNS and inflammatory responses, suggesting that NecroX-7 has potential therapeutic effects on steatohepatitis.

PE050 Clinical diabetes & therapeutics

Synthesis of lepidagathis hyalina nees: An investigation for novel drugs of anti-diabetic activities as probes for pharmacological cohort

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Objective Plants, being the major source of many drugs, have attracted scientists from ancient times. In the present era of medical engineering, plants play an equality important role in drug discovery and development. From this point of view to find out the domestic or industrial utilization (if any) of the plants, *Lepidagathis hyalina* Nees has been studied for anti-diabetic activities. *Lepidagathis hyalina* Nees is a branched annual herb and belongs to the family Acanthaceae Juss.. The stems, leaves, and roots of this herb are used for the remedy of killer diseases as well as debilitating diseases.

Methods The hot water and ethanol extracts of *Lepidagathis hyalina* Nees collected from the Bangladesh exhibited a significant hypoglycemic (blood glucose lowering) activity in both glucose-loaded and alloxan-induced diabetic rats.

Results Oral administration of glucose (1.5 g/kg body weight) increased the blood sugar level while the intraperitoneal administration of alloxan (40 mg/kg body weight) enhanced the blood sugar level much higher than that of the glucose-loaded rats. The hot water (0.8 g/kg body weight) and ethanol extracts (2 g/kg body weight) of *Lepidagathis hyalina* Nees reduced the elevated glucose level by 41.51% and 41.82% respectively in glucose-loaded rats as compared to the respective diabetic control rats. On the other hand, administration of hot water and ethanol extracts of *Lepidagathis hyalina* Nees decreased the blood sugar level by 46.21% and 45.13% respectively in alloxan-induced diabetic rats, when compared with that of diabetic control rats. Processing and physiochemical screening of *Lepidagathis hyalina* Nees is also carried out by the developed technologies.

Conclusion The work will increase the potentially of *Lepidagathis hyalina* Nees for the production of various pharmaceutical raw materials and new drugs of Bangladesh to a large extent. The plant is rapidly becoming endangered, it is important to perform scientific studies which may lead to discoveries of novel drugs.

PE051 Clinical diabetes & therapeutics

Comparison of efficacy and safety between metformin and carnitine orotate complex combination and metformin alone in subjects with non-alcoholic fatty liver disease: Results of a double-blind, placebo-controlled study

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Objective We compared the efficacy and safety between metformin and carnitine orotate complex combination and metformin alone in a 12-week, double-blind, randomized, placebo-controlled study in drug naïve patients with impaired glucose metabolism and fatty liver.

Methods Fifty-two patients with fasting glucose ≥ 100 mg/dL or HbA1c ≥ 6.5% and alanine aminotransferase (ALT) 40~250 IU/L were randomized to receive metformin (250 mg tid), or metformin (250 mg tid) and carnitine orotate complex (824 mg tid) for 12 weeks (n=26 in each group). The primary endpoint was the changes from baseline ALT level. The secondary endpoints were the changes of fasting glucose, HbA1c, aspartate aminotransferase (AST), urine 8-hydroxy-2′-deoxyguanosine (8-OHdG), a oxidative stress marker, and peripheral blood mitochondrial DNA (mtDNA) copy number.

Results Combined treatment of metformin and carnitine orotate complex reduced ALT level significantly: −51.5 ± 33.2 IU/L ($P < 0.001$) with significant difference with metformin alone (−16.7 ± 31.3 IU/L, $P = 0.015$). The changes in AST and HbA1c levels followed the same pattern but not statistically different: −10.5 ± 25.6 IU/L and 0.86 ± 1.01% for metformin and carnitine orotate complex vs. −7.6 ± 20.8 IU/L and 0.68 ± 0.86% for metformin alone, respectively. Urine 8-OHdG level decreased more by the treatment of metformin and carnitine orotate complex than metformin alone ($P = 0.033$) while mtDNA copy numbers were not different. No severe adverse events were observed in both groups.

Conclusion A 12-week treatment with metformin and carnitine orotate complex significantly improved liver function enzyme and reduced oxidative stress marker compared to metformin alone in patients with impaired glucose metabolism and fatty liver.

PE052 Clinical diabetes & therapeutics

Toe-brachial index is associated more strongly with progression of diabetic nephropathy than ankle-brachial index in type 2 diabetic patients

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Objective Atherosclerosis is more prevalent among people with chronic kidney disease (CKD) than among those with normal renal function. Ankle-brachial index (ABI) and toe-brachial index (TBI) are a simple useful method for assessing peripheral atherosclerosis. The aim of our study was to investigate whether ABI or TBI were more strongly associated with progression of diabetic nephropathy such as change of urinary albumin/creatinine ratio (ACR), serum creatinine levels and estimated glomerular filtration rate (eGFR).

Methods We recruited a total of 149 type 2 diabetics: 62 men (mean age 62.4 ± 12.1 years) and 87 women (mean age 60.3 ± 10.9 years) with CKD (≥ stage 2) by diabetic nephropathy and followed for 1.6±1.2 years. Renal function was evaluated by serum creatinine levels, estimated eGFR (calculated by the Cockcroft-Gault equation) and urinary ACR. Baseline-to-study end changes in eGFR were calculated, and yearly change of eGFR (mL/min/year) was computed. ABI and TBI measurements were performed with the subject in a supine position, and were determined as the ratio of ankle or toe systolic blood pressure to the brachial SBP, with both determined using an automatic device.

Results Overall, the mean age was 61.2 ± 11.0 years, duration of diabetes 13.8±10.5 years, HbA1C 7.9 ± 2.2%, ACR 1,635.2 ± 783.3 mg/gCr, serum creatinine 1.6 ± 1.1 mg/dL, and systemic BP 141.0 ± 23.7/91.5 ± 19.2 mmHg. Mean calculated GFR was 62.8 ± 27.1 mL/min/1.73m^2. ABI were 1.05 ± 0.24 (Rt.) and 1.01 ± 0.20 (Lt.). TBI were 0.73 ± 0.31 (Rt.) and 0.79 ± 0.22 (Lt.). Age, duration of diabetes, serum creatinine, ACR and eGFR were significantly correlated with ABI or TBI. Mean yearly change of eGFR was 7.2 ± 10.4 mL/min/year. Yearly change in the eGFR was negatively correlated with TBI, but not with ABI. By Univariate linear regression, TBI but not ABI showed a significant negative correlation with yearly change in the eGFR ($r = -0.309$, $P < 0.05$).

Conclusion This study demonstrated that TBI may be predictor of progression of diabetic nephropathy in patients with type 2 diabetes.

PE053 Clinical diabetes & therapeutics

Effects of D-α-tocopherol supplements on lipid metabolism in a high-fat diet-fed animal model

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Objective A high-fat diet up-regulates either insulin resistance or triglycerides, which is assumed to be related to the expression of peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ. The beneficial effects of vitamin E on insulin resistance are well known, however, whether vitamin E with a high-fat diet alters the expression of PPAR-α and PPAR-γ remains unknown. We investigated the effects of d-α -tocopherol supplementation on insulin sensitivity, blood lipid profiles, lipid peroxidation and the expression of PPAR-α and PPAR-γ in the high-fat (HF) diet-fed male C57BL/6J model of insulin resistance.

Methods The animals were given a regular diet (CON; 10% fat), a HF diet containing 45% fat, or a HF diet plus d-α-tocopherol (HF-E) for a period of 20 weeks.

Results The results showed that the HF diet produced insulin resistance and altered the lipid profile, specifically the triglyceride (TG) and total cholesterol (TC) levels ($P < 0.05$). In this animal model, supplementation of d-α-tocopherol improved significantly insulin resistance and the serum levels of TG, very-low-density lipoprotein-cholesterol (VLDL-C) ($P < 0.05$). It decreased the levels of malondialdehyde (MDA) in the serum as well as in the liver. Moreover, an increase in hepatic PPAR-α expression and a decrease in PPAR-γ expression were noted.

Conclusion In conclusion, the oral administration of d-α-tocopherol with a high-fat diet had positive effects on insulin resistance, lipid profiles, and oxidative stress through the expression of PPAR-α and PPAR-γ in mice.

PE054 Clinical diabetes & therapeutics

A case of polyglandular autoimmune syndrome type III

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Contents In patients with an autoimmune endocrine disease, there is a high risk of development of another autoimmune endocrine disorder. The coexistence of two or more autoimmune endocrine diseases is pathognomonic for polyglandular autoimmune(PGA) syndrome. The hallmark of PGA syndrome type III is the absence of adrenal insufficiency. Autoimmune thyroiditis and type 1 diabetes mellitus are the most common combination of autoimmune endocrine diseases reported. Autoimmune thyroiditis and latent autoimmune diabetes in adults are rarely reported. Recently, it is difficult to distinguish between type 1 diabetes and type 2 diabetes. A 31-year old man presented with polyuria, polydipisia, and weight loss of classic symptoms of immune-mediated diabetes. He was diagnosed with Graves' disease about 2 years ago. Serum glucose level was elevated (glucose 839 mg/dL, Hb A1c 11.7%). However, there was not ketoacidosis. Glutamic acid decarboxylase (GAD) antibody that is specific for immune-mediated diabetes was positive (serum anti GAD Ab 330 U/mL (< 1 U/mL)). In addition, the titers of thyroid microsomal antibody, TSH receptor antibody, and thyroglobulin antibody were all high. We report a case of PGA syndrome type III manifesting diabetes mellitus, Graves' disease, and vitiligo. In this adults patient with the presence of GAD antibody, the follow-up of clinical course is necessary and HLA halotypes testing is considered.

PE055 Clinical diabetes & therapeutics

Medical staff experience and acceptance of an insulin infusion protocol in a tertiary hospital in the philippines

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Objective To evaluate medical staff experience and acceptance of the protocol through a survey and focused group discussion.

Methods A survey followed by focused group discussions among the medical staff of the Medical and Central Intensive Care Units were done. Questionnaires were distributed to the nurses of the two ICU units and the medical residents who manned in these ICUs. The survey focused on assessment of their experience and acceptance of the insulin protocol. Focused group discussions were done after the survey to clarify and confirm the information derived from the survey.

Results A total of 110 medical staff (48 nurses and 62 medical residents) participated in the study. For nurses, most consider their knowledge of the protocol to be good. Majority believe the insulin protocol is effective in controlling hyperglycemia and preventing hypoglycemia. While 77% of nurses held that the protocol increases their workload due to frequent glucose checks and need for computations to adjust the insulin drip rates, majority (69%) agree that the protocol is easy to administer. Sixty-nine percent have high to very high level of satisfaction with the use of the protocol. Similarly, majority of medical residents who manned the ICUs believe that the protocol is effective in achieving glycemic control. While most felt that the protocol is not easy to administer and increases workload, majority would still opt to use the protocol for their patients. The staff believe that periodic training and provision for supplies were key factors in improving the protocol.

Conclusion Experience and acceptance of the insulin infusion protocol is generally excellent for nurses and physicians in the intensive care units. Despite an increase in workload, most believe the protocol to be effective and would advocate its use for ICU patients.

PE056 Insulin action & obesity

Effect of overfeeding in obese humans

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Objective Although obesity is associated with metabolic dysfunction and ectopic fat accumulation, it is unknown whether overfeeding and a moderate increase in body weight in obese subjects results in additional adverse effects on metabolic function and fat distribution. Therefore we evaluated the effect of overfeeding an additional 1000 kcal/day from fast food restaurants on insulin sensitivity and ectopic fat distribution in 11 obese subjects (1 male, age = 44 ± 10 y, BMI = 34 ± 3 kg/m^2).

Methods A two-stage (7 and 50 mU/m^2/min) hyperinsulinemic-euglycemic clamp procedure in conjunction with stable isotope tracer infusion was used to assess hepatic and skeletal muscle insulin sensitivity. Magnetic resonance (MR) spectroscopy, MR-elastography and MR-imaging were used to measure intrahepatic triglyceride (IHTG) content and stiffness, and visceral adipose tissue [VAT], respectively. These measurements were obtained at baseline and after a 6 ± 1% (5 ± 1 weeks) weight gain was achieved.

Results Overfeeding caused an increase in total body fat (12±4%), fat-free mass (2 ± 1%), and VAT (10 ± 13%) (all P-values < 0.05). IHTG content increased by 83 ± 51% (from 8 ± 11% to 12 ± 11%, $P < 0.01$), and liver stiffness (index of hepatic fibrosis) increased by 16 ± 22% (from 2.9 ± 0.4 kPa to 3.2 ± 0.6 kPa, $P < 0.05$). Hepatic insulin sensitivity, measured as the % suppression of endogenous glucose production during low-dose insulin infusion, decreased from 71 ± 10% to 64 ± 13% ($P = 0.05$). Skeletal muscle insulin sensitivity, measured as the % increase in glucose uptake during high-dose insulin infusion, decreased from 321 ± 124% to 248 ± 117%, ($P < 0.05$).

Conclusion These results demonstrate that overfeeding with moderate weight gain in already obese subjects causes further adverse effects on fat distribution and insulin sensitivity.

PE057 Insulin action & obesity

The roots of Atractylodes japonica Koidzumi promote adipogenic differentiation via activation of the insulin signaling pathway in 3T3-L1 cells

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Objective Type 2 diabetes (T2D) is a complex metabolic disorder characterized by insulin resistance and hyperglycemia. Peroxisome proliferator-activated receptor gamma (PPARγ) is a key transcription factor and plays an important role in the regulation of genes involved in adipogenic differentiation, glucose metabolism and insulin signal transduction.

Methods In this study, the effects of the root extract of *Atractylodes japonica* Koidzumi (Atractylodis Rhizoma Alba, ARA) on the differentiation of 3T3-L1 preadipocytes and the possible mechanism of glucose transport were investigated. 3T3-L1 cells were cultured with insulin and ARA extract.

Results In 3T3-L1 cells, ARA extract significantly enhanced adipogenic differentiation and upregulated the expression of PPARγ genes and protein in a dose-dependent manner. ARA also promoted glucose transport by increasing the glucose transporter 4 (GLUT-4), phosphatidylinositol 3-kinase (PI3K) and insulin receptor substrates-1 (IRS-1) levels.

Conclusion Our results suggest that ARA extract may be an attractive therapeutic agent for managing T2D via promoting the differentiation of adipocytes with the upregulation of PPARγ levels and the activation of the insulin signaling pathway.

PE058 Insulin action & obesity

Association between body mass index and glomerular filtration rate (GFR) in male workers

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Objective Overweight and obesity are well-established risk factors for cardiovascular disease and decline in kidney function in individuals with existing chronic kidney disease (CKD). Previous studies reported a positive association between body mass index (BMI) and CKD among men. In this context, we examined the relationship between BMI and CKD in a study of male workers.

Methods A total of 1,761 male, 30 years and older, untreated hypertension, diabetes and dislipidemia, were enrolled. Participants classified as 572 normal (BMI $<$ 23 kg/m^2), 478 overweight (BMI 23~25 kg/m^2) and 711 obese (BMI $\geq$ 25 kg/m^2). Anthropometry and biochemical parameters were measured and one time spot urine was collected for estimating urine-Na (UNa). The stages of CKD were defined according to the estimated glomerular filtration rate (GFR) based on recent guidelines of the National Kidney Foundation.

Results The mean of waist-circumference, percent body fat, lean body mass, waist-hip ratio, systolic blood pressure and diastolic blood pressure values were significantly higher in participants with more advanced BMI levels ($P < 0.001$). Total cholesterol, low density lipoprotein and triglyceride levels were significantly higher in the obesity group than the others ($P < 0.001$), and high density lipoprotein level was significantly lower in the obesity group than the other groups ($P < 0.001$). The mean spot UNa values were significantly higher in participants with more advanced BMI levels ($P < 0.01$). The estimated GFR (eGFR) significantly decreased with increasing BMI levels ($P < 0.001$), and the correlation coefficient between eGFR and BMI was -0.117 ($P < 0.001$). Increasing BMI levels were positively associated with CKD ($P < 0.001$).

Conclusion Since type 2 diabetes is obesity dependent, and obesity is the main aetiogical cause of type 2 diabetes. Higher BMI levels were negatively associated with GFR levels, and therefore positively associated with CKD among men.

PE059 Insulin action & obesity

Effects of exercise-induced weight loss on ratio of acylated and unacylated ghrelin in obese adolescent

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Objective Ghrelin induces growth hormone release from the pituitary gland, increases appetite and stimulates weight gain. In several reports, ghrelin increased in response to modest weight loss resulting from long-term exercise. Exercise is due to an increase in des-acylated ghrelin, not acylated ghrelin. We tested the effect of combined exercise on ratio of acylated and unacylated ghrelin during a 12-week aerobic and resistant training program in untrained overweight and obese adolescent.

Methods Twenty 13-year-old boys were randomly assigned to one of two groups: a control group who performed no additional exercise and an exercise group who performed a combined exercise. The combined exercise programme, consisting of aerobic exercise and resistance training, was performed by the experimental group under supervision for 12-week(three times a week) at 55~64% and 65~75% of maximum. At baseline and 12 weeks, body composition, lipid profile, total ghrelin and acylated ghrelin were measured.

Results There were significant differences between the groups in the pattern of change of weight ($P = 0.002$), BMI ($P = 0.04$), body fat percentage ($P = 0.03$), body fat mass ($P = 0.008$), lean body mass percentage ($P = 0.039$), TC ($P = 0.032$), LDL-C ($P = 0.039$), total ghrelin ($p = 0.004$), unacylated ghrelin ($P = 0.003$), ratio of acylated ghrelin ($P < 0.001$), and ratio of unacylated ghrelin ($P < 0.001$) levels during the 12-week study.

Conclusion The combined exercise program increases lean body mass percentage, total ghrelin, unacylated ghrelin, and ratio of unacylated ghrelin levels and decreases weight, BMI, body fat percentage, body fat mass, TC, LDL-C, and ratio of acylated ghrelin levels in previously untrained and overweight and obese adolescent. These findings suggest that exercise ameliorate appetite and energy metabolism through ratio of acylated ghrelin and unacylated ghrelin levels changing from 12-week combined exercise.

PE060 Insulin action & obesity

Adipocyte-specific deficiency of CRIF1 regulates browning of white adipose tissue in mice model

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Objective Promoting brown adipose tissue (BAT) function has a therapeutic potential to combat obesity. However, the amount and activity of BAT are very limited in humans. As an alternative strategy, inducing brown adipocyte like feature in white adipose tissue (WAT) has been investigated. The metabolic benefits of this conversion (browning effects) may include prevention of diet-induced obesity and increased insulin sensitivity. It has been known that browning effects of WAT in rodent models scan be brought by cold-exposures, and treatment with beta3-adrenoreceptor agonists or cytokines. However, the mechanism of this "browning" effect need to be solved. Therefore, we investigated the role of OXHPOS function of WAT in browning effects.

Methods We created mice lacking CRIF1, a regulator of mitochondrial OXPHOS function, in adipocytes using Cre/LoxP recombination. The mice were housed at room temperature in a 12hr light/dark cycle with free access to normal chow. Male adipocyte-specific CRIF1 knockouts and wild type mice between 7 and 9 weeks old were intraperitoneally injected daily with 10 mg/kg rosiglitazone or saline for 2 weeks. We performed histologic analysis by paraffin-embedded section, gene expression analysis by quantitative real-time PCR and protein analysis by Western blotting to evaluate the browning phenomena in WAT.

Results The adipocyte-specific CRIF1 knockout mice caused marked decrease of OXHPOS complex in adipocytes. The UCP1 protein levels of white adipose tissue was changed in adiponectin-*Cre* CRIF1 knockout mice.

Conclusion Adipocyte-specific deletion of CRIF1 Inhibits browning of subcutaneous white adipose tissue.The OXPHOS function in white adipocytes is related to browning effect.

PE061 Insulin action & obesity

The circumstances causing insulin resistance also induces FGF21 resistance by decreasing the activation of the downstream signals of FGF21 in human skeletal muscles

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Objective Insulin resistance and hyperinsulinemia are the hallmark features of non-insulin-dependent diabetes mellitus (NIDDM) and obesity, but the detailed pathogenesis underlying the initiation of insulin resistance is still poorly understood. Recently, fibroblast growth factor 21 (FGF21), a novel member of the FGF family, was identified as a potent metabolic regulator with specific effects on glucose and lipid metabolism.

We investigated the mechanisms involved in the induction of FGF21 resistance in human skeletal muscle of type 2 diabetes (T2DM) patients.

Methods We recruited 16 type 2 diabetic subjects and 12 subjects with normal glucose tolerance for this study. All subjects signed informed consent forms regarding the experimental procedures. The Institutional Medical Ethics Committee approved all methods.

Whole-body insulin-mediated glucose uptake was determined using a euglycemic hyperinsulinemic clamp test. A percutaneous biopsy sample of the vastus lateralis muscle was obtained from 15 to 20 cm above the knee using a Bergstrom needle.

Differentiated HSMMs were pretreated with palmitate at three different concentrations for 24 h, and then were stimulated for 10 min with recombinant FGF21 (100 ng/mL).

We measured levels of FGF21, FGF Receptor, FRS2, and ERK1/2 using antibodies specific for FGF21 (Abcam, Cambridge, MA), phospho-FGF Receptor (Tyr653/654), phospho r-FRS2-α (Tyr196), and phospho-ERK1/2 (Thr202/Tyr 204) (Cell Signaling technology, Danvers, MA), respectively.

Results Levels of FGF21 were significantly increased in skeletal muscles from T2DM subjects but levels of active FGF receptor and FRS2α were significantly decreased in skeletal muscles from T2DM subjects. Similarly, FGF21 increased levels of active FGF receptor, FRS2α and ERK1/2 in HSMMs but there were significantly decreased levels of FGF21-stimulated FGF receptor, FRS2α and ERK1/2 in HSMMs treated with palmitate.

Conclusion In conclusion, FGF21 resistance apparently was involved in insulin resistance in skeletal muscle in type 2 diabetes.

PE062 Insulin action & obesity

Inhibitory effect of KE-28, a Korean traditional herbal formula, on adipocyte differentiation in 3T3-L1 cells

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Objective KE-28 is a Korean traditional herbal prescription widely used to treat respiratory diseases. The present study was carried out to evaluate anti-obesity activity of KE-28 in vitro.

Methods KE-28 consists of 12 medicianal herbs and prepared using an herbal extractor for 2 h at 100℃. Preadipocyte 3T3-L1 cells were induced the differentiation into adipocytes by IMBX, dexamethasone and insulin with or without KE-28 for 8 days. Is inhibitory effect on adipogenesis was determined by oil red O staining, GPDH activity assay, leptin ELISA and triglyceride quantification assay.

Results Compared with the differentiated adipocytes, KE-28 treatment reduced lipid accumulation with no cytotoxicity in 3T3-L1 cells. KE-28 significantly inhibited the enzymatic activity of GPDH as well the contents of triglyceride in a dose-dependent manner. The amount of adipokine leptin in the media was dramatically decreased in a dose-dependent manner.

Conclusion Our finding implies that KE-28 could be suggested as a valuable anti-obesity medication. Further study will be necessary to verify its anti-obesity activity using in vivo experimental models.

PE063 Insulin action & obesity

Usefulness of various anthropometric measurements to predict insulin resistance in healthy Korean population

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Objective The aim of this study was to assess how effectively various anthropometric parameters can predict insulin resistance in healthy Korean adult population.

Methods We performed retrospective cross-sectional study in 6195 adult subjects to perform routine health check-up in Seoul St. Mary's hospital. Anthropometric parameters including body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) were measured to use standard methods. Percentage of body fat was determined by bioelectric impedance analysis (BIA). To estimate insulin resistance, the homeostatic model assessment of insulin resistance (HOMA-IR) was used. The stepwise regression models and receiver operating characteristics (ROC) curve analysis were performed to predict HOMA-IR.

Results The percentage of body fat was the best predictor of HOMA-IR in both sex. And WC and WHR were better than BMI to predict insulin resistance. ROC curve showed the percentage of body fat to be more sensitive in detecting insulin resistance than other parameters, but with less specificity.

Conclusion In healthy adult population, the percentage of body fat by BIA was better than WC, WHR, and BMI to predict insulin resistance.

PE064 Insulin action & obesity

High prevalence of papillary thyroid cancer in patient with hyperinsulinemia

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Objective Patient with insulin resistance have higher risk of thyroid nodules. However, the associations between hyperinsulinemia and thyroid cancer are uncertain. We evaluated the relationships between hyperinsulinemia and prevalence of papillary thyroid cancer.

Methods A total of 855 patients who underwent total thyroidectomy and 1298 patients underwent regular medical check up in Pusan National University Hospital were retrospectively reviewed in this study. Patients were grouped according to serum insulin level, fasting glucose level and the homeostasis model assessment of insulin resistance (HOMA-IR) index.

Results The prevalence of thyroid cancer was significantly correlated with increased insulin, glucose and HOMA-IR in the univariated analysis. These associations were persistent after adjusting for several confounding variables such as sex, age, BMI, smoking history, hypertension, previous thyroid disease, previous other cancer, total cholesterol and TSH level. The multivariated- adjusted odds ratio for prevalence of thyroid cancer in the highest quartile group of insulin, glucose and HOMA-IR were 2.85, 11.18 and 4.15 (all $P < 0.001$) compared to the lowest quartile group. However, insulin, glucose level and HOMA-IR were not associated with thyroid cancer severity such as cancer size, multifocality, microscopic invasion and lymph node metastasis.

Conclusion We conclude that hyperinsulinemia and insulin resistance were strongly associated with prevalence of papillary thyroid cancer in Korean population.

PE065 Insulin action & obesity

Effect of quercetin on gluconeogenesis and inflammatory alterations in ob/ob mice

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Objective Quercetin is an abundant flavonoid with anti-inflammatory action that relies on a wide range of mechanisms of action. It could modify the establishment of inflammation in adipose tissue during obesity. This study investigated the effect of quercetin treatment on obesity, inflammation and insulin sensitivity and its potential molecular mechanisms.

Methods The 7 week-old male lean C57BL6/J and ob/ob mice received HF diet (45% energy from fat) for 5 weeks. Quercetin injected intraperitoneally (i.p.) every day for 2 weeks at the dosage of 100 mg/kg body weight after 3 weeks of HF diet feeding. We measured insulin resistance index, adiposity and macrophage infilteration.

Results Obese mice presented significantly increased plasma levels of insulin, glucose and IL6, and insulin resistance compared with lean mice. Although quercetin supplementation was not significantly affected on these parameters in both of lean and obese mice with HF diet, it reduced fatty liver and fat weight. Quercetin supplementation significantly increased hepatic GK protein expression and significantly decreased PEPCK protein expression compared with HF diet in lean and obese mice. The mice fed HF with quercetin exhibited a significant reduction in the number of adipose cells expressed per area and a smaller mean cell circumference, radius, and area compared with the mice fed HF in both lean and ob/ob mice. Quercetin supplementation resulted in smaller in distribution of cell size, indicating that the reduction in total fat mass. Quercetin significantly reduced the production of IL-6 in lean mice and macrophage infilteration (F4/80+cells) of epididymal adipose tissue in lean and obese mice. In lean animals, F4/80-expressing cells were uniformly small, dispersed, and rarely seen in aggregates. The fraction of F4/80-expressing cells was greater in obese mice and greatest in the severely obese HF diet fed mice. Ouercetin reduced this macrophage infiltration in lean and obese mice.

Conclusion Quercetin significantly reduced the fatty liver and adiposity, which improved hepatic gluconeogenesis. Quercetin was able to inhibit microphage infilteration through maybe cytokine production in adipose tissue.

PE066 Insulin action & obesity

Changes in glucose and iron metabolism in the metabolically stressed hepatic cells

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Objective While iron is a vital requirement for normal cellular physiology, excess tissue/cellular iron level is a risk factor for diabetes, but the mechanisms underlying the association are incompletely understood. Excess iron could play a role in generating reactive oxygen species (ROS) which are thought to be responsible for mitochondrial dysfunction which could induce abnormal hepatic gluconeogenesis.

To explore the interacting pathways linking glucose and iron metabolism, we investigated the effect of excess iron or oligomycin-induced mitochondrial dysfunction on the formation of ROS, the extent of iron accumulation, the expression levels of proteins involved in iron-metabolism and gluconeogenesis in the SK-HEP-1 human liver cell line.

Methods The SK-HEP-1 cells were treated with 20 uM Fe-NTA for 24 h. Mitochondrial function was destroyed by 40 uM oligomycin, a mitochondrial ATPase inhibitor, for 24 h. To assess the effects of desferoxamine (DFO), an iron chelator, or n-acetylcysteine (NAC), a ROS scavenger, the cells were treated with for 2 h before the incubation with Fe-NTA or oligomycin.

Results Increased cellular iron, and increased expressions of ferritin and hepcidin (the iron storage and iron transport protein, respectively) with decreased expression of ferroportin (the iron efflux protein) were observed with Fe-NTA treatment. These changes were inhibited by DFO. While Fe-NTA increased ROS production and PEPCK expression, DFO and NAC inhibited those increments. Oligomycin-induced mitochondrial dysfunction increased ROS production and an iron accumulation, and changed the expressions of proteins involved in iron metabolism as well as gluconeogenesis.

Conclusion The iron overload in the liver cells stimulates hepatic gluconeogenesis through ROS production, similarly to the consequences induced by mitochondrial dysfunction. Mitochondrial dysfunction changed the cellular iron metabolism. Thus mitochondrial dysfunction and excess iron overload interact together on iron and glucose metabolism directly or indirectly. The excessive hepatic iron deposition can increase gluconeogenesis, and the risk for hyperglycemia.

PE067 Insulin action & obesity

Regulation of hepatic insulin sensitivity by NCoA6

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Objective NCoA6 is a transcriptional coactivator and regulates insulin secretion and beta-cell survival. The current study was performed to elucidate the role of NCoA6 in the regulation of insulin sensitivity.

Methods Glucose-stimulated insulin secretion was measured using islets isolated from wild type and $NCoA6^{+/-}$ mice. Intraperitoneal glucose, insulin and pyruvate tolerance tests were performed to compare glucose tolerance, insulin sensitivity, and gluconeogenic activity, respectively, between wild type and $NCoA6^{+/-}$ mice. To elucidate the regulation mechanism of insulin sensitivity by NCoA6, immunoblot analysis, chromatin immunoprecipitation analysis, qRT-PCR, and luciferase assay were employed.

Results Although islet cells from 10-week-old $NCoA6^{+/-}$ mice secreted less insulin than wild-type islets, there was no significant difference in glucose tolerance between $NCoA6^{+/-}$ and wild-type mice. However, $NCoA6^{+/-}$ mice did show increased insulin sensitivity compared to wild-type mice in insulin tolerance tests. Consistently, the levels of phosphorylated Akt were higher in $NCoA6^{+/-}$ hepatocytes than in wild-type hepatocytes after insulin treatment. Moreover, decreases in phosphoenolpyruvate carboxykinase mRNA in refed mice were more prominent in $NCoA6^{+/-}$ livers than in wild-type livers. Interestingly, the expressions of SOCS1 (suppressor of cytokine signaling-1) and SOCS3, well-known insulin signaling inhibitors, were decreased in $NCoA6^{+/-}$ hepatocytes and increased in NCoA6 overexpressing hepatocytes. Furthermore, NCoA6 was recruited to the promoter region of SOCS1 and potentiated the transcription by SREBP-1c (sterol regulatory element binding protein-1c). This transcription activating function of NCoA6 was diminished by mutations of SREBP-1c binding sites in SOCS1 promoter.

Conclusion These results suggest that NCoA6 negatively affects hepatic insulin sensitivity, at least in part, through induction of the insulin signaling inhibitors SOCS1 and SOCS3.

PE068 Insulin action & obesity

The association with serum vaspin and metabolic syndrome in healthy Korean subjects

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Objective Visceral obesity is associated with insulin resistance, type 2 diabetes, and cardiovascular diseases. Moreover, visceral adipose tissue-specific secretion of various adipokines may be responsible for these clinical consequences of visceral adipose tissue accumulation. Visceral adipose tissue-derived serpin (vaspin) was suggested as a novel adipokine related to obesity and its metabolic consequences. The aim of the present study was to investigate the relationship of serum vaspin levels with visceral adipose tissue (VAT) and components of metabolic syndrome (MetS).

Methods A cross-sectional analysis of healthy men (n = 97) and women (n = 156) for evaluation of clinical, laboratory, and anthropometric parameters were undertaken. Serum vaspin levels were determined. Abdominal VAT and subcutaneous adipose tissue were measured by computed tomography.

Results In a total of 253 subjects, 47 (18%) had MetS. Thirty three (34%) men and 14 women (9%) had MetS ($P < 0.001$). Mean serum vaspin level was significantly lower in men compared to women. There was no significant difference in mean serum vaspin level between the group with MetS and those without. However, in men, mean serum vaspin level was significantly lower in the group with MetS compared to those without. Mean serum vaspin level tended to decrease along to the number of MetS components. Serum vaspin level was negatively correlated with waist circumference, systolic and diastolic blood pressure, serum triglyceride, and abdominal VAT, but positively with high-density lipoprotein cholesterol. However, adjusting for sex, this correlation was disappeared.

Conclusion We found a sexual dimorphism in serum vaspin. Low serum vaspin levels are associated with MetS, especially in men. Serum vaspin levels are also associated most of components of MetS, such as visceral obesity, blood pressure, serum triglyceride, and high-density lipoprotein cholesterol, but this correlation might be caused by sex.

PE069 Insulin action & obesity

Increased ATP production by AMP-activated protein kinase is not associated with mitochondrial biogenesis in hepatocytes

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Objective AMP-activated protein kinase (AMPK) is an enzyme which plays a central role in the control of intracellular energy metabolism. AMP binding to the enzyme promotes its phosphorylation by the tumor suppressor LKB1, resulting in full activation. Once activated, the enzyme turns off biosynthetic pathways and at the same time turns on catabolic pathways, thus conserving ATP levels. In this study, we questioned whether the activation of AMPK is able to increase the production of ATP or not, and what mechanism might be involved.

Methods We employed AICA riboside (5-aminoimidazole-4-carboxamide -1-β-D-ribofuranoside) for activation of AMPK and Compound C for inhibition of AMPK. For cell culture experiment, we used Chang liver cells known as human normal hepatocytes and HepG2 cells known as human hepatocarcinoma cells. For ATP measurement, luciferin/luciferase assay was used with cell boiling method. Mitochondrial genomic DNA (mtDNA) was quantified by real-time qPCR with whole genomic DNA for analysis of mitochondrial biogenesis. Mitochondrial gene expression were measured by real-time qPCR. For animal model for this study, adenoviral-mediated AMPK gene transfer was employed for overexpression of AMPK in mice.

Results Activation of AMPK by AICAR showed increased ATP production in Chang liver cells, HepG2 Cells and AMPK-overexpressed murine liver. Treatment of Compound C as inhibitor of AMPK did not increase the production of ATP in both cells. Oxidative phosphorylation-related gene expression was increased by activation of AMPK while the expression was not affected by inhibition of AMPK. However, the amount of mtDNA was not changed by activation of AMPK or inhibition of AMPK.

Conclusion These results suggest that the activation of AMPK may induce the production of ATP. The mechanism of ATP production by AMPK might be increased gene expression of oxidative phosphorylation system and not be associated with mitochondrial biogenesis in hepatocytes.

PE070 Insulin action & obesity

Celecoxib improves mitochondrial biogenesis in fatty acids-induced insulin resistance in skeletal muscle

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Objective It is well known that mitochondrial dysfunction might play an important role in the pathophysiology of insulin resistance. And recently, several studies suggest that celecoxib, one of COX-2-selective inhibitors, has positive effect on insulin sensitivity. Here, we investigate the effect of celecoxib on insulin sensitivity and mitochondrial biogenesis in in-vivo and in-vitro studies.

Methods Twenty-week-old male OLEFT rats (n = 20) were separated into two groups: high fat diet fed and vehicle treated (n = 10); high fat diet fed and celecoxib (15 mg/kg) treated. Lean nondiabetic LETO rats were used as control. C2C12 myotubes were incubated in high palmitate condition (500 uM) with or without various doses of celecoxib (1, 3, 10, 30, and 50 uM) for 24 and 48 hours. To assess the mitochondrial biogenesis, nuclear peroxisome proliferator-activated receptor gamma coactivator-1a (PGC-1a), mitochondrial transcription factor A (Tfam), and nuclear respiratory factor-1 (Nrf1) expression were assessed by immunoblot.

Results Five-week treatment with celecoxib did not change body weight, food intake, and fasting plasma glucose level. However, celecoxib improved insulin sensitivity in high fat diet-fed OLEFT rats in OGTT. Electron microscopic findings of gastrocnemius muscle and mtDNA/nuclear DNA showed that celecoxib preserved mitochondrial density in diabetic rat muscle. In in-vitro studies, celecoxib increased nuclear PGC-1a expression in a dose- and time-dependent manner. High dose palmitate treatment decreased nuclear PGC-1a expression, however, simultaneous treatment with celecoxib preserved nuclear PGC-1a expression. Regarding Tfam and Nrf1, there were no differences.

Conclusion In summary, we have observed that celecoxib preserves mitochondria density and improves mitochondrial biogenesis in skeletal muscle in high fat diet-fed rats and palmitate-induced insulin resistance in C2C12 skeletal muscle cells.

PE071 Insulin action & obesity

Effects of nepetae spica extract in obese mice fed a high-fat diet

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Objective Obesity threatens to become the foremost cause of chronic disease in the world. Being obese can induce multiple metabolic abnormalities that contribute to diabetes, dyslipidemia, cardiovascular disease, glucose intolerance and other chronic disorders. It is becoming one of the greatest threats to global health in this millennium, with more than 1 billion overweight adults and of those, at least 300 million are clinically obese. Considerable advances have been made in diet, exercise and behavior approaches to treatment for obesity and new drugs with even better profile of pharmacological activity continues to be introduced on a regular basis. Thus, in spite of tremendous development in the field of allopath during the 20th century, plants still remain one of the major sources of drug in the modern as well as traditional system of medicine throughout the world.

Methods In this study, we elucidated that Nepetae Spica extract significantly inhibited lipid accumulation during 3T3-L1 adipocyte differentiation. Furthermore, Nepetae Spica extract reduced the body weight gain induced through feeding a high-fat diet to C57BL/6 mice.

Results The treatment of Nepetae Spica extract significantly reduced the adipose tissue weight to 2.7/100 g of body weight in high-fat mice. When their adipose tissue morphology was investigated for histochemical staining, the distribution of cell size in the high-fat diet groups was hypertrophied compared with those from Nepetae Spica extract-treated mice. In addition, in Nepetae Spica extract-treated mice, a significant reduction of serum triglyceride and T-cholesterol was observed at to 21% and 17%, respectively.

Conclusion The discovery of bioactive compounds from diet or dietary supplementation is one of possible ways to control obesity and to prevent or reduce the risks of various obesity-related diseases. These results support that Nepetae Spica extract is expected to create the therapeutic interest with respect to the treatment of obesity.

PE072 Insulin action & obesity

High fat diet-induced obesity is associated with hypothalamic inflammation in myeloid deletion of SIRT1 mice

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Objective Chronic inflammation is well known as a causal factor leading to the development of obesity, insulin resistance, and type 2 diabetes. Recent studies have shown that obesity results from the installation of an inflammatory process in the hypothalamus, which leads to resistance to the anorexigenic hormones leptin and insulin and finally to the defective regulation of food intake and energy expenditure. The important role that SIRT1, the leading situin family member, plays in immune response remains unclear. In this study, we investigate whether SIRT1 plays a pivotal role in regulating the inflammation and insulin resistance in the hypothalamus.

Methods C57B/6J wild type (WT) or myeloid cell-specific SIRT1 knockout (SIRT1 KO) mice were fed a normal diet (ND) or high fat diet (HFD) for 20 weeks. Metabolic parameters in serum were measured using ELISA and western blot and immunohistochemistry in liver, epididymal fat, and hypothalamus were performed.

Results Hepatic steatosis, macrophage infiltration, and insulin resistance were increased in HFD-fed SIRT1 KO mice compared to HFD-fed WT mice. In the hypothalamus, tumor necrosis factor-α (TNF-α) and Iba1 expression were increased in HFD-fed SIRT1 KO mice compared to HFD-fed WT. HFD induced acetylation of NF-kB p65 in the hypothalamus of both WT and SIRT1 KO mice. However, SIRT1 KO mice significantly displayed higher levels of acetylation of NF-kB p65. The phosphorylation of c-Jun N-terminal kinase (JNK) and insulin receptor substrate 1 (IRS-1) were also increased in the hypothalamus of HFD-fed SIRT1 KO mice compared to HFD-fed WT.

Conclusion These data suggest that SIRT1 is an important role for hypothalamic inflammation and insulin resistance in mice with chronic high fat diet.

PE073 Insulin action & obesity

Effects of caloric restriction on insulin sensitivity and antioxidant activity in ovariectomized rats

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Objective The influence of estrogen deficiency on the insulin resistance and risk of cardiovascular disease (CVD) is well known. Insulin resistance is associated with adverse changes in cardiovascular risk factors, such as obesity, high triglyceride levels, low levels of HDL-cholesterol (HDL-C) and increased levels of LDL-cholesterol (LDL-C). Many studies emphasized that caloric restriction (CR) is an important protective factor as well as the most safe and effective treatment for insulin resistance as well as CVD. The purpose of the study was to investigate the effects of caloric restriction on insulin resistance and cardio-metabolic risk biomarkers in ovariectomized (OVX) rats.

Methods Seven-week-old female Sprague-Dawley rats were randomized to sham-operated control fed ad libitum diet (SHAM-AD), sham-operated fed caloric restriction diet (SHAM-CR), ovariectomy-operated control fed ad libitum diet (OVX-AD), or ovariectomy-operated fed caloric restriction diet (OVX-CR). For 8 weeks, the OVX-AD group was pair-fed with the SHAM-AD group and the CR groups were fed diet with 50% fewer calories than their counterparts.

Results Cardio-metabolic risk biomarkers (glucose, insulin, TG, TC, LDL-C, HDL-C, SOD, MDA, GPx) were analyzed at the end of the experiment. HOMA-IR and QUICKI were calculated to using fasting levels of glucose and insulin. The results showed that serum levels of glucose, TG, TC, LDL-C, MDA, and GPx were highest in the OVX-AD group ($p < 0.05$). On the other hand, HDL-C levels were higher in the calorie restriction groups than in the ad libitum groups regardless of the operation. Calorie restriction significantly influenced serum levels of insulin, TG, HDL-C, LDL-C HOMA-IR, and QUICKI ($P < 0.05$). Ovariectomy significantly influenced serum levels of glucose, TC, GPx SOD, and HOMA-IR ($P < 0.05$).

Conclusion As a conclusion, the calorie restriction produced positive effects on insulin resistance as well as cardio-metabolic risk biomarkers, especially in ovariectomized rats.

PE074 Insulin action & obesity

Control of adipogenesis by F-box protein 9

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Objective F-box protein 9 (FBXO9) is a member of SCF (Skp, Cullin, F-box)-type ubiquitin E3 ligase, and acts as a recognizer of targets. However, the targets of FBXO9 have not been reported. In this study, we investigated the roles of FBXO9 in adipogenesis of 3T3-L1.

Methods FBXO9 is overexpressed or knocked-down using adenoviruses or siRNAs respectively in 3T3 L1 preadipocytes. The expression levels of adipogenic regulators during adipogenesis are determined using qRT-PCR and Western blot analysis. Differentiation of adipocytes is determined by Oil red-O staining analysis.

Results Expression of FBXO9 was increased 12 hours and peaked 48 hours after the addition of the differentiation inducers and sustained until day 6 of adipogenesis. When the FBXO9 was knocked down in 3T3-L1 preadipocytes, the adipogenesis was suppressed after the stimulus of differentiation. In contrast, when FBXO9 was knocked down two days after the differentiation induction, adipogenesis was not suppressed. In the condition of a knockdown of FBXO9 in preadipocytes, we examined the expression levels of adipogenic regulators including Wnt signaling molecules, C/EBP isoforms, PPARγ and MAPKs after the addition of the differentiation inducers. C/EBPβ was not fully induced and expression of PPARγ was almost completely inhibited by the knockdown of FBXO9. Reduction of the protein levels of Wnt signaling molecules, such as LRP6 and β-catenin, upon the induction of differentiation was attenuated by the knockdown of FBXO9.

Conclusion These results suggest that FBXO9 is involved in the adipogenesis at the early stage (day 0-2) and knock down of FBXO9 inhibits adipogenesis by affecting Wnt signaling or C/EBPβ expression or activity. To identify a more direct role of FBXO9 in adipogenesis, we need further studies for the regulation of Wnt signaling and C/EBPβ by FBXO9.

PE075 Insulin action & obesity

Effect of cilostazol on hepatic low-density lipoprotein receptor-related protein 1 (LRP1) expression suggests a possible mechanism for serum triglyceride reduction by cilostazol

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Objective Cilostazol, a selective phosphodiesterase 3 (PDE3) inhibitor, is a vasodilating and antithrombotic agent. The mechanism whereby cilostazol reduces plasma triglyceride is not completely understood. Here we investigated the effect of cilostazol on a remnant lipoprotein receptor, low-density lipoprotein receptor-related protein 1 (LRP1), which has been reported to play an essential role in clearance of circulating triglyceride in the liver.

Methods Total cellular expression, functional analysis, and transcriptional regulation of LRP1 were analyzed in human hepatoma cell lines (HepG2, Hep3B) incubated with various concentrations of cilostazol. Six-week-old C57BL/6 mice were subjected to high-fat diet (60% kcal) and cilostazol (30 mg/kg) treatment for 10 weeks to investigate the involvement of LRP1 in triglyceride reduction by cilostazol.

Results Cilostazol increased both mRNA and protein expression of LRP1 in HepG2 and Hep3B cells. In addition, enhanced transcriptional activity of the LRP1 promoter containing a peroxisome proliferator reponse element (PPRE) was observed upon cilostazol treatment. Electrophoretic mobility shift assays (EMSAs) confirmed that cilostazol activated peroxisome proliferator activated receptor-γ (PPAR-γ) binding to the PPRE of the LRP1 promoter. Cilostazol treatment enhanced the uptake of lipidated apoE3 and this effect was abolished when LRP1 was silenced by siRNA knockdown. A 10 week high-fat diet (60% kcal) induced hyperglycemia with high level of plasma triglycerides and reduced hepatic LRP1 expression in C57BL/6 mice. Treatment with cilostazol for the same period of time, however, successfully prevented this downregulation of LRP1 expression and significantly reduced plasma triglycerides.

Conclusion Our results demonstrated that cilostazol enhances LRP1 expression in liver by activating PPAR-γ binding to PPRE in the LRP1 promoter. Increased hepatic LRP1 may be essential for the reduction of circulating triglycerides by cilostazol.

PE076 Insulin action & obesity

Glucagon like peptide-1 receptor agonist directly reduced NAFLD through metabolic improvement

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Objective Non-alcholic fatty liver disease (NAFLD) is associated with insulin resistance, and metabolic syndrome. To reverse the NAFLD is helpful for treatment of insulin resistance condition. Recently many extrapancreatic effects of GLP-1 have been demonstrated. But, the direct effect of GLP-1 receptor agonist, exendin-4 (EX-4) on the liver is not clear. Therefore we investigated the direct effect of GLP-1 on the lipid metabolism in HEP3B cell line and in the liver of high fat (HF) fed dbdb mice.

Methods GLP-1 receptor was confirmed by realtime PCR and confocal microscopy in the HEP3B cell and Dbdb mice liver. HEP3B cell was treated with 0.5 mM palmitate with or without 100 nM exenitide treatment. 10 μg/kg Ex-4 was injected i.p to the HF fed dbdb mice for 6 weeks. Saline treatment mice and pair-feeding mice were control group. The mRNA expression of gene associated with lipid metabolism was examined by real time PCR. The protein expression was studied by Western blot.

Results EX-4 reduced fat accumulation and reduced lipogenic gene such as SREBP-1, DGAT-1 and increased the gene exression of fatty acid beta oxidation such as CPT-1, PPAR-alpha in HEP3B cell treated with 0.5 mM palmitate and HF fed dbdb mice. EX-4 could not reverse the autophagy induced by palmitate in the HEP3B and high fat fed mice.

Conclusion In conclusion, GLP-1 receptor agonist, EX-4 reduced hepatic fat accumulation through down regulation of lipogenic gene expression and up-regulation of lipid oxidation gene, rather than autophagy pathway.

PE077 Islet biology & insulin secretion, immunology & transplantation

Effect of GLP-1 analogues, exendin-4, on inhibition of islet fibrosis

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Objective Pancreatic islet fibrosis might be to lead the beta-cell loss and dysfunction in type 2 diabetes. Pancreatic stellate cells (PSCs) are known to be related to pancreatic fibrosis and inflammation, and are the result of extracellular matrix (ECM) protein synthesis. So far there was no report which demonstrates the effects of Ex-4 on PSCs. Therefore, we investigated the effect of GLP-1 analogues on activated PSCs in vitro and pancreatic islets fibrosis in vivo.

Methods PSCs cultured in low glucose (5.5 mM D-glucose) or high glucose (27.7 mM D-glucose) with or without 10 nM exendin-4 for 3 and 9 days.

Western blot analyses for the expressions of α-SMA and ECM proteins, such as CTGF and α-collagen I, were performed. Levels of TGF-β and angiotensin II in culture media are measured. For in vivo study, saline (control), Ex-4 (2.5 nM/kg/twice a day) and Insulin (control of glucose matched group) were injected into OLETF rats for 12 weeks. We analyzed pancreatic islet morphology, quantified beta-cells mass and the severity of islet fibrosis.

Results GLP-1R expression was induced with high glucose stimulation in PSCs. The protein level of a-SMA was increase by high glucose however attenuated by Ex-4 treatment for 3 days. CTGF and α-collagen I synthesis were increased for 9 days and also attenuated by Ex-4 treatment. Increased Angiotensin II and TFG-β concentration under high glucose were significantly reduced by Ex-4 treatment. Exendin-4 treatment also significantly decreased islet fibrosis area after 12wk treatment when compared with control group, whereas insulin treated group did not change.

Conclusion These results indicated that Exendin-4 may be useful not only diabetic agent but also anti-fibrotic agent in type 2 diabetes via ability to inhibit PSC activation, proliferation and reduce their synthesis of ECM proteins and improves islet fibrosis in OLETF rats.

PE078 Islet biology & insulin secretion, immunology & transplantation

Comparisons of risk factors of diabetes and cardiovascular disease according C-peptide levels

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Objective C-peptide is a one of the diabetes mellitus (DM) related factors as a marker of insulin secretion and production. We aimed to describe the levels of C-peptide in relation to risk factors of cardiovascular disease (CVD) in large population-based cohort.

Methods Data was obtained from 1,797 men (996 normal group, 728 IFG group, 73 DM group) who have not been diagnosed with diabetes and were participated in annual regular health check-ups in 2012. All subjects were divided into three subgroups according to C-peptide level (< 1.33 ng/mL, ≤ 1.33 - < 2.00 ng/mL, ≤ 2.00 ng/mL). The relationships between basal C-peptide and other clinical values were statistically analyzed.

Results Compared with the normal group, the mean C-peptide of IFG and DM groups were significantly higher after adjustment of age and BMI ($P<0.001$). All clinical parameters except low-density lipoprotein cholesterol (LDL), creatinine and homocysteine (Hcy) were significantly high across the C-peptide tertiles, including BMI, waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), triglyceride (TG), insulin, glycated hemoglobin (HbA1c), fasting blood sugar (FBS), Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and uric acid ($P < 0.05$). C-peptide demonstrated a statistically significant positive correlation with BMI, WC, SBP, DBP, creatine, TC, TG, insulin, HbA1c, FBS, HOMA-IR and uric acid, and negative correlation with HDL after adjustement of age ($P < 0.05$).

Conclusion C-peptide appears to be highly associated with risk of DM and CVD, suggesting that further large prospective study would be necessary to address these issues as well as to identify factors determining the C-peptide level in response to the development CVD.

PE079 Islet biology & insulin secretion, immunology & transplantation

Triiodothyronone (T3) induces the proliferation of insulin secreting pancreatic beta cell lines through the Akt pathway

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Objective Triiodothyronine (T3) has the growth stimulatory effect via the thyroid hormone receptors (TRs) in several cell lines. TRs expressions in pancreas confer the possibilities of pancreatic β cell proliferation by T3. The purpose of our study is to ascertain the mechanism of pancreatic β cell lines proliferation by T3 can be induced by Akt pathway.

Methods RIN5F and INS-1 cells were plated as a monolayer at a density of 4×10^4 and 2×10^5, cultured in RPMI 1640 with 10% FBS and 2-Mercaptoethaol, respectively, in six multiwells. After 48 hours, they were exposed to doses of T3 (10^{-7} M) or to vehicle alone. At 24, 48 and 72 hour of continuous exposure, viable cells were harvested and counted. Cell viability, proliferation and TRα1 and β1 expression in RIN5F and INS-1 cells were analyzed by Trypan Blue negative cell number in a Thomas's hematocytometer, FACS and Western blot. The proliferative mechanisms of INS-1 cell by T3 were proved by Akt pathway by Western blot.

Results Endogenous T3 influenced the proliferation of pancreatic β cell lines in the doses of 10^{-7} M with time dependent manner via Akt pathway.

Conclusion T3 stimulated the proliferation of RIN5F and INS-1 cells. This property would have very improtant clinical meanings, such as the selective thyroid hormone receptor agonists could be used as stimulating agent for the proliferation of pancreatic β cells to treat type 1 and type 2 diabetes mellitus. Further study will be done.

PE080 Islet biology & insulin secretion, immunology & transplantation

An endocrine response to glucose intake could be impaired or delayed in transgenic pigs, over-expressing PEA15

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Objective The objective of current study was to discover any physiological changes occurred in transgenic pigs which over-express PEA15 and also evaluate a potential of these animals as a disease model system for the investigation of diabetes and other related diseases.

Methods Using PEA15 pigs which has been created and bred by National Institute of Animal Science (NIAS), we have performed a line of experiments, including intravenous glucose tolerance test (IVGTT), oral glucose tolerance test (OGTT), analysis of two blood adipokines, adiponectin and resistin.

Results Results can summarized as these; (1) in IVGTT, blood glucose level in both PEA15 and control pigs surged immediately after glucose infusion and returned to a basal level within 30 min. (2) in OGTT, glucose clearing ability was significantly impaired in PEA15 pigs while glucose increase was not observed at all in control pigs. (3) blood resistin level was significantly increased in PEA15 pigs compared with control pigs. When the expression of resistin was quantified using qPCR in several organs, the expression was highest in adipose in control pigs. In PEA15 pigs, the expression was highest in muscle (7-fold compared with control muscle and 5-fold compared with adipose tissue).

Conclusion When our data combined, it can be concluded that the ability of pancreatic beta-cell to release insulin and control blood glucose was not impaired as no significant difference was found in IVGTT. However, since glucose clearing ability was significantly impaired or delayed in PEA15 pigs in OGTT, our data may suggest that endocrine responses that normally occur after glucose intake is not working properly in PEA15 pigs. Currently we are investigating blood insulin levels during IVGTT and OGTT. Regarding elevated blood resistin level in PEA15 pigs, we speculate that the over-exprssion of transfected gene in muscle is responsible for the elevated muscular resistin expression and high blood resistin level.

PE081 Islet biology & insulin secretion, immunology & transplantation

Resveratrol inhibits oxidative stress in pancreatic B-cells

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Objective Oxidative stress is one of the important mechanisms of b- cell failure in type 2 diabetes. Resveratrol (RSV), a type of natural phenol, has been reported antioxidant, anti-inflammatory, anti-cancer and blood sugar-lowering effects. In this study, we investigated the effects of RSV on dRib (2-deoxy-D-ribose)-induced oxidative stress in a pancreatic b- cell line.

Methods HIT-T15 cells and isolated rat islets were cultured with the indicated concentrations of dRib for 6 or 24 h after pretreatments with various concentrations of RSV. Cell viability was determined by MTT assay. Intracellular reactive oxygen species (ROS) was observed by dihydrorhodamine 123 (DHR123) staining, and primary rat islet insulin content was measured by ELISA method. Intracellular glutathione (GSH) level was detected by mBCl fluorescences. Western blot analysis was performed to determine the change of glutamate cysteine ligase (GCL) protein expression.

Results 2-Deoxy-D-ribose dose-dependently increased cytotoxicity & intracellular ROS levels and decreased intracellular GSH levels in HIT-T15 cells. RSV significantly reversed the dRib-mediated cytotoxicity & intracellular ROS increments and restored the dRib-induced GSH depletion. In addition, RSV significantly recovered the intracellular insulin content diminished by stimulation with dRib in isolated rat islets. Pretreatment with buthionine sulfoximine (BSO), a specific inhibitor of GCL, significantly reversed the protective effects of RSV against the dRib-induced cytotoxicity and GSH depletion in HIT-T15 cells. Stimulation with dRib dose-dependently suppressed GCL protein expression, but adding RSV significantly reversed the dRib-induced suppression of GCL protein.

Conclusion RSV was shown to protect pancreatic b-cells against the dRib-induced oxidative damage. Its mechanism might be a reversal in suppression of GCL protein expression by dRib.

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PE082 Islet biology & insulin secretion, immunology & transplantation

Induction mechanism of lipocalin-2 expression by co-stimulation with interleukin-1β and interferon-γ in RINm5F beta-cells

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Objective Lipocalin-2 (LCN-2) is known to act as an antiinflammatory or a proinflammatory mediator depending on cell types. Recently, LCN-2 has been recognized as an adipokine that links obesity and insulin resistance. However, there is no knowledge about the expression mechanism and the role of LCN-2 in pancreatic islet β-cells. Therefore, we examined molecular mechanisms by which proinflammatory cytokines interleukin-1β (IL-1β) and interferon-γ (IFN-γ) induce LCN-2 expression in RINm5F β-cells.

Methods RINm5F cells were treated with IL-1β and/or INF-γ. LCN-2 protein and mRNA expressions were examined by Western blot and Northern blot analyses. Transient transfection and luciferase reporter assay was performed to examine the LCN-2 promoter activity. Electrophoretic mobility shift assay (EMSA) was performed to examine the binding of NF-κB to promoter sites of LCN-2. In addition, iNOS and COX-2 expressions were examined by RT-PCR.

Results Unlike IL-1β, INF-γ alone did not induce LCN-2 mRNA and protein expression, however, IFN-γ significantly potentiated IL-1β-induced LCN-2 mRNA and protein expression. Meanwhile, INF-γ did not potentiate IL-1β -induced LCN-2 promoter activity, and promoter study using serially deletion constructs showed that NF-κB binding site was a key transcription factor in LCN-2 promoter activity. Also, INF-γ did not potentiate IL-1β-induced the band intensity of DNA-protein complex on NF-κB binding site of LCN-2 promoter. In addition, we found that LCN-2 expression was significantly increased compared with both iNOS and COX-2 under exposure to IL-1β, and that LCN-2 receptor was expressed in islet β-cells RINm5F and INS-1 cells.

Conclusion These findings suggest that IFN-γ significantly potentiated IL-1β -induced LCN-2 expression at mRNA and protein level but not at promoter level, and NF-κB binding site was a key factor in IL-1β-induced LCN-2 expression at transcriptional level. In addition, abundant expression of LCN-2 and LCN-2 receptor in β-cells implies that the interaction of LCN-2 and LCN-2 receptor plays a role in β-cell function.

PE083 Acute & chronic complications

Economic burden of diabetic peripheral neuropathy in Korea: Results from a population-based study of type 2 diabetic patients in Korea by Korean diabetes association diabetic neuropathy study group

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Objective This study was performed to assess the patient-level economic burden of diabetic peripheral neuropathy (DPN) through a cross-sectional survey including 4,000 patients with type 2 diabetes mellitus in Korea.

Methods A nation-wide, multi-center study was performed to estimate healthcare and non-healthcare cost, and productivity loss for recent 3 months in the patients with type 2 diabetes mellitus with and without DPN. DPN was defined as physician-diagnosed DPN or MNSI score over 2 points with abnormal monofilament test. Economic burden according to the presence of pain in DPN patients was also analyzed.

Results Mean age of study population was 60.94 ± 11.9 years and 33.5% (n = 1,338) of them had DPN. Monthly average number of visit to out-patient clinic was higher in the patients with DPN than those in the patients without DPN (1.26 ± 1.01 vs 1.04 ± 0.81, P 〈 0.0001). Total costs from health care, non-healcare and productivity loss were significantly higher in the patients with DPN than those in the patients without DPN (554,426 KRW vs 362,357 KRW, P 〈 0.0001). All parameters in productivity loss like away from work, days accoomplished less at work, and days missed work were were significantly worse in the patients with DPN compared with those in the patients without DPN. Total costs from health care, non-healcare and productivity loss were significantly higher in the DPN patients with pain (DPNP) than those in the DPN patients without pain (687,422 KRW vs 461,312 KRW, P = 0.0034). All parameters in productivity loss like away from work, days accoomplished less at work, and days missed work were were significantly worse in the patients with DPNP compared with those in the DPN patients without pain (non-DPNP).

Conclusion Our results suggest that the patient-level burden among DPN sufferers in Korea is significant, evidenced by health resource use and work/activity limitations. DPN was associated with greater healthcare cost and decreased work-productivity in Korean patients with diabetes. When combined with pain in DPN patient, economic burden from healthcare cost and productivity loss further increased compared with those of non-DPNP.

PE084 Acute & chronic complications

Effects of curcumin on diabetic nephropathy in type 2 diabetes rat model

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Objective In type 2 diabetic mellitus, diabetic nephropathy is the most common and a serious complication to lead the cause of mortality and morbidity. It is important that diabetic mellitus patients can be delayed for a long time into progressive diabetic nephropathy. In this study, we investigated whether curcumin could ameliorate diabetic nephropathy or not.

Methods At 25 weeks, we divided into three groups: LETO rats (CON), OLETF rats for diabetic control (DM) and curcumin-treated (100 mg/kg/day) OLETF rats (CUR + DM). At 45 weeks, we measured body, kidney and epididymal fat weights. We collected 24 hours urine sample for the assessment of albumin, creatinine, MCP-1, SOD and MDA. Plasma insulin, adiponectin, total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), and triglyceride (TG) were measured. To identify insulin resistance, we calculated using IPGTT, Kitt, HOMA-IR, and HOMA-beta. To confirm the damage of renal cortex, we measured glomerular basement membrane (GBM) thickness, slit pore density, MCP-1, VEGF, TGF-β1, collagen type IV, and nephrin in vivo and in vitro.

Results did not affect glucose control and insulin resistance. However it down-regulated serum lipid and also increased urine SOD level and plasma adiponectin level to epididymal fat/body weight ratio compared to OLETF rats. Additionally, it reduced albuminuria and GBM thickness with the restoration of slit pore density. In vitro study showed that it ameliorates nephrin whereas reduces inflammatory parameters such as ROS, MCP-1, VEGF, and TGF-β1 in high glucose induced podocyte cell lines, even though they did not show significant effects in vivo.

Conclusion We suggest that curcumin ameliorates diabetic nephropathy through the improved anti-lipid and anti-inflammatory effects.

PE085 Acute & chronic complications

The Relationship between disordered sleep and glucose level in Korean men

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Objective Poor quality of sleep has been associated with increased risk of diabetes mellitus(DM). Impaired fasting glucose (IFG) is an established risk factor for DM and cardiovascular disease. The purpose of this study was to investigate the relationship between sleep quality and glucose level in Korean men.

Methods A total of 4,316 subjects who participated in annual regular health check-ups in 2012 and have not been diagnosed with DM, hypertension and dyslipidemia. Subjects were divided into three group: 2,986 normal group, 1,245 IFG group, and 85 DM group. Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI).

Results In DM group, age, body mass index (BMI), waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP) and glyated hemoglobin (HbA1c) were significantly higher than other groups ($P < 0.001$). Also, the prevalence of disordered sleep was significantly higher in subjects with more advanced glucose levels ($P < 0.01$). The mean global PSQI score in normal group was significantly lower after adjustment of age and BMI than IFG and DM groups ($P < 0.01$). The global PSQI score demonstrated a statistically significant positive correlation with fasting blood glucose ($P < 0.05$), and adjustment for age and BMI did not alter the results ($P < 0.01$).

Conclusion In conclusion, subjects who are DM, or even only IFG, should be evaluated for global PSQI score and the presence of sleep disturbance. Sleep quality probably blood glucose regulation, and is closely correlated with increase of the cardiometabolic risk.

PE086 Acute & chronic complications

The relationship between arterial stiffness and metabolic syndrome in extensive cohort study

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Objective Metabolic syndrome (MS) is a cluster of cardiovascular risk factors and 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 MS.

Methods We recruited 8099 Korean subjects in extensive cohort from February 2006 to March 2010. Metabolic parameters, clinical characteristics, biochemical markers, ankle-brachial pressure index (ABI), and brachial-ankle PWV (baPWV) were obtained in each subject. The MS was defined by the National Cholesterol Education Program Adult Treatment Panel(NCEP) III criteria as three or more of five components where the cut-off point of waist circumference was modified for Korean as $\geq$ 90 cm in men and $\geq$ 80 cm in women according to the recommendation by WHO West Pacific Region..

Results Among 8099 subjects (Mean age 62.2 $\pm$ 9.25), prevalence of MS was 3715 cases (45.8%) according to the NCEP III criteria. The baPWV levels were significantly higher in patients with metabolic syndrome compared to subjects without metabolic syndrome (Rt;1622.54 $\pm$ 418.5 vs. 1478.24 $\pm$ 397.69, Lt;1628.32 $\pm$ 418.54 vs. 1483.56 $\pm$ 397.04, $P < 0.001$). The correlation between baPWV levels were significantly associated with blood pressure (BP), total cholesterol, fasting glucose, HDL, TG. The multiple regression analysis showed that the baPWV(right and left) was significantly associated with ABI(right and left) ($P < 0.05$).

Conclusion This study showed that patients with metabolic syndrome have elevated arterial stiffness in extensive cohort, suggesting a higher risk of cardiovascular disease.

PE087 Acute & chronic complications

A case associated with severe nonproliferative diabetic retinopathy (NPDR) in prediabetes

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Objective Diabetic retinopathy is considered the diabetes-specific microvascular complication. However, There is growing evidence that at glucose levels above normal but below the diabetes threshold diagnostic now referred to as prediabetes, there is also the risk of diabetic retinopathy. Retinopathy in predaibetes is present in 5~10% of subjects and typically has mild retinopathy. It is not clear why patients with prediabetes develop the complication. This is probably due to a combination of the effects of raised glucose, hypertension, dyslipidemia, genetic causes and insulin resistance.

Methods A 61-year-old woman was admitted with visual hallucination, persecutory delusion, insomnia, anxiety, and soliloquy which exacerbated since two weeks ago. She had blurred vision in right eyesight two years ago and in left eyesight two months ago. At admission, blood pressure was 110/70 mm Hg. Laboratory findings showed fasting serum glucose 115 mg/dL, total cholesterol 242 mg/dL, triglyceride 135 mg/dL, HDL-C 48 mg/dL, LDL-C 176 mg/dL, BUN 8 mg/dL, creatinine 0.46 mg/dL, HbA1c 5.9 %, insulin 2.28 μU/mL, C-peptide 0.84 ng/mL, urine microalbumin 11.4 mg/L, and urine ACR 0.012. Ophthalmologic examinations revealed neovascular glaucoma and severe NPDR in both eyes.

Results She underwent aspiration of cataract with intraocular lens implantation and anterior vitrectomy.

Conclusion Here we report a case associated with severe NPDR in prediabetes to illustrate the need for screening all patients with prediabetes, as we do in patients with type 2 diabetes.

PE088 Acute & chronic complications

Novel drug mechanism of Telmisartan: an inhibitor of voltage gated sodium channel inactivation in rat heart

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Objective Telmisartan, known as Angiotensin II receptor blocker (ARB) and partial PPAR-gamma agonist is a group of pharmaceuticals which modulate the renin-angiotensin -aldosterone system. It is mainly used for the management of hypertension, diabetic nephropathy and congestive heart failure. However, recent survey reported that myocardial infarction was occurred in telmisartan treated patients.

Methods We evaluated the effect of various dose of telmisartan on heart, cardiac myocytes and cardiac sarcolemmal ion channels. Hearts of 8 weeks SD rats were perfused with normal Tyrode's solution (control), telmisartan or losartan, another AngII antagonist, at the doses of 3, 10, 30 and 100 μM for 3 hours, respectively.

Results Telmisartan treatment, significantly induced myocardial infarction by 21% of total heart at 30 μM ($P < 0.0001$) and 63% at 100 μM ($P < 0.001$), but not in the control and same dose of losartan group. In the cardiac performance analysis and M-mode echocardiography, telmisartan treatment induced cardiac dysfunction including decreases in heart rate and coronary flow, hyper-contraction and arrhythmia. Confocal microscopy demonstrated that 30 μM of telmisartan significantly elevated intracellular Ca^{2+} level leading to hyper contracture and cell death. Patch clamp analysis revealed that telmisartan induced Na^+ overload via slowing in the inactivation of voltage-gated Na^+ current (I^{Na}) which leads to activation of reverse mode of NCX activity and following Ca^{2+} overload in isolated cardiac myocytes.

Conclusion As a new mechanism of drug action, telmisartan significantly delayed inactivation of voltage-gated Na^+ channel resulting cytosolic Na^+ overload, prolonged action potential duration and subsequent Ca^{2+} overload. Over threshold level (30 μM), this drug action potentially causes cardiac cell death and MI.

PE089 Acute & chronic complications

The preventive effect of uncarboxylated osteocalcin against free fatty acid-induced apoptosis through the activation of insulin signaling pathway in vascular endothelial cells

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Objective Osteocalcin (OC), one of the osteoblast-specific proteins, has been suggested to link between bone and energy metabolism. Regarding to atherosclerosis, there have been many studies which investigated the association between the serum levels of OC and atherosclerosis parameters, but conflicting results. OC, especially uncarbarboxylated OC (ucOC) has been suggested to be an active form of OC possessing insulin sensitizing effect and contribute to the pathogenesis of atherosclerosis. However, the potential mechanism of OC underlying it has not been fully elucidated. Furthermore, the independent effect of ucOC is largely unknown, especially in vascular cells. In present study, we examined whether ucOC 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 phosphatidylinositol 3-kinase (PI3-kinase)/Akt signaling pathways.

Methods We used human aortic endothelial cells (HAECs). Linoleic acid (LA) was used as a representative FFA. Apoptosis was measured by various methods, including a cell death enzyme-linked immunosorbent assay (ELISA) kit, a terminal deoxyribonucleotide transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL) analysis kit and Western blotting for cleaved caspase 3, cleaved PARP, and Bcl-xL.

Results Pretreatment with ucOC (30 ng/mL) prevented linoleic acid (LA)-induced apoptosis in insulin-simulated endothelial cells; this anti-apoptotic effect of ucOC was eliminated by pretreatment with wortmannin. Treatment of ucOC (ranged from 0.3 to 30 ng/mL) significantly increased the phosphorylation of Akt and endothelial nitric oxide synthase (eNOS) in a PI3-kinase dependent manner. The present study indicates that ucOC protects vascular endothelial cells from FFA-induced apoptosis through upregulation of the PI3-kinase/Akt signaling pathway.

Conclusion Our study is the first to demonstrate the independent effect of ucOC on vascular endothelial cells. Our results further suggest that ucOC could have beneficial effects on the atherosclerosis.

PE090 Acute & chronic complications

Prediction model of coronary artery disease in asymptomatic type 2 diabetes patients using multifacotorial risk stratification

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Objective Since asymptomatic coronary artery diseases (CAD) have higher mortality, it is important to distinguish who are at high-risk and need special imaging for CAD. So we developed a prediction model of CAD in asymptomatic type 2 diabetes mellitus (T2DM) patient.

Methods We performed Multidetector computed tomography (MDCT) 745 T2DM patients without chest pain or discomfort and assessed severity of stenosis according to results of MDCT. Anthropometric parameters, cardiovascular risk factors, medications (antidiabetic, antihypertensive, anticoagulant and lipid lowering agents), status of glucose control, lipid profile and the carotid intima media thickness (c-IMT) were evaluated. Variables which was used to analysis had be chosen by t-test and chi-square test. We developed the prediction model using neural network.

Results Among 745 patients, 55.3% of subjects had abnormal MDCT findings and 64 patients (20.1% of abnormal MDCT group) were treated with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). They had older age, longer duration of diabetes, higher c-IMT and plaque on c-IMT and higher postprandial glucose level. After adjustment of confounding factors, duration of diabetes, postprandial glucose level, c-IMT and c-IMT plaque was related with MDCT abnormality. The accuracy of prediction model using neural network was 95%.

Conclusion In this study, we developed a risk assessment model for CAD in T2DM. Using the assessment model, we expect we could predict CAD (accuracy, 95%) and advance further optimal evaluation and management of CAD, leading to prevention of coronary artery event about 55% of patients have abnormal MDCT finding, even though no typical symptoms in T2DM.

PE091 Acute & chronic complications

Metabolic syndrome is not suitable for screening of high CVD risk subjects in the patients with type 2 diabetes: analyses based on the KNHANES 2008

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Objective Patients who have metabolic syndrome(MS) are high cardiovascular disease (CVD) risk group, so they need aggressive treatment. But, for screening of high CVD group, there is no evidence that MS is superior to other known risk factors which are not involved in MS diagnostic criteria.

Methods Data from Korea National Health and Nutrition Examination Survey (KNHANES) 2008, which is national representative database, were used. MS was diagnosed using modified NCEP ATP III criteria. We analyzed the difference of clinical characteristics between MS subjects and non MS subjects. And we divided the subjects depending on glucose tolerance status, and compared clinical characteristics and number of subjects who have moderate or high CVD risk among those groups.

Results 18.5% of total subjects (n = 4,314) were classified as MS. Subjects who were MS have different clinical characteristics from who were not MS. 9.5% of MS subjects were DM patients, only 1% of non MS subjects were DM. ($P < 0.001$). But, non MS subjects were 30.9% of total DM patients. 10 year CVD risk was estimated by Framingham risk score. The prevalence of moderate (5~10%) and high(more than 10%) CVD risk subjects was significantly higher in MS subjects. ($P < 0.001$). But, in only DM subjects, there were no differences of clinical characteristics and prevalence of moderate and high CVD risk subjects between MS subjects and non MS subjects. Rather, the LDL in DM subjects without MS were significantly higher than DM subjects with MS ($P = 0.010$). These results were consistent even after multiple adjustments.

Conclusion The significance of MS for screening high CVD risk group in DM subjects is limited. Especially in Korea, the majority of DM patients did not accompany MS, so other important risk factors like LDL cholesterol may have more important role for screening high CVD risk group.

PE092 Acute & chronic complications

The effects of high glucose on the OPG/RANK/RANKL/TRAIL system in the progression of vascular calcification

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Objective Diabetes mellitus is frequently complicated by cardiovascular disease, such as vascular calcification and accelerated atherosclerosis. Recently, it has been known that the OPG/RANK/RANKL/TRAIL system may play a major role in vascular calcification and atherosclerosis. But, the possible effects of hyperglycemia on the OPG/RANK/RANKL/TRAIL system in the progression of vascular calcification are less clear.

Methods The primary cultured rat VSMCs obtained from thoracic aorta were divided into normal control group (NG, 5 mmol/L D-glucose), high glucose group (HG, 25 mmol/L D-glucose) and mannitol group (M, 5 mmol/L D-glucose plus 25 mmol/L mannitol) and stimulated with each glucose concentration and calcification medium for 2 weeks. We checked the calcium extent of VSMCs by von Kossa staining and the mRNA levels of OPG, RANKL, RANK, osteocalcin, and TRAIL were measured by RT-PCR. We also investigated the changes of expression of OPG, RANKL, RANK, osteocalcin, and TRAIL in HG group at 4, 7, 10, 14 days.

Results After 2 weeks of stimulation, the intensity of calcium staining was increased in HG group. The mRNA expression of RANKL, RANK, osteocalcin, and TRAIL were increased, but OPG expression was decreased in HG group. During 2 weeks, OPG expression was increased at 7, 10 days and decreased at 14 days. Meanwhile, expression of RANKL, RANK, osteocalcin, and TRAIL were increased to 14 days in HG group.

Conclusion High glucose may increase OPG mRNA expression with short-term stimulation, but decrease it with long-term stimulation in the process of vascular calcification. The expression of RANKL, RANK, and osteocalcin were increased persistently with high-glucose stimulation. As the expression of OPG was decreased, increased activity of TRAIL-induced apoptosis might be involved in the progression of vascular calcification with long-term hyperglycemic condition.

PE093 Acute & chronic complications

Anti-inflammatory effect of a novel selective 11β-hydroxysteroid dehydrogenase type 1 inhibitor (KR-66344) in LPS-activated J774 murine macrophages and mice

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Objective Type 2 diabetes causes a chronic low-grade inflammation and activation of the innate immune system that is closely involved in the pathogenesis of type 2 diabetes. 11β -hydroxysteroid dehydrogenase type 1 (11β–HSD1) as an endoplasmic reticulum-associated enzyme of a NADPH dependent reductase converts inactive cortisone to the active glucocorticoid cortisol, and is highly expressed in liver and adipose tissues. Recently, it is reported that 11β-HSD1 expression is regulated by pro-inflammatory cytokines and the relationship between 11β-HSD1, type 2 diabetes and inflammation has been demonstrated in diabetic mice models. In the present study, we investigated the anti-inflammatory effect of 2-(3-benzoyl)-4-hydroxy-1, 1-dioxo-2H-1,2-benzothiazine-2-yl-1-phenylethanone (KR-66344), a novel selective 11β-HSD1 inhibitor, in lipopolysaccharides (LPS)-activated murine J774.1 macrophages and C57BL/6J mice.

Methods The anti-inflammatory effect of KR-66344 was determined by reactive oxygen species formation assay and cell viability assay in LPS-activated J774.1 macrophages. For in vivo study, KR-66344 (30 mg/kg body weight) administrated by intraperitoneally 2 h before LPS treatment (i.v. 30 mg/kg body weight) in C57BL/6J mice. Six hours after LPS injection, mice were sacrificed. Furthermore, we examined by real-time PCR, western blotting and TUNEL assay for evaluating anti-inflammatory activity of KR-66344.

Results LPS increased 11β-HSD1 enzyme activity and expression in J774.1 cells, which KR-66344 inhibited in a concentration-dependent manner. In LPS treated macrophages, KR-66344 prevented the oxidative stress and cell death via suppressed the inflammation related cytokines and proteins and stimulated the expression of Heme oxygenase (HO)-1. These effects of KR-66344 were reversed by ZnPP, a HO-1 competitive inhibitor, in J774.1 macrophages. KR-66344 also suppressed the oxidative stress and apopotosis on spleen injury in LPS treated mice.

Conclusion It is suggested that a selective 11β-HSD1 inhibitor, KR-66344, may provide a new therapeutic window in the prevention and/or treatment of chronic inflammatory diseases with type 2 diabetes.

PE094 Acute & chronic complications

Nonalbuminuric proteinuria predict progression of type 2 diabetic nephropathy

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Objective Urinary leakage of proteins other than albumin (nonalbumin proteinuria, NAP) might indicate tubular damage rather than glomerular damage. The aim of this study was to evaluate the association of urinary NAP, a tubular damage marker, with the progression of type 2 diabetic nephropathy.

Methods The values of urinary NAP were calculated with total proteinuria and albuminuria values from each patient at baseline. In this prospective observational study, a total of 237 type 2 diabetic patients were followed up for 29 months (13~44 months).

Results Urinary NAPCR was significantly higher in the macroalbuminuria group than in the normo- and microalbuminuria groups (both $P < 0.001$) and they were also significantly different between the normo- and microalbuminuria groups ($P < 0.001$). Urinary NAPCR was positively correlated with urinary cystatin C as another urinary tubular marker. After adjusting for several clinical factors, NAPCR had significant association with the decline of eGFR ($r = 0.412$, $P < 0.001$). In patients with eGFR $\geq$ 60 mL/min/1.73 m^2 or/and normoalbuminuria, urinary NAPCR showed significant association with the decline of eGFR. In multivariate regression analysis, the number of patients who progressed to chronic kidney disease stage 3 or greater was higher in those in the upper tertiles of NAP than in those in the lower tertiles.

Conclusion The results of this study suggest urinary NAP may be predictor of the progression of type 2 diabetic nephropathy.

PE095 Acute & chronic complications

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 determined 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 were independently associated with indices of BPI-SF, MOS-Sleep, and EQ-5D and VAS.

Conclusion PDN patients had far advanced diabetic complications, which associated with decreased sleep adequacy and quality of life. There is a clear need for further research relating to prevention and treatment of DPN including the issues of sleep and quality of life.

PE096 Acute & chronic complications

Microabluminuria, but not reduced GFR, is independently associated wit arterial stiffness and carotid plaque in patients with Type 2 Diabetes

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Objective Both abluminuria and reduced estimated glomerular filtration rate (eGFR) have been shown to increase the cardiovascular disease in addition to chronic kidney disease. This study investigated the independent association between albuminuria and GFR with atherosclerotic vascular changes in patients with type 2 diabetes. Both abluminuria and reduced estimated glomerular filtration rate (eGFR) have been shown to increase the cardiovascular disease in addition to chronic kidney disease. This study investigated the independent association between albuminuria and GFR with atherosclerotic vascular changes in patients with type 2 diabetes.

Methods A cross-sectional analysis was performed among 712 subjects with type 2 diabetes. GFR was estimated by the Modification of Diet in Renal Disease formula. Albuminuria was assessed by urinary albumin-to-creatinine ratio (ACR) and categorized into normal, micro-and macroalbuminuria. Arterial stiffness was assessed by brachial-ankle pulse wave velocity (PWV) and carotid intima-media thickness (IMT) and plaque grade were assessed by B-mode ultrasonography.

Results PWV and plaque grade linearly increased according to normal, micro- and macroalbuminuria whereas no differences in IMT were observed between groups. There was no association between reduced eGFR (< 60 mL/min/1.73m^2) with PWV, IMT, and plaque grade. Albuminuria increased high PWV risk, with microalbuminuria and macroalbuminuria increasing high PWV (odds ratio 1.17 [95% confidence interval 0.68-2.00] and 3.14 (1.31-7.59), respectively; P for trend = 0.039) and plaque presence (1.90 [1.13-3.20) and 2.80 (1.19-6.61), respectively; P for trend = 0.009) after adjustment for cardiovascular risk factors. Further adjustment for eGFR did not change the significance. In multivariate linear regression analysis, ACR was independently associated with PWV ($\beta = 28.10$, $P < 0.001$) and plaque grade ($\beta = 0.08$, $P = 0.007$).

Conclusion Microalbuminuria is associated with arterial stiffness and plaque grade independently of reduced eGFR in subjects with type 2 diabetes. Long term follow-up studies, however, are needed to verify if microabluminruia has a greater impact on the development and progression of cardiovascular disease over reduced eGFR.

PE097 Acute & chronic complications

A critical role of activating transcription factor-3 on the transcriptional regulation of MCP-1 and macrophage infiltration in streptozotocin-induced diabetic nephropathy

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Objective Diabetic nephropathy (DN), a major cause of end-stage renal disease in the diabetic complication, is characterized by fibrosis of renal glomerulus and tubulointerstitial region. However, the exact molecular mechanisms by which metabolic syndrome such as diabetes may initiate and exacerbate chronic kidney disease (CKD) remain elusive. Here, we investigated whether ATF3, an oxidative stress marker, affects the development of diabetic kidney failure and especially, expression of inflammatory factors and infiltration of monocytes involved in fibrosis.

Methods Diabetic kidney failure rats were induced by injection of streptozotocin (STZ, 60 mg/kg, i.p.) and maintaining for 8-weeks.

Results The STZ-induced DN rats exhibited renal dysfunction, as evidenced by increased volume of renal glomerulus, thickened basement membrane, and increased mesenterium mass, which are consistent with higher levels of albuminuria, serum creatine, serum glucose, serum MCP-1 and TNF-a. CD68-positive cells were also significantly increased in the glomerulus and tubulointerstitial region of DN group. In quantitative RT2 PCR profiler array, MCP-1 was significantly increased in STZ-treated renal tissue, along with marked induction of ATF3. In NRK-52E cells, lipopolysaccharide or TNF-a-increased fibrosis and fibrosis-related gene expression were potentiated by ATF3 overexpression, which were strongly abolished by ATF3 siRNA. Interestingly, ATF3 acts as a direct transcriptional activator on MCP-1 gene expression by direct interaction with MCP-1 promoter. Furthermore, the conditioned media of LPS-treated macrophage RAW264.7 cells potently enhanced ATF3-mediated fibrosis, which were abolished by ATF3 siRNA and anti-TNF-a.1.

Conclusion Here, we know that ATF3 may acts as a novel transcriptional activator of MCP-1 gene expression and could lead to renal fibrosis by enhancing ECM accumulation and macrophage infiltration and thereby reveals a new aspect of the therapeutic mechanisms involved in DN.

PE098 Acute & chronic complications

Small dense LDL is associated with cardiac autonomic neuropathy in type 2 diabetes mellitus

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Objective This study was performed to investigate the relationship between small dense low density lipoproptein (sdLDL) and cardiac autonomic neuropathy (CAN) in the patients with type 2 diabetes mellitus

Methods A total 175 patients (96 men and 79 women) who have not taken lipid-lowering agents previously were consecutively enrolled in this study. LDL subfraction was determined with LipoPrintÔ LDL system, which fractionates LDL into seven parts (LDL1 through 7) according to the size and the extent of charge. And we analyzed mean LDL size and sdLDL proportion from the of LDL3 through 7 over whole LDL.

Results Mean age and the duration of diabetes were 56 ± 14 years and 10.3 ± 8.3 years, respectively. Subjects with CAN or diabetic nephropathy (DN) revealed significantly smaller mean LDL size and larger proportion of sdLDL compared with those without CAN nor DN in women. After adjusting for other confounding risk factors, sdLDL still remained the independent risk factors for CAN (i.e. mean LDL size, OR = 0.860, 95% CI 0.750-0.986, P = 0.031; sdLDL proportion, OR = 1.059, 95% CI 1.0021-1.119, P = 0.038) and DN (i.e. mean LDL size, OR = 0.858, 95% CI 0.775-0.949, P = 0.003; sdLDL proportion, OR = 1.069, 95% CI 1.025-1.115 P = 0.002) in women, but not in men.

Conclusion In this study, the more atherogenic, sdLDL was related to CAN and DN in women with type 2 diabetes.

PE099 Acute & chronic complications

Cardiovascular autonomic neuropathy and glycated hemoglobin in type 2 diabetic patients

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Objective The primary goal for control of glycaemia in diabetes is to return glycated haemoglobin (HbA1C) to a normal range to reduce chronic vascular complications. Cardiovascular autonomic neuropathy is related to increased risk of cardiovascular and all-cause mortality in patients with type 2 diabetes. Recently, intensive glycemic control was reported to be associated to increased mortality in type 2 diabetic patients. We aimed to assess CAN as a function of HbA1c in patients with type 2 diabetes.

Methods A total of 1,412 patients with type 2 diabetes were recruited. The cardiovascular autonomic function was assessed by deep breathing (E/I ratio), Valsalva and posture test.

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/m^2, respectively. Compared with HbA1C decile with the lowest hazard (median HbA1c 6.8%, IQR 6.7~6.9%), the adjusted odd ratio (OR) of CAN in the lowest HbA1c decile (5.9%, 5.5~6.1) was 1.70 (95% CI 1.04~2.79), and in the highest HbA1c decile (median 13.8%, IQR 12.8~15.1%) was 1.84 (95% CI 1.06~3.18).

Conclusion Low and high mean HbA1c values were associated with increased prevalence of CAN in type 2 diabetic patients.

PE100 Acute & chronic complications

Mean platelet volume in type 2 diabetes melllitus

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Objective Platelet activity and aggregation potential are essential components of thrombogenesis and atherosclerosis. The mean platelet volume(MPV), which is a marker of platelet size and platelet activity, can be conveniently measuring as part of whole blood count. It has been shown that MPV was significantly higher in diabetes mellitus. The aim of this study was to investigate the relationship among MPV, glycemic control and micro and macrovascular complications in type 2 DM without clinical cardiovascular disease.

Methods From August 2011 to August 2012, 270 Type 2 diabetic patients (129 male, 141 female) entering the diabetes care center of Incheon St. Mary's hospital were included in this study. Basic clinical information was required by a standardized questionnaire. Brachial-ankle PWV as a marker of stiffness of artery was measured and mean and maximal carotid IMT was evaluated by B-mode ultrasound. Platelet counts and MPV were measured using an automated blood cell counter. The fasting blood glucose levels, HbA1C and urine albumin/creatinine ratio (UACR) were also measured.

Results The mean age of study population was 56.71 ± 12 years in men, 58.56 ± 10.84 years in women and the mean duration of diabetes was 7.95 ± 7.89years and 7.71 ± 7.13 years, respectively. In men, MPV was significantly correlated with fasting glucose and HbA1c (r = 0.325 and r = 0.415, respectively, P = 0.000). In women MPV was significantly correlated with HbA1c (r = 0.323, P = 0.000). Multivariable analysis identified that MPV levels were independently associated with HbA1c in men and women (P = 0.000) but not diabetic vascular complications.

Conclusion Our results suggested a close relationship between poor glycemic control in type 2 DM. But, we did not find a significant correlation between MPV and diabetic micro- and macrovascular complications.

PE101 Acute & chronic complications

Validity of the medical outcomes study sleep scale in patients with painful diabetic peripheral neuropathy in Korea

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Objective A pain negatively influences sleep and quality of life of patients with painful diabetic neuropathy (PDN). A number of sleep questionnaires exist that are designed either to measure quality of sleep or impact of sleep problem on daily function or quality of life in patients with PDN. However, there is no convincing data on validation or reliability of these measures in patients with PDN in Korea. This study examined psychometric properties of Medical Outcomes Study (MOS)-Sleep Scale in patients with PDN based on a large population-based cross-sectional study in Korea.

Methods Measures of patients-reported outcomes (Brief pain index [BPI]-short form, MOS-Sleep Scale and EuroQoL Health [EQ-5D]) were documented. PDN was diagnosed if average daily pain intensity with visual analogue scale 4 or patients were taking medications about their current pain.

Results Patients with PDN were 577 (43.1% of DPN). Internal consistency reliability for MOS-Sleep Scale was estimated by Cronbach's alpha; it was ranged from 0.74 to 0.81 for the multi-item dimensions. The extent to which multiple items in a dimension were inter-correlated and form a dimension measuring a same underlying concept (Pearson correlation coefficients were ranged from 0.24 to 0.71, all $P < 0.001$). Each item of MOS-Sleep Scale was significantly correlated with average pain score and pain interference score (Pearson correlation coefficients ranged from 0.20 to 0.28 and from 0.29 to 0.40, respectively; all $P < 0.001$). In addition, correlations between the EQ-5D index and the MOS-Sleep Scales were ranging from -0.27 to -0.31 (all $P < 0.001$).

Conclusion The MOS-Sleep Scale had good reliable properties in the evaluation of PDN in Korean type 2 diabetic patients.

PE102 Acute & chronic complications

Atypical presentation of myocardial infarction : the philippine general hospital experience

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Objective Our primary objective is to determine the proportion of atypical presentation of MI in patients admitted in the Philippine General Hospital. Specifically, we aim to identify these atypical symptoms, to compare this population from those who presented typically and to identify associated factors for atypical presentation.

Methods We conducted chart review of patients diagnosed with myocardial infarction in the Philippine General Hospital during the period of October 2006 to September 2007.

Results Thirty eight percent (38%) of MI patients had atypical complaints. Dyspnea is the most common complaint (62%) followed by epigastric pain (8%) and syncope (8%). Four factors were significantly associated with atypical presentation: female (OR 11.54, 95% CI [1.46, 91.48]), heart failure (OR 7.31, 95% CI [1.28, 42.60]), decreased HDL (OR 13.7, 95% CI [1.14, 165]) and duration of smoking history (OR 1.05, 95% CI [1.0, 1.09]). Patients with atypical symptoms had significantly increased risk for mortality (OR 6.9 , 95% CI [1.24, 165]) and inhospital complications (OR 5.7, 95% CI [2.15, 16.21].

Conclusion A considerable proportion of patients with MI presented atypically. Dyspnea was the most common atypical symptom. They were shown to have poorer outcomes. Female gender, duration of smoking history, heart failure and low HDL are associated with atypical presentation.

PE103 Behavioral medicine & education

Measurement equivalence of touch-screen computerized and paper-based diabetes-specific quality-of-life questionnaires

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Objective Diabetes-specific quality-of-life instruments were originally developed as paper-and-pencil questionnaires. Current advances in technology have enabled the development of a computer-based questionnaire that provides various advantages over the paper-based mode of administration, such as automatic data entry, storage, and calculations. However, before implementing a computer-based questionnaire, its equivalence with the original paper-based questionnaire must first be demonstrated. This study was to test the measurement equivalence of the touch-screen computerized Diabetes-Specific Quality-of-Life questionnaire with its original paper-based counterpart. The times taken to complete the two modes of questionnaire, the user preference, and the ease of use were also explored.

Methods The study used a randomized crossover design. Participants were 208 adults diagnosed with diabetes from two university hospitals. Use of a personal computer almost every day was reported by 39.9% of the participants, and 83.2% had ever used an automated teller machine. Participants completed the paper and computer modes of the Diabetes-Specific Quality-of-Life questionnaire and were then questioned (on paper) regarding their preference and the ease of use of the modes. The measurement equivalence was evaluated using quadratic weighted kappa coefficient, ICC, and Cronbach's alpha comparisons.

Results The quadratic weighted kappa coefficient ranged from 0.703 to 0.823, and the ICCs ranged from 0.95 to 0.92 for the total scale and subscales. Cronbach's alpha values did not significantly differ between the two modes of questionnaire presentation. Among the participants, 82.7% preferred to use the computerized questionnaire, and 86.9% responded that this questionnaire was easy to use. There was no difference in the time taken to complete the two questionnaires.

Conclusion The touch-screen computerized Diabetes-Specific Quality-of-Life questionnaire was equivalent to its original paper-based counterpart. Participants preferred the computerized questionnaire over the paper-based questionnaire and reported that it was easy to use. The computerized Diabetes-Specific Quality-of-Life questionnaire may thus be feasible for use in clinical practice as an alternative to the original paper-based tool.

PE104 Behavioral medicine & education

Evaluation of education program based on empowerment model on promoting self-care among type 2 diabetic patients in Isfahan

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Objective Patient empowerment as an effective paradigm in self- care education and behavior change in diabetes care. This study examined the impact of pre, immediately and a-3 months, empowerment –based diabetes education to promoting self-care behaviors in type 2 diabetic patients in Isfahan city.

Methods This randomized control trial enrolled 140 adults with type 2 diabetes. Baseline, immediately and 3-months assessments measured self-care behaviors. In intervention group, participants received educational plan based on empowerment theory and control group received current education plan in the diabetes center. Patients in intervention group attended in five groups with 14 patients during 2 months intervention with group problem solving and peer support strategies based on empowerment theory constructs. Each scale was performed based on study goals in posttests separately. Collected data was analyzed using SSPSS software 11.5 version with statistical tests.

Results Response rate in first and 2th posttests was 100%. Self-care behaviors in total and some subscales such as nutrition, physical activity showed significant association in intervention group. Self-monitoring, adherence to treatment and inspection of foot had significant association in intervention group but there was no significant association within two groups. Smoking had a significant association in intervention group.

Conclusion Findings suggest that an empowerment based educational program is promising for improving and maintaining in some self-care subscales.

PE105 Behavioral medicine & education

Assessing the effectiveness of educational program based on empowerment model on diabetes distress and diabetes control among type 2 diabetes patients

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Objective Todays, patient empowerment is an effective plan towards behavior change in diabetes control. This study was conducted to assess evaluation of empowerment model on promoting diabetes distress and diabetes control among type 2 diabetes in Isfahan.

Methods This study was a RCT with 140 patients which was divided in two groups with Random allocation. In the baseline, demographic and health related variables were collected. In the intervention group, patients was divided in five groups with 14 patients and participate in the empowerment based education program using group problem based strategy and peer support based on model construct. In control group traditional educations done and all of patients filled the entire questionnaire the same. Empowerment goals assessed with diabetes distress and diabetes control with HbA1C. SPSS software version 11.5 using statistical tests were conducted.

Results Two groups had not any differences before the study (P 〉 0.05).Study findings revealed significant association in diabetes distress in intervention group and within two groups. Repeated measures test showed significant relation between two groups. Also, independent t- test revealed significant relation in 2 post tests. Pearson correlation coefficient showed a direct relation with HbA1C. It means that with decreasing diabetes distress, HbA1C decrease too.

Conclusion Findings revealed that education based empowerment model in intervention group using group problem based and peer support versus traditional education has effectiveness on diabetes distress and diabetes control.

PE106 Behavioral medicine & education

Assessing the effect of educational program based on small group on promoting knowledge and health literacy among women with type 2 diabetes referring to selected hospitals affiliated to Tehran University of Medical Sciences

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Objective Health Literacy is the capacity to which individuals have to obtain, process, and understand basic health information and services needed to make appropriate health decisions. Limited health literacy can reduce adults' ability to comprehend and adhere of treatment plans. This study was designed and implemented to assess effect of health education on promoting knowledge and health literacy in women with type 2 diabetes.

Methods This study was a randomize clinical trial which was conducted among 160 women with type 2 diabetes randomized in two experimental and controls groups. Tools of current study were a standard questionnaire (Test of functional health literacy in adults, TOFHLA) and knowledge was measured by self-administrated questionnaire. Intervention was performed in 6 educational sessions (45~60 minuts) in a form of small groups in experimental group. In order to analyzing data, SPSS16 software was performed and independent t- test, Kruskal-Wallis, Co-Variation, Chi-square were conducted.

Results Demographic variables of studied population in two groups was similar before intervention (P 〉 0.05). Before intervention there was not significant differences between the scores of Knowledge and Health Literacy in two groups (P 〉 0/05). After intervention, there was significant differences in the levels of knowledge and Health Literacy between experimental and control groups (P 〈 0.001).

Conclusion Study findings indicated that education with small group's strategy in experimental group, in comparison with current education has Effectiveness.

PE107 Behavioral medicine & education

Effects of nutritional intervention for prevention of diabetes in overweight and obese middle-aged women: Using HbA1c as an indicator of the intervention effects

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Objective Recently, HbA1c was adopted as a reliable screening recommendation for pre-diabetes. This study was performed to investigate the effects of nutritional interventions for the prevention of diabetes in middle-aged overweight women (BMI 23 or more) to test the reliability of HbA1c as primary indicator.

Methods Twenty overweight and obese middle-aged women finished the 12 week nutritional intervention study. Individual personalized nutrition counseling was performed every 2 weeks. The two main guidelines were 1) reduction of alcohol and alcohol associated high fat food and 2) reduction of fast-food, canned-food, ramen and high calorie snacks. Anthropometry (ht, wt, BMI, % of body muscle and fat, waist and hip circumference, blood pressure) and biochemical test (Fasting Blood Sugar (FBS), HbA1c, lipid profiles, CRP) were measured before and after the intervention.

Results After 12 weeks BMI (0wk: 27.5 ± 2.6 vs. 12 wk: 26.9 ± 2.9 kg/m^2, P = 0.005), waist circumference (0wk: 86.6 ± 2.6 vs. 12 wk: 84.02 ± 9.05 cm, P = 0.01), HbA1c (0 wk: 5.9 ± 1.0 vs. 12 wk: 5.6 ± 0.7 %, P = 0.001), LDL (P = 0.007), CRP (P = 0.003) was significantly decreased. However, FBS was increased from 97.5 ± 31.3 to 105.8 ± 20.4 mg/dL (P = 0.006). Carbohydrate (P = 0.001), fat (P = 0.000) and protein (P = 0.000) consumption was significantly decreased, while fiber intake was maintained.

Conclusion These results suggest that a mild nutrition intervention contribute effectively to prevent diabetes in overweight and obese women by applying new standard HbA1c level on pre-diabetes. The result of the dietary analyses suggests that the subjects successfully refrained from eating junk food and alcohol. While all the markers showed improved health result, FBS was not a reliable indicator, suggesting that HbA1c as a better marker for blood glucose regulation.

PE108 Behavioral medicine & education

Effect of physical activity difference according to the exercise education with accelerometer on clinical data of type II diabetic patients

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Contents The purpose of this case report was to determine effect of physical activity difference according to the exercise education with accelerometer on clinical data of type II diabetic patients. This study examined what effect did it have on clinical data of type II diabetic patients to make a difference in exercise education method by using accelerometer lifecorder that could monitor physical activity. In order to measure physical activity of total 16 type II diabetes patients, they were made to put on lifecorder, and were classified into 9 persons of experimental group, and 7 persons of control group. And physical activity analysis and education on importance and increase of physical activity were carried out for experimental group, and physical activity analysis and general exercise education were carried out for control group once a month, for 3 months. For data analysis, the mean and standard error were estimated; paired t-test was taken for measuring pre and post values in each group; and group differences were made for measures of one-way anova. Considering change before and after exercise education, FBS, PP2, HbA1C, Total-ch, BMI and Waist showed significantly decreasing tendency and HDL-Ch, Total Energy Expenditures, Physical Activity, Total Steps and Total Physical Activity Time showed significantly increasing tendency in experimental group. PP2, TG and BMI showed significantly decreasing tendency, and only Total Steps showed significantly increasing tendency in control group. Considering rate of change before and after exercise education between group, FBS, PP2, HBA1C, Total-Ch, TG, HDL, BMI, Waist and Total Energy Expenditure Activity were significant different. It is hard to represent effect of education due to a small number of subjects, but it may be useful in improving blood sugar, lipid, obesity, and activity to carry out exercise education through monitoring physical activity. And it can be deemed that physical activity is improved and obesity is consequently improved, by using equipment to monitor physical activity as education tool alone.

PE109 Behavioral medicine & education

Association of socioeconomic status with health behaviors and metabolic parameters in Korean type 2 diabetic patients

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Objective Lower socioeconomic status (SES) is associated with higher prevalence and incidence of diabetes. However, the characteristics of patients with type 2 diabetes according to SES, have not been well studied. The aim of this study is to investigate the association between SES and metabolic parameters and health behaviors in Korean Type 2 diabetic patients.

Methods A total of 4,584 type 2 diabetic patients from the Korean National Diabetes Program (KNDP) cohort who completed clinical evaluation and the physical activity and dietary intake questionnaire were included in this cross sectional study. Parameters of SES were monthly household income and education level, which were divided into 3 levels.

Results In men with type 2 diabetes, higher education level was associated with younger age, lower fasting and postprandial glucose, HbA1C, and urine alb/cr ratio, higher HOMR-IR, more current alcohol use, higher physical activity (total LTPA), energy intake, protein and fat intake. In women with type 2 diabetes, higher education level was associated with younger age, shorter diabetes duration, lower BMI, more energy intake with higher protein and fat intake, but low carbohydrate intake.

In men, higher income level was associated with younger age, shorter duration, higher BMI, lower postprandial glucose, HbA1C, lower Urine alb-Cr ratio, more current smoking, more current alcohol use, more physical activity (total LTPA), more energy intake with higher protein and fat intake but low carbohydrate content. In women with type 2 diabetes, higher income level was associated with younger age, shorter duration, more current alcohol use, more energy intake with higher protein and fat, but low carbohydrate content.

Conclusion In both men and women with type 2 diabetes, social economic status was associated with lifestyle factors. Both income and education was more strongly associated with glycemic control in men.

PE110 Behavioral medicine & education

Follow-up survey of women with gestational diabetes after childbirth

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Objective Gestational diabetes is known as a strong risk factor for type 2 diabetes, and it occurs between 2% to 5% in Korea. Thus, we would like to determine the state of new mothers who get gestational diabetes during pregnancy, education in managing their lives.

Methods The Endocrinology Internal Medicine assigned 22 patients with gestational diabetes, and a 75 g oral glucose tolerance test in the hospital after birth. To determine the management of mothers who had just given birth, we had used current medical records, lab data, and telephone surveys.

Results The subject data consisted of the following: average age of the subjects were 33.1, insulin-treated group 8 (36.3%), weeks at delivery 39 weeks, NSVD delivery method were 12 (54.5%), C/S 10 (45.5%), average neonatal weight 3430 g, pre delivery BMI was 23 kg/m^2, post delivery BMI was 24 kg/m^2, and the highest weight during pregnancy was 70.8 kg, which was insufficient for weight management. There were 9.7 weeks in which 75 g oral glucose tolerance tests performed, results acquired of phase DM 2 (9.1%), IFG 2 (9.1%), IGT 3 (13.6%), IFG + IGT 2 (9.1%), within normal limits 13 (59.1%), and for a period of breast feeding that lasted an average of 8.7 months, there were 20 (96%). The eating habits of the subjects are as follows: according to the survey, 13 (59.1%) subjects had regular meals, 4 (18.2%) had a tendency for overeating. The number of subjects that said yes to eating constantly was 16 (72%), and there were 8 (36%) subject that had more than the usual consumption of snacks between meals. The survey results from the weekly exercise regimen are as follows: the number of subjects that continued exercising the same as before and after pregnancy were 7 (31.8%), exercised at least 3 times a week was 8 (36%), the length of time was 34 minutes of each period of exercise, and the exercises consisted of walking, yoga, and aquarobics.

Conclusion As the survey studies show, the transition for eating habits of new mothers with diabetes have been quite good, however the transition for exercise habits and weight management following birth was not. In conclusion, we need to do more research on the daily life activities to better understand how to improve the quality of life for new mothers with diabetes.

PE111 Behavioral medicine & education

The current state of the management of patients with type 2 diabetes mellitus receiving treatment at general hospitals

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Objective It is well known that morbidity and mortality in patients with diabetes is influenced by diabetes complications, and that the long-term prognosis of patients with microvascular and macrovascular complications, such as chronic complications, can be greatly affected. Therefore, the proper management of diabetes and even the assessment of the management are very important.

Methods 2,059 patients receiving outpatient care at 10 general hospitals located in Seoul and Gyeonggi-do had been observed from 26 to 31, March 2012, in the areas of blood glucose management, complications management, and whether or not diabetes education was given.

Results The mean age, duration of diabetes, and HbA1c of the subjects were 60.9 ± 11.6years, 10.8 ± 8.2years, 7.4 ± 1.3%, respectively. The percentage of those achieving the goal of glycemic control (HbA1c 〈 7%) was 44.7%. 52.6% were controlled with blood pressure below 130/90 mm Hg, 43.1% were controlled with fasting glucose below 130 mg/dL, the percentage of those achieving the goal LDL-cholesterol (100 mg/dL 〈) was 66.3%. 72.8% were given oral hypoglycemic agents, 6.9% were given only insulin, 15.4% were given an insulin and oral hypoglycemic agent combination therapy. Performance Rates in fundus photogram examination within one year was 56.1% and microalbuminuria was 75.4%, respectively. 55.2% had a diabetes education experience at least once and 57.3% was educated in patients with diabetes duration of less than 10 years.

Conclusion Among type 2 diabetes patients in general hospitals, 45% reached target blood glucose, 45% did not receive diabetes education and Performance Rates in fundus photogram examination within 1 year was 56%. Finally the results showed the diabetes mellitus was not well-maintained. Thus, more aggressive education and testing need to be performed for better progresses.

PE112 Behavioral medicine & education

Dietary sodium intake among diabetic patients in KNHANES V-1

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Objective Hypertension (HTN) is common in diabetic patients and sodium restriction studies for hypertensive type 2 diabetic patients(T2D) showed favorable results in BP managment. Recently, lower 24-h urinary sodium excretion is paradoxically associated with an increased risk of all-cause and cardiovascular mortality in T2D. We briefly investigated the correlation among sodium intake and other cardiovascular markers in T2D.

Methods In a cross-sectional study sample with T2D in KNHANES V-1, sodium intake among age groups was explored using 24hour recall method and compared among different BMI, smoking, systolic and diastolic blood pressure groups (SBP/DPB).

Results Sodium intake was different among age groups in patients with T2D and well correlated with other cardiovascular markers.

Conclusion Sodium restriction was well correlated with multiple cardiovascular markers in T2D. These finding suggested that benefits of sodium restriction could not be restricted to mere BP lowering effect. Further investigation should be needed to confirm these observation and find underlying mechanisms.

PE113 Behavioral medicine & education

Effects of intensive dietary calorie restriction to reduce weight in obese women with type 2 diabetes after the 12 weeks intervention and 1 year follow-up of the intervention

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Objective Lifestyle intervention to reduce weight can improve glucose control and cardiometabolic risk factor in obese patients with type 2 diabetes, at least, as long as the intervention continues. We aimed to assess the changes of the weight, dietary composition and insulin resistance in obese women with type 2 diabetes after the 12 weeks dietary calorie restriction (12 w) and 1 year follow up of the intervention (1 y).

Methods A total 80 patients with type 2 diabetes were randomly assigned to intensive dietary intervention (IDI) group or control group. IDI group were recommended to reduce their usual dietary calorie by -500 kcal/d and provide biweekly individual intervention in 12w. Follow up assessments were performed after 1y. We measured the insulin resistance (IR) by HOMA-IR.

Results Of the 80 patients, 82.5% completed the 1y. Weight (-6.6% vs -0.3%, respectively, P 〈 0.001) and HbA1c showed larger reduction in IDI group than control group at 12w, however, no significant group differences were found in weight and HbA1c regain between 12w and 1y. In the IDI group, initial weight decreased at least 5% in 84.4 % and 63.3 % after 12w and 1y, respectively. IDI group showed larger reduction of carbohydrate intake and IR than control group at 12w, however, there was significant difference between the groups in carbohydrate intake but not in IR after 1y. The decrease of weight for 1y showed positive correlation with the decreased in weight and carbohydrate intake for 12w (r = 0.755, P 〈 0.001; r = 0.685, P 〈 0.001, respectively).

Conclusion A 12 week intensive dietary calorie restriction can induce significant weight loss (≥ 5%) in obese women with type 2 diabetes and maintain this loss in more than 60% of patients after 1y. The greater initial weight and carbohydrate reductions for 12w were associated with long term weight and carbohydrate intake maintenance.

PE114 Behavioral medicine & education

The effects of physical activity and obesity factor on brain nerve growth factor in children

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Objective Exercise leads to the release of certain neurotransmitters in the brain that alleviate pain, both physical and mental status. Physical activity is associated with a range of positive health outcomes, including fewer depressive symptoms. Physical activity increases expression of BDNF, which may enhance brain health. But the effects of physical activity on brain nerve growth factors for children are not clear. Therefore, the purpose of this study was to determine the effects of physical activity and obesity factor on brain nerve growth factor in children.

Methods Seventy-eight subjects were selected from one elementary school. We were measured variables of body composition, physical fitness, serum lipid, physical activity and brain nerve growth factor(insulin, BDNF, serotonin). The physical activity of day life changes were tested using the SenseWear Armband. The collected data were analyzed Total energy expenditure, Average METs, Time of 3.0 METs less than activity, Time of activity between 3.0 and 5.9 METs, Time of 6 METs over activity. The factors of brain nerve growth factor were BDNF (brain-derived neurotrophic factor), serotonin, insulin. Data analysis was done using PASW Statistics 18.0 program and included independent t-test, Pearson correlation coefficients and stepwise multiple regression.

Results The results of this study were as follows, BDNF in obese children was lower than the normal children. Muscle mass and insulin, BDNF, percent muscle mass and BDNF, serotonin, time of 6 METs over activity and BDNF were positively correlated. Percent body fat and BDNF were negatively correlated. The variables predict - ing Insulin were muscle mass and cardiorespiratory endurance. And predictors of BDNF were the muscle mass and time of 6 METs over activity. And predictors of serotonin were the percent muscle mass and muscular strength.

Conclusion The results indicate that it is necessary to improve brain nerve growth factor to increase muscle mass, time of 6 METs over activity in children.

PE115 Behavioral medicine & education

Knowledge, attitude, and practice of culinary botanicals for common diseases as well as killer diseases among the residents of Baltimore Maryland United States of America

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Objective Investigations on traditional healthcare have always offered immense scope for the development of new drugs and opportunities for alternative drug sources. The investigations were conducted in different neighborhoods and even urban areas of Baltimore within Maryland United States of America.

Methods The data adduced is based on personal interviews, observations, and experiences of elder residents in the Baltimore. Residents from different castes and immigrants such as Asian, Black or African American, Hispanic/Latino, White and people from urban area were carefully interviewed. The culinary botanicals are generally used in the form of staple food, leafy or fruit vegetables, spices or condiments. Voucher specimens were collected and identified by referring standard flora.

Results Information on 72 culinary botanicals belonging to 59 genera and 48 families are being communicated. Information regarding local remedies related especially to the culinary botanicals used as food and food adjuncts were recorded. The residents of Baltimore employ them also as local medicine in treating various human ailments. These are administered in the form of decoction, paste, oil, ash, juice, powder, extract, latex or in the form of a particular recipe. Even they are used raw or sometimes simply warmed. In many cases, they use them as a sole drug or occasionally supplemented by other botanicals or substances. They used these to combat common diseases such as migraine, rheumatic or joint pains, acidity, scabies, wounds, injuries, pimples, jaundice constipation, amoebic dysentery, cough, menstrual complaints, stomach-ache, tooth-ache, flatulence, burns, indigestion, eye-burning, fever etc. as well as killer diseases.

Conclusion It was found that some of the information has not so far been available in literature. The method of preparation and mode of action is also simple and convenient. The studies indicated that the knowledge is to be transferred properly by old people to younger generation and should be trained in collection and processing.

PE116 Behavioral medicine & education

Evaluation of predictive self-care behaviors on glycemic control in patients with type 2 diabetes

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Objective Diabete has no definite treatment. The most important treatment strategy employed to control diabete is adherence to self care behaviors that includes special diet, physical activity, blood glucose monitoring, daily foot care and taking the prescribed medicine. Purpose of this study was ditinctly recognition of adherence rate in different dimension of self-care behaviors and evaluating predictor potency of each dimension on glycemic control among type2 diabetic patients under coverage of diabetic clinic of Qom University of Medical Sciences.

Methods This descriptive and analytical study conducted as a cross sectional study among 275 Randomized patients that had Inclusion criteria. For data collection the «Summary of Diabetes self-care Activities Measure» (SDSCA), Cognitive Health Assessment Questionnaire, Beck Questionnaire and HbA1c test Was used . For data analysis bivariate correlations and multivariate linear regression in spss version17 was applied.

Results The final predictive variables regression model includedes education level, taking the medicine, Nutrition, physical activity and Blood glucose monitoring. This model has accounted for 66% of the variance of the HbA1c as a glycemic control indicator (P 〈 .001)

Conclusion In this study various dimension of diabetes self-care behaviors have different influence potency on metabolic control. Taking the medicine and nutritional dimention of self-care behaviors have the most influence on glycemic control.

PE117 Behavioral medicine & education

Application of BASNEF educational model for nutritional education among elderly patients with type 2 diabetes

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Objective The objective of this study was to determine the effects of nutritional educational program on glycemic control of elderly patients with type 2 diabetes.

Methods In this parallel randomized controlled educational trial, 100 diabetic elderly patients (≥ 60 years) were chosen (50 in control and 50 in test group). Nutrition education based on beliefs, attitudes, subjective norms and enabling factors (BASNEF model) was conducted. Dietary intake and glycemic indices as well as the components of the BASNEF model were assessed. The four 70-minute educational sessions were conducted in one month. Three months after training intervention, questionnaire was completed again and blood tests were performed.

Results Increased intake in the mean daily servings of fruits (0.91 ± 0.82 vs. 0.17 ± 0.79; P 〈 0.001), vegetables (0.87 ± 0.86 vs. 0.03 ± 1; P 〈 0.001) and dairy (0.35 ± 0.52 vs. and 0.12 ± 0.76; P 〈 0.001) were reported in the intervention group compared to the control group (P 〈 0.001). The amount of fruits, vegetables and dairy increased in the intervention group at the end of the study (P 〈 0.001). However, it was not significantly changed in the control group. HbA1c and fasting blood sugar (FBS) levels decreased significantly in the interventional group compared to the control group (P 〈 0.001). Comparing the amount of FBS and HbA1c at the end of the study with the baseline measurements showed significant reduction in interventional group (P 〈 0.001). However, there was no significant change in control group in this regard.

Conclusion BASNEF-based nutritional educational intervention improved dietary intakes as well as glycemic control 3 months after intervention.

PE118 Behavioral medicine & education

Change of insulin level during body weight loss might predict the weight regain in type 2 diabetes, but leptin did not

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Objective Substantial evidence indicates that biological adaptations to weight loss contribute to weight regain. Several hormones such as leptin, insulin, and ghrelin are instrumental in control of the appetite center.

Methods Total 46 women with type 2 diabetes were recruited for assessing weight regain after weight loss program with 3 month lifestyle modification. We assessed anthropometric parameters, abdominal fat using computed tomography, fasting serum levels of insulin and leptin at baseline, 1 month, 3 months, and 12 months for follow-up

Results At baseline, the mean age of subjects was 56 ± 8 years and BMI was 27.7 ± 2.4 kg/m^2. Body weight was decreased by 2.6 ± 2.3% at 1 month, by 5.7 ± 3.1% at 3 month, and regain by 0.5 ± 3.1% at 12 month. Weight regain (percent change) after lifestyle interventions was associated with percent decrease of insulin(r = -0.401 P = 0.014) at 1 month, but not with leptin (r = -0.129, P = 0.440) at 1 month during weight reduction. Abdominal fat regain was also associated with decrease of insulin at 1 month (r = -0.533, P = 0.001).

Conclusion In conclusion, when body fat stores fall, declining levels of insulin might be more important than those of leptin for regaining body weight in type 2 diabetes.

PE119 Behavioral medicine & education

Dietary intake and blood triglyceride level in men with impaired fasting glucose

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Objective Impaired fasting glucose (IFG) & elevated serum TG level are one of metabolic syndrome components. They were known as risk factors of cardiovascular diseases. Dietary modification is helpful to improve these risk factors and can prevent CVDs. We examined the dietary intake of adult men with IFG and dietary characteristics according to serum TG level.

Methods Subjects were 102 adult male out-patients with IFG visited clinical dietitian for nutrition counseling. We examined dietary habit and food intake using 24-hr recall method. Also we collected anthropometric and biochemical data.

Results Mean age and BMI of subjects were 45.6 years and 25.3 kg/m^2. Overweight or obese subjects were 75.5%. Mean FBS, HbA1c, LDL-cholesterol, HDL-cholesterol, and TG were 113.4 mg/dL, 5.6%, 118.0 mg/dL, 51.2 mg/dL and 164.4 mg/dL respectively. Energy consumption was 105.6% of requirement and C:P:F ratio was 5.6:2.6:1.8. In excessive energy intake subjects (≥ 120% of requirement), serum TG level was significantly higher than in subjects whose energy intake were less than 120% of requirement (220.0 mg/dL vs 146.4 mg/dL, P = 0.015). In hypertriglyceridemic (serum TG ≥ 150 mg/dL) subjects, percentage of CHO was higher than in normotriglyceridemic (serum TG 〈 150 mg/dL) subjects (57.7% vs 54.3%, P = 0.023). Intake amount of grains, sugars, and beverage were higher in hypertriglyceridemic subjects. Also the amount of alcohol drinking were significantly higher in hypertriglyceridemic subjects (5.4 vs 7.9 drinkings, P = 0.045). Frequently drinking subjects (6~7/week) had higher serum TG level than subjects drinking less than 1~2/week (156.0 vs 288.0 mg/d, P = 0.09) although there was no significant difference.

Conclusion These results suggested that CHO & alcohol drinking might have relation with serum TG level in adult men with IFG. Further researches will be needed to identify dietary characteristics and adequate dietary modification in persons with metabolic risk.

PE120 Behavioral medicine & education

Accuracy of the contents on diabetes from a high school textbook in Korea

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Objective Although a number of consumers get health information from internet, TV, and radio, they usually have confidence in the contents from textbooks. The purpose of this study is to access the accuracy of the contents on diabetes and related diseases from the newly developed high school textbook 'exercise and healthy life'.

Methods We reviewed five different versions of Korean high school textbook 'exercise and healthy life', and the diabetes related health informations were analyzed for accuracy.

Results Health professionals including diabetes specialists were not included among the authors in any chapters from these textbooks. In most of textbooks, the term "obesity" was defined by the body mass index of Caucasian standard, and pathogenesis of type 2 diabetes was described as the decreased insulin resistance. Moreover, they said that the etiology of type 1 diabetes was congenital cause. The diagnostic criteria for hypertension was listed over 160/95 mm Hg.

Conclusion Although recently the textbook 'exercise and healthy life' was developed, the accuracy of the contents on diabetes and related diseases is incorrent. Thus, health professionals including diabetes specialists should participate in developing the textbook for students to provide the reliable health informations about diabetes.

PE121 Epidemiology & genetics

Relationships between sarcopenic obesity and insulin resistance, inflammation, and vitamin D status: The Korean Sarcopenic Obesity Study (KSOS)

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Objective It has been suggested that insulin resistance, low-grade inflammation, and vitamin D deficiency are associated with obesity and sarcopenia. However, their relationships with sarcopenic obesity (SO) are unclear. We evaluated the impact of homeostasis model assessment of insulin resistance (HOMA-IR), high sensitivity C-reactive protein (hsCRP), and 25-hydroxyvitamin D (25[OH]D) levels on SO in Korean adults.

Methods This study included 493 apparently healthy adults (180 men and 313 women) enrolled in the Korean Sarcopenic Obesity Study (KSOS). Sarcopenia was defined as a skeletal muscle mass index (SMI) of 1 SD below the sex-specific mean value for a young reference group. Obesity was defined as a visceral fat area (VFA) $\geq$ 100 cm^2. We classified the participants into four sarcopenia/obesity groups based on both SMI and VFA.

Results The prevalence of SO was 17.8% in men and 24.9% in women. In women, the SO group had higher HOMA-IR and hsCRP levels compared to the non-SO group. In men, the 25[OH]D levels were significantly lower in the SO group than the non-SO group. Both hsCRP and HOMA-IR levels were negatively correlated with SMI and positively correlated with VFA in both men and women; whereas, 25[OH]D levels were positively correlated with SMI in both men and women. Multiple binary logistic regression analysis showed that HOMA-IR and 25[OH]D levels were independently associated with SO in men, while HOMA-IR and hsCRP were significant factors predicting SO in women.

Conclusion Insulin resistance, inflammation and vitamin D deficiency were associated with SO in a Korean adult population.

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