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Abstract book

2020 International Congress of Diabetes and Metabolism

18~19 September 2020
VIRTUAL CONGRESS

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2020 International Congress of Diabetes and Metabolism

September 18~19, 2020
Virtual Congress

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Korean Diabetes Association

Program at a Glance

LIVE Session

Time / Session	Channel A Clinical diabetes and therapeutics/Diabetic complications/Epidemiology	Channel B Behavioral medicine/Education/Clinical nutrition/Self-care	Channel C Basic & Translational Diabetes research (1)	Channel D Basic & Translational Diabetes research (2)
Friday 18 September, 2020				
09:00~09:10	Opening address			
09:10~11:10	S1 Diabetic complications 1	S2 Behavioral medicine/education (K)	S3 Molecular metabolism	S4 Integrated physiology
11:10~11:30	Break			
11:30~12:00	Plenary lecture 1			
12:00~12:30	Plenary lecture 2			
12:30~12:50	AW1 Sulwon Award			
12:50~13:10	Satellite symposium 1	Satellite symposium 2 (K)	Satellite symposium 3	Satellite symposium 4
13:10~14:00	Break			
14:00~16:00	S5 Clinical diabetes and therapeutics 1	S6 Self-care (K)	SP1 Debate session-SGLT2 inhibitor	CS1 Health insurance and government relation session
16:00~16:20	Break			
16:20~18:20	S7 Diabetic complications 2	S8 Clinical nutrition (K)	S9 Diabetes technology	S10 Basic research
Saturday 19 September, 2020				
08:30~08:50	Satellite symposium 5	Satellite symposium 6	Satellite symposium 7	Satellite symposium 8
09:00~11:00	S11 Clinical diabetes and therapeutics 2	S12 Epidemiology & genetics (K)	S13 Metabolomics in metabolic disease	
11:00~11:20	Break			
11:20~12:00	Plenary lecture 3			
12:00~12:10	Research contract			
12:10~12:30	AW2 Young Investigator Award			
12:30~12:50	Satellite symposium 9	Satellite symposium 10	Satellite symposium 11	
12:50~13:30	Break			
13:30~15:30	RG1 ICDM-AIBIS in AASD joint symposium	RG2 Research group on diabetic neuropathy session (K)	CS2 Diabetes and metabolism journal session	RG3 Research group on fatty liver disease session (K)
15:30~15:50	Break			
15:50~17:50	CS3 Diabetes prevention	RG4 Research group on diabetic vascular cell biology session	SP2 Precision medicine	SP3 AI drug target (K)
17:50~	Closing ceremony			

Program at a Glance

Video on Demand Session

VOD	Session
VOD1	Hot topic of diabetes epidemiology 1
VOD2	Hot topic of diabetes epidemiology 2
VOD3	International education course
VOD4	Cardiovascular disease across the life course in diabetic women
VOD5	Heterogenous adipose tissue and metabolic regulation
VOD6	Diagnosis and management of diabetic peripheral neuropathy; where are we now and where to go
VOD7	Mitochondrial dysfunction in diabetes and its complication
VOD8	Beta cell generation and regeneration

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PL-1

Diabetes care: post COVID-19 new normal

Kun-Ho Yoon

The Catholic University of Korea, Korea

The pandemic of coronavirus disease 2019(COVID-19) overwhelming the whole world, since the first case was reported in Wuhan, China in December 2019. As of on Aug. 8, 2020, worldwide, here have been 19,187,943 confirmed cases of COVID-19, including 716,075 deaths, reported to WHO. Although the fatality rate of COVID-19 is lower than that of SARS-CoV-1 and MERS-CoV, the absolute number of fatality in COVID-19 is extremely high because of high prevalence of COVID-19. Because of diabetes was significantly associated with worse outcomes, international diabetes associations including KDA have suggested strict glycemic control and prioritizing COVID-19 screening in elderly (aged ≥70 years) patients with diabetes to defend against COVID-19. KDA also suggest to refrain from going out or visiting crowded areas, put on a mask before visit a medical institution, avoid crowds, and avoid contacting someone with fever or respiratory symptoms. For blood sugar management, KDA suggest to make sure to keep oral medication and insulin administration more strictly than usual, conduct and check self-monitoring of blood sugar more frequently. Contact the community healthcare center is needed if there are any respiratory symptoms. If it is difficult to visit the doctor, consult through the phone helpline allowed temporarily by government. In this special COVID-19 pandemic environment, traditional way of healthcare through face-to-face contact so called analogue healthcare system might have a lot of prob-lems. It increases a chances of COVID-19 infection during clinic and hospital visit for only simple consultation or pre-scription refills and could not cover the patient's and physi-cian's needs. Modern digital healthcare system can provide pa-tients, family members, and healthcare professionals with sup-port during COVID-19 pandemic. For preparing the future another infectious disease pandemic attack, we have to prepare nationwide remote monitoring and couching system for the patients.

PL-2

Digital transformation of future medicine accelerated by COVID-19

Sungroh Yoon

Seoul National University, Korea

In this talk, I will first introduce the history and key development of artificial intelligence and big data and then present how the pandemic of COVID-19 is transforming many aspects of daily life all over the globe. In addition, I will explain how the future of medicine will be affected by the technological advances driving so-called non-contact economy. I will wrap-up the presentation by introducing the presidential committee on the 4th industrial revolution I am currently chairing.

PL-3

Pancreatic islet biology, function, and dysfunction: different pathways in different diabetes

Alvin C. Powers

Vanderbilt University, USA

A critical component of all forms of diabetes is reduced insulin secretion. This presentation will discuss new research that highlights different mechanisms leading to impaired islet function in human diabetes. The presentation will also discuss research approaches that are changing the understanding of the pathogenesis of islet dysfunction in type 1 and type 2 diabetes.

S1-1

SGLT2 Inhibitors and kidney protection beyond diabetes

David Z. Cherney

University of Toronto, Canada

The objective of this lecture is to review recent advances in the cardiovascular-renal-metabolic field, with a focus on trials that have demonstrated kidney protection. The discussion will also review insights into mechanisms responsible for kidney protection in people with and without underlying diabetes. Finally, the talk will review some of the ongoing trials in this area that target unmet needs in people with kidney disease.

S1-2

Diabetic medications and albuminuria

Soon Hyo Kwon

Soonchunhyang University, Korea

Increased urinary albumin excretion in diabetes is associated with renal and cardiovascular disease (CVD). The reduction in albuminuria in diabetes may reduce the risk of CVD events and slow the progression of diabetic kidney disease. The effects of new antidiabetic drugs such as as sodium-glucose cotransporter 2 (SGLT-2) inhibitors, and glucagon-like peptide 1 (GLP-1) receptor agonists, on the long-term outcomes in patients with diabetes are very promising. Recent studies indicate that SGLT2 inhibitors and GLP-1 receptor agonists reduce albuminuria compared with other conventional therapies such as and dipeptidyl peptidase 4 (DPP-4) inhibitors, sulfonylurea and placebo. The reduction of albuminuria may be associated with the cardiovascular and renal beneficial effects of these medications. The mechanisms of the albuminuria reduction are under investigated. Clinicians should consider these anti-diabetic medications therapy with blood pressure and cholesterol control for protection diabetic complications.

S1-3

Anti-diabetes drugs and GFR

Sang Soo Kim

Pusan National University, Korea

Diabetes has reached epidemic proportions in Korea and worldwide, and is associated with increased risk for chronic kidney disease (CKD) and end stage kidney disease (ESKD). The natural history of diabetic kidney disease (DKD) traditionally has been described as progressive albuminuria followed by a steady loss of glomerular filtration rate (GFR). However, the natural course of kidney function (GFR decline or trajectory) among people with diabetes (especially, type 2 diabetes) might be complex in real practice. A strong evidence demonstrated a consistent association between eGFR decline and subsequent development of hard renal endpoints (such as ESKD or renal death) from observational data and clinical trials. These data may support the use of GFR parameters (decline, changes or slope) as a surrogate endpoint for kidney disease progression in both real practice and clinical trials. Antidiabetic drugs have the potential for both benefit and harm to the kidneys and these effects play a pivotal role in patient-centered management overt DKD and. Studies on renal endpoints were also performed as pre-specified secondary outcomes in recent cardiovascular outcome trials (CVOTs). This review focuses on the clinical implication of eGFR decline as renal outcomes and the effects on renal outcomes of currently available anti-diabetic drugs.

S1-4

Multiomics approach in DKD research

Nan Hee Kim

Korea University, Korea

Diabetes is rapidly increasing worldwide, and approximately 40% of them will develop renal complications. Diabetic kidney disease (DKD) is the leading cause of end stage renal disease, which needs significant healthcare costs and results in early death. For several decades, investigators have sought to discover inherited risk factors and biomarkers for DKD. Several genome-wide association studies (GWAS) have been conducted for DKD with further meta-analysis of GWAS and comprehensive "single gene" meta-analyses now published. Despite these efforts, much of the inherited predisposition to DKD remains unexplained. Multi-omics approach including transcriptomic, proteomic, and metabolomic studies are being used to help elucidate the unknown mechanisms and possible biomarkers

in the development and progression of DKD. In this talk, I will summarize the recent progress of multi-omics studies in searching for the biomarkers of DKD.

S2-1

Recommendations for the good transition-how to transit?

Jae Hyun Kim

Seoul National University, Korea

During the long-term management of the type 1 diabetes (T1D from childhood to adulthood, transition, when the shift from childhood to adulthood occurs in many aspects, has a significant influence on diabetes care. Transition period corresponds to emerging adulthood, generally from late teens to early twenties. T1D patients in transition period are associated with unfavorable health outcomes including poor glycemic control, loss of follow-up, psychological problems, and increased acute and chronic complications. Therefore, proper management in the transition period is critical for improving clinical outcomes in T1D patients.

Although several guidelines and toolkits for transition care has already published, it is uncertain whether these recommendations are appropriately applied in the clinical practice. Many studies are performed on transition issues related to patients/family of T1D, adult providers, and pediatric providers, especially in Western countries. In a Korean study, transition care of T1D patients was a significant challenge to pediatric endocrinologists in Korea. Unfortunately, transition care for emerging adults with T1D remains to be investigated. Development of protocols for transition care for healthcare providers and improvement of diabetes self-management skills for patients are needed. In this lecture, current status of transition care and recommendations will be reviewed and suggestions for good transition will be discussed.

S2-2

"Live" diabetes education tool for transition

Jung Hwa Lee

Khyunghee University Hospital at Gangdong, Korea

Many adolescents with diabetes experience difficulties in blood sugar control as they transition into adults.

First, physically, as adolescents go through puberty, insulin resistance increases, and as a result, they experience poor blood sugar control. Second, he fears going into adulthood, where he has to think about the possibility of chronic diabetic complications psychologically. It is also becoming increasingly independent socially.

Education and counseling to help control blood sugar are needed during this transition period. We would like to find tools that help control blood sugar and help educational counseling through examples.

S2-3

Nutritional strategies during transition

Min Young Noh

Seoul St. Mary Hospital, Korea

'Emerging adult' is a newly recognized developmental period of life from the late teens through the twenties. During this period, emerging adults explore their identity and experience many new transitions, demands, expectations, and roles as they develop from dependent adolescents to independent young adults. This transition addresses the medical, psychosocial, educational, and vocational needs of the emerging adult with a lifelong chronic condition. Therefore, in this session, we will consider what nutritional management is needed in the emerging adult period and what areas should be of interest as educators.

S2-4

Exercise recommendations for good transition

Seung Jae Jeong

Samsung Medical Center, Korea

Adolescence is critical periods for developing movement skills, learning healthy habits, and establishing a firm foundation for lifelong health and well-being. Regular physical activity in adolescents promotes health and fitness. Compared to inactive people, physically active teenagers have higher levels of cardiorespiratory fitness and stronger muscles. They also typically have lower body fat and stronger bones. Physical activity also has brain health benefits for school-aged children, including improved cognition and reduced symptoms of depression.

But, pediatric diabetes is a challenging condition to manage for various physiological and behavioural reasons. Regular exercise is most important, but people with type 1 diabetes tend to be as inactive as the general people. For pediatric diabetes, regular exercise can improve health and wellbeing, and can help individuals to achieve their target lipid profile, body composition, and fitness and glycaemic goals.

Exercise guidelines for teenagers with pediatric diabetes are not much different from ordinary teenagers. School-age adolescents can gain significant health benefits by engaging in moderate physical activity for a period of up to 60 minutes each day. The activities should include aerobic activities as well as activities that strengthen the muscles and bones that fit the age. . Like adults, the total amount of physical activity is more important for achieving health benefits than is any one component (frequency, intensity, or duration) or specific mix of activities (aerobic, muscle strengthening, bone strengthening). Even so, bone-strengthening activities remain especially important for young adolescents because the greatest gains in bone mass occur during the years just before and during puberty. In addition, the majority of peak bone mass is obtained by the end of adolescence.

Teenagers in pediatric diabetes who are regularly active have a better chance of a healthy adulthood.

S3-1

Inflammasome modulation to treat NASH & liver fibrosis

Ariel Feldstein

University of California, USA

Cell death and inflammation are two central elements in the development of liver fibrosis and injury. Inflammasomes are intracellular multiprotein complexes expressed in both hepatocytes and non-parenchymal cells in the liver that are key regulators of inflammation and cell fate. They respond to cellular danger signals by activating caspase 1, releasing the proinflammatory cytokines IL-1β and IL-18, as well as initiating a novel pathway of programmed cell death termed "pyroptosis." This novel type of cell death is intrinsically pro-inflammatory because it is associated with the release of IL-1β and other intracellular content to the extracellular space including NLRP3 inflammasome particles that represent a novel mechanism to spread inflammasome signaling to adjacent cells. These downstream effectors of NLRP3 inlflammasome activation in the liver can initiate and perpetuate abnormal wound-healing responses with the principle cellular target being the activation of hepatic stellate cells. From the various inflammasomes, the NLRP3 inflammasome has been increasingly implicated in the pathogenesis of chronic inflammatory liver diseases, including non-alcoholic steatohepatitis, a disease process that is soaring and has evolved as a primary cause of liver fibrosis and need for liver transplantation. In this seminar, I will highlight the growing evidence for both indirect and direct effects of NRLP3 inflammasome activation in triggering liver fibrosis and its role for therapeutic intervention for treatment of Nonalcoholic Steatohepatitis (NASH).

S3-2

Cholesterol in the transition from steatosis to steatohepatitis

Jose C Fernandez-Checa

IIBB-CSIC, Spain

Cholesterol is a critical component of membrane bilayers that determine their physico chemical properties. Cholesterol accumulation plays a role in the progression of metabolic liver diseases and its regulation emerges as a potential target for intervention. Cholesterol trafficking in hepatocyte mitochondria determines mitochondrial function and susceptibility to oxi-

dative stress and inflammation-mediated cell death. Cholesterol accumulation in hepatic stellate cells and Kupffer cells plays a key role in the initiation of fibrogenesis and recruitment of inflammatory cells, contributing to the progression of steatosis to steatohepatitis.

S3-3

The cross talk between Hippo-YAP and AKT signaling in liver metabolic dysregulation and tumorigenesis

Dae Sik Lim

KAIST, Korea

Several in vitro studies have suggested that Hippo-YAP signaling regulates the AKT pathway components PI3K and PTEN. But the nature of crosstalk between the Hippo-YAP and AKT pathways in the regulation of liver homeostasis has remained unclear. Here, we investigated the possible role of cross talk between Hippo-YAP/TAZ and PTEN-AKT pathways in the liver. Deletion of both Pten and Sav1 in the liver (DKO) accelerates the development of Nonalcoholic fatty liver disease (NAFLD) and liver cancer in mice through hyperactivation of AKT. At the molecular level, activation of YAP/TAZ amplifies AKT signaling through direct up-regulation of IRS2 expression. Deletion of YAP/TAZ or activation of Hippo attenuated development of fatty liver in these DKO mice by down-regulating IRS2. Notably, increased YAP/TAZ expression was also associated with high level of IRS2-pAKT in the patient. Moreover, treatment with the AKT inhibitor MK-2206 attenuated NAFLD development and tumorigenesis in DKO mice. Our findings thus suggest that crosstalk between Hippo and AKT pathways at the level of YAP/TAZ-IRS2 contributes to the development and progression of NAFLD to liver cancer, and they therefore provide a basis for the development of new therapeutic interventions.

S3-4

New liver-secretory target molecule for insulin resistance

Sang Geon Kim

Seoul National University, Korea

The liver controls glucose and lipid metabolism as a central hub linking metabolic organs, governing whole-body energy metabolism. G protein-coupled receptors (GPCRs) sense neurohumoral signals outside the cell and activate intracellular signaling pathways through G protein. Since activation of multiple receptors converge on a single G protein, the level of G protein would affect net signal intensity via integration of different signals. This study investigated whether hyperglycemia in the setting of insulin resistance and obesity alters hepatic $G\alpha13$ level, and if so, whether this event affects systemic energy metabolism. In HCV-infected patients or animals with metabolic diseases, $G\alpha13$ level decreased in the liver as insulin sensitivity deteriorated. A hepatocyte-specific $G\alpha13$ knockout mouse line ($G\alpha13$ LKO) was created and utilized to explore $G\alpha13$ effect on systemic insulin sensitivity and the underlying basis. When subjected to high-fat diet model, $G\alpha13$ LKO mice exhibited defects in glucose uptake and insulin sensitivity in adipose tissue or skeletal muscle with no change in body weight gain, supporting the concept that decrease of $G\alpha13$ in hepatocytes provokes insulin resistance in other organs. Semi-quantitative LC-MS/MS analysis enabled us to extract a subset of "liver-enriched" "secretory" proteins up-regulated by $G\alpha13$ LKO. Of them, inter-α-trypsin inhibitor HC1 (ITIH1) was identified as a secretory mediator governing insulin receptor desensitization in peripheral organs. Moreover, $G\alpha13$ LKO promoted ITIH1 overexpression and O-GlcNAcylation in hepatocytes, reinforcing the inhibitory effect of hyaluronic acid on insulin sensitivity in fat and skeletal muscle by O-GlcNAc transferase induction. Collectively, hyperglycemia decreases $G\alpha13$ level in the hepatocyte, which facilitates ITIH1 overexpression and O-GlcNAcylation, and the secretion into bloodstream, fortifying hyaluronic acid-mediated insulin receptor desensitization in other metabolic organs, and exacerbating diabetic conditions.

S4-1

GLP-1 regulates neural structure under inflammatory condition

Ju Hyun Song

Chonnam National University, Korea

Glucagon-like peptide-1 (GLP-1) is a hormone mainly secreted from enteroendocrine L cells. GLP-1 and its receptor are also expressed in the brain. GLP-1 signaling has pivotal roles in regulating neuroinflammation and memory function, but it is unclear how GLP-1 improves memory function by regulating neuroinflammation. Here, we demonstrated that GLP-1 enhances neural structure by inhibiting lipopolysaccharide (LPS)-induced inflammation in microglia with the effects of GLP-1 itself on neurons. Inflammatory secretions of BV-2 microglia by LPS aggravated mitochondrial function and cell survival, as well as neural structure in Neuro-2a neurons. In inflammatory condition, GLP-1 suppressed the secretion of tumor necrosis factor-alpha (TNF-α)-associated cytokines and chemokines in BV-2 microglia and ultimately enhanced neurite complexity (neurite length, number of neurites from soma, and secondary branches) in Neuro-2a neurons. We confirmed that GLP-1 improves neurite complexity, dendritic spine morphogenesis, and spine development in TNF-α-treated primary cortical neurons based on altered expression levels of the factors related to neurite growth and spine morphology. Given that our data that GLP-1 itself enhances neurite complexity and spine morphology in neurons, we suggest that GLP-1 has a therapeutic potential in central nervous system diseases.

S4-2

New perspectives on the role of pericytes in diabetic retinopathy

Jun Yeop Lee

University of Ulsan, Korea

Diabetic retinopathy (DR) is a chronic and progressive microvascular complication, which remains an important cause of visual loss in working-age people. Pericyte dropout or loss has been suggested to have great consequences on blood vessel remodeling, and possibly causes the first abnormalities of the diabetic eye which can be observed clinically in DR. However, our group demonstrated that pericytes are not essential in the adult stable retinal blood vessels; and their selective depletion alone did not lead to a phenotype similar to DR (2017 Nat. Commun). In addition, we adapted a new fixation method which enables the visualization of α-smooth muscle actin (αSMA) along retinal capillaries. Diabetes induced less coverage of αSMA-positive pericytes overall, but they reached higher-order branches of the retinal capillaries, which was prominent in the aged mice. More αSMA-positive pericytes were observed in the choroid of diabetic mice, but the αSMA-positive expression reduced with aging (2020 Int J Mol Sci). This study suggested the potential role of smooth muscle cells and another significance of retinal pericytes in the pathogenesis of DR. This presentation will cover our recent research providing new perspectives on the role of pericytes in diabetic retinopathy.

S4-3

Clonal hematopoiesis as a novel risk factor for cardio-metabolic disorders

Chang Hee Jung

University of Ulsan, Korea

The accumulation of somatic mutations in hematopoietic stem/progenitor cells (HSPCs) is known to be an inevitable consequence of the process of aging. Some of these random mutations confer a competitive advantage to the mutant cells, leading to clonal expansion. This phenomenon is called as age-related clonal hematopoiesis (CH). The genes that were most commonly mutated in CH were DNMT3A, TET2 and ASXL1.
A number of studies have associated with CH with an increase in all-cause mortality. Although the presence of CH was associated with the increased risk of hematologic cancer, this only affected 0.5% to 1% of mutation carriers each year and did not explain the marked increase in all-cause mortality. Instead, the increased all-cause mortality was attributable to increased risk of cardiovascular disease (CVD). Based on these epidemiological data, several groups tried to elucidate the possible molecular mechanism underlying the presence of CH and CVD such as atherosclerosis, myocardial infarction and heart failure.
In addition to the causal link between CH and CVD, a modest and significant association between CH and type 2 diabetes was observed. In this talk,

I'd like to introduce the possible causal link between the loss of function in *DNMT3A*, the most frequently mutated gene in CH, and metabolic dysfunction including adipose tissue inflammation in mouse.

S5-1

Lack of a legacy effect in patients with diabetes and cardiovascular disease

Neda Laiteerapong

The University of Chicago, USA

Glycemic control is essential in the management of type 2 diabetes for decreasing the risk of diabetic complications. There has been evidence from the UKPDS that among patients with newly diagnosed diabetes, the benefits of intensive glycemic control (glycated hemoglobin~ 7% or 8.6 mmol/L) have long-term benefits (20 year) on microvascular complications and emerging benefits for macrovascular complications and mortality, even 10 years after intensive glycemic control. However, the benefits of intensive glycemic control (glycated hemoglobin<7%) on clinical outcomes varies based on the duration of diabetes and history of cardiovascular disease. Evidence from the three major modern type 2 diabetes trials (ACCORD, ADVANCE, and VADT) have found that intensive glycemic control may have small to negligible effects on rates of diabetic complications. The implication of these findings is that the legacy effects from intensive glycemic control may not exist for patients with type 2 diabetes and a high risk for, or pre-existing cardiovascular disease.

S5-2

Early intensive combination therapy in T2DM: pros and cons

Chang Hee Jung

University of Ulsan, Korea

There is clear evidence that achieving glycaemic targets reduces the risk of developing complications as a result of type 2 diabetes (T2D). Many patients, however, continue to have suboptimal glycaemic control because of issues that include unclear advice on how to achieve these targets as well as clinical inertia. The two management approaches recommended for patients newly diagnosed with T2D are stepwise and combination therapy, each of which has advantages and disadvantages. Recent clinical trial which examined the efficacy and safety by adopting the early intervention with a combination therapy of vildagliptin plus metformin (VERIFY study) has boosted up this issue again. In this session, let me discuss several advantages and disadvantages of initial combination therapy by comparing it with sequential therapy.

S5-3

Strategy to achieve remission of type 2 diabetes

Hyuk Sang Kwon

The Catholic University of Korea, Korea

Type 2 diabetes is traditionally considered as a progressive disease. Without changing lifestyle, A1C levels increase gradually over time and more drugs such as insulin are needed to control high blood sugar in diabetes. A recent study, DiRECT(Diabetes Remission Clinical Trial), tested whether calorie restriction would lead to diabetes remission. Intervention group ate 830 kcal day for 12 weeks, followed by 12 to 18 weeks on a stepped food re-introduction program, and finally a weight-loss maintenance program. One year later, 46% in the intervention group vs. 4% in the control group had achieved remission. According to the results of the last two years, maintenance of weight reduction is the key factor for predicting prolonged remission. This lecture will review the strategy for type 2 diabetes remission and its underlying mechanisms.

S5-4

Do we need to use SGLT2i/GLP-1RA in well-controlled diabetes with increased CV risk?

Roopa Mehta

INCMNSZ, Mexico

The presence of type 2 diabetes has traditionally been associated with increased cardiovascular risk. However, this risk is heterogeneous: the latest European guidelines, stratify patients according to risk categories, and provide advice accordingly. The results of cardiovascular outcome trials in diabetes have impacted these recommendations. Meta-analysis results clearly show that both SGLT2 inhibitors and GLP-1 receptor agonists show positive results in secondary prevention patients. The evidence for MACE in primary prevention (patients with multiple risk factors) is based only on subgroup analyses. However, both classes have shown benefit in hospitalization for heart failure and renal outcomes, independent of primary or secondary prevention. In addition, these benefits appear to be independent of baseline HbA1c. We now have a better understanding of the cardiovascular risk continuum in diabetes. Comprehensive treatment strategies should be implemented that are effective in reducing events the risk continuum.

S6-1

Motivational interviewing technique as a way of changing eating habits in diabetic patients with obesity

Seolhyang Baek

Dongguk University, Korea

Although a few investigators report that weight loss in obese diabetic individuals increased mortalities and let people associate with the obesity paradox, benefits of extra weight loss(i.e. diabetes remission) are still huge and hard to ignore. Even though current guidelines recommend 5~10% of body weight loss before treatment and lifestyle change with diet and exercise, many of diabetologists often meet obstacles.; A person never succeed his/her own weight loss. Another might have an awful response from patient when giving 'DONOT' messages. Maybe busy working hours of them does not allow to wait *gradually* occurred change. As a way of changing behavior, Prochaska and DiClemente introduced the transtheoretical model which ranges from pre-contemplation to maintenance and relapse prevention. When an individual is ready to change, however, ambivalence is usually anticipated. Motivational interviewing (MI) is a useful method that enhances motivation through the resolution of ambivalence. During this session, basic skills and principles of motivational interviewing are going to introduced along with barriers to implementing it.

S6-2

Medication for obesity treatment

Bo Yeon Kim

Sooncheonhyang University, Korea

Obesity is a serious and growing worldwide health challenge. Obesity is associated with type 2 diabetes, cardiovascular disease, osteoarthritis, some cancers, sleep apnea, asthma, and nonalcoholic fatty liver. The Korean Society for the Study of Obesity (KSSO) recommends that pharmacotherapy for obesity should be considered when intensive life style modifications fail to result in weight loss in obese patients with body mass index (BMI) ≥25 kg/m2 in Korean. Long-Term medications for enduring obesity have traditionally fallen into two major categories, centrally acting anorexiant medications and peripherally acting medications, such as orlistat.

Orlistat, liraglutide, naltrexone/bupropion ER, and phentermine/topiramate ER are well-tolerated and safe. The U.S. FDA asked the manufacturer of lorcaserin to voluntary withdraw the weight-loss drug lorcaserin from the market due to cancer risk, unfortunately.

In this paper, I provide an overview of the anti-obesity medications currently available for long-term treatment and individualization for obesity treatment. I reviewed the anti-obesity medications currently available for long-term treatment.

S6-3
Nutritional management in bariatric surgery
Mee Ra Kweon

Seoul National University Hospital, Korea

Morbid obesity is associated with several comorbidities such as hypertension, diabetes, cardiovascular disease and cancer. To avoid risk, multifactorial intervention must be implemented. Morbid obese subjects who failed dietary and medical treatment should be considered as candidates for bariatric surgery.

Bariatric surgery is considered the only effective method of achieving long-term weight loss and ameliorating obesity-associated comorbidities in morbidly obese patients. However bariatric surgery is associated with risks of nutritional deficiencies and malnutrition. Despite high caloric density, the diet of patients prior to bariatric surgery is often of poor nutrition quality and does not meet recommended dietary guidelines for micronutrient intake, making this an at-risk population for micronutrient malnutrition.

Since patients undergoing bariatric surgery are vulnerable to micronutrient deficiencies, close monitoring and supplementation are necessary. Therefore, postoperative nutritional follow-up and supplementation of vitamins and trace elements should be recommended.

Because of the pre- and postoperative dietary issues, Registered Dietitians(RDs) can assess, monitor, and counsel patients in order to improve adherence and reduce the risk of nutrient deficiencies.

The long-term outcome of bariatric patients relies on their adherence to lifetime dietary and physical activity changes. A comprehensive team approach is necessary to provide the best care to these. In those, structured nutrition counseling and education by qualified dietitians is essential part in the lifetime management of the patients.

In this lecture, we will look into nutritional management before and after bariatric surgery with actual hospital application case

S6-4
Nursing management of before and after bariatric surgery
Kyung Eun Bae

Sooncheonhyang University Hospital, Korea

According to the World Health Organization (WHO), obesity is a worldwide pandemic. Also, the Korean Society for Metabolic and Bariatric Surgery(KSMBS) predicted that the obese population continues to increase worldwide, and by 2030 more than half of adults will become overweight or obese.

The more obese, the higher the risk of developing diseases related to coronary artery disease, metabolic syndrome, cerebral infarction, non-alcoholic fatty liver, gout, as well as weight-related diseases (osteoarthritis, back pain, asthma, sleep apnea, varicose veins, tension urinary incontinence), reproductive endocrine system diseases (precocious puberty, menstrual abnormalities , Polycystic ovary syndrome, gynecomastia, erectile dysfunction, infertility and infertility), various cancers (breast cancer, colon cancer, liver cancer, biliary tract cancer, pancreatic cancer, kidney cancer, endometrial cancer, prostate cancer), which increases the mortality rate.

In obese patients, bariatric surgery treatment is the only treatment method for weight loss and weight-loss retention, and it has shown effective improvement in obesity-related diseases including type 2 diabetes, and also improves depression and somatoform disorders resulting from inferior appearance. As a result, the quality of life was improved and the mortality rate decreased.

As bariatric surgery has been officially recognized as a medical care benefit by Korean health insurance since January 2019, the demand for surgery has markedly increased and will continue to increase in the future.

Multidisciplinary treatment and long-term monitoring before and after surgery are essential in order to prevent complications and improve the safety and satisfactory results of bariatric surgery. In order to achieve such a successful bariatric surgery. the nursing management of before and after bariatric surgery is absolutely required, Therefore, we would like to find out more about the nursing management of before and after bariatric surgery that is actually performed in clinical practice.

S7-1
Blood glucose, antidiabetic drugs, and stroke risk
Meng Lee

Chang Gung University, Taiwan

Diabetes mellitus is a well-established risk factor of stroke. People with pre-diabetes on the basis of presence of impaired glucose tolerance has an independent risk of future stroke that is 20% greater than those with a normal glycemia. Pre-diabetes based on a more recent guideline recommended definition of impaired fasting blood glucose (100 to 125 mg/dL) is not linked to future stroke risk while patients with fasting blood glucose 110 to 125 mg/dL is linked to an increased stroke risk. Among people without baseline diabetes or cardiovascular disease, a fasting blood glucose level of <70 mg/dL is associated with an increased risk of stroke.

Lowering blood glucose with oral antidiabetic drugs is not necessarily associated with reduced cardiovascular events, and intensive glycemic control does not seem to prevent risk of stroke in diabetic patients. In patients at increased cardiovascular risk receiving metformin-based background therapy, certain GLP-1 receptor agonists and SGLT-2 inhibitors have a beneficial effect on some cardiovascular outcomes. Also, pioglitazone reduces recurrent stroke and major vascular events in ischemic stroke patients with insulin resistance, prediabetes, and diabetes mellitus. Combination of pioglitazone with a GLP-1 receptor agonist or an SGLT-2 inhibitor might reduce future stroke risk and mitigate potential side effects of pioglitazone, pending randomized controlled trials to confirm or rebut it.

S7-2
Hypoglycemia and brain
Ji-Young Kim

Inje University, Korea

The brain is a fine-tuned organ, taking 15% of whole cardiac output. It uses glucose as the only source of energy and therefore is sensitive to the level of blood glucose. Regardless of the type of diabetes mellitus, hypoglycemia affects brain function. Hypoglycemia is particularly the problem for older diabetic patients. This higher incidence among the older patients may be due to the impaired awareness of hypoglycemic warning symptoms, the reduced secretion of glucagon, or the altered psychomotor performance when the blood glucose is low which prevents the patient from taking steps to get out of the situation. Repeated exposure to hypoglycemia in diabetic patients is emerging as major clinical concerns since the strict control of blood glucose level has become popular in order to reduce diabetic complications. Although it is not infrequent to encounter patients showing altered consciousness and even seizure with extremely low blood glucose at emergency room, diabetic outpatients who are exposed to recurrent hypoglycemia are hardly noticed. The clinical impact of repeated exposure to hypoglycemia on cognitive function and cerebrovascular event is still under debate. In this review, the impact of repeated exposure to hypoglycemia on the brain, particularly focused on the cognitive function and cerebrovascular aspects will be discussed.

S7-3
Screening and diagnosis of diabetic peripheral arterial disease
Pil Hyung Lee

University of Ulsan, Korea

With the increasing prevalence of diabetes-related foot complications and the availability of endovascular treatment options, the screening and diagnosis of peripheral arterial disease (PAD) in patients with diabetes has become more important but has been less evolved without a strong evidence base. Annual clinical assessment (detailed medical history taking, palpating foot pulses, and skin characteristics) is recommended for all diabetic patients, yet, it does not reliably exclude PAD as they are less likely to report classic symptoms, and the reproducibility or agreement of physical examinations are poor. Thus, diagnostic tests to encompass macro and microcirculation are used in clinical practice. Global perfusion can be measured by hemodynamic assessment, such as ankle-brachial index, ankle pressure, and toe pressure, and anatomic assessment by using duplex ultrasound, computed tomographic angiography, or magnetic resonance angiography. These tools are routinely used in clinical practice to detect PAD and identify the location and degree of arterial obstruction in the lower extremities. However, these modalities' utility is reduced in small, heavily calcified tibial

and pedal arteries, which is typically involved in patients with diabetes. In addition, these techniques do not provide reliable information on the microcirculation, and could, therefore, underestimate the degree of functional limb ischemia. Studies to assess regional perfusion include laser doppler, transcutaneous oxygen pressure, or indocyanine green fluorescence angiography. Although these modalities can be performed at the bedside and are noninvasive, the main limitation is that they only provide information on perfusion in superficial tissues. Analysis of skin perfusion misses the muscle compartments, which determines symptomatic and functional limitations in PAD. Also, autonomic neural dysfunction and the presence of infection can significantly alter skin perfusion. Successful validation of novel imaging techniques, such as positron emission tomography, contrast-enhanced ultrasound, MRI (arterial spin labeling MRI, blood oxygenation level-dependent MRI), would present the opportunity of quantitative assessment of muscle perfusion and may ultimately help to improve limb salvage rates in diabetic patients with limb ischemia.

S7-4
Updated current treatment of DM PAD
Su Hong Kim

Busan Veterans Hospital, Korea

Introduction: The peripheral arterial disease caused by diabetes has become a common disease in relation to the aging of the population, and it has become a disease that is important to the survival as well as the quality of life of the patient.
Endovascular management for the claudicants: In many cases of patients complaining of claudication due to diabetic peripheral arterial disease, Endovascular treatment, not bypass surgery, has become the principle of treatment due to the inovation of the device and techniques
In TASC D lesions, which had previously been surgically treated, are also treating by endovascular treatment, and the development of atherectomy devices, drug-coated balloons, and drug eluting stents has greatly reduced the frequency of the restenosis and re-vascularization.
Endovascular management for the diabetic foot and critical limb ischemia: treatment goal of the diabetic foot has changed from reducing the frequency of amputation in the past to the wound healing, and recently the success rate of revascularization has risen rapidly with the development of special techniques such as distal vascular access, randez-vous technique, pedal planar loop technique, and channel wiring technique, which has greatly reduced the rate of amputation.
The success rate of the revascularization has increased rapidly, the major evaluation has almost disappeared from my own experience, and it has become common to perform minor amputation (toe or ray amputation) only, and it is believed to have had a significant impact on improving the patient's quality of life and survival rate.
Revascularization for the Diabetic foot and critical limb ischemia are considered to be the most important, and physician's thoughts and approaches for the treatment have important effects on the patient's quality of life and prognosis.
Please don't hesitate to consult to the interventionist to revascularize the blocked arteries even in below the ankle.

S8-1
The trend of nutritional intake in patients with DM
Shin Je Moon

Hallym University, Korea

The Korea National Health and Nutrition Examination Survey reported that the general population in Korea consumes approximately 1900-2000 Kcal daily. Koreans have been reported to consume more than 60% of their total energy through carbohydrates, approximately 15% through protein, and 22% through fat. This dietary pattern in Korea is different from that of Americans in the US who consume similar amounts of calories. Compared to Koreans, their proportion of protein and fat intake is relatively high, and the proportion of carbohydrate consumption is much lesser (45-50%). Considering these characteristics of Korean dietary habits, more specialized clinical nutritional therapy is needed for patients with diabetes in Korea.
The effectiveness of clinical nutrition therapy has been reported in various studies. A systematic review of the literature of 21 studies reported that clinical nutritional therapy reduced glycated hemoglobin by 0.3-2.0% in

type 2 diabetes and by 1.0-1.9% in type 1 diabetes. Considering the beneficial effects of clinical nutritional therapy on the treatment of diabetes, various clinical guidelines for diabetes emphasize the importance of appropriate clinical nutrition therapy. The 2019 Clinical Practice Guidelines for Diabetes in Korea also recommended that all patients at a high risk of diabetes and those with diabetes have to receive individualized clinical nutritional therapy. It is recommended that the total energy intake should be determined individually, according to their need to lose weight, treatment goals, and individual dietary preferences in patients with diabetes. However, the ideal proportion of carbohydrates, proteins, and fats has not been established.
This review discusses the existing literature on nutritional patterns of Koreans and analyzes recent dietary survey data to provide basic information for future studies on clinical nutritional therapy that are more specialized for patients with diabetes in Korea.

S8-2
Comparison of differences in health behavior and dietary intake according to diabetes awareness
Hae-Jeung Lee

Gachon University, Korea

TBD

S8-3
Assessment of current sodium intake recommendations in Korean diabetes patients
Jong Han Choi

Konkuk University, Korea

Lowering blood pressure is as important as blood glucose levels in delaying the development or progression of diabetic complications. Dietary sodium intake is associated with systolic and diastolic blood pressure, and uncontrolled hypertension is related to cardiovascular disease and mortality. Conversely, the reduction of sodium intake decreases hypertension, myocardial infarction, stroke, and resulting deaths. These observations have led to recommendations to reduce sodium consumption to improve population health. The appropriate sodium intake recommendations in diabetic patients vary on the guidelines depending on whether diabetes is classified as a high-risk group, and recommends within 1500 to 2400 mg per day. In Korea, there is no prospective study related to sodium intake despite much higher sodium intake than Western countries. Thus, Korean guidelines suggest the appropriate sodium intake relies on these international guidelines. It remains unclear how much the worldwide recommendations to reduce sodium consumption have decreased sodium intake in population and improved the prevalence and mortality of hypertension and cardiovascular disease. Despite these efforts, recent National Health and Nutrition Surveys have shown that there is no significant change in sodium intake in the United States. On the other hand, the sodium intake of Koreans significantly decreased according to the analysis of the Korean National Health and Nutrition Survey. Therefore, we will investigate how the reduction of sodium intake in Koreans has affected the improvement of hypertension, the occurrence, and deterioration of the cardiovascular disease. Besides, we will evaluate indirectly whether the current sodium intake recommendation is suitable in the absence of a prospective clinical study, especially in Korean diabetic patients.

S9-1
Use of FGM in insulin therapy for type 2 diabetes
Jun Sung Moon

Yeungnam University, Korea

Glucose monitoring is the key component for successful management of patients with diabetes. Though HbA1c and self-monitoring of blood-glucose (SMBG) by finger pricking are effective methods for assessing glucose exposure, there are limited to inform about glycemic variability.
Flash glucose monitoring (FGM) is a factory-calibrated sensor-based tech-

nology characterized by a small-sized patch lasting up to 14 days. On-demand sensor scanning provides patients with comprehensive glucose data, including current glucose levels, which are updated every minute, historical glucose readings from the last 8 hours, and trend arrows. Also, ambulatory glucose profiles (AGP) can be shared with the physician and their caregivers. Previous studies showing relevant benefits of FGM use in patients with type 1 and type 2 diabetes in terms of lesser hypoglycemic episodes. Besides, numerous evidences have suggested FGM might help increasing 'time-in-range' in terms of adequate glycemic control. Now FGM is also available in Korea and is increasing its use in clinical practice even though still lacking reimbursement policies. In this lecture, I will review the clinical update and practical tips for FGM.

S9-2

Adjustment of insulin therapy: new insights from CGM

Tae Jung Oh

Seoul National University, Korea

Continuous glucose monitoring (CGM) became a valuable tool for management of diabetes, especially for type 1 diabetes. A consensus report by the Advanced Technologies & Treatments for Diabetes (ATTD) guided us how to use CGM data in clinical practice. According to this recommendation, ambulatory glucose profile (AGP) enables clinicians and patients to work collaboratively in identifying problem areas. The International Diabetes Center (IDC) created a "9 Step" interpretation plan as follows: 1. Make sure there are adequate data for decision-making (ideally 14 days, at least 10 days). 2. If possible, mark directly on a printed copy of the AGP. 3. Once the report is "marked up," ask the patient to briefly describe and explain what he or she sees and why. 4. Look for patterns of low glucose readings. 5. Look for patterns of high glucose values. 6. Discuss areas where darker blue (50% of values) or lighter blue (90% of values) shaded areas are very wide. 7. Compare current AGP and CGM metrics to those from last visit (or contact), if available, and discuss progress. 8. Agree on an action plan consisting of one or two specific recommendations. 9. Print a copy of the marked-up AGP for the patient and store a PDF of the AGP into the EMR. In well-educated patients, we can discuss about personalized insulin therapy further using CGM data. In this lecture, I will discuss about how we can use the best of CGM.

S9-3

New insulin pumps and Open APS in Korea

Jae Hyeon Kim

Sungkyunkwan University, Korea

Diabetes technology including artificial pancreas (AP) has achieved remarkable progress in the past decades. The launch of the Medtronic MiniMed 670G system in 2017 and the subsequent release of the Tandem t:slim with Control-IQ system, the DANA RS pump compatible-CamAPS FX app in EU and the more recent announcement of the Medtronic MiniMed 780G system have come as answers to their prayers. However, all devices are inaccessible to most persons with T1D in Korea. Therefore, highly motivated and tech-savvy persons of the diabetes community have started developing open source artificial pancreas systems (Open APS) integrating CGM, insulin pumps, and smartphone technology to run their own do-it-yourself (DIY) AP algorithms to accomplish outstanding glycemic control. Online social network megatrends such as GitHub, CGM in the Cloud, and Twitter have been used to share these open source algorithms and expert user experiences, but these systems are not commercialized or regulated. Observational studies, and real-world patient stories revealed significant improvements in time in range (TIR), HbA1c levels, and quality of life after the initiation of Open APS. The use of the regularized CGM and insulin pump with unauthorized algorithms (DIYAPS) makes them off-label and has been a matter of grave concern. In addition, lack of safety data, funding or insurance coverage, ethical, and legal issues are barriers to the general acceptance of DIYAPS among persons with T1D. In this lecture, I will summarize existing DIYAPS studies including Korea and their advantages and disadvantages. In addition, I will introduce new insulin pumps available in Korea.

S9-4

Remote monitoring and education platform for CGM and SMBG

Jae Hyoung Cho

The Catholic University of Korea, Korea

With the development of information technology and the spread of smartphones, various diabetes management applications are being introduced. Through these management apps, patients can check and record their own blood sugar levels and obtain information on diet and exercise management. On the other hand, more advanced techniques have been applied recently, as well as self-sugar measurement, to identify their own changes in blood sugar through continuous blood glucose measurement, which can help them manage diabetes more effectively.

However, although the use of such applications has proven to be clinically effective for diabetes, they need to be used more long-term and effective in practice. It is necessary to communicate with the medical staff and identify the patient's condition based on blood glucose data, and to provide appropriate education, consultation and care accordingly. Therefore, self-sugar data or continuous blood glucose data, measured directly by them, should be efficiently communicated to the physician and the physician should be able to provide appropriate counseling accordingly.

Recently, a digital doctor-patient education platform has been introduced in Korea, increasing the number of users. This platform allows doctors to help patients manage diabetes by selecting the necessary training materials for patients in the doctor's office and providing them again with additional content and the patient receive and learn the most necessary and individualized teaching materials for him. Clinical studies on the effectiveness of this education platform have recently been underway at a university hospital for diabetes. The platform has been upgraded and put on a trial basis to make it more efficient for doctors to educate and treat patients by linking self-blood glucose data or continuous blood glucose data to the education platform. Through the linkage and concentration of these data, it is expected that it will not only help doctors treat patients but also be an effective tool for doctors' care and judgment by applying various analytical systems. iCare-D, a popular blood glucose management application in Korea, has been applied to link self-blood sugar, and data linkage with Free Style Libre is being attempted for continuous blood glucose data. Of course, this can only be used during doctor-patient interviews in the clinic, but can also be used for non-face-to-face education and care because it can be used to identify the patient's condition and provide appropriate messages when the doctor needs it. In this regard, the support of the medical policy is also necessary, so it is necessary to first prove the link between blood glucose data and its clinical effects, and then use it for non-face-to-face education and medical treatment so that more patients can receive appropriate education and counseling frequently so that they can be more efficient in managing diabetes.

S10-1

Hormonal and nutritional control of neuroendocrine circuits controlling feeding and glucose metabolism

Sebastien G Bouret

French Institute of Health and Medical Research, France

The growing prevalence of obesity and associated diseases such as type II diabetes is a major health concern, including among children. Epidemiological and animal studies suggest that alteration of the metabolic and hormonal environment during critical periods of development is associated with increased risks for obesity and type 2 diabetes in later life. There is general recognition that the developing brain is more susceptible to environmental insults than the adult brain. In particular, there is growing appreciation that developmental programming of neuroendocrine systems by the perinatal environment represents a possible cause for these diseases. This talk will summarize the major stages of hypothalamic development and will discuss potential periods of vulnerability for the development of hypothalamic circuits regulating feeding and glucose regulation. It will also provide an overview of recent evidence concerning the action of perinatal hormones (including leptin and ghrelin), nutrition (e.g., maternal obesity), and non-nutritive sweeteners in influencing development of hypothalamic circuits and how these developmental effects impact lifelong feeding and glucose regulations.

Abstracts

S10-2

Genetic identification of sweet taste neurons in the mouse brainstem

Ken-ichiro Nakajima

National Institute for Physiological Sciences, Japan

The gustatory system plays an important role in sensing appetitive and aversive tastes for evaluating food quality. In mice, taste signals are relayed by multiple brain regions, including the parabrachial nucleus (PBN) of the pons, before reaching the gustatory cortex via the gustatory thalamus. Recent studies show that taste information at the periphery and in the gustatory cortex is encoded in a labeled-line manner, such that each taste modality has its own neuronal pathway. Although the PBN consisting of multiple subnuclei has also been known to function as a hub to receive and transmit diverse information including signals of pain, hunger, and satiety, the molecular identity of gustatory neurons in the PBN is still unknown due to lack of molecular markers. Here we show that neurons expressing a transcription factor SatB2 localized in the waist area in the PBN are essential for sweet taste transduction. With cell ablation, in vivo calcium imaging, and optogenetics, we reveal that SatB2 neurons in the PBN encode positive valance and selectively transmit sweet taste signals to the gustatory thalamus.

S10-3

Paraventricular hypothalamus mediates diurnal rhythms of metabolism

Eun Ran Kim

Yonsei University, Korea

Diurnal patterns that include metabolism, and its associated energy expenditure and locomotion, when defective, are associated with obesity development. Although this correlation has been well described, the neural basis that regulates metabolism-related diurnal patterns remains unclear. Here we showed that mouse PVH neurons exhibit diurnal patterns in both GABA-A receptor $\gamma 2$ subunit expression and inhibitory inputs, which are both higher in the dark. Disruption of diurnal patterns in PVH GABAergic signaling by either cell type-specific $\gamma 2$ deletion, or replacing endogenous $\gamma 2$ expression with non-rhythmic ROSA26 knock-in mediated expression, led to loss of diurnal patterns and obesity. Chronic elevation in PVH neuron activity, which dampens PVH neuron diurnal activity, also diminished diurnal rhythmicity and caused obesity. Thus, we have identified that rhythmic GABAergic input to PVH is a neural basis for maintaining diurnal rhythmicity in metabolism, and that disruption of diurnal patterns as a major cause of obesity.

S10-4

A neural circuit mechanism for mechanosensory feedback control of ingestion

Sung-Yon Kim

Seoul National University, Korea

Mechanosensory feedback from the digestive tract to the brain is critical for limiting excessive food and water intake, but the underlying gut-brain communication pathways and mechanisms remain poorly understood. Here we show that, in mice, neurons in the parabrachial nucleus that express the prodynorphin gene (hereafter, PBPdyn neurons) monitor the intake of both fluids and solids, using mechanosensory signals that arise from the upper digestive tract. Most individual PBPdyn neurons are activated by ingestion as well as the stimulation of the mouth and stomach, which indicates the representation of integrated sensory signals across distinct parts of the digestive tract. PBPdyn neurons are anatomically connected to the digestive periphery via cranial and spinal pathways; we show that, among these pathways, the vagus nerve conveys stomach-distension signals to PBPdyn neurons. Upon receipt of these signals, these neurons produce aversive and sustained appetite-suppressing signals, which discourages the initiation of feeding and drinking (fully recapitulating the symptoms of gastric distension) in part via signalling to the paraventricular hypothalamus. By contrast, inhibiting the same population of PBPdyn neurons induces overconsumption only if a drive for ingestion exists, which confirms that these neurons mediate negative feedback signalling. Our findings reveal a neural mechanism that underlies the mechanosensory monitoring of ingestion

and negative feedback control of intake behaviours upon distension of the digestive tract.

S11-1

What is the ideal cholesterol level after stroke or TIA in Korean diabetic patients?

Beom Joon Kim

Seoul National University, Korea

LDL cholesterol is a well-known risk factor for atherosclerotic vascular diseases, including ischemic stroke. Statin and ezetimibe, which may effectively lower the LDL cholesterol level, have been reported to diminish the risk of incident stroke or its recurrence. Along with the Heart Protection Study and SPARCL trial, TST (Treat Stroke to Target) trial were published in late 2019. The TST trial randomized ischemic stroke or TIA survivors into the lower-target group (target LDL cholesterol <70 mg / dL) and the higher-target group (target LDL cholesterol 90 - 110 mg/dL), and followed-up to collect incidence of major cardiovascular events. Patients from the lower-target group had a significantly lower incidence of the primary endpoint during a median of 3.5 years, which suggested that strict LDL cholesterol management may be beneficial for atherosclerotic ischemic stroke or TIA patients. However, the point of association from the Korean subgroup favored the higher-target treatment, and the incidence of ICH was numerically higher. These two points raised concern on whether the TST trial results apply to Korean patients. In this lecture, the background and results of the TST trial will be summarized, and its generalizability to Korean stroke survivors will be discussed.

S11-2

Strategies to overcome residual risk In statins era

Kwang Kon Koh

Gachon University, Korea

In the present days, atherosclerosis has been one of the most important field in clinical and research medicine. Because it is closely related with cardiovascular and endocrine disorders such as coronary heart disease, cardiometabolic disorders, numerous researches to manage atherosclerosis have been performed. Low-density lipoprotein cholesterol concentration has been established as an independent risk factor for the development of atherosclerosis, and considerable effort has been committed to educate physicians and general public about the importance of lowering low-density lipoprotein cholesterol with statins. Although statins have already significantly improved cardiovascular outcomes, patients with low-density lipoprotein cholesterol target levels achieved by intense statins therapy still have significant remaining cardiovascular risks. Statins already play a central role in managing hyperlipidemia, however, residual risk with statins is an important field of managing remaining cardiovascular risks. Recent studies have suggested residual cholesterol and inflammation risks in causing cardiovascular events. In the current review, we will discuss these residual risks and suggest strategies to overcome residual risk in statins era.

S11-3

Fish oil and cardiometabolic diseases

Nam Hoon Kim

Korea University, Korea

Omega-3 (n-3) fatty acids, which are found abundantly in fish oil, exert pleiotropic cardiometabolic effects with a diverse range of actions. The important polyunsaturated fatty acids (PUFA) of fish oil are eicosapentanoic acid (EPA), and docosahexanoic acid (DHA). Their cardiometabolic effects ranged from anti-thrombosis ad endothelial stabilization to anti-arrhythmic potential. However, the precise mechanism responsible for cardiovascular health in humans are not well defined. Meanwhile, Cardiovascular outcome trials of n-3 fatty acids have shown quite conflicting, inconsistent results. From JELIS, ORIGIN, ALPHA-OMEGA trials to recent ASCEND, VITAL, REDUCE-IT trials, only high-dose EPA supplementation showed promising results, not low-dose ones or low-dose combination of EPA and DHA. So, there remains substantial unanswered questions about

n-3 fatty acids` cardiometabolic effects including dose-responses of physiological and clinical effects, whether only EPA has a beneficial cardiovascular effect, and whether the ratio of EPA and DHA is important. Here I will review the preclinical and clinical evidence of n-3 fatty acids and their supplements, and discuss the potential benefits and underlying mechanism.

S11-4

Big data based CVD risk prediction model in Korea

Seung-Hwan Lee

The Catholic University of Korea, Korea

It is well established that diabetes and related metabolic disturbances increase the risk of cardiovascular diseases (CVDs). Despite the observation that the incidence rate of CVD is decreasing, people with diabetes still have a 2-3 times greater risk of developing ischemic heart disease, myocardial infarction (MI), and cerebrovascular diseases. Therefore, efforts to prevent CVD through risk stratification are emphasized in the representative diabetes management guidelines. However, most of the widely used prediction models for cardiovascular disease are known to overestimate the risk of this disease in Asians. Using the Korean National Health Insurance System (NHIS) database, we generated risk models for predicting MI and stroke in middle-aged Korean subjects with type 2 diabetes. The original database was split into two datasets, the development cohort and the validation cohort for internal validation of the risk model. We identified potential risk factors for MI and stroke in people with type 2 diabetes based on the literature and selected variables that were most likely to have good predictive ability and available from the NHIS database. All the variables can be easily collected in routine clinical practice, and a web-based calculator was developed for easy application. We expect that our risk model will be a useful tool for identifying individuals at a high risk of developing MI and stroke, and this approach of risk assessment and intervention would improve the quality of care for patients with diabetes.

S12-1

Prediction of diabetes complications based on metabolomics: KNDP omics study

Choong Hwan Lee

Konkuk University, Korea

Case 1: We have identified the differences in metabolites with or without diabetic retinopathy (DR) in patients with type 2 diabetes mellitus (T2DM) who have had a disease duration of 15 years or more. For metabolite profiling, 32 case-control sets with adjusted clinical variables selected. Metabolomictes analysis revealed glutamine and glutamic acid were identified as the most accurate marker for the presence of DR in subjects. ROC analysis showed high diagnostic value of glutamine (AUC=0.671), glutamic acid (AUC=0.656) and its ratio (AUC=0.742) for DR. Our study suggests that glutamine, glutamic acid, and its ratio can be useful as new biomarkers to predict the prognosis of DR in elderly T2DM patients.
Case 2: We identified differences in plasma metabolites in subjects with type 2 diabetes (T2DM) with or without diabetic macular edema (DME) and a disease duration > 15 yrs. From metabolomic studies, 5 amino acids (asparagine, aspartic acid, glutamic acid, cysteine, and lysine), 2 organic compounds (citric acid and uric acid) and 4 oxylipins (12-oxoETE, 15-oxoETE, 9-oxoODE, 20-carboxy leukotriene B4) were identified as candidate multi-biomarkers which can guide DME diagnosis among non-DME subjects. Receiver operating characteristic curves revealed high diagnostic value of the combined 5 amino acids and 2 organic compounds (AUC = 0.918), and of the 4 combined oxylipins (AUC = 0.957). Our study suggests that multi-biomarkers may be useful for predicting DME in elderly T2DM patients

S12-2

Deep learning prediction for CVD and DM

Hyuk-Jae Chang

Yonsei University, Korea

Cardiovascular disease (CVD) are one of the major causes of death world-wide. For improved accuracy of CVD prediction, risk classification was performed using national time-series health examination data. The data offers an opportunity to access deep learning (RNN-LSTM), which is widely known as an outstanding algorithm for analyzing time-series datasets. The objective of this study was to show the improved accuracy of deep learning by comparing the performance of a Cox hazard regression and RNN-LSTM based on survival analysis. We selected 361,239 subjects (age 40 to 79 years) with more than two health examination records from 2002-2006 using the National Health Insurance System-National Health Screening Cohort (NHIS-HEALS). The average number of health screenings (from 2002-2013) used in the analysis was 2.9 ± 1.0. conventional prediction models were developed from the NHIS-HEALS data: a Cox hazard regression model and a deep learning model. In an internal validation of the NHIS-HEALS dataset, the Cox regression model showed a highest time-dependent area under the curve (AUC) of 0.79 (95% CI 0.70 to 0.87) for in females and 0.75 (95% CI 0.70 to 0.80) in males at 2 years. The deep learning model showed a highest time-dependent AUC of 0.94 (95% CI 0.91 to 0.97) for in females and 0.96 (95% CI 0.95 to 0.97) in males at 2 years. Layer-wise Relevance Propagation (LRP) revealed that age was the variable that had the greatest effect on CVD, followed by systolic blood pressure (SBP) and diastolic blood pressure (DBP), in that order. The performance of the deep learning model for predicting CVD occurrences was better than that of the Cox regression model. In addition, it was confirmed that the known risk factors shown to be important by previous clinical studies were extracted from the study results using LRP.

S12-3

Genomic landscape of type 2 diabetes in east Asians

Young Jin Kim

Korea National Institute of Health, Korea

Type 2 diabetes (T2D) is a common metabolic disease that is primarily caused by insufficient insulin production and/or secretion by the pancreatic ß cells, and insulin resistance in peripheral tissues. To date, several genome-wide association studies (GWAS) have revealed hundreds of T2D associated loci analyzing nearly one million individuals. However, most genetic loci associated with T2D have been identified in European populations (EUR). These European biased results may result in reduced accuracy in predicting T2D for non-Europeans. The relative contributions of different pathways to the pathophysiology of T2D may also differ between ancestry groups. For example, the prevalence of T2D is greater in East Asians (EAS) populations than in EUR among people of similar body mass index (BMI) or waist circumference. To identify new genetic associations and provide insight into the pathogenesis of T2D, we conducted the largest meta-analysis of T2D data analyzing 433,540 East Asian individuals (77,418 T2D cases and 356,122 healthy controls) from 3 biobanks and 20 different cohorts. As a result, 301 distinct association signals at 183 loci were discovered. Among them, 61 loci were newly implicated in predisposition to T2D. Common variants associated with T2D in both EAS and EUR exhibited strongly correlated effect sizes. When T2D genetic risk scores using discovered variants employed to access the prevalence of T2D in Koreans, genetically high risk group showed several times higher prevalence compared to those of median group. The results of our study implicate that association studies in diverse populations would provide additional loci and elucidate disease associated genes, biology, and pathways.

S12-4

The effectiveness of new diabetes drugs, SGLT2 inhibitors: real world evidence

Dae Jung Kim

Ajou University, Korea

Recent cardiovascular outcome trials have demonstrated a significant reduction in major adverse cardiovascular events, death, and hospitalizations for heart failure with sodium-glucose cotransporter-2 inhibitors (SGLT-2i) in patients with T2D, most of whom had established cardiovascular diseases. Randomized controlled trials (RCTs) has been well established as the gold standard for evaluating drug efficacy and safety. However, RCTs have limitations because the study design and study outcomes cannot be translated into real clinical practice.
There are large large pharmacoepidemiological study for SGLT2 inhibitors—CVD-REAL (Comparative Effectiveness of Cardiovascular Outcomes

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in New Users of Sodium-Glucose Cotransporter-2 Inhibitors) and EMPRISE (EMPagliflozin CompaRative EffectIveness and SafEty). As I participated as a researcher of Korea in these studies of cardiovascular effects and safety of SGLT2 inhibitors, I would like to share the results and my experiences in this symposium.

S13-1
The fate of circulating glucose
Joshua D. Rabinowitz

Princeton University, USA

I will present isotope tracer studies interrogating glucose metabolism - both consumption and production. Through these studies, conducted in mouse, I will present evidence that carbohydrate metabolism operates differently than commonly assumed. Most cells, especially in the fasting state, do not catabolize circulating glucose via glycolysis. Instead, they acquire glycolytic intermediates from glycogen breakdown and gluconeogenesis. Circulating glucose is, however, avidly consumed by relatively rare highly glycolytic cells, which rapidly convert it into circulating lactate. This lactate is a major circulating fuel, feeding TCA metabolism throughout the body. The active production of lactate from glucose, and also gluconeogenic conversion of lactate into glucose, are robust features of metabolism, occurring across feeding, fasting, and even ketogenic diet. Implications of this metabolic network usage for glucose and redox homeostasis will be discussed.

S13-2
Mitochondria, metabolism and cellular decisions
Jared Rutter

University of Utah, USA

Mitochondria are dynamic and complex organelles that play a central role in all aspects of biology, including energy production, intermediary metabolism, and apoptosis. These broad cellular functions also place mitochondria as a central player in human health and disease. We have focused recently on deciphering the biochemical and cellular functions of conserved uncharacterized mitochondrial proteins. This has revealed new mechanisms for several critical aspects of mitochondrial function, including the Mitochondrial Pyruvate Carrier (MPC), which is required for efficient mitochondrial pyruvate uptake. By perturbing the metabolic program of cells, MPC manipulation profoundly affects cellular decisions impacting stem cell homeostasis and uncontrolled proliferation. This observation suggests that metabolism is not a passive bystander in determining the behavior of cells, but instead plays a decisive role. One of our major future goals is to determine the mechanisms whereby metabolism and metabolites affect behaviors via direct modulation of proteins involved in signaling, transcription and other regulatory mechanisms. This information will then enable us to impinge on these mechanisms for therapeutic benefit in many disease states.

S13-3
Different compositions of proteins and lipids from human ectopic fat omics analysis
Sung Hee Choi

Seoul National University, Korea

We have been interested in the different characteristics and composition of Ectopic fat depots, such as visceral or pericardial fat, because it is important key feature of many metabolic diseases including diabetes and cardiovascular diseases. In humans, there were many studies that higher amounts of ectopic fats are significantly associated with altered metabolic parameters. Despite their pathological significance, proteomic and lipodomic analysis of human adipose tissue that characterize their functions and are associated with metabolic diseases were lacking. Here, we present the validation of human ectopic fat proteomes and the results of differentially regulated lipid of visceral, pericardial, and subcutaneous fats in non-DM and T2DM patients with coronary artery disease (CAD).
Lipid composition of ectopic fats (visceral and pericardial) in T2DM patients with CAD showed significant difference in Cer, PC, LPA, and DG. Will

be presented in the lecture in more detail subspecies. In both visceral and pericardial fats, there were six upregulated proteins including VCAN, TOM1 as well as five downregulated proteins including APOE, CYB5R3 were validated in independent cohort with same disease. Our finding will add the understanding of pathophysiology of atherosclerosis and the contribution of T2DM in CAD.

S13-4
Microbial metabolites as inter-kingdom signaling messengers
Ara Koh

Sungkyunkwan University, Korea

Increasing evidence indicates that interactions between the gut microbiota, diet, and the host contribute to the development of number of diseases from intestinal diseases, metabolic diseases and even to neurological disorders. Beyond the previous association studies between metabolic status and microbiota composition, accumulating data suggest that the microbiota may affect host metabolic phenotypes through the production of metabolites, which would contribute to the development or treatment of diseases. These bioactive microbial metabolites, sensitive fingerprints of microbial function, can act as inter-kingdom signaling messengers via penetration into host blood circulation and tissues. This seminar will focus on the microbially produced metabolite imidazole propionate and how it potentially contributes to the pathogenesis of type 2 diabetes. In addition, I will also briefly describe our ongoing research about investigating potential role of imidazole propionate on inter-individual variations in anti-diabetic drug response.

CS1-1

Introduction and signification of pilot project of telemedicine in type 1 DM

Jung Kyu Lee

MOHW, Korea

CS1-2

Current status of pilot project of telemedicine in type 1 diabetes and insurance policy of diabetic education

Jae Hyun Kim

Seoul National University, Korea

Self-care is an essential part for the management of type 1 diabetes (T1D). Skills including administration of insulin, self-monitoring of blood glucose, carbohydrate count and integrative application of these skills are necessary for better glycemic control. Especially, technological advances in diabetes cares increased the T1D population using continuous glucose monitoring and continuous subcutaneous insulin infusion. Continuous and repetitive education is very important for the appropriate glycemic control.

In Korea, education program for T1D patients was carried out in hospital setting during admission. After diagnosis of T1D, diabetes education was irregularly provided. Diabetes education is not covered by the National Insurance System of Korea, which increase financial burden to T1D patients. Appropriate diabetes education customized to situation of T1D patients will help achieve better glycemic control and reduce acute and chronic diabetes complications of diabetes, and improve quality of life and better health outcomes.

In Korea, pilot project of telemedicine in T1D has begun since 2020. In this pilot project, diabetes education consists of three components: education from doctors; education from diabetes nurse educators or dietitians during the hospital visit; and teleconsulting using telephone and text message. A total of 42 hospitals participated in this project. Whether T1D patients are in hospital or at home, diabetes cre team provide an appropriate education program using face-to-face counseling, telephone or text message.

This pilot project has an important implication for diabetes care, because diabetes education included in the national insurance system for the first time. Although there might be trials and errors, improvement of self-care skills and glycemic control, or reduction of acute and chronic complications should be monitored in the long term. This program should be the first step toward setting up the nationally proved education program for T1D patients.

CS2-1

Essential role of protein arginine methyltransferase 1 in pancreas development by regulating protein stability of neurogenin 3

Hyun Ki Kim

KAIST, Korea

Background: Protein arginine methyltransferase 1 (PRMT) is a major enzyme responsible for the formation of methylarginine in mammalian cells. Recent studies have revealed that PRMT1 plays important roles in the development of various tissues. However, its role in pancreas development has not yet been elucidated.
Methods: Pancreatic progenitor cell-specific Prmt1 knock-out (Prmt1 PKO) mice were generated and characterized for their metabolic and histological phenotypes and their levels of Neurog3 gene expression and neurogenin 3 (NGN3) protein expression. Protein degradation assays were performed in mPAC cells.
Results: Prmt1 PKO mice showed growth retardation and a severely diabetic phenotype. The pancreatic size and β-cell mass were significantly reduced in Prmt1 PKO mice. Proliferation of progenitor cells during the secondary transition was decreased and endocrine cell differentiation was impaired. These defects in pancreas development could be attributed to the sustained expression of NGN3 in progenitor cells. Protein degradation assays in mPAC cells revealed that PRMT1 was required for the rapid degradation of NGN3.
Conclusion: PRMT1 critically contributes to pancreas development by destabilizing the NGN3 protein.

CS2-2

Myricetin protects against high glucose-induced beta-cell apoptosis by attenuating endoplasmic reticulum stress via inactivation of cyclin-dependent kinase 5

Udayakumar Karunakaran

Yeungnam University, Korea

Background: Chronic hyperglycemia has deleterious effects on pancreatic β-cell function and turnover. Recent studies support the view that cyclin-dependent kinase 5 (CDK5) plays a role in β-cell failure under hyperglycemic conditions. However, little is known about how CDK5 impair β-cell function. Myricetin, a natural flavonoid, has therapeutic potential for the treatment of type 2 diabetes mellitus. In this study, we examined the effect of myricetin on high glucose (HG)-induced β-cell apoptosis and explored the relationship between myricetin and CDK5.
Methods: To address this question, we subjected INS-1 cells and isolated rat islets to HG conditions (30 mM) in the presence or absence of myricetin. Docking studies were conducted to validate the interaction between myricetin and CDK5. Gene expression and protein levels of endoplasmic reticulum (ER) stress markers were measured by real-time reverse transcription polymerase chain reaction and Western blot analysis.
Results: Activation of CDK5 in response to HG coupled with the induction of ER stress via the down regulation of sarcoendoplasmic reticulum calcium ATPase 2b (SERCA2b) gene expression and reduced the nuclear accumulation of pancreatic duodenal homeobox 1 (PDX1) leads to β-cell apoptosis. Docking study predicts that myricetin inhibit CDK5 activation by direct binding in the ATP-binding pocket. Myricetin counteracted the decrease in the levels of PDX1 and SERCA2b by HG. Moreover, myricetin attenuated HG-induced apoptosis in INS-1 cells and rat islets and reduce the mitochondrial dysfunction by decreasing reactive oxygen species production and mitochondrial membrane potential ($\Delta\varphi$m) loss.
Conclusion: Myricetin protects the β-cells against HG-induced apoptosis by inhibiting ER stress, possibly through inactivation of CDK5 and consequent upregulation of PDX1 and SERCA2b.

CS2-3

Asian subpopulations may exhibit greater cardiovascular benefit from long-acting glucagon-like peptide 1 receptor agonists: a meta-analysis of cardiovascular outcome trials

Yu Mi Kang

University of Ulsan, Korea

Background: Based on reported results of three large cardiovascular outcome trials (CVOTs) of glucagon-like peptide 1 receptor agonists (GLP-1 RAs), we aimed to investigate the overall effect of GLP-1 RAs on major adverse cardiovascular events (MACEs) and to identify subpopulations exhibiting the greatest cardiovascular (CV) benefit.
Methods: Three CVOTs reporting effects of long-acting GLP-1 RAs were included: LEADER (liraglutide), SUSTAIN-6 (semaglutide), and EXSCEL (exenatide once weekly). In all studies, the primary endpoint was three-point MACE, comprising CV death, non-fatal myocardial infarction, and non-fatal stroke. Overall effect estimates were calculated as hazard ratios and 95% confidence intervals (CIs) using the random-effects model; subgroup analyses reported in the original studies were similarly analyzed.
Results: Overall, statistically significant risk reductions in MACE and CV death were observed. Subgroup analysis indicated a significant racial difference with respect to CV benefit (P for interaction <0.001), and more substantial risk reductions were observed in subjects of African origin (relative risk [RR], 0.78; 95% CI, 0.60 to 0.99) and in Asians (RR, 0.35; 95% CI, 0.09 to 1.32). However, post hoc analysis (Bonferroni method) revealed that only Asians exhibited a significantly greater CV benefit from treatment, compared with white subjects (P<0.0001).
Conclusion: Long-acting GLP-1 RAs reduced risks of MACE and CV deaths in high-risk patients with type 2 diabetes mellitus. Our findings of a particularly effective reduction in CV events with GLP-1 RA in Asian populations merits further exploration and dedicated trials in specific populations.

CS2-4

The risk of myocardial infarction and ischemic stroke according to waist circumference in 21,749,261 Korean adults: a nationwide population-based study

Jung Hwan Cho

Sungkyunkwan University, Korea

Background: Waist circumference (WC) is a well-known obesity index that predicts cardiovascular disease (CVD). We studied the relationship between baseline WC and development of incident myocardial infarction (MI) and ischemic stroke (IS) using a nationwide population-based cohort, and evaluated if its predictability is better than body mass index (BMI).
Methods: Our study included 21,749,261 Koreans over 20 years of age who underwent the Korean National Health Screening between 2009 and 2012. The occurrence of MI or IS was investigated until the end of 2015 using National Health Insurance Service data.
Results: A total of 127,289 and 181,637 subjects were newly diagnosed with MI and IS. The incidence rate and hazard ratio of MI and IS increased linearly as the WC level increased, regardless of adjustment for BMI. When the analyses were performed according to 11 groups of WC, the lowest risk of MI was found in subjects with WC of 70 to 74.9 and 65 to 69.9 cm in male and female, and the lowest risk of IS in subjects with WC of 65 to 69.9 and 60 to 64.9 cm in male and female, respectively. WC showed a better ability to predict CVD than BMI with smaller Akaike information criterion. The optimal WC cutoffs were 84/78 cm for male/female for predicting MI, and 85/78 cm for male/female for predicting IS.
Conclusion: WC had a significant linear relationship with the risk of MI and IS and the risk began to increase from a WC that was lower than expected.

CS2-5

PF-04620110, a potent antidiabetic agent, suppresses fatty acid-induced NLRP3 inflammasome activation in macrophages

Jong-Seok Moon

Soonchunhyang University, Korea

Background: Chronic inflammation has been linked to insulin resistance and type 2 diabetes mellitus (T2DM). High-fat diet (HFD)-derived fatty acid is associated with the activation of chronic inflammation in T2DM. PF-04620110, which is currently in phase 1 clinical trials as a selective acyl-CoA:diacylglycerol acyltransferase-1 (DGAT1) inhibitor, is a potent anti-diabetic agent that may be important for the regulation of chronic inflammation in T2DM. However, the mechanisms by which PF-04620110 regulates fatty acid-induced chronic inflammation remain unclear.
Methods: PF-04620110 was used in vitro and in vivo. DGAT1-targeting gRNAs were used for deletion of mouse DGAT1 via CRISPR ribonucleoprotein (RNP) system. The activation of NLRP3 inflammasome was measured by immunoblot or cytokine analysis in vitro and in vivo.
Results: Here we show that PF-04620110 suppressed fatty acid-induced nucleotide-binding domain, leucine-rich-repeat-containing receptor (NLR), pyrin-domain-containing 3 (NLRP3) inflammasome activation in macrophages. In contrast, PF-04620110 did not change the activation of the NLR family, CARD-domain-containing 4 (NLRC4), or the absent in melanoma 2 (AIM2) inflammasomes. Moreover, PF-04620110 inhibited K+ efflux and the NLRP3 inflammasome complex formation, which are required for NLRP3 inflammasome activation. PF-04620110 reduced the production of interleukin 1β (IL-1β) and IL-18 and blood glucose levels in the plasma of mice fed HFD. Furthermore, genetic inhibition of DGAT1 suppressed fatty acid-induced NLRP3 inflammasome activation.
Conclusion: Our results suggest that PF-04620110 suppresses fatty acid-induced NLRP3 inflammasome activation.

CS2-6

High proportion of adult cases and prevalence of metabolic syndrome in type 1 diabetes mellitus population in Korea: a nationwide study

You-Bin Lee

Sungkyunkwan University, Korea

Background: The prevalence and incidence of type 1 diabetes mellitus (T1DM) in all age groups and the prevalence of metabolic syndrome in patients with T1DM in Korea were estimated.

Methods: The incidence and prevalence of T1DM between 2007 and 2013 were calculated using the Korean National Health Insurance Service (NHIS) datasets of claims. Clinical characteristics and prevalence of metabolic syndrome in individuals with T1DM between 2009 and 2013 were determined using the database of NHIS preventive health checkups.
Results: The prevalence of T1DM in Korea between 2007 and 2013 was 0.041% to 0.047%. The annual incidence rate of T1DM in Korea in 2007 to 2013 was 2.73 to 5.02/100,000 people. Although the incidence rate of typical T1DM was highest in teenagers, it remained steady in adults over 30 years of age. In contrast, the incidence rate of atypical T1DM in 2013 was higher in people aged 40 years or older than in younger age groups. Age- and sex-adjusted prevalence of metabolic syndrome in patients with T1DM was 51.65% to 55.06% between 2009 and 2013.
Conclusion: T1DM may be more common in Korean adults than previously believed. Metabolic syndrome may be a frequent finding in individuals with T1DM in Korea.

CS3-1

Korean diabetes prevention study

Jeong-Taek Woo

Kyung Hee University, Korea

Diabetes and its complications are a major health problem and cause of mortality in Korea. The prevalence of diabetes in Korea has increased from 1.5% to 13.0 % in the past 40 years.
In particular, the serious problem is that the prevalence of diabetes in the young population increases, and prevalence of prediabetes is about 25% in people over 30 years of age.
Therefore, national efforts to introduce for diabetic prevention are urgently needed to reduce the epidemic of diabetes in Korea.
Unfortunately, no randomized controlled clinical studies aimed at establishing an objective basis for diabetes prevention had been conducted in Korea. However, the national project, the Korean Diabetes Prevention Study (KDPS) was organized to conduct multi-center clinical trials for the prevention of diabetes.
The goals of KDPS are as follows: (1) to develop a diabetes prevention program (lifestyle intervention and medication) that is suitable for Koreans at high risk for diabetes; (2) to conduct a prospective, randomized, controlled study and establish a cost-effective intervention program; and (3) to contribute to the national diabetes prevention program and promote public health by disseminating the results of the study.
The KDPS is underway on two different settings: a hospital-based intervention study (H-KDPS) with three intervention groups and a community web-based intervention study (community web-based Korean Diabetes Prevention Study [C-KDPS]) with two intervention methods. The results of this study are expected to contribute to the establishment of a unique diabetes prevention strategy that reflects the characteristics of Koreans.

CS3-2

Japanese standard configuration for personal health records (PHR) for diabetes mellitus

Naoki Nakashima

Kyushu University, Japan

It has been expected a large amount of data, related to diabetes mellitus and other non- communicable diseases, will be generated in the era of information. However, databases constructed without standardized data item sets should be limited in their usefulness. To address this, the Collaborative Committee of Clinical Informatization in Diabetes Mellitus was established in 2011 by the Japan Diabetes Society and Japan Association for Medical Informatics. The committee has developed core item sets and self-management item sets for diabetes mellitus, hypertension, dyslipidemia, and chronic kidney disease in collaboration with the Japanese Society of Hypertension, Japan Atherosclerosis Society, Japanese Society of Nephrology, and Japanese Society of Laboratory Medicine, as well as a mapping table that aligns the self-management item sets with the Japanese standardized codes for laboratory testing. The committee also determined detailed specifications for implementing the four self-management item sets in personal health record (PHR) applications, using international clinical guidelines to facilitate risk stratification, the generation of alerts using information and communications technology systems, the avoidance of data input errors, and the generation of reminders to input the self-management item set

data. The approach developed by the committee may be useful for combining databases for various purposes (such as for clinical studies, patient education, and electronic medical record systems) and for facilitating collaboration between PHR administrators.

CS3-3
Defeating type 2 diabetes: global challenges and new solutions
A. David Napier

University College London, UK

With well over four hundred million people globally living with type 2 diabetes, were diabetes a country it would be the third largest country in the world. Yet, with only half of those people diagnosed, for many living with the condition the experience remains nonclinical. Moreover, with low adherence rates across the globe the numbers in treatment who manage their diabetes without significant complications also remain very low.
To address the limited impact of biomedicine on the rise of diabetes, new strategies for assessing the diverse roles of complex, non-biomedical drivers of the illness must be developed. Moreover, as urban populations grow, large cities carry a disproportionately higher diabetes disease burdens than previously.
In response to these new trends, University College London joined Novo Nordisk and the Steno Diabetes Center in 2014 to launch a first-of-its-kind public private partnership. This partnership, Cities Changing Diabetes, seeks to understand the complex drivers of diabetes through new, action-oriented, interdisciplinary research strategies, and new cross-sectoral alliances with local governments, public health departments, community organizations, and patient groups. Focusing on both diabetes prevention and management outside of clinical settings, Cities Changing Diabetes in now working with 28 cities globally whose public health departments represent the needs of more than 200 million people.
The goals of the programme are to apply a deeper understanding of the social and cultural drivers of diabetes vulnerability and its lived experience, and to reverse the rapid rise of both diabetes and its key risk factor, obesity. Through prevention programmes based on feasible changes in policy, practice, and behavior, and through better care pathways and management programmes for those already living with the disease, Cities Changing Diabetes works to reverse the diabetes epidemic and towards defeating this serious global challenge.

CS3-4
City changing project in Busan city
Jeong Hyun Park

Inje University, Korea

In Busan city, the percentage of people age over 65 years is highest, and the numbers of people age under 14 years is lowest, among all the large cities in South Korea. The standardized mortality rate, and age-standardized mortality due to ischemic heart disease of Busan city is highest among the 7 large cities in South Korea. The number of people living in Busan city is about 3 million. Because Busan is a rather big city, the health status including the prevalence of chronic degenerative diseases including diabetes mellitus shows heterogenous distribution. The prevalence of diabetes greatly varies according to the specific regions of the Busan city i.e. the higher income areas showed lowest prevalence of diabetes. The urbanization would be a strong risk factor for the development of non-communicable degenerative diseases including obesity, hypertension, hyperlipidemia, and diabetes mellitus, because it usually being accompanied by so-called westernization of life style. But in the highly urbanized cities like Busan city, much heterogeneities of the prevalence and the quality of medical care exists in the city. For reducing the burden of diabetes mellitus of Busan city, the interventions to solve the inequalities of health related parameters are mandatory.

RG1-1
The mitochondrial-encoded peptide regulates CD4+ T cells and prevents autoimmune diabetes
Young Min Cho

Seoul National University, Korea

Mitochondria are principal metabolic organelles that are increasingly unveiled as immune regulators. However, the connection between mitochondrial-regulated immunity and type 1 diabetes (T1D), an autoimmune metabolic disorder, is largely unclear. Here, we provide evidence for the mitochondrial-encoded peptide (MDP) in preventing the progression of T1D by modulating CD4+ T cell function. MDP treatment significantly delayed the onset of diabetes in the NOD mouse model of T1D and preserved insulin-producing capacity. MOTS-c modulated CD4+ T cell subset composition by increasing Treg and depleting TH1 cell fractions in the spleen and pancreas of NOD mice. Consistently, adoptive transfer of MDP-c-treated NOD splenocytes to NOD-SCID mice failed to transmit autoimmune diabetes. At the cellular level, MOTS-c altered T cell metabolism by promoting OXPHOS and impeding glycolysis, compatible with the metabolic profile of Treg cells. MDP treatment suppressed the activation of CD4+ T cells derived from T1D and healthy individuals. Together, these results reveal that autoimmune diabetes can be regulated by a peptide that is encoded in the mitochondrial genome, which uniquely holds translational potential as a mitochondrial-encoded therapeutic target for T1D.

RG1-2
Defective BCAA metabolism contributes to pancreatic beta cell dysfunction in type 2 diabetes
Kenneth Cheng

The Hong Kong Polytechnic University, China

Type 2 diabetes is characterized by peripheral insulin resistance and defective insulin secretion in pancreatic ß-cell. Metabolomics analysis indicated that elevation of circulating levels of branched chain amino acids (BCAA including leucine, isoleucine and valine) is strongly associated with insulin resistance, obesity and an increased risk of future type 2 diabetes in human. Recent studies define a causal link between defective BCAA metabolism and peripheral insulin resistance in type 2 diabetes. For instance, chronic overload of BCAA and toxic lipid synergistically cause insulin resistance via induction of insulin receptor substrate degradation in the obese animal models. However, whether aberrant BCAA metabolism contributes to the progression of ß-cell failure has never been explored. By using metabolomics and different animal models, we recently found that defective BCAA metabolism is a major contributor of ß-cell dysfunction in type 2 diabetes. The expression of key enzymes responsible for BCAA catabolism is aberrant in diabetic ß-cells, leading to incomplete catabolism of BCAA and subsequent impairment of insulin secretion. The findings can help to design a new therapeutic approach for type 2 diabetes, an incurable and deadly disease that afflicts more than 420 million individuals worldwide.

RG1-3
Stomach-pancreas crosstalk in glucose homeostasis
Weizhen Zhang

Peking University, China

X/A-like cells, a group of unique endocrine cells in gastric oxyntic mucosa, produce and secret ghrelin to influence energy balance. Whether gastric X/A-like cells affect pancreatic fibrosis and subsequent glucose homeostasis remains unclear. We aimed to examine effects of mTORC1 signaling in X/A-like cells on ghrelin, pancreatic fibrosis and glucose metabolism. For this goal, we established a Ghrl-cre transgene in which the cre enzyme is expressed in X/A-like cells under the control of ghrelin-promoter. TSC-1flox/flox mice were bred with Ghrl-cre mice to generate Ghrl-TSC1-/- (TG) mice, within which mTORC1 signaling was activated in X/A-like cells. Ghrelin expression, glucose metabolism and pancreatic fibrosis were analyzed.
Activation of mTORC1 signaling by deletion of TSC1 gene in gastric X/A-like cells induced spontaneous pancreatic fibrosis. This alteration was associated with reduced insulin expression and secretion, as well as impaired glucose metabolism. Activation of mTORC1 signaling in gastric X/A-like cells reduced gastric and circulating ghrelin levels. Exogenous ghrelin re-

versed pancreatic fibrosis and glucose intolerance induced by activation of mTORC1 signaling in these cells. Rapamycin, an inhibitor of mTOR, reversed the decrease of ghrelin levels and pancreatic fibrosis.
In conclusion, activation of mTORC1 signaling in gastric X/A-like cells induces spontaneous pancreatic fibrosis and subsequently impairs glucose homeostasis via suppression of ghrelin. We thus identify a novel stomach-pancreas crosstalk pathway.

RG1-4

Ubc9-mediated SUMOylation regulates oxidative stress and ER stress in the pancreatic β cells

Cong-Yi Wang

Tongji Medical College, China

Although SUMOylation has been recognized in regulation of various cellular processes, but its exact function in the pancreatic β cells is yet to be fully addressed. Since β cells are easily assaulted by oxidative stress and endoplasmic reticulum (ER) stress, we induced Ubc9 (the only E2 SUMO-conjugating enzyme) deficiency in 8-wk old B6 mice by tamoxifen injection (Ubc9fl/fl-Ins1-ER-cre). Remarkably, mice with Ubc9 deficiency in the pancreatic β cells manifested abnormal insulin/proinsulin (immature insulin form) secretion and developed diabetes spontaneously. Histological and ultrastructural analysis revealed a significant loss of β cell mass along with ER/mitochondria morphological abnormalities. Specifically, loss of Ubc9 impaired β cell anti-oxidative capability as manifested by the decreased expression of anti-oxidative genes coupled with reactive oxygen species (ROS) accumulation, and provoked ER stress signals. By proteomic analysis of SUMOylation substrates in both human and mouse islets, we characterized a novel SUMOylation regulatory axis, which synergistically regulates AKT/GSK3β phosphorylation to impact NRF2 stability and transcriptional activity, thereby improving anti-oxidative stress capability. Moreover, SUMOylation of Pdi (protein disulfide isomerase) family proteins regulates their enzymatic activity, protein binding capability, cellular localization and stability, thereby regulating ER stress and insulin maturation in the pancreatic β cells. Collectively, our data support that SUMOylation function is required for β cells to defend oxidative stress and ER stress, and to process insulin maturation.

RG1-5

GLP-1 agonist prevents β cells from apoptosis through improving mitochondrial function and suppressing prolonged AMPK activation

Tien-Jyun Chang

National Taiwan University, Taiwan

Accumulation of methylglyoxal (MG) contributes to glucotoxicity and mediates beta cell apoptosis. The molecular mechanism by which GLP-1 protects MG-induced beta cell apoptosis remains unclear. Metformin is a first-line drug for treating type 2 diabetes associated with AMPK activation. However, whether metformin prevents MG-induced beta cell apoptosis is controversial. Here, we explored the signaling pathway involved in the anti-apoptotic effect of GLP-1, and investigated whether metformin had an anti-apoptotic effect on beta cells. MG treatment induced apoptosis of beta cells, impaired mitochondrial function, and prolonged activation of AMP-dependent protein kinase (AMPK). The MG induced pro-apoptotic effects were abolished by an AMPK inhibitor. Pretreatment of GLP-1 reversed MG-induced apoptosis, and mitochondrial dysfunction, and suppressed prolonged AMPK activation. Pretreatment of GLP-1 reversed AMPK activator 5-aminoimidazole-4-carboxamide riboside (AICAR)- induced apoptosis, and suppressed prolonged AMPK activation. However, metformin neither leads to beta cell apoptosis nor ameliorates MG-induced beta cell apoptosis. In parallel, GLP-1 also prevents MG-induced beta cell apoptosis through PKA and PI3K-dependent pathway. In conclusion, these data indicates GLP-1 but not metformin protects MG-induced beta cell apoptosis through improving mitochondrial function, and alleviating the prolonged AMPK activation. Whether adding GLP-1 to metformin provides better beta cell survival and delays disease progression remains to be validated.

RG1-6

GLP-1 receptor agonists and β-cell mass

Daisuke Yabe

Gifu University, Japan

Glucagon-like peptide-1 receptor (GLP-1R) agonists exert their glucose-lowering effects through amelioration of the impaired secretions of insulin and glucagon, two fundamental defects in the pathogenesis of type 2 diabetes, without increasing hypoglycemia risk (Diabetes Obes Metab. 2017;19(3):442-447). We have clinically demonstrated that glucose-lowering effects of GLP-1R agonists depend on levels of remaining pancreatic β-cell function (J Diabetes Investig. 2013; 4(6):585-94; J Diabetes Complications. 2015; 29(8):1203-10; J Diabetes Complications. 2016 Sep-Oct;30(7):1385-92; J Diabetes Investig. 2018; 9(4):822-830). However, it remains unknown whether remaining β-cell mass or insulin secretory capacity of each β-cell are responsible for glucose-lowering effects of GLP-1R agonists. We have recently demonstrated, using GLP-1R-targeting probe 111 Indium-labeled exendin-4 derivative, that remaining -cell mass correlates with post-treatment glycohemoglobin and glucose area under curve during an oral glucose tolerance test (R2 = 0.76 and 0.80; P < 0.01 and <0.01, respectively), indicating that remaining β-cell mass determines glucose-lowering effects of GLP-1R agonists (J Diabetes Investig. 2020 Apr 23. doi: 10.1111/jdi.13281). We thus turned to investigate strategies to enhance β-cell mass in vivo to restore glucose-lowering effects of GLP-1R agonists in patients with reduced β-cell mass. As a first step, we have recently developed a novel tool that specifically labels replicating -cells by the fluorescent ubiquitination-based cell cycle indicator Fucci2a in β-cells to facilitate evaluation of β-cell proliferation in vivo (Diabetes. 2020 Aug 7. doi: 10.2337/db20-0290). Three-dimensional imaging of optically cleared pancreas tissue from these mice enabled quantification of replicating β-cell in the islets and morphometric analysis of the islets following known mitogenic interventions such as insulin receptor antagonist S961, diet-induced obesity, pregnancy and partial pancreatectomy. Furthermore, we have succeeded in intravital imaging of β-cell proliferation. With this novel model, we're positioned to screen chemical libraries to find molecules that potentially enhance β-cell proliferation. In the current talk, I'd like to discuss potential therapeutics targeting β-cell mass by providing our clinical and basic data on GLP-1R agonists and β-cell mass.

RG2-1

New perspective in diabetic neuropathy: from the periphery to the brain

Tae Jung Oh

Seoul National University, Korea

Diabetic neuropathy is common microvascular complication of diabetes and related with foot ulceration, poor quality of life and increase of mortality. Among diverse forms of diabetic neuropathy, distal symmetrical polyneuropathy (DSPN) is the most common form of diabetic neuropathy. However, the underlying mechanism is not yet fully understood. According to the data of autopsy and neuro-image studies, pathology of spinal cord and brain involved in DSPN. For example, cross-sectional area of cervical spinal cord is reduced in patients with DSPN compared to those without DSPN. In addition, grey matter volume localized to the primary somatosensory cortex is decreased in patients with DSPN. From the recent studies using advanced technology, maladaptive alteration of both peripheral and central nervous system arose as an important contributor in DSPN. To understand this pathophysiology, diverse functional image tools have been developed. In this lecture, I will discuss current evidences about how central nervous system is related with DSPN. Even though there is still a large gap between understanding pathophysiology of DSPN and development of therapeutics, I think this topic is worthy to discuss.

RG2-2

Painful and painless diabetic neuropathies: what is the difference?

Seong-Su Moon

Dongguk University, Korea

Diabetic peripheral neuropathy is one of the most common complications of diabetes, ranging from devastating to asymptomatic status. The symp-

toms manifested by patients are various and the courses are not sequential, which makes the diagnosis not simple. Although the symptoms cannot be dichotomized, the symptoms are categorized as positive and negative. Depending on the affected legion of the nervous system, symptoms can be different. Pain is a typical positive symptom alleviating the quality of life of patients with diabetic peripheral neuropathy. Previous studies have shown that clinical manifestations of painful and painless diabetic neuropathy are not exclusive. Several hypothetical theories of neuropathic pain generation are suggested while pathogenetic mechanisms of painful diabetic peripheral neuropathy are still elusive. It is crucial to understand the characteristics of painful and painless diabetic neuropathy when we treat patients. At this talk, the difference between painful and painless diabetic neuropathy will be addressed in clinical, epidemiological, and pathogenetic aspects.

RG2-3
Disease modifying therapies for diabetic neuropathy-P present strategies and emerging solutions
Chong Hwa Kim

Sejong General Hospital, Korea

Diabetic peripheral neuropathies (DPN) are a heterogeneous group of disorders caused by neuronal dysfunction in patients with diabetes. They have differing clinical courses, distributions, fiber involvement (large or small), and pathophysiology. These complications are associated with increased morbidity, distress, and healthcare costs. Pathogenetic treatments aim to impact favorably the underlying pathophysiological aberrations encountered in DPN by targeting different elements in the pathways leading to neurovascular dysfunction. Optimal glucose control represents the only broadly accepted therapeutic option though evidence of its benefit in type 2 diabetes is unclear. A number of pathogenetic treatments are recommended in clinical guidelines for the management of DPN, including Alpha lipoic acid (ALA), benfotiamine, actovegin, and gamma linoleic acid etc. A number of symptomatic treatments are recommended in clinical guidelines for the management of painful DPN, including antidepressants such as amitriptyline and duloxetine, the γ-aminobutyric acid analogues gabapentin and pregabalin, opioids, and topical agents such as capsaicin.
However, monotherapy is frequently not effective in achieving complete resolution of pain in DPN. There is a growing need for head-to-head studies of different single-drug and combination pharmacotherapies.

RG3-1
Current evidence for NAFLD treatment
You-Cheol Hwang

Kyung Hee University, Korea

Nonalcoholic fatty liver disease (NAFLD) is the most common chronic liver disease worldwide and shows diverse disease spectrum from simple steatosis, nonalcoholic steatohepatitis (NASH), cirrhosis to cancer. Unfortunately, however, the pathophysiologic mechanism is not fully understood yet and there is no approved pharmacotherapy. In this talk, I would like to introduce the drugs currently available for the treatment of NAFLD/NASH and their pharmacologic action mechanisms. In addition, I will briefly provide an overview of drug targets currently under development.

RG3-2
Treatment of non-alcoholic fatty liver disease with focus on non-pharmacologic option
Ji Hye Huh

Hallym University, Korea

Non-alcoholic fatty liver disease (NAFLD) is a spectrum of liver disease, from steatosis to liver cirrhosis in individual who does not consume alcohol in significant amount. The prevalence of NAFLD in Korea was estimated around 30%, this condition related to the increased incidence of metabolic disorders. Current understanding of NAFLD pathogenesis is the third-hit theory, in which insulin resistance resulting in free fatty acid accumulation that triggers inflammation causing fibrosis and hepatocyte death, and these

conditions are not followed by adequate hepatocyte proliferation.
Treatment of NAFLD requires both non-pharmacologic and pharmacologic interventions. Life style intervention includes restricting calories, low saturated fat and low sugar diet, and also physical activity. In patients unresponsive to lifestyle changes and pharmacotherapy, bariatric surgery is an option for reducing weight and metabolic complications, with stable results in the long-term. Liver transplantation is an accepted procedure in NASH patients with end-stage liver disease.
In this session, I would like to talk about evidences regarding treatment of non-alcoholic fatty liver dsease with focus on non-pharmacologic options.

RG3-3
Treatment Of NAFLD: effect of anti-diabetic medication
Jae Hyuk Lee

Hanyang University, Korea

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disease characterized by hepatic steatosis in the absence of excessive alcohol consumption. NAFLD may progress to cirrhosis and is likely an important cause of cryptogenic cirrhosis.
Pharmacologic therapy can be used to promote weight loss in patients who fail to achieve their goals through diet and exercise alone. For patients with diabetes mellitus, the presence of NASH can inform the choice of glucose lowering therapy in some cases. Although initial therapy for type 2 diabetes mellitus is typically with metformin, which does not improve liver histology, the beneficial impact on liver histology with certain other insulin-sensitizing agents could be a consideration when choosing a second-line agent for patients with NASH who cannot take metformin or need additional glucose-lowering therapy.
In patients with diabetes mellitus and biopsy-proven NASH, pioglitazone improves fibrosis as well as inflammation and steatosis. Although less well studied, liraglutide also appears to improve liver biopsy evidence of NASH. The potential benefits of these drugs must be balanced with their associated adverse effects. For example, use of pioglitazone is limited because it is associated with increased risk of weight gain, heart failure, and fractures.

RG3-4
Treatment of NAFLD: non-diabetic drugs
Yeon Seok Seo

Korea University, Korea

TBD

RG4-1
Simple and faster way to create vascular cell specific KO mouse
Ho Lee

NCC-GCSP, Korea

Recent technological advances have led to fast-track generation of sophisticated mouse models that more closely mimic human disease in terms of genetic composition, interactions of mutant cells with their microenvironment, and drug response. Recently, CRISPR/Cas9 has been developed in genome editing which is becoming an indispensable element of the genetic toolbox in mice. It enhances the efficiency of gene targeting or modification, and additionally save time and cost for generation of mouse models.
In the field of vascular biology, enormous insight has been gained by using conditional knockout mouse in which specific gene is temporarily or spatially manipulated within endothelial. Numerous models are available to constitutively or inducibly modulate gene expression in all or a specified subset of endothelial cells.
Here, I will introduce and summarize what is known about commonly-used endothelial-specific Cre and CreERT2 transgenic mouse models and how these mice are used in vascular biology field.

RG4-2

How to make early diabetic retinopathy mouse model

Jeong Hun Kim

Seoul National University, Korea

Angiogenesis-related Blindness (ARB) includes representative vision-threatening diseases: age-related macular degeneration, diabetic retinopathy (DR), and retinopathy of prematurity. As their names imply, each disease is related with aging, diabetes, and preterm birth, respectively. We coined the term, ARB, to emphasize the common mechanism of these vision-threatening disorders, pathologic angiogenesis.

In particular, as research on diabetes is actively performed, there are several validated animal models for diabetes and some of them are utilized for the investigation of DR. These animal models basically demonstrate induced hyperglycemia as the main characteristic of animal models. In other words, the elevation of serum glucose that is spontaneously, chemically, or surgically induced leads to pathologic events similar to those in patients with diabetes and DR. As previously mentioned, animal models of this category show the pathologic features regarding structural abnormalities or the dissociation of neurovascular units of the retina: 1) pericyte loss, 2) thickening of BM, 3) acellular capillaries or capillary dropout, and 4) increased vascular permeability. Unfortunately, retinal neovascularization in DR is not definite in animal models of DR with induced hyperglycemia.

In this lecture, I would like to introduce basic techniques of in vitro and in vivo experiments on tranlational research in DR for beginners as clinician-scientists of diabetes.

RG4-3

How to make diabetic albuminuria and/or glomerulosclerosis mouse model

Sungjin Chung

The Catholic University of Korea, Korea

Over the last few decades, rodent animals have been instrumental in numerous experimental studies, and in an area of diabetic kidney research they have also provided important information about how diabetic renal complication starts and progresses through time, helping to make us understand the pathogenesis of human diabetic nephropathy better. Especially, the mouse has become the main experimental model used in research for diabetic renal physiology and pathology due to its easy manipulation, short gestation times and relatively high genetic homology with humans. The more important thing is that an ideal rodent model of diabetic nephropathy should exhibit the characteristic of renal histology in the glomeruli and tubulointerstitial area, with increased albuminuria and a decline in renal function. However, current diabetic mouse models have shown to be seemingly bounded by some major limitations including the fact that most of murine models just replicate a few parts of human diabetic kidney disease. Most of the mice usually chosen as animal models of diabetic kidney disease show a different degree of resistance to the development of diabetic nephropathy as the susceptibility to kidney disease is clearly influenced by the genetic background of the strain. Many researchers have tried to develop novel and different rodent strains demonstrating typical findings of diabetic nephropathy but there have still been some arguments on which model could be more suitable one mimicking features of human diabetic nephropathy. Therefore, a critical need to explore and characterize novel mouse models that provide clinically relevant representations of human diabetic nephropathy should be met in the near future. Until then, it is clear that knowledge of the differences in genotypes and phenotypes among current diabetic mouse models leads to a better understanding of pathophysiology of diabetic kidneys and helping researchers assess the effects of the new therapeutic tools against diabetic nephropathy.

RG4-4

Mouse models for progression and regression of atherosclerosis

Jae-Hoon Choi

Hanyang University, Korea

Atherosclerosis is a chronic inflammatory disease due to various causes including hyperlipidemia, hypertension, obesity so on. Atherosclerosis is initiated with increased lipid accumulation in the subintimal space and oxidative modification of lipids, and progressed by the interactions among modified lipoproteins, immune cells such as macrophages and T cells, and non-immune vascular cells such as smooth muscle and endothelial cells during hyperlipidemic condition. Mouse model is most favored to study human diseases for its rapid reproduction, genetic manipulation ability. However, mouse is highly resistant to atherosclerosis because of different lipid profile compared to humans. In mouse, the majority of cholesterol is transported via high density lipoproteins (HDL) and retain low concentration of LDL and very low density lipoproteins (VLDL). Therefore, the genetic manipulation on lipid metabolism genes is required to induce hyperlipidemia and atherosclerosis in mouse. In this session, I will introduce the genetically engineered mouse models for hyperlipidemia and atherosclerosis. Furthermore, I will also present the atherosclerosis-regression model to study the molecular and cellular mechanisms of plaque resolution.

SP1-1

VERTIS-CV Study - how can we interpret the results?

Jeong Hyun Park

Inje University, Korea

The VERTIS cardiovascular (CV) outcomes trial has a primary objective to demonstrate non-inferiority of ertugliflozin versus placebo on major adverse CV events: time to the first event of CV death, nonfatal myocardial infarction, or nonfatal stroke. Secondary objectives are to demonstrate superiority of ertugliflozin versus placebo on time to the composite outcome of CV death or hospitalization for heart failure, CV death, and the composite outcome of renal death, dialysis/transplant, or doubling of serum creatinine from baseline. Patients ≥40 years old with T2DM (HbA1c 7.0-10.5%) and established atherosclerotic cardiovascular disease (ASCVD) were randomized 1:1:1 to once daily double-blind placebo, ertugliflozin 5 mg or 15 mg added to existing therapy. Total 8246 patients were randomized. Mean age was 64.4 years, 11.0% were ≥75 years old, and mean diabetes duration was 12.9 years with screening HbA1c of 8.3%. At entry, coronary artery disease, cerebrovascular disease, and peripheral arterial disease were present in 76.3%, 23.1%, and 18.8% of patients, respectively. HF was present in 23.1%, and Stage 3 kidney disease in 21.6% of patients. Ertugliflozin reduced HbA1c, body weight, and SBP compared with placebo, and reductions were sustained over the course of the study. Ertugliflozin added to guideline-directed secondary prevention therapies was noninferior compared with placebo for MACE, achieving the primary objective of the study. A 30% risk reduction in HHF, a prespecified end point not part of the hierarchical testing sequence, was observed with ertugliflozin relative to placebo. Ertugliflozin was well tolerated, with a safety profile consistent with previous studies of ertugliflozin. The incidences of UTIs and GMIs were significantly higher in the ertugliflozin group vs placebo.

SP1-2

ALL SGLT2 inhibitor are same – pros

Young Min Cho

Seoul National University, Korea

SGLT2 inhibitors are under spotlight due to its unique property protecting the cardiovascular system and the kidney. Several SGLT2 inhibitors are available and they share similar chemical structure resembling glucose molecule. The mechanism of glucose lowering is removal of glucose through urine by inhibiting its tubular reabsorption. Therefore, glucose lowering efficacy of these drugs are largely identical. Cardiovascular outcomes studies have shown similar reduction in cardiovascular events and hospitalization for heart failure. However, study-to-study variations were noted possibly due to differences in the study populations. In this debate session, I will show recent evidence supporting the class effect of the SGLT2 inhibitor.

SP1-3

ALL SGLT2 inhibitor are same – cons

Gwan Pyo Koh

Jeju National University, Korea

Many cardiovascular outcome trials (CVOTs) of new antidiabetic agents has been conducted since Dr. Nissen raised the issue of myocardial infarction risk of rosiglitazone. The CVOTs were intended to ensure cardiovascular safety of those, however the EMPA-REG OUTCOME trial demonstrated that empagliflozin significantly reduced the risk of major adverse cardiovascular events (MACE), heart failure, progressive kidney disease and mortality. After that, canagliflozin also improved cardiovascular and renal outcomes in the CANVAS and CREDENCE trials. Dapagliflozin reduced the risk of heart failure (HF) and kidney disease but not MACE in the DECLARE-TIMI 58 trial. Most recently, ertugliflozin did not show cardiovascular or renal benefit, it showed only HF benefit in the VERTIS-CV trial. In CVOTs, taken together, the four sodium-glucose cotransporter inhibitors (SGLT2i) consistently reduced the HF risk, but they have variable effects on MACE, kidney disease and mortality. Why are they different? I think SGLT2i prevents the progression of HF rather than atherosclerosis. So the outcome parameters excluding HF may vary depending on the study design, subjects and circumstances in CVOTs with SGLT2i. A further study is required to identifying the action mechanism and cardiovascular effect of SGLT2i.

SP2-1

Making AI meaningful in diabetes management

Seong Ki Mun

Virginia Tech, USA

The use of artificial intelligence (AI) and machine learning (ML) tools are topics of great interests throughout many industries as massive amount of digital data has been accumulated ubiquitously. Digital industries have been promoting exiting new products and services to healthcare sector. However, broad clinical adoption of AI is many years away. In diabetes management, we see 4 categories of AI tools, Automated Retinal Screening, Clinical Decision Support, Predictive Population Risk Stratification and Patient Self-Management Tools. Diabetes community have been developing these systems, except retinal screening, for many years using rule based statistical methods with limited success. The question here is, would AI-based tools experience better clinical adoption. This presentation will discuss the progress made primarily in retinal screening and clinical decision support systems in order to highlight some new and old persistent challenges R&D and clinical deployment of AI tools. Some of the major issues include the availability of structured or operational data, quality of data, ability to deal with heterogenous nature of healthcare processes, and lastly, integration of new tools to clinical workflow. The eventual success of global adoption of AI in healthcare will noticeably depend on its ability to offer substantial productivity improvements and at the same time more patient centric care via mass customization based on the concept co-production that involves a patient as an end-user.

SP2-2

Mission and vision of the all of us researcher workbench

Andrea Ramirez

Vanderbilt University , USA

The All of Us (AoU) Research Program is committed to the ambitious mission of collecting health data from a million or more participants, with a focus on those under-represented in biomedical research, to accelerate discovery in precision medicine. At this scale, downloading a dataset and storing it locally is expensive, impractical, and increases security risks. Moreover, many researchers will not have the necessary computational or security infrastructure to perform local analyses on large datasets. To address these challenges, AoU aims to "bring researchers to the data" by creating a cloud-based analytical platform to help users test hypotheses in silico and readily and efficiently work within an environment that meets robust security and regulatory requirements. This platform, the All of Us Researcher Workbench, includes layers of functionality to address researcher needs at all stages of research design and execution.
Three important innovations in the Workbench are designed to meet the needs of today's researcher. First, the access process includes identity verification, ethics training, and data use attestation, enabling the first of its kind "passport model" based on researcher identity, not a specific research proposal. Second, custom tools have been built to create datasets for analysis, by identifying relevant cohorts and biomedical concepts. These tools enable exploration and characterization in a graphical user interface, allowing researchers to focus on their question of interest. Third, a cloud-based Jupyter notebooks environment supporting R and Python provides easy access to powerful compute and seamless sharing of analyses for reproducibility and collaboration. These three key elements are supported by an integrated help desk and extensive documentation including a data dictionary, code snippets, and a library of tutorial workspaces, pre-implemented phenotypes, and example analyses.
This presentation will provide an overview of the initial Workbench analysis suite, including tools for study cohort identification and characterization for feasibility testing, data exploration and covariate selection, and analysis.

SP3-1

An artificial intelligence-aided interactive platform for explainable target identification

Hee Jung Koo

Standigm Inc., Korea

Identifying an appropriate disease target is an essential task to be solved for the successful development of therapeutics. Based on this need, we suggest

a novel artificial intelligence-aided target identification approach, iCLUE-ASK™, to make a breakthrough in deciphering the target identification task with exploiting the vast resources.

iCLUE-ASK™ is comprised of three components distinct from conventional methods: a heterogeneous graph database, an explainable prediction algorithm, and an interactive user interface.

First, we constructed a massively-linked heterogeneous graph database by integrating the preexisting knowledge related to diseases, targets, and drugs and the relationships surrounding these entities. It contains not only the information from curated public databases but also the relations extracted from published abstracts using natural language processing technology. It comprehensively recognizes diverse biological entities presented in the multiple sentences and detects gene-disease associations in real-time, thus enables us to keep our database up to date.

Second, we developed a target prioritization algorithm based on the constructed database. We developed a deep neural network aided by the attention mechanism, one of the state-of-the-art techniques in recent AI studies that gives more accurate results and better explainability.

Third, we provide an interactive user interface for browsing the predicted targets and exploring the supporting evidence visualized as a graph connecting the disease and target through important paths. iCLUE-ASK™ also supports a customized analysis for users who want to apply their own datasets to acquire more focused results on their disease-of-interest. In the same context, users can validate their hypotheses in silico before initiating experiments or get ideas that lead to new hypotheses from the prediction results and evidence.

iCLUE-ASK™ officially opens in September, and we expect our platform to aid target researchers by being an in silico testbed and conferring a novel insight.

SP3-2

Application of machine learning in target discovery

Hyeon Joo Yim

LG Chem, Korea

New drug development begins with the selection of targets that will change the state of the disease. A proper target must be able to significantly change the state of the disease when modulating its activity. The use of literature information and rich omics data accumulated by the development of modern biology as well as the high-level analysis of these data using deep learning or machine learning provide new challenges and opportunities for target discovery. In the field of new drug discovery research and development, cooperation with these new technologies, training appropriate experts internally, and various attempts are needed to integrate rapidly developing new areas.

SP3-3

AI-based systematic target discovery for metabolic diseases

Joong Hoon Park

Seoul National University, Korea

The scarcity of new targets and unmet medical needs are challenging in the new drug R&D for metabolic diseases. Here, we developed an AI-based systematic target discovery approach (Artificial Intelligence of Target Discovery; AITD) for metabolic diseases through phenotypic analysis of knock-out (KO) mice, integrated bioinformatics analyses incorporating empirical evidence provided by experts. Using the phenotype information of 11,181 KO mouse strains collected from International Mouse Phenotyping Consortium (IMPC) release 10.1 and Mouse Genome Informatics (MGI) 6.14, qualitative and quantitative analysis revealed 4,363 metabolic genes significantly influencing body composition, glucose homeostasis, dyslipidemia and NAFLD-associated phenotypes. Among them, the annotated genes in cellular function, protein-protein interaction, and/or signaling pathway were subjected to natural language processing-based literature mining, and 1,495 genes participating in type 2 diabetes, obesity, the disorder of lipid metabolism, and NAFLD were identified. It was confirmed that 733 genes without functional abnormalities in the cardiovascular system, central nervous system, and respiratory system were enriched in fatty acid metabolism and PPAR signaling pathway. Analysis of target novelty revealed that 110 ligand-coding genes and 189 receptor-coding genes were in the preclinical stage at most. To validate the clinical relevance of these genes, mRNA levels in liver, fat, and muscle tissues of obese and obese/

diabetic patients were comparatively analyzed, and 54 novel genes were discovered for metabolic diseases with high druggability. AITD is proposed as the cornerstone for the discovery of new druggable targets and new drug R&D for metabolic diseases.

AW1

Control of fuel homeostasis by Rho-kinase

Kim Young-Bum

Harvard University, USA

Type 2 diabetes is a rapidly growing health problem, affecting 29 million people in the United States and over 350 million worldwide and together with obesity presents an overwhelming economic burden. Thus, studies are urgently required to improve our understanding of the disease process to plan more effective therapeutic approaches to limit and/or reverse the disease. Our studies have identified ROCK1 (Rho-kinase 1; Rho-associated coiled-coil-containing kinase 1) as a key regulator of insulin sensitivity, hepatic steatosis, and adiposity, that provide promising insights into the pathogenesis of type 2 diabetes and obesity. In particular, we show that peripheral ROCK1 controls glucose metabolism and insulin sensitivity, whereas hypothalamic ROCK1 acts to dominantly regulate feeding behavior and body-weight homeostasis. In this talk, I will share the data of our on-going Rho-kinase studies and offer a new paradigm in which Rho-kinase is a critical determinant of fuel homeostasis.

AW2

It's time to build high level of real-world evidence in diabetes and metabolism research

Nam Hoon Kim

Korea University, Korea

Advance in diabetes therapeutics, especially drug therapy, has been mainly driven by large-scale randomized controlled trials (RCTs). Not surprisingly, clinical guidelines adopt RCTs and meta-analysis of RCTs as the highest level of evidence. However, there being inherent limitations of RCT including limitation of generalizability. As well, it was not an area that individual researchers could easily attempt due to huge budget. Real-world data (RWD) are data relating to patient health status and the delivery of health care routinely collected from a variety of sources. Real-world evidence (RWE) is the clinical evidence from RWD, which is playing an increasing role in health care decisions specifically for drug usage, or the potential benefits or risks of therapeutics. Despite essential limitations or biases of RWE, well designed, well construct studies could hopefully bridge the gap between RCT and unprocessed RWD. Here I introduce some strategy and examples to overcome the limitations of RWE, to the high level of RWE.

SS1

SGLT2 Inhibition: role in T2D and related complications

David Z. Cherney

University of Toronto, Canada

Dr. David Cherney, one of the leading researchers of SGLT2 inhibitors in the world, has been elucidating benefits of SGLT2 inhibitors from early and demonstrated the TGF hypothesis as a mechanism of action. In this lecture, Dr. Cherney will lead us through the paths, where number of large scaled CVOTs for antidiabetic drugs have paved for the past decade. It would give us opportunity to learn recent insights from the mechanisms to clinical implications around the multiple benefits we have observed from SGLT2 inhibitors class now being explained based on the systematic review and potential inter-organ connectivity as the cardio-renal metabolic axis. The burden of cardio-renal complications and mortality from the long journey of type 2 diabetes remain significant. Emerging clinical evidences and guidelines are now leading us toward the new era how we may better approach to address major complications of type 2 diabetes, which resonates the findings from EMPA-REG Outcome trial and comprehensive clinical programs for empagliflozin, becoming one of the essential part of T2D treatment. The discussion may further help us to define the role of empagliflozin in managing T2DM, combined comorbidities and death where mechanistic translation would play important role.

SS2

The multiple benefits of SGLT-2i: ideal option for Asian T2DM patients

Bo Kyung Koo

Seoul National University, Korea

Recent guidelines on glucose lowering agents for type 2 diabetic patients recommend that a GLP-1 receptor agonist or SGLT2 inhibitor should be considered independently of baseline HbA1c or individualized HbA1c target to reduce MACE, heart failure, cardiovascular death or chronic kidney disease (CKD) progression for patients with high-risk ASCVD risk or CKD risk. For patients with or without established atherosclerotic CVD, but with HFrEF (EF ⟨45%) or CKD (eGFR 30 to ≤60 ml min-1 [1.73 m]$^{-2}$ or UACR ⟩30 mg/g, particularly UACR ⟩300 mg/g), the level of evidence for benefit is greatest for SGLT2 inhibitors. Ipragliflozin (SUGLAT®), one of SGLT2 inhibitors on Korean market, has various clinical trials on combination therapy in Asian Patients. It brings significant improvement on HbA1c, blood pressure, body weight, visceral fat and non-fatty liver disease as reported in other SGLT2 inhibitors. In addition, its relatively low SGLT2 selectivity compared to dapagliflozin or empagliflozin and no effect on LDL cholesterol might be strengths of ipragliflozin distinguished from other SGLT2 inhibitors.

SS3

The beneficial effects of lobeglitazone combination therapy

Soo Lim

Seoul National University, Korea

Lobeglitazone is a PPARγ agonist, which has favorable effects in adipogenesis, insulin sensitivity, and cell cycle regulation. We recently compared the efficacy and safety of an initial triple therapy using metformin, sitagliptin, and lobeglitazone with a stepwise approach using sulfonylurea and metformin in new-onset, drug-naïve patients with T2D (9.0%-12.0% of HbA1c). After 12 months of treatment, HbA1c levels decreased significantly in both groups: from 10.7%±1.0% to 6.7%±1.3% in the triple group, and from 10.5%±1.0% to 7.3%±1.2% in the conventional therapy group. At 12 months, achievement of the HbA1c target (⟨7.0%) was higher in the triple group than in the conventional group (70% vs 52%, p⟨0.01). Dynamic indexes related to β-cell function and insulin sensitivity improved, and albuminuria reduced significantly only in the triple group. Another recent study evaluated the efficacy and safety profile of lobeglitazone compared with sitagliptin as an add-on to metformin in patients with type 2 diabetes for 24 weeks. The mean changes in HbA1c of the lobeglitazone and sitagliptin groups were -0.79% and -0.86%, respectively; the between-group difference was 0.08% (95% CI, -0.14%~0.30%), showing non-inferiority. Lobeglitazone has also proven its anti-inflammatory and antiatherogenic properties in two rodent models. Lobeglitazone treatment (0.3 and 0.9 mg/kg) caused a significant decrease in the intima-media ratio compared with control rats.

Consistent with this, in ApoE(-/-) mice fed a high-fat diet, lobeglitazone treatment (1, 3, and 10 mg/kg) for 8 weeks reduced atherosclerotic lesion sizes in the aorta compared with the control mice in a dose-dependent manner. Of note, treatment with lobeglitazone over 52 weeks showed no detrimental effect on the BMD compared to the placebo. Collectively, a lot of evidence suggests that lobeglitazone improves glucose homeostasis by decreasing insulin resistance without side effects.

SS4

Strategic T2DM treatment in broad range of patients

Eun Seok Kang

Yonsei University, Korea

Diabetes, one of four top-priority non-communicable diseases (NCDs) targeted for action by world leaders, is a serious public health problem. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades. Diabetes is a complex, chronic illness requiring continuous medical care with multifactorial risk-reduction strategies apart from glycemic control. When caring for diabetic patients, strategically optimized treatment is especially important because of the multitude of variables involved in the decision-making process, including therapeutic choices, disease duration, presence of complications and comorbid conditions, and economic factors in broad range of patients. So strategic treatment individualized is strongly supported by current guidelines, ADA 2020.

Combination therapy is the one of strategic treatments in terms of more rapid achievement of glycemic control, use of lower doses of individual agents, complementary modes of action, etc. So more than 70% of patients received combination therapy and more than 1/4 patients received triple combination therapy. There are various drug options to consider as a combination therapy for better outcome so we are looking at what drug class has benefit-risk to accomplish strategic treatment individualized.

In this lecture I will talk about strategic treatment options focused on Sitagliptin and Ertugliflozin what evidences they can provide for optimized treatment and how they can suggest therapeutic strategies for better outcomes.

SS5

Clinical values of the new basal insulin & GLP-1 fixed ratio co-formulation

Young Min Cho

Seoul National University, Korea

Two major injectables for treatment of type 2 diabetes are basal insulin and GLP-1 receptor agonists (GLP-1RA). They have complementary mechanism of action, prompting combination therapy to tackle multiple pathophysiological defects causing and sustaining hyperglycemia. Co-formulation of long-acting insulin and long-acting GLP-1RA are particularly effective in reducing hyperglycemia while avoiding increased risk of hypoglycemia and weight gain. In this lecture, I will focus on clinical values of the fixed ratio co-formulation of insulin degludec and liraglutide.

SS6

The power of one pill, NesinaAct for T2DM patients

Dae Jung Kim

Ajou University, Korea

The various combination therapy of oral anti-diabetic drugs for the management of type 2 diabetes mellitus (T2DM) are suggested. We consider the beneficial combination based on not only insulin resistance with protecting and/or restoring β-cell function but also insulin secretion. And the most important factor of treatment is to control glucose level.

For being synergistic partner in the treatment of T2DM, illustrated the potential benefits of combination therapy with pioglitazone and DPPIVi with respect to: (1) addressing pathophysiologic mechanisms underlying T2DM; (2) maintenance of sustained and effective glycemic control; (3) overall safety benefit; and (4) effect on CV risk and long-term outcomes. Patho-physiologically, it is logical to combine insulin sensitizers with incre-

tin agents and these different mechanisms of action are covered with the combination of alogliptin, pioglitazone. By protecting β-cell function early on, it may be possible to prevent later deterioration and type 2 diabetes complications. Also, both of alogliptin and pioglitazone demonstrated CV safety and have abundant evidences (EXAMINE/ PRO-active)

In this lecture I attempt to address the synergistic benefits with DPPIVi and pioglitazone combination, that should be considered when providing optimized treatment and suggesting therapeutic strategies for better outcomes in T2DM patients.

SS7

All statins are the same in safety and outcome for Asian?

Hyuk Sang Kwon

The Catholic University of Korea, Korea

Pitavastatin is characterized for its potent LDL-C lowering as well as TG-lowering and stable HDL-C elevating effects. In TOHO-LIP trial published in Internal Journal of Cardiology 2020, Pitavastatin therapy compared with atorvastatin more prevents cardiovascular events in hypercholesterolemic patients with one or more risk factors for atherosclerotic diseases despite similar effects on LDLC levels. Moreover, clinical trials performed in Europe and Japan so far have not shown adverse effect of pitavastatin on glucose metabolism. In this presentation, the role of pitavastatin in management of diabetic dyslipidaemia patients with special emphasis on Asian population will be discussed.

SS8

From CVOTs to practice: focused on GLP-1 receptor agonists

Sin Gon Kim

Korea University, Korea

In terms of design of cardiovascular outcome trials (CVOTs), there are limitations, such as the lack of generalisability (i.e. participants often are at high risk for a CV event or death to provide an adequate number of events) and relatively short term periods for assessing potential harms or benefits. Therefore, recent CVOTs cannot be entirely representative of the general population, and the findings of such trials can be extrapolated to a wider population only with considerable caution.

CVOTs of GLP-1 receptor agonists (RA) vary in their sizes, designs, and patient populations, of which seven including ELIXA, LEADER, SUSTAIN-6, EXSCEL, Harmony, REWIND and PIONEER-6 have reported outcomes. Among them, REWIND was more representative of the population of patients with T2DM than other GLP-1 RA CVOTs. At baseline, only 3114 (31.5%) had established CVD, whereas 6787 (68.5%) had CV risk factors. In addition, the high proportion of women (46.3%) was included in this trial and baseline HbA1c level was just 7.3% close to real practice.

Despite the low proportion of patients with established CVD, REWIND reduced the relative risk of 3-points MACE by 12% (HR 0.88, 95% CI [0.79, 0.99]; P=0.026) over a median follow-up of 5.4 years with the primary outcome occurring in 594 (12.0%) and 663 (13.4%) patients in the dulaglutide and placebo arms, respectively. As a result, in 2020, dulaglutide became the first agent in the US with a label indication to reduce the risk of MACE in adults with T2DM who have established CVD or multiple CV risk factors.

In this lecture, I will summarize the recent CVOTs of GLP-1 RA and evaluate the value of REWIND trial in clinical practice.

SS9

Advanced clinical outcomes on 24hr glucose control-based on EVERGREEN study

Gyuri Kim

Sungkyunkwan University, Korea

The importance of glycemic variability is emphasized to reduce diabetic complications by diabetes guideline as continuous glucose monitoring system (CGMS) develops. Dipeptidyl peptidase-4 (DPP-4) inhibitors have shown to be associated with less fluctuation in blood glucose levels in both hypoglycemic and hyperglycemic status in a glucose-dependent manner. There were several studies to investigate the clinical efficacy of glycemic

variability in the treatment of type 2 diabetes mellitus (T2DM) but these studies had a relatively short follow-up duration and a small number of participants.

In this session, we will talk about the efficacy and safety of Evogliptin compared to Linagliptin, comparing changes in HbA1c and CGM parameters for 12 weeks and extension period of 12 weeks in inadequately controlled patients with T2DM.

SS10

See the unseen: SGLT2 inhibitor's glucose control with renal benefit in T2DM

Eunjung Rhee

Sungkyunkwan University, Korea

Sodium-glucose co-transporter 2 inhibitor(SGLT2i) is a novel class of anti-diabetic drug that binds to SGLT2 in S3 segment of renal proximal tubule and inhibits reabsorption of glucose to circulation. Expression of SGLT2 is known to be increased in kidney of patients with typ2 diabetes mellitus. SGLT2i is a good glucose-lowering strategy for halting the vicious cycle of glucotoxicity in patients with type 2 diabetes mellitus. The results from recent clinical trials of SGLT2i show significant effects on cardioprotection and renoprotection of this drug in patients with type 2 diabetes. Recent guidelines adapted these results and suggested a new paradigm for the selection of anti-diabetic drugs next to metformin for the patients with or without cardiovascular disease and chronic kidney disease. In this talk, I would like to review the recent results of the effects of SGLT2i on heart and kidney in patients with type 2 diabetes mellitus.

SS11

Get the time in range: review of clinical evidence on the use of CGMs

Jong Chul Won

Inje University, Korea

The three factors in diabetes management are decreased glycated hemoglobin (HbA1c), decreased glucose variability, and avoid or minimize hypoglycemia. In addition, Time In Range (TIR) was announced at the 2019 International consensus an important indicator of diabetes monitoring. TIR refers to the portion of time spent in the appropriate glucose range for 24-hour period. Even if the level of HbA1c, which is the average blood sugar for 3 months, may be the same, the TIR may vary. TIR can be checked through Continuous Glucose Monitoring (CGM) and Ambulatory Glucose Profile (AGP) reports showing changes in glucose level over a 24-hour period. The effectiveness obtained by using FreeStyle Libre for diabetes management has been proven through several clinical trials. Representatively, through the IMPACT study in type 1 diabetes patients and the REPLACE study in type 2 diabetes patients, it was confirmed that the use of FreeStyle Libre increases the number of blood glucose measurements, TIR, and decreases the time of hypoglycemia. In addition to the RCT study, in the Real-World study, the group using FreeStyle Libre showed a significant decrease in HbA1c compared to the control group, and the patient's satisfaction was higher.

VOD1

B vitamin intake and diabetes risk: a 30-year prospective follow-up study

Ka Kahe

Columbia University, USA

To prospectively examine intakes of folate, vitamin B6, and vitamin B12 in relation to diabetes incidence in a large U.S. cohort.

A total of 4,704 American adults aged 18-30 years and without diabetes were enrolled in 1985-1986 and monitored until 2015-2016 in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Dietary assessment was conducted by a validated dietary-history questionnaire at baseline, in 1992-1993, and in 2005-2006. The cumulative average intakes of folate, vitamin B6, and vitamin B12 were used in the analyses. Incident diabetes was ascertained by plasma glucose levels, oral glucose tolerance tests, hemoglobin A1c concentrations, and/or antidiabetic medications.

During 30 years (mean 20.5 ± 8.9) of follow-up, 655 incident cases of diabetes occurred. Intake of folate, but not vitamin B6 or vitamin B12, was inversely associated with diabetes incidence after adjustment for potential confounders. Compared with the lowest quintile of total folate intake, the multivariable-adjusted hazard ratios (95% CI) in quintile 2-5 were 0.85 (0.67-1.08), 0.78 (0.60-1.02), 0.82 (0.62-1.09), and 0.70 (0.51-0.97; P trend = 0.02). Higher folate intake was also associated with lower plasma homocysteine (P trend < 0.01) and insulin (P trend < 0.01). Among supplement users, folate intake was inversely associated with serum C-reactive protein levels (P trend < 0.01).

Intake of folate in young adulthood was inversely associated with diabetes incidence in midlife among Americans. The observed association may be partially explained by mechanisms related to homocysteine level, insulin sensitivity, and systemic inflammation.

VOD2

Using registries to describe disease phenotypes and prognosis in people with young-onset diabetes

Andrea Luk

The Chinese University of Hong Kong, Hong Kong

The Hong Kong Diabetes Register (HKDR) was established in 1994 at the Prince of Wales Hospital, Hong Kong, as part of a quality improvement initiative in which people with diabetes underwent a structured assessment of their metabolic control and diabetes-related complications. The web-based Joint Asia Diabetes Evaluation (JADE) programme is an extension of the HKDR protocol and include a standardised template to guide clinical assessment implemented in 11 regions in Asia since 2007. The HKDR has accrued over 23,000 people with diabetes followed prospectively for development of major clinical events and the JADE database includes 100,000 people with comprehensive disease characterisation. Recently, the data bank containing electronic medical records of the 7.3 million Hong Kong residents attending public healthcare services is made available externally for research and from this data repository, 800,000 people with diabetes have been identified. Using these databases, we reported the Asian diabetes phenotype characterised by low body mass index and young age of diabetes onset. Up to one in five people with diabetes were diagnosed before the age of 40 years. People with young-onset diabetes have higher lifetime risks of diabetes-related complications and consume more healthcare resources than their usual-onset counterparts. We estimated that a person with young-onset diabetes will spend approximately 100 days in hospital by the age of 75 years. Furthermore, the life expectancy of a person with diabetes at the age of 40 years is shortened by 7-8 years. Whilst mortality rates have declined for most people with diabetes, improvements were not observed in the young. The challenge in the management of young-onset diabetes is compounded by the heterogeneity in the underlying cause and clinical phenotypes. Treatment algorithms incorporating genetic and clinical biomarkers to guide drug therapy in young people are desirable but this will require vigorous evaluation in well-executed clinical trials. There are windows of opportunity to intervene early in the clinical trajectory of people with young-onset diabetes who are most likely to benefit from metabolic legacy.

VOD3-1

Oral hypoglycemic agents: how to combine them

Sung Hwan Suh

Dong-A University, Korea

Type 2 diabetes mellitus (T2DM) is caused by both decreased secretion of insulin and insulin sensitivity. Thus, a therapeutic approach targeted toward the diverse pathogenesis of T2DM leads to successful glycemic control. Insulin injection is the most effective treatment available for managing hyperglycemia. However, despite the advantages of insulin therapy, poor adherence is a big challenge for both the physician and patients. Metformin should be started at the time T2DM is diagnosed unless there are contraindications. Because T2DM is a progressive disease in many patients, maintenance of glycemic targets with monotherapy is often possible for only a few years, after which combination therapy is necessary. In addition, if the HbA1c target is not achieved after approximately 3 months, you should consider a combination of metformin or proceed to multiple-drug combination. Several new oral hypoglycemic agents (OHAs) have been developed over the past decades, and unlike the conventional drugs, they have unique mechanisms of action that are targeted toward a specific organ. In addition, most clinical studies have reported that the synergy of combination therapy is more efficacious and safer than monotherapy. In this lecture, we will discuss the pharmacokinetics, pharmacodynamics and safety profiles of currently available OHAs for patients with T2DM.

VOD3-2

Recent insulin and non-insulin injectables: how did they change our practice?

Hae Jin Kim

Ajou University, Korea

Many patients with type 2 diabetes mellitus (T2DM) eventually require and benefit from insulin therapy. Basal insulin alone is the most convenient initial insulin regimen, beginning at 10 units per day or 0.1-0.2 units/kg/day, depending on the degree of hyperglycemia. Longer-acting basal analogs (U-300 glargine or degludec) may provide stable glycemic control and are associated with a reduced risk of hypoglycemia compared with previous-generation basal insulin analogs (U-100 glargine and detemir). If basal insulin has been titrated to an acceptable fasting blood glucose level and A1C remains above target, we can consider advancing to combination injectable therapy. The combination of basal insulin with a GLP-1 receptor agonist (GLP-1 RA) is increasing in popularity because these pharmacologic actions complement one another. Other options for treatment intensification include stepwise additional injections of prandial insulin or stopping the basal insulin and initiating a premixed insulin twice daily. Each approach has its advantages and disadvantages.

GLP-1 RAs have robust A1C lowering properties, and are usually associated with weight loss and lipid and BP reductions. The risk of hypoglycemia with GLP-1 receptor agonists is low, and they reduce fluctuations in both fasting and postprandial glucose levels by stimulating glucose-dependent insulin secretion and suppressing glucagon secretion. Especially, the GLP-1 RAs with proven CV benefits should be considered in T2DM patients with established CVD. Recent guidelines recommend that GLP-1 RAs are the preferred choice to insulin for most patients with T2DM who fail to achieve the glycemic target with oral antihyperglycemic agents. The most common side effects of GLP-1 RAs are nausea, vomiting, and diarrhea, though these tend to diminish over time.

VOD3-3

Diabetic microvascular complications: how to diagnose and manage them?

Mikyung Kim

Keimyung University, Korea

Diabetes mellitus (DM) is a serious, chronic, and progressive disease. Diabetic patients suffer from increased risks for many debilitating and life-threatening health conditions, including cardiovascular disease, blindness, kidney failure, and lower-limb amputation. Approximately 415 million adults have diabetes and an estimated 642 million adults will be diagnosed with diabetes by 2040. Therefore, DM is considered to be one of the global health emergencies.

Abstracts

The goals of treatment for diabetes are to eliminate symptoms related to hyperglycemia and reduce the long term complications of DM. Chronic complications associated with hyperglycemia include microvascular and/or macrovascular complications. Microvascular complications include eye disease, neuropathy, and nephropathy; macrovascular complications include coronary heart disease, peripheral arterial disease, and cerebrovascular disease. Many large clinical studies show intensive glucose control therapies can reduce microvascular complications. For the prevention of chronic complications, patients should be assessed whether they have these complications or risk factors and should be treated for them. This session will discuss how to screen microvascular complications and manage risk factors to delay them.

VOD3-4
Diabetic macrovascular complications: where do we stand now?
So Hun Kim

Inha University, Korea

Macrovascular complications are atherosclerotic cardiovascular diseases (ASCVD) that are the main cause of morbidity and mortality in patients with diabetes. People with diabetes have an increased risk of heart attacks, heart failure and sudden death. Research have shown the benefits of reducing the modifiable risk factors for atherosclerosis. Modifiable risk factors include dyslipidemia, smoking, high blood pressure, diabetes, central obesity and physical activity. Current management focuses on lifestyle intervention, antihypertensive therapy, control of LDL cholesterol, and antiplatelet therapy. Recent cardiovascular outcome trials have shown benefits of SGLT2 inhibitors and GLP-1 receptor agonists in patients with type 2 diabetes and established cardiovascular disease or those with high cardiovascular risk. Current treatment strategies for prevention and management of cardiovascular disease in diabetes will be reviewed.

VOD3-5
Glycemic variability: how can we avoid it?
Eunjung Rhee

Sungkyunkwan University, Korea

Glycemic variability is considered as the fourth component of glycemic control, next to fasting, postprandial glucose and HbA1c. The importance of glycemic variability has been emphasized since the development of incretin therapy and continuous glucose monitoring system (CGMS). Recent studies obtained from CGMS usage show close relations between glycemic fluctuation and oxidative stress in humans. Postprandial glycemic spike strike the endothelial wall and increased the oxidative stress in the vessels. Recent studies show that increased mean amplitude of glycemic excursion (MAGE), which is a marker of glycemic variability, may predict future cardiovascular events in those who were admitted to hospital due to acute myocardial infarction. Therefore, it is time to measure and try to reduce glycemic variability to prevent cardiovascular complication in patients with diabetes. In this talk, I would like to introduction recent concepts of glycemic variability and its relationship with diabetic complications. In addition, I will introduce currently available CGMS and artificial pancreas, for the future.

VOD4-1
Cardiovascular disease in women with diabetes: epidemiologic perspectives in Korea
Hyejin Lee

Ewha Womans University, Korea

Cardiovascular disease (CVD) is the leading cause of death in both men and women. Although age-standardized rates of CVD are substantially higher in men than women, CVD is the leading cause of morbidity and mortality in women worldwide.
Reports from recent studies suggest that diabetes confers a higher risk of CVD in women compared to men. Diabetes increase the risk of CVD by three to four times in women and two to three times in men, after adjusting for other risk factors. Although nondiabetic women have fewer cardiovascular events than nondiabetic men of the same age, this advantage appears to be lost in the context of diabetes. Unfortunately, there appears to be a heavy risk-factor burden in women with diabetes, and younger women appear especially sensitive to CVD risk factors. In addition, there are risk factors that are specific to women, including gestational diabetes mellitus and polycystic ovarian syndrome, which affect CVD risk.
I describe the differences in CVD in men and women, and possible mechanisms for increased cardiovascular risk associated with diabetes in women. Furthermore, I present CVD epidemics in Korean diabetic women with National Sample Cohort database released from the Korean National Health Insurance Service.

VOD4-2
CVD risk in women of reproductive age; focusing on polycystic ovary syndrome
Bulent Yildiz

Hacettepe University, Turkey

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age affecting up to one in five women. The syndrome is characterized by androgen excess, ovulatory dysfunction and polycystic ovarian morphology (PCOM). The manifestations of the syndrome are heterogenous but commonly includes irregular menstrual cycles, infertility, and clinical signs of androgen excess such as hirsutism and acne. Beyond reproductive and dermatologic features, PCOS is a life-long condition associated with cardiometabolic dysfunction which may confer an increased risk for cardiovascular disease later in life. However, longitudinal studies of well-defined cohorts are limited. Currently available international guidelines recommend assessment and monitoring of cardiovascular risk in comprehensive clinical care of women with PCOS.

VOD4-3
Management of cardiovascular risk in peri and postmenopausal women with diabetes
Catherine Kim

University of Michigan, USA

TBD

VOD5-1
Adipose tissue progenitor cells & fat tissue development
Patrick Seale

University of Pennsylvania, USA

Our research program focuses on the development and remodeling of adipose tissues. Impaired adipocyte differentiation leads to insulin resistance, whereas promoting adipocyte differentiation ameliorates obesity pathogenesis. Our lab has utilized single cell gene expression analyses to identify and profile different types of progenitor cells in adipose tissues. In subcutaneous white fat tissue, we identified a population of mesenchymal progenitor cells marked by DPP4 expression that are highly proliferative and possess multi-lineage differentiation capacity. DPP4+ cells reside mainly within a fluid-filled connective tissue layer called the reticular interstitium that envelops adipose tissue lobes. DPP4+ interstitial progenitor cells (IPCs) have the potential to give rise to committed preadipocyte cells, marked by expression of ICAM1 and Pparg. In addition to serving as a reservoir of new adipocytes, we posit that DPP4+ interstitial progenitor cells (IPCs) contribute to tissue fibrosis under pathologic conditions. More recent studies in our lab have focused on the development of brown adipose tissue (BAT) depots, including the perivascular adipose tissue (PVAT). These studies have identified two distinct types of brown adipocyte progenitor cells: fibroblasts and smooth muscle cells. Ongoing studies are focused on understanding the molecular pathways that control adipogenic commitment and differentiation of these progenitor cells under various conditions.

VOD5-2

Molecular control of de novo adipogenesis in obesity

Rana K Gupta

University of Texas Southwestern, USA

The activation of de novo adipocyte differentiation, or "adipogenesis," in the setting of caloric excess is a protective mechanism to ensure safe energy storage in white adipose tissue (WAT) and prevent against ectopic lipid accumulation and insulin resistance. Highly committed adult adipocyte precursor cells (APCs) reside within the adipose tissue vasculature as a specialized subset of PDGFRβ+ mural cells. In adulthood, APCs undergo adipogenesis in a WAT-depot specific manner; however, the mechanisms underlying regional variation in APCs activity in obesity remain unknown. Here, we reveal that HIF1α-induced PDGFRβ signaling within WAT PDGFRβ+ cells drives inhibitory serine 112 (S112) phosphorylation of PPARγ, the master regulator of adipogenesis. Levels of PPARγ S112 phosphorylation in WAT PDGFRβ+ cells are regulated in a depot-dependent manner, with levels of PPARγ S112 phosphorylation in PDGFRβ+ cells inversely correlating with their capacity for adipogenesis upon high fat diet feeding. HIF1α suppression in PDGFRβ+ progenitors promotes subcutaneous and intra-abdominal adipogenesis, healthy WAT remodeling, and improved metabolic health in obesity. These metabolic benefits are mimicked by treatment of obese mice with the PDGFR antagonist, Imatinib, which promotes adipocyte hyperplasia and glucose tolerance in a progenitor cell PPARγ-dependent manner. Our studies unveil a mechanism underlying depot-specific responses of APCs to caloric excess, and highlight the potential for APCs to be targeted pharmacologically to improve metabolic health in obesity.

VOD5-3

The cellular and functional heterogeneity of thermogenic fat

Shingo Kajimura

Harvard University, USA

I will discuss our recent study on beige adipocyte progenitors.

VOD6-1

Advances in the pathogenesis and diagnosis of diabetic neuropathy

Rayaz A. Malik

Weill Cornell Medicine, Qatar

Both metabolic and microvascular mechanisms play an important role in the pathogenesis of human diabetic neuropathy. There is increasing evidence for the role of lipids and inflammation. Clinical trials have on the whole failed to show benefits in patients with diabetic neuropathy. Even improved glucose control has shown that at best it prevents progression of DPN in T1DM and has no impact in T2DM. There are small studies showing a benefit with blood pressure and lipid lowering therapies as well as after weight loss with bariatric surgery on DPN. The current approach to the diagnosis of diabetic neuropathy is flawed. The focus is on symptoms and the simple, but inadequate assessment of neurological deficits using loss of vibration sensation and monofilament testing. There are currently no FDA approved treatments and we have the enviable record of 100% failure rate in clinical trials of diabetic neuropathy. The focus of diagnostic and clinical trial endpoints is on the large fibres, instead of the more abundant and clinically relevant small fibers, which mediate pain, tissue blood flow and inflammation, all key to the genesis of foot ulceration. The assessment of small fibres has mainly relied on thermal thresholds, but they are not commonly available and lack sensitivity for detecting repair. Sudomotor dysfunction is an important measure which has relevance to foot ulceration; but is again not commonly assessed. Skin biopsy is a potential alternative for imaging small fibers and has been advocated as an end point for trials of diabetic neuropathy. However, it is an invasive and time-consuming technique, which requires laboratory expertise. However, several recent trials deploying IENFD have failed. We have pioneered the novel ophthalmic technique of corneal confocal microscopy (CCM) that allows a rapid, non-invasive means to identify early sub-clinical small fibre damage, even in subjects with IGT and predicts the development of diabetic neuropathy, foot ulceration and Charcot. It also shows an improvement in corneal nerve morphology following pancreas and kidney transplantation, multiple risk factor intervention and ARA290, a first in class erythropoietin analogue.

VOD6-2

Diabetic neuropathy: perception beyond the seam of the periphery

Solomon Tesfaye

University of Sheffield, UK

Diabetic peripheral neuropathy (DPN) is a common, debilitating and distressing complication of diabetes. Most patients develop painless, insensate distal nerve damage which increases the risk of foot ulceration and subsequent amputation. Amputation is not only devastating in its impact on the person with diabetes and their family, leading to loss of independence and livelihood; it is also very expensive in material terms and results in only 50% surviving for two years. Around a quarter of all diabetic patients also develop a chronic painful condition mainly affecting the legs which can result in considerable disability and suffering. Many such patients with painful DPN have depression, anxiety, fear and stress, and do not sleep well. There is thus an urgent need to detect DPN early by using objective, validated point-of-care devices as clinical exam or the use of the 10 gram monofilament is not reliable. Early detection will lead to an earlier intervention to reduce risk factors for the development of DPN.

There has also been emerging evidence that DPN may not be as its name suggest, and may involve the central nervous system. We have reported the involvement of the spinal cord in DPN on MRI. More recently we have reported the involvement of the brain in DPN by demonstrating: 1) thalamic neuronal dysfunction using MR Spectroscopy, 2) increased thalamic vascularity in painful DPN on MR perfusion imaging and disruption of the resting state network connectivity on functional MRI. If we are able to develop non-invasive, objective biomarkers of painful DPN this would be a great advance as it would serve as a target for the development of new drugs for this distressing condition. The symptomatic management of painful DPN continues to pose considerable challenge to clinicians as less than 50% of patients respond to current drugs. Innovative, head-to-head and combination trials of new and existing drugs are required. We have obtained $4.8 m funding from the UK NIHR to conduct such a trial. Finally, there is early evidence that a patient's pain phenotype may determine response to treatment although further studies are required.

VOD7-1

CD38 inhibition decreased renal oxidative stress in diabetic kidney disease by restoring of Sirt3 activation

Daisuke Koya

Kanazawa University, Japan

Mitochondrial oxidative stress is a significant contributor to the pathogenesis of diabetic kidney disease (DKD). We previously showed that mitochondrial oxidative stress in the kidneys of Zucker diabetic fatty rats is associated with a decreased intracellular NAD+/NADH ratio and NAD+-dependent deacetylase Sirt3 activity, and increased expression of the NAD+-degrading enzyme CD38. In this study, we used a CD38 inhibitor, apigenin, to investigate the role of CD38 in DKD. Apigenin significantly reduced renal injuries, including tubulointerstitial fibrosis, tubular cell damage, and pro-inflammatory gene expression in diabetic rats. In addition, apigenin down-regulated CD38 expression, and increased the intracellular NAD+/NADH ratio and Sirt3-mediated mitochondrial antioxidative enzyme activity in the kidneys of diabetic rats. In vitro, inhibition of CD38 activity by apigenin or CD38 knockdown increased the NAD+/NADH ratio and Sirt3 activity in renal proximal tubular HK-2 cells cultured under high-glucose conditions. Together, these results demonstrate that by inhibiting the Sirt3 activity and increasing mitochondrial oxidative stress in renal tubular cells, CD38 plays a crucial role in the pathogenesis of DKD.

VOD7-2

Lipid-related mitochondrial dysfunction in diabetic kidney diseases

Alessia Fornoni

University of Miami, USA

Fibroblasts from patients with Tangier disease carrying ATP-binding cassette A1 (ABCA1) loss-of-function mutations are characterized by cardiolipin accumulation, a mitochondrial-specific phospholipid. Suppression of ABCA1 expression occurs in glomeruli from patients with diabetic kidney

disease (DKD) and in human podocytes exposed to DKD sera collected prior to the development of DKD. We demonstrated that siRNA ABCA1 knockdown in podocytes led to reduced oxygen consumption capabilities associated with alterations in the oxidative phosphorylation (OXPHOS) complexes and with cardiolipin accumulation. Podocyte-specific deletion of Abca1 (Abca1fl/fl) rendered mice susceptible to DKD, and pharmacological induction of ABCA1 improved established DKD. This was not mediated by free cholesterol, as genetic deletion of sterol-o-acyltransferase-1 (SOAT1) in Abca1fl/fl mice was sufficient to cause free cholesterol accumulation but did not cause glomerular injury. Instead, cardiolipin mediates ABCA1-dependent susceptibility to podocyte injury, as inhibition of cardiolipin peroxidation with elamipretide improved DKD in vivo and prevented ABCA1-dependent podocyte injury in vitro and in vivo. Collectively, we describe a pathway definitively linking ABCA1 deficiency to cardiolipin-driven mitochondrial dysfunction. We demonstrated that this pathway is relevant to DKD and that ABCA1 inducers or inhibitors of cardiolipin peroxidation may each represent therapeutic strategies for the treatment of established DKD.

VOD7-3

Mitochondrial quality and lipid metabolism

Quan Chen

Nankai University, China

Mitophagy is a cellular process that selectively removes damaged mitochondria via autophagy. It is essential for mitochondrial quality control and is suggested to play a role in metabolic homeostasis. We have previously characterized that FUNDC1 is a mitophagy receptor that mediates mitophagy via its direct interaction with LC3. We further addressed the potential role of defective mitophagy in the pathogenesis of metabolic disorders. Mice with germline knockout of Fundc1 resulted in defective mitophagy in white adipose tissue (WAT) and developed more severe obesity and insulin resistance due to the hyperactivation of MAPK/JNK when fed a high-fat diet (HFD). Interestingly, mice with skeletal-muscle-specific ablation of FUNDC1 were protected against high-fat-diet-induced obesity with improved systemic insulin sensitivity and glucose tolerance. Skeletal-muscle-specific ablation of FUNDC1 in mice caused decreased muscle fat utilization and endurance capacity during exercise. FUNDC1 deficiency in muscle elicited a retrograde response in muscle that upregulated FGF21 expression, thereby promoting the thermogenic remodeling of adipose tissue. We recently found that saturated fatty acids, but not unsaturated ones, can directly impact on FUNDC1 dependent mitophagy and impairs mitochondrial quality. Thus, these findings reveal FUNDC1-dependent mitophagy regulates cellular and systemic metabolism.

VOD8-1

Single cell approaches to understand and improve functional maturation of stem cell derived ß-cells

Francis Lynn

University of British Columbia, Canada

Differentiated human embryonic stem cells hold great promise in the treatment of diabetes; however, most current approaches for generating ß-cells result in cells with blunted function. Using single cell RNA sequencing we have defined genes that are important for beta cell differentiation and maturation and have used this information to guide new approaches for deriving more functional ß-cells. My talk will highlight some recent advances we have made towards understanding and improving the functional maturation of stem cell-derived ß-cells.

VOD8-2

Identify pancreatic islets resident progenitors

Yi Arial Zeng

Chinese Academy of Sciences, China

It has generally proven challenging to produce functional β cells in vitro. Here, we describe a novel Procr+ cell population in adult mouse pancreas through scRNAseq. The cells reside in islets, do not express differen-

tiation markers and feature epithelial-to-mesenchymal transition (EMT) characteristics. By genetic lineage tracing, Procr+ islet cells undergo clonal expansion and generate all four endocrine cell types during adult homeostasis. Sorted Procr+ cells, representing ~1% of islet cells, can robustly form islet-like organoids when cultured at clonal density. Exponential expansion can be maintained over long time periods by serial passaging, while differentiation can be induced at any time point in culture. β cells dominate in differentiated islet organoids, while α, δ and PP cells occur at lower frequencies. The organoids are glucose-responsive and insulin-secreting. Upon transplantation in diabetic mice, the organoids reverse disease. These findings demonstrate that the adult pancreatic islet contains a population of Procr+ endocrine progenitors.

VOD8-3

Lineage dynamics of pancreatic development at single-cell resolution

Julie Sneddon

University of California, San Francisco, USA

The mammalian pancreas arises through a series of coordinated events, including specification, proliferation, differentiation, and maturation. Despite substantial progress in understanding some of the signaling events underlying these processes, a global view of the timing and dynamics of these processes in the developing human pancreas was not previously possible. We have constructed a transcriptional atlas of the developing pancreas that serves as a guidebook for endocrine development, identifying novel intermediate progenitor states and lineage relationships, and characterizing cellular dynamics across developmental time. Application of a novel clustering algorithm has enabled our identification of multiple distinct endocrine progenitor populations in the developing human pancreas. In addition, lineage reconstruction analysis has led to new insights about divergences between the process of beta cell specification in mouse vs. human tissue. We have further identified candidate transcriptional regulators mediating progression along the differentiation trajectory towards the beta cell lineage. Lastly, we have integrated genome editing techniques into a stepwise differentiation platform for generating beta cells from human pluripotent stem cells (hPSCs), thereby establishing a platform for interrogating the function of putative transcriptional regulators of human endocrine cell fate identified in our study. In summary, these studies have revealed heretofore unknown pre-beta cell progenitor states in the developing human pancreas. In addition to contributing to our knowledge about the basic developmental biology of this organ, this work will also provide important clues as to which cellular states should be recapitulated in vitro in directed differentiation experiments aimed at generating truly bona fide beta cells from hPSCs for patients with diabetes.

VOD8-4

Engineering gastric tissues for insulin production

Joe Q. Zhou

Cornell University, USA

Autologous tissue regeneration and repair can be enabled by direct reprogramming of adult cells in the body, a technology with potential wide applications in regenerative medicine. My laboratory has been developing direct reprogramming approaches to produce insulin-secreting cells for autologous cell therapy to treat diabetes. Using a set of defined beta-cell developmental master regulators, we carried out an in vivo genetic screen in mouse and made the surprising discovery that epithelial cells of the antral stomach are particularly amenable for direct conversion to insulin+ cells. The induced murine gastric insulin+ cells have molecular and functional hallmarks of pancreatic beta cells, can secrete insulin in response to high glucose, and suppress hyperglycemia in an experimental form of diabetes. Human antral gastric tissues can be obtained from individual patients through routine biopsy. We developed a method to culture biopsy-derived human gastric stem cells as flat colonies and massively expand them into billions of cells. Using sequential expression of genetic factors and chemical compound treatment, cultured human GI stem cells can be induced to develop into insulin+ cells, form islet-like aggregates, and secrete insulin upon glucose challenge. The aggregates can be grafted into mouse hosts and secret insulin for long periods of time. With these studies, we aim to develop a new approach with which personalized insulin+ cells can be produced in large numbers and used in cell therapy for diabetes,

and in particular, Type 1 Diabetes.

Main symposia

Research group and commitee sesions

Special and award session

Corporate symposia

Video on demand session

Oral presentations

Poster exhibitions

Oral presentations

Role of Mig-6 as a regulator of Energy Homeostasis in brown adipocyte through modulating thermogenesis

Sorim Choung[1,2]*, Ji Min Kim[2], Kyong Hye Joung[2], Hyun Jin Kim[2], Bon Jeong Ku[1,2]

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Objective: Due to special ability to dissipate energy as heat, BAT has a therapeutic potential to combat obesity, diabetes and metabolic syndrome. Mitogen-inducible gene 6 (Mig-6) is a negative regulator of the EGFR signal. Mig-6 is known as a tumor suppressor gene. Recently, Mig-6 has an important role in the regulation of cholesterol homeostasis and lipid metabolism in the liver. In previous study, the association between EGFR signaling and metabolic disorder such as NAFLD. However, the roles of Mig-6 in BAT remain poorly understood. In the present study, we investigated the metabolic role of Mig-6 in BAT.

Methods: Immortalize brown adipocytes were transfected siRNA targeting Mig-6 after differentiation. We generated mice specifically enhancing Mig-6 in BAT using a genetic strategy based on the Cre-ROSA recombination. We fed normal chow or high fat to KI mice for 12 weeks. Body weights and food intake were observed weekly. We conducted GTT and ITT. KI mice were measured energy expenditure by using indirect calorimetry system. Tissues staining was performed. Biochemical parameters was measured using mice serum. Western blot and quantitative polymerase chain reaction (Q-PCR) performed to analyze related genes.

Results: Here we showed that the inhibition of Mig-6 decreases the expression of thermogenesis relative genes, UCP1 and Elovl3, in the BAT cell. Mig-6 KI mice showed better metabolic phenotypes, including improved glucose tolerance and reduction of body weight. In the accelerated obese condition, transgenic mice induced the improvement of glucose tolerance, fasting glucose level and lipid levels. Importantly, Mig-6 up-regulated the expression of thermogenesis relative genes (UPC1, Pgclα, Cieda, PPARα, Elovl3), consistent with the increased UCP1 in the BAT of mice. Mig-6 KI mice on HFD improved insulin sensitivity, glucose tolerance and energy metabolism.

Conclusion: These results together suggest that Mig-6 acts as potential factor improving obesity by regulating thermogenesis in the BAT.

C1q/TNF-related protein-9 attenuates palmitic acid-induced endothelial cell senescence via increasing autophagy

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Asan Medical Center, Internal Medicine[1], Yonsei University Wonju College of Medicine, Internal Medicine[2], Hallym University Sacred Heart Hospital, Internal Medicine[3], Asan Institute of Life Science, Endocrinology and Metabolism[4]

Objective: Autophagy is an important process in the pathogenesis of atherosclerosis. C1q/tumor necrosis factor-related protein 9 (CTRP9) is the closest adiponectin paralog. CTRP9 has purported anti-aging and anti-atherogenic effects, but its roles in autophagy and endothelial senescence are unknown. The aim of this study was to evaluate whether CTRP9 prevents palmitic acid (PA)- induced endothelial senescence by promoting autophagy.

Methods: After no treatment or pre-treatment of human umbilical vein endothelial cells with CTRP9 prior to PA treatment, the level of senescence was measured by senescence associated acidic β- galactosidase staining and the level of hyperphosphorylated pRB protein. Autophagy was evaluated by LC3 conversion and the level of p62/SQSTM1, a protein degraded during autophagy. Autophagosome- lysosome fusion was detected by fluorescence microscopy.

Results: Pre-treatment with CTRP9 attenuated PA- induced endothelial senescence. CTRP9 increased the conversion of LC3-I to LC3-II, and decreased the level of p62 in time- and dose- dependent manners. Although both CTRP9 and PA treatment increased the LC3 conversion, treatment of PA increased p62 and decreased the fusion of autophagosomes and lysosomes, which represented decreased autophagic flux. However, pre- treatment with CTRP9 recovered the autophagic flux inhibited by PA. AMP- activated kinase (AMPK) activation was involved in LC3 conversion and decreased p62 induced by CTRP9.

Conclusion: CTRP9 inhibits PA- induced endothelial senescence by recovering autophagy and autophagic flux through AMPK activation.

Gut-derived serotonin regulates hepatic steatosis and ER stress in alcoholic liver disease

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KAIST, GSMSE[1], NIH, Division of metabolic disease[2]

Objective: Serotonin (5-hydroxytryptamine (5-HT)) is a monoamine neurotransmitter that has various functions in central and peripheral tissues. Upon high-fat diet (HFD), gut-derived serotonin (GDS) synthesized by enterochromaffin cells has been reported to travel to the liver through portal vein and regulate hepatic steatosis via serotonin receptor 2A (HTR2A) signaling. However, the role of GDS in alcoholic liver disease remains to be elucidated.

Methods: To examine the role of GDS and hepatic HTR2A signaling in alcoholic liver disease, both gut-specific Tph1 knockout (Tph1 GKO) and liver-specific Htr2a knockout (Htr2a LKO) mice were fed a Lieber-DeCarli diet containing 5% ethanol for 4 weeks. Then, liver tissues were examined by histological analysis, triglyceride quantification, western blot, and quantitative PCR.

Results: we demonstrate that inhibition of GDS synthesis ameliorates alcoholic liver disease through the reduction in HTR2A signaling. Plasma serotonin concentrations were increased in both ethanol-fed mice and human with alcoholic liver disease. Gut-specific Tph1 knockout (Tph1 GKO) mice fed a Lieber-DeCarli diet containing 5% ethanol for 4 weeks exhibited improved steatosis and decreased expression of genes involved in lipogenic pathway. Also, liver-specific Htr2a knockout (Htr2a LKO) mice phenocopied Tph1 GKO mice. Moreover, endoplasmic reticulum (ER) stress markers were decreased in both Tph1 GKO and Htr2a LKO mice.

Conclusion: Thus, these data suggest that GDS plays a crucial role in alcoholic liver disease and that inhibition of serotonin to HTR2A signaling can afford attractive approach to treat alcoholic liver disease.

The role of serotonin signaling through HTR2A/2B in visceral adipose tissue

Won Gun Choi*, Seung Yeon Lee, Inseon Hwang, Wonsuk Choi, Jueun Kim, Hwajin Kim, Hail Kim

KAIST, GSMSE

Objective: Serotonin (5-hydroxytryptamine, 5-HT) is a bioamine and has diverse functions. 5-HT plays a distinct role depending on whether it is synthesized in the brain or in the periphery. Recent studies demonstrated that peripheral 5-HT has a significant role in regulation of systemic energy homeostasis. It induces lipid accumulation in liver and inhibits the UCP1 dependent thermogenesis in brown adipose tissue. However, it has not been completely elucidated how 5-HT influences visceral white adipose tissue dysfunction although visceral white adipose tissue is a major player in the development of obesity-related insulin resistance.

Methods: Htr2b flox/flox mice were crossed with Adiponectin-Cre mice to generate adipose tissue-specific Htr2b knockout (Htr2b FKO). At 12 weeks of age, mice were fed a standard chow diet (SCD), high- fat diet (HFD, 60% fat calories).

Results: In this study, we found that the expression of Htr2a and Htr2b were increased in visceral adipose tissue upon high fat diet (HFD) feeding. Additionally, both adipocyte specific Htr2a knockout mice and adipocyte specific Htr2b knockout mice showed improved insulin sensitivity, attenuated hepatic steatosis, inflammation and adipocytes hypertrophy. Most of all, HTR2B promotes adipocyte lipolysis via phosphorylation of HSL in obesity. These data suggested that 5-HT signaling through HTR2A or HTR2B can play an important role in visceral adipose tissue dysfunction.

Conclusion: Therefore, unveiling the mechanism of 5-HT signaling through HTR2A/2B in adipose tissue can broaden our understanding of the pathophysiological insight in obesity.

OP05   Basic & Translational diabetes research

Growth differentiation factor 15 protects from aging-related systemic inflammation in humans and mice

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Objective: Mitochondrial dysfunction is associated with aging-mediated inflammatory responses, leading to metabolic deterioration, development of insulin resistance, and type 2 diabetes. Growth differentiation factor 15 (GDF15) is an important mitokine generated in response to mitochondrial stress and dysfunction, however, the implications of GDF15 to the aging process are poorly understood in mammals.

Methods: Bioinformatics analysis of the Innocenti et al. dataset and GTEx dataset was conducted. Hepatic and adipose immune cells from WT and GDF15 KO old (20-month-old) mice were analyzed using flow cytometry.

Results: In this study, we identified a link between mitochondrial stress-induced GDF15 production and protection from tissue inflammation on aging in humans and mice. We observed an increase in serum levels and hepatic expression of GDF15 as well as pro-inflammatory cytokines in elderly subjects. Circulating levels of cell-free mitochondrial DNA were significantly higher in elderly subjects with elevated serum levels of GDF15. In the BXD mouse reference population, mice with metabolic impairments and shorter survival were found to exhibit higher hepatic Gdf15 expression. Mendelian randomization links reduced GDF15 expression in human blood to increased body weight and inflammation. GDF15 deficiency promotes tissue inflammation by increasing the activation of resident immune cells in metabolic organs, such as in the liver and adipose tissues of 20-month-old mice. Aging also results in more severe liver injury and hepatic fat deposition in Gdf15-deficient mice. Although GDF15 is not required for Th17 cell differentiation and IL-17 production in Th17 cells, GDF15 contributes to regulatory T cell-mediated suppression of conventional T cell activation and inflammatory cytokines.

Conclusion: Taken together, these data reveal that GDF15 is indispensable for attenuating aging-mediated local and systemic inflammation, thereby maintaining glucose homeostasis and insulin sensitivity in humans and mice.

OP06   Basic & Translational diabetes research

DETECTION OF DIABETES MELITUS FOR WOMEN AND PREPARATION OF HEALTHY MENU USING THE ADAPTIVE NEURO FUZZY INFERENCE SYSTEM (ANFIS) AND GENETIC ALGORITHM (GA) APPROACHES

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Objective: This study aims to create a model for the preparation of a healthy food menu based on the number of calorie needs per day so that it meets the criteria for balanced nutrition and fulfills food variations in the form of staple foods, side dishes, vegetables, and fruit.

Methods: In this study, the Adaptive Neuro-Fuzzy Inference System (ANFIS) method and Genetic Algorithm (GA) are used to provide food serving recommendations that meet the type of menu and the number of portions ideal for DM sufferers. Pima Indian Diabetes dataset as data of diabetics. The Pima dataset was taken from the UCI Machine Learning Repository from the Institute of Diabetes and Digestive and Kidney Diseases in the United States, data taken from the Pima Indian women. Food data as food menu data is taken from the Indonesian Food Composition Table which consists of staple foods, side dishes, vegetables, and fruit which totals 312 food data along with energy, protein, fat, and carbohydrate values.

Results: The results obtained from this study are modeling on ANFIS that has been used in this study can provide results with the best accuracy of 89.1% for accuracy training and 72.1% for accuracy testing with epoch = 2000 to determine whether or not someone has diabetes. The best results obtained from the GA process were 98.9% for the fulfillment of nutrients achieved with the highest fitness value in the number of generations = 40, the number of chromosomes = 10, the number of patients = 10 and the combination of crossover rate and mutation rate was 0.6:0.8.

Conclusion: The proposed method gets very good grades and produces a healthy menu that meets optimal nutrition and the achievement of food diversity in accordance with the four pillars of balanced nutrition of the Indonesian Ministry of Health.

OP07   Basic & Translational diabetes research

Association between family history of diabetes and increased carotid atherosclerosis

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Objective: The purpose of this study was to assess the association between family history of diabetes and increased carotid intima-media thickness (IMT), a maker of subclinical atherosclerosis, among middle aged Korean population

Methods: This cross-sectional study included community-dwelling adults of 3,958 (1,397 Men and 2,561 women) aged 30 to 64 years from the Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort. Family history of diabetes was confirmed through face-to-face interviews using standardized questionnaires according to pre-set protocol. Carotid IMT was assessed by B-mode ultrasonography; increased IMT was defined as top quartile of the IMT values in total participants. Multivariate logistic regression was used to assess independent association between family history of diabetes and increased IMT.

Results: Family history of diabetes was significantly associated with increased carotid IMT (odds ratio [OR] 1.24; 95% confidence interval [CI], 1.04-1.47), after adjusting for sex, age, body mass index, systolic blood pressure, total cholesterol, triglyceride, hemoglobinA1c, smoking, alcohol-drinking, exercise and medication uses for hypertension, dyslipidemia and diabetes. Similar findings were observed in sex-stratified analysis, but the association was more significant in women (OR 1.31; 95% CI, 1.05-1.64) than in men (OR 1.31; 95% CI, 0.97-1.76) probably due to larger sample size for women.

Conclusion: Family history of diabetes positively was associated with increased carotid IMT. This finding suggests that asking the family history of diabetes may help to better identify high-risk groups of atherosclerotic cardiovascular disease.

OP08   Basic & Translational diabetes research

SGLT2 inhibitor decreases senescent cells in the kidney of type 2 diabetes mouse model

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Objective: Metabolic stress may accelerate cellular senescence, leading to further deterioration of metabolism and development and/or progression of complications. SGLT2 inhibitors induces negative energy balance and alter whole body metabolism, which may potentially affect aging process. In this study, we examined the effects of an SGLT2 inhibitor, dapagliflozin, on cellular senescence of the kidney in a diabetic mouse model.

Methods: Dapagliflozin (1 mg/kg) or glimepiride (2.5 mg/kg) or vehicle was administrated daily via oral gavage for 8 weeks in db/db mice. Body weight, blood glucose level, and food intake were measured during treatment. After 8 weeks of treatment, we evaluated expressions of aging markers (p21, p16, p53) and oxidative stress levels in kidney. We also explored potential mechanisms of above observations focusing on beta-hydroxybutyrate (BHB) using HK-2 cells.

Results: The dapagliflozin (db/db+SGLT2i) group and the glimepiride (db/db+SU) group showed no changes in body weight compared to the vehicle (db/db+vehicle) group, but showed a significant decrease in blood glucose. Total food intake was increased in the db/db+SGLT2i group compared to the db/db+vehicle group. Gene expression of aging markers was increased in the db/db+vehicle group compared to the db/m group, and this increase was markedly reversed in the db/db+SGLT2i group, but not in the db/db+SU group. In the db/db+SGLT2i group, ROS level was also reduced compared to the db/db+vehicle or db/db+SU group. BHB concentrations were increased after dapagliflozin treatment, and BHB attenuated H_2O_2-induced cellular senescence in HK-2 cells.

Conclusion: This study demonstrated that progression of aging was significantly inhibited by SGLT2 inhibitor in the kidney of db/db mice. In addition, BHB has the potential to mediate the anti-aging effect of dapagliflozin in the kidney.

Oral presentations

IDENTIFICATION OF DIABETES MELLITUS (DM) USING ARTIFICIAL NEURAL NETWORK (ANN) WITH BACKPROPAGATION METHOD AND SIGMOID ACTIVATION FUNCTION

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Objective: Diabetes is one of the most common illnesses and serious chronic diseases in Indonesia today. Diabetes Mellitus (DM) which is commonly known as diabetes is a disease characterized by hyperglycemia (an increase in blood sugar levels) that is persistent and varied, especially after eating. This disease is not easy to be accurately recognized by the public. So we need to develop a system that can identify accurately.

Methods: The system was built using artificial neural networks with backpropagation methods and sigmoid activation functions. For the methods, the backpropagation Neural Network Architecture used is as follows: (1) 8 input layers, because there are 8 categories used as input data for ANN, namely: (a) The number of times pregnant; (b) 2-hour plasma glucose concentration in an oral glucose test; (c) Diastolic blood pressure (mm Hg); (d) Triceps fold thickness (mm); (e) 2-hour serum insulin (mu U / ml); (f) Body Mass Index (weight in kg / (height in m2)); (g) Diabetes genealogical functions; (h) Age (years), (2) 2 output layers, i.e. output = 1, it means that the person has diabetes, and if output = 0 then that person does not have Diabetes and (3) 5 Hidden layer with diabetes data obtained from UCI machine learning repository there are 768 data, with details of 500 affected by diabetes and 268 not affected by diabetes.

Results: The results showed that this method successfully classified diabetics and non-diabetics disease with close to 100% accuracy in training 8 times for ANN in diabetes.

Conclusion: The conclusion obtained is that it can be said that it is good to do identification based on the accuracy level that is produced close to 100%.

Deciphering the mechanism of the loss of β cell identity in mouse model for early diabetes

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Objective: The purpose of this study was to describe and decipher the mechanism of β cell dedifferentiation.

Methods: Prmt1 floxed (Prmt1fl/fl) [MGI: 4432476] mice were crossed with Pdx1-CreERT2 [MGI: 2684321] mice to generate Prmt1 βiKO mice. Immunofluorescent staining, H&E and immunohistochemical (IHC) staining, transmission electron microscopy was performed for imaging analysis. Glucose tolerance test (GTT), oxygen consumption rate (OCR), Glucose-stimulated insulin secretion (GSIS) was performed for functional analysis. For single cell RNAsequencing, islets from 3 biological replicate mice was harvested and were dissociated to single cell level. Single cell libraries were generated using the Chromium single cell 3' library and gel bead kit V3.

Results: Prmt1 knock-out in adult β cells resulted in early and progressive diabetic phenotype. β cells in Prmt1 βiKO mouse were functionally and morphologically immature and the protein level of mature β cell markers were decreased. Single cell transcriptomic analysis of Prmt1 βiKO β cells revealed groups of β cell subpopulations that serially ranged from transcriptomic normal β cells to the stressed β cells and immature β cells. Stressed β cells were increased in mRNA expression of both Insulin and ER stress-related genes whereas immature β cell population were decreased in mRNA expression of insulin, insulin biosynthesis gene and β cell transcription factors. Metabolic challenge in βiKO mice resulted in robust 'loss of identity' in β cells with profound proteomic and transcriptomic change. Pseudotemporal analysis revealed a biological meaningful wave of transcriptomic changes.

Conclusion: Prmt1 βiKO β cells recapitulates the phenotype of type2 diabetes β cells. Single cell analysis of Prmt1 βiKO β cells can provide a novel insight on how β cells lose their identity in type 2 diabetes.

Changes in inflammatory cytokines in the liver of OLETF rats

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Objective: Obesity results in accumulation of ectopic fat in the liver. That involved in the expression of inflammatory cytokines and induces insulin resistance. However, the changes in inflammatory cytokine expressions in the liver according to the stage of type 2 diabetes are still unknown. The purpose of the present study was to investigate these changes focusing on accumulation of ectopic fat in the liver.

Methods: Otsuka Long-Evans Tokushima Fatty (OLETF) rats were used as models of type 2 diabetes with obesity and Long-Evans Tokushima Otsuka (LETO) rats served as healthy controls. TAG levels in the liver and mRNA expression levels of inflammatory cytokines (TNFα, IL-6, IL-1β, IL-10) were measured at 8, 20, 30 and 60 weeks old.

Results: At 8 weeks old, TAG levels were significantly higher in OLETF rats than in LETO rats. The levels in OLETF rats were significantly increased from 8 to 20 weeks old, and then significantly decreased from 30 to 60 weeks old. At 8 weeks old, there were no significant differences in TNFα expression levels between animal strains. TNFα expression levels in OLETF rats significantly increased from 8 to 20 weeks old, and then were decreased from 30 to 60 weeks old. There were no significant differences in IL-1β and IL-10 expression levels of OLETF rats among the weeks old. IL-6 expression levels were below the detection limit at all weeks old in both strains.

Conclusion: These results suggested that accumulation of ectopic fat in the liver induces TNFα expression and the changes could depend on accumulation of ectopic fat. Ectopic fat in the liver could involve in insulin resistance at the early stage of type 2 diabetes with obesity. Additionally, insulin resistance at the progressive stage could be caused by TNFα from the liver with ectopic fat.

Changes in inflammatory cytokines in the epididymal adipose tissue of OLETF rats

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Objective: Inflammatory cytokines derived from adipose tissue are involved in impaired glucose tolerance associated with obesity. However, the changes in inflammatory cytokine expressions in adipose tissue with the progression of type 2 diabetes are still unknown. In the present study, we examined changes in chronic inflammation-related cytokines in adipose tissue of type 2 diabetes with obesity.

Methods: OLETF and LETO rats were used as models of type 2 diabetes with obesity and healthy controls, respectively. Oral glucose tolerance test was performed at 8, 20, 30 and 60-week-old. Additionally, expression levels of IL-6 and IL-10 in the epididymal adipose tissue were measured as inflammatory cytokine and anti-inflammatory cytokine, respectively.

Results: Glucose tolerance was impaired in OLETF rats at 8-week-old and the intolerance deteriorated with age. There was no significant difference in IL-6 expression level between animal strains at the 8-week-old. However, IL-6 expression level in OLETF rats was significantly increased from 8 to 30-week-old, and significantly decreased from 30 to 60-week-old. IL-6 expression level in LETO rats was increased from 8 to 30-week-old and decreased from 30 to 60-week-old, but insignificant. IL-10 expression level in OLETF rats was significantly increased from 8 to 20-week-old, and decreased after 20-week-old.

Conclusion: The results suggest that IL-6 derived from epididymal adipose tissue have no involvement in impaired glucose tolerance in the early stage of type 2 diabetes with obesity. Conversely, at the progressive stage, increased IL-6 and decreased IL-10 expression in epididymal adipose tissue could induce glucose intolerance. The contributory causes of glucose intolerance differ from the stage of type 2 diabetes, and inflammatory cytokines derived from epididymal adipose tissue could be involved in the progression, not the initiation.

OP13 Basic & Translational diabetes research

Use of RNA-seq to identify differentially expressed genes in gestational diabetes mellitus among Filipino pregnant women

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Objective: This study aimed to use RNA sequencing technology to identify differentially expressed genes in gestational diabetes mellitus (GDM) among Filipino pregnant women.

Methods: Participants were gathered according to inclusion and exclusion criteria. Blood samples were collected during the first, second, and third trimesters of pregnancy for the biochemical testing and RNA sampling. A total of 80 pregnant women, 40 GDM diagnosed, and 40 nonGDM, were included in the study. Tempus™ Spin RNA Isolation Kit was used to isolate RNA. After validating the quality and quantity of RNA extracts, the RNA library was prepared. RNA sequencing was done using NovaSeq 6000 System. Data were analyzed using various bioinformatics tools.

Results: A total of 2,129 DEGs were identified, including 1,348 upregulated and 781 downregulated genes in GDM and nonGDM. Focusing on DEGs common between GDM and nonGDM in all trimesters of pregnancy, there were a total of 104 upregulated genes in GDM and 71 upregulated genes in nonGDM, 21 genes of which are common to both. There were a total of 2,265 downregulated genes in GDM and 2,702 in nonGDM, 2,181 are common to both conditions. Of intriguing interest, the DEGs found in the first trimesters of pregnancy may be used as potential early biomarkers of GDM. The following are some of the remarkable genes that may act as a potential biomarker to GDM: (1) hepatic PTPRG stimulated by inflammation in obese/T2DM mice and positively correlated with insulin resistance; (2) HSF1 regulates autophagy which is enhanced in high glucose levels in GDM pregnancy and (3) other pseudogenes that may act as health regulators in GDM.

Conclusion: The identification of differentially expressed genes in GDM could advance our knowledge in determining the risk of GDM development and potentially may be used as molecular targets for the prevention and treatment of the condition.

OP14 Basic & Translational diabetes research

Palm Oil-Derived Tocotrienol-Rich Fraction Preserves Normal Retinal Vascular Structures in Streptozotocin-Induced Diabetic Rats

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Objective: Retinal vessel dilatation, breakdown of blood-retinal barrier, increased vascular permeability and retinal angiogenesis are the hallmark features of diabetic retinopathy (DR). Expression of Angiopoietin-2 (Ang-2) and Protein Kinase C (PKC) have been identified to play a role. Therefore, we investigated the effect of tocotrienol-rich fraction (TRF), a potent antioxidant, towards retinal vascular changes, level of Ang-2 and PKC in rats with streptozotocin (STZ)-induced DR.

Methods: Sprague-Dawley rats were divided into three groups; control rats (NC) received oral vehicle treatment whereas diabetic rats received either vehicle (DV) or 100 mg/kg of TRF treatment (DT). All treatments were given daily through oral route for 12 weeks. Diabetes was induced with intraperitoneal injection of STZ (55 mg/kg body weight), whereas control rats received intraperitoneal injection of citrate buffer. Treatment was started once the rats were diabetic (48 hours post-STZ injection) and at 0 (baseline), 6 and 12 weeks post-treatment, fundus photographs were taken, and average diameter of retinal veins and arteries were measured. After 12 weeks of treatment, rats were euthanized, and retinas were collected for measurement of Ang-2 and PKC expression using ELISA.

Results: Retinal venous diameter was increased in DV group at week 12 compared to baseline (p<0.01) as well as when compared to DT (p<0.001) and NC group (p<0.001). However, no significant difference was seen in arterial diameter. Retinal venous diameter in DT group at 12 weeks was reduced compared to baseline (p<0.01).In NC, retinal vessels diameter remained unchanged throughout the study period. Preservation of the retinal vascular diameter was associated with significantly reduced expression of retinal Ang-2 and PKC protein levels of DT compared to DV group (p<0.001 and p<0.01 respectively).

Conclusion: Oral TRF supplementation preserves retinal vascular architecture in STZ-induced diabetic rats. This effect of TRF is associated with reduction of retinal Ang-2 and PKC expression.

OP15 Basic & Translational diabetes research

Diagnostic utility of maternal serum cortisol in gestational diabetes mellitus among Filipinos: a multi-marker approach

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Objective: The prevalence of gestational diabetes mellitus (GDM), a common complication during pregnancy, is increasing worldwide and yet, preventive healthcare to pregnant women is not given emphasis. Diagnostic test utilized is oral glucose tolerance test (OGTT), a test that requires patients to drink a sweet sugar solution and submit several blood specimens. This test is done late in the second trimester or early third trimester, where complications already exist. With this, it is crucial to identify potential markers that may identify the disease earlier and using techniques that are more convenient. To address this, we sought to determine the possibility of using maternal serum cortisol (MSC) as a potential complementary marker to diabetes-associated parameters for GDM diagnosis.

Methods: With ethical approval, 158 case and control-matched pregnant women were recruited and subjected to 75-g OGTT. Hemoglobin A1c (HbA1c), lipid profile, fasting insulin levels, and fasting MSC were also assayed.

Results: Levels of fasting MSC were found to be significantly higher among the GDM group than the non-GDM group. Partial correlation (adjusted for the participant's age and BMI) showed no association between MSC with 75-g OGTT, HbA1c, and HOMA-IR. Whereas, a positive linear correlation was observed with certain lipid profile parameters. Using the ROC curve, cut-off points for fasting blood glucose (FBG), HbA1c, HOMA-IR, and MSC were determined. MSC yielded an AUC > 0.6 (p < 0.001), which indicates a poor discrimination for a diagnostic marker. When combined with other diabetes-associated parameters, most notably FBG, specificity, and the positive predictive value of MSC significantly increases.

Conclusion: Our study suggests that the use of FBG alone is more superior to the use of MSC or a combination of the two. Further studies across various geographic locations and among different ethnic groups should be conducted to determine the applicability of the results in our population.

OP16 Basic & Translational diabetes research

Renalprotective effect of Ganoderic acid against renal dysfunction in type II diabetes via alteration of TGF-β

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Objective: In the current experimental study, we scrutinize the nephroprotective effects of ganoderic acid against high-fat diet/streptozotocin-induced type II diabetes mellitus and explore the underlying mechanism.

Methods: STZ used to induce type II diabetes and rats were received the oral administration of ganoderic acid and glibenclamide post-induction diabetes and estimation the body weight, food intake, blood glucose, plasma insulin, biochemical, antioxidant, proinflammatory cytokines and inflammatory mediators, respectively.

Results: Dose dependently treatment of GA significantly (P<0.001) reduced the blood glucose level (78%), food intake (54%), Hb1c (55.5%), HOMA-IR (50.5%) and increased the plasma insulin (65.7%), body weight (18%). GA significantly altered the antioxidant level in renal tissue via down-regulated the MDA (56.7%) and up-regulated the SOD (76.5%), GSH (70.5%), GPx (65.5%) and CAT (60.5%), respectively. GA altered the renal parameters such as BUN (68.5%), creatinine (60.2%), serum protein (60.5%). GA decreased the expression of TGF-β (46.6%), COX-2 (65.3%), iNOS (68.7%) and PGE2 (59.9%) and ameliorated the structural alteration in renal tissues.

Conclusion: Collectively, we can conclude that ganoderic acid reduced the renal dysfunction in type II diabetic rats via alteration of the inflammatory pathway.

OP17 Basic & Translational diabetes research

Hypertension and Insulin Resistance as Transition Factors to Type 2 Diabetes from Prediabetes: Evidence from a Prospective Cohort Study of 10 Years in South Korea

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Objective: The aim of this study is to examine whether hypertension or insulin resistance (IR) are valid transition factors to Type 2 Diabetes (T2DM) from prediabetes. Among all people with prediabetes, to distinguish those with high risk from those not is the first essential step to allocate the right resources to the right people in the alleviation of T2DM epidemics and its social burden.

Methods: We evaluated 2265 middle-aged South Korean examinees with prediabetes at baseline in the Korean Genome and Epidemiology Studies (KoGES) during the follow-up period of 10 years. Incident T2DM was defined as FPG≥126mg/dl, PPG≥200mg/dl, HbA1c≥6.5%, physician-diagnosed T2DM or if self-reported to have prescribed of oral medication or insulin.

Results: During 8.24 person-years, we identified 469 incident T2DM cases (21%). The incidence of T2DM increased with hypertension or IR with the adjusted hazard ratios (HRs) of 1.595 (CI: 1.209-2.105). Compared to those with only hypertension (Adjusted HR, 1.342 [CI: 1.045-1.723]), those with hypertension and IR show a clearly larger HR (Adjusted HR, 2.593 [CI: 1.802-3.733]). Meanwhile, hypertension did not show any relevance in survival analysis of regression to normal among all prediabetes while IR did, such that those prediabetes with IR are less likely to improve back to normal (Adjusted HR, 0.824 [CI: 0.555-1.293]; 0.569 [CI: 0.353-0.918]).

Conclusion: The middle-aged South Koreans with prediabetes who have hypertension or insulin resistance are likely to develop T2DM, and thus they deserve special attention for timely intervention. Among those with prediabetes who have hypertension, those with IR are especially likely to develop T2DM.

OP18 Basic & Translational diabetes research

Pre-diabetes-diabetes morbidity study according to fasting blood glucose level: difference in morbidity by age group

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Objective: This study is about age-related differences in prediabetes-diabetes morbidity according to two different prediabetes standards of fasting plasma glucose (FPG) levels. It will provide how the risks of developing Type 2 Diabetes (T2DM) from prediabetes differ by each FPG threshold and age group.

Methods: The National Health Insurance Service-National Health Screening Cohort (NHIS-HEALS) comprised of 304,080 people in 2004 without any previous history of high glucose levels above the normal. Among 304,080, those who develop prediabetes with FPG levels of 100-110mg/dL are those with 'first diabetes', while those who have prediabetes with FPG levels of 110-125mg/dL have 'second diabetes'. Among three groups of normal, first prediabetes and second prediabetes, there are four age groups: 40-49 years-old, 50-59 years-old, 60-69 years-old or ≥70 years. Until the end of follow-up, 2013, T2DM incidence is defined as anyone who was prescribed of T2DM (ICD-10th codes: E1100-E1190) in the NHIS-HEALS claims data.

Results: The adjusted incidence rate of T2DM per 10 person-years among those with 1st prediabetes at 40s is 2378.55 at 40s, 3158.8 at 50s, 4485.18 at 60s and 5274.11 at 70s while among 2nd prediabetes is 4391.06 at 40s, 5641.71 at 50s, 7061.7 at 60s and 7358.01 at 70s. Those in 40s have higher HR than HRs of 50s, 60s, 70s at 1st prediabetes (40s: 1.994 [1.913-2.079], 50s: 1.521[1.467-1.577], 60s: 1.236 [1.189-1.284], 70s: 1.113[1.054-1.176]). Also, those in 40s have highest HR at 2nd prediabetes among HRs of other age groups at 1st or 2nd prediabetes (3.415 [3.252-3.587]).

Conclusion: The middle-aged South Koreans (40-79 years old) with FPG from 110-125mg/dL have higher risks of developing T2DM among other age groups or among others with less FPG levels.

OP19 Basic & Translational diabetes research

Impact of Urgently Initiated Telemedicine Due to COVID-19 on Glycemic Control in Patients with Diabetes

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Objective: To investigate the impact of telemedicine due to COVID-19 on glycemic control in patient with diabetes

Methods: We retrospectively analyzed the mean HbA1c and change in glycated hemoglobin level in patients with diabetes who undertook telemedicine because of COVID-19 and those who did face to face care (non-telemedicine group). We compared the mean HbA1c and delta HbA1c between telemedicine group and non-telemedicine group that were enrolled at the same period.

Results: The mean HbA1c levels of patients were significantly higher after than before the telemedicine period (7.47±1.24% vs 7.28±1.13%, p ⟨ 0.05). Mean delta HbA1c was significantly higher in the telemedicine than in the non-telemedicine group (0.20±0.68% vs 0.04±0.94%, p ⟨ 0.05). Delta HbA1c was significantly greater in patients with shorter duration of diabetes, fewer oral hypoglycemic agents, no insulin, fewer comorbidities, and higher baseline HbA1c.

Conclusion: Telemedicine may worsen glycemic control in patients with diabetes during public health crises.

OP20 Basic & Translational diabetes research

Small RNA Profile of Urinary Extracellular Vesicles in Obese Type 2 Diabetes Patients - Before and After the Bariatric Surgery

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Objective: Small RNA in the urinary extracellular vesicle (EV) serves to regulate gene expression, but the expression pattern of obesity is still uncertain. We aimed to profile small RNAs of urinary EVs in obese type 2 diabetes mellitus (T2DM) patients before and after 6 months of bariatric surgery compared to those of healthy volunteers (HVs).

Methods: Age-sex matched HVs and obese T2DM patients (n=6 each) were recruited. Small RNA profile of urinary EVs were analyzed using RNA sequencing. To evaluate the effect of weight loss on obese T2DM patients, small RNA profiles of urinary EVs 6 months after bariatric surgery were also assessed.

Results: Total numbers of small RNAs in urinary EVs by RNA sequencing were 5205. Obese T2DM patients had differential expression of 1343 small RNAs in urinary EVs compared to HVs (fold change ≥ 2 & P-value ⟨ 0.05). Bariatric surgery changed the expression levels of 372 small RNAs. Among those, compared to HVs, 228 small RNAs were found to be either upregulated in obese T2DM and downregulated after bariatric surgery or downregulated in obese T2DM and upregulated after bariatric surgery. Sixty-one (3 piRNAs, 4 snRNAs, 54 tRNAs) small RNAs were upregulated in obese T2DM and downregulated after bariatric surgery and 167 (2 miRNAs, 12 piRNAs, 7 snoRNAs, 131 snRNAs, 15 tRNAs) small RNAs were downregulated in obese T2DM and upregulated after bariatric surgery.

Conclusion: Compared to HVs, obese T2DM patients showed a distinct urinary EVs small RNA profile. Weight loss after bariatric surgery may have changed the small RNA profiles of urinary EVs in obese T2DM patients.

OP21   Clinical diabetes and therapeutics

Predictive Performance of HbA1c for Incident Diabetes Compared with Glucose Tolerance Test in Obese Population: A Prospective Population-Based Cohort Study

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Objective: To examine whether HbA1c test would be suitable screening tool for detecting high-risk subjects for diabetes compared to oral glucose tolerance test (OGTT) according to accompanied obesity.

Methods: In this prospective population-based cohort study, both OGTT and HbA1c tests were performed and continued every two years up to 12 years among individuals with non-diabetic state at baseline (aged 40-69 years, N = 7,512). Incident diabetes was established by a doctor, HbA1c ≥ 6.5%, and/or fasting plasma glucose (FPG) ≥126 mg/dL, and/or 2-hour postprandial glucose level (2hPG) based on OGTT ≥200 mg/dL. Discriminative capacities of high HbA1c (≥ 5.7%) versus high 2HPG (≥ 140 mg/dL) for predicting incident diabetes were compared using Cox-proportional hazard regression and C-index.

Results: During the median 11.5 years of follow-up period, 1341 (17.6%) developed diabetes corresponding to an incidence of 22.1 per 1,000 person-years. Isolated high 2hPG was associated with higher risk for incident diabetes (hazard ratio [HR] 4.29, 95% CI 3.56-5.17) than isolated high HbA1c (HR 2.79, 95% CI 2.40-3.26, P < 0.05). In addition, high 2hPG provided better discriminatory capacity than high HbA1c (C-index 0.79 versus 0.75, P < 0.05). Meanwhile, the HR (3.95 with 95% CI 3.01-5.18 versus 2.82 with 95% CI 2.30-3.46) and discriminatory capacity of incident diabetes (C-index 0.75 versus 0.75) between two subgroups became comparable in obese population.

Conclusion: Even though overall inferior predictive capacity of HbA1c test than OGTT, HbA1c test might plays a complementary role in identifying subjects at high risk for diabetes in the obese population with increased sensitivity.

OP22   Clinical diabetes and therapeutics

Changes in Target Achievement Rates After Statin Prescription Changes at a Single University Hospital

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Objective: We investigated changes in low-density lipoprotein cholesterol (LDL-C) target achievement rates (<70 and <100 mg/dL) when the prescription changed from various statins to Lipilou, a generic formulation of atorvastatin

Methods: This study was a retrospective cohort study of patients who had been prescribed Lipilou for >3 months at Seoul National University Hospital from 2012 to 2018. For patients who were treated with a previous statin before the prescription of Lipilou, changes in target achievement rates of LDL-C <70 and <100 mg/dL were confirmed 3-6 months after the prescription of Lipilou

Results: Among the 683 enrolled patients, when their prescription was changed to Lipilou, the target achievement rate of LDL-C was significantly increased for LDL-C <70 mg/dL (from 22.1% to 66.2%, p<0.001) and 100 mg/dL (from 26.8% to 75.3 %, p<0.001). In particular, when moderate-low potency statin was changed to Lipilou (10 mg), the target achievement rates for LDL-C <70 mg/dL (from 28.9% to 66.7%, p<0.001) and 100 mg/dL (from 42.2% to 86.7%, p<0.001) was significantly increased. The change from moderate-high potency statin to Lipilou (20mg) showed an increased target achievement rates for LDL-C <70 mg/dL (from 33.3% to 80.0%, p=0.008) and 100 mg/dL (from 40.0% to 73.3%, p<0.025).

Conclusion: We cannot simply conclude whether Lipilou is superior to other statins. However, when target LDL-C were not reached with previous statin treatments, a high target achievement rate could be achieved by changing the prescription to Lipilou. Physicians should always consider aggressive statin prescription changes for high target achievement rates

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OP23   Clinical diabetes and therapeutics

Efficacy and safety of Anagliptin after switching from other dipeptidyl peptidase-4 inhibitors in type 2 diabetes with insufficient glucose control: A 12-week interim report

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Objective: The objective of this study was to evaluate the glucose control effect of anagliptin after switching from other DPP4is in patients with T2DM who had inadequate glycemic control.

Methods: This study was designed as a non-interventional, single group, open-label, multi-center observational study. Patients with T2DM whose HbAlc levels were ≥ 7% despite of taking DPP4is, other than anagliptin, were enrolled. Patients took DPP4is for at least 8 weeks, regardless of whether by monotherapy or combination therapy. After switching to anagliptin, all subjects maintained their regimen for 24 weeks in condition that events of FPG >13.4 mmol/L or HbA1c > 10.0% did not occur. Although the primary endpoint was the change in HbA1c after 24 weeks, the data from baseline to week 12 was used for analysis in this interim report. We also performed subgroup analysis by demographics and medical history of T2DM.

Results: Total 1,761 subjects were enrolled for this study. In the overall efficacy set (1,178 subjects), change in HbA1c at 12 week from baseline was -0.59±0.95 % (p<0.0001). At week 12, the percentage of patients achieving HbA1c ≤ 7.0% was 33.6% and that of achieving HbA1c ≤ 6.5% was 10.4%, respectively. In the subgroup analysis by previous 8 different DPP4i, all of the intra-group difference by previous DPP4i was statistically significant (p<0.0001 each) whereas inter-group difference was not significant. In the safety set (1,415 subjects), a total of 62 AEs were reported in 53 subjects. Hypoglycemic event was reported in just 1 subject (0.07%).

Conclusion: This study demonstrated that switching to anagliptin from other DPP4is resulted in significant improvement in HbA1c at week 12 of treatment from baseline in patients with T2DM. Anagliptin can be considered as a successful and safe alternation for T2DM patients with insufficient glucose control who are currently taking other DPP4is.

OP24   Clinical diabetes and therapeutics

Asian Subpopulations May Exhibit Greater Cardiovascular Benefit from Long-Acting Glucagon-Like Peptide 1 Receptor Agonists: An updated meta-analysis including the HARMONY, REWIND and PIONEER 6 trials

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Objective: In 2019, we presented a meta-analysis of cardiovascular outcome trials (CVOTs) concerning long-acting glucagon-like peptide-1 receptor agonists (GLP-1RAs). After our report, three other CVOTs were published. We synthesized previous and recent CVOTs to examine the overall effect of long-acting GLP-1RAs on major adverse cardiovascular events (MACEs) and to confirm subpopulations exhibiting the greatest CV benefit.

Methods: Six CVOTs were included: LEADER (liraglutide), SUSTAIN-6 (semaglutide), EXSCEL (exenatide once weekly), HARMONY (albiglutide), REWIND (dulaglutide) and PIONEER 6 (oral semaglutide). Overall effect estimates were calculated as relative risks (RRs) and 95% confidence intervals (CIs) using the random-effects model; subgroup analyses reported in the original studies were similarly analyzed.

Results: Overall, significant risk reductions in MACE and CV death were observed. Evaluation of patients on the basis of race showed trends of MACE risk reductions in subjects of White race (RR, 0.89; 95% CI, 0.82 to 0.96) and Asians (RR, 0.50; 95% CI, 0.29 to 0.86). Black race did not show the statistically significant CV benefit from long-acting GLP-1 RAs (RR, 0.95; 95% CI, 0.67 to 1.37).

Conclusion: Long-acting GLP-1 RAs reduced risks of MACE and CV deaths in high-risk patients with type 2 diabetes mellitus. Our findings from synthesized data including recently published CVOTs support a particularly effective reduction in CV events with GLP-1 RA in Asian populations.

Oral presentations

The study population of recent cardiovascular outcome trials shows indirectness against real-world inpatients and outpatients with diabetes

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Objective: Recent cardiovascular outcome trials changed the therapeutic strategy of guidelines for type 2 diabetes. We aimed to compare the characteristics of patients from real-world hospital settings and those from recent pragmatic randomized trials.

Methods: This electronic medical records (EMR)-based retrospective observational study investigated the patients with diabetes from the inpatient and outpatient settings in West China Hospital of Sichuan University from 1/1/2011 to 30/6/2019. We identified patients meeting the inclusion criteria of a pragmatic randomized trial (EMPA-REG OUTCOMES) based on EMR and compared their baseline characteristics (including demographic, metabolic (BP, lipid), kidney function, treatment) with the trial data using the student's t-test for continuous variables and Chi-square test for categorical variables in R-Studio (R Pack Version 3.6.1).

Results: We included 48,257 inpatients and 36,857 outpatients with diabetes where 8,389 (17.4%, 8,389/48,257) inpatients and 2,646 (7.2%, 2,646/36,857) outpatients met the inclusion criteria for the EMPA-REG OUTCOMES trial, respectively. Compared to the trial population, the real-world inpatients meeting the eligibility criteria of EMPA-REG OUTCOMES had fewer males, older age, lower BMI, higher blood pressure, similar lipid profiles, higher eGFR, less proteinuria, fewer metformin users, more insulin users, fewer anti-hypertensive drug users, and fewer aspirin users, while the outpatients meeting the eligibility criteria had fewer males, similar age, worse lipid control, fewer metformin users, fewer insulin users, fewer anti-hypertensive drug users, and fewer aspirin users.

Conclusion: The trial population in EMPA-REG OUTCOMES represents only 1/6 of the inpatients and 1/13 of the outpatients with diabetes in the Chinese tertiary medical center. Both potential eligible inpatients and outpatients showed different baseline characteristics, with fewer users of metabolic drugs in the current study population. The interpretation of EMPA-REG OUTCOMES results should be cautious with its indirectness of the study population in China.

Comparison of the Effects of Sodium-glucose co-transporter 2 Inhibitor and Thiazolidinedione Treatment on Risk of Stroke among Patients with Type 2 Diabetes

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Objective: Influential guidelines recommend using SGLT-2i preferentially among antidiabetic drugs in patients with diabetes and ASCVD. Although CVOTs with SGLT-2i showed reduction in risk of 3-point major adverse cardiovascular events (MACE), they did not demonstrate beneficial effect on stroke. In addition, a meta-analysis reported adverse effect of SGLT-2i for stroke. On the contrary, pioglitazone, a type of TZD, showed to reduce recurrent stroke risk in two large RCTs. The aim of this study was to compare the effect of SGLT-2i and TZD on the risk of stroke among patients with type 2 diabetes.

Methods: Using the Korean National Health Insurance Service data, we compared a 1:1 propensity score-matched cohort of patients who were new users of SGLT-2i (n = 81,548) and TZD (n = 81,548) from January 2014 to December 2018. The primary outcome was stroke. The secondary outcomes were MI, CV death, 3-point MACE, and hospitalization for heart failure (HF).

Results: During the follow-up, 1,815 patients were newly hospitalized for stroke. The incidence rate of stroke was 5.30 and 5.36 per 1,000 person-years for TZD and SGLT-2i group, respectively. The hazard ratio of stroke was 0.992 (95% CI: 0.867-1.136) in SGLT-2i-treated patients compared with TZD-treated patients. There was no clear difference in risk of MI (HR: 1.022, 95% CI: 0.805-1.296), CV death (HR: 0.839, 95% CI: 0.661-1.066), 3-point mace (HR: 0.969, 95% CI: 0.873-1.074) between two groups. Hospitalization for HF was significantly decreased in SGLT-2i-treated patients (HR: 0.628, 95% CI: 0.430-0.917). Results were consistent regardless of prior CV disease.

Conclusion: In this real-world data, the risk of stroke was comparable in patients with type 2 diabetes treated with SGLT-2i vs TZD.

Low Fasting Glucose and C-peptide Levels Were Associated with Superior Response of Insulin Degludec/Aspart compared to Basal Insulin

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Objective: Efficacy of degludec/aspart (IDegAsp) compared to basal insulin in type 2 diabetes has not been established. We investigated efficacy of change from basal insulin to IDegAsp, and searched for related clinical factors.

Methods: We collected medical records of adults with type 2 diabetes, treated with basal insulin during 2017~2020 in 3 referral hospitals. Among them, those who initiated once-daily IDegAsp and continued ≥6 months were enrolled. Control group under continuous basal insulin was selected by 1:1 Propensity-score-matching (PSM) for baseline HbA1c and insulin dose. Delta-fasting plasma glucose (△FPG) was calculated by [measured-FPG – predicted-FPG].

Results: A total of 324 patients were using basal insulin without change in other anti-diabetic agents. Among them, 87 patients were recruited to IDegAsp group. A control group was matched for age, sex, BMI, DM duration, HbA1c, and insulin dose. After 6 months, HbA1c decreased more in the IDegAsp group compared to the control (-0.55±0.78 vs -0.26±1.02% p=0.037). Baseline FPG was significantly lower in the IDegAsp group (124.2±38.4 vs 148.0±50.6 mg/dL, p=0.001), therefore, we drew 'predicted FPG' by regression analysis with baseline FPG and HbA1c. Next, we divided the IDegAsp group according to difference between the measured-FPG and the predicted-FPG (that is △FPG), and each control was selected by further matching with baseline FPG. We found reduction of HbA1c in the IDegAsp group was significantly superior to that in the control group only in the lower △FPG group (each n=39, -0.53±0.74 vs -0.10±1.34% p=0.043). Hypothesizing that low △FPG could come from insulin deficiency, correlation analysis was done between fasting c-peptide and △FPG, and a significant correlation was observed (r=0.167, p=0.026), even after adjustment with age, sex, weight, and GFR.

Conclusion: We observed that IDegAsp was more effective than basal insulin in patients with lower FPG than predicted from HbA1c, which was associated with insulin deficiency.

Trends and risk factors in hospital admission for hypoglycemia with type 2 diabetes in Korea

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Objective: Due to the development of several new classes of anti-hyperglycemic drugs with a low risk of hypoglycemia, hypoglycemia-related hospitalizations are expected to decrease during past decades. We aimed to examine nationwide incidence trends and risk factors of hospitalization for hypoglycemia with type 2 diabetes in Korea.

Methods: We conducted repeated cross-sectional analyses using a Korean National Health Insurance Service-National Sample Cohort from 2006 to 2015. Logistic regression analysis was performed to investigate possible risk factors. Hypoglycemic events were defined as hospitalization or a visit to an emergency department with a primary or secondary diagnosis of hypoglycemia using ICD-10 codes.

Results: During the study period, the prevalence of type 2 diabetes continuously increased. The percentage of patients prescribed sulfonylurea, and α-glucosidase inhibitor decreased while those who prescribed metformin, and dipeptidyl peptidase-4 inhibitor increased. The number of admissions for hypoglycemia with type 2 diabetes increased from 183 in 2006, to 412 in 2013 and then modestly decreased to 388 in 2015. Accounting for the prevalence of type 2 diabetes, age-standardized incidence of hypoglycemic admission per 1,000 diabetic patients increased from 5.996 to 8.240 between 2006 and 2010, and then fell to 6.448 in 2015. The trends are mainly attributed to those in subjects aged 65 or above. Predictors of hypoglycemic hospitalization included female sex, older age, multiple comorbidities, and sulfonylurea usage.

Conclusion: Decreased sulfonylurea use might be the cause of decreased incidence of hypoglycemia requiring hospitalization from 2010 to 2015. Although incidence of hypoglycemia requiring hospitalization decreased, absolute number of hypoglycemia-related admission is still a major burden. Interventional strategies to reduce the hypoglycemia-related hospitalization should be implemented particularly for older women with multiple comorbidities.

OP29   Clinical diabetes and therapeutics

Prevalence of metabolic syndrome and its risk factors in Mongolian population: Fourth national WHO STEPS Survey of Noncommunicable diseases

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Objective: To determine prevalence of the metabolic syndrome (MetS) and its related risk factors in Mongolian population.

Methods: In 2019, the 4th national STEPS survey was conducted in 377 sampling units using WHO STEP wise approach to estimate the prevalence of lifestyle-related primary and intermediate-risk factors for developing non-communicable diseases. Randomly selected 6654 Mongolians aged 15-69 were involved in this study. MetS was diagnosed when the presence of central obesity (waist circumference: for men≥90 cm, women≥80 cm), in addition to two or more of the other four factors for the IDF definition of MetS: central obesity, raised triglycerides ≥150 mg/dl, low HDL-cholesterol (<1.03 mmol/l and <1.29 mmol/l in men and women separately), blood pressure ≥130/≥85 mm Hg, and diabetes or fasting glucose >5.6 mmol/l.

Results: MetS was present in 1851 (28.6%) subjects; prevalence was 26.8% (784) in men and 30.4% (1078) in women (p<0.05). There was a significant age-related increase in its prevalence (p<0.05) showing the prevalence of MetS was relatively common in people aged 45-69-year-old. Furthermore, the prevalence of MetS was significantly high in urban (30.5%) when compared to rural area (25.4%). Among components of MetS, central obesity and increased blood pressure was common in Mongolian population. The prevalence of central obesity and increased blood pressure was 53.0% and 44.0% respectively. Regard to other lifestyle-related risk factors, the prevalence of physical inactivity, lower daily consumption of fruits and vegetables and smoking was greater among Mongolian people. In accordance with the presence of unhealthy-lifestyle, one in three of 15-69 years-old people and one in two of 45-69 years-old people had high risk of non-communicable diseases. Above mentioned lifestyle-related risk factors were common in the metabolic syndrome group (p<0.05).

Conclusion: The prevalence of metabolic syndrome was 28.6% in Mongolian population. Implementation of lifestyle-related prevention should be at this high-risk people.

OP30   Clinical diabetes and therapeutics

Co Q10 improves vascular reactivity in male diabetic rats by enhancing insulin sensitivity and antioxidant effect

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Objective: To investigate the potentiating effect of Co-Q10 with insulin in treatment of diabetes and to study its effect on vascular reactivity and metabolic parameters in diabetic rats.

Methods: Fifty male albino rats were divided into five groups, control, diabetic untreated, diabetic insulin-treated, diabetic Co-Q10-treated, and diabetic combined-treated groups. After 8 weeks rats were anesthetized to measure the in-vivo aortic blood pressure and vascular reactivity to norepinephrine (NE) and Acetylcholine (Ach). Then serum samples were taken to measure fasting glucose, fasting insulin, C-peptide, malondialdehyde (MDA) and antioxidant level using Tatal antioxidant capacity(TAC). Also, blood samples for estimation of glycosylated Hb (HbA1c) and the homeostasis model assessment- Insulin Resistance (HOMA-IR) was calculated.

Results: Diabetic untreated group showed significant increase in fasting blood glucose, HbA1c, HOMA-IR, C-peptide, MDA, blood pressure parameters and a significant decrease in TAC and vascular reactivity to NE and Ach. Insulin treatment of diabetic rats significantly improved theses parameters compared to diabetic untreated group. Co-Q10 treatment of diabetic rats ameliorated these effects with marked reduction in HOMA-IR and increasing the antioxidant level compared to diabetic untreated group.

Conclusion: Combined intake of Co-Q10 with insulin in the treatment of diabetes is beneficial to reduce the dose of given insulin as it decreased the insulin resistance with better metabolic control. Also, it has a strong antioxidant effect with an improvement of vascular reactivity to both NE & Ach that protects the diabetic patient from cardiovascular complications

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OP31   Clinical diabetes and therapeutics

Association of plasma branched-chain amino acids with patients of type 2 diabetes mellitus among Indian population - A case control study

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Objective: Amino acids have a vital role in protein synthesis and are also important intermediaries of intracellular signalling for cell growth. Among the amino acids, branched-chain amino acids (BCAAs) are essential amino acids viz leucine, isoleucine and valine and they are catabolized in both liver and skeletal muscles. Over the past few years, plasma BCAAs are linked to metabolic disease, but their relevance for the prediction of type 2 diabetes mellitus (T2DM) development is unclear. Most of the studies on the association of plasma BCAAs and T2DM have been done on western populations, while evidence in Asian populations is sparse and also ethnic differences in patterns of associations between amino acids and T2DM have been observed. The objective of the study is to determine the plasma branched-chain amino acids (BCAA) and their association with insulin resistance in patients with T2DM among Indian adults.

Methods: In this analytical cross-sectional study, a total of 100 subjects were studied and blood samples were subjected for glucose, insulin and BCAAs analysis. Insulin resistance was estimated by homeostasis model assessment (HOMA) and BCAAs association with HOMA of insulin resistance (HOMA-IR) were assessed using Spearmen Rank Correlation.

Results: Our study has shown a significant increase in FBS (p<0.001) and HOMA-IR (p < 0.001) in patients with T2DM compared to healthy controls. The plasma levels of BCAAs were significantly higher (p=0.03) in subjects with type 2 diabetes than in control subjects. Spearman Rank Correlation analyses revealed a non-significant (p=0.21) but positive association between BCAAs and type 2 diabetes (Rho: 0.27).

Conclusion: The high concentrations of BCAAs in T2DM supports the findings in the western population and BCAAs may serve as a novel biomarker for T2DM and could be involved in unknown pathways in type 2 diabetes pathophysiology.

OP32   Clinical diabetes and therapeutics

The Effects of Glucose Lowering Agents on Secondary Prevention of Coronary Artery Disease in Patients with Type 2 Diabetes

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Objective: Patients with diabetes have worse outcome after primary PCI (percutaneous coronary intervention) and have higher risk of repeated PCI compared to patients without diabetes. This study sought to evaluate and compare the effects of anti-diabetic drugs on secondary prevention of myocardial infarction among patients with type 2 diabetes mellitus (T2DM).

Methods: We analyzed the general health check-up dataset and claim data of the Korean National Health Insurance Service (NHIS) of 199,714 diabetic participants (age ≥ 30) who underwent PCI between 2010 and 2013. Those who underwent PCI within 1 year from the date of their first PCI (n=38,541) and those who expired within 1 year (n=36,452) were excluded. Participants were classified according to their prescription records of glucose lowering agents. The primary endpoint was the incidence rate of coronary revascularization and study participants were followed up from 2010 to 2017.

Results: A total of 35,348 patients were analyzed in this study. Metformin and dipeptidyl peptidase-4 inhibitor (DPP-4i) significantly decreased the risks of revascularization in total study population (adjusted hazard ratio [aHR] 0.744, and 0.926, respectively; p < 0.001). In obese patients with body mass index (BMI) ≥ 25 kg/m2, the patients treated with TZD exhibited decreased risk of revascularization than those who were not treated with TZD (aHR 0.789, 95% CI 0.64 - 0.973). Patients who were treated with metformin and DPP-4i showed decreased risk of revascularization regardless of their BMI.

Conclusion: The risk of repeated revascularization was lower in diabetic patients treated with metformin and DPP-4i, and in obese patients treated with TZD compared to those who did not treated with each agents. This results suggest that physicians should choose appropriate glucose lowering agents for the secondary prevention of coronary artery disease.

OP33   Clinical diabetes and therapeutics

Effect of Ranolazine on Glycemic Control in Diabetic Patients: A meta-analysis

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Objective: Severel strudies reported ranolazine is an antianginal drug with hypoglycemic effects. We conduct meta-analysis of randomized controlled trials (RCTs) to assess the effect of ranolazine on glycemic control for adults with diabetes.

Methods: Two databases, including PubMed and Cochrane Library, were systematically searched for literature until June 2020 to find RCTs which compared the effect of ranolazine versus placebo on haemoglobin A1c (HbA1c) and/or fasting plasma glucose (FPG). We used mean differences in HbA1c and FPG and analyzed the data with random-effects model for meta-analyses using Revman 5.3.

Results: Four RCTs involving 2675 participants were included in the meta-analysis. The result suggested that ranolazine has significant different on HbA1c -0.47% (95% CI -0.55% to -0.39%; p⟨0.00001). There was no significant difference in FPG between ranolazine and placebo groups (-2.86 mmol/L, 95% CI -9.54 to 3.82; p=0.40).

Conclusion: Ranolazine improves glycemic control by significantly improves HbA1c.

OP34   Diabetes care & Education

The impact of COVID 19 pandemic and Economic status on diabetes care in Sudan, 2020

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Objective: The whole world is facing the current COVID-19 pandemic, the most serious health crisis in modern times. This pandemic affects all people but it's serious in the case of diabetes. Although Sudan has a well-established healthcare system, yet it has so many drawbacks mainly due to economic and managerial reasons. The aim of this study is to give an insight over the diabetes care in Sudan, Assess the patient's access to medications, and assess the situation from both economic status and patients prospective.

Methods: This research was done from many electronic databases: Ministry of health and WHO Sudan reports and direct observation from hospitals and public pharmacies.

Results: The economic situation of Sudan and COVID 19 crisis led to a negative impact on nutrition; Since the implementation of the complete curfew in Sudan, the closure of markets, lack of vegetables, fruits, and the lack of basic food, led to poor nutritional states in diabetics. It also affected Daily exercises which are one of the most important parts of treatment, as curfew reduced the daily exercise; resulted in failure to regulate blood sugar levels. And it also affected the patients follow up due to decrease in medical staff in hospitals and closure of most follow up clinics by 62%. It also affected the Availability of the medications; treatment was deficient in all hospitals and pharmacies by 65%, which led to the monopoly of the remaining medicines and sold at a double price.

Conclusion: Due to the Covid-19 crisis and the bad economic status of the country, lack of healthy food, poor follow up and unavailability of medications; Diabetic patients face a higher chances of experiencing serious complications especially when infected with the virus.

OP35   Diabetes care & Education

Self-Glucose Monitoring Among Cambodian Diabetic Patients Using Diabetic Health App "CarnetDia"

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Objective: CarnetDia App is the first Diabetic Health App developed in Cambodia and released to the public since September 2018. CarnetDia App aims to raise the awareness among Cambodians. And patients could register and record their glycemia in order to send to their healthcare providers. Diabetic Mobile Health Apps have been increasingly applied in diabetes self-monitoring. And it appears that those technologies could effectively help patients to manage their diabetes. However not all diabetic patients are able to use those tools. This study was to analyze the frequencies and timetables of self-blood glucose monitoring among Cambodian diabetic patients using CarnetDia App.

Methods: We analyzed the records of the patients who registered and recorded their glycemia in CarnetDia App. Since the release in September 2018 there were 4.943 users (iOS 2.473 and Android 2.470).

Results: Among 4.943 users, there have been 779 users who have registered to record their glycemia (Male 72% Female 28%). According to the age groups we observed: 10-19y: 9, 20-29y: 171, 30-39y: 238, 40-49y: 93, 50-59y: 131, 60-69y 114, 70-79y: 17, ⟩ 80y: 6. On average patients had 2 or 3 glycemia checked per week and most of it done before breakfast. Timetables of checked glycemia before meals: before breakfast 64%, before lunch 3% and before dinner 11%. Timetables of checked glycemia after meals and others: 2H after breakfast 5%, 2H after lunch 6%, 2H after dinner 10% and before going to bed 1%. The geographic distribution of the registered users: 70% live in the capital and 30% live in diferrent provinces.

Conclusion: We observed that on average the registered users self-checked the glycemia 2 or 3 times a week but overwhelmingly did before breakfast. It seemed that younger patients (from 30-39 years old) have temptations to record their glycemia in the cellphone more than older patients.

OP36   Diabetes care & Education

Effects of Social Distancing on Diabetes Self-management in Elderly Diabetes during COVID-19 Pandemic

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Objective: From March 22, 2020 to May, 2020, intense social distancing was implemented in South Korea, and so far, the South Korean government has decided to maintain its social distancing although easing some restrictions. The aims of this study were to examine the impact of social distancing on glycemic control and physical activity in older adults with diabetes.

Methods: Adults aged 60 to 90 who had type 2 diabetes and blood glucose tests from March to June 2019 and those who performed follow-up blood glucose test from May to July 2020, were asked questions in the International Physical Activity Questionnaire (IPAQ). The results of blood glucose tests of March to June 2019 and April to July 2020 were compared.

Results: A total of 96 men and 133 women (Mean 73.6 year, SD=7.4) participated in this survey. Total physical activity was reduced by COVID-19 social distancing (1755 MET-min/week vs 2296 MET-min/week, p⟨0.01). The levels of glycated hemoglobin (7.4±1.0% vs 7.2±0.9, p=0.00) and fasting glucose (139.29±33.5 vs 133.5±28.0 mg/dL, p=0.01) in 2020 were increased compared to year 2019, respectively.

Conclusion: Social distancing during COVID-19 pandemic caused negative effects in diabetes self-management in elderly patients with type 2 diabetes.

OP37 Diabetes complications- basic & translational

Early-Life Famine Exposure and Risk of Cardiovascular Diseases in Later Life: Findings From the REACTION Study

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Objective: Previous studies reported that early-life exposure to undernutrition is associated with the risk of diabetes mellitus and metabolic syndrome in adulthood, but the association with risk of cardiovascular disease (CVD) later in life remains unclear. The current study aimed to investigate whether exposure to Chinese famine in early life is associated with risk of CVD.

Methods: We used data from REACTION (Risk Evaluation of Cancers in Chinese Diabetic Individuals: A Longitudinal) Study, which recruited a total of 259 657 community-dwelling adults aged 40 years or older from 25 centers across mainland China between 2011 and 2012.

Results: Compared with the nonexposed participants, those who had been exposed to famine in early life had a significantly increased risk of total CVD, myocardial infarction, stroke, and coronary heart disease. In the multivariable-adjusted logistic regression model, the odds ratios (95% CI) for total CVD, myocardial infarction, stroke, and coronary heart disease in fetal famine exposure were 1.35 (1.20-1.52), 1.59 (1.08-2.35), 1.40 (1.11-1.78), and 1.44 (1.26- 1.65), respectively; those odds ratios in childhood famine exposure were 1.59 (1.40-1.81), 2.20 (1.52-3.20), 1.82 (1.45-2.28), and 1.80 (1.56-2.09), respectively; and those in adolescent famine exposure were 1.52 (1.27-1.81), 2.07 (1.28-3.35), 1.92 (1.42-2.58), and 1.83 (1.50-2.24), respectively. The main finding of our study is that, compared with those who lived in the less severely affected famine area, individuals in the severely affected famine area had significantly increased risk of total CVD in all 3 exposed groups.

Conclusion: Early-life exposure to undernutrition is associated with significantly increased risk of CVD in later life, especially among those who were in the severely affected famine area.

OP38 Diabetes complications- basic & translational

Oral Administration of Palm Oil-derived Tocotrienol-Rich Fraction Reduces Retinal Oxidative Stress in Rat Model of Streptozotocin-Induced Diabetic Retinopathy

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Objective: The second commonest microvascular complication in diabetes mellitus is diabetic retinopathy (DR). Neurodegeneration during early DR development is associated with oxidative stress (OS), which is prominent with chronic hyperglycemia. Palm oil-derived tocotrienol-rich fractions (TRF), a potent antioxidant, may provide protection against DR development. Therefore, we investigated the effect of TRF on the expression of retinal antioxidants and extent of lipid peroxidation in rats with streptozotocin-induced diabetic retinopathy.

Methods: Male Sprague-Dawley rats weighing 200-250 grams were divided into normal control rats (N) which was injected intraperitoneally with citrate buffer and rats which were injected intraperitoneally with streptozotocin (55 mg/kg body weight). STZ-injected rats with blood glucose of more than 20mmol/L were considered diabetic. Diabetic rats were further subdivided to diabetic-control (DV) and diabetic-treated (DT) groups. N and DV group received vehicle treatment, whereas DT received TRF treatment (100 mg/kg body weight) via oral gavage daily for 12 weeks. At the end of experimental period, rats were euthanized, and retinal tissues were collected for hematoxylin and eosin (H&E) staining and immunoassay for detection of reduced glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD). Retinal lipid peroxidation level was also measured by estimating malondialdehyde (MDA) level.

Results: Retinal morphometric analysis from H&E staining showed reduction in retinal cell count (RCC) of DV compared to N (p<0.01), whereas DT showed increased RCC compared to DV (p<0.05). Higher retinal GSH level was seen in DT compared to DV (p<0.05), and this was comparable to that in N. Similar observations were also found for the CAT and SOD levels. Lower retinal MDA level was seen in N and DT compared to DV (p<0.001).

Conclusion: Oral administration of TRF reduces retinal lipid peroxidation and increases retinal antioxidants levels in rats with streptozotocin-induced diabetic retinopathy, which in turn seems to restore normal RCC and morphology.

OP39 Diabetes complications-clinical

Total iron intake per se and the relative intake to polyunsaturated fatty acid, and diabetic peripheral neuropathy

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Objective: The associations of iron intake, polyunsaturated fatty acid (PUFA) intake and complications of diabetic peripheral neuropathy (DPN) has not been studied. We investigated the associations of iron intake, PUFA intake and risk of DPN.

Methods: We analyzed the data of 147 subjects with type 2 diabetes from an ongoing prospective observational study. Dietary nutrient intake was estimated using 3-day food records. DPN was diagnosed using the Michigan Neuropathy Screening Instrument-Physical Exemination (MNSI-PE) ≥ 2.5. Dietary nutrients were compared between subjects with or without DPN by analysis of covariance adjusting total energy intake. The association between dietary iron intake, iron to PUFA ratio (iron/PUFA) with the presence of DPN was analyzed using logistic regression models.

Results: The prevalence of DPN was 46.3%. Iron intake after adjusting for total energy intake was significantly higher in subjects with DPN compared to those without DPN (9.9 ± 3.6 vs. 10.9 ± 4.0, p = 0.041). In addition, iron /PUFA was significantly higher in subjects with DPN (1.1 ± 0.4 vs. 1.4 ± 0.8, p = 0.005). MNSI-PE scores were positively correlated with iron intake (r = 0.189, p = 0.022) and iron/PUFA (r = 0.276, p = 0.001). In the logistic regression analysis, we found that iron intake was associated with the risk of DPN after adjustment for total energy intake, sex, age, BMI, SBP, diabetes duration, HbA1c, and HOMA-IR (OR 1.138 [95% CI 1.002 1.292] p = 0.046). We also found the significant association between the iron/PUFA and the presence of DPN (OR 2.400 [95% CI 1.157 4.982] p = 0.019).

Conclusion: Dietary iron intake and the relative iron intake to PUFA was associated with DPN. The present study suggested the importance of dietary iron intake pattern in subjects with DPN, and it might be a possible intervention target for preventing or treating DPN.

OP40 Diabetes complications-clinical

Correlation between serum low density lipoprotein cholesterol levels and cognitive functions of type 2 diabetes mellitus patients: A cross-sectional study

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Objective: While cholesterol is essential for cognitive function, elevated cholesterol is associated with cognitive impairment. We aim to investigate the association between serum cholesterol, especially for low density lipoprotein cholesterol (LDL-C) levels and cognitive functions of type 2 diabetes mellitus (T2DM) patients.

Methods: 196 patients with T2DM were recruited. 3-hydroxy-3-methylglutaryl CoA reductase (HMG-CoA reductase) levels were measured. Clinical parameters and neuropsychological tests were compared between mild cognitive impairment (MCI) patients and controls. Goodness of fit was accessed to determine the linear or U-shaped relationship between cholesterol and cognitive function. Correlation and regression were curry to explore the relationship between cognition decline and cholesterol.

Results: Although no significance of HMG-CoA reductase, total cholesterol (TC), and LDL-C levels were detected in 77 patients with MCI, compared with 119 patients without MCI, HMG-CoA reductase is significantly associate to TC, LDL-C and MoCA. Inverted-U-shaped association was determined between LDL-C and MoCA. Additionally, the cut point of LDL-C is 2.79 mmol/l. Each unit increment/decrement of LDL-C increased the MCI risk by 60.8% or 139.1% above or below the cut point receptively. LDL-C is positively related to Trail Making Test B (TMTB), while negatively associated to Auditory Verbal Learning test-delayed recall (AVLT-DR) in patients with LDL-C (>2.79 mmol/l). Moreover, LDL-C (<2.79 mmol/l) is positively associated with Clock Drawing Test (CDT).

Conclusion: Inverted-U-shaped correlation between serum LDL-C and global cognitive function exist in T2DM patients. While higher LDL-C damage executive function and scene memory, lower LDL-C impairs visual space function.

OP41 Diabetes complications-clinical

SGLT2 Inhibitor Prescription Pattern In Diabetic Kidney Disease In A Real-World Setting

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Objective: For patients with type 2 diabetes(T2D) and diabetic kidney disease(DKD), a sodium-glucose cotransporter 2 inhibitor(SGLT2i) should be considered in patients with an estimated glomerular filtration rate(eGFR) ≥30 mL/min/1.73 m2 and urinary albumin ⟩30 mg/g creatinine. In this study, we analyzed the prescription patterns of glucose-lowering medications in T2D according to chronic kidney disease (CKD) stage in real practice.

Methods: During six months (2019~2020), we reviewed 3673 consecutive T2D patients visiting an endocrinology outpatient clinic from four teaching hospitals in Seoul Metropolitan Area, Korea. We classified DKD based on the eGFR and albuminuria (A1, ⟨30; A2, 30-299; A3, ⟩300mg/g). There were CKD stage 1=50%; 2=37%; 3=11%; 4&5=2.5%, respectively. Atherosclerotic cardiovascular disease (ASCVD) or heart failure(HF) status in each CKD stage was 24%, 38%, 51%, 68%, respectively.

Results: Overall, there were 931(25%) SGLT2i initiators. SGLT2i initiators in each CKD stage and albuminuria (A1; A2; A3) category was as follows. CKD 1 (30%; 48%; 44%); CKD 2 (18%; 25%; 35%); CKD 3 (9%; 8%; 12%). A2 or A3 with eGFR ≥30 (n=976) was analyzed according to SGLT2i use. ASCVD characteristics in this group were coronary artery disease 25%, stroke 15%, heart failure 3%, and peripheral arterial occlusive disease 2%. In this high-risk group, compared with SGLT2i non-users, SGLT2i initiators (n=303, 31%) was tended to be younger (56 vs. 66) and with higher heart failure(6 vs. 2%). They also had higher BMI (28 vs. 26), worse HbA1C levels (8.1 vs. 7.5), and higher eGFR (90 vs. 74). ASCVD was comparable (33 vs. 38%).

Conclusion: In contrast to clinical guidelines, a small proportion of T2D with CKD is currently treated with SGLT2i in real-world clinical practice. Physicians still take a glucocenric approach instead of focusing on reducing renal events. Other limiting factors for failing to initiate SGLT2i are old age and lower eGFR.

OP42 Diabetes complications-clinical

The Long-term Risk of Altered Hepatic Steatosis Status on Type 2 Diabetes Mellitus: a Community-based 15-year Prospective Cohort Study

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Objective: We investigated the long-term effects of changes in hepatic steatosis (HS) status on incident type 2 diabetes mellitus (T2DM).

Methods: The study included 3,512 subjects drawn from the 2001-2016 Korean Genome and Epidemiology Study. Participants with alcohol consumption ⟩ 40 g/day (⟩ 20 g/day for women) and those with T2DM at baseline were excluded. HS was defined as a liver fat score (LFS) ⟩ -0.64 or HS index (HSI) ≥ 36. Changes in HS status were assessed using LFS and HSI values from the 2001-2002 and 2003-2004 surveys divided into four groups: sustained healthy liver, improved HS, progression of HS, and persistent HS. The 15-year T2DM risk according to HS status was assessed by Cox-regression analysis after adjusting for covariates.

Results: T2DM developed in 200 participants (5.7%) after a mean of 13.4 years (range, 4-15 years). As HS status worsened, the incidence and risk of T2DM increased (p for trend ⟨ 0.001, based on LFS and HSI data). The risk of T2DM was higher in those who ever had HS than the sustained healthy liver group (LFS: hazard ratio [HR], 1.832-2.799 and HSI: 2.380-3.132, p ⟨ 0.05 compared with the remaining groups). The persistent HS group was at higher risk of developing T2DM than the improved HS group (HR = 1.876 based on LFS, p⟨0.05).

Conclusion: Changes in HS status differently affect the risk of T2DM. Although maintenance of a healthy liver is ideal, efforts made to improve HS reduce the risk of incident T2DM.

OP43 Diabetes complications-clinical

Association of coronary artery calcification with atherosclerotic carotid artery and increased brachial-ankle pulse wave velocity in patients with type 2 diabetes mellitus: A cross-sectional study

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Objective: No single surrogate marker for atherosclerosis is recommended for the prediction of cardiovascular disease (CVD) in patients with diabetes as yet. We analyzed the relationship between coronary artery calcium score(CACS) and intima-media thickness (cIMT), plaques in carotid artery and brachial-ankle pulse wave velocity(baPWV) in patients with type 2 diabetes without underlying CVD history.

Methods: In 1,058 patients with type 2 diabetes without underlying CVD (mean age 58 years) who attended department of endocrinology and metabolism, Kangbuk Samsung Hospital in Korea between January 2008 and December 2014, in whom CACS were measured, relationship between CACS and cIMT of right common carotid artery, total number of carotid artery plaques and right baPWV were analyzed. Presence of coronary artery calcification (CAC) was defined by CACS⟩0. CACS was measured by multi-detector computed tomography and cIMT and presence of carotid plaques were assessed by carotid ultrasonogram.

Results: Of the 1,058 subjects, 485 (45.8%) had CAC. In a multivariable-adjusted model, the odds ratio (OR) for CAC increased as the quartiles of cIMT increased (OR 1.160, 95% CI 1.448~1.669 for 4th quartile of cIMT). The risk of CAC also increased as baPWV levels increased as the quartiles of baPWV increased (OR 1.693, 95% CI 1.056~2.716 for 4th quartile of rt baPWV). The increasing number of carotid plaques was associated with significantly increased risk for CAC (OR 18.763, 95% CI 4.3~81.876 for ≥4 plaques).

Conclusion: Increasing number of carotid plaques, cIMT and baPWV valuse were positively associated with CAC risk in a large number of Korean patients with type 2 diabetes and without underlying CVD history. Among them, the number of carotid artery plaques showed most significant association with presence of CAC.

OP44 Diabetes complications-clinical

Novel Classification of Adult-onset Diabetes Mellitus in Korea

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Objective: Due to its heterogeneous traits, type 2 diabetes needs to be more specifically classified. We conducted subgroup analysis for Korean diabetes and compared the characteristics and diabetic complications between each subgroup.

Methods: We enrolled 57,105 patients with diabetes who visited Seoul National University Hospital between 2004~2019. We conducted cluster analysis using k-means clustering based on five variables including age, body mass index, HbA1c, and homeostatic model assessment 2 of β-cell function and insulin resistance at the first visit. Diabetic kidney disease was defined by the urine albumin to creatinine ratio and glomerular filtration rate. Coronary artery disease and stroke were assessed by using procedures and International Classification of Disease-10 codes.

Results: Among 18,715 patients who had all the variables for clustering, patients clinically diagnosed type 1 diabetes and latent autoimmune diabetes in adults were classified to cluster 1;severe autoimmune diabetes (n=640, 3.5%). Other type 2 diabetes patients were sub-classified to cluster 2;severe insulin-deficient diabetes (n=3206, 17.3%), cluster 3;severe insulin-resistant diabetes (n=1661, 8.9%), cluster 4;mild obesity-related diabetes (n=4459, 24.1%), and cluster 5;mild age-related diabetes (n=8566, 46.2%). During the median 6.3 years of follow up, patients in cluster 3 had significantly higher risk of diabetic kidney disease–albuminuria (Hazard ratio 2.41, 95% confidence interval 2.03~2.87), chronic kidney disease at least stage 3A (2.64, 2.36~2.96) and end-stage renal disease (8.32, 6.62~10.47)–compared to cluster 5, even though the glycemic control assessed by HbA1c was comparable. Patients in cluster 3 had 1.4 times higher of coronary artery disease (1.43, 1.19~1.72) and 1.5 times higher of stroke (1.54, 1.25~1.91) than did patients in cluster 5.

Conclusion: We classified Korean diabetes into five subgroups with different characteristics and risk of diabetic complications. Individuals in cluster 3 with severe insulin-resistant diabetes had significantly higher risk of diabetic kidney disease and macrovascular complications than individuals in cluster 4 and 5 with similar HbA1c.

OP45   Diabetes complications-clinical

Mild cognitive impairment and type 2 diabetes in Elderly Mongolians: initial results

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Objective: To investigate the association of type 2 diabetes (T2D) with the presence of mild cognitive impairment (MCI) in elderly Mongolians and to investigate the vascular shifts in MRI examination in people with suspected MCI.

Methods: In this hospital-based study, we involved 65 patients aged 60 years and older. Upon obtaining the informed consent, each subject was interviewed and screened for T2D. The mini-mental state examination (MMSE) was used to assess cognitive function in each subject. MRI examinations were performed at different institutions on 1.5-T MRI scanner. Regression analyses were performed to evaluate risk of MCI with T2DM.

Results: MCI was present in 24 (36.9%) subjects and the mean score of MMSE was 23.9±0.6 (range of 9 and 30). Compared with people with diabetes, the prevalence of MCI in the present study was more frequent than the prevalence of MCI for the people without diabetes in almost same ages (mean age was 65.3±6.4 and 67.1±6.1 in people with and without TDM, p>0.05): prevalence of MCI was 42.3% and 31.3% in people with and without diabetes respectively (p

Conclusion: The present study shows the high prevalence of MCI with T2DM among the elderly Mongolians. Our study reveals needs for further large-scale interdisciplinary investigations, especially on vascular MCI to fully elucidate the problem of early diagnosis in dementia in Mongolia.

OP46   Clinical diabetes and therapeutics

Efficacy and Safety of monotherapy with Enavogliflozin in Korean Patients with Type 2 Diabetes Mellitus: Results of a 14 week, multi-center, randomized, double-blind, placebo-controlled, phase 2 trial

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Objective: The aim of this study was to evaluate the efficacy and safety of enavogliflozin, a newly developed sodium-glucose co-transporter 2 inhibitor, compared with placebo in patients with Korean type 2 diabetes mellitus (T2DM).

Methods: Participants with glycated hemoglobin (HbA1c) of 7.0-10.0%, entered a 2-week, single-blind, placebo run-in period, followed by a 12-week, double-blind period during which participants were randomized 1:1:1:1 to receive enavogliflozin (0.1, 0.3, or 0.5mg) or placebo. The primary efficacy endpoint was the change from baseline in HbA1c at week 12. Pre-specified secondary endpoints included change in fasting plasma glucose (FPG), proportion of patients reaching HbA1c <7.0%, and proportion of patients achieving a reduction of >0.5% of HbA1c. Adverse events (AEs) were recorded throughout the study.

Results: Overall, 194 patients were included in the full analysis set (placebo: n=46, enavogliflozin 0.1mg: n=49, enavogliflozin 0.3mg: n=50, enavogliflozin 0.5mg: n=49). Patients with 0.1, 0.3, and 0.5mg enavogliflozin significantly reduced HbA1c compared with placebo at week 12 (-0.79%, -0.89%, -0.92%, -0.08%, respectively; P <0.001). Mean change of FPG from baseline at week 12 were -30.0 ± 28.0 mg/dL, -31.5 ± 29.3 mg/dL, -27.9 ± 33.3 mg/dL and 1.96 ± 19.2 mg/dL in patients with the enavogliflozin 0.1, 0.3, 0.5mg and placebo, respectively. The proportion of patients reaching HbA1c <7.0% were significantly higher in the enavogliflozin 0.1, 0.3, and 0.5mg groups than in the placebo group (42.9%, 44.0%, 61.2%, 17.4%, respectively). More patients had HbA1c reduction >0.5% with enavogliflozin 0.1, 0.3, and 0.5mg versus placebo (61.2%, 72.0%, 65.3%, 26.1%, respectively). Overall AEs were reported in 20.4%, 16.0%, 22.0%, and 16.0% with enavogliflozin 0.1, 0.3, and 0.5mg and placebo, respectively. The incidence of hypoglycemia and genital infection were similar across groups.

Conclusion: Once-daily enavogliflozin monotherapy for 12 weeks was an effective, safe and well-tolerated treatment for Korean patients with T2DM.

Poster exhibitions

Correlation Between Malondialdehyde Levels and Dismutase Superoxide Activity of Testicular Organs After Intervention of Fermented and Non-Fermented Soybean Milk (Glycine max) in Hyperlipidemic Rats

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Objective: Hyperlipidemia is a risk factor for type 2 diabetes mellitus. Oxidative stress in hyperlipid condition can correlate with levels of malondialdehyde (MDA) and superoxide dismutase (SOD) activity. Increased oxidative stress results in damage to testicular cells and the risk of infertility. This study aimed to determine the correlation of MDA levels and SOD activity in the testicular organs of hyperlipidemia rat after intervention with fermented and non-fermented soy milk (Glycine max).

Methods: The subjects are male Wistar (Rattus norvegicus) strain rats 2-3 months with body weight 200-300 grams divided into 4 groups (K+, K-, P1, and P2). Group of K+, P1, and P2 were given quail egg yolk for 2 weeks with a dose of 5 ml while a group of K- were only given fed ad libitum. For the next 2 weeks, P1 group was given non-fermented soy milk (5 ml), and fermented soy milk (5 ml) for P2 group. All rats terminated to taken the testicular organ to measure the level of MDA and SOD activity. All data were statistically analyzed with one way ANOVA and Pearson test for the correlation. Values were considered significant at p⟨0,05.

Results: Mean of MDA level (nmol/gram) in rats was 0,95 ± 0,75 in K-group, 8,64 ± 0,13 in K+ group, 4,20 ± 0,93 in P1 group, 2,12 ± 0,18 38 in P2 group. Mean of SOD activity (%) in rats was 82,03 ± 1,62, 17,97 ± 2,06, 53,51 ± 2,15 and 70,31 ± 2,38. The One-Way ANOVA test showed significant differences activity between group with p⟨0,001 and Post Hoc test p⟨0,001. Pearson test of MDA level and SOD activity showed negative correlation with p⟨0,001 and r=-0.985.

Conclusion: There is a negative correlation between malondialdehyde levels and superoxide dismutase activity in the testicular organs of hyperlipidemic rats.

A Porous Microcarrier with External/interconnected Architecture for Cultivation of Pancreatic β Cell Spheroids

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Objective: Developing cellular products to treat type 1 diabetes mellitus (T1DM) faces the unique challenge of autoimmunity. It would be ideal to protect transplanted β cells with engineered materials.

Methods: We fabricated the desired microcarriers by using a coaxially assembly capillary microfluidic device for 3D culture of islet organoids. In this system, silicone oil was utilized as the inner and outer phase, while Na-alginate and poly ethylene glycol diacrylate (PEGDA) hybrid solution was employed as the middle phase. Cell viability of islet organoids during the long-term culture was tested. The glucose-stimulated insulin release (GSIS) and potassium-stimulated insulin secretion (KSIS) assays were carried out for the evaluation of the glucose responsiveness of β cells in the microcarriers.

Results: A porous microcarrier was produced utilizing a simple capillary microfluidic device for the culture of pancreatic β cells, with external/interconnected cores encapsulated in the hydrogel. Due to the architecture of microcarriers, the exchange of necessary substances such as nutrient and oxygen were facilitated, this promoted the formation of 3D islet multicellular spheroids. The cells exhibited a better cell viability than those cultured in matrigel without microcarriers, ascribing to the spherical architecture of cells. The islet multicellular spheroids exhibited more sensitive GSIS response, and the result of KSIS assay was consistent with the GSIS assay, indicating the maturation of islet organoids. It was not only attributed to the 3D architecture of the microcarriers, but also the assistant of the connected windows for the informational communication.

Conclusion: The communicational efficiency among multicellular spheroids was reinforced by small-scale windows between the cores, bolstering the function of β cells. The characters made the novel microcarrier we proposed promising for the cultivation of islet organoids, the tissue engineering and the regenerative medicine, drug screening and cell therapy for diabetes care.

Protein oxidation is increased among Filipinos with Gestational Diabetes Mellitus

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Objective: Gestational diabetes mellitus (GDM) is an idiopathic disorder affecting 18 million pregnant women annually with cases still on the rise. Despite the recognized associated complications of GDM, its pathophysiological mechanism remains unclear. Findings have suggested that oxidative stress (OS) is significantly increased in GDM, which may have considerable clinical implications in the pathophysiology of GDM. This study aims to evaluate the maternal blood oxidative stress in GDM and non-GDM pregnant women.

Methods: A cross-sectional study was conducted involving pregnant women on their 2nd or 3rd trimester of gestation (n=60; 30 with GDM, 30 non-GDM). Plasma protein carbonyl (PC) was measured using DNPH assay to assess protein oxidative damage. Plasma 8-hydroxy-2'-deoxyguanosine (8-OHdG) was assayed through ELISA to determine DNA oxidative damage, and total antioxidant capacity (TAC) was evaluated using a colorimetric assay to determine the antioxidative defense.

Results: Higher plasma protein carbonyl was observed in the GDM group indicating a higher protein oxidative damage than the non-GDM group (p=.0059). 8-OHdG and TAC levels did not differ significantly among the two groups (p=⟩0.05).

Conclusion: These findings may suggest that oxidation status is increased in GDM, especially protein oxidation, which may contribute to the pathophysiology of GDM.

Role of sirtuin-1 (SIRT1) in hypoxic injury in pancreatic β-cells

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Objective: β-cells are highly sensitive to hypoxic damage due to their high oxygen dependence. β-cells exposed to hypoxia can be fatally damaged in some circumstances by several mechanisms. We investigated the role of sirtuin-1 (SIRT1) under hypoxic injury in INS-1 cells.

Methods: To induce hypoxic damage in INS-1 cells, we used an anaerobic chamber system. SRT1720 (1 mM) and GW4064 (100 nM) were used as SIRT1 activator. For suppression of SIRT1 expression, si-SIRT1(100 pmol/ml) was added. We measured cell viability, apoptosis, the levels of inflammatory cytokines (tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) by ELISA), and reactive oxygen species (ROS, by CM-H2DCFDA) under hypoxic conditions. Real-time PCR and Western blot analysis (SIRT1, FXR, HIF-1α, vascular endothelial growth factor (VEGF), β-actin) were performed.

Results: Cell viability was significantly reduced to 71% and 40% after 4 and 6 h of hypoxic conditions, respectively. Apoptosis increased significantly 2.8-fold and 5.3-fold after 4 and 6 h of hypoxia, respectively. SIRT1, FXR, and VEGF expressions were significantly reduced at the mRNA and protein level during hypoxic treatment. But HIF-1α expression tended to increase as the time in the anaerobic chamber increased. Hypoxic damage significantly increased the TNF-α, IL-6 and ROS levels in INS-1 cells in a time-dependent manner. However, the reduced cell viability and increased inflammatory cytokines levels from hypoxic damage were ameliorated by SIRT1 activation.

Conclusion: SIRT1 activation has shown a protective effect on pancreatic β-cells exposed to hypoxia by attenuating apoptosis, inflammation and the ROS response. We suggest that SIRT1 may play an important role in improving β-cell survival under hypoxic damage.

PE07   Basic & Translational diabetes research

NTS inflammation in high fat diet-induced obesity

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Objective: In the adult rodent brain, POMC- expressing neurons are located in the arcuate nucleus (ARC) and the nucleus tractus solitarius (NTS). Previously, we reported that obese mice on a high-fat diet (HFD) display macrophage accumulation and increased vascular permeability in the hypothalamic arcuate nucleus. However, it remains unclear whether these changes can be also detected in NTS of the HFD-fed mice. Therefore, we investigated whether HFD could increase vascular permeability and inflammation in NTS.

Methods: C57BL/6 (C57) male mice were fed either a standard chow diet or a HFD, and maintained under a controlled temperature with a 12-h light-dark cycle. Following cardiac perfusion and fixation, we conducted immunostaining for Glial fibrillary acidic protein (GFAP) and Ionized calcium- binding adapter molecule 1 (Iba1) to measure HFD- induced neuroinflammation. To evaluate the increase in vascular permeability, we examined extravascular leakage of Evans blue and fluorescein- conjugated lectin.

Results: We observed a significant increase in Iba1 and GFAP immunoreactivity in NTS as well as hypothalamic ARC during chronic HFD feeding, compared with CD fed mice. Also, HFD increased Evans blue and fluorescein- conjugated lectin extravasation due to increased vascular permeability in ARC and NTS.

Conclusion: HFD promotes inflammation and vascular permeability in NTS and hypothalamic ARC. Further studies to understand the molecular mechanisms related with neuronal function would be of interest.

PE08   Basic & Translational diabetes research

Iron overload disturbed pancreatic β cells functions via alteration of Ca+2 homeostasis

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Contents: There are growing evidences that iron overlord is related to the metabolic syndrome, but the underlying mechanisms are still not clearly understood. To examine precise molecular mechanisms of iron overload on the pancreatic β cell functions, we established cell model using INS-1 rat insulinoma pancreatic β cells and studied the effects of iron. By increasing the concentration of Fe-NTA, the accumulation of cellular ferritin and labile iron level were increased, and concomitantly the cell viability was decreased. To determine β cell functions, we measured glucose stimulated insulin secretion (GSIS) in INS-1 cells. While GSIS was already disturbed by 24h treatment of Fe-NTA, the expression of glucose transporter 2 (Glut2) and insulin was reduced by prolonged exposure of iron. Corresponding to the insulin secretion, cellular ATP level, on which insulin secretion is dependent, was drastically reduced by excess iron and recovered by the pre-treatment of iron cheater, DFO. GSIS in pancreatic β cells was initiated by the rapid influx of Ca+2 into the cell. To start over Ca+2 influx signal again, the elevated Ca+2 was promptly sequestered by the calbidin or absorbed into the ER or pumped outside of the cells, thereby low steady state [Ca+2]i is maintained. Therefore, we next examined whether excess iron changes the Ca+2 channels and Ca+2 binding proteins. Excess iron caused up-regulation of IP3R, on the contrary, down-regulation of PMCA, NCX, SERCA and calbindin, which all together resulted in the abnormal elevation of cytosolic steady state [Ca+2]i. Co-treatment of DFO reverted the alterations in the expression patterns of Ca+2 channels, indicating that iron overload specifically disturbed intracellular Ca+2 homeostasis. In conclusion, our results showed that iron accumulation caused alteration of calcium homeostasis and abnormal elevation of steady state [Ca+2]i, thereby induced failure of the pancreatic β cell functions.

PE09   Basic & Translational diabetes research

Association of sEGFR levels with cholesterol in subjects with type 2 diabetes mellitus

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Objective: Relationship between metabolic disorders and serum soluble epidermal growth factor receptor (sEGFR) levels remains poorly understood. The aim of this study was to investigate the relationship between sEGFR and serum lipid profiles in diabetic subjects.

Methods: A total of 161 subjects aged 18 years or older with 103 subjects with newly diagnosed type 2 diabetes mellitus (T2DM) and 58 subjects with normal glucose tolerance (NGT) were recruited from the department of endocrinology at Chungnam National University hospital. We divided diabetic patients into two groups [67 with dyslipidemia group (T2DM with dyslipidemia) and 36 with non-dyslipidemia group (T2DM without dyslipidemia)] according to the NCEP ATP-III criteria of dyslipidemia. Blood samples were collected in the morning after an overnight fast >8 hours. The fasting serum sEGFR level was measured using a quantitative sandwich enzyme immunoassay technique with an enzyme-linked immunosorbent assay (ELISA). Demographic findings and serum sEGFR were compared among three groups. Serum sEGFR were also correlated with clinical factors using linear regression analysis.

Results: There was significant difference of serum sEGFR level among three groups (T2DM with dyslipidemia: 87.0±18.0ng/mL, T2DM without dyslipidemia: 79.8±10.4 ng/mL, NGT: 75.1±19.7 ng/mL, p=0.001), and significant difference was found only in the comparison between DM with dyslipidemia and NGT in the post-hoc analysis (p=0.001). In linear regression analysis, serum sEGFR was significantly correlated with TC (r=0.325, p⟨0.001), LDL-C (r=0.270, p=0.001), HDL-C (r=-0.168, p=0.037), and TGs (r=0.211, p=0.008) in total subjects. HbA1c (r=0.428, p⟨0.001), fasting glucose (r=0.386, p⟨0.001), PP2 glucose (r=0.397, p⟨0.001) also showed significant association with serum sEGFR levels. In multivariate linear regression analysis, both fasting glucose (partial r=0.294, p⟨0.001) and TC (partial r=0.202, p=0.012) were significantly correlated with serum sEGFR.

Conclusion: Serum sEGFR levels are associated with serum lipid and glucose profiles. T2DM and dyslipidemia are important factors affecting serum sEGFR levels.

PE10   Basic & Translational diabetes research

The role of astrocytic primary cilia in prevention of obesity

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Objective: The primary cilia are a microtubule-based hair-like sensory organelle present in the surface of most mammalian cells. They detect extracellular cues and transduce these signals into cells. The dysregulation of primary cilia can cause various diseases, including congenital anomalies, neurodevelopmenta l disorders, obesity, and cancer. In the mature brain, both neurons and astrocytes contain a single primary cilium. The pathophysiological impacts of neuronal primary cilia on obesity and mental disorders are well recognized, but the physiological functions of astrocytic primary cilia related with metabolic disorder remain unclear. In the present study, we investigated the role of astrocytic primary cilia in the context of energy metabolism.

Methods: To generate mice with astrocyte-specific ciliary dysfuction, astrocyte marker glial fibrillary acid protein (GFAP)- creERT2 mice were mated with intraflagellar transport protein (IFT) 88-floxed mice. Gene knockdown was induced by intraperitoneal injection of tamoxifen for 5 days at 7 weeks- old. Body weight and food intake were monitored under the feeding condition of a normal chow diet (CD) or a high fat diet (HFD). Body composition was analyzed using dual- energy X-ray absorptiometry (DEXA). Energy expenditure was determined by comprehensive Lab Animal Monitor System (CLAMS).

Results: The female GFAP- IFT88-knockout (KO) mice on both of HFD and CD exhibited significant increase in body weight compared to wild type (WT). On the contrary, in case of male mice, KO showed increased body weight on a CD, but not on HFD. Under the HFD condition, female KO showed decreased energy expenditure (EE) compared to WT, while there was no significant di ff erence between gen o types in male mice. The KO mice in both male and female showed a significant lower respiratory exchange ratio (RER) compared to WT.

Conclusion: Our findings imply an important role for astrocytic primary cilia in mediating anti- obesity effect.Further studie s to explore the molecular mechanisms that could explain these results are warranted.

Prediction of Diabetic Retinopathy Using Serum Proteomic Profiling

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Objective: Diabetic retinopathy is the most frequently occurring complication of diabetes. Screening for diabetic retinopathy is recommended to facilitate early detection and treatment. We examined whether technologies identify novel serum protein makers associated with diabetic retinopathy.

Methods: Healthy volunteers, diabetic patients and diabetic retinopathy patients were prospectively enrolled in the study. We measured baseline characteristics, several metabolic parameters. The study assessed the serum cytokine profiles of healthy volunteers, diabetes and diabetic retinopathy patients using antibody array.

Results: Cytokine profiling antibody array features 310 unique antibodies for profiling cytokines and related biomarker in serum. Among these proteins, we identified 8 up-regulated and 4 down-regulated proteins in the diabetic retinopathy patients compared with diabetic patients. And these proteins are likely involved in angiogenesis and neovascularization.

Conclusion: Patients with diabetic retinopathy have a distinct cytokine expression profile compared with healthy volunteers or diabetic patients. To characterize the specific biomarkers involved in prediction of diabetic retinopathy, further studies are needed.

Effect of L-glutathione on antioxidant enzyme and Bax/Bcl2 ratio in the testes of diabetes-induced C57BL/6NTac mice

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Objective: The study was conducted to determine the effect of L-glutathione on testicular antioxidant enzyme level, testicular morphology and the ratio of Bax/Bcl-2 to preserve spermatogenesis in diabetes-induced C57BL/6NTac mice.

Methods: Male C57BL/6NTac mice weighing 20-25 grams (16-weeks old) were randomly divided into four groups (n=6): Non-diabetic control group (Group C), non-diabetic GSH treated group (Group G), STZ-induced diabetic group (Group D) and diabetic-induced GSH-treated (Group DGSH). Doses of 15 mg/kg of GSH were administered intraperitoneally, weekly for 42 days. On Day-43, all mice were euthanized, and testes were removed for evaluation of antioxidant enzyme activities by measuring total antioxidant capacity (TAOC), reduced glutathione (GSH) level, superoxide dismutase (SOD) activity, and catalase (CAT) activity. The testes were also processed for histological studies using haematoxylin and eosin stains. Reverse transcription-qualitative polymerase chain reaction (RT-qPCR) of Bax and Bcl-2 genes were performed with RNA extracted from the testes. Data were analysed using one-way ANOVA.

Results: L-glutathione increased TAOC level, increased GSH and decreased SOD activity in Group DGSH mice, relative to the Group D mice (p<0.01). There was an increase in the diameter of the seminiferous tubules, a decrease in the diameter of the seminiferous lumen, and an increase in the length of the seminiferous epithelium of the testis in Group DGSH mice compared to the Group D mice (p<0.01). Expression ratio of Bax/Bcl-2 was found to be significantly decreased in Group DGSH mice, compared to the Group D mice (p<0.01).

Conclusion: L-glutathione at 15 mg/kg bw enhanced defense against diabetes-induced testicular oxidative stress and decreased damage to seminiferous tubules by improving testicular morphology. [Study funding: Funding by the Ministry of Higher Education Malaysia grant no FRGS 5/3 (273/2019)]

L-glutathione alleviates testicular oxidative stress in streptozotocin-induced diabetic mice

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Objective: This study was conducted to investigate the effect of L-glutathione supplementation on oxidative stress (OS) markers and antioxidant gene expression in C57BL/6NTac diabetic mice.

Methods: Twenty-four male C57BL/6NTac mice, 16 weeks of age, were divided into four groups; C, G, D, and DGSH (n=6). Diabetic mice (Groups D and DGSH) were injected with streptozotocin (STZ) at 50 mg / kg bw in 0.1 ml of Na-Citrate buffer. Control mice (Groups C and G) were injected with an equal dose of Na-Citrate buffer. L-glutathione at 15 mg/kg bw was intraperitoneally administered to the Group DGSH mice weekly. Testes were collected for evaluation after 42 days of treatment. To assess oxidative damage, serum and testicular tissue malondialdehyde (MDA) and 8-hydroxy deoxyguanosine (8-OHdG) were measured. The mRNA expression of antioxidant enzymes, superoxide dismutase 1 (Sod1) and glutathione peroxidase 1 (Gpx-1) in the testes were quantified using a real time-quantitative polymerase chain reaction (RT-qPCR). Data were then analysed using one-way ANOVA.

Results: Significant decreased of testicular MDA and 8-OHdG were observed in Group DGSH mice compared to the Group D (p<0.01). However, significant elevation of serum MDA was observed in Group DGSH mice, relative to the mice in the Group C. While for mRNA expression, Sod1 and Gpx-1 were upregulated in Group DGSH when compared to Groups D and G, respectively.

Conclusion: Conclusion: Oxidative stress (OS) state in testes were confirmed by the elevated levels of MDA and 8-OHdG in Group D. Enhanced Sod1 and Gpx-1 expression in Group DGSH showed that L-glutathione at 15 mg/kg bw was able to minimize the harmful effects of diabetes. Present data indicated the existence of several processes that contribute to, and possibly interact with, impaired testicular function in diabetic mice, some of which are potentially susceptible to therapeutic interventions with L-glutathione. [Funding: Ministry of Higher Education Malaysia FRGS 5/3 (273/2019)]

PREVALENCE OF Overweight and Obesity in health promotion center

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Objective: Obesity defined by body mass index and waist circumference can affect the epidemiology. Anthropometric indicators, overweight and obesity belong to intermediate risk factors for MS.

Methods: Among adults aged ≥19 years who participated in the Health promotion center between 2019, a total of 405 subjects (199 men and 206 women) were analyzed according to BMI and waist circumference. General obesity was defined as BMI ≥ 25 kg/m2 and abdominal obesity was defined as WC ≥ 90 cm in men and ≥ 80 cm in women, both of which were based on the WHO criteria.

Results: Trained staff performed anthropometric measurements of weight, height and waist and hip circumferences in 405 survey participants aged 19-60 years. Anthropometric measurements were utilized to calculate BMI and estimate the mean WHC in order to determine the prevalence of overweight by age, and gender. The mean body weight was 75.1 kg (95%CI 73.3-74.6) in the male population, while the mean height was 165.4 cm (95%CI 165-160.4). The corresponding indicators for females were 65.3 kg (95%CI 64.6-66.0) and 156.8 cm (95%CI 156.5-157.2). The mean WC among the study population was 91.4 cm (95% CI 86.6-88.5). The measurement results showed that this indicator was 0.7 cm more for men compared to women, being 91.8 cm (95%CI 90.3-107.3) in men, and 92.1 cm (95%CI 90.6-107.7) in women.

Conclusion: The mean BMI in the study population was 27.3, which is elevated compared to the WHO-recommended values. Collated by gender, the mean BMI was 27.8 in men, and 26.8 in women. According to the BMI risk assessment, 61.9% of the 19-60 year-old subject was overweight or obese, with 43.9% overweight and 18% obese. proportion of overweight or obese women in all age groups was relatively high compared to their male counterparts. The prevalence of central obesity was 73.5% in the 19-60 year-old.

PE17 Basic & Translational diabetes research

Serum Uteroglobin (UG), a biomarker for vascular inflammation in adults with type 2 diabetes mellitus

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Objective: Main pathophysiology of type 2 diabetic mellitus (T2D) and coronary artery disease is chronic vascular inflammation and decreased endothelial function. Statin is drug with anti-inflammatory effects against coronary artery disease. Because uteroglobin (UG), also known as secretoglobin family 1A member 1 (SCGB1A1), is a multifunctional protein with anti-inflammatory properties, we investigate the change of serum UG levels before and 3 months after statin treatment in patients with T2D.

Methods: This study enrolled 63 patients with T2DM who have no medical history with statin treatment. We measured blood chemistry, lipid profiles, fasting glucose insulin, and c-peptide. Fasting serum UG levels were measured using a quanti¬tative sandwich enzyme immunoassay technique with an en¬zyme-linked immunosorbent assay kit. To confirm arterial stiffness and stenosis, we also measured the brachial-ankle pulse wave velocity (baPWV).

Results: The average age of T2DM patients in this study was 57.6 (± 9.1) years, and the disease period was 57.6 (± 1.5) months. The male and smoker were 31, accounting for 49.2% of all participants and 22, accounting for 34.9%. Medical history for hypertension was 33 participants, accounting for 52.4%. The average value (cm/s) of the right and left PWV was 1535 (± 35) and 1557 (± 36). Fasting glucose and HbA1C levels were not significant change before and 3 months after treatment. As expected, total cholesterol, LDL cholesterol and triglycerides were significantly lower and HDL cholesterol was significantly higher after treatment. Interestingly, the serum UG levels increased after treatment with metformin in patients with T2DM.

Conclusion: Statin treatment in T2D patients with arterial stiffness increased serum UG levels. This results suggests that circulating UG might be a biomarker for vascular inflammation in T2D.

PE18 Basic & Translational diabetes research

Advanced nano material sensors detecting glycation of proteins through portable home-based diabetes device

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Objective: The emergence of nanotechnology and implications of nanomaterials in diabetes research enable us to develop the novel and advanced nanomaterial-based sensors. Since more than 4.7 million world population is suffering from diabetes and the frequent measurements of blood glucose concentration is required, the development of home based, rapid and portable devices have shown promising future. It has been noted that if patients get the measurements of the proportion of protein glycosylation (Glycated Hemoglobin and Glycated Albumin), then under a longer period of time, the personalized measures for improved diabetes management is achieved.

Methods: A combination of electrochemical studies, FTIR, SEM and XRD were performed to evalute the characterization of nanomaterials and sensor performances.

Results: Here advanced nanomaterials play a bridge to fill the gap over the traditional noninvasive and invasive monitoring sensors for diabetes. The combination of synthesized nanocomposites such as AuNPs embedded N-doped rGO and Pd NPs modified MoS2 for the preparation of electrodes sensors have shown promising future. These nano - composites characterized and further used for the biosensing of glycation of blood proteins, glycated hemoglobin (HbA1c) and glycated albumin (GA). The results obtained through characterization and analysis revealed the hierarchical modification of the working electrodes and successful immobilization of enzyme over the nanocomposite modified working electrode surface.

Conclusion: An electrochemical analysis demonstrated that N-doped rGO and Pd-NPs modified MoS2 composites film provides an effective electrochemical response with enhanced conductivity for the selective detection of HbA1c and GA in a wide concentration range.

PE19 Basic & Translational diabetes research

A meta-analysis on the association of plasminogen activator inhibitor-1 levels among women with previous history of gestational diabetes mellitus

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Objective: Prior reports suggest that women with previous history of gestational diabetes mellitus (GDM) are at high risk for developing diabetes and cardiovascular disorders. Plasminogen activator inhibitor-1 or PAI-1 has been demonstrated to be associated with both insulin resistance and cardiovascular disorders and has been linked to early atherosclerosis in women with history of GDM. Conflicting results of the association of PAI-1 with GDM has been observed, which prompted us to perform a meta-analysis on this association.

Methods: Relevant literature that contained data on the association of PAI-1 with previous history of GDM was searched in PubMed. Form this; eight studies were included in the meta-analysis. The needed data were extracted by two of the authors and were analyzed. Computation of both the standardized mean difference (SMD) and 95% confidence interval (CI) was carried out in Review Manager ver. 5.3.

Results: The overall results were not combinable due to the high degree of heterogeneity, which prompted us to identify the source using Galbraith's plot. Four studies were identified to be as outliers and were removed in the subsequent analysis. The post-outlier outcomes are homogenous and significant. Based on our results, women with previous history of GDM have higher levels of PAI-1 compared to patients without history of GDM.

Conclusion: Overall, our results demonstrate a significant association of GDM history with PAI-1 levels. However, further studies must be performed to verify our claims before being applied clinically. 3

PE23 Basic & Translational diabetes research

Lobeglitazone ameliorates hepatic fat accumulation and changes oxylipin profile in a rat model of obesity and type 2 diabetes

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Objective: Thiazolidinediones, acting as peroxisome proliferator-activated receptor gamma (PPARγ) ligands, has been reported to reduce hepatic steatosis in human and animals. However, the underlying mechanism remains largely unknown. The purpose of this study was to investigate changes in hepatic metabolites in response to treatment with lobeglitazone (LOBE), a PPARγ ligand in an animal model of obesity and type 2 diabetes.

Methods: Male obese and diabetic OLETF rats were orally administered either vehicle (CONTROL) or LOBE (1mg/kg) fed on high fat/ high carbohydrate diet for 15 weeks. Blood and liver tissue were harvested after overnight fasting at the end of study. Biochemical and histological assessment were performed in plasma and liver. Metabolites in plasma and liver were analyzed via metabolomic analyses.

Results: OLETF rats that received LOBE showed decreased in hepatic fat accumulation in liver and improvement of lipid profiles in liver and plasma including total cholesterol, triglyceride and free fatty acid compared to CONTROL rats. LOBE treatment significantly altered levels of metabolites, including oxylipins (oxygenated fatty acid derivatives) in the plasma and liver, which are strongly correlated with metabolic parameters and potential hepatic biomarkers.

Conclusion: Our results demonstrate that LOBE can regulate oxylipin metabolism in a rat model of obesity and type 2 diabetes, which could contribute to the improvement of hepatic steatosis.

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PE24 Basic & Translational diabetes research

A novel regulatory mechanism of insulin secretion by protein phosphatase 1

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Objective: In the previous study, we observed that calyculin A, a non-selective inhibitor of protein phosphatse (PP), decreased insulin secretion while ML-7, a myosin light chain kinase inhibitor, enhanced insulin secretion. In this study, we aimed to identify specific type of PPs affecting insulin secretion and evaluate its regulatory role in pancreatic beta-cells.

Methods: To identify the specific PPs that regulate insulin secretion, INS-1E cells were transfected with siRNA for PP1, PP2A, and PP2B. Specific inhibitors for PP1, PP2A, and PP2B (tautomycin, fostriecin, and cyclosporin A, respectively) was also used. Insulin was measured under high-glucose conditions. Exocytosis of insulin granule was evaluated using a pH-sensitive fluorescent protein fused with neuropeptide Y (NPY-GFP).

Results: Glucose-induced insulin secretion (GSIS) was significantly decreased in INS-1E cells treated with tautomycin (20nM), but neither with fostriecin (20nM) nor cyclosporinA (1μM). Transfection of siRNA for PP1, PP2A, and PP2B showed similar results. To determine the possible substrates of PP1, we measured 20 kDa myosin light chain of 20 (MLC20) phosphorylation in INS-1E cells. MLC20 phosphorylation increased immediately after high glucose stimulation and then decreased over time. It was also significantly increased by treatment of calyculin A or tautomycin. To determine if PP1 affects exocytosis during insulin secretion process, fluorescent images were obtained in INS-1E cells transfected with siRNA for PP1, PP2A and PP2B. Under high glucose condition, NPY-GFP signal decreased in INS-1E cells treated with PP1 siRNA, but not with PP2A or PP2B siRNA.

Conclusion: Our results showed a novel regulatory mechanism of insulin secretion by PP1, which involves in phosphorylation of MLC20 and exocytosis of insulin granules.

PE25 Basic & Translational diabetes research

Regulation of Adipsin Expression by Endoplasmic Reticulum Stress in Adipocytes

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Objective: Adpsin is an adipokine that stimulates insulin secretion from β-cells and improves glucose tolerance. Its expression has been found to be markedly reduced in obese animals. However, it remains unclear what factors lead to downregulation of adipsin in the context of obesity. Endoplasmic reticulum (ER) stress response is activated in various tissues under obesity-related conditions and can induce transcriptional reprogramming. Therefore, we aimed to investigate the relationship between adipsin expression and ER stress in adipose tissues during obesity.

Methods: C57BL/6N mice were randomly divided into two groups fed either a normal chow diet (ND; n = 8) or a high-fat diet (HFD; n = 16). After 8 weeks, the HFD-fed mice were randomly divided into two subgroups: an HFD group (n = 8); an HFD plus 4-PBA group (HFD + 4-PBA; n = 8). The HFD group and the HFD + 4-PBA group were fed with an HFD and intraperitoneally administered with vehicle or 4-PBA (1 g/kg per day) once daily for additional 4 weeks, respectively. After pretreatment with chemical chaperones, 3T3-L1 adipocytes were incubated with thapsigargin (10 nM) or tunicamycin (5 μg/mL) for 24 h.

Results: We observed that obese mice exhibited decreased levels of adipsin in adipose tissues and serum and increased ER stress markers in adipose tissues compared to lean mice. We also found that ER stress suppressed adipsin expression via adipocytes-intrinsic mechanisms. Moreover, the ER stress-mediated downregulation of adipsin was at least partially attributed to decreased expression of peroxisome proliferator-activated receptor γ (PPARγ), a key transcription factor in the regulation of adipocyte function. Finally, treatment with chemical chaperones recovered the ER stress-mediated downregulation of adipsin and PPARγ in vivo and in vitro.

Conclusion: Our findings suggest that activated ER stress in adipose tissues is an important cause of the suppression of adipsin expression in the context of obesity.

PE26 Basic & Translational diabetes research

Visfatin exacerbates hepatic inflammation and fibrosis in a methionine-choline-deficient diet induced mouse model of nonalcoholic steatohepatitis

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Objective: Non-alcoholic fatty liver disease (NAFLD) ranges from simple steatosis to non-alcoholic steatohepatitis, which is characterized by hepatic inflammation that can progress to fibrosis, cirrhosis and hepatocellular carcinoma. The progression of NAFLD is still poorly understood. Visfatin, an adipocytokine, was reported to induce pro-inflammatory cytokines and can be associated with liver fibrosis. We investigated the role of visfatin on hepatic inflammation and fibrosis in a methionine-choline-deficient (MCD) diet induced steatohepatitis mouse model.

Methods: Three groups of 8-week-old male C57BL/6J mice were studied for 2 weeks: 1) saline-injected control diet group; 2) saline-injected MCD diet group; and 3) visfatin-injected MCD diet group (n=8/group). Mice were intravenously injected every day with saline or 10 μg of recombinant murine visfatin for 2 weeks. Histologic assessment of liver, and biochemical and molecular measurements of endoplasmic reticulum (ER) stress, oxidative stress, inflammation, and fibrosis were performed in livers from these animals.

Results: Treatment with visfatin increased liver weight of MCD-diet fed mice without changing ALT, AST and liver fat content. Visfatin elevated the serum CC chemokine ligand (CCL) 20 and CXC chemokine ligand (CXCL) 8, and increased hepatic mRNA expression of CXC chemokine receptor (CXCR) 1, CXCR2, CXCL2, and CCL2. The intravenous injection of visfatin increased inflammatory cell infiltration (indicated by F4/80, CD68, ly6G, and CD3 mRNA expression) in the liver. Visfatin also increased the expression of pro-inflammatory cytokines (IL-1β, TNF-α, and IL-6) and activated the fibrosis markers (cTGFβ, TIMP1, collagen 1A2, collagen 3A2, αSMA, Fibronectin, and Vimentin). Livers of mice injected with visfatin showed an upregulation of the ER stress and oxidative stress and activation of JNK signaling.

Conclusion: These results suggest that visfatin aggravates hepatic inflammation with inducing ER stress and oxidative stress, and exacerbates fibrosis in MCD diet fed mouse model of steatohepatitis.

PE27 Basic & Translational diabetes research

Muscle attenuation of metabolically healthy and metabolically unhealthy obese individuals

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Objective: Metabolically healthy obese (MHO) is defined as the absence of metabolic complication. However, it remains unclear whether MHO exists. Increased ectopic adipose tissue infiltration in skeletal muscles is associated with metabolic disturbances. We compared the fat infiltration in muscle among MHO, metabolically unhealthy obese (MUO) individuals and healthy control.

Methods: In this retrospective study, healthy control (n=65) and obese individuals (n=169) who underwent bariatric surgery were enrolled. We divided obese individuals into MHO and MUO patients by Adult Treatment Panel III. For the assessment of myosteatosis, Hounsfield unit histogram analysis (HUHA) and average CT Hounsfiled unit (HU) measurements were performed on axial precontrast images at L3 level using commercial 3D analysis software (Aquarius iNtuition v4.4.12®, TeraRecon). One radiologist drew region of interest (ROI) along the outline of bilateral psoas muscles, bilateral paraspinal muscles and abdominal wall muscles. The HUHA is expressed as a percentage and volume of the ROI and can be classified into three category: the ROI: -190 ≤ A ⟨ -30, -29 ≤ B ⟨ 29, 30 ≤ C ⟨ 150, representing intermuscular adipose tissue (IMA), low attenuation muscle (LAMA), and normal attenuation muscle (NAMA), respectively.

Results: The number of MHO and MUO individuals were 27 (16%) and 142 (84%) respectively. The IMA and LAMA of obese patients were significantly higher than non-obese patients (p⟨0.001). The NAMA of obese patients was significantly lower than non-obese patients (p⟨0.001). However, the IMA, LAMA and NAMA of MHO patients did not differ from those of MUO individuals after covariates adjustment.

Conclusion: This study would suggest that the fat infiltration in skeletal muscle of MHO did not differ from that of MUO individuals.

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PE28 Basic & Translational diabetes research

Melatonin ameliorates Dapagliflozin-induced diabetic ketoacidosis by inhibiting lipolysis and hepatic ketogenesis in type 2 diabetic mice

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Objective: Sodium-glucose cotransporter-2 inhibitors (SGLT2i) are effective hypoglycemic agents that can induce glycosuria. However, there are increasing concerns that they might induce diabetic ketoacidosis. This study investigated the effect of melatonin on SGTL2i-induced ketoacidosis in insulin-deficient type 2 diabetic (T2D) mice.

Methods: To obtain an insulindeficient T2D mouse model, high fat-fed mice were injected with low-dose streptozotocin and nicotinamide. 6-week-old C57BL/6 mice were fed a high-fat diet (HFD) for 4 weeks. High fat-fed mice were injected with streptozotocin (150 mg/kg) and nicotinamide (1000 mg/kg) and were then fed a HFD continuously for 2 weeks. The mice were treated with an intraperitoneal injection of 1 mg/kg dapagliflozin in 10% DMSO-containing saline at 10:00 AM after 4-hour food deprivation. Melatonin was administered intraperitoneally shortly before the treatment with dapagliflozin. Six hours after the injection of dapagliflozin, plasma, urine, and tissue samples were collected.

Results: The SGLT2i dapagliflozin reduced blood glucose level and plasma insulin concentrations in T2D mice, but induced increases in the concentrations of plasma β-hydroxybutyrate, acetoacetate, and free fatty acid and a decrease in the concentration of plasma bicarbonate, resulting in ketoacidosis. Melatonin inhibited dapagliflozin-induced ketoacidosis without inducing any change in blood glucose level or plasma insulin concentration. In white adipose tissue, melatonin inhibited lipolysis and downregulated phosphorylation of PKA, HSL, and perilipin-1. In liver tissue, melatonin suppressed cellular cyclic AMP levels and downregulated phosphorylation of PKA, AMPK, and acetyl-CoA carboxylase (ACC). In addition, melatonin increased hepatic ACC activity, but decreased hepatic CPT1a activity and acetyl-CoA content. These effects of melatonin on lipolysis and hepatic ketogenesis were blocked by pretreatment with melatonin receptor antagonist or PKA activator.

Conclusion: Collectively, these results suggest that melatonin can ameliorate SGLT2i-induced ketoacidosis by inhibiting lipolysis and hepatic ketogenesis though cyclic AMP/PKA signaling pathways in T2D mice. Thus, melatonin treatment may offer protection against SGLT2iinduced ketoacidosis.

PE29 Basic & Translational diabetes research

Melatonin attenuates cisplatin-induced acute kidney injury through dual suppression of apoptosis and necroptosis

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Objective: Melatonin is well known to modulate the sleep-wake cycle. Accumulating evidence suggests that melatonin also has favorable effects such as anti-oxidant and anti-inflammatory properties in numerous disease models. It has been reported that melatonin has therapeutic effects against cisplatin-induced acute kidney injury (AKI). However, mechanisms underlying the therapeutic action of melatonin on the renal side-effects of cisplatin therapy remain poorly understood.

Methods: Seven-week-old male C57BL/6N mice were randomly grouped into the following groups (n = 10 for each group): Control, cisplatin alone, and melatonin in combination with cisplatin. For cisplatin treatment, mice received an intraperitoneal injection with 15 mg/kg cisplatin (dissolved in 0.9% normal saline). To evaluate the potential effects of melatonin on the renal side-effects of cisplatin therapy, mice were injected intraperitoneally with 20 mg/kg melatonin for 3 days before and 2 days after cisplatin treatment. Mice were sacrificed 72 h after cisplatin injection.

Results: In this study, we showed that melatonin treatment significantly ameliorates cisplatin-induced acute renal failure and histopathological alterations. Increased expression of tubular injury markers was largely reduced by melatonin. Melatonin treatment inhibited caspase-3 activation and apoptotic cell death. Moreover, protein levels of key components of the molecular machinery for necroptosis were decreased by melatonin. Melatonin also attenuated nuclear factor-kB activation and suppressed expression of pro-inflammatory cytokines. Consistent with in vivo findings, melatonin dose-dependently decreased apoptosis and necroptosis in cisplatin-treated mouse renal tubular epithelial cells.

Conclusion: Collectively, our findings suggest that melatonin ameliorates cisplatin-induced acute renal failure and structural damages through dual suppression of apoptosis and necroptosis. These results reveal a novel mechanism underlying the therapeutic effect of melatonin against cisplatin-induced AKI and strengthen the idea that melatonin might be a promising therapeutic agent for the renal side-effects of cisplatin therapy.

PE30 Clinical diabetes and therapeutics

The association between renal fat amount and renal threshold for glucose

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Objective: The role of kidney in glucose homeostasis has become an attractive research topic in the fields of pathogenesis and management of diabetes mellitus. In addition to its important role in gluconeogenesis and glucose utilization, the kidney maintains glucose homeostasis primarily through glucose reabsorption. Moreover, visceral lipid accumulation is involved in a variety of physiological aberrations. However, little is known regarding the potential role of lipid accumulation in renal glucose reabsorption. The aim of this study was to investigate the association between renal fat amount and renal threshold for glucose (RT).

Methods: 20 healthy subjects and 20 subjects with diabetes were recruited in this study. We examined the renal fat amount using magnetic resonance imaging (MRI). RT of each subject was assessed. Clinical parameters and demographic characteristics were assessed. Pearson correlation analysis and partial correlation analysis were carried out to analyze the association between renal fat amount and RT.

Results: Individuals with BMI $\geq$ 24kg/m2 exhibited significantly higher renal fat fraction (RFF) than those with BMI $\langle$ 24kg/m2 (p $\langle$ 0.05). RFF was positively associated with BMI and waist-to-hip ration (WHR). Moreover, significant and positive associations of BMI, WHR, and RFF with RT were found. The correlation between RFF and RT was strongest (r = 0.647, p $\langle$ 0.001). However, after adjusting for mean blood glucose, age, gender, diabetes status, estimation of the glomerular filtration rate (eGFR) and blood pressure (BP), RFF was still positively associated with RT, whereas BMI and WHR were not significantly correlated with RT. Furthermore, when further controlling for BMI and WHR, the positive association of RFF with RT still remained significant.

Conclusion: Renal fat amount may be a crucial determinant of RT. Our study provides evidence that excessive lipid accumulation in the kidney may play an important role in increased renal glucose reabsorption.

PE31 Clinical diabetes and therapeutics

Trends of diabetes and prediabetes prevalence among Korean Adolescents From 2007 to 2018

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Objective: To provide updated prevalence data and to estimate changes in the prevalence of diabetes among Korean adolescents by sex and age between 2007 and 2018.

Methods: We used the data of children and adolescents (8,718 subjects aged 10 to 18 years) from the Korea National Health and Nutrition Examination Survey IV-VII (KNHANES 2007-2018). The recent prevalence of diabetes and pre-diabetes estimated by using the latest KNHANES VII. The linear trends were estimated by comparing 3-year KNHANES cycles according to sex and by using logistic regression.

Results: The prevalence of diabetes and pre-diabetes was 0.298% (95% CI, 0.289-0.308) and 7.914% (95%CI, 0.43-0.49). The prevalence of diabetes was a significant increase from 0.189 to 0.430 during KNHANE IV and VII. A positive linear trend is significant for diabetes (p trends=0.006) in only male subjects. The prevalence of pre-diabetes was a significant increase from 5.86 to 12.08 in both sexes. During KNHANES IV and VII, the prevalence of obesity increased significantly.

Conclusion: Between 2007 and 2018, the prevalence of diabetes among Korean adolescents increased. Further studies are required to determine the causes of these increases.

PE32 Clinical diabetes and therapeutics

Dulaglutide may be an Effective Tool for Replacement of Prandial Insulin in Patients with Type 2 Diabetes

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Objective: Multiple daily insulin injection (MDI) therapy is used in type 2 diabetes (T2DM) patients for strict glycemic control. The use of glucagon-like peptide-1 receptor agonist (GLP-1RA) is increasing in T2DM patients, and dulaglutide, a weekly injectable GLP-1RA, has demonstrated effectiveness when added to basal insulin. In the present study, we examined whether the efficacy of dulaglutide is comparable to three injections of bolus insulin in patients with type 2 diabetes (T2DM) undergoing MDI after kidney transplantation.

Methods: Thirty-seven kidney transplant recipients with T2DM, who switched from MDI to basal insulin and dulaglutide, were retrospectively analyzed. Change in HbA1c, fasting plasma glucose (FPG), body weight, and total daily insulin dose during 6 months were evaluated.

Results: The combination of basal insulin and dulaglutide is comparable to three injections of prandial insulin for glycemic control (7.1% vs 7.0%, 95% CI: -0.526 to 0.278, p=0.534). The combination of basal insulin and dulaglutide showed reduction of FPG by 9.7mg/dl (95% CI: 2.085 to 41.537, p=0.031), body weight by 4.9 kg 95% CI: 2.872 to 6.979, p

Conclusion: Once weekly dulaglutide may be an effective alternative for thrice-daily prandial insulin in patients with type 2 diabetes currently on MDI. Further large, prospective studies for patients on MDI will be needed.

PE33 Clinical diabetes and therapeutics

Prevance of Diabetes and Impaired Glucose Tolerance in Urban and Rural population In Nepal

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Objective: The rationale of this study was to determine the prevalance of Diabetes and Impaired Glucose Tolerance in Urban and Rural population In Nepal

Methods: Analytical cross sectional study involving men and women >30 years of age from urban and Rural population in Nepal.Total of 100 patients were selected. Glucose Tolerance status was denned by World health Organisation criteria and was based on 75-g oral glucose tolerance test.

Results: out of 100 subjects,the prevalence of diabetes was more than twice as high among the urban population(12.7%) and among the rural ppulation (6.2%).Diabetes was more prevalent among the male than women (8.4% vs 4.7%).IGT was found in an additional 15.2 % of male and 6.8 % of female.The combined prevalance of diabetes and IGT in the population >45 years is 36.2% (diabetes 14% and IGT 22.2%). Of the people identified with with diabetics 40% were not previously diagnosed

Conclusion: Hence, the study revealed that prevalence of diabetes was high in urban population . older male population are at the risk of developing diabetes and IGT.Obesity and family history of diabetes are associated with increases odd of developing diabetes in urban population.Rural population are at lower risk mainly because of their daily physical activities as population in rural areas earn their living by more physical activities as compared to population of urban areas.

PE34 Clinical diabetes and therapeutics

The Beneficial Role of Early Screening of Gestational Diabetes Mellitus: A Case Report of Gestational Diabetes Mellitus in a Rural Hospital of South Sumatra, Indonesia

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Contents: Gestational Diabetes Mellitus (GDM), which defined as any glucose intolerance during pregnancy, is associated with complicated maternal and fetal outcomes. Screening for GDM is typically done at 24-28 weeks of gestation. In this case, A 46-year-old woman, a housewife, presented to regional general hospital of Muaradua, South Ogan Komering Ulu, South Sumatra, Indonesia at six weeks of gestation of her fifth pregnancy in August 2019. There was a case history of type 2 diabetes as her mother was diabetic. Then, A 75 g oral glucose tolerance test (OGTT) was performed. The fasting plasma glucose was 130 mg/dl and 2 h value was 225 mg/dl. The diagnosis of GDM was made and insulin therapy in the form of three times daily injections of insulin aspart and once daily injection of insulin detemir was started. Follow ups were done at intervals of 2-4 weeks counting on the glycaemic control achieved. Her average fasting and two hours plasma glucose values were 88 mg/dl and 116 mg/dl. At 37 completed weeks, an elective caesarean section was planned. A live and healthy female baby was delivered weighing 3500 g. The baby had an uncomplicated neonatal course. The patient's plasma glucose values returned to normal by the next morning and insulin injections were stopped. At six weeks postpartum, she underwent a 75 g OGTT, which was normal. She was informed of her high risk of developing type 2 diabetes mellitus in her later life and was advised to maintain normal body weight by appropriate dietary modifications and regular physical activity. She was also advised to undergo a 75 g OGTT every 3 years. This case report shows that GDM screening early in the pregnancy, preferably in the first antenatal visit, and insulin therapy have a definite beneficial role in improving the outcome of the pregnancy.

PE35 Clinical diabetes and therapeutics

Effectiveness of Vitamin D Supplementation in Patients with Type 1 Diabetes Mellitus: A Systematic Review

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Objective: A systematic review was conducted to determine the effectiveness of vitamin D supplementation as adjunctive therapy in patients with type 1 diabetes mellitus.

Methods: A systematic review was carried out based on the Cochrane Collaboration methodology. Randomized controlled trial articles were obtained from Pubmed, Google Scholar, Wiley Online Library and Science Direct published until December 2019.

Results: There were 7 research articles with a total of 300 participants who met the criteria and were then included in this systematic review. All types of vitamin D and their analogues (alphacalcidol, cholecalcidol or calcitriol) in the study were given orally, in addition to administering insulin. This supplement is given over a span of 3 to 24 months (average duration of 12.4 months). Overall, vitamin D supplementation has a positive effect as adjunctive therapy in patients with type 1 diabetes mellitus. Against the immune system, vitamin D strengthens the suppressive capacity of regulatory T cells (Tregs), but does not significantly change the percentage of Tregs in the circulation. Changes in the glucometabolic process are also seen with this supplementation, such as decreased HbA1c levels, lower insulin dosage requirements and increased C-peptide levels that reflect the preservation of pancreatic beta cell function.

Conclusion: Oral administration of vitamin D as an adjunct therapy of insulin is effective, both in enhancing immunomodulatory and glucometabolic function in patients with type 1 diabetes mellitus.

PE36 Clinical diabetes and therapeutics

Greater Reductions in HbA1c and Body Weight with Once-Weekly Semaglutide vs Comparators Across Baseline BMI Subgroups: a Post Hoc Analysis of SUSTAIN 1-5 and 7-10 (Originally presented at ADA 2020)

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Objective: In the SUSTAIN trials, once-weekly subcutaneous semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1RA) approved for treatment of type 2 diabetes, significantly reduced HbA1c and body weight (BW) vs all comparators (placebo, sitagliptin, exenatide extended release, insulin glargine, dulaglutide, canagliflozin and liraglutide), with a safety profile consistent with the GLP-1RA class. Patient factors (e.g. body mass index [BMI]) may impact therapeutic choices and treatment goals. This post hoc analysis of SUSTAIN 1-5 and 7-10 explored changes from baseline in HbA1c and BW with semaglutide vs comparators by baseline BMI subgroups.
Methods: On-treatment without rescue medication data were evaluated in the full analysis set. Estimated treatment differences (ETDs) for change in HbA1c and BW from baseline to end of treatment were calculated for semaglutide 0.5 or 1.0 mg vs comparator by baseline BMI (⟨25; ≥25-⟨30; ≥30-⟨35 and ≥35 kg/m2). Treatment by subgroup (BMI) interaction was analysed using a mixed model for repeated measurements, for each trial separately.
Results: Overall, 572, 1,867, 2,103 and 2,217 subjects with BMI ⟨25, ≥25-⟨30, ≥30-⟨35 and ≥35 kg/m2, respectively, were evaluated. The ETDs for the changes in HbA1c and BW from baseline to end of treatment favoured semaglutide vs comparators (ETD ⟨0) in most subgroups. In general, treatment-by-subgroup interactions were nonsignificant (p⟩0.05), except for a generally greater HbA1c reduction with semaglutide 0.5 mg vs dulaglutide 0.75 mg across increasing BMI subgroups in SUSTAIN 7 (p=0.03), and a generally greater BW reduction with semaglutide 1.0 mg vs insulin glargine across increasing BMI subgroups in SUSTAIN 4 (p=0.005).
Conclusion: In the SUSTAIN trials, once-weekly subcutaneous semaglutide generally resulted in greater HbA1c and BW reductions vs comparators across BMI subgroups. Understanding the expected relative effects of semaglutide on glycaemia and BW by baseline BMI may further inform patient-centred therapeutic choices and treatment goals.

PE37 Clinical diabetes and therapeutics

Identifying Risk Predictors for Gastrointestinal Adverse Events with Once-weekly Semaglutide (Presented originally at ADA 2020)

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Objective: Gastrointestinal adverse events (GI AEs) are common with glucagon-like peptide-1 receptor agonists (GLP-1RAs). We aimed to identify risk predictors for GI AEs with once-weekly semaglutide to support clinicians identify high-risk patients.
Methods: Data from SUSTAIN 1-10 and two SUSTAIN Japanese trials were used to assess the effects of age, region, ethnicity, diabetes duration, gender, renal function, smoking status, HbA1c, body weight (BW), alanine aminotransferase and bilirubin on the incidence of GI AEs with semaglutide vs non-GLP-1RA comparators (exenatide extended release, dulaglutide and liraglutide were excluded). Changes in HbA1c and BW were assessed by GI AE status.
Results: Frailty (age, renal impairment, smoking) and female gender were associated with marginally higher risk of GI AEs than non-frailty and male gender, regardless of treatment. With semaglutide, patients with lower baseline BW were at higher risk of GI AEs vs those with higher BW. With comparators, lower baseline BW was associated with lower risk than higher BW. These results were confirmed by formal statistical analysis (data not shown). Semaglutide reduced HbA1c and BW across the trials, regardless of GI AEs.
Conclusion: GI AEs are hard to predict although they tend to be more common in frail vs non-frail patients and females vs males, regardless of treatment. Semaglutide reduced HbA1c and BW regardless of the presence/absence of GI AEs.

PE38 Clinical diabetes and therapeutics

Once-Weekly Semaglutide 1 mg vs Empagliflozin 25 mg as Add-On to Metformin Monotherapy in Patients with Type 2 Diabetes: a Meta-Regression Analysis of Individual Patient Data (Originally presented at ADA 2020)

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Objective: There are no published head-to-head trials of once-weekly semaglutide 1 mg vs once-daily empagliflozin 25 mg in type 2 diabetes (T2D), therefore we indirectly compared the pooled once-weekly semaglutide arms in SUSTAIN 2, 3 and 8 with the empagliflozin arm in PIONEER 2.
Methods: This analysis used individual patient data for patients on metformin monotherapy in the once-weekly semaglutide arms of SUSTAIN 2, 3 and 8 and the empagliflozin arm in PIONEER 2. Although all trials had similar inclusion criteria and duration, meta-regression analyses adjusting for potential effect modifiers and prognostic factors further controlled for differences in design and population.
Results: Mean baseline characteristics were similar with once-weekly semaglutide and empagliflozin (age: 56 vs 58 years, diabetes duration: 7 vs 8 years, BMI: 33 vs 33 kg/m2, HbA1c: 8.2% vs 8.1%, respectively). Semaglutide reduced mean HbA1c by -1.4 vs -0.8%-point with empagliflozin (p⟨0.001), and body weight by -5.3 vs -3.7 kg with empagliflozin (p⟨0.001). Complementary analyses, which were performed to assess robustness of these findings, supported these results. A significantly greater proportion of patients on semaglutide vs empagliflozin also achieved HbA1c targets and clinically relevant weight-loss targets.
Conclusion: In this indirect comparison, pooled once-weekly semaglutide 1 mg provided significantly greater HbA1c reduction and body weight loss compared with empagliflozin 25 mg in patients with T2D on metformin monotherapy.

PE39 Clinical diabetes and therapeutics

HbA1c levels and rates of hypoglycemia with insulin degludec U200 and insulin glargine U300 stratified by kidney function subgroups: post hoc analysis from the CONCLUDE trial (Originally presented at ADA 2020)

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Objective: CONCLUDE was a randomized, open-label, treat-to-target trial in participants with T2D, who received basal insulin ± oral antihyperglycemic drugs (OADs) and had ≥1 baseline hypoglycemia risk factors, including moderate kidney impairment.
Methods: Participants were randomized to degludec U200 or glargine U300 (± OADs). CONCLUDE demonstrated no significant difference in the overall symptomatic hypoglycemia rate with degludec U200 vs glargine U300 in the maintenance period (primary endpoint, tested for superiority). However, lower rates of nocturnal symptomatic and severe hypoglycemia in the maintenance period (exploratory secondary endpoints) were observed with degludec U200 vs glargine U300. The current post hoc analysis investigated these hypoglycemia endpoints and HbA1c stratified by baseline estimated glomerular filtration rate (eGFR) subgroups (⟨60, 60-⟨90, ≥90 mL/min/1.73 m2).
Results: The treatment differences in the change in HbA1c from baseline to end of treatment across baseline eGFR subgroups were not significantly different from each other (interaction: p=0.842) . For the rate ratios for hypoglycemia endpoints (overall symptomatic hypoglycemia, nocturnal symptomatic hypoglycemia and severe hypoglycemia), treatment differences across baseline eGFR subgroups were not significantly different to each other (interaction: p⟩0.05). The RRs for treatment difference in overall symptomatic hypoglycemia for the eGFR subgroups (⟨60, 60-⟨90, ≥90 mL/min/1.73 m2) were (0.89[0.57;1.39]95% CI; p=0.919), (0.80[0.59;1.09] 95% CI; p=0.919) and (0.80[0.58;1.09] 95% CI; p=0.919). The RRs for treatment difference in nocturnal symptomatic hypoglycemia for the eGFR subgroups (⟨60, 60-⟨90, ≥90 mL/min/1.73 m2) were (0.44[0.23;0.87]95% CI; p=0.299, (0.57[0.37;0.89] 95% CI; p=0.299) and 0.81[0.52;1.28] 95% CI; p=0.299. The RRs for treatment difference in severe symptomatic hypoglycemia for the eGFR subgroups (⟨60, 60-⟨90, ≥90 mL/min/1.73 m2) were (0.22[0.03;1.23]95% CI; p=0.957), 0.17[0.02;0.72] 95% CI; p=0.957) and 0.25[0.01;1.91] 95% CI; p=0.957)
Conclusion: Irrespective of kidney function, degludec U200 and glargine U300 resulted in similar HbA1c, and hypoglycemia rates were consistent with the primary analyses.

Efficacy of Oral Semaglutide According to Background Medication: An Exploratory Subgroup Analysis of the PIONEER Trial Program (Originally presented at ADA 2020)

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Objective: The PIONEER program investigated once-daily oral semaglutide (3, 7, 14 mg or flexibly dosed) versus comparators in patients with type 2 diabetes (T2D). This exploratory subgroup analysis evaluated the effect of background medications on glycated hemoglobin (HbA1c) and body weight (BW) reductions at the end of trial (26–78 weeks) in five PIONEER trials (3–5, 7–8).

Methods: Data were analyzed using the trial product estimand from patients who received oral semaglutide or comparator (sitagliptin 100 mg, liraglutide 1.8 mg, or placebo) based on background medication: metformin, sulfonylurea, sodium-glucose co-transporter 2 inhibitor (SGLT2i), insulin or combinations.

Results: Baseline characteristics were generally similar across subgroups. Greater reductions in HbA1c and BW were generally observed with oral semaglutide versus comparators, regardless of background medication. HbA1c reductions for oral semaglutide 14 mg versus placebo were greater in PIONEER 4 (-1.2 vs 0.1% [metformin]; -1.1 vs 0.4% [SGLT2i±metformin], PIONEER 5 (-1.3 vs 0.1% [metformin]; -1.1 vs -0.2% [sulfonylurea±metformin]; -1.1 vs -0.1% [insulin±metformin] and PIONEER 8 (-1.5 vs 0.1% [insulin]; -1.1 vs -0.0% [insulin+metformin]). Oral semaglutide 14 mg or flexibly dosed reduced HbA1c versus sitagliptin in PIONEER 3 (-1.2 vs -0.6% [metformin]; -1.0 vs -0.3% [sulfonylurea±metformin]) and PIONEER 7 (-1.4 vs -0.9% [metformin]; -1.3 vs -0.6% [metformin]; -1.3 vs -0.8% [metformin±SGLT2i]; -1.5 vs -0.6% [combinations]), respectively. HbA1c reductions were similar versus liraglutide (PIONEER 4; -1.2 vs -0.9% [metformin]; -1.1 vs -1.1% [SGLT2i±metformin]) but, as with other comparators, BW reductions were greater (-5.0 vs -3.0 kg [metformin]; -5.0 vs -3.7 kg [metformin±SGLT2i]). In general, there were no statistically significant interactions between treatment and subgroups. Estimated treatment differences were consistent within each trial and background medication subgroups.

Conclusion: These findings support the use of oral semaglutide across a broad population of patients with T2D in combination with other commonly used glucose-lowering agents.

Glycemic and Body Weight Responses to Oral Semaglutide in the PIONEER Trial Program (Originally presented at ADA 2020)

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Objective: The PIONEER phase 3 clinical trial program investigated glycemic response and other efficacy endpoints in patients with type 2 diabetes who were randomized to the glucagon-like peptide-1 analog oral semaglutide (3, 7 or 14 mg once daily), placebo or an active comparator (empagliflozin [25 mg], sitagliptin [100 mg] or liraglutide [1.8 mg] once daily). We aimed to evaluate and compare the efficacy responses for oral semaglutide and comparators across trials.

Methods: A post-hoc analysis of the PIONEER 1-5 and 8 trials was conducted to assess the response of any reduction in glycated hemoglobin HbA1c (%) and/or body weight (%), and a clinically relevant composite endpoint of HbA1c reduction ≥1% and body weight loss ≥5%, with oral semaglutide 14 mg versus comparators at the end of treatment (26-78 weeks). The trial product estimand was used.

Results: Across trials, any reduction in HbA1c was observed in higher proportions of patients with oral semaglutide (89-95%) than with placebo (51-64%) or active comparators (82-88%). A simultaneous reduction in both HbA1c and body weight was seen in 72-86% of patients treated with oral semaglutide 14 mg. The composite of HbA1c reduction ≥1% and body weight loss ≥5% was achieved by 27-41% of patients with oral semaglutide 14 mg, 1-8% of patients with placebo, 11% of patients with sitagliptin 100 mg, 18% of patients with liraglutide 1.8 mg, and 20% of patients with empagliflozin 25 mg. Within each trial, the odds of achieving HbA1c reduction of ≥1% and body weight loss of ≥5% with oral semaglutide 14 mg were significantly greater versus all comparators (p<0.0001).

Conclusion: These results demonstrate that oral semaglutide 14 mg was more effective than comparators for providing any HbA1c reduction, or both an HbA1c reduction ≥1% and body weight loss ≥5%.

Effect of Oral Semaglutide with or without Background SGLT2i in Patients with Type 2 Diabetes: Subgroup Analysis of PIONEER 4 (Originally presented at ADA 2020)

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Objective: Glucagon-like peptide-1 receptor agonists (GLP-1RAs) and SGLT2 inhibitors (SGLT2is) are widely used to treat type 2 diabetes (T2D) but trial data on their combined use are limited. We report the first data on oral semaglutide in combination with SGLT2i.

Methods: This was a post-hoc subgroup analysis of the 52-week, double-blind, double-dummy PIONEER 4 trial (NCT02863419), in which patients with T2D uncontrolled on metformin with or without SGLT2i were randomized 2:2:1 to once-daily oral semaglutide 14 mg, s.c. liraglutide 1.8 mg or placebo. Glycated hemoglobin (HbA1c) and body weight (BW) data are presented for the trial product estimand (on trial product without rescue medication).

Results: In total, 183 (26%) of 711 patients were receiving SGLT2i treatment at baseline and continued throughout trial. Compared with patients not receiving SGLT21s, subgroups of patients receiving SGLT2i had a lower percentage of females (SGLT2i: 37.8-45.2%; no SGLT2i: 48.3-52.1%), slightly longer mean T2D duration (SGLT2i: 8.2-8.7 years; no SGLT2i: 7.0-7.6 years) and higher BW (SGLT2i: 95.2-98.0 kg; no SGLT2i: 91.7-94.6 kg). Changes in HbA1c and BW were similar in patients with SGLT2i versus those without SGLT2i who were receiving oral semaglutide (HbA1c: -1.1 vs -1.2%; BW: -5.0 vs -5.0 kg), s.c. liraglutide (HbA1c: -1.1 vs -0.9%; BW: -3.7 vs -3.0 kg) and placebo (HbA1c: 0.4 vs 0.1%; BW: -1.1 vs -1.3%). Occurrence of most gastrointestinal adverse events was similar in patients on GLP-1RA with vs without SGLT2i (e.g. nausea: 20.3 vs 19.4% [oral semaglutide 14 mg]; 19.2 vs 17.5% [liraglutide 1.8 mg]; 2.8 vs 3.8% [placebo]).

Conclusion: Improvements in HbA1c and BW after one year as well as safety profile were similar in patients on oral semaglutide with or without background SGLT2i.

Efficacy and Safety of Oral Semaglutide When Added to Basal, Premix, or Basal-Bolus Insulin (Originally presented at ADA 2020)

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Objective: An exploratory subgroup analysis of the 52-week, double-blind PIONEER 8 trial (NCT03021187) evaluated the effect of background insulin regimen (basal, premixed, or basal-bolus) with/without metformin on the efficacy and safety of oral semaglutide.

Methods: Patients (N=731) with type 2 diabetes treated with insulin were randomized to once-daily oral semaglutide (3, 7, or 14 mg) or placebo. Endpoints included change from baseline in HbA1c, body weight (BW), and total daily insulin dose at week 52, assessed for the treatment policy estimand.

Results: Baseline age and HbA1c were similar across insulin regimen subgroups (8.1-8.4%) whereas BW was greater (86.9-93.0 kg vs 83.4-85.4 and 76.7-85.4 kg) and diabetes duration was longer (15.3-17.4 years vs 12.7-15.2 and 13.0-15.8 years) in patients on basal-bolus versus basal and premix subgroups, respectively. There were greater dose-dependent HbA1c and BW reductions with oral semaglutide 3, 7 and 14 mg versus placebo (basal: -0.6, -0.9, -1.3 vs -0.3% and -0.9, -1.5, -4.1 vs 0.9 kg; premix: -0.9, -0.8, -1.1 vs -0.2% and -1.9, -1.6, -3.3 vs -0.1 kg; basal-bolus: -0.5, -0.7, -1.1 vs -0.2% and -0.1, -2.6, -3.6 vs 0.3 kg). Total daily insulin dose at week 52 was decreased for patients on basal (oral semaglutide 7 and 14 mg; -13 and -2 U), premix (14 mg; -5 U), and basal-bolus (3, 7, and 14 mg; -4, -10, -9 U). Most hypoglycemic episodes were in patients on basal-bolus insulin. Fewer patients had severe or blood glucose-confirmed symptomatic hypoglycemia with oral semaglutide versus placebo (basal: 10.4-15.8% vs 20.0%; premix: 18.8-22.2% vs 34.4%) except in the basal-bolus subgroup (39.7-50.7% vs 37.5%).

Conclusion: Oral semaglutide reduced HbA1c and BW in a dose-dependent manner, and reduced insulin dose regardless of background insulin regimen, with a safety profile similar to other glucagon-like peptide-1 receptor agonists.

PE44   Clinical diabetes and therapeutics

Triglyceride and glucose index and risk of gestational diabetes: a nationwide population-based cohort study

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Objective: The main pathophysiology of gestational diabetes mellitus (GDM) is aggravation of preexisting insulin resistance during pregnancy. Triglyceride-glucose (TyG) index is a well-validated surrogate marker of insulin resistance. We aimed to evaluate the association between pre-pregnancy TyG index and GDM in primipara women.

Methods: A total of 380,208 women who underwent a Korean national health screening exam within 2 years before their first delivery, between January 1, 2012, and December 31, 2015, were included. The TyG index was calculated as ln [triglyceride (mg/dL) × fasting plasma glucose (FPG) (mg/dL)/2]. Multiple logistic regression analysis was performed to evaluate the risk of incident GDM according to the quartile of TyG index.

Results: Among the 380,208 primipara women, GDM developed in 17,239 women (4.53%). Multiple logistic regression analysis adjusted for risk factors showed an odds ratio of 1.80 for GDM (95% confidence interval 1.72-1.89) in the highest quartile compared with the lowest quartile. A 1-standard deviation (SD) increase in the TyG index was associated with a 33% increased risk of GDM in the fully adjusted model. Particularly, a 1-SD increase in the TyG index was associated with an 88% increased risk of GDM requiring insulin therapy. A 1-unit increase in the TyG index significantly increased the risk of GDM and GDM requiring insulin treatment by 1.86 and 3.93 times, respectively. The impact of a high TyG index on the incidence of GDM was more profound in the subjects aged ≥35 years, with obesity, with impaired fasting glucose, who are current smokers, and with a family history of diabetes (P for interaction = 0.001).

Conclusion: Increased pre-pregnancy TyG index is associated with a risk of GDM. Elevation of the TyG index may be an early predictor of GDM.

PE45   Clinical diabetes and therapeutics

Systematic approach on the discovery of druggable targets for metabolic diseases

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Objective: The scarcity of new targets and unmet medical needs are challenging in the new drug R&D for metabolic diseases. Here, we developed an AI-based systematic target discovery approach (Artificial Intelligence of Target Discovery; AITD) for metabolic diseases through phenotypic analysis of knock-out (KO) mice, integrated bioinformatics analyses incorporating empirical evidence provided by experts.

Methods: Using the phenotype information of 11,181 KO mouse strains collected from International Mouse Phenotyping Consortium (IMPC) release 10.1 and Mouse Genome Informatics (MGI) 6.14, qualitative and quantitative analysis revealed 4,363 metabolic genes significantly influencing body composition, glucose homeostasis, dyslipidemia and NAFLD-associated phenotypes.

Results: Among them, the annotated genes in cellular function, protein-protein interaction, and/or signaling pathway were subjected to natural language processing-based literature mining, and 1,495 genes participating in type 2 diabetes, obesity, the disorder of lipid metabolism, and NAFLD were identified. It was confirmed that 733 genes without functional abnormalities in the cardiovascular system, central nervous system, and respiratory system were enriched in fatty acid metabolism and PPAR signaling pathway. Analysis of target novelty revealed that 110 ligand-coding genes and 189 receptor-coding genes were in the preclinical stage at most. To validate the clinical relevance of these genes, mRNA levels in liver, fat, and muscle tissues of obese and obese/diabetic patients were comparatively analyzed, and 54 novel genes were discovered for metabolic diseases with high druggability.

Conclusion: AITD is proposed as the cornerstone for the discovery of new druggable targets and new drug R&D for metabolic diseases.

PE46   Clinical diabetes and therapeutics

Serum levels and placenta mRNA expression of interferon-gamma and soluble PD-L1 in pregnant women with GDM

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Objective: The present study aims to investigate the serum levels and mRNA expression in placenta of interferon-gamma and soluble PD-L1 in GDM.

Methods: A total of 34 pregnant women with normal glucose tolerance(NGT) and 35 pregnant women with gestational diabetes mellitus(GDM) were studied. The serum levels of interferon-gamma (IFN-γ) and soluble PD-L1 (sPD-L1) were measured at 36-40 weeks of pregnancy. We measured the mRNA expression of IFN-γ and sPD-L1 in placenta of pregnant women with NGT (n=6) and GDM (n=7).

Results: The serum IFN-γ level was lower significantly in GDM group than NGT group(184.973±41.88 vs 259.825±120.70, P=0.002). There was no difference in serum sPD-L1 levels between both groups (911.50±245.86 vs 849.82±261.23, P=0.434). Serum IFN-γ levels were correlated with BMI (r=- 0.255), but not with age, glucose and weight gain during pregnancy. The mRNA expression of IFN-γ and sPD-L1 in placenta was increased in subjects with GDM compared with pregnant women with NGT.

Conclusion: These results suggest that IFN-γ could be associated with pathophysiology of GDM, although it is not yet known where IFN-γ was secreted mainly and whether changes of IFN-γ level were caused or byproducts. And increased mRNA expression of PD-L1 could indicate a biological link between PD1-PDL1 signaling and GDM.

PE47   Clinical diabetes and therapeutics

High-intensity Interval Training is not Superior to Moderate-intensity Continuous Training for Reducing Levels of Plasminogen Activator Inhibitor-1 in Women with Type 2 Diabetes

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Objective: Elevated levels of plasminogen activator inhibitor-1 (PAI-1) have been reported in obese patients with type 2 diabetes and are associated with a predisposition to coronary and cerebral thrombosis. Recently, high-intensity interval training (HIIT) has been suggested for type 2 diabetes by the international guidelines showing several superior health benefits compared to the traditional moderate-intensity continuous exercise (MICT). Therefore, the primary purpose of this study was to assess the effect of HIIT on PAI-1 compared to MICT in women with type 2 diabetes.

Methods: Eighteen women with type 2 diabetes were assigned in two groups; HIIT group (n1=8, 42.1 ± 6.8 yrs, 33.1 ± 4.95 kg/m2) and MICT group (n2=10, 41.1 ± 2.9 yrs, 35.2 ± 2.6 kg/m2). The anthropometrics, PAI-1, and glycosylated hemoglobin (HbA1c) were measured. A graded symptom-limited exercise testing was done for the patients prior to exercise training to determine the peak heart rate (HRpeak). Patients in the HIIT group exercised for 4 × 4 min at 85%-90% of HRpeak with 3-min active recovery in between. Patients in the MICT group exercised for about 40 min at 65%-75% of HRpeak. Paired and Unpaired t-tests were used for statistical analysis.

Results: PAI- has reduced significantly in the HIIT (p=0.0003) and the MICT (p=0.0001) groups with no significant difference between the two groups (p=0.352). Likewise, HbA1c has reduced in the HIIT (p=0.0001) and the MICT (p=0.0002) groups with no significant difference between them. The BMI showed non-significant changes in either group.

Conclusion: The study sample may be too small to draw a conclusion; yet this study can suggest that, compared to the HIIT, the less physically demanding moderate-intensity continuous walking may be an effective lifestyle therapy for elevated PAI-1 levels in obese women with type 2 diabetes who may be physically unfit or may have cardiopulmonary, musculoskeletal/neurological limitations to exercises of higher intensity.

Characteristics of insulin and glucagon secretion pattern in Korean patients with diabetes

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Objective: The causes of diabetes have been explained mainly due to insufficiency of insulin action. However, it is known that glucagon also plays an important role in blood glucose homeostasis. There are still limitations of knowledge about how glucagon contributes in diabetes. This study was performed to investigate the change of insulin and glucagon levels in Korean patients with various patterns of blood glucose levels.

Methods: Patients who visited Hanyang University Hospital for diabetes screening tests from May 2009 to January 2015 with no diabetic treatment experience were enrolled. After fasting for at least eight hours, 75g glucose load tests were performed and insulin and glucagon concentrations were measured at 0, 30, and 120 minutes. According to glucose load test results, the subjects were classified as normal, fasting glucose control disorder, and postprandial glucose control disorder. The difference of insulin and glucagon pattern among groups was analysed

Results: Overall, the more severe the diabetes, the more delayed the glucagon reduction after glucose loading and the delayed response to the increase in insulin secretion were observed. In group-to-group comparison, the glucagon level of the fasting glucose disorder group was initially elevated after glucose load than the normal group and was not inhibited later. The postprandial glucose disorder group showed a tendency to delayed insulin response in the early stages after glucose load compared to the normal group, but to continue the insulin increase until later.

Conclusion: In this study, we observed that fasting glucose disorder is more related to glucagon and postprandial glucose control is related to Insulin. Considering that several complex factors are involved in glucose control, this result might be further investigated.

Prevention of type 2 diabetes with lifestyle intervention merging public health center resources and a web-based system: The Community-based Korea Diabetes Prevention Study

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Objective: The aims of this study are to the effectiveness of the web-based lifestyle modification (LSM) program to prevent or delay the onset of diabetes in pre-diabetes in community settings.

Methods: We performed a community-based randomized intervention trial for preventing the diabetes using a web-based lifestyle intervention program conducted in two public health centers. 415 subjects (mean age, 54 years; mean body-mass index, 26.3 kg/m2) who diagnosed pre-diabetes were randomly assigned to the LSM and standard management (SM) groups and followed for 22 months. The subjects assigned to the LSM group received 29 sessions for 22 months to achieve their goals for individual weight loss, physical activity, and balanced diet compared with SM groups who received the standard management program. The primary outcome was incidence of type 2 diabetes. A 75-g oral glucose-tolerance and HbA1c tests were performed every 6 months.

Results: The subjects assigned to the LSM and SM groups were 207 and 208, respectively (191 males and 224 females). The average follow-up was 16.5 months. Body weight decreased by 0.65 kg in the SM group and by 1.10 kg in the LSM group (P=0.123). The cumulative incidence of diabetes after trial was 5.6 percent in the LSD group and 10.2 percent in SM group. The incidence of diabetes was 5.96 and 2.98 cases per 100 person-years in the SM and LSM group. The risk of developing diabetes in the LSM group was 0.52 (p = 0.115) times lower than that of the SM group, but the number of new cases was small, so there was no statistical significance.

Conclusion: Web-based program used by public health center personnel is an effective and acceptable way to provide advice and support on lifestyle modifications to prevent type 2 diabetes in pre-diabetes in community setting.

DPP4-inhibitor Linagliptin Improves Glycemic Control in Type-2 Diabetes Mellitus with Renal Impairment : A Systematic Review

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Objective: Diabetes mellitus is a metabolic disease which is characterized by chronic condition of hyperglycemia due to impairment of insulin secretion, insulin dysfunction, or both. The most common type of diabetes mellitus is type 2 diabetes mellitus (T2DM). Diabetes mellitus is associated with the risk of renal disease, and the presence of both T2DM and cardiovascular disease increased the risk of death. Linagliptine is one of dipeptidyl peptidase-4 (DPP-4) inhibitors that is used in the management of patients with type 2 diabetes mellitus (T2DM) and renal impairment (RI). A systematic literature review was performed to compare the efficacy and safety of DPP-4 inhibitors in patients with T2DM and RI.

Methods: We searched the medical literature and registers of trials for randomized controlled trials of the effect of Linagliptin in type 2 diabetes mellitus patient with renal impairment. We used databases such as Pubmed for literature searching process. Selected literatures are those therapeutic studies with relevant to the clinical question and met the inclusion-exclusion criteria. The keywords that we used were "Linagliptin" AND "Diabetes mellitus" AND "Renal impairment" or "Renal dysfunction"

Results: Total 3 studies were identified. The study population covered in this systematic review are predominantly patients with type 2 diabetes with renal impairment. After 52 weeks, linagliptin reduced HbA1c levels by 0.6% (baseline 7.8-8.4%) versus placebo in the overall population. HbA1c reductions were similar at weeks 12 and 52. ates of adverse events (AEs) and changes involving renal function were similar in the active- and placebo-treated groups.

Conclusion: From this systematic review, we can conclude that linagliptin potentially improves glycemic control in patients with RI without increasing the risk of HEs or overall AEs.

Sleep quality and health-related quality of life in patients with type 2 diabetes mellitus patients: A cross-sectional study

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Objective: The objective of this study is to measure the relationship between sleep quality and health-related quality of life (HRQOL), in the Indian population with type 2 diabetes mellitus (T2DM).

Methods: A cross-sectional study, included a total of 300 patients with T2DM. All participants were responding to the Pittsburgh Sleep Quality Index (PSQI) and European Quality of Life-5 Dimensions Questionnaire (EQ-5D). A PSQI global score ≥ 5 was defined as poor sleep quality. EQ-5D visual analogue scale (VAS), determining the overall health status. Logistic regression analysis was used to examine the association between PSQI and EQ-5D. All the study data were analysed using the SPSS software version 20.0. Values of $p < 0.05$ were considered statistically significant.

Results: The mean age of included participants were 57.56. Majority of the participants (55.3%) were identified as "poor sleepers" and female (31.3%) contributing higher proportion. Poor sleepers had significantly lower the HRQoL ($p < 0.001$). After adjustment, poor sleep quality was significantly associated with a lower HRQoL; EQ-5D index (OR= 1.080, 95%, CI: 1.015 - 1.148, $p < 0.05$), and EQ-5D VAS (OR= 1.092, 95%, CI: 1.021 - 1.176, $p < 0.01$). Overall the EQ-5D index and EQ-5D VAS were found to be an independent predictors of sleep quality.

Conclusion: Poor sleep quality is prevalent in Indian T2DM population, and it imparts negative impact on several dimensions of EQ-5D that characterising the daily activities performance. Therefore, further real-world studies are needed to determine the causal relationship between T2DM patients and measure of objective sleep and their impact on health.

PE55   Clinical diabetes and therapeutics

G6PD deficiency is associated with renal impairment in T2DM

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Objective: Diabetes and its complications including renal impairment are the consequences of increased oxidative stress. Glucose-6-phosphate dehydrogenase (G6PD) protects from harmful oxidative metabolites. G6PD deficiency hence can lead to diabetes and its complications including renal impairment. If any association between G6PD deficiency and damage to kidney exists in diabetic population then screening for G6PD deficiency will help identify the susceptible patient and can prevent them from renal impairment in the long run.

Methods: Healthy volunteers and diabetic with or without renal impairment were selected. Body Mass Index and blood pressure were recorded. G6PD activity, hemoglobin, glycated hemoglobin, uric acid, and creatinine were measured. Urine was tested for the presence of proteinuria. Glomerular filtration rate (eGFR) was estimated with the Modification of Diet in Renal Disease Study (MDRD) Equation. Statistical analysis was done with open software LibreOffice 6.3.3 and SPSS version 22.0.

Results: The mean G6PD level of healthy control was 84.27 ± 9 and that of diabetic patient and diabetic patients with renal impairment were 65.05 ± 5.35 and 46.64 ± 6.56 respectively. There was only one participant (4.55%) with G6PD deficiency among healthy controls whereas the proportion of participants having normal, mild to moderate, and severe degree of G6PD deficiency were 77.27%, 13.64%, and 9.09%, respectively for diabetic patient while 40.91%, 22.73%, and 36.36% for those with renal impairment.

Conclusion: The prevalence of G6PD deficiency was higher in diabetics with renal impairment than with diabetes alone suggesting the relation between G6PD activity and diabetes with renal impairment.

PE56   Clinical diabetes and therapeutics

Low muscle mass and risk of developing type 2 diabetes in Korean women with gestational diabetes mellitus

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Objective: The purpose of this study is to evaluate if low muscle mass increases the risk of type 2 diabetes (T2D) in women with gestational diabetes mellitus (GDM).

Methods: A total of 317 women with GDM (mean age: 34.9 ± 3.7 years) was prospectively evaluated for the incidence of T2D. GDM was diagnosed with 75g or 100g oral glucose tolerance test (OGTT) during 24-28 week gestational age. Postpartum glycemic status was evaluated with 75g OGTT at 6-8 weeks after delivery and appendicular skeletal muscle (ASM) was assessed with bioelectrical impedance analysis. ASM was divided by BMI and this index was divided into 3 tertiles. The hazard ratio for the incidence of T2D was assessed according to muscle mass tertiles.

Results: After the median follow up duration of 29.4 months, the highest group had 57% and 75% risk reduction in incident prediabetes and T2D compared to the lowest group (p=0.006 and p=0.01, respectively). After adjusting maternal age, hypertension, body weight, waist circumference, family history of T2D, degree of gestational hyperglycemia by index pregnancy OGTT, breast feeding and extent of weight gain after delivery, the highest group had 83% and 65% lower risks developing prediabetes and T2D (p=0.002 and p=0.024, respectively). The risks demonstrated a significant inverse association for developing prediabetes and T2D according to ASM/BMI tertiles (p for trend=0.002) for the trend of which indicated the lowest group developed more prediabetes and T2D than higher groups.

Conclusion: The low muscle mass defined by ASM/BMI index was associated with an increased risk of T2D in Korean women with GDM.

PE57   Clinical diabetes and therapeutics

Differences of stress, depression, fatigue & sleep quality in gestational diabetes mellitus and normal pregnancy

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Objective: This study was a case-control study to compare the stress, depression, fatigue, and sleep quality between gestational diabetes mellitus and normal pregnancy.

Methods: The study subjects were 49 gestational diabetes mellitus women and 51 normal pregnant women who were matching with gestational diabetes mellitus women by age, gestational age and number of birth. Research tools were used with numerical rating scale and gestational stress measurement tools, depressed measurement tools (CES-D), fatigue measurement tools, sleep quality measurement tools (VSH Scale) and Canopy 9 Professional 4.0 (IEMBIO, Gangwon do, Korea) equipment. Data were analyzed by frequency, percentage, average and standard deviation, two Independent sample t-test, Fisher's exact test and x2-test using SPSS 24.0.

Results: The subjects of this study were 49 pregnant women and 51 normal pregnant women. The general and obstetric characteristics of the two groups were identical. The results of this study showed that stress, depression and fatigue in pregnant diabetic pregnant women were significantly higher than normal pregnant women and the quality of sleep was similar.

Conclusion: Individualized counseling to assess stress, depression, and fatigue in antenatal care for gestational diabetes and development of training and nursing intervention programs to reduce it.

PE58   Clinical diabetes and therapeutics

Pre-pregnancy metabolic syndrome and insulin administration in gestational diabetes: a nationwide population-based cohort study

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Objective: To evaluate the relationship between pre-pregnancy maternal metabolic syndrome and insulin administration in gestational diabetes mellitus (GDM) to diminish the burden of insulin use during pregnancy.

Methods: This was a population-based retrospective cohort study conducted using data from the National Health Information Database of Korea. We identified all deliveries from January 1, 2011 to December 31, 2015 (N = 1,214,655). Among the deliveries, we identified mothers with pre-pregnancy health checkup records and without previous diabetes history (N = 325,208). Hazards of insulin use in GDM were calculated based on pre-pregnancy obesity and metabolic syndrome.

Results: Hazards of insulin use in GDM increased proportionately with an increase in the pre-pregnancy body mass index (BMI) and waist circumference (WC). After the adjustment for clinical factors, high BMI group ($\geq$30 kg/m2) and high WC group ($\geq$100 cm) were significantly associated with higher hazard ratios (HRs) (HR 4.161, 95% Confidence interval [CI] 3.381-5.121, P < 0.001 and HR 2.563, 95% CI 1.769-3.712, P < 0.001, respectively). The presence of pre-pregnancy metabolic syndrome significantly increased the hazard of insulin use in GDM (0.54% vs. 5.04%). In the presence of central obesity (WC $\geq$ 85 cm) or obesity (BMI $\geq$ 25 kg/m2), HRs of insulin use in GDM were 1.603 (95% CI 1.023-2.511) and 2.637 (95% CI 2.275-3.056), respectively, after adjustment for clinical factors.

Conclusion: Pre-pregnancy obesity, central obesity, and metabolic syndrome increase the hazard of insulin use in GDM in Korean mothers.

Impact of social distancing due to COVID-19 on the changes in HbA1c level in patients with type 2 diabetes

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Objective: To investigate the impact of social distancing due to COVID-19 on glycemic control in patients with type 2 diabetes.

Methods: The study period was divided up according to the timing of the COVID-19 outbreak in Daegu (18 Feb, 2020). Period 1 was defined as 18 November to 17 February, and Period 2 was defined as 18 February to 17 May. Data were collected for the same dates during the 3 years (COVID-19 Cohort (2019-2020), non-COVID-19 Cohort 1 (2018-2019) and Cohort 2 (2017-2018)). Of 74,636 patients who visited the five tertiary hospitals in Daegu and had their HbA1c levels measured during the designated periods, the patients in each cohort who had this parameter measured during both Periods 1 and 2 were enrolled. A total of 20,087 patients were enrolled. We retrospectively analyzed the change in glycated hemoglobin level (DHbA1c) in patients with type 2 diabetes who undertook social distancing because of COVID-19. We compared the DHbA1c between COVID-19 and non-COVID-19 cohorts.

Results: The mean HbA1c levels of the non-COVID-19 cohorts were decreased in Period 2 than in Period 1, whereas the mean HbA1c level of the COVID-19 cohort did not differ between the two periods. The mean DHbA1c of the COVID-19 cohort was significantly higher than those of the non-COVID-19 cohorts. Subgroup analysis showed that social distancing significantly increased the mean HbA1c level of participants of <50 years. The DHbA1c of participants of <50 years and with HbA1c <7.0% in the COVID-19 cohort showed larger changes than other subgroups. After adjustment for age, sex, and baseline HbA1c level, the adjusted DHbA1c level in the COVID-19 cohort remained significantly higher than those in the two other cohorts.

Conclusion: Social distancing negatively impacts blood glucose control in patients with type 2 diabetes, especially those who are younger and have good blood glucose control.

Legacy effects of adiponectin correlated with body weight in type 2 diabetes

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Objective: Adiponectin is a hormone produced primarily by adipocyts. It has been known that have an inverse relationship with body mass index (BMI). However, in some studies, adiponectin had positive correlation results with BMI. To date, studies have not been able to confirm the distinct relationship between body weight or BMI and adiponectin in patients with diabetes.To examine the effects of the formerly obesity affects current adiponectin in patients with diabetes, an observational study was performed.

Methods: 323 admitted patients or outpatient, who visited Kyungpook National University Hospital, conducted a cross-sectional cohort study. Among 323 patients with type 1 diabetes, acute hyperglycemia, missing data, or thiazolidinedione users were excluded, and a total of 236 patients were analyzed. Based on BMI, BMI<25: non-obese (n), BMI≥25: obese (o), present-non-obese patients were grouped to formerly obese&now normal (on, n=46) and in the past&present normal group (nn, n=117).

Results: Adiponectin was statistically significantly reduced in the group (on), which was currently normal and formerly obesity (8.8 vs 7.0, p=0.027). There were no differences between the two groups in other characteristics or laboratory markers. Regression analysis confirmed the association of adiponectin with each variable: current BMI, positive correlation with body weight (standard coefficients beta= 0.256, 0.356, p=0.013, 0.017, respectively), past maximum BMI, maximum A negative correlation with body weight (beta=-0.366, -3.511, p<0.001, p=0.001, respectively) was found to be statistically significant. It is still statistically significant even if each is adjusted by age, sex, and BMI. Odds ratio between two groups (nn, on), adiponectin was statistically significant (OR=0.90, 95% CI= 0.82-0.99). Groups with formerly obese appear to have decreased adiponectin by approximately 10% compared to nn group.

Conclusion: In conclusion, formerly obesity has an independent effect on the current adiponectin level even after correcting the current weight was normal.

The effects of psychological insulin resistance on the intensive care of type 2 diabetes in patients treated with insulin

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Objective: Many patients with type 2 diabetes (T2D) are reluctant to initiation and maintenance of insulin therapy partly due to the negative attitude for insulin. This study aims to examine the effects of psychological insulin resistance (PIR) and diabetes-related distress on intensive diabetes management in patients treated with insulin.

Methods: Validated structured questionnaires - Insulin Treatment Appraisal Scale (ITAS) and the Problem Areas In Diabetes (PAID) - were used in 271 patients with T2D who were treated with insulin at least 6 months. Multiple regression model was conducted to determine the association between the psychological aspects and glycated hemoglobin (HbA1c).

Results: The participants' (144 [53.1%] male and 127 [46.9%] female) mean age was 59.9±12.3 years; the mean durations of diabetes and insulin therapy were 16.1±9.3 and 4.8±4.9 years, respectively. The total scores of negative and positive appraisal of ITAS and PAID were 45.5±8.8, 15.0±2.1 and 67.3±14.1, respectively. The top 3items presenting the highest scores on negative treatment appraisal were "Diabetes has gotten worse", "Failure recognition on pre-insulin treatment", and "Getting worry from family/friends" (the number [%] for "Agree", 197(72.7%), 189(69.8%), and 163(60.1%), respectively). In total, the negative appraisal scores of ITAS questionnaires were significantly associated with poor glycemic control after adjustment for confounding factors. Only female showed a positive relationship between positive ITAS scores and lower HbA1c ("taking insulin helps to improve my health", β±SE, -0.50±0.21, P<0.05). Meanwhile, diabetes-related distress such as "discomfort", "mood instability", and "efforts to diabetes-care" were associated with lower HbA1c in female (all P<0.05).

Conclusion: This study demonstrated that negative treatment appraisals were associated with poor glycemic control. Moreover, given our findings that the positive appraisal of insulin had a significant impact on good glycemic control, providing positive reinforcement and supportive care could help with glycemic control in T2D patients receiving insulin therapy.

THREE C'S (CHECK ,CHANGE AND CONTROL) HYPERTENSION

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Objective: Check Change and control (three c's) is an intensive blood pressure intervention Program targeting poorly controlled hypertension in patients with chronic disease ex,Diabetes . it is patient centered care module focus on the patient participation in treatment plan with the guidance of multidisciplinary team. The three steps intervention include check patient's blood pressure, change their life style and control of drug therapy according to latest guidelines

Methods: Prospective Quality improvement project on 34 patients poorly controlled blood pressure who attended Qatar university health center. The inclusion criteria for the sample were patients from 20-75 years old, with hypertension and with other chronic disease like diabetes. excluded patients were with secondary hypertension ex Pheochromocytoma , tumor and patients with severe kidney disease Patients were called to attend health center for consultation in which meeting is done with patient, pharmacist, physician and nurse for combined comprehensive consultation. patient is educated how to take accurate readings, change lifestyle, improve medication adherence

Results: Out of 34 patients with raised BP reading we excluded 16 patients as blood pressure normalized on next PHCC attendances. Only 6 patients out of 18 attended following 3 phone calls. 2 of which did not require intervention as blood pressure readings normalized and out of the 4 patients 3 had a BP decrease more than 10 mm hg following intervention and the fourth patient didn't attend the follow up appointment.

Conclusion: Although the number of the responded patients to the treatment methodology is not high but the patients who received the intervention and education has very impressive improvement where of nearly two thirds of patients are uncontrolled did not attend for intervention when called 3 times. So poorly controlled blood pressure should not be an indicator for quality of health care organization or professionals as many other related factors are in play

PE63 Diabetes care & Education

Education and Management of Lifestyle in Type 2 Diabetes : A Systematic Review

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Objective: Education for lifestyle modification aimed at reducing energy intake and increasing physical activity is the principal therapy for overweight and obese patients with type 2 diabetes

Methods: The study is a literature review of scientific article through several online database including PubMed and ClinicalKey using keywords related to the clinical query. The results were assessed based on the title and abstract on the articles.

Results: Several stduy about Education and Management in Type 2 Diabetes have been colected. From the relating articles, nonpharmacological therapy plays an important role in the management of type 2 diabetes. Before therapy with treatment, lifestyle modification is recommended for someone with type 2 diabetes, so it gave good health quality.

Conclusion: Lifestyle modification is highly recommended for someone with type 2 diabetes. Losing weight, eating fruit, vegetables and a low-fat diet, especially animal fat, and balanced with physical activity can help reduce blood sugar significantly compared with medical therapy

PE64 Diabetes care & Education

Prevalence of glucose intolerance in adult Mongolians: results of a nationwide survey

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Objective: To evaluate the prevalence of glucose intolerance in the urban and rural areas in Mongolia

Methods: We used data from 4th national WHO STEPS survey which sampled 377 units from urban and rural areas in Mongolia. Randomly selected 6654 Mongolians (4315 urban and 2337 rural subjects) aged 15-69 were involved in this study. According to WHO criteria, glucose metabolism was defined as normal, impaired fasting glycemia (IFG) and diabetes mellitus (DM) based on fasting capillary blood glucose level and self-reports of diagnosis by a physician.

Results: the prevalence of DM and IFG in general population was 8.3% and 17.4% respectively. The prevalence of DM was greater in urban: 8.9% in the urban and 7.3% in the rural populations (p⟨0.05). However, the prevalence of IFG was slightly higher in rural subjects: 16.6% and 18.7% in urban and rural subjects respectively. Furthermore, there was a gender difference showing that higher prevalence of DM and IFG in men: The prevalence of DM and IFG was 10% and 19.2%, respectively, in men, and 6.7% and 15.7% in women. In both sexes, the prevalence of DM increases with age: the highest prevalence of DM in various age groups was men aged 45-64-years-old (15.5%) and women aged 55-69-years-old (13.7%) respectively. Regard to the risk factors related to diabetes, the prevalence of obesity was higher in urban and rural subjects in both men and women thereby indicating that the higher prevalence of DM was mostly explained by the association between obesity and glucose intolerance. The percentage of obesity was 49.4% (including overweight) as defined as BMI≥25kg/m2. According to waist circumference criteria (for men≥90 cm, women≥80 cm) the central obesity was 53.0% in general population.

Conclusion: The prevalence of the population with glucose intolerance was higher in Mongolia, higher than the survey findings in 1999 and 2013.

PE65 Diabetes care & Education

Knowledge, attitude and practice of metformin extended-release tablets among clinicians in China: A cross-sectional survey

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Objective: Metformin extended-release (XR) is the once daily preparation of the drug. The aim of the study was to investigate the knowledge, attitude and practice of metformin XR tablets among clinicans.

Methods: We conducted a cross-sectional online survey among endocrinologists, general practitioners, and internists, who are taking routine care of patients with type 2 diabetes in the primary, secondary, and tertiary hospitals in Sichuan Province, China. We designed an online questionnaire including the demographic information, the knowledge, attitude and practice about metformin XR tablets. We decribed the results using SPSS version 25.

Results: We included 161 participants, 68% of which were females and 64% were from the tertiary hospitals. The mean age of the participants was 39.5±7.8 years (ranged between 22-62 years). Only 8.1% of the participants correctly answered the knowledge questions. Over 80% of the participants preferred metformin XR to metformin immediate release (IR) and believed the effectiveness of metformin XR is superior, and 62.7% believed metformin XR has less side effect. However, none of these attitudes are well supported by the evidence. Majority of the clinicians (85.7%) prescribed metformin XR only because the patients need metformin, while only 47% of the participants prescribe the drug because the patients asked for once daily preparation.

Conclusion: Our study identified clear gaps in the clinicians' knowledge, attitude and practice of metformin XR tablets from different levels and specialties in China. Clinical guidance on specific anti-diabetic drugs and close collaboration between the clinicians and the clinical pharmacists are warranted.

PE68 Diabetes complications- basic & translational

Liraglutide improved the cognitive function of diabetic mice via the receptor of advanced glycation end products down-regulation

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Objective: Hyperglycemia, associated with advanced glycation end products (AGEs) and its receptor (RAGE), is a well-recognized risk factor of cognition decline. We aim to investigate the effect of Liraglutide on cognitive function of diabetic mice and the mechanism in this progress.

Methods: db/m mice without diabetes and db/db mice, were used in this present study. Liraglutide was used to remedy diabetic mice. Neuros and the level of RAGE in hippocampus were showed by immunofluorescence. And then, PC12 cells or HT22 cells exposure AGEs were treated with liraglutide. Receptor of GLP-1 (GLP-1R) and RAGE were measured. Co-immunoprecipitation assay were carried out to detect the interaction between GLP-1R and RAGE.

Results: Compared to db/m mice, diabetic mice showed decreased cognitive function. Moreover, lower GLP-1 level in plasma and local GLP-1R level in hippocampus were detected in db/db mice. In addition, More RAGE was detected in diabetic mice than those without diabetes. However, decreased GLP-1R and increased RAGE levels were reversed by liraglutide in vivo. Additionally, we found decreased cellular activity in cells with AGEs in vitro. Moreover, AGEs up-regulated RAGE in PC12 and HT22 cells. However, GLP-1 improved the cell activity damaged by AGEs. Although we did not discover RAGE in the mixture pulled down by the antibody of GLP-1R, elevated RAGE induced by AGEs was restored by liraglutide in PC12 and HT22 cells.

Conclusion: We demonstrated that the cognitive function of diabetic mice was improved by liraglutide via the down-regulation of RAGE.

Potential Biomarker of Glycated Albumin (GA) in the Evaluation of Glycemic Control in Patients With Diabetes and Chronic Kidney Disease: Systematic Review

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Objective: The aim of this review is to know potential biomarker of glycated albumin in the evaluation of glycemic control in patients with diabetes and chronic kidney disease

Methods: The study is a systematic review of scientific article through several online database including PubMed and ClinicalKey using keywords related to the clinical query. Our review was arranged by 55 Journals selected by this method.

Results: Several study about glycated albumin as glycemic control biomarker in patients with diabetes and chronic kidney disease have been colected. Study from Tigan,2017 showed that GA is superior to HbA1c in assessing blood glucose control in diabetes patients with advanced CKD with total patient 3928. Other study showed that GA significantly reflected glycemia control in diabetic patients with predialysis CKD that HbA1c serum (P=0.005).

Conclusion: Glycated Albumin is a short-term marker of glycemia that has been evaluated as an alternative test to A1C in patients with DM. If compared to A1C, GA is more reliable to evaluate glycemic variability. Also, it is especially indicated for patients on hemodialysis and its levels are not affected in the presence of anemias or hemolytic processes. Compared to the fructosamine test, GA is more advantageous, since it is not influenced by other serum proteins.

Derived Time-in-range is Associated with MACE in T2D: DATA From the DEVOTE Trial (Originally presented at ADA 2020)

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Objective: There is a need to validate time-in-range (TIR; percentage of time with plasma glucose between 70 and 180 mg/dL (3.9-10.0 mmol/L) as a surrogate endpoint for long-term clinical outcomes.

Methods: We used data from patients with 8-point glucose profiles (8pp) from the double-blind cardiovascular outcomes trial, DEVOTE (NCT01959529). In total, 7637 patients with T2D and either established CVD or at high risk for CVD were included in the trial. The primary endpoint in DEVOTE was time to first MACE. The 8pp were collected at 1 year, 2 years and end-of-trial. Median length of follow-up was 2 years. For 5644 patients, 8pps with at least 7 points existed. Among the 681 major adverse cardiovascular events (MACEs) in DEVOTE, 360 were among patients with 8pps. Individual TIR was derived as the proportion of the 8pp within range. A Cox model was used to estimate the association between derived TIR and time to first MACE. Hazard ratios (HR) were estimated for patients with TIR>70% vs TIR≤70%, and for TIR>70% and TIR 50-70% vs TIR≤50%.

Results: Patients with TIR >70% had the lowest observed incidence of MACE compared to lower TIR categories. Derived TIR was >70% for 65% of the patients. Estimated rate of first MACE was lower for TIR >70% and TIR 50-70% vs TIR≤50% and for TIR>70% vs TIR≤70% (HR: 0.74 [0.60;0.91]95% CI; p⟨0.01). The associations were maintained when analyses were adjusted for baseline characteristics.

Conclusion: Derived TIR was associated with rate of first MACE for T2D patients in DEVOTE.

Role of hyperglycemia in the pathogenesis of Na+/K+ disturbance

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Objective: The diabetic patients may develop electrolyte imbalance. This study aims to determine an inverse relationship between serum sodium (Na+) and potassium (K+) levels in diabetic patients.

Methods: This cross-sectional was conducted in KIST Medical College and Teaching Hospital, Lalitpur, Nepal over a period of 2 months (June to July 2016). Total of 135 patients (65 male and 70 female) diagnosed with type 1 and type 2 diabetes mellitus of age ranged from 14 to 85 years were included in this study. Fasting blood glucose (FPG) level was analyzed with semiautomatic analyzer- humalyzer 3000 by Glucose oxidase/Peroxidase method and Na+ and K+ levels were analyzed with ion selective electrodenova electrolyte. The relationship among serum Na+ level, serum K+ levels and FPG levels were determined by linear regression and ANOVA with software SPSS version 20. A 95% confidence interval was used.

Results: Serum Na+ level was insignificantly negatively correlated (r=-0.091, p=0.296) with FPG level while a positive correlation of serum K+ level (r=0.235, p=0.006) was seen with FPG level and an inverse relation between serum Na+ and K+ was found. Age showed insignificant negative correlation with serum Na+ (r= -0.203, p=0.018), insignificant positive correlation with K+ (r=0.067, p=0.443) and insignificant negative correlation with FPG (r= - 0.045, p=0.608).

Conclusion: Hyperglycemia disrupts the balance of serum Na+ and K+ in uncontrolled diabetes mellitus. This study showed hyponatraemia and hyperkalaemia with increased hyperglycemia i.e. there is inverse relation between serum Na+ and K+ levels and it is dependent plasma glucose level.

BIOMARKERS IN EARLY DETECTION FOR HEART FAILURE IN PATIENTS WITH DIABETES MELLITUS

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Objective: to find alternative biomarkers for the development of chronic heart failure (CHF) in patients with diabetes mellitus (DM).

Methods: A total of 155 patients (14 men and 61 women) with type 1 and type 2 diabetes, aged 34 to 84 years, were examined. All patients underwent standard clinical and laboratory examination, with an assessment of the levels of pro-inflammatory cytokines (IL-6, TNF-alpha), chemokines (MIG, RANTES), growth factors (FGF-23, VEGF-A). A renal function was assessed based on the serum creatinine, GFR was calculated according to the CKD-EPI formula, albuminuria was assessed as albumin/creatinine ratio (A/K). An echocardiographic examination was conducted according to the standard protocol with the calculation of dimensional, volume and speed characteristics. Statistical analysis was performed using smSTATA 14.2 for Mac (2018).

Results: The levels of BNP and proBNP were identified as CHF in 57% DM patients. The levels of BNP and proBNP positively correlated with the levels of homocysteine, uric acid, IL-6, CRP, hsCRP, A/K, creatinine, cystatin C, TNF-alpha, chemokines (MIG, RANTES), growth factors (FGF-23, VEGF-A) (p ⟨0.05). According to multiple regression analysis, predictors for increasing proBNP were IL-6, A/K, creatinine (ß=0.70, p⟨0.001, ß=3.51, p=0.01, ß=0.97, p=0,01, respectively). ROC analysis determined the highest diagnostic significance of creatinine for predicting heart failure. The significance of IL-6 was higher than A/K (AUC-0.777). So, when the level of IL-6 (AUC-0.789) was 3.1 mg/ml, the sensitivity and specificity for increasing proBNP concentration were 71.9% and 71.2%, respectively.

Conclusion: IL-6 might be an independent predictor of the development of heart failure in patients with diabetes.

PE77 Diabetes complications-clinical

Risk factors for development and progression of diabetic retinopathy in patients with diabetes mellitus

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Objective: To define stages of diabetic retinopathy (DR) in patients with diabetes mellitus, to investigate risk factors for development and progression of diabetic retinopathy

Methods: The study included 60 patients with diabetes mellitus, who were served by the cabinets of endocrinology and ophthalmology in out-patients department's the General Hospital for Special Servants of Mongolia. We assumed risk factors of DR to answer the questionnaire, to measure anthropometric indices and to perform laboratory examination of HbA1C. Changes of DR were diagnosed by the indirect ophthalmoscopy. Statistical evaluation of the study was performed be SPSS 26.0 software.

Results: The prevalence of DR was 51.67%, the mean age of participants 52 ± 11.5 years, mean of diabetes duration of 9.017 ± 5.6463 years, mean of HbA1C $9.3695\pm2.14430\%$ and mean body mass index (BMI) was 28.8 kg/m2. Among DR patients, the number of mild, moderate, severe non-proliferative diabetic retinopathy (NPDR) patients and proliferative diabetic retinopathy (PDR) patients were 4 (6.67%), 16 (26.67%), 4 (6.67%) and 7 (11.66%), respectively. BMI, age, sex, smoking or blood pressure were no significant difference for patients with and without DR. However, there was a significant difference between different status of employment groups $(x(2)=7.122, P=0.028)$, as well as between insulin therapy group and non-insulin therapy group $(x(2)=8.763, P=0.033)$. The multivariate logistic regression analysis demonstrated the risk factors for DR occurrence were hemoglobin A1c (HbA1c) (OR=0.707, 95%CI: 0.525-0.954, P=0.023) and duration of diabetes (OR=0.835, 95%CI: 0.744-0.938, P=0.002).

Conclusion: The occurrence of DR in patients was associated with duration of diabetes, HbA1c. Increased HbA1c level and longer duration of diabetes were independent risk factors for DR in diabetic patients. Good glycemic and regular screening to detect diabetic retinopathy is highly recommended as timely intervention can prevent most diabetic causes of blindness.

PE78 Diabetes complications-clinical

Advanced liver fibrosis is independently associated with an increased risk of chronic kidney disease in patients with type 2 diabetes

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Objective: Non-alcoholic fatty liver disease (NAFLD) is associated with chronic kidney disease (CKD) in different patient populations. However, the causal relationship between NAFLD and the development of CKD is uncertain, particularly in patients with type 2 diabetes mellitus (T2DM). We aimed to investigate the association between NAFLD and the risk of incident CKD in patients with T2DM.

Methods: In this large, longitudinal cohort study of Korean patients with T2DM, 3,188 patients with preserved renal function were recruited. NAFLD was defined as the presence of hepatic steatosis on ultrasonography without any other causes of chronic liver diseases. The severity of NAFLD was assessed based on the NAFLD fibrosis score (NFS). Advanced liver fibrosis was defined as NFS 〉 0.675. CKD was defined as estimated glomerular filtration rate (eGFR) 〈 60 mL/min/1.73 m2.

Results: At baseline, 1,729 (54.2%) patients had NAFLD, of whom 94 (5.4%) had advanced liver fibrosis. During the follow-up of 8.3 ± 3.6 years, 472 (14.8%) patients developed incident CKD, 220 (15.1%) in the non-NAFLD group, 226 (12.8%) in hepatic steatosis alone group and 26 (27.7%) in advanced liver fibrosis group. There was no increased risk of incident CKD in the NAFLD group compared with the non-NAFLD group (p = 0.79). However, among patients with NAFLD, advanced liver fibrosis was associated with an increased risk of CKD (adjusted hazard ratio [HR] 1.78 (95% confidence interval [CI] 1.14-2.76, p=0.011).

Conclusion: Advanced liver fibrosis in NAFLD is independently associated with an increased risk of incident CKD in patients with T2DM.

PE79 Diabetes complications-clinical

Triglyceride glucose waist circumference is a better predictor of the progression of coronary artery calcium compared with other indices of insulin resistance: a longitudinal observational study

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Objective: The triglyceride glucose (TyG) index, a product of triglyceride and fasting glucose, is a reliable marker for insulin resistance; however, few studies have investigated the efficiency of TyG-related markers that combine obesity markers with TyG index. This study aimed to investigate the association between coronary artery calcification (CAC) progression and the TyG-related markers in adult Koreans.

Methods: We enrolled 1,145 asymptomatic participants who underwent repeated CAC score measurements during routine health examinations. Homeostasis model assessment of insulin resistance (HOMA-IR), TyG index, TyG-BMI (body mass index), and TyG-WC (waist circumference) were subsequently analyzed. Progression of CAC was defined as (1) incident CAC in a CAC-free population, or an (2) increase of ≥2.5 units between the baseline and final square root of the CAC scores participants with detectable CAC at the baseline examination.

Results: According to the quartiles of each parameter, the subjects were stratified into four groups. The prevalence of progression increased with the TyG-WC quartile (15.0%, 24.1%, 31.0%, and 32.2%, respectively; P 〈0.001). The multivariate-adjusted odds ratio [95% confidence interval (95% CI)] for CAC score progression was 1.70 (1.06-2.72) when the highest and lowest TyG-WC index quartiles were compared. Furthermore, the predictability of TyG-WC for CAC progression was better than the other indices by the area under the curve (AUC) (AUCHOMA-IR = 0.543, AUCTyG = 0.557, AUCTyG-BMI = 0.583, and AUCTyG-WC = 0.600).

Conclusion: The TyG-WC index predicted CAC progression better than other markers of insulin resistance and could be a potential marker of future coronary atherosclerosis.

PE80 Diabetes complications-clinical

Adropin's level and lipid profile correlation in patients with type 2 diabetes mellitus comorbid with essential hypertension and obesity

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Objective: Recent studies suggested adropin as a substantial player in the development of endothelial dysfunction and dyslipidemia through its participation in the glucose and lipid metabolism and energy homeostasis. The aim of our study was to investigate the association of adropin with lipid profile in diabetic patients under the influence of the essential hypertension and obesity.

Methods: 121 patients with essential hypertension were enrolled into the investigation. They were divided into 2 groups: the first one (n = 64 patients, 38 females, average age – 57.8 ± 7.89 years) was only with hypertension, and the second one (n = 57, females – 31, age – 59.1 ± 9.73) – hypertension comorbid with 2TDM and obesity. Serum adropin level was measured by ELISA. We examined total cholesterol (TC), LDL-C, HDL-C, triglycerides (TG).

Results: The group with comorbid 2TDM and obesity showed statistically increased TC, LDL-C (P〈0.05) without significant differences in HDL-C, TG compared with the first group. The serum level of adropin was statistically decreased in the comorbid group (1.93 ± 0.59 ng/ml vs 2.87 ± 0.61 ng/ml, P〈0.05). A moderate nagative correlation was found between TG (r=0.41) and LDL-C (r=0.58) and adropin levels (p〈0.01) and positive correlation with HDL-C (r=0.39; p〈0.05) in the patients with only hypertension. In contrast, the group with comorbidity did not revealed correlation of adropin and TC (p = 0.043) and TG (p = 0.059), and HDL-C (p=0.482) the only LDL-C was statistically correlated with the adropin's level in the first group (r=0.29; p=0.021).

Conclusion: The presence of 2TDM and obesity lead to diminished level of adropin in hypertensive patients. In patients with comorbidity, the link between serum adropin levels and lipid profile is not so significant as in patients with essential hypertension only, probably, due to severe low level of adropin in such group of patients.

Glucose variability and frailty in older patients with diabetes: a pilot study using continuous glucose monitoring

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Objective: To assess the relationship between glucose variability and frailty.

Methods: Forty-eight type 2 diabetic patients aged ≥65 years were enrolled. The FRAIL scale was used for frailty assessment, and participants were classified into 'healthy & pre-frail' (n = 24) and 'frail' (n = 24) groups. A continuous glucose monitoring (CGM) system was used for a mean of 6.9 days and standardized CGM metrics were analyzed: mean glucose, glucose management indicator (GMI), coefficient of variation, and time in-, above-, and below- range (TIR, TAR, and TBR).

Results: The mean age was 79.6 years [range 65-96] and the male to female ratio was 1.82:1. The demographics did not differ between groups. However, among the CGM metrics, mean glucose (178 mg/dL vs. 207 mg/dL), GMI (7.8% vs. 8.8%), and TAR in the post-breakfast (45% vs. 76%), post-lunch (36% vs. 70%), and post-dinner (44% vs. 70%) were higher in the frail group (all p<0.05). After multivariate adjustments, the post-lunch TAR (OR = 1.034, p = 0.029) affected the prevalence of frailty.

Conclusion: Higher glucose variability with marked daytime postprandial hyperglycemia is significantly associated with frailty in older patients with diabetes.

Optimal blood pressure to prevent stroke recurrence in adults with stroke: a nationwide cohort study

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Objective: Optimal target blood pressure (BP) for recurrent stroke prevention in patients with a prior history of stroke has not clearly addressed.

Methods: We performed a retrospective cohort study using the Korean National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) data. The hazards of stroke recurrence were analyzed according to the systolic BP (SBP) or diastolic BP (DBP) ranges measured during baseline health examinations between 2009 and 2010 among 402,652 adults aged 40 years or more with a history of stroke. This population was followed for diagnosis of nonfatal stroke, ischemic stroke and intracranial hemorrhage, until December 2016.

Results: During a median follow-up of 5.6 years, 39,523 nonfatal strokes, 32,025 ischemic strokes and 7,985 intracranial hemorrhages developed. When the SBP of 120-129 mmHg and the DBP of 70-79 mmHg were set as references, SBP of 100-109 mmHg and DBP of 60-69 mmHg were associated with a lower risk of developing recurred stroke, regardless of stroke type. SBP of <100 mmHg was associated with an increased risk of ischemic stroke in all population. When participants were divided into two groups according to anti-hypertensive use, SBP of 100-109 mmHg and DBP of 60-69 mmHg were associated with a lower risk of recurred stroke among non-uses of anti-hypertensive medication. In contrast, among antihypertensive users, lowering SBP below 120 mmHg did not lower the risk of stroke recurrence. Moreover, SBP of <100 mmHg was associated with an increased risk of ischemic stroke.

Conclusion: This study supports that BP control targeting SBP of 100-109 mmHg and DBP of 60-69 mmHg may reduce stroke recurrence in adults with prior history of stroke. However, it would be appropriate not to lower SBP below 100 mmHg among anti-hypertensive users to prevent recurrent stroke.

The association between sex-specific relative muscle mass and coronary artery calcification

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Objective: Low muscle mass has been an emerging risk factor for cardiovascular disease (CVD). We investigated whether relative skeletal muscle mass is associated with existing CAC which is a marker of subclinical atherosclerosis in a large population.

Methods: A total of 21,069 adults free of CVD who underwent a health checkup examination including cardiac tomography estimation of CAC scores were enrolled in this cross-sectional study. Relative muscle mass was presented using the skeletal muscle mass index (SMI) [SMI (%) = total appendicular muscle mass (kg)/body weight (kg) x 100] was estimated by bioelectrical impedance analyzer. Based on the distribution of Agatston scores, the participants were divided into CAC score categories of 0 (no CAC), greater than 0 to 100 (minimal to mild CAC), greater than 100 to 400 (moderate CAC), or greater than 400 (severe CAC).

Results: Of the 21,069 subjects, 13,425 (63.7%) subjects had no CAC, 5,437 (25.8%) had minimal to mild CAC, 1,160 (5.5%) had moderate CAC, and 597 (2.8%) had severe CAC. Log-transformed CAC score increased across sex-seperated SMI tertile. In a multivariate logistic regression analysis, the highest tertile was inversely associated with the presence of total CAC (adjusted odds ratio [AOR] = 0.86, 95% confidence interval [CI] = 0.78-0.95; p = 0.002), the presence of moderate and severe CAC (AOR = 0.84, 95% CI = 0.73-0.98; p = 0.018), and the presence of severe CAC (AOR = 0.72, 95% CI = 0.54-0.95; p = 0.020), compared with the lowest sex-seperated SMI tertile. Each 1% increase in sex-seperated SMI as a continuous variable also showed an inverse association with CAC presence.

Conclusion: Low skeletal muscle mass was significantly associated with higher risk of CAC, supporting sarcopenia as an independent risk factor of CVD.

Cardiovascular outcomes and safety of SGLT-2 Inhibitors compared with DPP-4 Inhibitors in older patients with type 2 diabetes

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Objective: Large-scale studies about cardiovascular (CV) disease benefits and safety of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in older patients with type 2 diabetes (T2D) remain rare. Therefore we compared cardiovascular outcomes and adverse events in older patients with T2D newly initiating on SGLT2i or dipeptidyl peptidase-4 inhibitors (DPP-4i).

Methods: This retrospective cohort study used a national health insurance database. Age ≥65 year patients with T2D who newly started SGLT-2i or DPP-4i from September 2014 to December 2016 were included. In total, 15699 propensity score matched pairs of SGLT-2i and DPP-4i new users were examined. Cox proportional hazards models were used to calculate the hazard ratios (HR) and 95% confidence intervals (CI) for CV and safety outcomes.

Results: The SGLT2i group were associated with lower risks for hospitalization for heart failure (HHF) (HR 0.86; 95% CI 0.76-0.97), all-cause death (HR 0.85; 95% CI 0.75-0.98), all-cause death or HHF (HR 0.86; 95% CI 0.78-0.94), stroke (HR 0.86; 95% CI 0.77-0.97) compared to the DPP4i group. The risks of DKA, fracture, and hypoglycemia were similar between both groups, however genital infection (HR 2.44; 95% CI 2.22-2.67), and urinary tract infection (HR 1.05; 95% CI 1.00-21.11) were more frequent with SGLT2i use versus DPP4i use.

Conclusion: Our findings suggest SGLT2i has CV benefits and can be used safely in older patients with T2D.

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DIABETES & METABOLISM JOURNAL

Aims and Scope

The aims of the Diabetes & Metabolism Journal are to contribute to the cure of and education about diabetes mellitus, and the advancement of diabetology through the sharing of scientific information on the latest developments in diabetology among members of the Korean Diabetes Association and other international societies.

    The Journal publishes articles on basic and clinical studies, focusing on areas such as metabolism, epidemiology, pathogenesis, complications, and treatments relevant to diabetes mellitus. It also publishes articles covering obesity and cardiovascular disease. Articles on translational research and timely issues including ubiquitous care or new technology in the management of diabetes and metabolic disorders are welcome. In addition, genome research, meta-analysis, and randomized controlled studies are welcome for publication.

    The editorial board invites articles from international research or clinical study groups. Publication is determined by the editors and peer reviewers, who are experts in their specific fields of diabetology.

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