POSTER PRESENTATION
ABSTRACTS
PP1: Molecular and Cellular Biology of Diabetes #1

PP1-1 A role for SNARE binding protein p34 in GLUT4-vesicle recycling
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Glucose transporter 4 (GLUT4) is the major insulin-responsive glucose transporter expressed in muscle and adipose tissue and plays an important role in whole body glucose homeostasis. In the basal state, GLUT4 is sequestered in several intracellular compartments, one of which has come to be known as insulin-responsive compartment (IRC). The IRC is a tissue specific compartment that is a target of insulin signaling cascade, however, its precise nature is unclear. Here, we report a novel mechanism to regulate IRC and glucose transport in adipocytes. First, we investigated the intracellular localization of p34 in adipocytes, and found that p34 was localized in the perinuclear region and exhibited the partial co-localization with GLUT4 at basal condition. Next, we show that p34 can bind syntphin, a Qc-SNARE, localized at trans-Golgi area. Third, we determined the role of p34 on insulin stimulated glucose transport in p34 silenced cells. P34 knockdown by siRNA decreased insulin responsive glucose uptake by 20%. These data suggested that p34 may have a role on GLUT4 entry into IRC and regulate GLUT4-reacquiring required for proper glucose transport.

PP1-2 Exendin-4 inhibits interleukin-1β-induced iNOS expression at the protein level in RinN5F β-cells
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Cytokines such as interleukin-1 beta (IL-1β) stimulate iNOS expression and nitrite (NO) overproduction leading to the β-cell damage. Meanwhile, glucagon-like peptide-1 (GLP-1) and its potent analog exendin-4 (EX-4) were well known for β-cell proliferation. However, the protective mechanisms of GLP-1 in β-cells exposed to cytokines were not fully elucidated. Therefore, the effects of EX-4 on the IL-1β-induced iNOS gene expression were investigated employing RinN5F β-cells. EX-4 inhibited IL-1β-induced iNOS protein expression and NO production. However, Northern blot and promoter analyses showed that EX-4 failed to inhibit IL-1β-induced iNOS mRNA expression and iNOS promoter activity. By electrophoretic mobility shift assay (EMSA), EX-4 did not alter the binding activity of NF-κB to the iNOS promoter. Consistent with the EMSA result, EX-4 did not inhibit nuclear translocation of p65. We also tested the effect of EX-4 on iNOS mRNA stability. Actinomycin D chase experiments showed that EX-4 did not affect the decay rate of iNOS mRNA and the promoter assay using the construct containing 3′-untranslated region of iNOS showed that EX-4 did not alter the stability of iNOS mRNA. Meanwhile, forskolin significantly inhibited IL-1β-induced iNOS protein, which was reversed by H-89, a protein kinase A (PKA) inhibitor. Moreover, EX-4 pretreatment restored IL-1β-induced decrease in CAMP toward control level. Additionally, cycloheximide chase study demonstrated that EX-4 significantly accelerated iNOS protein degradation. We, therefore, concluded that EX-4 inhibited IL-1β-induced iNOS protein and nitrite production via CAMP/PKA system irrespective of both transcriptional and posttranscriptional mechanisms of iNOS gene and this inhibitory effect of EX-4 appears to be regulated at posttranslational level.

PP1-3 Establishment of new clonal pancreatic β-cell lines (MIN6-K) useful for study of incretin/CAMP signaling
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Incretin/CAMP signaling is critical for potentiation of insulin secretion. Although several cell lines of pancreatic β-cells are currently available, there are no cell lines suitable for investigation of incretin/CAMP signaling. In the present study, we have newly established pancreatic β-cell lines (named MIN6-K) from the IT16 mouse, which develops insulinoma. MIN6-Kβ cells respond to both glucose and incretins such as glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP), as is the case in pancreatic islets, while MIN6-K20 cells responded to glucose, but not to incretins. Despite the difference in incretin-potentiated insulin secretion between these two cell lines, the accumulation of cAMP after stimulation of GLP-1 these cells is comparable in these cells. Interestingly, we found that incretin responsiveness is drastically induced by formation of pseudosilts from MIN6-K20 cells to a level comparable to that of pancreatic islets. Thus, these cell lines represent useful for studying incretin/cAMP signaling in β-cells.

PP1-4 Preadipocyte factor-1 induce transdifferentiation of pancreatic ductal cells into insulin secreting beta-cells
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Preadipocyte factor-1/Delta like 1 homolog (Pref-1/Dlk 1) is widely expressed in embryonic tissues, whereas in adult postnatal, its expression is limited. Although it is involved in cell development, differentiation and regeneration in various tissues, the function of Pref-1 is not cleared yet in pancreas. To extend our understanding for the role of Pref-1 in pancreas, we analyzed the intracellular signaling pathway of Pref-1 in pancreatic duct cell line, PANC-1. Purified soluble Pref-1 (Pref-1-mFc) treatment increased Akt, ERK1/2 and FOXO1 phosphorylation, and ERK1/2 and FOXO1 phosphorylation were blocked by PD98059, but not Akt phosphorylation in PANC-1 cells. We also observed that the activation of Pref-1 increased PDX1 and insulin genes transcription, whereas it decreased FOXO1. After overexpression of Pref-1 gene in PANC-1 cells, extracted proteins were analyzed by 2-DE and identified by MALDI-TOF. Protein which have protective effect against hypoxia-induced cell apoptosis and Rab GTPase-activating protein which might be related with AKT phosphorylation were increased by Pref-1 gene overexpression. We conclude that Pref-1 expression was regained in adult pancreatic cells during proliferation and might play an important role for the regeneration and differentiation of endocrine pancreas through phosphorylation of ERK1/2, FOXO1 and increased PDX-1 expression.

PP1-5 Expression of Pdx1 mediates differentiation from mesenchymal stem cells into insulin-producing cells
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The transplantation of insulin-producing cells is a promising approach for the treatment of insulin-dependent diabetes mellitus; however, lack of pancreas donors limits its application. Pancreatic ductal homeobox 1 (Pdx1) plays a key role in the differentiation of various non-β-cells into insulin-producing cells, but the potential mechanism remains to be clarified. The purpose of this study was to confirm that the expression of Pdx1 could mediate the differentiation of rat mesenchymal stem cells (MSCs) into insulin-producing cells, and evaluate the potential molecular mechanisms in the process that Pdx1 activates transcription of insulin gene. In this study, glucose-stimulated insulin secretion was obviously detected in MSCs transfected with Pdx1 cDNA by insulin release assay and the islet-like structure formed in Pdx1-expressing MSCs was stained into black-red by diithizone, while the native MSCs were opposite. In addition, we uncovered the close relationships among the expression of Pdx1, insulin and Ngn3 genes, whose expression indicated parallel changes after high glucose challenge, and the fluctuation of Pdx1 and Ngn3 partly resulted in the unstable release of insulin. Taken together, these findings demonstrated the effective role of Pdx1 gene in inducing insulin-producing cells, which may shuttle to the nucleoplasm of MSCs under high glucose, then initiate the expression of native transcription factors Ngn3 and recruit other proteins, resulting in transactivation of the relevant genes including insulin and generation of beta cell phenotype. Accordingly, these results would provide new insights that may be applicable to improve β cell replacement strategies and enhance diabetes therapy in the future.
Hepatocytes are excellent candidates for generating beta-cell surrogates for autologous transplantation, because liver and pancreas share a common bipotential precursor cell within the embryonic endoderm so that transdif-
fereientiation of hepatocytes to beta cells is easier than other germ-line cells. In this study, we try to transdifferentiate neonatal pig hepatocytes (NPHPCs) to insulin producing cells on the basis of our rodent data. In our previous study, we induce transdifferentiation of mouse primary hepatocytes into insulin producing cells by adenovirally transduction of Ad-PP1-1/VP-16, BETAA2 and MafA. NPHPCs were isolated from the liver of 3-day-old neonatal pig. The cells were cultured for 6 days in low serum and high glucose containing cytokines such as human hepatocyte growth factor (HGF), epidermal growth factor (EGF) after adenoviral transduction and formed pseudo-islet clusters by suspension cultures. Gene expression was determined cells were stained for insulin antibody. Insulin contents were measured with radioimmunoassay kit. Real-time PCR of isolated islets shows that albumin expression was significantly decreased in adenovirally transduced NPHPCs while insulin expression was strongly observed. Other pancreatic gene also induced in transduced NPHPCs but not in control NPHPCs. Consistent with PCR data, insulin was found in 10% of adenovirus-transduced group in immunohistochemical staining, but not in control group. The insulin content was increased in the transduced cells. In conclusion, we shows that neonatal pig hepatocytes could be induce to insulin producing cells by adenoviral transduction, which could provide basis of searching for alternative transplantable beta cell source for the treatment of diabetes mellitus.

**PP1-6**

*In vitro transdifferentiation of neonatal pig hepatocytes to insulin-producing cells using adenoviral transduction*

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*Development of anti-fibrosis coating on the alginate capsules for xenogenic islet transplantation*

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Microencapsulated pig islets are attractive alternative for islet transplantation. However early failure of transplanted islets by severe fibrosis still need to be overcome. The aim of this study is to establish the appropriate strategy for minimizing the fibrosis around the microcapsulated pig islets with anti-fibrosis coating with chitosan-dexamethasone 21-phosphate and polyethylene glycol-rapamycin. To optimize the anti-fibrosis coating on alginate microcapsule, we adjusted the polymerization solution and anti-fibrosis coating condition including chitosan-dexamethasone 21-phosphate and polyethylene glycol-rapamycin. Coated dexamethasone or rapamycin released gradually over time more than 21 days after coating. The islet cell viability in the microcapsules was tested by AO/PI staining until 14 days after encapsulation. Naked islets, alginate and each anti-fibrosis coating encapsulated islets were showed similar viability. Each anti-fibrosis coating alginate or alginate monolayer encapsulated porcine islets were transplanted to peritoneal cavity of type 1 diabetic mouse. Although the blood glucose levels of diabetic mice were normalized by transplantation both of anti-fibrosis coating alginate and alginate capsule, fibrosis infiltration of two different anti-fibrosis coating capsules surface were significantly decreased than alginate only capsules. The anti-fibrosis coating microencapsulated xenogenic islet transplantation might minimize the fibrosis.

**PP2: Molecular and Cellular Biology of Diabetes #2**

**PP2-1**

**Adiponectin modulates gluconeogenesis by inhibiting CREB coactivator TORC2**

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Adiponectin activates AMP-activated protein kinase (AMPK) in skeletal muscle cells and adipocytes, thereby lowers blood glucose through promoting glucose uptake and utilization in peripheral tissues. However, in hyperglyce-
mia conditions, increase in circulating adiponectin inhibits hepatic glucose output through unknown mechanisms. In response to fasting, transducer of regulated CAM response element binding protein (CREB) activity 2 (TORC2) is de-phosphorylated at Ser171 and transported to the nucleus, where it stimulates gluconeogenesis through binding to CREB, while AMPK inhibits the gluconeogenic process by promoting TORC2 phosphorylation and blocking its accumulation at the nucleus. In this study, we showed that in human hepatocyte L-02, adiponectin could promote AMPKα phosphorylation at Thr172 and thereby disrupts TORC2 activation. Under high glucose treatment, TORC2 was de-phosphorylated and degraded after over-expression of adiponectin. In conclusion, we showed that adiponectin could modulate gluconeogenesis through AMPK-CREB-TORC2 key enzymes in the gluconeo-
genic signaling pathway.

**PP2-2**

**Mechanisms that globular adiponectin reverses apoptosis in human umbilical vein endothelial cells intervention with AGEs**

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METHODS: Human Umbilical Vein Endothelial Cells (HUVECs) were cultured with different concentrations of AGEs for 24 h or 48 h, one group cells were pretreated with adiponectin (gAD). Cellular viability was detected by MTT. Cellular apoptotic rate was detected by flow cytometry with Annexin V-FITC/PI double stained. Both Bax and Bcl-2 were measured by western blot. Adiponectin receptor1 (AdipoR1) mRNA was determined by RT-PCR.

RESULTS: Cellular viability decreased gradually with increasing concentrations of AGEs, but cellular apoptotic rate increased on contrary. With 200 mg/L AGEs, gAD suppressed cellular apoptotic rate sharply versus to the
PP2-3
Pathophysiological roles of adiponectin/AdipoRs in mitochondrial bioenergetics via AMPK/SIRT1/PPAR-γ
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Mitochondrial dysfunction seems to be associated with insulin resistance. However, the upstream mechanisms for the physiological and pathophysiological regulation of mitochondrial bioenergetics are not well clarified. Here, we show that muscle-specific disruption of adiponectin (Ad) receptor (AdipoR1) resulted in decreased activation of AMP-activated protein kinase (AMPK)/SIRT1 by adiponectin as well as decreased expression and increased acetylation of PGC-1α. Decreased mitochondrial content and enzymes such as cytochrome c (Cyt c), decreased oxidative type I myofibers and increased oxidative stress-detoxifying enzymes such as catalase and manganese superoxide dismutase (SOD2), decreased molecules involved in fatty-acid oxidation such as medium-chain acyl-CoA dehydrogenase (MCAD), thereby leading to increased oxidative stress and increased tissue triglyceride content in skeletal muscle. Moreover, muscle-specific AdipoR1 knockout mice exhibited increased phosphorylation of S70 kinase and JNK and also increased serine phosphorylation of IRS-1 as well as decreased glucose transporter (GLUT) 4 expression and decreased Akt activation by insulin, which were associated with decreased rates of glucose disposal (Rd).
Importantly, all these alterations could result in insulin resistance and decreased exercise endurance. These data suggested that AdipoR1 appears to play causal roles in mitochondrial dysfunction and insulin resistance seen in diabetes.

PP2-4
Acetyl-L-carnitine improves mitochondrial dysfunction and insulin resistance in OLETF rats
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It has been shown that acetyl-L-carnitine (ALC) level is decreased in type 2 diabetes mellitus, which might be associated with the mitochondrial dysfunction and insulin resistance. Mitochondrial dysfunction could lead to the state of insulin resistance, defects in insulin secretion and is associated with the development of complications. ALC treatment was shown to improve insulin resistance, but the effects of ALC on mitochondrial function and insulin resistance in type 2 diabetes are not known. Thus, the aim of this study was to investigate the effects of ALC on mitochondrial function and insulin resistance in an animal model of type 2 diabetes mellitus, i.e., Otsuka Long-Evans Tokushima Fatty (OLETF) rats and their control strain Long-Evans Tokushima Otsuka (LETO) rats. Both oxygen consumption and the expression of complexes in oxidative phosphorylation were significantly increased after intraperitoneal injection of injections with rats (100 mg or 200 mg kg−1·day−1) ALC for 8 weeks. The treated rats also showed higher expressions of genes related to mitochondrial energy metabolism (PGC-1α, NRF-1) and caloric restriction (Sirt1), consistent with the increase in energy expenditure. ALC treatment increased the phosphorylation of Akt at Ser473, AMP-activated protein kinase (AMPK) at Thr172 and carnitine palmitoyltransferase (CPT)-1 and suppressed IRS-1 phosphorylation at Ser307. Manifestations of the metabolic syndrome such as white adipose tissue weight, degree of insulin resistance, dyslipidemia, and fatty liver were significantly ameliorated without change in food intake. Our data suggest that ALC may play an important role in improvement of insulin resistance through the effects on mitochondrial function.

PP2-5
Vaspin expression is regulated by metabolic hormones in 3T3-L1 adipocytes
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Recently, vaspin was identified as an adipokine with insulin-sensitizing effects, which is predominantly secreted from visceral adipose tissue. In this study, we have investigated the regulation of vaspin gene expression in 3T3-L1 adipocytes in different settings known to be associated with energy homeostasis and alterations in insulin sensitivity, as well as in pathophysiological conditions related to metabolic syndrome. A marked increase in vaspin expression was observed during differentiation, with a 1.7-fold increase between preconfluent and 2-day confluent cells even before differentiation was initiated. A further 3.8-fold increase was induced from day 0 to day 8 of differentiation (overall six fold). Overnight incubation with dexamethasone increased vaspin expression in adipocytes (100 μM-1.6 fold). High glucose increased vaspin secretion by 6.6-fold at 25 mM, pioglitazone by 1.6-fold at 100 μM, and fenofibrate by 1.5-fold at 100 μM. All other treatments decreased vaspin expression. Vaspin expression decreased with insulin by 37–53% at 10–100 nM, 48% with palmitate at 1 mM, 15–40% with tumour necrosis factor-alpha (TNF-α) at 10–20 ng/ml. Taken together, the level of vaspin is regulated physiologically by multiple hormones and metabolic factors. Our results suggest that vaspin expression level could be associated with status of metabolic disorders. The definite mechanism of vaspin action remains to be elucidated.

PP2-6
Etiological role of the glucose intolerance locus on chromosome 1 in the Spontaneously Diabetic Torii rat
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The Spontaneously Diabetic Torii (SDT) rat is an animal model of non-obese type 2 diabetes. To identify genes responsible for diabetes in SDT rats, we previously performed a quantitative trait locus (QTL) analysis for glucose tolerance using (BN × SDT) F1 × SDT backcrossed rats, and mapped three QTLs, Gisdt1, Gisdt2, and Gisdt3, associated with glucose intolerance on rat chromosome 1, 2, and X, respectively. In this study, we have clarified the etiological role of the Gisdt1 locus on chromosome 1. We produced reciprocal congenic strains carrying the Gisdt1 region of the SDT rat on the BN genetic background and vice versa (BN.SDT-Gisdt1 and SDT.BN-Gisdt1 congenic strains). At 12 weeks of age, frequently-sampled intravenous glucose tolerance test (FS-IVGTT) was performed, and gene expression in the liver was analyzed by microarray and quantitative RT-PCR. At the fasting state, BN.SDT-Gisdt1 strains showed higher Homeostasis Model Assessment-Insulin Resistance (HOMA-IR) values compared with BN rats, suggesting insulin resistance. In addition, BN.SDT-Gisdt1 strains exhibited higher expression of genes involved in gluconeogenic pathway compared with BN rats. In contrast, SDT.BN-Gisdt1 strains showed lower expression of those genes compared with SDT rats. These results suggest that the Gisdt1 locus is involved in hepatic insulin resistance.
group and diabetes group. OGTT was performed every 4 weeks from the 30th to 42nd week. mRNA levels of Chemerin and CMKLR1 in adipose tissue of the LETO rats and OLETF rats were determined by real-time PCR. mRNA expressions of Chemerin and CMKLR1 in subcutaneous and visceral adipose tissue in diabetes group and rosiglitazone group were significantly higher than that in LETO group \( P < 0.01 \), while Chemerin expression in rosiglitazone group was lower than that in diabetes group \( P < 0.01 \). Expressions of Chemerin and CMKLR1 mRNA in visceral adipose tissue were higher than that in subcutaneous adipose tissue \( P < 0.01 \) and \( P < 0.05 \). There was no correlation between Chemerin and CMKLR1 \( P > 0.05 \). Average maximal diameter of subcutaneous and visceral adipocyte in diabetes group was increased compared with that of LETO group \( P < 0.01 \). However, average maximal diameter of visceral adipocyte in rosiglitazone group was reduced compared to the diabetes group \( P < 0.01 \). Chemerin and its receptor CMKLR1 are up-regulated in OLETF rats, which can be inhibited by rosiglitazone. Chemerin and CMKLR1 may be involved in the pathogenesis of obesity, insulin resistance and type 2 diabetes.

PP3-2
Effects of SIRT1 on NO secretion and E-selectin expression in high glucose cultured endothelial cells
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To investigate the roles of SIRT1 in the development of diabetic atherosclerosis, seven Otsuka Long-Evans Tokushima Fatty (OLETF) rats and eight non-diabetic Long-Evans Tokushima Otsuka (LETO) rats were included. Real-time PCR was used to detect SIRT1 mRNA expression in abdominal aorta at the 42nd week. SIRT1 mRNA level in OLETF group was significantly lower than that in control group. To further investigate the roles of SIRT1 on the function of endothelial cells in high glucose, HUVEC were treated with SIRT1 activator resveratrol for 24 h before cultured in high glucose medium for 48 h. Method based on nitric acid reductase was used to analyze the NO content in the supernatant. Cells were collected to analyze the expression of endothelial nitric oxide synthase (eNOS), E-selectin and SIRT1. In order to verify the dependence of resveratrol on SIRT1, the effects of resveratrol on cells treated by SIRT1 siRNA were also examined. Compared with control cells, high glucose decreased NO secretion. Resveratrol treatment increased the expression of SIRT1 and the secretion of NO. After interfering the expression of SIRT1 using SIRT1 siRNA, the effects of resveratrol on NO secretion was impaired. SIRT1 also counteracted the other pro-atherosclerotic effects of high glucose, including the up-regulating roles of high glucose on the expression of eNOS mRNA. In conclusion, decreased expression of SIRT1 in artery may involve in the development of diabetic atherosclerosis, and SIRT1 activator may have great promise in the prevention and therapy of atherosclerosis in diabetic patients.

PP3-3
Effects of metformin on SIRT1 mRNA expression in abdominal aorta of the OLETF rats
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OBJECTIVE: To investigate SIRT1 expression in abdominal aorta of rats with spontaneous type 2 diabetes mellitus and the effect of metformin treatment on SIRT1 expression.

METHODS: Seventeen Otsuka Long-Evans Tokushima Fatty (OLETF) rats were randomly divided into the model group and treatment group (received metformin gavage for 12 weeks). Non-diabetic Long-Evans Tokushima Otsuka (LETO) rats of the same genetic background were included in the normal control group. Real-time PCR was used to detect SIRT1 mRNA expression in abdominal aorta.

RESULTS: Level of SIRT1 mRNA in the model group was significantly lower than that in the control group \( (P < 0.05) \). However, in the metformin treatment group, SIRT1 mRNA expression was significantly increased than that of the model group \( (P < 0.05) \).

CONCLUSION: Down-regulation of SIRT1 in artery may involve in the initiation and development of type 2 diabetes mellitus and associated vascular diseases. Metformin may have a protective role though activating SIRT1 expression.
**PP3-4**

**Effects of ER stress induced by tunicamycin on the activity of endothelial nitric oxide synthase**

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**BACKGROUND:** Metabolic diseases including obesity and diabetes are causally related to the development of atherosclerosis, which is known as an inflammatory disease. Endoplasmic reticulum (ER) stress has been known to link between metabolic stress and inflammation. However, the effect of ER stress on the endothelial nitric oxide synthase (eNOS) activity in vascular endothelial cells, which has an important role in regulating endothelial function, is currently unclear. In this study, we investigated the effect of ER stress on eNOS activity and the effects of various drugs on vascular ER stress.

**METHOD:** Human aortic endothelial cells (HAECs) were used in whole experiments. Tunicamycin (Tm) was used to induce ER stress. We measured the phosphorylation of eNOS and examined whether protein kinase C (PKC) is involved in this pathway using GFX, a PKC inhibitor. To identify the specific isoform of PKC involved in ER stress-induced eNOS inactivation, we also measured cytosolic and membranous forms of PKC βII and PKCδ.

**RESULTS:** Treatment of Tm decreased the phosphorylation of eNOS at the site of Ser1177 but increased it at Thr495 site. Tm-induced changes in ENOS phosphorylation were reversed with GFX pretreatment. Tm induced translocation of PKCδ but not PKC βII from the cytosolic to membrane fraction. ALA and rosiglitazone, but not telmisartan decreased ER stress and ER stress-induced ENOS inactivation.

**CONCLUSION:** Tm-induced ER stress inactivates ENOS by activating PKCδ. ER stress-induced ENOS inactivation might lead to decrease in NO bioavailability, endothelial dysfunction and eventually atherosclerosis. ALA and rosiglitazone might be used to reverse ER stress-induced endothelial dysfunction.

**PP3-5**

**Withdrawal**

**PP3-6**

**Clusterin deficiency accelerates neointimal hyperplasia after vascular injury**

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**OBJECTIVE:** Clusterin is induced in vascular smooth muscle cells (VSMCs) during atherosclerosis and injury-induced neointimal hyperplasia. However, its functional roles in VSMCs and endothelial cells remain controversial and elusive. This study was undertaken to clarify the role of clusterin in neointimal hyperplasia and elucidate its underlying mechanism of action.

**METHODS AND RESULTS:** Adenovirus-mediated overexpression of clusterin (Ad-Clu) inhibited TNF-alpha-stimulated expression of monocyte chemotactic protein-1, fractalkine, cell adhesion molecules, and matrix metalloproteinase-9, leading to repression of VSMC migration. Both Ad-Clu and secreted clusterin suppressed VSMC proliferation by inhibiting DNA synthesis, but not by inducing apoptosis. Ad-Clu upregulated p53 and p21cip1/waf1 but downregulated cyclins D and E, leading to suppression of PRB phosphorylation and subsequent induction of G1 arrest. Moreover, clusterin deficiency augmented VSMC proliferation in vitro, and neointimal hyperplasia was accelerated in cuff- or wire-injured femoral arteries of clusterin deficient (Clu KO) mice in vivo. Additionally, clusterin diminished TNF-alpha-induced apoptosis of human umbilical vein endothelial cells (HUVECs) and restored endothelial nitric oxide synthase (eNOS) expression suppressed by TNF-alpha.

**CONCLUSION:** These results suggest that upregulation of clusterin during vascular injury and atherosclerosis may be a protective response against, rather than a causative response to, the development of neointimal hyperplasia.

**PP3-7**

**PPAR δ-mediated anti-inflammatory mechanisms inhibit streptozotocin-induced diabetic nephropathy**

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Activation of the nuclear hormone receptor peroxisome proliferator-activated receptor δ (PPARδ) has been shown to improve insulin resistance, adiposity, and plasma HDL levels. Recently, several studies reported that activation of PPARδ is atheroprotective, however, the effect for the renal function remains unclear. Here we report the renoprotective effect of PPARδ activation in a model of streptozotocin (STZ)-induced diabetic nephropathy. In this model, the PPARδ agonist GW0742 (1 mg/kg) was administered to C57BL/6 mice for 8 weeks after inducing diabetes. Administration of GW0742 decreased the urinary albumin excretion without altering blood glucose level. Macrophage infiltration, mesangial matrix accumulation, and type IV collagen deposition were substantially attenuated. Inflammatory gene expression in the kidney cortex, such as MCP-1, IL-6, TNF-α, were also suppressed. These results revealed that the actions of PPARδ activation attenuate the progression of STZ-induced diabetic nephropathy by inhibiting inflammatory process.

**PP3-8**

**Sitagliptin is more beneficial in non-obese diabetic mice models**

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This study was conducted to determine whether treatment with sitagliptin (SITA) and pioglitazone (PIO) resulted in different effects on glucose homeostasis and β-cell dynamics in non-obese and obese animal models of type 2 diabetes. Akita mice and db/db mice were used as lean and obese models, respectively, and divided into the control group, and SITA or PIO treatment group. Blood glucose levels were significantly decreased in both SITA and PIO group regardless of mice models. With the intraperitoneal glucose tolerance test, SITA-treated group showed decreased area under the curve glucose (AUCg) and glycemic excursion significantly only in Akita mice by contrast, PIO group was effective in both mice. Both SITA and PIO preserved normal islet structure and increased β-cell ratio in the islets. SITA evidenced a higher proliferation rate of beta-cells in Akita mice in addition to lower rate of apoptosis rate, whereas PIO showed only lower rate of apoptosis without difference of proliferation rate. Taken together, SITA had a more profound glucose lowering effect and improved β-cell dynamics by increasing the beta-cell proliferation besides decreasing apoptosis only in the lean mice, whereas PIO had similar glucose lowering effect in both mice model and preserved β-cell only by decreasing apoptosis.

**PP4-1**

**Effect and mechanism of rosiglitazone on pbk expression of insulin resistance rat skeletal muscle**

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**AIM:** To study the effect of insulin sensitivity agonist, rosiglitazone on pbk expression and phosphorylation level of insulin resistant rat’s skeletal muscle induced by hexadecanocan acid.

**METHODS:** Insulin resistant rat skeletal muscle cell model was induced by hexadecanocan acid. There were four groups: normal skeletal muscle group (NG), insulin resistance group (IR), insulin resistance rosiglitazone intervention group (RI). The four groups were treated with insulin. Then, the pbk expression and phosphorylation level were tested with Western blotting.
RESULTS: The pkb expression of skeletal muscle in group RO decreased compared with normal control group, but higher than that in group IR. Compared with group RL, the pkb expression of skeletal muscle in group RO was higher, too. But, there was no significance. However, pkb473 serin phosphorylation level in group RO increased significantly compared with group IR (P<0.05). pbk473 serin phosphorylation level in group RL decreased significantly compared with group RO (P<0.05).

CONCLUSION: Rosiglitazone can increase pkb473 serin phosphorylation level which is related with PI3K route in insulin signal transduction and further improve insulin resistance.

PP4-2 Expression of PPARγ target genes is selectively modulated by desumoylation of PPARγ in C2C12 myotubes
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Peroxisome proliferator-activated receptor-γ (PPARγ) is a member of the nuclear hormone receptor superfamily and functions as a transcriptional regulator in various tissues. It has been reported that modification of PPARγ by the small ubiquitin-like modifier (SUMO) plays an important role in PPARγ transcriptional activity. In this study, we investigated how expression of PPARγ target genes is modulated by sumoylation of PPARγ in C2C12 myotubes. We used an overexpression system of SUMO specific protease 2 (SENP2) which specifically desumoylates PPARγ-SUMO conjugates. Expression of fatty acid translocase (CD36) and fatty acid binding protein 3 (FABP3) genes was induced by SENP2 but expression of ADRP, another PPARγ target gene, was not affected by SENP2 overexpression in C2C12 myotubes. Chromatin immunoprecipitation analysis showed that desumoylation of PPARγ increased its binding activity to both a recombinant PPRE and endogenous PPREs of the target genes, suggesting that sumoylation of PPARγ primarily inhibits its DNA binding activity. These results suggest that expression of PPARγ target genes is selectively regulated by sumoylation of PPARγ, and sumoylation of PPARγ modulates the DNA binding activity of PPARγ.

PP4-3 Roles of PKC zeta and AMPK in regulating glucose homeostasis in muscle cells
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Activation of PI3 Kinase (PI3K) and AMP Kinase (AMPK) signaling pathways result in cellular glucose uptake although the integration of these pathways in the maintenance of glucose homeostasis remains elusive. Berberine, an active component extracted from the Chinese herb, huanglian, enhances glucose uptake by activating AMPK. We have previously shown that protein kinase C zeta (PKC zeta) is an important molecule in insulin-activated PI3K pathway by regulating actin remodeling resulting in translocation of glucose transporter type 4 (GLUT4) from perinuclear region to plasma membrane. Using insulin sensitive muscle cell lines, we found that the effect of co-stimulation of insulin and berberine on glucose uptake was less than their summative effect. Using specific inhibitors to key kinases of both pathways, we found that PKC zeta was a common signal for the insulin effects on protein kinase B (PKB) activation and AMPK inhibition. In the presence of berberine, PKC zeta caused AMPK activation which attenuated the insulin effect on PKB while insulin attenuated that of berberine on AMPK via PKC zeta. These results suggest that PKC zeta plays an important switching role in PI3K and AMPK signaling pathways on glucose uptake.

PP4-4 Endothelial insulin signaling regulates capillary recruitment and glucose uptake in skeletal muscle
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Insulin actions in the skeletal muscle (SKM), especially in myocytes, has attracted much attention and the underlying mechanism has been largely elucidated. However, the mechanism how insulin delivery into the SKM interstitium is regulated remains to be elucidated. To clarify this issue, we generated mice with endothelial-cell-specific knockout of Irs2 (ETIrs2KO) mice, which is one of the major Irs isoforms expressed in the endothelial cells (ECs). Insulin-stimulated phosphorylation of Akt and endothelial nitric oxide synthase (eNOS) was significantly reduced in the ECs of the ETIrs2KO mice. Insulin-induced capillary recruitment (CR) and increase of interstitial concentrations of insulin were significantly impaired in the ETIrs2KO mice. The glucose infusion rate (GIR) and rate of glucose disappearance (Rd) were significantly reduced in the ETIrs2KO mice. To determine whether improvement of insulin signaling in the ECs with restoration of insulin-induced eNOS phosphorylation might restore glucose uptake by the SKM, we administered a stable prostaglandin (PGI) 2 analogue to the ETIrs2KO mice; this agent has been reported to increase the expression levels of eNOS mRNA and protein. This treatment restored the insulin-stimulated phosphorylation level of eNOS in the ETIrs2KO mice. The insulin-induced CR and interstitial concentrations of insulin were restored in the PGI2 analogue-treated ETIrs2KO mice. Consequently, the GIR and Rd were completely restored in the PGI2 analogue-treated ETIrs2KO mice. These data suggest that impaired insulin signaling in the ECs causes attenuation of the insulin-induced CR and increase of interstitial concentrations of insulin, consequently, reducing the glucose uptake by the SKM. We propose a novel paradigm: endothelial insulin signaling regulates CR and glucose uptake in the SKM.

PP4-5 Rooibos tea (Aspalathus linearis) anti-diabetic or diabetogenic: A dose response study
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The present study was conducted to investigate the effects of a low (0.5%) and a high (1.0%) dose of the aqueous extracts of Rooibos tea (RT) (Aspalathus linearis) in a streptozotocin (STZ)-induced diabetes model of rats. Six-week-old male Sprague-Dawley rats were fed a commercial pellet diet for 1 week and thereafter divided into four groups namely Normal Control (NC), Diabetic Control (DBC), Rooibos Tea Low (RTL, 0.5%) and Rooibos Tea High (RTH, 1.0%). Diets were induced an intraperitoneal injection of streptozotocin (STZ; 65 mg/kg body weight) in all groups except the NC group. After 4 weeks feeding of experimental diets, the food and drinks intake and weekly blood glucose levels were significantly (P<0.05) increased in the RT-consumed groups compared to the DBC group however, body weights were not different between these groups. The results of the intraperitoneal glucose tolerance test (IPGTT) revealed significantly lower glucose tolerance in the RT-consumed groups compared DBC group. Only serum insulin concentration was significantly increased in the RTL group compared to the DBC and RTH group. Serum HDL-cholesterol concentrations were significantly increased in the DBC and RTL groups compared to the RTH group when serum total cholesterol, LDL-cholesterol, triglycerides, fructosamine levels and liver weight, relative liver weight and liver glycogen concentrations were not influenced by the consumption of RT. Data of this study suggest that the low (0.5%) or the high (1.0%) dose of RT has no anti-diabetic but may have some diabetogenic effects in this STZ-induced type 1 diabetes model of rats.

PP4-6 Effects of honeybush tea (Cyclopia intermedia) in a streptozotocin-induced diabetes model of rats
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The present study was conducted to examine the effects of two dietary dosages of honeybush tea (HBT) (0.5 and 1.0 %) in a streptozotocin (STZ)-induced diabetes model of rats. Six-week-old male Sprague-Dawley rats were fed a commercial rat pellet diet for 1 week and then randomly divided into four groups: Normal Control (NC), Diabetic Control (DBC), Honeybush Tea Low (HBTL, 0.5 %), and Honeybush Tea High (HBTH, 1.0 %). Diabetes was induced in all groups except the NC group by an intraperitoneal injection of STZ (65 mg/kg body weight). The NC group was injected with citrate buffer only. After 4 weeks supplying of HBT, although food and tea intakes were significantly increased in the tea consumed groups compared to the DBC group however body weights were not significantly different between these groups. The weekly blood glucose concentrations were not significantly
PP4-7
Effects of metformin and swimming exercise on Visfatin protein expression levels in different tissues of obesity rats
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Visfatin which preferentially expresses in viscera adipose tissue may play a role in the glucolipid metabolism of obesity rats. Metformin and swimming exercise can down-regulate Visfatin protein expression in subcutaneous adipose tissue and perirenal adipose tissue but has no influence on that of muscle tissue.

PP4-8
Role of 12-hydroxyeicosatetraenoicacid(12-HETE) in diabetic cardiomyopathy
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Adverse effects of hyperglycemia on cardiomyocytes is known as pathogenesis of diabetic cardiomyopathy. But precise mechanism underlying diabetic cardiomyopathy is still unknown. On the other hand, it has been reported that 12-lipoxygenase (12-LO) which gene is one of the arachidonate cascade pathway plays a dominant role in the development of arteriosclerosis and the cell growth of cardiac fibroblast. Moreover, it has been also reported that 12-LO knockout mice were highly resistant to diabetes development compared with control mice. Therefore, 12-LO pathway may play a part in the diabetic cardiomyopathy. Then, we examined the role of 12-lipoxygenase (12-LO) which gene is one of the arachidonate cascade pathway in cardiomyopathy by using the diabetic cardiomyopathy rat model. The diabetic cardiomyopathy rat was induced by a single percutaneous injection of streptozotocin. Echocardiogram revealed Fractional Shortening was decreased in the cardiomyopathy rat model compared with that of control rats. When we extracted RNA from the heart and examined, not only natriuretic peptide (BNP), a marker of cardiac failure, but also mRNA level of 12-LO and its protein expression levels were reduced in the heart tissue of diabetic cardiomyopathy rat model compared with that of control rats. The in vitro study demonstrated that hyperglycemia stimulation induced 12-LO and 12-HETE expression which promoted cardiomyocyte apoptosis. These results together suggest that 12- HETE may play a part in the pathogenesis of diabetic cardiomyopathy.

PP5: Pathophysiology and Diagnosis of Diabetes #1
PP5-1
Surveillance study on Hemoglobin A1C by JDS for China, Korea and Japan in 2009
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Hemoglobin A1C (HbA1c) is the most important parameter to assess the glycemic control of diabetic patients. Many different routine methods claiming to measure Hba1c are currently used by clinical laboratories. For global harmonization, the IFCC reference method is based on the quantification of hexapeptides and glycated hexapeptides decomposed from the N-terminal of the β-chains by either a mass spectrometry technique or capillary electrophoresis. However, regional standardization of HbA1c measurement by using NGSP-traceable methods is progressed in North America, China, Korea and other Asia countries except Japan. For example, the harmonization of between-methods, methodolable improvement is seen in Japan. International Expert Committee of American Diabetes Association (ADA) was reported on the role of the A1C assay in the diagnosis of diabetes in 2009. Diabetes should be diagnosed by using diabetes control problems trial (DCCT) values when (A1C) is equal to or greater than 6.5%. The study was performed in the end of March after February and the routine laboratories were divided distribution and the measurement. Three kinds of specimens were distributed to participating laboratories as frozen blood which constituted three concentration levels. The target values of these specimens were set with designated comparison method (IDS values) and NGSP SRLs (NGSP values) and the data of measurements were with a bias. And also the IFCC values by the IFCC method as reference values were evaluated. We will present the detail of the results of this surveillance study on the Meeting.

PP5-2
Cut-point of glycated hemoglobin (HbA1c) for the diagnosis of Chinese type 2 diabetes (T2DM)
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OBJECTIVES: The use of HbA1c for the diagnosis of diabetes has been recommended by a joint Expert Commitee of ADA, the European Association for the Study of Diabetes and the International Diabetes Federation. In this study we try to find out the diagnostic cut-point of HbA1c for Chinese type 2 diabetes (T2DM) and to expore it clinical significance in determining insulin resistance and islet cell function.
METHOIDS: One thousand seven hundred and sixty Chinese were tested HbA1c and were conducted OGTT and insulin release test. These data were statistically analyzed by using SPSS 12.0 software base on the 1998 WHO diagnostic criteria of diabetes. The levels of HOMA-IR, B30/G30, HOMA-B, and AUCi were compared between different levels of HbA1c.
RESULTS: (1) Obtained from ROC curve, the diagnostic cut-point of HbA1c for Chinese T2DM was 6.2% (sensitivity and specificity were 77.1 and 74.3%). The diagnostic cut-point of impaired glucose regulation (IGR) was 5.9% (the sensitivity and specificity were 55.3 and 66.8%). (2) With the increasing in HbA1c, HOMA-IR was increased and B30/G30 was decreased progressively (P < 0.05). HOMA-B was decreased when HbA1c was higher than 6.2% (P < 0.05). AUCi showed an upward trend as HbA1c was under 7.0% and was decreased as HbA1c was higher than 7.0% (P < 0.05).
CONCLUSIONS: Our results suggested that the appropriate diagnostic cut-point of HbA1c for Chinese T2DM is 6.2%. HbA1c is not suited for diagnosis of IGR. To a certain extent HbA1c can reflect the state of insulin resistance and islet β cell function.

PP5-3
Evaluation of plasma thioredoxin levels in patients with diabetes mellitus
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Thioredoxin has been found as an electron donor to ribonucleotide reductase, and induced by many forms of oxidative stress and released from cells. In order to investigate the changes in thioredoxin levels and oxidative stress biomarkers in diabetes mellitus, we have evaluated plasma thioredoxin, glutathione, high-sensitive CRP (hsCRP) and urinary 8-OHdG levels in patients with diabetes mellitus and healthy controls. Fifteen Japanese patients with diabetes mellitus (D group) and 11 healthy controls were enrolled in this study. In patients with diabetes mellitus mean duration of diabetes were 7.7 years. Mean age of patients with diabetes and healthy controls were 60 ± 4 and 41 ± 4 years, respectively. Mean HbA1c was 7.88 ± 0.48 % for patients with diabetes mellitus, and was 5.08 ± 0.17 % for controls. Plasma levels of thioredoxin in D group was 36.0 ± 4.7 ng/mL, which was significantly higher than 24.2 ± 2.7 ng/mL in ND group (P < 0.05). In ND group plasma total glutathione concentration was significantly decreased as HbA1c was higher than 7.0% (P < 0.05). AUCi showed an upward trend as HbA1c was under 7.0% and was decreased as HbA1c was higher than 7.0% (P < 0.05).

PP5-4
Liver glycogon levels in patients with diabetes mellitus
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Serum insulin, serum fructosamine, other serum lipids concentrations and liver weights were influenced by the consumption of tea. Data of this study suggest that either low (0.5%) or high (1.6%) dose of HST has no anti-diabetic effects and may have some diabetogenic effects at least in this experimental condition.

PP5-5
Evaluation of thioredoxin levels in patients with diabetes mellitus
T. Hye1, T. Kurose1, K. Watanabe1, M. Hishizawa1, D. Yabe1, M. Fukushima2 and Y. Seino2
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Thioredoxin has been found as an electron donor to ribonucleotide reductase, and induced by many forms of oxidative stress and released from cells. In order to investigate the changes in thioredoxin levels and oxidative stress biomarkers in diabetes mellitus, we have evaluated plasma thioredoxin, glutathione, high-sensitive CRP (hsCRP) and urinary 8-OHdG levels in patients with diabetes mellitus and healthy controls. Fifteen Japanese patients with diabetes mellitus (D group) and 11 healthy controls were enrolled in this study. In patients with diabetes mellitus mean duration of diabetes were 7.7 years. Mean age of patients with diabetes and healthy controls were 60 ± 4 and 41 ± 4 years, respectively. Mean HbA1c was 7.88 ± 0.48 % for patients with diabetes mellitus, and was 5.08 ± 0.17 % for controls. Plasma levels of thioredoxin in D group was 36.0 ± 4.7 ng/mL, which was significantly higher than 24.2 ± 2.7 ng/mL in ND group (P < 0.05). In ND group plasma total glutathione concentration was significantly decreased as HbA1c was higher than 7.0% (P < 0.05). AUCi showed an upward trend as HbA1c was under 7.0% and was decreased as HbA1c was higher than 7.0% (P < 0.05).
38.1 ± 1.0 µg/mL, and in D group it was 33.0 ± 1.0 µg/mL, significantly lower than in controls (P < 0.01). Plasma thioredoxin concentration showed significant positive correlation with HbA1c (r = 0.495, P = 0.05), while the total glutathione showed a negative correlation with HbA1c (r = -0.387, P < 0.05). On the other hand, urinary 8-OHdG levels in D group revealed no apparent difference with those in ND group. Plasma hsCRP levels in D group also showed no apparent difference compared to those in ND group. Accordingly, plasma thioredoxin and glutathione levels may reflect the real time redox state in patients with diabetes mellitus.

PP5-4
Vascular inflammation in patients with impaired glucose tolerance and type 2 diabetes: Analysis with FDG-PET/CT
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Background: Type 2 diabetes mellitus (T2DM) is associated with an increased risk of atherosclerotic cardiovascular disease. Vascular inflammation is a key factor in both the pathogenesis and outcome of atherosclerosis. 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is a promising tool for indentifying and quantifying vascular inflammation within atherosclerotic plaques. This study was designed to examine the vascular inflammation measured using FDG-PET in patients with impaired glucose tolerance (IGT) and T2DM, in comparison with age- and gender-matched control subjects with normal glucose tolerance (NGT).

Methods and Results: We investigated vascular inflammation using FDG-PET in ninety age- and gender-matched subjects with different glucose tolerance (30 NGT subjects, 30 IGT subjects and 30 T2DM subjects). Vascular 18F-FDG uptake was measured as both the mean and maximum blood-normalized standardized uptake value (SUV), known as the target-to-background ratio (TBR). Both mean and maximum TBR measurements were significantly different based on glucose tolerance, although the carotid intima-media thickness measurements were not significantly different. The maximum TBR values in patients with IGT and T2DM were significantly increased compared to the normal subjects. In addition, subjects with metabolic syndrome (MetS) had increased maximum TBR values compared to those without MetS. Age-, gender- and BMI-adjusted maximum TBR levels were positively correlated with triglyceride, hemoglobin A1c (HbA1c), insulin resistance, high-sensitivity CRP (hsCRP) and Framingham risk score, and were negatively correlated with high density lipoprotein (HDL) cholesterol and adiponectin levels.

Conclusions: The results of the present study suggest that IGT and T2DM are associated with vascular inflammation in carotid atherosclerosis detected by FDG-PET.

PP5-5
Association of endothelial function with carotid arterial stiffness in type 2 diabetic patients
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Endothelial dysfunction is a predictive surrogate marker of cardiovascular event. However, it’s measurement in a clinical setting is accompanied by technical and equipment issues about reliability and precision. Recently, a novel ultrasound equipment for measurement of endothelial function, UNEXEF18G (Unex Co. Ltd., Japan), has been developed, which make it possible to evaluate more local and precisely than previous equipments. Using such an equipment, we aimed to clarify its clinical usefulness and the association between endothelial function, flow-mediated and nitroglycerin-induced dilatation (FMD and NMD), and carotid arterial stiffness, stiffness parameter a measured by high resolution ultrasound with phase-locked echotracking system (ProSound 6500, Aloka Co.Ltd., Japan) in 107 type 2 diabetic patients [age, 65 ± 11 (SD) years old; duration of diabetes, 14 ± 10 years]. In all type 2 diabetic patients, FMD was 6.9 ± 4.2%, ranging from 0.7 to 19.2%, and NMD 11.8 ± 6.4%, 0.5 to 28.9%. On simple regression analysis, both FMD and NMD were significantly inversely associated with stiffness parameter a (r = -0.234, P = 0.018 and r = -0.294, P = 0.005, respectively). On multiple regression analysis, only systolic blood pressure was found to be a common significant independent contributor to FMD (â = -0.281, P = 0.009), NMD (â = -0.222, P = 0.041) and stiffness parameter a (â = 0.302, P < 0.05). In conclusion, both FMD and NMD are associated with functional stiffness property of carotid artery in type 2 diabetes and may share common mechanism(s) for development of arterial stiffening in type 2 diabetes.

PP5-6
Analysis of clinical characteristics in emergent patients with ketosis-onset diabetes
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Objective: To investigate the presence of islet auto-antibodies in patients with ketosis-onset diabetes, and to analyze their clinical characteristics.

Methods: The lipid profile, random plasma glucose, hemoglobin A1c, pancreatic function and islet auto-antibodies [glutamic acid decarboxylase antibody (GAD-Ab), protein tyrosine phosphatase antibody (IA2-Ab)] were examined in a total of 133 diabetic patients with ketosis-onset. The blood pressure, weight and diabetes family history were also recorded. This cohort was divided into three categorical groups based on the presence or absence of auto-antibodies (A+ or A-) and B cell functional reserve (B+ or B-): group 1, A+ (including A+B+ and A+B-); group 2, A+B+; group 3, A-B-.

Results: (1) The positive rates of GAD-Ab and IA2-Ab were 27.8 and 16.5%, respectively. And that of either of the 2 antibodies was 29.3%. (2) Group 1 had earlier age onset, lower body mass index(BMI), higher level of random plasma glucose and high density lipoprotein cholesterol (HDL) compared with group 2 and group 3 (P < 0.01). There were 48.2% patients in group 2 having diabetes family history, higher than the other 2 groups. In addition, group 2 had higher level of triglyceride (TG) compared with group 1 (P < 0.05) and higher level of fasting C peptide and postprandial C peptide compared with group 1 and group 3 (P < 0.01).

Conclusions: Diabetic patients with ketosis-onset showed different clinical characteristics significantly. Auto-antibodies and B cell functional reserve may help to identify the subtypes of diabetes, leading to different therapeutic strategies.

PP5-7
Hypertension, hyperglycemia, and hyperlipidemia associated with high IgA levels among school children in Taiwan
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Background: Little is known regarding immunoglobulin A (IgA) in association with diabetes in children. We investigated the associations between IgA and hypertension, hyperglycemia (fasting glucose ≥ 100 mg/dL) and hyperlipidemia (total cholesterol ≥ 200 mg/dL) for school children.

Methods: From 1992 to 2000, the nationwide mass urine screening was conducted to identify proteinuria, glucosuria, and/or hematuria for all school children aged 6–18 years in Taiwan Province. Urine screening positive students received health check-up including blood tests.

Results: Among 92517 students with screening positive, 1874 (2.0%) had IgA levels ≥ 400 mg/dL. Students with elevated IgA were more prevalent with hypertension (13.0 vs 8.8%, P < 0.0001), hyperglycemia (20.9 vs 14.0%, P < 0.0001), and hyperlipidemia (15.4 vs 11.5%, P < 0.0001), compared with other screening positive students with normal IgA. The multivariate logistic regression analysis showed that students with high IgA had the odds ratios of 1.29 (95% confidence interval [CI] = 1.12–1.49) for hypertension, 1.52 (95% CI = 1.35–1.70) for hyperglycemia, and 1.33 (95% CI = 1.16–1.52) for hyperlipidemia.

Conclusion: Our findings show that hypertension, hyperglycemia, and hyperlipidemia are associated with IgA among school children found abnormal in urine screening.
A case of fulminant-like type 1 diabetes accompanied by erythema and swelling of the pancreas

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A 55-year-old man visited our hospital with a common-cold-like symptom and fever. After 3 days, he had erythema multiforme and was medicated with betamethasone. After 5 days, he suddenly had general fatigue, developed thirst and polyuria. He was admitted to our hospital with suspicion of severe type 1 diabetes mellitus (BG: 807 mg/dl, HbA1c 6.5%, arterial pH: 7.285, i-ketone: ++). CT scan revealed swelling of the pancreas, spleen, and liver. Not only GAD and IA-2 antibody but also ICA were negative, and his HLA typing was DRB1 0405, DQ01 0401. The serum antibody to various viruses such as coxsackie, and Epstein-Barr were undetectable. After the treatment for his hyperglycemia with intensive insulin therapy, the second CT scan showed normalization of pancreas, spleen, and liver size. The erythema multiforme has disappeared after 7 days. The plasma C-peptide level has been completely depleted after 8 months. In this case, we could observe the abrupt onset of fulminant-like type 1 diabetes preceded by erythema multiforme. Reports of the swelling of the pancreas, spleen, and liver and return to normal size in the course of treatment are rare.

Pathophysiology and Diagnosis of Diabetes #2

The characteristics of patients with both fasting and postprandial glucose were controlled by basal insulin therapy

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Basal insulin treatment is frequently used in type 2 diabetes, but the successful control of postprandial glucose is challenging. Type 2 diabetes show heterogeneous response to various treatment. Since each type 2 diabetic patient has different glucose excursions, basal insulin can control both fasting and postprandial glucose levels in some patients. We tried to find out their characteristics related to the differences in insulin sensitivity and pancreatic beta cell dysfunction. After fasting glucose was optimized by insulin glargine, two oral agents were initiated and then crossed over after second wash out. During wash out period, only basal insulin can control postprandial glucose as well as fasting glucose in 22% of patients. They have significantly young age (51.8 vs 58.3 years) and low basal hemoglobin A1c (HbA1c) (7.6 vs 8.5 %) than patients whose postprandial glucose were not controlled by basal insulin only. Their duration of disease (8.2 vs 10.0 years) and the requirement of basal insulin (0.28 U/kg vs 0.37 U/kg) were less than others, but they were not significant. Homeostasis model analysis (HOMA) beta, corrected insulin response (CIR) and Insulin-to-glucose ratio (IGR) were significantly higher in the controlled group. Controlled group showed significantly low Mean average glucose excusion (MAGE) and Average daily risk range (ADRR). Basal insulin could control both fasting and postprandial glucose in 22% of type 2 diabetes in our study. They are younger and have low basal HbA1c and low glucose excursion. Their makers of beta cell function are better than non-controlled group.

Age-dependent decline in beta cell function assessed by an oral glucose tolerance test-based disposition index

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Although a large body of evidence suggests that glucose tolerance declines progressively with age, it remains unclear whether pancreatic beta cell function also deteriorates in an age-dependent manner. Oral glucose tolerance test (OGTT)-based analogs of the disposition index have recently been proposed and shown to be of clinical utility. In the present study, we evaluated the effect of age on beta cell function as assessed with such an OGTT-based analog (oral disposition index). A total of 110 Japanese normoglycemic subjects (aged 22–59 years) was divided into decadal age groups (20s, 30s, 40s, and 50s) and subjected to an OGTT. The oral disposition index was calculated as the product of the Matsuda index and the ratio of the area under the insulin curve to the area under the glucose curve for 0–120 min during the OGTT (AUCglu/AUCins). We found that the oral disposition index declines with age in the study subjects, whereas such an age-dependent decline was not observed for other indexes of insulin secretion including homeostasis model assessment of beta cell function (HOMA-beta), the insulomogenic index, and AU(C)ins/AUCglu. Our results suggest that the oral disposition index is a sensitive measure of beta cell function and that a natural decline in beta cell function likely begins in early adulthood and progresses with age.

Association between family history of type 2 diabetes and beta cell function in Korean type 2 diabetic patients

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Type 2 diabetes is characterized by progressive beta cell dysfunction and insulin resistance. Family history of type 2 diabetes has been known to be associated an increased risk of developing the disease. However, few studies have evaluated the effects of family history on beta cell function. We studied association between family history of type 2 diabetes, clinical characteristics and beta cell function in type 2 diabetic patients. A total of 1,401 patients with type 2 diabetes mellitus (type 2 DM) were recruited. After adjustment for age and gender, fasting C peptide level was associated negatively with diabetes mellitus (DM) duration and positively with body mass index (BMI) in type 2 diabetic patients. The patients with family history of type 2 diabetes had higher A1C, higher low density lipoprotein (LDL)-cholesterol, and lower fasting C-peptide levels than the patients without family history. When divided according to the tertiles of DM duration, there were significant differences of fasting C-peptide levels in patients with family history of type 2 diabetes. However, there were no significant differences in patients without family history. In a multivariate analysis, family history of type 2 diabetes was an independent determinant for the lowest tertile of fasting C-peptide level after adjustment of age, gender, BMI, hypertension, A1C, and dyslipidemia. This study suggests that diabetic patients with family history of type 2 DM may be associated with more deterioration of beta cell function than patients without family history.

Impaired super early phase insulin secretion and its genetic restriction in Japanese type 2 diabetes and controls

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BACKGROUND AND AIMs: We previously demonstrated that insulin secretion at super-early phase (i.e. 0–30 min) during oral glucose tolerance test (OGTT) is severely reduced in untreated Japanese patients with short duration of type 2 diabetes (T2DM). Here, we investigated insulin secretion at super early phase in T2DM, impaired glucose tolerance (IGT) and control subjects, and their single nucleotide polymorphisms (SNPs) in two genes that have been implicated in pancreatic beta cell function.

MATERIALS AND METHODS: Japanese untreated T2DM (n = 33; age 56 ± 1; hemoglobin A1c (HbA1c) 6.5 ± 0.2%; duration 2.1 ± 0.4 years), IGT (n = 20; age 55 ± 2; HbA1c 5.4 ± 0.1%) and age-matched controls (n = 35; age 47 ± 2; HbA1c 5.2 ± 0.0%) were subjected to OGTT. Blood samples were collected at 0, 5, 10, 20 and 30 min after the ingestion to measure serum insulin and plasma glucose. SNPs in KCNQ1 and TCF7L2 were measured by the ASPCR methods.

RESULTS: Insulin secretion at super early phase was significantly reduced in T2DM compared to controls, reproducing our previous results. The super early phase of insulin secretion was reduced in Individuals carrying risk alleles...
for two KCNQ1 SNPs (rs2237892 and rs2237895). None of TCF7L2 SNPs was correlated with insulin secretion at super early phase.

**Conclusion:** Our results confirm that insulin secretion at the super early phase is already reduced in Japanese patients with short duration of T2DM. The current results suggest that KCNQ1 but not TCF7L2, plays a role in insulin secretion at super early phase.

### PP6-5 Withdrawal

### PP6-6

**Plasma GIP and GLP-1 levels are associated with distinct factors after glucose loading in Japanese subjects**

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Gastric inhibitory polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) are major incretins that potentiate insulin secretion from pancreatic β-cells. Plasma GIP and GLP-1 levels after food intake or glucose loading have been well evaluated in Caucasian subjects, and a defective incretin effect is reported in type 2 diabetes, suggesting that a reduced incretin effect is associated with postprandial hyperglycemia in type 2 diabetes. However, they have not been characterized well in Japanese and other Asians. In this study, we measured plasma GIP and GLP-1 levels during oral glucose tolerance test (OGTT) in 17 Japanese normal glucose tolerance (NGT) subjects, and evaluated the factors associated with GIP and GLP-1 secretion (area under curves (AU(C)) of GIP and GLP-1 during OGTT) using simple regression and multiple regression analyses. GIP secretion was positively associated with BMI and AUCs of CPR and glucagon, while GLP-1 secretion was negatively associated with AUC of glucose loading. The insulinogenic index (early-phase insulin secretion) was the most strongly associated with GIP secretion and HOMA β-cell (basal insulin secretion) was the strongest factor in GLP-1 secretion among the four indices of insulin secretion and insulin sensitivity. These results show that various distinct factors during OGTT are associated with GIP and GLP-1 secretion in Japanese subjects.

### PP6-7

**Intact glucagon-like peptide-1 levels are not decreased in Japanese patients with type 2 diabetes**

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Impaired secretion of glucagon-like peptide 1 (GLP-1) has been suggested to contribute to the deficient incretin effect in patients with type 2 diabetes mellitus (T2DM). Recent studies, however, have not always supported this notion. Since Japanese patients with T2DM usually have severe impairment in the early-phase of insulin secretion, the measurement of incretin secretions in Japanese T2DM patients would be useful for assessing the association between incretin levels and insulin secretion. We conducted an oral glucose tolerance test (75 g) (OGTT) and meal tolerance test (480 kcal) (MTT) for subjects with normal glucose tolerance (NGT, n = 12), subjects with impaired glucose tolerance (IGT, n = 7), and T2DM patients (n = 21). The tests were carried out according to a 5-min study periods on separate occasions. Intact GLP-1, GIP, and dipeptidyl peptidase-IV (DPP-IV) were measured by ELISA. T2DM exhibited an impaired early phase of insulin secretion and a reduction in glucagon suppression. There were no significant differences in GLP-1 or GIP levels at each sampling time among NGT, IGT, and T2DM after the ingestion; hence the incremental areas under the curve (IAUC) for the three groups were quite similar. The levels of DPP-IV, a limiting enzyme for the degradation of incretins, were comparable among the three groups. The GLP-1/IAUC was not correlated with IAUCs of insulin, C-peptide, or glucagon determined by the OGTT or the MTT. We concluded that intact GLP-1 levels are comparable between non-diabetics and T2DM, suggesting that impaired insulin secretion in Japanese T2DM is not attributable to defect in GLP-1 secretion.

### PP6-8

**Characterization of the candidate genes involving prostaglandin metabolism in type 2 diabetes**

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It is now broadly accepted that low-grade chronic inflammation associated with obesity leads to the onset of Type 2 diabetes (T2D). Previously, we have shown that the substrates of the prostaglandin reductase 2 (PTGR2) could modulate PPARγ activity. Therefore, the aim of this study was to investigate genetic association of single nucleotide polymorphism (SNPs) within candidate genes involved in prostaglandin metabolisms, and cumulative effect of these SNPs on T2D. We genotyped 65 tag SNPs of 12 candidate genes in a group of 1520 T2D cases and 1520 non-diabetic controls. In a single SNP analysis, we found that there were some nominal significant association of rs1937840, rs2153407, rs3827354, rs2076113, rs2284060, rs10817193 with T2D, but the significance was abolished after correction for multiple testing. In haplotype analysis, we demonstrated that AKR1G3 haplotype were highly associated with T2D (with permutation P < 0.05). We also analyzed the potential cumulative effect by using a genetic score. Odds ratios for T2D were 2.07 (95% confidence interval, 1.61 to 2.66) in subjects with greater than 62 risk alleles compared with those with less than 54 risk alleles. In summary, we found that the genes involved in prostaglandin metabolism might be associated with pathogenesis of T2D. These data also suggest a gene-dose effect of the examined gene variants involved in prostaglandin metabolisms on T2D. Further biological studies will be required to substantiate the role of some of the candidates in glucose metabolism.

### PP7-1 Withdrawal

### PP7-2

**The relation of age and metabolic disorders in population of Bali, Indonesia**

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A cross sectional study on metabolic syndrome (MS) and glucose intolerance in seven villages population of Bali, Indonesia was conducted. Three hundreds and ten elderly (aged >60 years) and 168/142 out of 1840 total subjects were involved. The prevalence of impaired fasting glucose (IFG) and diabetes mellitus (DM) were 2% in the elderly compared to in the younger groups (21.4 vs 11.7; 11.7 vs 4.8; respectively). Blood pressure (BP) and fasting blood sugar (BS) levels were higher in the elderly than in the younger groups (113.7 vs 117.7 mmHg, 102.7 vs 93.0 mg/dL, respectively; P < 0.001). No difference of triglyceride and HDL-C levels between 2 groups. The elderly, although have lower WC (75.8 vs 80.9 cm; P < 0.001), revealed higher prevalence of MS compared to the younger group [22.9 vs 17.3%; P = 0.028; prevalence risk 1.423 (CI = 1.043–1.944)]. The prevalence risk of the each components of MS for the occurrence of MS were: elevated triglyceride [30.2 (CI, 14.5–63.1)]; elevated fasting BS [8.5 (CI, 4.5–15.8)]; elevated WC [8.1 (CI, 4.3–15.0); reduced HDL-cholesterol [4.4 (CI, 2.4–7.9)]; and elevated BP [3.7 (CI, 1.9–7.2)].

**Conclusions:** Compared to the younger group, the elderly have higher (2x) prevalence of IFG and DM; lower prevalence of central obesity but higher MS. Old aged (>60 years) has 1.4x risk for MS than younger aged and elevated triglyceride was the most important risk factor for MS.
PP7-3
Metabolic syndrome predicts new onset of type 2 diabetes in Japanese-Americans –Hawaii-Los Angeles-Hiroshima study–
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Objective: The impact of metabolic syndrome as one of risk factors for the incidence of type 2 diabetes has been reported in some races. However, there is few information regarding whether it might be associated with risk of type 2 diabetes among Japanese. The aim of this study was to investigate the association between metabolic syndrome and development of type 2 diabetes in Japanese-Americans. Although their genetic background is similar to Japanese people, they have undergone a rapid and intense westernization of their lifestyle.

Methods: Nine hundred and twenty eight Japanese-Americans were enrolled between 1992 and 2007. The study population consisted of 379 men and 549 women who did not have diabetes as ascertained by a 75-g glucose tolerance test at baseline. We adopted a modified criterion defined by AHA/NHLBI for the diagnosis of metabolic syndrome, in which elevated waist circumference was estimated as equal or more than 90 cm in men, or 80 cm in women. The average of follow-up period was approximately 6.8 years.

Results: One hundred and sixteen new cases of diabetes were diagnosed during the follow-up period. Metabolic syndrome was significantly associated with increased risk of type 2 diabetes. The multivariable-adjusted hazard ratio of type 2 diabetes for subjects with metabolic syndrome compared with those without metabolic syndrome. Meanwhile, components of metabolic syndrome except for impaired fasting glycemia were not associated with a significantly increased risk of type 2 diabetes.

Conclusions: The presence of metabolic syndrome independently predicts the development of type 2 diabetes in Japanese-Americans.

PP7-4
Prevalence of prediabetes in a Korean population
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Background: Concerns about prediabetes, and the prevalence of this disease have been increasing. In most populations, IGT is considerably more prevalent than IFG. But there were few population-based studies in South Korea. This study was performed to examine the prevalence of and prediabetes in a rural area of South Korea.

Methods: From August to November 2003, 1,773 subjects over the age 20 were selected randomly out of 101,104 residents of Dalseong country in Daegu, South Korea. All subjects were carried out with fasting and 2 h postprandial plasma glucose measurements. Prediabetes was defined according to American Diabetes Association 2003 criteria. Subjects with prediabetes were classified into three categories of glucose tolerance; isolated impaired glucose tolerance (I-IGT), and combined IFG and IGT (C-IFG/IGT).

Results: Age-adjusted overall prevalence of prediabetes was 18.5% (I-IFG 13.2%, I-IGT 2.6%, C-IFG/IGT 2.7%), and men in their forties and women in their fifties showed the peak prevalence. The prevalence of prediabetes rose along with increasing age (P for trend <0.01). The prevalence of I-IGT tends to increase across all age groups, but that of I-IFG tends to plateau in middle age. In Koreans, I-IFG is considerably more prevalent than I-IGT and C-IFG/IGT.

Conclusions: The prevalence of prediabetes was slightly lower than those of previous results of other regions in South Korea. The prevalence of prediabetes in men was increasing at younger age than in women. I-IFG is considerably more prevalent than I-IGT and C-IFG/IGT in a Korean population.

PP7-5
The effect of lifestyle and dietary habit on the age onset of newly developed type 2 DM, based on the DCMP 2001, Taiwan
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Background: To evaluate the effect of lifestyle and eating habit on the age onset of type 2 diabetes mellitus (T2DM).

Material and Methods: From 2003 to 2006, 6147 diabetes were randomly and cumulatively recruited in DCMP 2001. The baseline of lifestyle (I : no smoking, no alcoholic and regular exercise; II : smoking and/or alcoholic and/or no exercise) and individualized nutritional assessment were achieved. The macronutrient consumptions of daily caloric intakes were classified under 10 Groups, G1: 45% < carbohydrate ≤ 50% and 30% < fat ≤ 35% and 15% < protein ≤ 20%, G2a, G2b, G2c, G3a, G3b, G3c, G4a, G4b, and G4c (G2: CHO > 50%, G3: CHO ≤ 45%, G4: 45% < CHO ≤ 50%; x: fat > 35%, b: fat ≤ 30%, c: 30% < fat ≤ 35%). The newly developed T2DM (n = 1326) living on either lifestyle I (n = 489) or lifestyle II (n = 837) was categorized into two groups, high fat (G3a and G4a, n = 555) and low fat (G2b and G2c, n = 574) diet eaters respectively.

Results: The case and percentage distributions in different age ranges of onset of disease in newly developed T2DM living on lifestyle I and lifestyle II and with either high fat or low fat diet were demonstrated in Fig. 1 and Table 1. There were statistically significant difference in the age of onset of diabetes among these 4 groups of newly developed T2DM (P < 0.001).

Conclusion: Combination of both lifestyle I and low fat diet would be considered as a feasible, effective and non-pharmaceutical regimen for 8–10 years delay in the development of T2DM.

PP7-6
Diabetes and impaired fasting glucose in Mongolian population
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Aims: The aims of the study is to assess the prevalence of diabetes and impaired fasting glucose (IFG) and compare the risk factors between diabetes and IFG in the Mongolian population.

Methods: Data of demographic characteristics, life style risk factors family history of diabetes and hypertension, medical history and fasting plasma glucose obtained and analyzed for all individuals.

Results: Total 3411 Mongolians aged 15–64 were recruited as study subjects. The overall prevalence of diabetes and IFG were 8.2% (± 0.05CI) and 12.3% (± 0.05CI). About 23.1% (± 0.01CI) of the surveyed population engaged only in low levels of physical activity or have had physical inactivity and 22.2% (± 0.05CI) had elevated blood pressure. In regard to body mass index erisk categories 31.6% (± 0.1CI) of the population aged 15–64 years was overweight and obese.

Conclusions: IFG were common among Mongolian population. IFG has partly same risk factors as diabetes, and prevalence of some cardiovascular risk factors and number of risk factors in diabetes were higher than that in IFG.

PP7-7
Blindness with childhood-onset type 1 diabetes in Japan, 2000–2005: Characteristics of blind patients
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Background: Among patients with childhood-onset type 1 diabetes, progressive retinopathy has resulted in blindness even recently in Japan.

Objective: To investigate the characteristics of blind patients with childhood-onset type 1 diabetes in Japan.
Objective: To investigate the effects of obesity on the prevalence of the metabolic syndrome (MS) and its relation to the levels of adipokines in a large population-based study of schoolchildren in Beijing area.

Methods: A total of 3,315 schoolchildren (Male/Female: 1.792/1,723) were selected from the Beijing Child and Adolescent Metabolic Syndrome Study, a representative sample of 19,593 children aged 6-18y in 2004. Examination included anthropometry, body composition by BIA; pubertal development, and levels of fasting lipid profile, insulin, leptin, resistin and adiponectin. The overweight status was defined according to International Obesity TaskForce (IOTF) BMI cut-offs and the MS was diagnosed by a modified IDF definition in 2005.

Results: In general, the prevalence of MS increased with the severity of overweight and reached about one fifth in overweight and obese children (Male/Female: 19.8% vs 17.4%). The prevalence of the MS increased significantly with increasing insulin resistance (HOMA-IR) after adjustment of obesity (BMI by age and Z-score). The level of leptin increased and adiponectin decreased with the increasing of obesity and numbers of MS component, even after adjustment for gender and pubertal development, but no similar trend was observed in resistin levels.

Conclusions: The prevalence of the MS was high among overweight and obese schoolchildren in Beijing and it increased with worsening of obesity. Biomarkers of the increased risk of adverse cardiovascular outcomes, such as hyperleptinemia and hypoadiponectinemia, are already present in these children.

PP8-2
Metabolic syndrome in Japan: Importance of increased waist circumference
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Obesity is defined as a condition of excessive body fat accumulation mainly in adipose tissue, which increases the risk of type 2 diabetes, hypertension, dyslipidemia and cardiovascular disease (CVD), and ultimately death. Body mass index (BMI) measures general obesity, but cannot take into account the distribution of body fat. In contrast, waist circumference is one of the indices of abdominal obesity. Considerable attention has been paid to the metabolic syndrome over the past two decades, and heated arguments have arisen about the importance of increased waist circumference. Current widely used diagnostic criteria for the metabolic syndrome, including the Japanese original criteria published in 2005, adopt abdominal obesity as defined by waist circumference. The cut-off points, 85 cm for men and 90 cm for women at the level of the umbilicus in Japan, were based on the original cross-sectional data from Japanese and the corresponding values for the visceral fat area (VFA) of 100 cm² at the level of the umbilicus, rather than a specific value of BMI. Since April in 2007, we have performed a nationwide survey to establish original evidence for diagnosis and management of the metabolic syndrome by integrating twelve cohort studies in Japan, through which the importance of increased waist circumference is expected to be elucidated.

PP8-3
The association of weight change and body composition with glycemic progression in subjects without history of diabetes
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We performed an observational study whether changes in weight and body composition affects the glycemic progression in subjects without diabetes in 4 years of follow-up period in a community cohort. Among the subjects who participated in a medical check-up program in 2004 and repeated the check-up in 2008, 29,339 subjects (mean age 39 years) without history of diabetes and showed fasting blood glucose lower than 126 mg/dL in 2004 were selected for this study. Data on anthropometric measurement and metabolic parameters were obtained in 4 years of interval. Body composition analyses were performed with bioelectric impedance analyzer. Skeletal muscle index (SMI%) was calculated with lean mass / weight × 100. After 4 years, 1.5% of the participants developed diabetes mellitus, 13.1% progressed to more advanced glycemic status. The odds ratio for glycemic progression increased, as the quartiles for percent weight change in 4 years increased, and subjects who had more than 5% increase in percent weight showed 2.3-fold increased risk for glycemic progression compared with those who lost more than 5% weight during 4 years. Among the components of body composition, increase in waist-hip ratio was the mostly significant predictor for glycemic progression. The proportions of progresses increased as the quartiles of changes in weight, percent body fat and WHR increased and as the changes in SMI decreased. Body weight gain, increased WHR and decreased skeletal muscle significantly predict increased risk for glycemic progression in subjects without history of diabetes.

PP8-4
The ApoB/ApoA1 ratio is associated with metabolic syndrome and its components in a Chinese population
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In this study, we assessed whether the apolipoprotein B/apolipoprotein A1 ratio (ApoB/ApoA1) is related to metabolic syndrome (MS) and its components in an urban Chinese population. A total of 709 community residents were enrolled. Metabolic syndrome was defined according to the International Diabetes Federation definition in 2005. The high ApoB/ApoA1 group was defined as the gender-specific upper quartile of the ApoB/ApoA1 ratio. Insulin resistance (IR) was defined as the upper quartile of Homa-IR. The ApoB/ApoA1 ratio was significantly higher in subjects with MS, compared to those without (P < 0.05). After adjusting for age and gender, subjects with MS (OR = 3.3) or IR (OR = 2.3) were more likely to be in the high ApoB/ApoA1 group. The ApoB/ApoA1 ratio increased significantly as the number of MS components increased (P < 0.05). Taken together, these data demonstrate that the ApoB/ApoA1 ratio is strongly associated with MS and its components in an urban Chinese population.

PP8-5
Westernization of life style enhances the influence of metabolic syndrome to atherosclerosis
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Background and Purpose: Comparison of Japanese-Americans with native Japanese makes it possible to clarify the effects of life style westernization in various diseases. The aim of this study was to investigate
relationship between life style westernization and influence of metabolic syndrome to atherosclerosis.

**Methods:** We compared carotid intima-media thickness (CIMT) between the subjects with metabolic syndrome diagnosed by modified AHA/NHLBI definition and the others among 478 Japanese-Americans or 279 native Japanese aged from 40 to 79 years.

**Results:** CIMT in the subjects with metabolic syndrome was greater than that in the subjects without metabolic syndrome regardless of the age in Japanese-Americans. Contrary, there was no significant difference in CIMT between the subjects with metabolic syndrome and the others in native Japanese. In Japanese-Americans, metabolic syndrome had significant association with CIMT after adjustment of age, sex, smoking status, and LDL cholesterol level in multivariate linear regression model. On the other hand, such relationship was not found in native Japanese.

**Conclusion:** The impact of metabolic syndrome on atherosclerosis was greater in Japanese-Americans than in native Japanese. The result suggests that life style westernization may have influence to enhance atherogenic effect of metabolic syndrome.

**PP9-2 Relation of homocysteine and homocysteine-related vitamins to bone mineral density in Japanese patients with diabetes**

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**Objective:** Elevation of homocysteine (Hcy) is associated with an increased risk of osteoporosis and fracture, although it is known whether high Hcy level affects bone in diabetic patients. In this study, we investigated relation of homocysteine and B-vitamin status indicators to bone mineral density (BMD) in Japanese diabetic patients.

**Methods:** Femoral neck BMD was measured by DXA method in 154 diabetic patients (92 men and 62 women). Values of dietary B6, B12 and folate intake were evaluated using food frequency questionnaire. Serum B6 and plasma Hcy levels were measured by high performance liquid chromatography, and serum levels of B12 and folate were measured by the micro bioassay methods.

**Results:** Dietary B6, B12 and folate intake values were significantly associated with serum vitamin levels. Plasma Hcy levels showed significantly negative correlations with dietary B6 intake, folate intake and serum folate level. Femoral neck BMD was related negatively to plasma Hcy levels ($R = -0.219 \pm 12289; P = 0.007$) and positively to folate intake ($R = 0.185 \pm 12289; P = 0.023$).

**Conclusion:** These data suggest that elevated Hcy due to folate insufficiency may be a potential factor for reduced BMD in diabetic patients.

**PP9-3 Withdrawal**

**PP9-4 Correlation between fetuin-A and matrix Gla protein levels in diabetic and non-diabetic subjects**

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Vascular calcification is frequently found in hemodialysis and/or diabetic patients. Fetuin-A is a well-characterized circulating inhibitor of calcification. As expected, several reports have shown that low fetuin-A levels were associated with high morbidity and mortality for dialysis patients, possibly through accelerated vascular calcification. Furthermore, we recently demonstrated that fetuin-A levels were inversely associated with vascular calcification in subjects without renal dysfunction, suggesting the role of fetuin-A as a calcification inhibitor regardless of renal function. Several other bone-associated proteins, such as the matrix Ga protein (MGP), osteoprotegerin (OPG), and osteopontin (OPN), are also known to inhibit vascular calcification. However, little is known about the relationship between fetuin-A and these calcification inhibitors. In this study, we examined the association of fetuin-A with MGP, OPG, and OPN. We consecutively enrolled 92 nondiabetic and 38 diabetic subjects who were suspected to have coronary artery diseases. Serum levels of fetuin-A, MGP, OPG, and OPN were measured using ELISA. In nondiabetic subjects, fetuin-A level was significantly correlated with MGP level ($\rho = 0.242, P = 0.021$). The fetuin-A level was not correlated with OPG ($\rho = 0.048, P = 0.649$) and OPN ($\rho = 0.007, P = 0.948$) levels. On the other hand, there was no association of fetuin-A with MGP ($\rho = 0.224, P = 0.173$), OPG ($\rho = 0.265, P = 0.107$), and OPN ($\rho = 0.154, P = 0.349$) in diabetic subjects. We found the positive correlation between fetuin-A and MGP levels in nondiabetic subjects. Fetuin-A may collaborate with MGP to inhibit vascular calcification.

**PP9-5 Serum C3: A better inflammatory marker of insulin resistance than hs-CRP in non-diabetic Chinese**

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To compare the associations of C3 and hs-CRP with metabolic risk factors and insulin resistance, 664 non-diabetic Chinese aged 20–80 years were recruited. Insulin resistance was defined as the upper quartile of HOMA-IR. Results showed C3 and hs-CRP were significantly higher in subjects with
insulin resistance than those without. In a logistic regression model, including age, gender, SBP, DBP, TG, TC, high-density lipoprotein cholesterol (HDL-c), both C3 and hs-CRP were independently associated with insulin resistance. When hs-CRP or waist circumference was included in the model, C3 remained significantly associated with insulin resistance. However, the correlation between hs-CRP and insulin resistance disappeared after C3 or waist circumference entering. Conclusively, compared with hs-CRP, serum C3 had a stronger association with insulin resistance, independent of waist circumference, blood pressures and serum lipids.

PP9-6 The impact of glucose control on the prognostic factors of patients with head and neck cancers
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Introduction: Some reports reveal that hyperglycemia is harmful for postoperative wound healing. Some patients with cancers may have dysglycemia. We investigated whether preoperative hyperglycemia is associated with increased incidence of postoperative prolonged in-hospital stay and complication in patients with head and neck cancers undergoing concurrent chemoradiation therapy (CCRT) after surgery.

Methods: Preoperative fasting glucose values before surgery were retrieved for 60 patients with head and neck cancers (male: 56; female: 4). We observed the association of preoperative fasting hyperglycemia values with the prognostic factors of patients undergoing concurrent chemoradiation therapy after surgery.

Results: Preoperative fasting hyperglycemia values higher than 110 mg% are associated with prolonged in-hospital stay, increased body weight loss, and increased incidences of in-hospital complication.

Conclusion: Our data indicate that preoperative fasting hyperglycemia is a risk factor for prolonged in-hospital stay and complications in patients with head and cancer undergoing CCRT and surgery.

PP9-7 To explore the related cause of hypoglycemia unawareness in type 2 diabetes mellitus
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The most reason inducing severe hypoglycemia is hypoglycemia unawareness (HU). If we can know what cause the occurrence of HU, we will decrease the incidence of the severe hypoglycemia. However, there are not many studies related with this subject in Taiwan. Therefore, the purpose of this study was to explore the related cause of HU in type 2 DM patient. This will be a cross-sectional correlation study. Convenient sampling will be conducted from April 2008 to June 30 2009 at medical center of Tainan County in Taiwan. Forty-four people with hypoglycemic symptoms and forty-seven people without the symptoms of hypoglycemia and all of them have the blood sugar below 70 mg/dl are included in this study. The research tools include heart rate variability monitor with high validity and reliability and biological investigation test. SPSS/PC software (version 17.0) was used to analyze the data. The results show HU is closely related to the disease duration and the renal function (MDRD). In logistic regression analysis it shows that incidence of HU is increased by 7% with increased one-year disease duration, and increased by 2% with increase in MDRD score by 1. As we can know, the longer disease duration and renal dysfunction are the two most important factors related with HU. Health care provider should be cautious while taking care of this kind of patients in order to decrease the occurrence of severe hypoglycemia.

PP9-8 Characterization of the severe hypoglycemia in type 2 diabetes according to c-peptide level
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Severe hypoglycemia is a major barrier to tight glycemic control in diabetes. The risk is associated with c-peptide negativity (decreased insulin secretion). We aimed to describe clinical characteristics of the type 2 diabetic patients admitted for severe hypoglycemia according to c-peptide level. We retrospectively analyzed 83 episodes of severe hypoglycemia between January 2008 and December 2009. We collected data on the event, concomitant risk factors, diabetic complications and current medications. We divided the patients according to c-peptide level (c-peptide < 0.5 ng/ml, N = 27; c-peptide > 0.5 ng/ml, N = 56). The study subjects were 68 ± 12 years old and 33 (39.8%) men and 50 women (60.2%). The duration of diabetes was 13 ± 9 years and diabetic retinopathy was present in 9 (10.8%); diabetic nephropathy in 26 (31.3%); microalbuminuria/macroalbuminuria/elevated creatinine in 40/6/10 (48.2%/7.2%/12.0%); macrovascular complications in 6 (7.2%). The patients with low c-peptide were younger (64 ± 12 years vs 70 ± 12 years, P = 0.03) and more commonly on insulin treatment compared to the control (89% vs 50%, P < 0.01). HbA1c level was higher in the group with low c-peptide compared to that of control (8.9 ± 1.8% vs 7.1 ± 1.6%, P < 0.01). However they did not differ in terms of diabetes duration, prevalence of diabetic micro- and macrovascular complications.

Conclusion: Type 2 diabetic patients with low c-peptide developed severe hypoglycemia despite they showed poorer glycemic control. Studies investigating optimal treatment for these patients are needed to be followed.

PP10: Diabetes Complications #1

PP10-1 The role of sFlt-1 in the modulation of angiogenesis in diabetes mellitus
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Vascular disease is a major complication of diabetes mellitus (DM), and in patients with peripheral arterial disease (PAD), diabetes is a major risk factor for the development of critical limb ischemia (CLI) and subsequent limb loss. Abnormalities in factors that regulate normal endothelial function and angiogenesis likely contribute to diabetic vascular complications. Vascular endothelial growth factor (VEGF) likely plays a key role in the regulation of angiogenesis and collateral blood vessel formation in PAD, and evidence indicates that VEGF may also serve as an endothelial maintenance factor. In preclinical studies, mice fed a high-fat diet develop type 2 diabetes mellitus (DM2), and following surgically-induced hind limb ischemia, these mice display abnormal angiogenesis and limb perfusion. Recent data from our lab indicate that these abnormalities in angiogenesis are accompanied by evidence of diminished VEGF signaling (decreased phospho-Akt and -eNOS). Moreover, ischemic diabetic mice demonstrate a marked increase in expression of a soluble splice variant of full-length VEGF receptor-1, known as soluble Flt-1(sFlt-1), that acts as an endogenous inhibitor of VEGF-mediated angiogenesis. This acts as an endogenous inhibitor of VEGF-mediated angiogenesis. Currently, little is known about the mechanisms responsible for deficient angiogenesis in patients with diabetes mellitus and PAD. Our data suggest that a VEGF receptor signaling defect, analogous to insulin resistance, may be responsible for the observed vascular defects in diabetes. Therefore, we hypothesize that diminished skeletal muscle VEGF signaling and angiogenesis in type 2 diabetes mellitus are due to increased sFlt-1 expression.

PP10-2 Homocysteine was related with peripheral arterial disease among the elderly with type 2 diabetes only in male
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Objective: To find a novel risk factor for peripheral arterial disease (PAD) in the elderly.

Methods: A cross sectional study involving 70 out of 146 elderly with type 2 diabetes patients (>60 years) at Geriatric Out-patient Clinic, Sanglah Hospital was conducted. Age (right ABI, r = -0.396, P < 0.001; left ABI, r = -0.509, P < 0.001), lying systolic blood pressure (right ABI, r = -0.267, P = 0.013), concentration of 2 hpp plasma glucose (right ABI, r = -0.384, P = 0.002; left ABI, r = -0.396, P < 0.001), and smoking (right ABI, r = -0.268, P = 0.012; left ABI, r = -0.267, P = 0.013), concentration of 2 hpp plasma glucose (right ABI, r = -0.384, P = 0.002; left ABI, r = -0.396, P < 0.001).
has positive correlation with age ($r = 0.315; P < 0.004$). Homocysteine also has positive correlation with age ($r = 0.315; P = 0.004$).

Conclusions: Some traditional risk factors (age, lying systolic blood pressure, and 2 hpp plasma glucose) were related with PAD in the elderly with type 2 diabetes. Homocysteine had correlation with ABI only in male. Age was the most important risk factor for PAD, both directly and indirectly through homocysteine (only in male).

**PP10-5**  
**Diabetic foot in Mongolia**  
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**AIMS:** The aim of this study was to evaluate the diabetic foot among type 2 diabetic patients in Mongolia.

**METHODS:** This study included 262 type 2 diabetic patients (133 male, 129 female), with a mean age of 59.13 ± 11.03 years and a mean diabetes duration of 5.25 ± 5.8 years. The diabetic foot damage diagnosed by means of Practical Guidelines from the International Working Group on the Diabetic Foot. The foot inspection was included brief questionnaire and clinical examination (deformities, dry skin, callus, infection and ulceration). Nerve damage examined by 128 Hz tuning fork, 10 g monofilament, pin prick, cotton wool, temperature sensation, muscle strength and achilles reflexes. Vascular damage examined by foot pulses and ABI.

**RESULTS:** People at some point in their life time were with foot ulcer, skin on the feet so dry that cracked open and had amputation in 48(24.1%), 37(18.6%) and 4(1.5%) patients. Foot deformity, dry skin, callus, fissure, infection and ulceration were in 42(16.1%), 223(86.5%), 188(72.0%), 32(12.3%), 70(26.8%) and 27(10.3%). Nerve and vascular damage were diagnosed in 178(68.0%) and 55(31.1%) patients. Poor glycemic control, hypertension, dyslipidemia and hypercoagulation were in 218(87.6%), 131(30.0%), 122(53.8%) and 129(55.2%) patients. All 262(100%) participants answered they haven’t any podiatrist in their country.

**CONCLUSIONS:** We have diabetic foot problem but we haven’t diabetic foot care in Mongolia. We need podiatrist and diabetic foot clinic in Mongolia.

**PP10-6**  
**Association of serum adiponectin concentration with HRV in non diabetic offspring of type 2 diabetic patients**  
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**OBJECTIVE:** To study the association of serum adiponectin concentrations with reduced analysis of heart rate variability (HRV) in non diabetic offspring of type 2 diabetic patients.

**METHODS:** Thirty one type 2 diabetic subjects had 91 offsprings, 67 offsprings with FPG no more than 5.6 mmol/L were divided into two groups according to the outcomes of oral glucose tests (OGTTs): normal glucose tolerance (NGT) group ($n = 32$) and impaired glucose tolerance (IGT) group ($n = 35$). Twenty-five control subjects were recruited for the study. Serum adiponectin concentrations were measured. HRV was determined from 24-h Holter recording.

**RESULTS:** There are significant differences in SDNN, SDANN, rMSSD, TP, LF, HF, fasting insulin and adiponectin concentrations within the three groups, in body mass index (BMI), TG, HDL-c between IGT and the rest two groups. Serum adiponectin concentrations in non diabetic offspring of type 2 diabetic patients were negatively related to BMI, fasting insulin concentration, and positively related to HDL-c, SDNN, SDANN, rMSSD, TP, LF, HF.

**CONCLUSION:** The autonomic impairment is associated with insulin resistant and the altered serum adiponectin concentrations.

**PP10-7**  
**Pupillary light reflex in patients with diabetes mellitus**  
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In order to investigate the relationship between pupillary signs of patients with diabetes mellitus and diabetic conditions, we have evaluated the parameters obtained in the pupillary light reflex test in patients with diabetes mellitus. A total of 89 randomly chosen patients with diabetes mellitus who have no apparent neuropathy or mild diabetic neuropathy were selected for this study. The pupillary light reflex test was performed on both eyes using a portable infrared video-pupillography system (Iriscodex Dual C-1064); Hamamatsu Photonics). The measured parameters of the pupillary light reflex test are as follows; D1, initial diameter in the dark before light stimulus (mm); D2, minimum diameter after light stimulus; CR, constriction ratio (CR = (D1-D2)/D1); VC, the maximum velocity of constriction (mm/s). Median
Objective: To explore the relationship between Arg913Gln Polymorphism of SLC12A3 gene Arg913Gln polymorphism and type 2 diabetic complications, we have evaluated fasting plasma C-peptide levels and microvascular complications in obese and nonobese patients with type 2 diabetes.

Methods: Three hundred and seventy patients with type 2 diabetes were divided into two groups, with/without the presence of nonalcoholic fatty liver disease (NAFLD). PCR-sequencing was used to detect genotypes of Arg913Gln polymorphism of SLC12A3 gene for groups. Genotypic and allelic frequencies and clinical characteristics were compared among the groups.

Results: Three genotypes were detected, i.e. GG, GA and AA genotype. In comparison with control groups frequencies of GA ± AA genotype and A allele in T2DM group showed elevated tendency (p<0.05 for each). There were no significant differences in genotypic or allelic frequencies among DN0, DN1 and DN2 groups. The T2DM with GA ± AA genotype group exhibited increased TG, AER, FINS and HOMA-IR (P values were 0.047, 0.048, 0.001 and 0.002, respectively) when compared with GG genotypic group.

Conclusions: Our data suggested that Arg913Gln<G/A> polymorphism of SLC12A3 gene were not significantly associated with T2DM and DN in Shanghai Han populations. Because T2DM with GA ± AA genotype showed significant elevation in AER when compared with GG genotype, suggesting that the Arg913Gln<G/A> polymorphism of SLC12A3 gene may predict the increase of albuminuria in T2DM patients in Shanghai Han populations.

PP11-5 Withdrawal

PP11-6 Progression of estimated glomerular filtration rate associated with values of toe brachial index in type 2 diabetes

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Objective: To analyze the clinical features of coronary artery disease (CAD) patients with or without the presence of nonalcoholic fatty liver disease (NAFLD).

Methods: A total of 234 subjects aged 66.6 ± 10.5 were divided into non-NAFLD group and NAFLD group according to ultrasonography. After coronary angiography was performed, non-NAFLD group were further divided into subgroups, including NCAD subgroup CAD subgroup, isolate NAFLD subgroup (INAFLD) and CAD with NAFLD subgroup (CAD&FLD).

The sever of CAD was assessed according to the coronary stenosis index (CSI). Definition for central obesity followed the Guideline on Prevention and Treatment of Blood Lipid Abnormality in Chinese Adults.

Results: Ultrasonography revealed NAFLD in 62 patients (26.5%). In patients with NAFLD, the incidence of central obesity was higher than those without NAFLD (83.9% vs 48.8%, P < 0.001). The frequency of CAD accompanied with NAFLD was more common in subjects under the age of 65 than those over 65 years old (59.5% vs 40.5%, P = 0.025). CSI score was similar in CAD subgroup and CAD&FLD subgroup (P > 0.05), however the age of patients in CAD&FLD subgroup is significantly lower compared to the CAD subgroup (P = 0.006). Logistic regression suggested central fat was the only independent risk factor of NAFLD (β = 1.701, P < 0.001). Multiple stepwise regression analysis showed that age was the single parameter that best predict CSI score. However, in subjects over 65 years old waist circumference was the only independent factor affecting CSI score.

Conclusion: This implies CAD accompanied with NAFLD was more common in the middle age subjects. In patients with NAFLD, it is important to explore the patients for cardiovascular disease.
and toe-brachial index (TBI) in progression of CKD are largely unexplored. We consecutively collected 1461 (male/female: 1055/406) type 2 diabetes (mean age of 57.1 ± 12.9 years) (mean ± SD) who received ABI & TBI examinations in outpatients clinic at central Taiwan from October 2008 to August 2009. Estimated glomerular filtration rate (eGFR) were obtained by the Modification of Diet in Renal Disease Study equation.

RESULTS: In baseline examinations, 2.8 % of participants had ABI value less than 0.9, & 5.7% had the TBI value less than 0.6. Lower values of eGFR are independently associated with both low ABI & low TBI. Repeating renal function measured 3–6 months later showed that 118 out of 473 developed CKD progression downwards. Low TBI values were significantly associated with CKD progression. The predictors of eGFR progress more than 10 ml/ 

RESULTS: Serum Apelin levels in the patients were significantly higher than those in the normal control group. Serum Apelin levels were significantly higher in the non plaque group than those in the plaque group. Multiple stepwise regression analysis showed that serum Apelin level was influenced mainly by insulin resistance index and serum cholesterol level, while the logistic regression showed serum Apelin level may be a protective factor of atherosclerosis in early type two diabetes patients.

CONCLUSION: In early type two diabetes, low serum Apelin level may be a predictor of atherosclerosis and Apelin may be an inhibitory factor for atherosclerosis.

Bone morphogenic protein 4 as an emerging biomarker of subclinical atherosclerosis in patients with type 2 diabetes

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Recent studies suggest that bone morphogenic protein 4 (BMP-4), which is produced in vascular endothelial cells by oscillatory shear stress, may act as a pro-inflammatory and pro-atherogenic cytokine in the vessel wall. We evaluated the relationship between serum BMP-4 levels and subclinical atherosclerosis in type 2 diabetes. A total of 174 asymptomatic diabetic patients were recruited and their clinical and biochemical characteristics were collected. The degree of atherosclerosis was evaluated by measuring carotid intimal-medial thickness (IMT) and the cardio-ankle vascular index (CAVI). When subjects were divided into tertiles by serum BMP-4 levels, carotid IMT (P = 0.008) and CAVI (P = 0.014) were lower in proportion to BMP-4 levels. Serum BMP-4 levels were inversely correlated with hsCRP levels (P = 0.050) after adjustment for age, sex, duration of diabetes, systolic blood pressure, body mass index (BMI), HbA1c, and LDL-cholesterol. Serum BMP-4 levels were downregulated in high carotid IMT (>0.9 mm; P = 0.036), high CAVI (>9; P = 0.028), and high hsCRP (>3 mg/L; P = 0.023) subgroups. After adjustment for age, sex, duration of diabetes, systolic blood pressure, and BMI, BMP-4 levels remained independently associated with carotid IMT (P = 0.028) and CAVI (P = 0.008) in patients with type 2 diabetes. Serum BMP-4 levels have a consistent inverse relationship with hsCRP levels, and with carotid IMT and CAVI independent of conventional risk factors. These results suggest that BMP-4 may be a novel atherosclerotic biomarker in asymptomatic patients with type 2 diabetes.

Vaspin serum concentrations in type 2 diabetic patients with carotid plaque

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AIMS: We examined whether serum vaspin levels are associated with the presence of carotid plaque in early stage of type 2 diabetes.

METHOD: Sixty-one type 2 diabetic patients within 3 years of diagnosis were divided into two groups by the presence or absence of carotid plaque. Twenty two age-matched apparently healthy controls were included. Serum vaspin was measured by enzyme-linked immunosorbent assay.

RESULTS: Fasting serum vaspin concentrations were higher in the diabetic subjects without carotid plaque than controls (0.65 ± 0.27 vs 0.46 ± 0.13 ng/ml, < 0.01). However, circulating vaspin was lower in the diabetic subjects with carotid plaque than those without (0.53 ± 0.24 vs 0.65 ± 0.27 ng/ml, < 0.05). Logistic regression analysis showed that SBP and fasting serum vaspin levels were significantly associated with the presence of carotid plaque.

CONCLUSIONS: Serum vaspin levels were significantly associated with the presence of carotid plaque in type 2 diabetic patients.
In conclusion, EGCG inhibited TNF-α-mediated PAI-1 production and induced endothelial cell senescence. We investigated the relation between PWV, media thickening in the carotid artery (IMT) and examined d-ROMs and BAP.

**Method:** Fifteen people hoped for PWV and 34 people who hoped for carotid echogram whom a clinical survey had a checkup. d-ROMs and BAP measured it with FRAS4. PWV(cm/sec) with a product made in Korin Corporation, and maxIMT(mm) measured greatest thickening value with a carotid echogram. We examined the correlation of the PWV, maxIMT, d-ROMs, BAP, metabolic syndrome-related factor with a rank-difference correlation of spearman.

**Results:** In PWV measurement group, PWV significantly related BAP $r = -0.86$, waist $r = 0.55$, mean BP $r = 0.63$, HDLcho $r = -0.52$ ($P < 0.05$). BAP significantly related with waist $r = -0.58$, mean BP $r = 0.51$. In maxIMT measurement group, maxIMT significantly related BAP $r = -0.38$, age $r = 0.70$, mean BP $r = 0.51$, FBS $r = 0.45$. BAP significantly related TG $r = -0.51$. d-ROMs did not accept meaningful correlation.

**Conclusion:** The decrease of BAP related to PWV increase and an IMT thickening then was risk factor of the arteriosclerosis development, and useful as screening of the arteriosclerosis.

**PP12-6**

**Green tea (-)-Epigallocatechin gallate inhibits TNF-α-induced PAI-1 production from vascular endothelial cells**

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The role of tumor necrosis factor-alpha (TNF-α) in contributing to obesity-associated cardiovascular and metabolic risk has gained much attention. TNF-α could increase plasminogen activator inhibitor 1 (PAI-1) expression in the pathophysiology of obesity-related cardiovascular diseases. (-)-Epigallocatechin gallate (EGCG), the major catechin derived from green tea, has multiple beneficial effects to reduce cardiovascular disease but the effects of EGCG on vascular endothelial TNF-α-induced PAI-1 production is not known. In this study, we investigated the mechanisms by which EGCG may inhibit TNF-α-induced PAI-1 production in human umbilical vein endothelial cells (HUVEC). TNF-α-increased PAI-1 production in both a concentration and time-dependent manner. Inhibitors of extracellular signal-regulated kinases 1/2 (ERK1/2), PD98059, decreased TNF-α-induced PAI-1 production. EGCG prevented TNF-α-mediated PAI-1 production and reduced phosphorylation of ERK1/2. In addition, EGCG attenuated TNF-α mediated down-regulation of TNF-α receptor 1 (TNFR1), but not TNFR2. In conclusion, EGCG inhibited TNF-α-induced PAI-1 production. Moreover, EGCG inhibited ERK1/2 phosphorylation as well as TNF activation of TNFR1, which subsequently resulted in reduced PAI-1 production. These data provide a novel mechanism where the green tea (-)-epigallocatechin gallate, EGCG, could provide direct vascular benefits in inflammatory cardiovascular diseases.

**PP12-7**

**Effect of aspirin on high glucose-induced senescence of endothelial cells**

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**Background:** Endothelial cell senescence is accelerated under high glucose condition, which may contribute to the vascular complications in the diabetics. This study aimed to investigate the effect of aspirin on high glucose-induced endothelial cell senescence.

**Methods:** Human umbilical venous endothelial cell were cultured in Dulbecco’s modified Eagle’s medium (DMEM) with different treatments including the normal glucose (5.5 mmol/L), high glucose (33 mmol/L), aspirin (0.01–1.00 mmol/L) with high glucose. 300 umol/L L-NAME was added to the cultured medium when needed. After 48 h, SA-β-gal staining was used to evaluate the senescence. Total nitric oxide (NO) production and NO synthase (NOS) activity were measured using Griess reaction and molecular probes of 3-amino-4-aminomethyl-2,7-difluorescin, diacetate. The level of intracellular reactive oxygen species was monitored by flow cytometry using 2',7'-dichlorofluorescein diacetate. Asymmetric dimethylarginine (ADMA) concentration was determined by high-performance liquid chromatography.

**Result:** Exposure to 33 mmol/L glucose for 48 h significantly increased the number of SA-β-gal positive cells. Co-incubation with aspirin markedly inhibited SA-β-gal activity dose-dependently. Aspirin increased NOS activity with eNOS protein expression unchanged but increased NO levels and alleviated oxidative stress. Consistent with these findings, caveolin-1 expression, caveolin-1/eNOS interaction and ADMA accumulation were also decreased. All the inhibitory effects of aspirin on senescent were completely obliterated by L-NAME, the NOS inhibitor.

**Conclusion:** The anti-senescent effects of aspirin are fulfilled by increasing NO production via the up-regulation of NOS activity and preventing caveolin-1 expression, caveolin-1/eNOS interaction and ADMA accumulation.

**PP12-8**

**Effects of atorvastatin on expression of RAGE mRNA of aorta in GK rats and HUVECs in vitro**

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**Objective:** To investigate the effect of atorvastatin on expressions of receptor for advanced glycation end products (RAGE) and to discuss the potential anti-atherosclerosis mechanisms of atorvastatin.

**Methods:** Five healthy Wistar rats (normal control group) and 9 GK rats divided randomly into two groups: diabetic group and atorvastatin-treated diabetic group (20 mg/Kg qd ) were fed with the high fat diet for 12 weeks. RAGE mRNA and MCP-1 mRNA of aorta were detected using RT-PCR. Ultra microstructure of aorta was observed using transmission electron microscopy (TEM). The cultured human umbilical vein endothelial cells were divided into six groups randomly. RAGE mRNA in endothelial cells was detected via real-time PCR in each groups.

**Results:** In vivo, compared with normal control group, the expressions of RAGE mRNA and MCP-1 mRNA of aortas in diabetic control group rats were significant increased. Decreases of RAGE mRNA and MCP-1 mRNA were observed in aortas of treated-diabetic group compared with diabetic control group. There was significant correlation between levels RAGE mRNA and MCP-1 mRNA ($r = 0.48$, $P = 0.031$). Pathomorphological changes of aorta were similar in each groups observed by TEM. In vitro, the levels of RAGE mRNA in endothelial cells incubated with glucose or AGEs were higher than that of the control group. RAGE mRNA expressions were decreased by atorvastatin treatment.

**Conclusions:** The expression of RAGE is elevated in the early stage of atherosclerosis in diabetic rats. Atorvastatin could prevent the progression of atherosclerosis partly by decreasing the expression of RAGE.
PP13: Clinical Trials of Diabetes

PP13-1 The gender difference of plasma lactate levels in type 2 diabetes and the effect of metformin on that
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OBJECTIVE: To investigate gender difference of the plasma lactate levels (LA) in type 2 diabetes mellitus patients with normal renal and hepatic function, and the effect of metformin on gender difference of the LA levels.

METHODS: Thousand twenty one type 2 diabetes mellitus inpatients with normal renal and hepatic function were collected. The LA and other biochemical indexes were determined. Then analysed the related influencing factors of LA levels, and compared the blood lactate levels of different groups treated with or without metformin and all Cr and ALT subgroups levels, as well as age subgroups.

RESULTS: 1. The LA levels of treated with metformin group was higher significantly than without-metformin group, and no lactic acidosis was found. 2. Spearman correlation analysis showed LA levels had a positive association with gender, metformin and BMI apart from Cr and ALT (P < 0.01). Multivariate logistic regression analysis showed that gender, Cr, ALT and metformin were independent correlated factors of hyperlactacidemia. 3. The female LA levels were obviously higher than males in total group and two subgroups treated with or without metformin (P = 0.000). And the female LA levels were notably higher by comparing with male in Cr and ALT subgroups, as well as each age subgroup especially when age was less than 45-years old (P = 0.021).

CONCLUSIONS: There are gender differences of LA levels in diabetic patients, and the effect of metformin on the plasma lactate levels (LA) of different gender in diabetic patients is different. The plasma LA level in females especially the postmenopausal women are prone to rise.

PP13-2 Comparative glycemic variability of two a-glucosidase inhibitors by using CGM
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The aim of study is to compare Glucose variability in patients given miglitol or acarbose by using continuous glucose monitoring (CGM). Nine type 2 diabetic patients treated with any a-GI (median age: 56.0, HbA1c 6.0% and body mass index 22.7) were enrolled in the study. They were hospitalized for 4 days, and were given miglitol 50 mg or acarbose 100 mg before meal in a non-blinded fashion on day two and vice versa on day three in a randomized crossover design. They had test meals on days two and three. We used CGM and compared the magnitude of increase in glucose levels (MIG), the time to peak glucose levels (TPG) from baseline, and the area under the glucose curve (AUC) from pre-meal baseline to baseline after each meal. No significant differences were seen between those given miglitol and those given acarbose in MIG, TPG and AUC after each meal. The range of increase in glucose levels from baseline was significantly narrower in those given miglitol than in those given acarbose, 30 and 60 minutes after lunch (30 min, 0.8 vs 31.9 mg/dL, P < 0.0001; 60 min, 36.8 vs 72.2 mg/dL, P < 0.0001) and 30, 60 and 90 min after dinner (30 min, 2.9 vs 24.0 mg/dL, P = 0.0210; 60 min, 38.4 vs 72.0 mg/dL, P < 0.0001; 90 min, 66.2 vs 88.8 mg/dL, P = 0.0103). Miglitol is effective to suppress the post prandial glucose excursions until 60–90 min after meal compared to acarbose.

PP13-3 Efficacy and safety of glipizide GITS for treatment of type 2 diabetes: A multi-center clinical study
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To investigate the efficacy and safety of glipizide GITS for the treatment of type 2 diabetes. 675 type 2 diabetic patients from 21 centers with poor glycemic control after life style intervention or oral hypoglycemic drug treatment other than glipizide GITS were included in this multi-center, open-labeled and self-controlled clinical study. Patients were switched to glipizide GITS treatment for 12 weeks. After treated by glipizide GITS for 12 weeks, these patients had decreased HbA1c by 1.48% ± 1.20%, decreased fasting blood glucose by 2.47 ± 1.38 mmol/L and decreased mean postprandial blood glucose by 3.64 ± 2.63 mmol/L. 52.21% of patients achieved HbA1c < 6.5% and 83.21% achieved HbA1c < 7.0%. A majority of patients obtained the glycemic target by only 5–10 mg/dl glipizide GITS, the percentages were 97.0% in former lifestyle intervention group, 95.8% in former non-insulin secretagogue therapy group and 88.7% in former insulin secretagogue therapy group. The incidence of mild hypoglycemia was 4.59% and incidence of severe hypoglycemia was 0.15%. In addition, since glipizide GITS is convenient to use and has more advantages to improve quality of life, 99% of patients switched from other insulin secretagogue to glipizide GITS preferred glipizide GITS as their treatment. In conclusion, glipizide GITS is an effective and safe hypoglycemic agent and could greatly improve the quality of life for type 2 diabetic patients.

PP13-4 Role of pancreatic β cell function for long term glycemic control of pioglitazone in type 2 diabetes
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Recent studies showed the glycemic durability efficay of rosiglitazone monotherapy and showed that the pioglitazone add-on therapy had a good long-term efficacy and tolerability type 2 diabetes. But, the variables affecting long-term efficacy are uncertain. So, we examined the long-term glycemic durability of pioglitazone early add-on therapy and analyzed the variables affecting long-term efficacy in type 2 diabetes. A 48 months prospective observation study were performed in patients with type 2 diabetes. To the patients enrolled (n = 211), pioglitazone (15 mg) add-on therapy (to sulphonylurea and/or metformin) was maintained. One hundred and eight patients completed this study. At baseline, HbA1c was 7.62 ± 1.50%, fasting plasma glucose was 140.4 ± 33.6 mg/dL. The mean change from baseline was in HbA1c: -0.40 ± 1.50%, in fasting plasma glucose: -9.1 ± 44.9mg/dl, in triglyceride: -58.25 ± 207.3 mg/dl, in HOMA-IR: -0.39 ± 1.11, and in body weight 0.85 ± 3.26 kg. At month 48, 64.6% of patients showed good glycemic durability with HbA1c < 7%. In these group, there were significantly shorter duration of diabetes (3.3 ± 3.4 vs 5.7 ± 4.8 year), lower baseline HbA1c (7.06 ± 1.48 vs 8.20 ± 1.24%) and higher baseline β cell function (HOMAβ 45.00 ± 33.80 vs 32.96 ± 20.80) than the other group with HbA1c > 7%. According to baseline HOMAβ, patients divided to tertile (tertile 1: 74.18 ± 31.46, tertile 2: 32.86 ± 4.88, tertile 3: 16.84 ± 5.37). At month 48, tertile1 showed significantly lower HbA1c than tertile 3 (6.60 ± 0.57% vs 7.42 ± 1.48). As compared with tertile 3 (55%), more percent of patients (80%) in tertile 1 were less than HbA1c 7%. These study suggest that long-term glycemic control in pioglitazone add-on therapy is associated with preserved β cell insulin secreting function.

PP13-5 Effect of Rosiglitazone on glucose tolerance in newly diagnosed type 2 diabetes patients
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OBJECTIVE: To analyze the effect of Rosiglitazone on glucose tolerance in newly diagnosed type 2 diabetes patients.

METHODS: Fifty eight newly diagnosed type 2 diabetic patients were treated with Rosiglitazone (4–8 mg/day) for 12 weeks. Oral glucose tolerance test (OGTT) and insulin release test was performed before and after treatment. According to the results of OGTT after treatment, the patients were divided into 2 groups: group A (glucose tolerance restored) and group B (glucose tolerance not restored). Baseline characteristics and the changes of insulin resistance and β cells function were compared.

RESULTS: Thirty two cases of 58 patients' glucose tolerance were restored: 17 cases were restored to NGT, 13 returned to IGT, 3 recovered for IFG, 26 cases...
glucose tolerance were not mitigation. After treatment, HbA1c of group B decreased from 7.2 ± 0.9 to 6.4 ± 0.59% and HbA1c of group A decreased from 7.1 ± 0.7 to 5.6 ± 0.55% (P < 0.05). Compared to group B, the patients of group A were younger and had shorter course of disease (P < 0.05); HOMA-B and MBCI and early phase insulin secretion of group A were better than that of group B before and after treatment respectively (P < 0.05), while HOMA-IR was lower than that of group B (P < 0.05).

Conclusion: Rosiglitazone could obviously improve insulin resistance of newly diagnosed type 2 diabetes patients, thus facilitate the restoration of their islet β cells function and glucose tolerance. The impact factors of glucose tolerance restoration included age, diabetes duration, HbA1c, β cells function and insulin resistance.

PP13-6
The outcome of the diabetic care with the use of the Traditional Chinese Medicine
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Global diabetes prevalence estimates, derived from population-based data using oral glucose tolerance tests, maybe at least attend to 300 million people by 2030. In 2001, diabetes mellitus quality improvement program was launched in Taiwan into which all patients were incorporated for the management of the medical care. The purpose of this study is to discuss whether using Traditional Chinese Medicine and Western Medicine simultaneously affects the outcome of the diabetic patients. The subjects were admitted to the program from 2001 to 2003. The baseline of their data was recorded while patients joined the program, while the endpoint of theirs was assumed in one year. The research frame, discussing the relationship between the Chinese and Western medicine and the outcome, is on the basis of the Model of Health Behaviour proposed by R. M. Andersen. Generally speaking, the findings of this paper shows the relationship between the change of HbA1c and the outcome of diabetes mellitus patients using Chinese and Western medicine was not statistically significant compared with others who had taken Western Medicine only; however, when we specifically analysed the effect of individual Chinese herbal medicine, patients who used Zhu-Ye Shu-Gao Tang (one important prescription which had been used hundreds years) got the larger decline of HbA1c compared with others (P < 0.05).

PP14-1
Lipid Metabolism and Diabetes

PP14-1
Lipid partitioning after uninephrectomy
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This longitudinal study addressed the sequential events and metabolic consequences of lipid partitioning following uninephrectomy. Adult male Sprague-Dawley rats were randomized into sham operation (n = 15) or left uninephrectomy (UNX, n = 18). At 1 and 3 months post nephrectomy, three rats from each group were sacrificed for histopathological examination of adipocyte differentiation and lipid accumulation. Renal protein expression of the lipogenic peroxisome proliferator-activated receptor-gamma (PPAR-gamma), HMG-CoA reductase (HMGCGR) and adiponectin receptor was detected by western blot and immunofluorescence microscopy. Blood lipids, glucose, insulin and renal functions were longitudinally measured up to 10 months after operation. The UNX rats progressively developed lipodystrophy of subcutaneous and visceral adipose depots with failure of adipocyte differentiation and lipid storage, followed by blood lipid elevation and ectopic lipid deposition with cellular lipid peroxidation, and renal adipogenesis with chronic inflammatory infiltration. Despite having standard diet, normal food consumption and normal body weight, the uninephrectomized rats with defective lipid partitioning manifested a myriad of homeostatic disturbances including insulin resistance, hyperglycemia, adiponectin resistance and upregulation of PPAR-gamma; and HMGCGR. Disordered lipid partitioning from adipose depots to circulation and non-adipose tissues and non-adipose cells contributes to homeostatic disturbances and lipogenic activation.

PP14-2
Effects of MTP gene on the hypolipidaemic response to statins in type 2 Diabetes dyslipidemia
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Objective: To investigate the relationship between microsomal triglyceride transfer protein (MTP) gene and the effects of simvastatin and atorvastatin on type 2 Diabetes dyslipidemia.

Methods: Five hundred and sixty four type 2 diabetes mellitus (DM) patients with hypercholesterolemia were treated with simvastatin 20 mg/d or atorvastatin 10 mg/d for 4 weeks. MTP-493G/T polymorphism was detected by PCR-RFLP and DNA sequence analysis.

Results: (1) Both simvastatin and atorvastatin therapies significantly decreased the levels of total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and triglycerides (TG) (P < 0.05), there were no significant differences between two groups. (2) The MTP-493G/T polymorphism was found in both simvastatin and atorvastatin groups, and the phenotype distribution of the two groups did not differ significantly. (3) TG and very-low density lipoprotein-cholesterol (VLDL-C) in patients with MTP-493T/G or G/T gene are significantly higher than that in MTP-493G/G gene patients (TG 2.47 ± 1.63 vs 1.98 ± 1.35, VLDL-C: 0.79 ± 0.37 vs 0.58 ± 0.24), (P < 0.05). (4) The change of TC and LDL-C in patients with MTP-493T/T or G/T gene are significantly decreased compared with MTP-493G/G gene carriers.

Conclusions: Single nucleotide mutation of G/T of MTP-493 genes has significant influence on dyslipidemia in type 2 Diabetes. The common genetic variation of MTP promoter seems has implication for the effect of statins.

PP14-3
Roles of lipid transfer proteins in determining cellular cholesterol efflux to serum in type 2 diabetes mellitus
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Objective: Cholesterol efflux from cells is an early step of reverse cholesterol transport (RCT) and the capacity of serum to induce cellular cholesterol efflux has been shown to be impaired in type 2 diabetes. Phospholipid transfer protein (PLTP) and cholesterol ester transfer protein (CETP) are the major lipid transfer proteins in the circulation and are involved in RCT. The present study determined whether activities of these lipid transfer proteins are important determinants of cellular cholesterol efflux to serum in type 2 diabetes.

Methods: Two hundred and six type 2 diabetic patients (104 male, 102 female) were recruited. Serum PLTP and CETP activities were measured by radiometric assays. Cholesterol efflux to serum was determined by measuring the transfer of [3H] cholesterol from Fu5AH cells to the medium containing the tested serum.

Results: There were no significant differences in serum CETP (134.9 ± 46.5 arbitrary units (AU) vs 124.8 ± 46.4 respectively) and PLTP activities between female and male subjects (130.5 ± 35.5 AU vs 126.6 ± 32.0 respectively), but female subjects had higher cellular cholesterol efflux to serum (14.1 ± 3.4% vs 13.1 ± 2.6, P = 0.03). On univariate analysis, cellular cholesterol efflux to serum correlated with serum CETP, PLTP, HDL and apo AI. On multiple linear regression analysis, serum PLTP activity and HDL were the major independent determinants of cellular cholesterol efflux to serum, accounting for 29% and 14% of the variability.

Conclusion: Serum PLTP activity (but no CETP) was independently associated cellular cholesterol efflux to serum in type 2 diabetes mellitus.

PP14-4
Withdrawal

PP14-5
Investigation of rate of achievement of LDL-C goals in patients with type 2 diabetes mellitus
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Objective: To evaluate the rate of achievement of LDL-C goal and the factors associated in type 2 diabetes dyslipidemia.

Methods: One hundred and sixty patients (113 male, 47 female) with type 2 diabetes mellitus were included in this study. The patients were divided into three groups according to their achievement for LDL-C goal (group A: > 10%, group B: 0-10%, group C: < 0%).

Results: There were no significant differences in the characteristics of the three groups. However, the patients who achieved the LDL-C goal (group A) had significantly higher rate of smoking and heavier body weight than the other two groups.

Conclusion: The rate of achievement of LDL-C goal in type 2 diabetes mellitus was low, and smoking and body weight were associated with this outcome.
PP15-2
Dietary habit in Japanese type 2 diabetic patients
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Dietary habit has been linked to lifestyle related diseases, such as type 2 diabetes mellitus (DM). Traditional Japanese diet, in which principal food is rice, is thought to be healthier than Western diet. However, rice consumption per person in Japan has been decreasing. On the contrary to this decrease of rice consumption, the number of diabetic patients has been increasing dramatically. This change of dietary habit is thought to be responsible, at least partly, for the increase of diabetes in Japan. To investigate the difference in dietary habit between DM and non-diabetic controls (C), we made the questionnaire survey in DM group (310 men and 215 women, Age: 65.9 ± 11.3 year, HbA1c: 6.9 ± 1.2 %, BMI: 23.2 ± 3.5 kg/m²) and C group (379 men and 679 women, Age: 60.6 ± 14.1 year, BMI: 22.3 ± 3.0 kg/m²). Rice consumption per person per meal was 760.6 ± 364.8 g in DM group and 728.8 ± 294.9 g in C group, respectively (not significantly different). There were no significant differences in the frequencies of skipping breakfast, and night snacks between DM and C groups. However, the frequency of taking snacks between lunch and dinner was significantly higher in C group. The frequency of slow eater who takes more than 15 min at breakfast was significantly higher in group C. The frequency of slow eater who takes more than 15 min at breakfast was significantly higher in C group. The frequency of slow eater who takes more than 15 min at breakfast was significantly higher in C group.

PP15-3
A study on the in-hospital diabetes39 with the high-fiber formula substitution for the traditional breakfast
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INTRODUCTION: Due to the dietary habits, it was a big challenge in Taiwan that how diabetes could increase their high-fiber intake when eating breakfast. The present study was to substitute the high-fiber formula for the diabetes39 breakfast and tried to observe their change of sugar blood before or after eating.

RESEARCH METHOD AND SUBJECTS: With the regressive analysis of the two groups39 change of sugar blood, the researcher observed 30 subjects who had the traditional breakfast in Taiwan, and 30 in-hospitals type 2 diabetes who received indigestible dextrin formula, an exchange of vegetables and cereal.

RESULT: To increase 1.7 g dietary fibers intake when subjects receive high-fiber formula diet that could alleviate the rising range of blood sugar after eating.

DISCUSSION: To substitute the indigestible dextrin for traditional breakfast could increase the dietary fibers intake and alleviate the profile of sugar blood after eating.
**PP15-4**
Effects of small sized-rice bowl on dietary energy and macronutrient composition in obese patients with type 2 diabetes

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The energy intake from carbohydrate was 68.0% in Korean diabetes and the main carbohydrate source is rice. This study was to evaluate the effects of a small sized rice bowl on dietary energy intake and composition of macronutrient in obese patients with type 2 diabetes mellitus. Total 54 obese patients (male; 27, female; 27) with type 2 diabetes were enrolled in the study. The 3-day dietary records were analysed for total energy intake and composition of macronutrient, before and 2 weeks after small sized (male; 300 cc, female; 200 cc) rice bowl based education were given. At baseline, the average age of male was 56.0 ± 7 years, female 59.1 ± 6 years, and the body mass index (BMI) of male was 27.3 ± 1.7 kg/m², female 28.4 ± 2.4 kg/m². Total energy intake was decreased significantly both in male and female by -96.4 ± 103 kcal (P < 0.001), -199.9 ± 224 kcal (P < 0.001) respectively, the proportion of carbohydrate intake was reduced in all groups (male; -3.7 ± 6.2%, P=0.005, female; -3.1 ± 6.0%, P = 0.015, respectively) which fit in the recommendation of Korean Diabetes Association (RKDA). The proportion of protein intake was increased significantly in male (P = 0.004), but not in female. The proportion of fat intake was increased significantly in all groups which fit in RKDA. Body weight was decreased in male, by -0.4 ± 0.5 kg, but not in female. Rice bowl-based meal plan was effective in control of the dietary intakes and balanced of macronutrient composition in the Korean obese persons with type 2 diabetes.

**PP15-5**
A study on the dietary burden of low glycemic load diet intake for the control of in-hospital diabetes

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**INTRODUCTION:** The study of low GL (glycemic load) diet was aimed at the subjects who were not in hospital or who received the long-term food interference. The current research was to observe the sugar blood change of the in-hospital diabetes who received the low GL diet intake and the ordinary diet intake before or after they ate.

**METHOD AND SUBJECTS:** Eighteen in-hospital diabetes (median age: 58.5, range: 32–75) who registered metabolic clinic. Males were 44.4% and females were 55.6%. With the random and cross-over experiment design, subjects received the low GL diet (one day GL < 80/day), had the ordinary diet one day, and measured their sugar blood.

**RESULT:** In comparison with the ordinary food intake, diabetes who received low GL diet certainly could hold their profile of sugar blood over effectively. In addition, it was good for the control of patients39 condition.

**PP16: Diabetes Education and Care #2**

**PP16-1**
Impact of treatment for diabetes on quality-of-life in patients with type 2 diabetes

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**BACKGROUND AND AIMS:** Physical and psychological conditions of patients, which could be referred to as quality of life (QOL), affect self management of diabetes. To understand relationship between QOL and clinical outcome of patients, we performed a DQOL measure developed to measure QOL of patients in the Diabetes Control and Complications Trial study.

**METHODS:** A total of 113 Japanese out-patients with type 2 diabetes (male, 69/ female, 44; age, 65.0 ± 10.6 years; duration of diabetes, 13.5 ± 9.2 years; HbA1c, 7.0 ± 1.8%; BMI, 24.4 ± 4.2) were recruited for the DQOL measure. Relationship between each item in the DQOL measure and HbA1c were analyzed by multiple regression.

**RESULTS:** Following five items in the DQOL measure were significantly associated with HbA1c: ‘How satisfied are you with the time it takes to determine your sugar level?’, ‘How satisfied are you with the time you spend exercising?’, ‘How satisfied are you with your leisure time?’, ‘How satisfied are you with life in general?’, ‘How often do you worry that you will get complications from your diabetes?’ Significant relationship between severity of diabetic complications and following three items in the DQOL measure were observed: ‘How satisfied are you with the time you spend exercising?’, ‘How satisfied are you with life in general?’. Significant relationship between severity of diabetic complications and following three items in the DQOL measure were observed: ‘How satisfied are you with life in general?’, ‘How satisfied are you with your leisure time?’, ‘How satisfied are you with your sleep?’. Several items in the DQOL measure were correlated well with HbA1c and severity of diabetic complications in most patients. Wide range of satisfaction in quality-of-life in each patient could improve self-management of the disease and medical outcome.

**PP16-2**
Adjuvant CAM improves the quality of life in patients with type 2 diabetes: A randomized controlled trial

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**OBJECTIVE:** Quality-of-life (QOL) should be an important consideration while choosing therapeutic options for patients with diabetes. In order to assess the effect of CAM on the QOL of the patients, we compared the QOL of 2 groups of patients with type 2 diabetes who have received integrative medicine therapy (multiple western drugs adjuvant CAM, IMT) and multiple west drugs therapy (MWDT).

**METHODS:** Seventy-four subjects were enrolled to receive regular monthly visits for clinical assessment. The QOL of patients was assessed by a previously developed Diabetes Quality of Life (DQOL) and Short Form-36 (SF-36) questionnaires. Outcomes were measured at 0 and 3 months.

**RESULTS:** After the run-in period (baseline), there were no significant differences between two groups in terms of biochemical indications or QOL scores. An increase in Satisfaction (63.7 ± 16.9 vs 56.9 ± 13.7, P = 0.059) and Impact (77.5 ± 15.6 vs 60.1 ± 13.7, P = 0.022) of the DQOL questionnaires was observed in the IMT group. The IMT group showed an obvious difference in the QOL scores for Physical Function, Bodily Pain, Validity, and Role Limitation (emotional) subscales when compared to the baseline. The MWDT group showed slight improvement in each dimension when compared to the baseline; however the difference is not significant. After the 3-month intervention, there were significant differences in the QOL scores for the most important indicators, including physical function, bodily pain, validity, and role limitation (emotional) between the IMT and MWDT groups.

**CONCLUSIONS:** Adjuvant CAM can improve partial dimensions of QOL in patients with type 2 diabetes.

**PP16-3**
Effect of Tai Chi exercise on biochemical profiles and oxidative stress indicators in obese type 2 diabetic patients

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**BACKGROUND:** Tai Chi Chuan is a type of exercise that can promote the cardiovascular functions and life quality of people. Tai Chi exercise (a simplified form of Tai Chi Chuan) is easier and gentler.

**OBJECTIVE:** The aim of this study was to validate the effects of this simplified exercise in obese diabetic patients.

**METHODS:** Hospital-based obese diabetic patients (aged 40–70, BMI 30–35) were randomly selected and grouped into Tai Chi exercise and conventional exercise groups. They practiced three times a week, including one practice day, and measured their sugar blood.
Roles: After 12 weeks, the hemoglobin A1C values of the experimental group did not decrease (8.9 ± 2.7%; 8.3 ± 2.2%, P = 0.066); but the BMI (33.5 ± 4.8: 31.3 ± 4.2, P = 0.038) significantly decreased. Serum lipid in patients with type 2 diabetes was increased in the D group compared to control. The percentage changes in body fat and fat/lean mass were greater in the D group than in the control group. Insulin resistance by the homeostatic model assessment, total body fat mass, and markers of endothelial function are not fully known in type 2 diabetic patients. In this study, 1580 consecutive patients with type 2 diabetes were included. The major findings were: 1. Total energy intake was decreased in OIG (< 0.05). In the effect of glycemic control, the elderly patients had higher serum creatinine, triglycerides, and creatinine than the non-elderly. We suggest that improving lifestyle modification for non-elderly patients should be considered in the education program.

**PP16-5**

**Metabolic control in elderly patients and non-elderly patients with type 2 diabetes mellitus**

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**Background:** Lifestyle modification plays an important role in metabolic control. Apparently, elderly and non-elderly patients have different lifestyle. We analyze the metabolic control between elderly and non-elderly patients with type 2 diabetes mellitus.

**Patients and Methods:** In this study, 1580 consecutive patients with type 2 diabetes and who enrolled to our shared care program for DM during 2009 July to 2009 Nov were analyzed. According to their age, patients were divided into two groups those with age under (n = 913) and those with age equal to or older than 65 years (n = 667).

**Results:** HbA1c was significantly lower in elderly diabetic patients (7.9 ± 1.4% vs 8.3 ± 1.7%, P < 0.0001). In the elderly patients, the BMI was significantly lower (25.7 ± 3.9 vs 26.4 ± 4.2, P < 0.05). The elderly patients had higher systolic BP and lower diastolic BP. In lipid profile, HDL-C was not significantly different in both groups, but the elderly patients had lower total cholesterol (178.3 ± 35.5 (n = 659) vs 186.0 ± 37.0 (n = 896), P < 0.0001) and LDL-cholesterol (107.6 ± 31.6 (n = 648) vs 114.9 ± 32.9 (n = 884), P < 0.0001). The elderly patients had higher serum creatinine (1.07 ± 0.66 vs 0.92 ± 0.54, P < 0.0001) and lower eGFR (69.7 ± 24.1 vs 87.3 ± 25.4, P < 0.0001).

**Conclusion:** The elderly patients have better metabolic control in hyperglycemia and dyslipidemia than the non-elderly. We suggest that improving lifestyle modification for non-elderly patients should be considered in the education program.

**PP16-6**

**Body weight loss from an energy-restricted diet improves endothelial function and increases adiponectine to leptin ratio**

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The effects of weight loss from an energy-restricted diet on endothelial function and markers of endothelial function are not fully known in type 2 diabetic patients. We investigated the effect of weight loss from an energy-restricted diet on endothelial function and adipokines. Twenty-seven subjects (body mass index = 27.8 ± 3.6 kg/m², aged 55.8 ± 6.7 years) were assigned to an dietary energy-restricted (D; −500 kcal/day) or control group for 12 weeks. We assessed the endothelial function by the brachial artery flow-mediated dilation (FMD), insulin resistance by the homeostatic model assessment, total body fat mass by dual-energy X-ray absorptiometry and leptin and adiponectin at baseline and at the end of 12-week intervention. After 12 weeks, FMD was increased (60.1%, P < 0.05) and HOMA-IR (-37.9%, P < 0.01) and total fat mass (-4.4 kg, P < 0.001) was decreased in the D group compared to control. The adiponectin (+33.4%, P < 0.029) was increased and leptin was decreased (-35.2%, P < 0.05) and the adiponectin to leptin ratio (ALR, 143.6%, P < 0.001) was increased in the D group compared to control. The percentage changes in FMD had positive correlation with the changes in ALR (r = 0.666, P < 0.001). Body weight loss from an energy-restricted diet was effective in improving endothelial function in type 2 diabetic patients. The improvement in endothelial function might be correlated with increase in ALR.
for diabetes prevention and care. This utility of this intervention should be evaluated in a longer term demonstration with a larger population, to better understand the potential sustainability and long-term effectiveness for the prevention and management of diabetes.

PP17: Diabetes Education and Care #3

PP17-1
Diabetes Conversation Map™: Assessing learning and stages of change for self-management by a questionnaire

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AIMS: Diabetes Conversation Map™ is a novel educational tool that engages a group of patients with interactive learning of information relevant to diabetes. The group setting and interactive discussion is designed for mutual exchange of challenges and successes in self-management of diabetes, and helps building confidence for their self-management. Here, we assessed learning knowledge and stages of change for self-management using a questionnaire developed in this study.

METHODS: A total of 108 Japanese patients with diabetes and their families (male 59.3%; age, 63.3 ± 11.0 years; duration of diabetes, 10.7 ± 10.2 years) were recruited. Sessions of “Living with Diabetes”, one of 4 Diabetes Conversation Map™ programs covering general knowledge on diabetes were performed with a group of 5–10 patients. Each session was facilitated by a diabetologist. Participants answered the questionnaire before and after the session.

RESULTS: Understanding of knowledge related to diabetes significantly improved after the session, and the degree of the improvement correlated well with duration of diabetes. Understanding of behaviors and conditions affecting blood glucose levels, and that of symptoms related to hyperglycemia or hypoglycemia significantly improved after the session. Stages of change for self-management were not affected by the session because most patients had already been in stages of preparation, action or maintenance. However, many participants realized importance of setting goals for self-management after the session.

CONCLUSIONS: While effects on long-term clinical outcomes need to be evaluated in the future, Diabetes Conversation Map™ is a powerful educational tool to improve understanding of knowledge and importance of self-management of diabetes.

PP17-2
Diabetes foot care knowledge: A survey of registered nurses in Hong Kong

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PURPOSE: Diabetes and its related foot problems pose serious public health threat worldwide and in Hong Kong. One strategy to minimize diabetic foot problems and lower limb amputation incidence is to develop competence in diabetes education and specific knowledge in diabetes foot care of healthcare professionals. While effort has been invested to develop competence in diabetes education of Registered Nurses, little is known about their foot care knowledge level.

METHODS: A cross-sectional survey was conducted with a cohort of nurses who undertook a post-registration course in diabetes nursing. A Disease Foot Care Knowledge Scale, DFKS, previously developed and validated in Hong Kong was administered.

SUMMARY OF RESULTS: All nurses, 65, upon enrolling to the course participated in the study. Their mean age was 32.7 years old. The mean DFKS score of the sample was 41.4 out of a possible total of 65 scores. Most nurses gave wrong answers, 0 score, to items about applying surgical spirit between toes as a risk factor, 83.1 percent, woollen socks as suitable footwear, 75.4 percent, and normal saline as appropriate solution for minor wound care, 73.8 percent. Twenty two nurses with and 45 nurses without diabetes specialty working experience obtained similar scores. Twenty eight nurses with prior training in foot care did better than those without.

CONCLUSIONS: Although this is a small sample and participants were recruited from a single setting, findings provide pointers to professional education for registered nurses to strengthen their capacity in diabetes foot care.

PP17-3
Medication adherence and associated factors among outpatients with type 2 diabetes

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Type 2 diabetes constitutes a growing public health concern due to the risk of long-term complications. Control of blood glucose and other preventive measures are known to decrease this risk. Medication adherence is one of important behaviors to affect glycemic control and its influencing factors can provide meaningful information.

OBJECTIVE: To investigate the relationship between strength of medication adherence and its related influencing factors in type 2 diabetes.

METHODS: A cross-sectional evaluation was performed in 185 Taiwanese adult outpatients aged 40 years and older with type 2 diabetes of more than 2 years duration who had also received at least one individualized dietitian-led nutrition education session and one nurse-led diabetes education session. They responded to a self-reported survey questionnaire, with interviewer assistance if required, on adherence to diabetes medication use and on factors affecting their self-care. Spearman correlation was used to examine the associations between medication adherence and all characteristics and influencing factors.

RESULTS: 79% of the patients regularly (defined as often or always) took their medications. Patients who took their diabetic medications had lower HbA1c levels and fewer chronic complications. Medication adherence was highly correlated with less environmental barriers such as busy life, traveling, irregular life pattern (P < 0.001) and also correlated with their quality of life. Conclusions: Better medication adherence with improvement in lower HbA1c levels. Environmental barriers and quality of life may play important roles to medication adherence.

PP17-4
Usefulness of the diabetes one-stop clinic

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In the management of diabetic patients, there are procedural difficulties such as inter-department cooperation and patients’ difficulty in visiting the clinic frequently. To overcome this, we have set up the diabetes one-stop clinic. In this study, we investigated its usefulness. We studied 108 patients visiting the one-stop clinic at St. Mary’s Hospital in Seoul from January 2006 to January 2008. Blood and urine sampling, the evaluation of retinopathy, neuropathy and foot deformities by an ophthalmologist and a podiatrist from 8:00 am to noon, food education and buffet at lunch by a dietician, and prescription by a diabetologist at 1:00 pm were made. Patient satisfaction survey was conducted.

The glycemic status of the study subjects (one-stop subjects) was compared with that of diabetic subjects receiving conventional management, who were matched for age, gender, and duration of diabetes (control subjects), n = 100. The one-stop subjects were mostly satisfied with convenience and quality of the clinic: the mean score of satisfaction was 8.8 out of 10. There was no difference in HbA1c level at baseline between the one-stop subjects and control subjects (7.9 ± 2.0 vs 8.0 ± 1.8%, P = 0.728). After 1 year, HbA1c
level in the one-stop subjects decreased significantly from 7.9 ± 2.0 to 6.9 ± 0.9% (P < 0.001), and fasting serum glucose level from 164.9 ± 51.9 to 137.1 ± 26.0 mg/dL (P < 0.001). And the one-stop subjects showed lower HbA1c level compared with the control subjects (6.9 ± 0.9 vs 7.3 ± 1.2%, P = 0.005). In conclusion, the diabetes one-stop clinic is useful and convenient for the management of diabetic patients.

**PP17-5**

**Employees slimming of health promotion**

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The purpose of this study is to find out people obtain metabolic syndrome and try to correct their behavior in eating and exercising and improve all related data. This research used the quasi-experiment methodology. All people enrolled in this study are the employees of a medical center in Taiwan from September 9 to December 15 2008. All processes follow the regulation of IRB. There are 27 employees complete this research. All employees are divided into 8 groups. 8 weeks of courses are arranged in this study. The courses include discussion the risk of overweight, the importance of regular exercise, and correct eating habit. The nutrition department prepares low calorie meal and high fiber crackers for them. We tailor-made an approach for each person. We obtain their biochemistry and physiological datum before and after the study. Data were analyzed with the SPSS 17.0 program. The results show that BW, BMI, waist circumference, blood sugar, and TG are significant improved a lot. Diet and exercise behavior are also improved. The employees whose attendance rate is more than 50% have significant improved in body weight, BMI, waist circumference compared to those who have lower attendance rate during the study. From the results we know that the more they attend the courses the more chances for them to change their mind and behavior. Although we can see the obvious effects in 3 months, the most important thing is long-term observation.

**PP17-6**

**Differences in knowledge level of diabetes between urban and rural Vietnamese populations**

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AIMS: To promote effective health management for the prevention and treatment of diabetes (DM), it is important to recognize the knowledge level of DM in each area-urban and rural-to impart proper and practical education.

METHODS: A cross-sectional questionnaire-based survey was conducted on a randomly chosen population from both the urban (N = 1516) and rural (N = 2217) areas of Vietnam. The participants were asked to answer whether they had ever been diagnosed as DM, and asked to describe their awareness of DM, such as methods of diagnosis, risk factors, and complications. Further, they were asked to mention the sources of their knowledge.

RESULTS: Self-reported DM prevalence of the urban and rural subjects were 6.9% and 2.0%, respectively. Approximately 60% of the urban subjects responded to blood test as a method of diagnosis, whereas among the rural subjects, less than 30% did. Among the listed choices, both urban and rural subjects considered excessive sweet intake and obesity as the major risk factors for DM. Approximately 60% of the urban subjects and less than 26% of the rural subjects recognized renal failure and blindness as complications, but few subjects recognized amputation as a diabetic complication—both in the urban and rural areas. TV and radio were the most commonly cited sources by both urban and rural subjects.

CONCLUSIONS: Certain differences were observed in knowledge level of DM between the urban and rural Vietnamese populations. Information and education for DM must be tailored to suit the subjects in each residential area.