Background: Cytomegalovirus (CMV) is readily transmitted from seropositive solid organ donors to CMV seronegative recipients (CMV-mismatch) despite the use of antiviral prophylaxis and can cause highly morbid and even fatal illness. Type 1 diabetic patients are known to have reduced odds of CMV seropositivity when compared with potential donors. Therefore, the proportion of transplant recipient who has CMV-mismatch in islet cases is significantly higher than that in solid organ transplant (SOT). Our previous study has shown that there is a lower rate of CMV transmission in islet transplant recipients. It is unclear if the recent modification of islet transplant induction protocol has an impact on the rate of transmission.
Methods: Our study was an observational retrospective study comparing the rate of transmission of CMV, in CMV mismatched islet transplant recipients (n = 45) to a control group of CMV mismatched SOT recipients (n = 27) corresponding to the same donor at the University of Alberta Hospital from March 1999 to May 2014.
Results: CMV mismatched islet transplant recipients were less likely to have CMV transmission (8.9%) than CMV mismatched SOT recipients (78%) despite receiving tissues from the same donors. CMV transmission rates in islet transplant had increased due to the recent modification of induction protocol.
Conclusions: Low number of contaminating leukocytes due to stringent retrieval and purification process of islet, the success of immunosuppression protocols in maintaining low rejection rate along with low cytokine response which might promote CMV reactivation and the lack of surgical procedure which might lead to pro-inflammatory state that reactivates CMV in recipients are the postulated reasons for the lower transmission rate in islet transplant cases. The recent intensification of islet transplant induction protocol which renders islet recipients more immunosuppressed than before might have contributed to the higher rate of CMV transmission in this current cohort than the one from our previous study.

PH-04

Identifying a new pathway to regulate AMPK activity under metabolic stress

Eijiro YAMADA[1]*, Shuichi OKADA[1], Ryo SHIBUSAWA[1], Yuko TAGAYA[1], Aya OSAKI[1], Yoko SHIMODA[1], Tsugumichi SAITO[1], Claire BASTIE[2], Jeffrey PESSIN[2], Masanobu YAMADA[2]. [1]*Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Mabashi, Japan;* [2]*Department of Medicine, Albert Einstein College of Medicine, Bronx, NY, United States of America*

Metabolic stress is associated with diabetes and insulin resistance and these patho-physiologies are linked with dysfunctions of nutrient-sensors such as AMP-dependent protein kinase (AMPK). Additionally pro-inflammatory cytokines such as TNFα secreted from adipose tissue contributes to chronic low-grade inflammation and whole body insulin resistance. Previously we reported that Fyn knull mice display increased energy expenditure and fatty acid oxidation due to increased AMPK activity in peripheral tissues. More recently, we demonstrated that Fyn regulates AMPK activity not only indirectly via its action on LKB1, but also by direct modulation of AMPK activity through Y426 phosphorylation of the α subunit. To investigate how Fyn regulates AMPK activity, we made AMPK α-Y426F mutant and examine functional interactions of the α subunit with the β and γ subunits. Although co-immunoprecipitation demonstrated no significant difference in β and γ subunit binding, the α-Y426F mutant displayed increased kinase activity compared to the wild type α subunit. These data suggested that Fyn-dependent tyrosine phosphorylation of AMPK α subunit on Y426 regulates its intra-molecular activity.
To assess this pathway has a critical role under metabolic disease, we further investigated the signaling crosstalk between Fyn and pro-inflammatory cytokines, TNFα on AMPK regulation. Time course analyses revealed that acute treatment with TNFα (10 ng/mL for 12 h) enhanced AICAR (2 mM, 10 min) dependent phosphorylation of the AMPK α subunit on the activation T172 site. In contrast, prolonged incubation with TNFα (24–36 hr) suppressed AICAR stimulated T172 α subunit phosphorylation. In parallel, TNFα increased Fyn tyrosine kinase activity and siRNA knockdown of Fyn prevented the chronic TNFa inhibition of AICAR-stimulated AMPK T172 α subunit phosphorylation. Taken together, these data suggest that prolonged stimulation of TNFα blunts AICAR dependent AMPK activation through Fyn-dependent tyrosine phosphorylation of AMPK α subunit.

PH-05

High molecular weight adiponectin and lipid profile in the type-2 diabetes mellitus-Mets

Deasy ARDIANY[1]*, Askandar TJOKROPRAWIRO[1], Ari SUTJAHJO[1], Agung PRANOTO[1], Sri MURTIWI[1], Soebagijo ADI[1], Sony WIBISONO[1]. [1]*Surabaya Diabetes and Nutrition Centre - Dr. Soetomo Teaching Hospital Faculty of Medicine Airlangga University, Surabaya, Indonesia*

Background: Dyslipidemia is a major component of the metabolic syndrome (Mets) and a strong risk factor for the development of cardiovascular disease. High Molecular Weight (HMW) Adiponectin is an adipocyte-derived hormone that enhances insulin sensitivity. It plays an important role in glucose and lipid metabolism. Plasma HMW adiponectin level is decreased in patients with type 2 diabetes. The effects of dyslipidemia on plasma HMW adiponectin levels in human subjects have not yet been studied.
Aim: To investigate the correlation between HMW adiponectin level and lipid profile in the type-2 diabetes mellitus (T2DM)-Mets patients.
Method: This is a cross sectional study with T2DM-Mets patients who came to the outpatient clinic of Soetomo Hospital in Surabaya during January 2010 to December 2012. Subjects met the inclusion and exclusion criteria were measured their HMW adiponectin level in plasma using ELISA method. Index lipid profile measured were serum high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), LDL/HDL ratio and TG/HDL ratio. The study was approved by the local Research Ethics Committee and subjects gave written informed consent.
Results: Forty T2DM-Mets patients consisted of 16 (40%) males and 24 (60%) females who met inclusion and exclusion criteria were enrolled in this study. Their mean of age was 51 ± 5.2 years old, duration of illness was 16.49 ± 23.4 months, HMW adiponectin level was 2,195.6 ± 4.6 ng/mL, A1C level was 8.52 ± 0.9%, BMI was 26.62 ± 4.5 kg/m^2, LDL-C level was 148.35 ± 31.1 mg/dL, triglyceride level was 173.00 ± 100.2 mg/dL, HDL-C level was 48.15 ± 8.93 mg/dL, LDL/HDL ratio was 3.15 ± 0.7, and TG/HDL ratio was 3.78 ± 2.4. Spearman's correlation analysis showed that HMW adiponectin level was significantly correlated with triglyceride level and TG/HDL ratio ($p = 0.009$; $r = -0.407$ and $p = 0.014$; $r = -0.387$, respectively). However, no significant correlation found with HDL-C, LDL-C, and LDL/HDL ratio.
Conclusion: Triglyceride cholesterol and TG/HDL ratio are correlated with HMW adiponectin level in this T2DM-MetS population.

PH-06

Fluoxetine treatment impairs E-cadherin-mediated cell adhesion and altered calcium homeostasis in pancreatic beta cells

Huang-Yu CHANG[1], Shu-Ling CHEN[1], Yun-Wen CHEN[1]*. [1]*Department of Pharmacology, College of Medicine, National Cheng Kung University, Taiwan*