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Jonas, Izabella; Nyakas, Csaba; Doornbos, Mark; Vaanholt, Lobke M.; Garland Jr., Theodore; Visser, G. Henk; Dijk, Gertjan van

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T1:PO.110

Prevalence of TCF4 gene microsatellite alleles in obese hypertensive patients

Sarzani Riccardo¹, Pietrucci Francesca¹, Salvi Fabio¹, Caraceni Daniele¹, Lancioni Letizia¹, Cafarelli Fiammetta¹, Lorenzetti Barbara¹, Trotta Fabiana M¹, Dessi-Fulgheri Paolo¹, Rappelli Alessandro¹

¹Ancona University Politecnica Delle Marche, Ancona, Italy

Obesity is increasing worldwide together with its companions hypertension and type 2 diabetes. The obese hypertensive patients are usually at high cardiovascular risk because derangements of glucose and lipids metabolism are also present. A study in 3 different populations suggested a relationship between the TCF4 gene microsatellite DG10S478 allele "X" (with more than 5 TTC repetitions) and type 2 diabetes. This genetic marker may be especially useful to identify patients with susceptibility to diabetes in a population with high cardiovascular risk and increased incidence and prevalence of diabetes. Thus, the objectives of this study were: 1) identify the carriers of TCF4 allele X among obese hypertensives; 2) verify the prevalence of the X allele in comparison to healthy subjects. We studied 131 obese hypertensives without diabetes, and 146 healthy subjects as control population. Genotyping of the microsatellite was performed by PCR and direct sequencing. The allelic frequencies were similar (allele X = 37.4%) to those found in the previous published study on 3 different population. We didn't find a higher allele X frequency in obese hypertensives compared to the control group (39.7% vs. 35.3%, $P=0.323$). Furthermore, there were no allele X-related differences in BMI and waist among groups ($P=0.76$). We conclude that, although TCF4 X allele could be useful to identify obese hypertensives that might develop diabetes, its prevalence is not increased in this population. Thus, accordingly to the previous published work, allele X associates with type 2 diabetes through mechanisms not linked to obesity and related consequences.

T1:PO.112

Emotionality of mice selectively bred for high wheel-running activity

Jonas Izabella¹, Nyakas Csaba^{1,2}, Doornbos Mark¹, Vaanholt Lobke M.¹, Garland Jr. Theodore³, Visser G. Henk¹, van Dijk Gertjan¹

¹University of Groningen, Netherlands; ²Semmelweis University, Budapest, Hungary; ³University of California, Riverside, USA

Our previous research showed that female mice selectively bred for high voluntary wheel running activity are resistant against high fat diet-induced obesity, despite increased high fat intake in these mice relative to female controls. Since high fat feeding relates to brain serotonin levels and mood regulation, we investigated whether selected mice 1) have altered diet selection when given a choice of fat and carbohydrates, 2) have different performances in behavioral tests (i.e., plus maze, open field, complex maze), and 3) have differences in biogenic amine levels in discrete brain regions relative to controls. When given choice, selected mice strongly preferred high carbohydrate diet over the fat diet, irrespective of the regular diet (i.e., chow or high fat food). Secondly, selected animals had a higher level of anxiety, as evidenced by higher closed-arm occupation in the plus maze relative to controls, but selected animals were more explorative in open field and complex maze. Finally, levels of serotonin, but not of the 5HT metabolite 5HIA, were markedly suppressed in prefrontal cortices of selected females and males, an effect that was more pronounced in animals feeding the high fat diet than those feeding chow. The results indicate that low brain serotonin levels in high activity mice may underlie reduced fat selection and their increased state of anxiety. They do not explain, however, the higher level of spontaneous activity and explorative behaviour in these selected mice.

T1:PO.111Effects of PGC-1 α on endothelial function and apoptosis

Park Joong-Yeol¹, Won Jong Chul¹, Lee Ki-Up¹, Lee Woo Je², Ko Kyung Soo², Song Kee-Ho³

¹University of Ulsan College of Medicine, Seoul, Korea; ²Inje University College of Medicine, Seoul, Korea; ³Konkuk University School of Medicine, Seoul, Korea

Aims: Central obesity is associated with increased cardiovascular morbidity and mortality. It has been proposed that increased lipid accumulation in vascular tissue and the consequent increase in oxidative stress may be a missing link between obesity and atherosclerosis. The peroxisome proliferators-activated receptor (PPAR)- γ coactivator 1- α (PGC-1 α) is a transcriptional coactivator playing an important role in energy metabolism. PGC-1 α is present in vascular cells, but its role in vascular endothelial cells has not been established. In this study, we examined the effect of adenoviral overexpression of PGC-1 α (Ad-PGC-1 α) in human aortic endothelial cells (HAECs) on apoptosis induced by linoleic acid (LA).

Methods: Effect of PGC-1 on HAECs apoptosis was evaluated by ELISA, WST-1 assay, and caspase activity. Using Ad-PGC-1 and ANT-1 siRNA, effect of PGC-1 and ANT-1 on reactive oxygen species (ROS) production, fatty acid oxidation (FAO) and mitochondrial membrane potential (mtMP) were analyzed.

Results: PGC-1 α prevented LA-induced endothelial apoptosis. PGC-1 α also reduced LA-induced increases of antioxidant enzyme expression and ROS accumulation at basal state. LA decreased the activity of adenosine nucleotide translocase (ANT), and increased mtMP. In the Ad-PGC-1 α -infected HAECs, activity and the mRNA expression of ANT-1 were increased and LA did not increase mtMP. siRNA against ANT-1 reversed the changes induced by PGC-1 α .

Conclusion: These data suggest that PGC-1 α functions as a physiologic regulator of ROS generation in endothelial cells and that part of this effect is mediated by ANT-dependent increase in FAO.

T1:PO.113Rosiglitazone reduce macrophage and chemokine expression but increase chemokine receptor expression in human adipose tissue *in vivo*

Bruun Jens M.¹, Paulsen S.K.¹, Kim K.W.¹, Christiansen T.¹, Pedersen S.B.¹, Richelsen B.¹

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Visceral obesity is a chronic low-grade inflammatory state associated with insulin resistance, type 2 diabetes, and cardiovascular disease. Human adipose tissue (AT) seems to be involved in the abovementioned deleterious health effects of obesity through the production of inflammatory proteins. Rosiglitazone is a PPAR- α agonist with known anti-diabetic effects and reported anti-inflammatory effects. Aim of the study was to investigate the long-term effects of Rosiglitazone (4mg daily) on AT mRNA levels of macrophage specific markers [CD14, CD68], chemokines, and chemokine receptors in six abdominally obese male subjects (mean age: 50.2 \pm 2.9 yrs, mean BMI: 29.3 \pm 1.0 kg/m², mean waist: 98.7 \pm 1.2 cm). AT-biopsies were obtained from the subcutaneous abdominal AT-depot at baseline, after 3, and 6 months, at which time AT-mRNA levels were quantified using a real time RT-PCR method. Rosiglitazone reduced mRNA levels of CD14 ($P<0.05$), CD68 ($P<0.01$), MCP-1 ($P<0.01$), MIP-1 ($P<0.05$), and IL-8 non-significant ($P=0.06$) but increased mRNA levels of the equivalent chemokine receptors: CCR2 ($P<0.05$), CXCR2 ($P<0.05$), and CXCR1 non-significant ($P=0.07$). In conclusion, Rosiglitazone was for the first time found to exert anti-inflammatory effects in human AT *in vivo*, reducing mRNA levels of macrophage specific markers [CD14, CD68] and various chemokines. In parallel, increasing mRNA levels of the equivalent chemokine receptors were found. This suggests, that a complex interaction may exist between AT-inflammation and the need for chemokines to attract cell-types involved in tissue homeostasis [e.g. macrophages, leucocytes].