Abstracts

T3:P3-025
THE KIR 6.2 GENE E23K SNP IN RELATION TO DM2 IN CZECH POPULATION
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Aims: The Kir 6.2 gene product is a subunit of the inwardly rectifying ATP-sensitive K+ channel, which is involved in the regulation of insulin secretion. Kir 6.2 E23K is considered as a DM2 risk-altering SNP. We decided to determine the allelic and genotypic frequencies in DM2 patients, in offspring of DM2 patients, and in the healthy adult Czech population. The aim was to compare genotypic distribution between these groups and to study the possible association with biochemical and anthropometric parameters related to DM2.

Methods: The study included 293 DM2 patients (age 59±7), 108 offspring (age 38±10), and 177 controls (age 32±11). The E23K substitution was detected by the PCR-RFLP method (BamHl).

Results: The 23K allele frequency did not differ between the diabetic, offspring, and controls (38.2%, 40.3%, 39.5%, respectively). However, genotypic distribution in controls was different in comparison to offsprings (EE/EK/KK): 40.11%/40.68%/19.21% vs. 31.48%/55.48%/12.04%, respectively (χ²=7.04; p=0.03). In the controls, the assessment of beta-cell function using the OGTT-derived indices revealed a higher stimulated glucose levels (G1, p=0.001; G2, p=0.001; G4, p=0.003) and lower insulinogenic index (G1/G2-G3/G4, p=0.012), as well as lower disposition indices in the KK carriers compared to the EE genotype.

Conclusions: The association of the Kir 6.2 E23K with DM2 was not confirmed. Nevertheless, in healthy adults without a family history of DM2, the KK carriers exhibited reduced in the insulinogenic index and in disposition indices.

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T3:P3-026
ROLE OF GENETIC POLYMORPHISMS IN THE RISK OF MICROALBUMINURIA (OLIVETTI HEART STUDY)
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Aims: To analyze the association between microalbuminuria (MA) and single-nucleotide polymorphisms (SNPs) of potentially relevant candidate genes in a population-based investigation.

Methods: Anthropometry, blood pressure (BP), HOMA index, MA (albumin excretion rate>20 μg/min) and common SNPs of ten candidate genes were evaluated in 243 untreated male participants in the 2002-03 follow-up examination of the Olivetti Heart Study.

Results: Age, BMI, BP and HOMA were positively associated with MA (p<0.01). Polymorphism in the GRK4 gene (p=0.01) and PAI-1 (p=0.04) were associated with MA independently of age, BMI, BP and HOMA. OR (95% CI) for MA were 0.194 (0.043-0.872) for subjects homozygous for the rare A142V variant of GRK4 (compared with homoyzogotes for the more common variant) and 0.483 (0.239-0.978) for subjects homozygous for the rare 4G/5G variant of PAI-1 compared with all others. The ANP clearance receptor (NPRC) C1-55A polymorphism (p=0.06) was also marginally associated with MA.

Conclusions: GRK4 and PAI-1 genetic variation is associated with risk of MA in male individuals independently of BMI, BP and insulin resistance.

T3:P3-027
TRANSCRIPTIONAL EFFECTS OF EXOGENOUS LEPTIN ADMINISTRATION IN HUMAN WHITE ADIPOSE TISSUE
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Aims: To know whether leptin has transcriptional action in human white adipose tissue (WAT) and to identify its gene targets.

Methods: 10 obese men (mean BMI=33) have received 60 mg of pegylated recombinant leptin (PEG -leptin). The subcutaneous WAT was taken before and at the highest leptin concentration in the blood (1000X than normal serum leptin concentration), 3 days after the treatment. Pangenomic microarrays were performed from WAT of 7 patients before and after leptin treatment. Significant genes were obtained, thanks to statistical analysis SAM (significance analysis assay), and were annotated with Gene Ontology (GO).

Results: The analysis of results showed that leptin mostly downregulated the gene expression in WAT. Using a false discovery rate of 5%, we obtained 1822 upregulated and 100 downregulated genes under leptin treatment. These genes are implicated in different functional pathways including morphogenesis, signal transduction and inflammation.

Conclusions: Leptin injection in human has a major suppressing effect in WAT gene expression and particularity on gene involved in inflammation process.

T3:P3-028
A QTL ON CHROMOSOME 2P INFLUENCES FAT MASS IN ADULTS FROM THE FELS LONGITUDINAL STUDY
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Introduction: Recent linkage studies have identified or suggested many quantitative trait loci (QTL) influencing various measures of adiposity, but the most frequently studied phenotype has been the body mass index (BMI). Relatively few studies have examined more direct measures of adiposity.

Aims: The goal of this study was to conduct an initial whole-genome scan for QTL influencing hydrostatically determined fat mass in randomly ascertained adults.

Methods: The study sample consisted of a subset of 563 men and women aged 18 to 76 years from 83 kindreds drawn from the Fels Longitudinal Study. The fat mass (FM) of each subject was calculated from their underwater weight at their most recent exam. Of the 563 study subjects, 344 have been genotyped for 377 autosomal markers spaced approximately every 10 cm. A variance components-based linkage analysis method was used to analyze these data and obtain multipoint LOD scores.

Results: The heritability of FM was highly significant at 0.57 ± 0.11. A significant peak LOD score of 3.05 for linkage of FM to a QTL on chromosome 2 at 2 cm (2p25.3) was obtained.

Conclusions: The peak LOD score found in this study for linkage of fat mass to chromosome 2p is very near the ACP1 gene, which has been suggested to influence various measures of adiposity and related Metabolic Syndrome risks. Further work will focus on associations between fat mass and polymorphisms in the ACP1 and other positional candidate genes.

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