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JOINT EVENT ON
13th Euro Obesity and Endocrinology Congress
and
16th World Congress on Nutrition and Food Chemistry
September 18-20, 2017 | Zurich, Switzerland

J Nutr Food Sci 2017, 7:5(Suppl)
DOI: 10.4172/2155-9600-C1-048

Overlapping Genetic Aspects of Type 2 Diabetes Mellitus and Obesity

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Statement of the Problem: Diabetes mellitus is considered a major public health problem worldwide. Susceptibility to diabetes is influenced by both genetic and environmental determinants. Both Type 2 Diabetes (T2D) and obesity are associated frequently and considered as key components of metabolic syndrome. The purpose of this study is to test for 16 independent single nucleotide polymorphisms (SNPs) in established T2D and obesity susceptibility loci by GWAS in a sample of Egyptian patients to find out if there is shared genetic background underlying both disease entities. Genotyping was performed using OpenArray® protocol on the QuantStudio™ 12K Flex Real-Time PCR System. A custom array was designed to facilitate cost-effective analysis of selected SNPs related to glycolysis, gluconeogenesis, inflammation, insulin signalling, and immune function. Findings: Seven gene variants showed significant association with the risk of T2D patients including FCGRA2, STAT4, CELSR2, PPARG, EXT2 rs3740878, GCKR, PTGS1. Factors that significantly affect T2D were obesity ($p<0.001$) and GCKR ($p=0.001$) and PTGS1 ($p=0.001$) gene variants. Gene variants that showed significant or borderline effect on obesity were MTHFD1, EXT2 rs3740878, GCKR and PTGS1 ($p=0.03$, 0.017, 0.059, 0.006) respectively. Conclusion & Significance: Overlapping genetic aspects should be considered and the presence of risk alleles of different genes together could contribute to the risk of T2D or obesity or both. The MTHFD1 and EXT2rs3740878 gene variants significantly affect obesity and not shared with T2D. Gene variants that showed combined effect on both disease entities were GCKR and PTGS1. These findings provide a basis for future studies on a larger scale. More stress on the risk gene variants that have a combined impact on both diabetes and obesity is recommended to improve risk prediction and preventive strategies.

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