Gene-Gene Interaction between \textit{APOA5} and \textit{USF1}: Two Candidate Genes for the Metabolic Syndrome

Objective: The metabolic syndrome, a major cluster of risk factors for cardiovascular diseases, shows increasing prevalence worldwide. Several studies have established associations of both apolipoprotein A5 (\textit{APOA5}) gene variants and upstream stimulatory factor 1 (\textit{USF1}) gene variants with blood lipid levels and metabolic syndrome. \textit{USF1} is a transcription factor for \textit{APOA5}.

Methods: We investigated a possible interaction between these two genes on the risk for the metabolic syndrome, using data from the German population-based KORA survey 4 (1,622 men and women aged 55–74 years). Seven \textit{APOA5} single nucleotide polymorphisms (SNPs) were analyzed in combination with six \textit{USF1} SNPs, applying logistic regression in an additive model adjusting for age and sex and the definition for metabolic syndrome from the National Cholesterol Education Program's Adult Treatment Panel III (NCEP (AIII)) including medication.

Results: The overall prevalence for metabolic syndrome was 41%. Two SNP combinations showed a nominal gene-gene interaction (p values 0.024 and 0.047). The effect of one SNP was modified by the other SNP, with a lower risk for the metabolic syndrome with odds ratios (ORs) between 0.33 (95% CI = 0.13–0.83) and 0.40 (95% CI = 0.15–1.12) when the other SNP was homozygous for the minor allele.
Nevertheless, none of the associations remained significant after correction for multiple testing. Conclusion: Thus, there is an indication of an interaction between APOA5 and USF1 on the risk for metabolic syndrome.

Stichworte:  Metabolic syndrome; Cardiovascular risk; SNP; APOA5; USF1

Zeitschriftentitel:  Obesity Facts

Jahr:  2009

Band:  2

Heft / Issue:  4

Seiten:  4

Volltext / DOI:  http://doi.org/10.1159/000227288

Verlag / Institution:  S. Karger GmbH

Verlagsort:  Freiburg, Germany

Print-ISSN:  1662-4033

E-ISSN:  1662-4033

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- Kollektionen > Open Access Publikationen > Verlage > Karger
- Kollektionen > Open Access Publikationen > 2009

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