Genetic variants in the USF1 gene are associated with low-density lipoprotein cholesterol levels and incident type 2 diabetes mellitus in women: results from the MONICA/KORA Augsburg case-cohort study, 1984-2002.

OBJECTIVE: Upstream transcription factor 1 (USF1) regulates genes of glucose and lipid metabolism. Polymorphisms in the USF1 gene showed association with familial combined hyperlipidemia and lipid parameters. The aim of our study was to examine the associations between USF1 polymorphisms and lipid parameters as well as incident type 2 diabetes mellitus (T2DM) in German Caucasians. DESIGN: We genotyped eight polymorphisms in the USF1 gene in 2067 middle-aged (35-74 years) individuals including 498 incident T2DM cases and 1569 non-cases of the population-based case-cohort study from the MONICA/KORA Augsburg project. METHODS: Six polymorphisms and their haplotypes were analyzed using multivariable linear regression and Cox proportional hazards models. RESULTS: Polymorphism rs3737787 was inversely associated with incident T2DM in women with decreased risk for female heterozygotes compared with women homozygous for the major allele (Hazard ratio=0.57; 95% confidence intervals: 0.38-0.87; P=0.008). After correction for multiple testing, significance remained. Polymorphisms rs3813609 and rs1556259 were significantly associated with reduction in
low-density lipoprotein (LDL) cholesterol (p(NOM)=0.001; p(NOM)=0.00002) in women. Analyses also indicated associations of haplotypes with LDL cholesterol in women, but the association lost statistical significance after correction for multiple testing. Total serum cholesterol (TC) and high-density lipoprotein (HDL) cholesterol were weakly associated (P<0.05) with USF1 polymorphisms in women. No significant associations were found in men. CONCLUSIONS: In this large population-based study, statistically significant associations of USF1 polymorphisms with incident T2DM and LDL cholesterol were found in women, but not in men. Genetic variants in the USF1 gene showed weak or no associations with TC and HDL cholesterol.