SNP43 of CAPN10 and the Risk of Type 2 Diabetes in African-Americans: The Atherosclerosis Risk in Communities Study

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Recently, an A-to-G variant in intron 3 (SNP43) of the calcium-activated neutral protease 10 gene (CAPN10) was identified as a possible type 2 diabetes susceptibility gene through positional cloning Mexican-Americans. We conducted cross-sectional and prospective studies to evaluate the relation between SNP43 and type 2 diabetes and related traits in middle-aged African-American participants of the Atherosclerosis Risk in Communities Study, a population based longitudinal study. At baseline, 269 prevalent diabetes cases and 1,159 nondiabetic control subjects were studied. Those with the G/G genotype were more likely to have diabetes than those with the A/G or A/A genotype (odds ratio [OR] 1.41, 95% CI 1.00-1.99, P = 0.05). In the prospective study, 166 of the control subjects developed incident diabetes for individuals with the G/G genotype did not differ significantly from those with at least one copy of the A allele (23.3 vs. 19.5 per 1,000 person years, P = 0.29). Pooling prevalent and incident diabetic cases together, individuals with the G/G genotype were approximately 40% more likely to have diabetes than those without (OR 1.38, 95% CI 1.04-1.83, P = 0.03). Because of the high frequency of the G allele (0.88), approximately 25% of the susceptibility to type 2 diabetes in African-Americans may be attributed to the G/G genotype at SNP43 of CAPN10, although most of the subjects with the G/G genotype did not develop diabetes over the 9 years of follow-up. We conclude from this large prospective study that the G allele of SNP43 of CAPN10 or another allele or gene that is in linkage disequilibrium with it increases susceptibility to type 2 diabetes in African-Americans.

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