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

Michael J. Garant, W. H. Linda Kao, Frederick Brancati, Josef Coresh, Tejal M. Rami, Craig L. Hanis, Eric Boerwinkle, and Alan R. Shuldiner

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 longitudincal 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 disequalibrium with it increases susceptibility to type 2 diabetes in African-Americans.

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