SNP43 of calcium-activated neutral protease (CAPN10) is associated with Type 2 diabetes in African Americans: the Atherosclerosis Risk in Communities (ARIC) study

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In Mexican Americans, an A/G variant in intron 3 of CAPN10 (SNP43) has been shown to be associated with type 2 diabetes in a recessive mode of inheritance. Therefore, we conducted cross-sectional and prospective studies to evaluate the association between SNP43 and type 2 diabetes in middle-aged African-American participants of the ARIC study, a population-based longitudinal study. Diabetes was defined by self report or by serum glucose levels. At baseline, 269 prevalent cases and 1,159 controls were selected from 3,268 African-American ARIC participants. In the cross-sectional study, the frequency of the G allele was slightly higher in cases than in controls (90.0% vs 87.1% respectively, p = 0.07). However, the prevalence of G/G genotype was significantly higher in cases than in controls (82.5% vs 76.4% respectively, p = 0.03). Assuming a recessive mode of inheritance, those with G/G genotype were more likely to have diabetes than those without (odds ratio = 1.42, 95% confidence interval: 1.00, 2.01). In the prospective study, 166 of the controls developed incident diabetes for individuals with G/G genotype was higher than that for those without (23.3 vs 19.5 per 1,000 person-years respectively, p = 0.29). Pooling all prevalent and incident cases together, individuals with G/G genotype were about 40% more likely to have diabetes compared to those without (odds ratio = 1.38, 95% confidence interval: 1.03, 1.85). All associations between G/G genotype and diabetes were independent of age, sex, and body-mass index. In contrast, neither the G allele nor G/G genotype was associated with glucose and insulin levels, body-mass index, waist-to-hip ratio, or waist circumference in this cohort. These results suggest that either the G allele of SNP43 of CAPN10, or another allele that is in linkage disequilibrium with it, may contribute to the risk of type 2 diabetes in African-Americans in a recessive manner.

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