LETTER

Association between chromosome 2p16.3 variants and glaucoma in populations of African descent

Jiao et al. (1) recently reported significant association of three SNPs on chromosome 2p16.3 (rs12994401, rs10202118, and rs1533428) with an increased risk of primary open-angle glaucoma (POAG) in the Barbados population. In an effort to replicate these findings, we genotyped these three SNPs in our African-American and Ghanaian (West African) datasets. The research was reviewed and approved by the Institutional Review Board of Duke University Medical Center and for Ghanaian subjects, by the Noguchi Memorial Institute of Medical Research of the College of Health Sciences at the University of Ghana.

Table 1. Association results for three SNPs on chromosome 2p16.3 for POAG cases and controls

		African-American samples*				Ghanaian samples†		
SNPs	Allele	MAF (controls)	MAF (cases)	*P* value‡	OR (95% CI)	MAF (controls)	MAF (cases)	*P* value‡
rs12994401	T	0.102	0.057	0.003	0.53 (0.35–0.81)	0.046	0.072	0.216
rs10202118	T	0.509	0.477	0.332	0.90 (0.73–1.11)	0.466	0.399	0.082
rs1533428	T	0.351	0.374	0.358	1.11 (0.89–1.40)	0.426	0.434	0.735

MAF, minor allele frequency; OR, odds ratio; CI, confidence interval.
*African-American dataset includes 382 POAG cases and 275 controls.
†Ghana dataset contains 170 POAG cases and 132 controls.
‡*P* value from log-additive model adjusted for sex.

The African-American dataset included 382 cases and 275 controls, and the Ghanaian dataset contained 170 cases and 132 controls as previously described (2).

Genotyping of blood DNA was performed with TaqMan allelic discrimination assays according to the standard protocols (Applied Biosystems). We required 95% genotyping efficiency and matching genotypes of quality-control samples within and across all plates to include samples in the statistical analysis. Within each population, genotype frequencies of cases and controls were compared by logistic regression with adjustment for gender using SAS software (SAS Institute).

All markers were in Hardy–Weinberg equilibrium ($P > 0.05$) in cases and controls from both populations. Only rs12994401 was significantly associated with an increased risk of POAG in the African-American population ($P = 0.003$) (Table 1). We observed no linkage disequilibrium (LD) between the three SNPs in either population based on r^2 ($r^2 < 0.35$ for all SNP pairs in the respective cases and controls). Although we identified a modest association with POAG risk in the African-American population, risk was conferred by the C allele at rs12994401 rather than the T allele as reported by Jiao et al. (1). T allele frequencies in our African-American controls and the Barbados controls were nearly identical. Thus, this discrepancy may be attributed to population differences in the POAG cases. The Barbados population is believed to be fairly homogenous with only 10% European admixture (3), whereas African Americans have ~21% European admixture (4). Lack of LD between rs12994401 and rs1533428 in our datasets strongly contrasts with a D′ value of 0.72 between these SNPs in the Barbados population. The lack of an observed association in the Ghanaian population may be because of population differences or reduced statistical power, because this smaller dataset had only 42% power (at 5% significance level) to detect an odds ratio of 0.5 for a minor allele frequency of 6%. In summary, we identified a significant association between SNP rs12994401 and POAG in the North Carolina African-American population with a different risk allele than reported for Barbados. As previously discussed (5), this suggests that the as yet unidentified causal variant in this region of chromosome 2 has different levels of LD with the genotyped SNP in these distinct populations of African descent. More studies will be necessary to identify the true causal variant(s) for POAG in this genomic region.

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The authors declare no conflict of interest.

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