Association of Glaucoma Risk Genes with Retinal Nerve Fiber Layer in a Multi-ethnic Asian Population: The Singapore Epidemiology of Eye Diseases Study

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PURPOSE: Genome-wide association studies have identified several genes associated with glaucoma. However, their roles in the pathogenesis of glaucoma remain unclear, particularly their effects on retinal nerve fiber layer (RNFL) thickness. The aim of this study was to investigate the associations between the identified glaucoma risk genes and RNFL thickness.

METHODS: A total of 3843 participants (7,020 healthy eyes) were enrolled from the Singapore Epidemiology of Eye Diseases (SEED) study, a population-based study composing of three major ethnic groups-Malay, Indian, and Chinese-in Singapore. Ocular examinations were performed, and spectral-domain optical coherence tomography (SD-OCT) was used to measure circumpapillary RNFL thickness. We selected 35 independent glaucoma-associated genetic loci for analysis. An linear regression model was conducted to determine the association of these variants with circumpapillary RNFL, assuming an additive genetic model. We conducted association analysis in each of the three ethnic groups, followed by a meta-analysis of them.

RESULTS: The mean age of the included participants was 59.4 ± 8.9 years, and the mean RFNL thickesss is 92.3 ± 11.2 μm. In the meta-analyses, of the 35 glacuoma loci, we found that only SIX6 was significantly associated with reduction in global RNFL thickness (rs33912345; ? = -1.116 um per risk allele, P = 1.64E-05) , and t

CONCLUSIONS: Of the 35 glaucoma identified risk loci, only SIX6 is significantly and independently associated with thinner RNFL. Our study further supports the involvement of SIX6 with RNFL thickness and pathogensis of glaucoma.

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