GWAS identifies two common loci associated with pigment dispersion syndrome/pigmentary glaucoma and implicate myopia in its development

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PURPOSE: To identify genetic variants associated with pigment dispersion syndrome and pigmentary glaucoma in unrelated patients, and to further understand the genetic and potentially causal relationships between pigment dispersion syndrome and associated risk factors.

DESIGN: A two-stage genome-wide association meta-analysis with replication and subsequent in-silico analyses including Mendelian randomisation.

SUBJECTS: A total of 574 cases with pigmentary glaucoma and/or pigment dispersion syndrome and 52,627 controls of European descent.

METHODS: Genome-wide association analyses were performed in four cohorts and meta-analysed in three stages: first a discovery meta-analysis of three cohorts, secondly replication was performed in the fourth cohort, thirdly all four cohorts were meta-analysed to increase statistical power. Two-sample Mendelian randomisation was utilised to determine whether refractive error and intraocular pressure exert causal effects over pigment dispersion syndrome.

RESULTS: Significant association was present at two novel loci for pigment dispersion syndrome/pigmentary glaucoma. These loci and follow up analyses implicate the genes GSAP (lead SNP: rs9641220, p=6.0x10-10) and GRM5/TYR (lead SNP: rs661177, p=3.9x10-9) as important factors in disease risk. Mendelian randomisation showed significant evidence that negative refractive error (myopia) exerts a direct causal

effect over pigment dispersion syndrome (p=8.9x10-7) .

MAIN OUTCOME MEASURES: A) The association of genetic variants with pigment dispersion syndrome and, B) whether myopia exerts causal effects over pigment dispersion syndrome.

CONCLUSIONS: Common SNPs relating to the GSAP and GRM5/TYR genes are associated risk factors for the development of pigment dispersion syndrome and pigmentary glaucoma. Although myopia is a known risk factor, this study is the first to use genetic data to demonstrate that myopia is, in part, a cause of pigment dispersion syndrome and pigmentary glaucoma.

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