# New insights into the genetics of primary open-angle glaucoma based on meta-analyses of intraocular pressure and optic disc characteristics

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Primary open-angle glaucoma (POAG) , the most common optic neuropathy, is a heritable disease. Siblings of POAG cases have a ten-fold increase risk of developing the disease. Intraocular pressure (IOP) and optic nerve head characteristics are used clinically to predict POAG risk. We conducted a genome-wide association meta-analysis of IOP and optic disc parameters and validated our findings in multiple sets of

POAG cases and controls. Using imputation to the 1000 genomes (1000G) reference set, we identified 9 new genomic regions associated with vertical cup disc ratio (VCDR) and 1 new region associated with IOP. Additionally, we found 5 novel loci for optic nerve cup area and 6 for disc area. Previously it was assumed that genetic variation influenced POAG either through IOP or via changes to the optic nerve head; here we present evidence that some genomic regions affect both IOP and the disc parameters. We characterized the effect of the novel loci through pathway analysis and found that pathways involved are not entirely distinct as assumed so far. Further, we identified a novel association between CDKN1A and POAG. Using a zebrafish model we show that six6b (associated with POAG and optic nerve head variation) alters the expression of cdkn1a In summary, we have identified several novel genes influencing the major clinical risk predictors of POAG and showed that genetic variation in CDKN1A is important in POAG risk.



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