DNA analysis reveals genetic variants that make individuals susceptible to form of glaucoma prevalent in Asian countries

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Glaucoma is the leading cause of irreversible blindness in the world. A form known as primary open angle glaucoma (POAG) predominantly

affects Europeans and Africans, whereas primary closed angle glaucoma (PACG) mostly affects Asians. Despite the high levels of blindness caused by PACG in Asian countries, scientists lacked the information that could confirm the disease's genetic basis and provide a starting point to tackle the problem.

An international research team, including Chiea-Chuen Khor at the A*STAR Genome Institute of Singapore and Eranga Vithana and Tin Aung from the Singapore Eye Research Institute, has now identified three genetic variants that make individuals susceptible to PACG.

Glaucoma results from damage to the optic nerve that is caused by reduced drainage of fluid in the eye. In POAG, fluid flows correctly in the eye, but cannot drain because there is damage to the trabecular meshwork—the structure that is responsible for the drainage. In PACG, the gap through which fluid flows from the back to the front of the eye is closed, preventing it from reaching the trabecular meshwork (see image).

Khor and co-workers enrolled patients with PACG from multiple countries, including Singapore, Hong Kong, China, India, Malaysia, Vietnam, Saudi Arabia and the UK. The researchers compared these patients' DNA sequences with those of healthy controls to identify specific genetic characteristics that were consistently over-represented in the patients. They performed the process in two stages; to test the results from the first stage, they repeated the analysis with a second, independent set of patients.

In total, Khor and co-workers compared 3,771 patients with 18,551 controls. The analysis revealed three genetic variants strongly associated with PACG, implicating three genes in the disease: PLEKHA7, COL11A1 and PCMTD1.

"This is the first time that heritable determinants underlying PACG have been robustly discovered," says Khor. "Many clinicians suspected a genetic cause, but were unable to prove it. We have definitively identified three genes that are important." Khor also points out that it makes sense for these genes to be involved: "The genes identified, in particular PLEKHA7 and COL11A1, are strongly expressed in eye tissue at the suspected site of pathology."

Identification of genetic variants that make patients susceptible to PACG provides researchers with a foundation upon which to develop ways of tackling the disease. For example, susceptibility to PACG could be assessed by genetic analysis, providing a predictive test, and this work could lead to the identification of drug targets.

More information: Vithana, E. N., Khor, C.-C., Qiao, C., Nongpuir, M. E., George, R. et al. Genome-wide association analyses identify three new susceptibility loci for primary angle closure glaucoma. *Nature Genetics* 44, 1142–1146 (2012). www.nature.com/ng/journal/v44/ … 10/full/ng.2390.html

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