World-first glaucoma gene discovery

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(Medical Xpress) -- An Australian research team led by Flinders University researchers has discovered two new genes that could open the way to new treatments for blinding glaucoma.

Their findings are published online this week in the prestigious international science journal, Nature Genetics.

The study established that 18 per cent of the population carry risk variants at these two genes, making them up to three times more likely to develop severe glaucoma than those that don't.

Other unknown factors also influence the overall risk for an individual.

The team, headed by Associate Professor Jamie Craig and Research Fellow Dr Kathryn Burdon (pictured) from the Department of Ophthalmology at Flinders University, involved groups from five other Australian universities on the ground-breaking survey of 4500 patients from every state in Australia and New Zealand.

"Although open angle glaucoma is the most common form of the disease, it is poorly understood and difficult to diagnose in its early stages," Associate Professor Craig said.

"Many cases still remain undiagnosed until irreversible loss of vision has occurred," he said.

"Our discovery will help replace routine monitoring and hit-and-miss treatment for glaucoma, by identifying patients at the highest risk of going blind. It opens the pathway to developing completely new ways of treating patients that could delay disease progression and prevent blindness."

Glaucoma is the collective name for eye diseases causing irreversible loss of peripheral vision, often associated with too much pressure developing inside the eyeball. It is the leading cause of irreversible blindness worldwide, affecting an estimated 300,000 people in Australia, of which half are currently undiagnosed.

"This study is the culmination of five years' work. Before anyone else in the world, our South Australian team achieved these outstanding results," Associate Professor Craig said.

Dr Burdon said that as part of its ongoing research, the team will examine how these genes relate to other biological measures that are relevant to glaucoma.

"By combining genetics with a better understanding of factors such as the pressure in the eye and how the optic nerve looks, we may be able to develop earlier diagnostics for glaucoma," Dr Burdon said.

More information: Genome-wide association study identifies susceptibility loci for open angle glaucoma at TMCO1 and CDKN2B-AS1, *Nature Genetics* (2011) doi:10.1038/ng.824

Abstract

We report a genome-wide association study for open-angle glaucoma (OAG) blindness using a discovery cohort of 590 individuals with severe visual field loss (cases) and 3,956 controls. We identified associated loci at TMCO1 (rs4656461[G] odds ratio (OR) = 1.68, P = 6.1 × 10?10) and CDKN2B-AS1 (rs4977756[A] OR = 1.50, P = 4.7 × 10?9). We replicated these associations in an independent cohort of cases with advanced OAG (rs4656461 P = 0.010; rs4977756 P = 0.042) and two additional cohorts of less severe OAG (rs4656461 combined discovery and replication P = 6.00 × 10?14, OR = 1.51, 95% CI 1.35 - 1.68; rs4977756 combined P = 1.35 × 10?14, OR = 1.39, 95% CI 1.28 - 1.51). We show retinal expression of genes at both loci in human ocular tissues. We also show that CDKN2A and CDKN2B are upregulated in the retina of a rat model of glaucoma.

Provided by Flinders University