BioSpectrum the business of Bio & Health Sciences ASIA EDITION

Gene mutation discovered that can prevent Glaucoma

07 July 2017 | News

Singapore-led discovery of rare gene mutation and identification of five new susceptibility loci will help illuminate the disease biology.

Singapore - In the largest study on any cause of glaucoma to date, an international research collaboration on Exfoliation Syndrome – a major form of glaucoma – has found a mutated gene that can prevent glaucoma, the leading cause of irreversible blindness worldwide.

Jointly led by A*STAR's Genome Institute of Singapore (GIS) and the Singapore Eye Research Institute (SERI) of the Singapore National Eye Centre (SNEC), the study involved more than 120,000 individuals from 36 countries across six continents. The study has recently been published in Nature Genetics.

Exfoliation Syndrome (XFS) is an age-related eye disease where abnormal whitish flakes are deposited in the front of the eye (iris, ciliary body, lens and zonules), and abnormalities in connective tissues may appear in parts of the body. The disease occurs globally in approximately 60 to 70 million people. In the eye, the disease often leads to an increase in eye pressure, or glaucoma, which can result in visual impairment and blindness.

Since the 2007 publication of an Icelandic study and subsequent validation attempts by research groups from around the world, it is known that common genetic variants in one gene, the *LOXL1* gene, show a strong association with XFS. However, the association with common genetic markers at *LOXL1* are reversed depending on ethnic group, thus rendering the health implications unclear. In this latest study, the researchers uncovered a rare protective mutation in the *LOXL1* gene. The mutation, p. Y407F, was found to offer protection against XFS instead, thereby leading to the prevention of secondary glaucoma. The mutation offers a 25-fold protection against XFS, the largest ever seen for a common, complex disease.

"Naturally occurring genetic variants are hard to find, but once discovered, they pinpoint potential druggable targets. These are what we call 'accidents and experiments of nature'. The *LOXL1* p. Y407F rare variant reported in this study is one of these examples," explained Dr Khor Chiea Chuen, one of the study's corresponding authors and Principal Investigator of Human Genetics at the GIS. In addition, the researchers also discovered five new susceptibility gene loci in XFS – specifically POMP, TMEM136, AGPAT1, RBMS3 and SEMA6A. This will help deepen the researchers' understanding of XFS and how the disease process works.

Prof Aung Tin, Executive Director of SERI and Deputy Medical Director of SNEC, and lead author of the paper said, “This was the largest ever genetic study for glaucoma, and with so many centres and patients from 36 countries involved, it was very challenging to coordinate the research with most of the work being done in Singapore. The findings are very exciting as it can lead to the development of new therapies for glaucoma.”