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Singapore scientists discover genes responsible for cornea blindness

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Scientists at Singapore Eye Research Institute and A*STAR's Genome Institute of Singapore have succeeded in identifying genes for central corneal thickness that may cause potentially blinding eye conditions. These eye conditions include glaucoma, as well as the progressive thinning of the cornea, which may eventually lead to a need for corneal transplantation.

The authors jointly led a multi-centre study involving 55 hospitals and research centres around the world. They performed a meta-analysis on more than 20,000 individuals in European and Asian populations. Their findings were published in the prestigious science journal, *Nature Genetics* (January 6, 2013).

Central corneal thickness (CCT) is associated with potentially blinding eye conditions such as keratoconus, a condition where the cornea progressively thins and takes on a more conical shape that may eventually require transplantation. CCT has an estimated heritability up to 95% and may determine the severity of one's glaucoma and assist eye doctors in identifying patients with high risk for progression. In fact, it is one of the leading causes of corneal transplantation worldwide.

The Singapore team has had remarkable success identifying the most CCT-associated loci to date prior to this collaborative world-wide effort, by identifying 6 distinct genetic loci in two papers published in 2011 and 2012 via sample collections involving Singaporean Chinese, Indians, and Malays, as well as Beijing Chinese. However, none was found to be

associated with common eye diseases like this study has now shown. Overall this new study identified a total of 27 associated loci, including 6 for the keratoconus.

These observations suggest that most of the CCT-associated loci identified from populations of European descent are shared with Asian populations. These findings show that Singapore is well placed globally in eye and genetics research in finding causes for sight threatening conditions. Eye doctors can in the future through genetic analysis better manage such patients, preventing regression of their conditions.

Prof Aung Tin, Deputy Director, Singapore Eye Research Institute (SERI) and a senior consultant ophthalmologist and Head of Glaucoma Service at Singapore National Eye Centre and a co-author of the paper, said, "This was a tremendous achievement, involving many centres from several countries around the world. Singapore played a major role in this work, especially SERI's population based studies of 10,000 Chinese, Malay and Indian people."

Assoc Prof Eranga Vithana, Associate Director, Basic and Experimental Sciences, SERI and a co-author of the paper, said, "This paper identified 6 novel genetic variants that confer increased risk of keratoconus, a condition for which genes were not very forthcoming prior to this study. It once again underlined the inevitability of large scale collaborative studies to unravel genes for common complex diseases and also the advantage of having well characterized large cohorts."

Assistant Professor Khor Chiea Chuen, Principal Investigator, Division of Human Genetics, Genome Institute of Singapore-an institute of the Agency for Science, Technology and Research (A*STAR) and the paper's co-lead author, said, "Yet again, this paper underscores the power of modern genetic approaches studied in very large sample sizes in revealing the hereditable basis of normal human traits, and how the

extremes of which may give rise to common diseases."

Prof Ng Huck Hui, Executive Director of the Genome Institute of Singapore said, "I am very pleased that the Genome Institute of Singapore is a part of an international effort to dissect the genetics of eye conditions such as keratoconus and glaucoma. Genomics remains a very powerful tool to identify the link between genetic variations and phenotypes. This study that focuses on central corneal thickness illustrates the value of large scale genetics studies in identifying potential pathways that underlie specific human phenotypes."

Prof Wong Tien Yin, Executive Director of SERI and Chair, Dept of Ophthalmology, National University Health System (NUHS) and the paper's senior corresponding author said, "The investment of SERI in population-based studies over the past decade is now paying off with major discoveries in the causes of common eye diseases. This is a team effort and included more than 50 over clinicians, clinician-scientists, research scientists, research staff, statisticians and most importantly, our patients, who have contributed to the collection of these samples."

Adjunct Assoc Prof Jodhbir S Mehta, Head and Senior Consultant, Cornea Service at Singapore National Eye Centre said, "This is a great achievement in collaborative research and offers new insights into keratoconus."

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