



MEDIA RELEASE FOR IMMEDIATE RELEASE

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DISCOVERED GENES REVEAL NOVEL INSIGHTS INTO BIOLOGY OF GLAUCOMA

Findings provide deeper understanding of the disease which affects mainly ageing Asians, and open up new possibilities for the delivery of precision medicine

SINGAPORE – An international research collaboration has revealed eight genes strongly associated with primary angle-closure glaucoma (PACG), the most prevalent form of glaucoma in Singapore, and Asia. These eight genes¹ provide unexpected insights into the disease process of glaucoma, and how the shape of the eye could contribute to the disease even in currently healthy, asymptomatic people. The collaboration was jointly led by Dr Khor Chiea Chuen from A*STAR's Genome Institute of Singapore (GIS) and Prof Aung Tin from Singapore Eye Research Institute (SERI), Singapore National Eye Centre (SNEC) and National University of Singapore (NUS).

The study involved more than 10,000 patients from 24 countries and the findings were reported in the prestigious scientific journal *Nature Genetics*. This paves the way to identify potential new drug targets to treat glaucoma, and build up genetic predictors that could help to screen and to direct treatment for individuals at risk of becoming blind from glaucoma.

Although it is preventable, glaucoma is the most common cause of irreversible blindness worldwide. PACG is responsible for a high proportion of blindness in Asia; with up to 80 percent of the estimated 15 million people afflicted with PACG living in Asia².

¹ Five of these eight genes are newly discovered by the GIS-SERI team, with the other three previously reported by the same group in 2012

² Quigley, H.A. & Broman, A.T. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol* 90, 262-7 (2006)

Epidemiological risk factors of PACG include advancing age, the female gender, as well as being of East Asian ethnicity. There are also ocular risk factors such as hyperopia and smaller anatomical dimensions of the eye. Having seen glaucoma patients at the SNEC and SERI for more than 20 years, Prof Aung noticed that PACG is fairly common in elderly Singaporean Chinese, and that the disease appears to run in families, thus raising the possibility that there could also be a hereditary basis for PACG.

For much of the past decade, the search for susceptibility genes for PACG has not been fruitful mainly because earlier genomic technology and methods did not allow deep and broad searches across the entire genome to occur concurrently. Recent advances in genomic technology have made possible an unprecedentedly broad and unbiased search for genes associated with disease in the human genome, sparking GIS and SERI/SNEC to collaborate again in the search for human genetic variants which could cause PACG. Other collaborating centres in Singapore include National University Health System, Tan Tock Seng Hospital and Changi General Hospital.

Prof Aung, Executive Director of SERI and the consortium leader who initiated the project, said, "It was very exciting but also challenging to coordinate this project from Singapore as it involved so many samples from more than 100 centres in 24 countries around the world. We hope our findings will be a major contribution to the understanding of PACG, which is a particularly important cause of glaucoma and visual loss/blindness in Singapore and Asia. This research is a great example of successful international multi-centre collaborative research; we are grateful to all our study participants and collaborators, as well as funding bodies in Singapore such as National Research Foundation and National Medical Research Council, who funded this work."

Dr Khor, co-lead author of the study and Principal Investigator of Human Genetics at the GIS, said, "Research on complex genetic diseases such as PACG needs to be undertaken in large enough numbers so that as many people as possible are represented. The findings we present here are averaged across more than 10,000 patients from 24 countries."

"This very large multi-ethnic study of angle-closure glaucoma has identified five new genes contributing to this important cause of blindness. This unprecedented analysis provides a comprehensive genetic profile of angle-closure glaucoma, and these findings will suggest important areas of research that may lead to new strategies to screen, prevent and treat this devastating disease," added Prof Janey L. Wiggs, who holds the post of Paul Austin Chandler Professor of Ophthalmology at the Harvard Medical School. Prof Wiggs is also the Massachusetts Eye and Ear Infirmary's Associate Chief of Ophthalmology Clinical Research, and Associate Director of Howe Laboratory.

GIS Executive Director Prof Ng Huck Hui said, “As Singapore faces the challenge of a rapidly ageing population, the need to research the genetics of age-related diseases, like glaucoma, also increases. Considering how prevalent PACG is in Asian populations, this discovery is significant as researchers continue to work towards precision medicine. It allows for better clinical decision-making which ultimately leads to improved healthcare outcomes for the public. This collaboration also reaffirms the importance of cross-institutional efforts; bringing our capabilities together results in high-impact research.”

IMAGE



The study leaders: Prof Aung Tin (left) of Singapore Eye Research Institute and Dr Khor Chiea Chuen (right) of the Genome Institute of Singapore

Notes to Editor:

The research findings described in this media release can be found in the scientific journal *Nature Genetics*, under the title, “Genome-wide association study identifies five new susceptibility loci for primary angle closure glaucoma” by Chiea Chuen Khor^{1,2,3,124}, Tan Do^{4,124}, Hongyan Jia^{5,124}, Masakazu Nakano^{6,124}, Ronnie George^{7,124}, Khaled Abu-Amero^{8,9,124}, Roopam Duvessh^{10,124}, Li Jia Chen^{11,124}, Zheng Li¹, Monisha E Nongpiur², Shamira A Perera², Chunyan Qiao⁵, Hon-Tym Wong¹², Hiroshi Sakai¹³, Mônica Barbosa de Melo¹⁴, Mei-Chin Lee², Anita S Chan², Yaakub Azhany¹⁵, Thi Lam Huong Dao⁴, Yoko Ikeda¹⁶, Rodolfo A Perez-Grossmann¹⁷, Tomasz Zarnowski¹⁸, Alexander C Day^{19,20,21}, Jost B Jonas²², Pancy O.S. Tam¹¹, Tuan Anh Tran²³, Humaira Ayub²⁴, Farah Akhtar²⁵, Shazia Micheal²⁶, Paul T K Chew²⁷, Leyla A Aljasim²⁸, Tanuj Dada²⁹, Tam Thi Luu³⁰, Mona S Awadalla³¹, Naris Kitnarong³², Boonsong Wanichwecharugruang^{33,34}, Yee Yee Aung³⁵, Jelinar Mohamed-Noor³⁶, Saravanan Vijayan¹⁰, Sripriya Sarangapani³⁷, Rahat Husain^{2,38}, Aliza Jap^{2,38}, Mani Baskaran², David Goh², Daniel H Su², Huaizhou Wang⁵, Vernon K Yong¹², Leonard W Yip¹², Tuyet Bach Trinh²³, Manchima Makornwattana³⁹, Thanh Thu Nguyen⁴⁰, Edgar U. Leuenberger^{41,42}, Ki-Ho Park⁴³, Widya Artini Wiyogo^{44,45}, Rajesh S Kumar⁴⁶, Celso Tello⁴⁷, Yasuo

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The *Nature Genetics* paper can be accessed online from:
<http://www.nature.com/ng/journal/vaop/ncurrent/full/ng.3540.html>

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About A*STAR's Genome Institute of Singapore (GIS)

The Genome Institute of Singapore (GIS) is an institute of the Agency for Science, Technology and Research (A*STAR). It has a global vision that seeks to use genomic sciences to achieve extraordinary improvements in human health and public prosperity. Established in 2000 as a centre for genomic discovery, the GIS will pursue the integration of technology, genetics and biology towards academic, economic and societal impact.

The key research areas at the GIS include Human Genetics, Infectious Diseases, Cancer Therapeutics and Stratified Oncology, Stem Cell and Regenerative Biology, Cancer Stem Cell Biology, Computational and Systems Biology, and Translational Research.

The genomics infrastructure at the GIS is utilised to train new scientific talent, to function as a bridge for academic and industrial research, and to explore scientific questions of high impact.

For more information about GIS, please visit www.gis.a-star.edu.sg

About Singapore Eye Research Institute (SERI)

Established in 1997, the Singapore Eye Research Institute (SERI) is Singapore's national research institute for ophthalmic and vision research. It is the research arm of Singapore National Eye Centre, and affiliated to the National University of Singapore (NUS) and the Duke-NUS Medical School.

In two decades, SERI has grown from a team of 5 to over 220 staff, and more than 100 distinguished adjunct faculty members to become the largest eye research institute in the Asia-Pacific region. Collectively, our clinician-scientists and researchers have published more than 2,000 peer-reviewed papers supported by over S\$200 million in competitive research grants. SERI has trained more than 150 current and past graduate students; and has been conferred over 350 national & international awards and 105 patents.

Today, SERI is recognized as a pioneering center for high quality eye research in Asia, with breakthrough discoveries that has translated to significant paradigm shift in eye care delivery.

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