MEDIA RELEASE
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DISCOVERED GENE ALLOWS A PEEK INTO THE FUTURE ON EYE DISEASE

Study opens new possibilities for scientists to create genetic tests and future treatments for Exfoliation Syndrome

Singapore — An international research collaboration led by Singaporean researchers have led to the discovery of a mutated gene that renders people highly susceptible to a severe eye disorder called Exfoliation Syndrome (XFS). The study involved 8,400 patients from 17 countries and was reported in the prestigious scientific journal, *Nature Genetics*.

The scientists found that Singaporean Chinese with the mutation are 40 to 56 percent more likely to develop XFS some time in their lives compared to Singaporean Chinese without the mutation. They also noted that Singaporean Indians with the mutation are between 19 to 25 percent more likely to develop XFS some time in their lives compared against Singaporean Indians without the mutation. This figure is in stark contrast to the global average of 16 to 25 per cent of similar individuals likely to develop XFS. The study is led by researchers from A*STAR's Genome Institute of Singapore (GIS) and the Singapore Eye Research Institute (SERI).

XFS usually develops in people above the age of 60 years old and is characterised by the body's inability to remove abnormal protein deposits from inside the eye. The accumulation of these protein deposits clogs the eye's drainage mechanism that results in a build-up of fluid and pressure in the eye in a condition called Glaucoma. If left untreated, a person with glaucoma can become permanently blind.

The gene believed to be responsible for XFS is called CACNA1A. The scientists found that CACNA1A affects the body's calcium transport channels, which are important for many vital biological functions. Those who carry the CACNA1A gene have faulty calcium transport channels that hinder normal bodily functions, such as the eye's ability to efficiently remove abnormal protein deposits.

A*STAR's Dr Khor Chiea Chuen from GIS said, "Glaucoma is one of the most common eye diseases in Singapore and around the world. With this knowledge, we can now concentrate our efforts to develop therapeutic solutions to address and normalise the calcium signalling function in order to reduce the risk of XFS and the development of glaucoma."

SERI Executive Director and Senior Consultant and Head of Glaucoma Service, Singapore National Eye Centre, Prof Aung Tin said, "This is an exciting discovery as the pathway we have found could be a target for new therapies and medications to prevent or treat this type of glaucoma."

“On a personal level,” added Prof Aung, “the project was extremely stimulating and interesting as we were working with more than 90 collaborating sites from 17 different countries in Asia, Europe, Australia, Africa, North America and South America. It was a huge honour for us in Singapore to be coordinating and leading this global study of such scale and impact.”

Prof Robert Ritch, Shelley and Steven Einhorn Distinguished Chair, Professor of Ophthalmology and Surgeon Director and Chief (Glaucoma Services) at The New York Eye and Ear Infirmary said, “This new gene may not only explain some of the manifestations of Exfoliation Syndrome, but may also help us explain why associated systemic diseases occur in conjunction with it. This discovery opens doors to further elucidation, understanding, and perhaps new treatments for Exfoliation Syndrome.” Prof Ritch is also the founder, medical director and chairman of the Scientific Advisory Board at The Glaucoma Foundation.

“This is a very important study showing association of a novel DNA variant with disease risk in populations throughout the world,” added Janey L. Wiggs, who holds the post as the Paul Austin Chandler Associate Professor of Ophthalmology at the Harvard Medical School. Prof Wiggs jointly supervised the project.

“Exfoliation Syndrome is a debilitating disorder affecting many people in the world. The study is highly relevant to local as well as some foreign populations. The next step after this study is to capture the value from this new knowledge and turn it into health outcomes, such as to develop a genetic test to screen for XFS and new treatments for individuals carrying the CACNA1A gene,” said Prof Ng Huck Hui, Executive Director, GIS.

Notes to Editor:

The research findings described in the media release can be found in the *Nature Genetics* journal, under the title, “A common variant mapping to *CACNA1A* is associated with susceptibility to Exfoliation syndrome” by Tin Aung*1,2,3, Mineo Ozaki*4,34, Takanori Mizoguchi*5, R Rand Allingham6*, Zheng Li7, Aravind Haripriya8, Satoko Nakano9, Steffen Uebe10, Jeffrey M. Harder11, Anita S.Y. Chan1,2, Mei Chin Lee1, Kathryn P. Burdon12,13, Yury S. Astakhov14, Khaled K. Abu-Amero15,16, Juan C. Zenteno17,18, Yildirim Nilgün19, Tomasz Zarnowski20, Mohammad Pakravan21, Leen Abu Safieh22, Liyun Jia23, Ya Xing Wang24, Susan Williams25, Daniela Paoli26, Patricio G Schlottmann27, Lulin Huang28,29,30, Kar Seng Sim7, Jia Nee Foo7, Masakazu Nakano31, Yoko Ikeda32, Rajesh S Kumar33, Morio Ueno32, Shin-ichi Manabe34, Ken Hayashi34, Shigeyasu Kazama35, Ryuichi Ideta36, Yosai Mori37, Kazunori Miyata37,38, Kazuhisa Sugiyama39, Tomomi Higashide39, Etsuo Chihara40, Kenji Inoue41, Satoshi Ishiko42, Akitoshi Yoshida43, Masahide Yanagi44, Yoshiaki Kiuchi44, Makoto Aihara45, Tsutomu Ohashi46, Toshiya Sakurai47, Takako Sugimoto38, Hideki Chuman38, Fumihiko Matsuda48, Kenji Yamashiro49, Norimoto Gotoh49, Masahiro Miyake48,49, Sergei Y. Astakhov14, Essam A. Osman15, Saleh A. Al-Obeidan15, Ohoud Owaidhah21, Leyla Al-Jasim21, Sami Al Shahwan21, Rhys A. Fogarty12, Paul Leo50, Yaz Yetkin19, Çilingir Oğuz19, Mozhgan Rezaei Kanavi21, Afsaneh Naderi Beni21, Shahin Yazdani21, Evgeny L. Akopov14, Kai-Yee Toh7, Gareth R

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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.

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About the Singapore Eye Research Institute

Established in 1997, SERI is Singapore's national research institute for ophthalmic and vision research. SERI's mission is to conduct high impact eye research with the aim to prevent blindness, low vision and major eye diseases common to Singaporeans and Asians. Serving as the research institute of the Singapore National Eye Centre, and directly affiliated to the Yong Loo Lin School of Medicine, National University of Singapore, as well the Duke-NUS Graduate Medical School, SERI undertakes vision research in collaboration with local clinical ophthalmic centres and biomedical research institutions, as well as major eye centres and research institutes throughout the world.

SERI has grown from a founding team of five in 1997 to a faculty of 220, encompassing clinician scientists, scientists, research fellows, PhD students and support staff. This makes SERI one of the largest research institutes in Singapore and the largest eye research institute in Asia-Pacific. The institute has amassed an impressive array of publications totalling 2,100 scientific papers as of November 2014, and has secured 212 external peer-reviewed competitive grants worth $197 million. As of November 2014, SERI's faculty has been awarded over 300 national and international prizes and filed over 90 patents.

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