

MEDIA RELEASE
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**RESEARCHERS FIND LINK BETWEEN EYE DISEASE AND
DEGENERATION OF THE BRAIN**

A scientific study of African populations discovers that the beta-amyloid gene is associated with an increased risk of the most common form of glaucoma

SINGAPORE – A global research team led by scientists from Singapore and the United States has discovered new evidence that there is an underlying link between degeneration of the eye and brain. They found that genetic variation at a beta-amyloid gene was significantly associated with increased risk of Primary Open Angle Glaucoma (POAG), the most common form of glaucoma and the leading cause of irreversible blindness worldwide. The association was identified specifically in people with African ancestry. The high-risk variant was common in African populations (around 20%), but essentially absent in all other ancestral groups.

The findings from this research confirmed a common suspicion that glaucoma may not simply be an eye disease, but also linked to degeneration of the brain. Two lines of evidence were established – First, genetic variation at a beta-amyloid gene family was observed to be significantly associated with POAG risk. Second, beta-amyloid deposits were also significantly increased in eye and brain tissues of patients with POAG compared to unaffected individuals. This links degeneration of the eye to possible degeneration of the brain as beta-amyloid is one of the best-known causes for nerve cell death in Alzheimer's disease and dementia.

The global research team consisted of scientists and clinicians from the Agency for Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS), Singapore Eye Research Institute (SERI), Singapore National Eye Centre (SNEC), Duke University, Duke-NUS Medical School, partner institutions (including the University of California San Diego, UCSD, and the University of California San Francisco, UCSF), as well as leading eye centres around the world. The study was published in the Journal of the American Medical Association (JAMA) on 6 November 2019.

Another recently conducted study on a large multi-ethnic sample, the Genetic Epidemiology Research On Adult Health & Aging (GERA) cohort in the USA, confirmed the highest prevalence of POAG in African ancestry individuals (16.1%) compared to East Asians (9.9%) and Europeans (7.4%)¹.

¹ Choquet H, Paylakhi S, Kneeland SC, et al. A multiethnic genome-wide association study of primary open-angle glaucoma identifies novel risk loci. Nature communications. 2018;9(1):2278.

However, African populations have been understudied and under-represented in genomic research. This is despite our understanding that modern humans originated in Africa approximately 200,000 years ago, and 99% of the human evolutionary experience has been in Africa². African populations hold a treasure trove of unexplored genomic information which could provide solutions to combat various diseases, including glaucoma. Hence, the team studied POAG in Africans and African-descent populations to obtain biological and clinical insights, which may have been unavailable in European and Asian studies.

The JAMA study on African populations presented new findings which are expected to change the way researchers perceive glaucoma. Scientists have also begun to look for neuroprotective mechanisms, which could illuminate new ways to treat the disease.

Dr Michael A Hauser, Professor of Medicine and Ophthalmology at the Duke University Medical Center, said, “Glaucoma in Africans is severe, striking early and often leading to blindness. Our data shows that glaucoma in Africa has a different genetic structure than glaucoma in Europe or Asia. We hope that our work to better understand African glaucoma will help preserve sight in people of African ancestry around the world.”

Dr Khor Chiea Chuen, Group Leader at GIS, said, “Family members of patients with glaucoma have a genetically higher chance of contracting glaucoma. The earlier the age of onset and the more severe the disease, then the higher the likelihood that the patient and family members are genetically predisposed and should therefore explore potential interventions.”

Professor Aung Tin, Executive Director of SERI and Professor at Yong Loo Lin School of Medicine, National University of Singapore, said, “This was a huge multi-national effort with much of the research conducted in Singapore. The findings are very interesting as it shows the diverse genetic make-up of glaucoma in different populations from around the world. We need to better understand the role of this gene in the glaucoma disease process, so that we can develop new therapies in the future.”

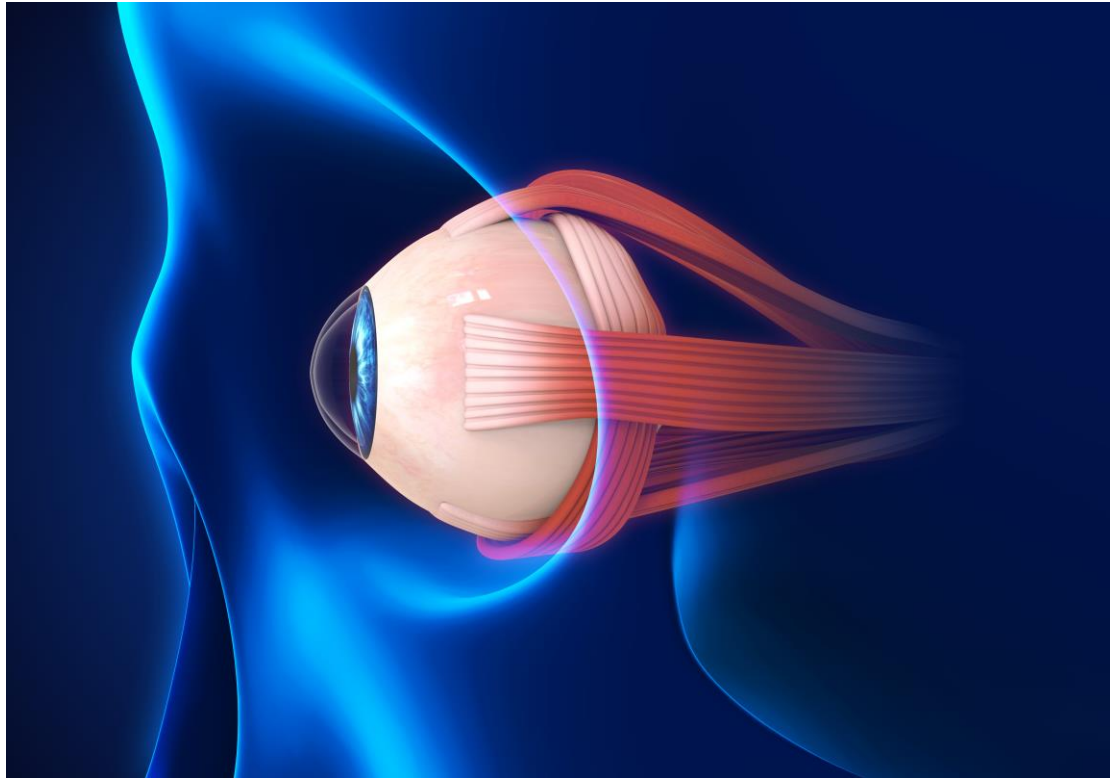
Professor Neil Risch, Director, Center for Human Genetics, UCSF and Lamond Family Foundation Distinguished Professor in Human Genetics, said, “This important finding for POAG research was only possible because of the collegiality and collaboration of nearly all major groups with POAG subjects of African descent. As is typical in studies of this type, very large samples are required, and this study represents by far the largest collection of POAG subjects of African descent in the world, derived from many countries and continents.”

Professor Patrick Tan, Executive Director of GIS, said, “These findings are crucial in efforts to pinpoint why certain groups of people suffer from severe glaucoma, particularly early on in life. It also suggests that degeneration of the

² <https://www.sciencedirect.com/science/article/pii/S0092867417311315?via%3Dihub>

eye and brain could be mechanistically related. This research may lead to solutions to slow down disease onset and lower disease severity.”

IMAGES



This is a three-dimensional photo of the human eye. Glaucoma could be genetic and is triggered in the front chamber of the eye.

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Notes to Editor:

The research findings described in this media release can be found in the scientific journal *JAMA*, under the title, “Association of genetic variants with primary open angle glaucoma among individuals with African ancestry” by The Genetics of Glaucoma in people of African Descent (GGLAD) consortium.

The authors of the paper are:

Michael A Hauser, PhD^{1,2,3+}; R Rand Allingham, MD^{2,3+}; Tin Aung, MD, PhD^{3,4+}; Carly J Van Der Heide, MD⁵⁺; Kent D Taylor, PhD^{6,7+}; Jerome I Rotter, MD⁶⁺; Shih-Hsiu J Wang, MD, PhD⁸⁺; Pieter WM Bonnemaier, MD^{9,10+}; Susan E Williams, MD¹¹⁺; Sadiq M Abdullahi, MD¹²; Khaled K Abu-Amero, PhD¹³; Michael G. Anderson, MD⁵; Stephen Akafo MD¹⁴; Mahmoud B Alhassan MD¹²; Ifeoma Asimadu, MD¹⁵; Radha Ayyagari, PhD¹⁶; Saydou Bakayoko, MD^{17,18}; Prisca Biangoup Nyamsi, MD¹⁹; Donald W Bowden, PhD²⁰; William C Bromley, MD²¹; Donald L Budenz, MD²²; Trevor R Carmichael, MD, PhD¹¹; Pratap Challa, MD²; Yii-Der Ida Chen, PhD^{6,7}; Chimdi M Chuka-Okosa, MD²³; Jessica N Cooke Bailey, PhD^{24,25}; Vital Paulino Costa, MD²⁶; Dianne A Cruz, MS²⁷; Harvey DuBiner, MD²⁸; John F Ervin, BA²⁹; Robert M Feldman, MD³⁰; Miles Flamme-Wiese, BSE⁵; Douglas E Gaasterland, MD³¹; Sarah J Garnai, BS³²; Christopher A Girkin, MD³³; Nouhoum Guirou, MD^{17,18}; Xiuqing Guo, PhD⁶; Jonathan L Haines, PhD^{24,25}; Christopher J Hammond, MD³⁴; Leon Herndon, MD²; Thomas J Hoffmann, PhD^{35,36}; Christine

M Hulette, MD⁸; Abba Hydera, MD³⁷; Robert P Igo, Jr, PhD²⁴; Eric Jorgenson, PhD³⁸; Joyce Kabwe, MD³⁹; Ngoy Janvier Kilangalanga, MD³⁹; Nkiru Kizor-Akaraiwe, MD^{15,40}; Rachel W Kuchtey, MD, PhD⁴¹; Hasnaa Lamari, MD⁴²; Zheng Li, MD, PhD⁴³; Jeffrey M Liebmann, MD⁴⁴; Yutao Liu, PhD^{45,46,47}; Ruth JF Loos, PhD^{48,49}; Monica B Melo, PhD⁵⁰; Sayoko E Moroi, MD, PhD³²; Joseph M Msosa, MD⁵¹; Robert F Mullins, PhD⁵; Girish Nadkarni, MD^{48,52}; Abdoulaye Napo, MD^{17,18}; Maggie C Y Ng, PhD²⁰; Hugo Freire Nunes, PhD⁵⁰; Ebenezer Obeng-Nyarkoh, MA²¹; Anthony Okeke, MD⁵³; Suhanya Okeke, MD^{15,40}; Olusegun Olaniyi, MD¹²; Olusola Olawoye, MD⁵⁴; Mariana Borges Oliveira, MD⁵⁰; Louise R Pasquale, MD^{55,56}; Rodolfo A. Perez-Grossmann, MD⁵⁷; Margaret A Pericak-Vance, PhD⁵⁸; Xue Qin, PhD⁵⁹; Michele Ramsay, PhD⁶⁰; Serge Resnikoff, MD, PhD^{61,62}; Julia E Richards, PhD^{32,63}; Rui Barroso Schimiti, MD⁶⁴; Kar Seng Sim, MS⁴³; William E Sponsel, MD^{65,66}; Paulo Vinicius Svidnicki, PhD⁵⁰; Alberta AHJ Thiadens, MD, PhD⁹; Nkechinyere J Uche, MD^{23,40}; Cornelia M van Duijn, PhD⁹; José Paulo Cabral de Vasconcellos, MD, PhD²⁶; Janey L Wiggs, MD, PhD^{67,68}; Linda M Zangwill, PhD¹⁶; Neil Risch, PhD^{35,36,38+}; Dan Milea, MD, PhD³⁺; Adeyinka Ashaye, MD⁵⁴⁺; Caroline CW Klaver, MD, PhD^{9,69+}; Robert N Weinreb, MD¹⁶⁺; Allison E Ashley Koch, PhD¹⁺; John H Fingert, MD, PhD⁵⁺; & Chiea Chuen Khor, MD, PhD^{3,43+}

¹Department of Medicine, Duke University, Durham, NC, ²Department of Ophthalmology, Duke University, Durham, NC, ³Singapore Eye Research Institute, Singapore, ⁴Singapore National Eye Center, Singapore and Duke-NUS Medical School, Singapore, ⁵Department of Ophthalmology and Visual Sciences, Carver College of Medicine, University of Iowa, Iowa City, IA, ⁶The Institute for Translational Genomics and Population Sciences, Department of Pediatrics, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, ⁷Department of Pediatrics, Harbor-University of California, Los Angeles Medical Center, Torrance, CA, ⁸Department of Pathology, Duke University, Durham, NC, ⁹Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands, ¹⁰Rotterdam Eye Hospital, Rotterdam, The Netherlands, ¹¹Division of Ophthalmology, Department of Neurosciences, University of the Witwatersrand, Johannesburg, South Africa, ¹²National Eye Centre, Kaduna, Nigeria, ¹³Department of Ophthalmology, College of Medicine, King Saud University, Riyadh 11411, Saudi Arabia, ¹⁴Unit of Ophthalmology, Department of Surgery, University of Ghana Medical School, Accra, Ghana, ¹⁵Department of Ophthalmology, ESUT Teaching Hospital Parklane, Enugu, Nigeria, ¹⁶Department of Ophthalmology, Hamilton Glaucoma Center, Shiley Eye Institute, University of California, San Diego, La Jolla, CA, ¹⁷Institut d'Ophtalmologie Tropicale de l'Afrique, Bamako, Mali, ¹⁸Université des sciences des techniques et des technologies de Bamako, Bamako, Mali, ¹⁹Service spécialisé d'ophtalmologie, Hôpital Militaire de Région No1 de Yaoundé, Yaoundé, Cameroun, ²⁰Department of Biochemistry, Center for Diabetes Research, Wake Forest School of Medicine, Winston-Salem, NC, ²¹Center for Human Genetics, Bar Harbor, ME, ²²Department of Ophthalmology, University of North Carolina, Chapel Hill, NC, ²³University of Nigeria Teaching Hospital, Ituku Ozalla, Enugu, Nigeria, ²⁴Department of Population and Quantitative Health Sciences, Case Western Reserve University, Cleveland, OH, ²⁵Institute for Computational Biology, Case Western Reserve University, Cleveland, OH, ²⁶Department of Ophthalmology, Faculty of Medical Sciences, University of Campinas, Campinas, Brazil, ²⁷Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, ²⁸Clayton Eye Care Center Management, Inc., Marrow, GA, ²⁹Kathleen Price Bryan Brain Bank and Biorepository, Department of Neurology, Duke University, Durham, NC, ³⁰Ruiz Department of Ophthalmology & Visual Science, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, ³¹The Emmes Corporation, Rockville, MD, ³²Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, MI, ³³Department of Ophthalmology and Visual Sciences, University of Alabama Birmingham, Birmingham, AL, ³⁴Section of Academic Ophthalmology, School of Life Course Sciences, FoLSM, King's College London, London, United Kingdom, ³⁵Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA, ³⁶Institute for Human Genetics, University of California San Francisco, San Francisco, CA, ³⁷Sheikh Zayed Regional Eye Care Centre, Kanifing, The Gambia, ³⁸Kaiser Permanente Northern California (KPNC), Division of Research, Oakland, CA, ³⁹Department of Ophthalmology, Saint Joseph Hospital, Kinshasa, Limete, Democratic Republic of the Congo, ⁴⁰The Eye Specialists Hospital, Enugu, Nigeria, ⁴¹Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center, Nashville, TN, ⁴²Clinique Spécialisée en Ophtalmologie Mohammedia, Mohammedia, Morocco, ⁴³Genome Institute of Singapore, Singapore, ⁴⁴Bernard and Shirlee Brown Glaucoma

Research Laboratory, Harkness Eye Institute, Columbia University Medical Center, New York, NY, ⁴⁵Cellular Biology and Anatomy, Augusta University, Augusta, GA, ⁴⁶James & Jean Culver Vision Discovery Institute, Augusta University, Augusta, GA, ⁴⁷Center for Biotechnology & Genomic Medicine, Augusta University, Augusta, GA, ⁴⁸The Charles Bronfman Institute for Personalized Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, ⁴⁹The Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, ⁵⁰Center for Molecular Biology and Genetic Engineering, University of Campinas, Campinas, Brazil, ⁵¹Lions Sight-First Eye Hospital, Kamuzu Central Hospital, Lilongwe, Malawi, ⁵²Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, ⁵³Nigerian Navy Reference Hospital, Ojo, Lagos, Nigeria, ⁵⁴Department of Ophthalmology, University of Ibadan, Ibadan, Nigeria, ⁵⁵Icahn School of Medicine at Mount Sinai, Department of Ophthalmology, New York, NY, ⁵⁶Channing Division of Network Medicine, Brigham and Women's Hospital, Boston, MA, ⁵⁷Instituto de Glaucoma y Catarata, Lima, Peru, ⁵⁸John P Hussman Institute for Human Genomics, University of Miami Miller School of Medicine, Miami, FL, ⁵⁹Duke Molecular Physiology Institute, Duke University, Durham, NC, ⁶⁰Sydney Brenner Institute for Molecular Bioscience, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, ⁶¹Brien Holden Vision Institute, Sydney, Australia, ⁶²School of Optometry and Vision Science, University of New South Wales, Sydney, Australia, ⁶³Department of Epidemiology, University of Michigan, Ann Arbor, MI, ⁶⁴Hoftalon Hospital, Londrina, Brazil, ⁶⁵San Antonio Eye Health, San Antonio, TX, ⁶⁶Eyes of Africa, Child Legacy International (CLI) Hospital, Msundwe, Malawi, ⁶⁷Harvard University Medical School, ⁶⁸Massachusetts Eye and Ear Hospital, Boston, MA, ⁶⁹Department of Ophthalmology, Radboud University Medical Center, Nijmegen, The Netherlands
+ Drs. Hauser, Allingham, Aung, Van Der Heide, Taylor, Rotter, Wang, Bonnemaijer, Williams, Risch, Milea, Ashaye, Klaver, Weinreb, Ashley Koch, Fingert, and Khor contributed to the work equally.

Author contributions: Drs Hauser (mike.hauser@duke.edu) and Khor (khorcc@gis.a-star.edu.sg) had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis

For media queries and clarifications, please contact:

Lyn Lai
Officer, Office of Corporate Communications
Genome Institute of Singapore, A*STAR
Tel: +65 6808 8258
Email: laiy@gis.a-star.edu.sg

Ravi Chandran
Corporate Communications
Singapore National Eye Centre
Tel: +65 8121 8569
Email: ravi.chandran@sneec.com.sg

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.a-star.edu.sg/gis.

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The Agency for Science, Technology and Research (A*STAR) is Singapore's lead public sector agency that spearheads economic oriented research to advance scientific discovery and develop innovative technology. Through open innovation, we collaborate with our partners in both the public and private sectors to benefit society.

As a Science and Technology Organisation, A*STAR bridges the gap between academia and industry. Our research creates economic growth and jobs for Singapore, and enhances lives by contributing to societal benefits such as improving outcomes in healthcare, urban living, and sustainability.

We play a key role in nurturing and developing a diversity of talent and leaders in our Agency and research entities, the wider research community and industry. A*STAR's R&D activities span biomedical sciences and physical sciences and engineering, with research entities primarily located in Biopolis and Fusionopolis. For ongoing news, visit www.a-star.edu.sg/.

About Singapore Eye Research Institute (SERI)

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. 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. In addition, SERI has over 250 adjunct faculties from various eye departments, biomedical institutes and tertiary centres in Singapore.

SERI has amassed an impressive array of more than 3,585 scientific papers as of July 2019, and has secured more than \$314 million in external peer-reviewed competitive grants. To date, SERI's faculty has been awarded more than 568 national and international prizes and filed more than 130 patents. Serving as the research institute of the Singapore National Eye Centre and affiliated to the

Duke-NUS Medical School, National University of Singapore, 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. Today, SERI is recognized as a pioneering centre for high quality eye research in Asia, with breakthrough discoveries that has translated to significant paradigm shift in eye care delivery. For more information, visit www.seri.com.sg

About Singapore National Eye Centre (SNEC)

Singapore National Eye Centre was incorporated in 1989 and commenced operations in 1990. It is the designated national centre within the public sector healthcare network, and spearheads and coordinates the provision of specialised ophthalmological services with emphasis on quality education and research. Since its opening in 1990, SNEC has achieved rapid growth and currently manages an annual workload of 400,000 outpatient visits and 40,000 major eye surgeries and lasers.

Ten subspecialties in Cataract and Comprehensive Ophthalmology, Corneal and External Eye Disease, Glaucoma, Neuro-Ophthalmology, Oculoplastics, Pediatric Ophthalmology and Strabismus, Refractive Surgery, Ocular Inflammation and Immunology, Medical Retina and Surgical Retina have been established to provide a full range of eye treatments from comprehensive to tertiary levels for the entire spectrum of eye conditions.

SNEC was accorded the Excellence for Singapore Award in 2003 for achieving excellence in the area of Ophthalmology, thrusting Singapore into international prominence. In 2006, SNEC received the first Minister for Health Award for public health. Clinician scientists from Singapore National Eye Centre and Singapore Eye Research Institute were awarded the prestigious President's Science and Technology Award in 2009, 2010 and 2014 for their outstanding contributions in translational, clinical and epidemiological research in cornea, retina and glaucoma. Visit us at www.snec.com.sg.