

MEDIA RELEASE

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For Immediate Publication

Largest non-European study of diabetes genetics finds novel diabetes genes that may help explain how disease develops in East Asian individuals

International team of researchers aims to identify genetic targets that can enhance precision medicine efforts and treatment of diabetes

SINGAPORE — In the largest non-European diabetes genetics study to date that involved 433,540 East Asian individuals from China, Hong Kong, Japan, the Philippines, Singapore, South Korea, Taiwan and USA, an international team of 113 investigators co-led by five senior authors,¹ including Dr Xueling Sim from NUS Saw Swee Hock School of Public Health (NUS SSHSPH) and Dr Karen Mohlke from University of North Carolina, identified 61 new genetic variants associated with Type 2 diabetes (T2D).

Findings include discovery of variants near genes involved in skeletal muscle, and pancreatic functions as well as in alcohol metabolism (e.g. *GDAP1*, *PTF1A*, *SIX3*, *ALDH2*), and also in genes linked to higher levels of fat around the belly in East Asian individuals, e.g. *NID2*. These genes had not been linked with T2D before and may help explain why East Asian individuals get T2D even though they are not obese based on their body mass index (BMI) measurements. The study was published in prestigious scientific journal, *Nature*, on 6 May 2020.

“While a recent study of 900,000 European individuals discovered many new genetic variants linked to T2D², we were still able to make novel findings as we were studying such a large number of East Asian individuals, where these variants are more common. The identified variants are relatively rare in Europeans and thus missed in the European studies,” said Dr Sim. She added, “We learnt over the years that European and East Asian individuals share many T2D genetic variants, but studying East Asian individuals in such an unprecedented collaborative scale allows us to expand the number of genetic variants associated with diabetes. This can help us understand population differences in the development of T2D.”

¹ The co-senior authors of the paper include Dr Xueling Sim, PhD, Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore; Dr Karen Mohlke, PhD, Department of Genetics, University of North Carolina at Chapel Hill School of Medicine; Dr Bong-Jo Kim, MD, PhD, Center for Genome Science, National Institute of Health, Cheongjusi, South Korea; Dr Robin Walters, PhD, Nuffield Department of Population Health, University of Oxford; Dr Takashi Kadowaki, MD, PhD, Department of Diabetes and Metabolic Diseases, University of Tokyo, Japan.

² Mahajan A, Taliun D, Thurner M, et al. Fine-mapping type 2 diabetes loci to single-variant resolution using high-density imputation and islet-specific epigenome maps. *Nat Genet.* 2018;50:1505-1513.

The researchers made another striking observation: genetic variants can act through multiple close-by genes in different tissues to influence T2D development. For example, one gene may influence the production of insulin in the pancreas, while another gene close by could affect the use of insulin in the muscle.

“These results help further our understanding of the genetic basis for T2D across populations and provide new targets for T2D drug discovery,” said Dr Karen Mohlke of the University of North Carolina, one of the co-senior authors.

“Genetic variants are present in all our genomes, some of which predispose individuals to disease like T2D. Due to differences in the population history, some variants are more common in one population than another. This study emphasizes the importance of including large numbers of individuals from different parts of the world in these studies, so that we can better understand the cause of diseases. Singapore, with its multi-ethnic populations from different parts of the world is an ideal environment for studying this,” said Professor E Shyong Tai, Senior Consultant from the Division of Endocrinology at the National University Hospital and Professor at the NUS SSHSPH.

These results serve as a valuable public resource for precision medicine efforts in diabetes. The next steps are to identify which genes are altered by the genetic variants and to determine which of these genes may be targets for new diabetes drugs and treatments.

The large scale study brought together 23 cohort studies from the Asian Genetic Epidemiology Network (AGEN), a consortium with over 10 years of collaborative history. It includes local cohort studies such as the Singapore Population Health Studies (SPHS), the Singapore Chinese Health Studies (SCHS) from NUS SSHSPH, and the Singapore Epidemiology of Eye Diseases (SEED) studies from the Singapore Eye Research Institute (SERI).

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About the National University Health System (NUHS)

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Institutions in the NUHS Group include the National University Hospital, Ng Teng Fong General Hospital, Jurong Community Hospital and Alexandra Hospital; three National Specialty Centres - National University Cancer Institute, Singapore (NCIS), National University Heart Centre, Singapore (NUHCS) and National University Centre for Oral Health, Singapore (NUCOHS); the National University Polyclinics (NUP); Jurong Medical Centre; and three NUS health sciences schools – NUS Yong Loo Lin School of Medicine (including the Alice Lee Centre for Nursing Studies), NUS Faculty of Dentistry and NUS Saw Swee Hock School of Public Health.

With member institutions under a common governance structure, NUHS creates synergies for the advancement of health by integrating patient care, health science education and biomedical research.

As a Regional Health System, NUHS works closely with health and social care partners across Singapore to develop and implement programmes that contribute to a healthy and engaged population in the Western part of Singapore.

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About the NUS Saw Swee School of Public Health

Building upon decades of experience in research, training and practice in epidemiology and public health, the Saw Swee Hock School of Public Health (SSHSPH), under the National University of Singapore, was established in October 2011 as Singapore's first and only full-fledged national public health tertiary education institution. The School is also a member of the National University Health System (NUHS).

The School aims to continually foster healthier communities in Singapore and the region, and impact public health programmes and policies through its robust educational programmes and translational cross-disciplinary research work on cohort studies and life course epidemiology, infectious disease research, health technology assessment, health promotion, workplace safety and health, health systems evaluation and health services research. An interdisciplinary approach — augmented by rigorous training, applicable research and regional partnerships — places SSHSPH at the forefront of public health knowledge discovery and practice in Asia.

The School actively collaborates with many partners including the London School of Hygiene & Tropical Medicine, Karolinska Institutet, Harvard School of Public Health and University of Michigan School of Public Health. Its flagship programme, the Master of Public Health (MPH) degree, attracts students from a wide range of disciplines from within Singapore and throughout the region.

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