



[For immediate release](#)

MEDIA RELEASE

Novel approach to treat and prevent Type 2 diabetes: SGH and NUS Medicine study

Singapore, 17 November 2022 — Bile acids, a digestive juice, may hold the key to a new way of treating and preventing Type 2 diabetes.

However, bile acids do more than just helping with food digestion. They also act as signalling molecules and control various body functions, including the regulation of blood sugar. Diabetes develops when the body loses its ability to maintain normal blood sugar, and studies have found that the bile acid composition of patients with Type 2 diabetes is different. This unique bile acid profile is controlled by the *CYP8B1* gene, which makes an enzyme necessary for bile acid synthesis. But until now, the link between *CYP8B1*, diabetes risk and glucose control in humans has not been identified.

From the Bench

A study team from Singapore General Hospital (SGH) and Yong Loo Lin School of Medicine at National University of Singapore (NUS Medicine) found that pre-clinical models without the *CYP8B1* gene have a bile acid composition that is different from those with Type 2 diabetes. This change improves the ability of insulin to lower blood glucose and protects them against developing Type 2 diabetes. Realising this, the researchers embarked on a project to investigate whether the same is also true in humans.

“One approach to investigate the relationship between *CYP8B1* and diabetes risk is to study the health status of individuals who lack the gene due to naturally occurring gene mutations. Such ‘loss-of-function mutations’ however, were not known to be present in humans. We also did not know whether the mutations would exert the same protective effects against diabetes,” said Dr Tan Hong Chang, the co-lead investigator of this project and Senior Consultant at the SGH’s Department of Endocrinology.

This prompted the researchers to analyse stored DNA samples of over 8,000 volunteers from other studies to look for individuals with loss-of-function mutations in *CYP8B1*. The team eventually found about 140 individuals and invited them for a follow-up comparison study.

To Bedside

From 2016 to 2018, study volunteers with the mutations were matched with individuals without mutations of the same age, gender, race, and BMI, and underwent detailed metabolic studies at the SingHealth Investigational Medicine Unit. Hyperinsulinemic-euglycemic clamp studies were performed to measure how well they metabolised glucose and how sensitive they were to insulin. The results in humans confirmed the team's findings in pre-clinical models– volunteers with *CYP8B1* loss-of-function mutations had significantly better insulin sensitivity and were better at regulating blood glucose in the normal range. Furthermore, these volunteers were also found to have reduced amounts of fat in their liver and a better lipid profile compared to those without the mutations.

Back to Bench

The researchers did not stop there.

They headed back into the laboratory to identify the molecular pathway that is responsible for the difference in those with the *CYP8B1* mutations.

Dr Roshni R Singaraja, Assistant Professor, Department of Medicine and Cardiovascular Research Institute, NUS Medicine, and co-lead investigator of the study said: "Since the *CYP8B1* mutations in our study volunteers protects them against Type 2 diabetes, developing a drug to reduce the enzyme activity of this bile acid gene should confer the same benefit for everyone else. It could also be used as a glucose lowering agent for those with the chronic disease."

The study team is now exploring different methods to target this gene and hope to develop new treatment options to treat and prevent Type 2 diabetes which is on the rise globally. Despite the ongoing war against diabetes in Singapore, the prevalence of diabetes increased from 8.8 per cent in 2017 to 9.5 per cent in 2020. The number of Singaporeans suffering from diabetes is estimated to hit 1 million by 2050.

World Diabetes Day is commemorated annually on 14 November.

The findings of the joint study were published in peer-reviewed medical journal, *The Journal of Clinical Investigation*, in September 2022 (<https://doi.org/10.1172/JCI152961>).

For media enquiries, please contact:

Carol Ang (Ms)
Communications Department
Singapore General Hospital
Mobile: 98455354
Email: carol.ang@sgh.com.sg

Amanda Yap
Communications
NUS Yong Loo Lin School of Medicine
Mobile: +65 8157 0881
Email: medajy@nus.edu.sg

--- End ---

About Singapore General Hospital

Singapore General Hospital, a member of Singapore Health Services, is the public sector's flagship hospital. Established in 1821, SGH is Singapore's largest acute tertiary hospital with 1,700 beds and national referral centre offering a comprehensive range of more than 40 clinical specialties on its campus. Every year, about 1 million Singaporeans benefit from medical care delivered by its 800 specialists. As an academic healthcare institution and the bedrock of medical education, SGH plays a key role in nurturing doctors, nurses and allied health professionals, and is committed to innovative translational and clinical research in her continual strive to provide the best care and outcomes to her patients. www.sgh.com.sg

About the NUS Yong Loo Lin School of Medicine (NUS Medicine)

The NUS Yong Loo Lin School of Medicine is Singapore's first and largest medical school. Our enduring mission centres on nurturing highly competent, values-driven and inspired healthcare professionals to transform the practice of medicine and improve health around the world.

Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through our doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is one of the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2023 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2022).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>