# PRESS RELEASE

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## NUS Medicine researchers unlock the potential of genetic glycoengineering to advance vaccines and therapeutics technology

*Singapore, 16 October 2023* – A novel glycoengineering platform, created by the laboratory of Assistant Professor Chris Lok-To Sham from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), is poised to revolutionise future production of vaccines and therapeutics to fight infectious diseases. Glycoengineering aims to manipulate sugars to produce useful carbohydrates. This innovative platform simplifies the customising and production of sugar carbohydrates known as glycans that plays a crucial role in various therapeutic applications.

Sugar-adding enzymes called glycosyltransferases (GTs) produce glycans and control the structural diversity of glycans. The team found that the capsular polysaccharide (CPS), the sugar layer which encases many bacteria have extreme diversity, where its enzymes can be exploited to build many customised glycans.

“These enzymes are like Lego. The more types of Lego bricks you have, the more unique types of glycans you can build,” explained Asst Prof Chris Sham from the Department of Microbiology and Immunology at NUS Medicine. Armed with this knowledge, Asst Prof Chris Sham and his graduate student Su Tong from the Department of Microbiology and Immunology, together with their team from the Infectious Diseases Translational Research Programme at NUS Medicine, took advantage of the diverse pathways of the bacterial CPS and the ease of modifying its pathways to create this novel glycoengineering platform. This platform provides increased versatility in modifying GTs, facilitating the engineering of newly-customised glycans.

Customised glycans, essential for diverse therapeutic applications, requires a versatile platform capable of the insertion, deletion, substitution and general modification of glycan linkages. The team found that by relaxing the specificity of the precursor transporters, they could broaden the range of residues entering the cytoplasm. This innovation enables the production of customised glycans with unprecedented flexibility.

“The process of customising glycans, or glycoengineering, is made more challenging because it mostly relies on in-vitro approaches. These issues affect the efficient production of vaccines and other biological therapeutics. The new platform circumvents this challenge by demonstrating the possibility to genetically manipulate and engineer new glycans, giving rise to new knowledge about GTs, which ultimately signals an important advancement in glycoengineering,” Su Tong said.

To date, the team has already celebrated significant achievements, including the successful synthesis of clinically relevant glycans such as the Galili antigen, blood group antigens and Lewis antigens. These glycans can contribute to positive outcomes in the areas of organ

transplants and blood transfusion when antibody rejection occurs in situations where the patient's blood group is incompatible with the donor, resulting in severe inflammation and cell death.

Asst Prof Chris Sham is optimistic about the future development of this glycoengineering platform in creating more glycans for a broad variety of specific needs. "The current focus is to make glycans found in mammals, but in the future the team hopes to use this novel platform technology and adapt it to multiple bacterial species to generate more useful carbohydrates for other applications, such as countering immunological paralysis and graft rejection."

The paper was published in Science Advances on 6 September 2023, titled *Rewiring the pneumococcal capsule pathway for investigating glycosyltransferase specificity and genetic glycoengineering*.

**For media enquiries, please contact:**

Amanda YAP
Assistant Manager, Communications
Yong Loo Lin School of Medicine
National University of Singapore
Email: medajyjy@nus.edu.sg

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy; environmental and urban sustainability; treatment and prevention of diseases; active ageing; advanced materials; risk management and resilience of financial systems; Asian studies; and Smart Nation capabilities such as artificial intelligence, data science, operations research and cybersecurity.

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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 Asia's leading medical schools 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 2023).

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