

PRESS RELEASE

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NUS researchers uncover new differences in bacteria's sugar coat to aid pneumococcal vaccine development

Singapore, 17 April 2023 – Many disease-causing bacteria like Streptococcus pneumoniae (S. pneumoniae) are encased in a sugar layer called the capsular polysaccharide (CPS). This layer is often essential for infections. In a ground-breaking discovery by scientists from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), features of the CPS that help the bacteria to colonise the human respiratory tract were identified. The research showed that the structures of the CPS capsule and its types of linkages and combinations matter greatly in allowing the bacteria to better attach and survive on the lining of the upper and lower human respiratory tracts.

To challenge the widely-held notion that structurally diverse CPS capsules in *S. pneumoniae* perform the same function in promoting bacterial colonisation, the team, led by Assistant Professor Chris Lok-To Sham and graduate student, Jade Chun Ye-Yu, from the Infectious Diseases Translational Research Programme at NUS Medicine, constructed bacterial mutants displaying one of the 84 types of CPS found in *S. pneumoniae*. The mutants were then introduced to respiratory cells to investigate their abilities to bind to the respiratory tracts. Using a molecular barcode to distinguish the strains, the team examined whether varying CPS in these mutants would affect binding on the nasal and bronchial cells.

The results showed that the CPS with rhamnose sugar residues bound poorly to the airway cells, while CPS with glycan motifs bound strongly. The experiment demonstrated that the structural configurations and the types of CPS play important roles in the strength of attachment and survival on the human airway.

"In the past, scientists recognised that the proteins found in bacteria are not by chance, and they do serve a purpose. Bacteria have shown a preference for certain types of sugars on their capsules, and a specific linkage of sugars. Our research proves that some of these combinations benefit the bacteria because they aid in colonising the human respiratory tract. This finding will shed more light on the range of CPS types to be included in future vaccines, as current vaccines against *S. pneumoniae* do not cover the many types of CPS produced by the bacteria," added Jade Chun, who is also from the Department of Microbiology and Immunology at NUS Medicine.

S. pneumoniae is a major driver of pneumonia, septicaemia, and meningitis. Collectively, these infections are among the leading causes of morbidity and mortality in the elderly and young children. To fight against these deadly infections, pneumococcal vaccines are administered to stimulate antibody production to the CPS. However, the bacteria can manipulate their CPS structure to evade these antibodies. This biochemical warfare results in more than a hundred types of CPSs produced by S. pneumoniae, which increases the challenge of producing effective vaccines. While the diversity of CPS is well appreciated, what actually makes the CPS a lethal weapon for the bacteria remains unclear.

The findings have been published in <u>The Proceedings of the National Academy of Sciences</u> (PNAS), a peer-reviewed journal of the National Academy of Sciences (NAS).

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The National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education, research and entrepreneurship, with a focus on Asian perspectives and expertise. We have 16 colleges, faculties and schools across three campuses in Singapore, with more than 40,000 students from 100 countries enriching our vibrant and diverse campus community. We have also established our NUS Overseas Colleges programme in more than 15 cities around the world.

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, research centres of excellence, corporate labs and more than 30 university-level research institutes 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, cuttingedge 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 2023).

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