



PRESS RELEASE

3 AUGUST 2022 | FOR IMMEDIATE RELEASE

NUS scientists engineer probiotic to prevent infection of large intestine

Singapore, 3 August 2022 – Scientists from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) have created a probiotic to restore bile salt metabolism, found in the gastrointestinal tract, to counter the onset and effects of *Clostridium Difficile Infection* (CDI).

CDI is the infection of the large intestine or colon that leads to infectious diarrhoea, caused by an infectious bacterium known as *Clostridium*. Most cases of CDI have been observed to occur in those who have been taking antibiotics or just finished their course of antibiotics.

The administration of antibiotics in the treatment of CDI causes an imbalanced gut microbiome, known as dysbiosis, which can disrupt other microbiome processes such as bile salt metabolism. The dysregulation of bile salt metabolism can activate dormant *Clostridioides difficile* spores, leading to CDI, causing severe diarrhoea and colitis – inflammation of the large intestine, or a reinfection of CDI.

A team of researchers, led by Associate Professor Matthew Chang, from the Synthetic Biology Translational Research Programme at NUS Medicine and [NUS Synthetic Biology for Clinical and Technological Innovation](#) (SynCTI), engineered a probiotic that can detect the occurrence of antibiotic-induced microbiome imbalance and express an enzyme that can regulate the bile salt metabolism upon detection. This probiotic contains a genetic circuit that comprises a genetically encoded sensor, amplifier and actuator.

The team used an *E. coli* probiotic strain as the host because of its proven safety record in humans and its gram-negative nature makes it compatible with the current CDI therapy that uses antibiotics targeting gram-positive bacteria. The sensor in this probiotic, detects the presence of sialic acid, a gut metabolite that is indicative of microbiome imbalance. The actuator produces an enzyme that can regulate the bile salt metabolism, activated by the sensor, and it reduces the germination of the *Clostridioides difficile* spores that causes CDI, when induced by the sialic acid sensor. The team also included an amplifier in the probiotic which amplifies the activation by the sensor and increases the production of the enzyme, reducing the germination of the *Clostridioides difficile* spores by 98%. Experiments showed that the probiotic significantly reduced CDI in laboratory models, as demonstrated by a 100% survival rate and improved clinical outcomes.

Assoc Prof Chang is encouraged by this advancement that sheds more light on the gut environment and how it can be manipulated to create less invasive treatment strategies. He says, “This scientific innovation gives a better understanding on how we can control the microenvironment in the body, without needing to exert direct lethality to kill the *Clostridioides difficile* bacterium, give additional drugs, or use invasive methods to rid the infection. Our perspectives have shifted towards studying how we can come up an antimicrobial strategy to

complement and assist the natural biological processes in the body to help limit the onset of infection. This is useful when considering the development or improvement of future therapeutics for CDI.”

The paper was published in *Nature Communications* in July 2022, and can be accessed here: <https://www.nature.com/articles/s41467-022-31334-z>.

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About National University of Singapore (NUS)

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

The Yong Loo Lin School of Medicine, National University of Singapore (NUS 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 Asia's leading medical schools and ranks among the best in the world (Times Higher Education World University Rankings 2022 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/>