



PRESS RELEASE

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NUS Medicine pioneers ground-breaking technique to deliver drugs directly to the brain

This landmark study using the nasal bacteria technique promises new treatments for neurological disorders by bypassing the blood-brain barrier

Singapore, 18 February, 2025 – Scientists at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) have developed a ground-breaking technique to deliver therapeutic molecules directly to the brain, bypassing the blood-brain barrier.

Led by Dr Haosheng Shen, lead researcher from the Synthetic Biology Translational Research Programme, NUS Medicine and the NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI) this novel approach utilises a naturally occurring nasal bacterium, *Lactobacillus plantarum* (Lp), which was genetically engineered to produce therapeutic compounds and release them through a specific nose-to-brain pathway. Their research was published in leading life sciences journal, [Cell](#).

The blood-brain barrier (BBB) plays a crucial role in protecting the brain from harmful substances but also poses significant challenges to delivering medications for neurological conditions. Existing drug delivery methods often struggle with limited efficiency and require invasive procedures. To address these challenges, the team identified a strain of Lp with a natural affinity for the olfactory mucosa, a specialised tissue located in the upper part of the nasal cavity responsible for the sense of smell. This tissue also provides a direct pathway to the central nervous system, enabling targeted intranasal drug delivery.

However, intranasal drug delivery to the brain is hindered by the small surface area of the olfactory mucosa and the rapid clearance of drugs by the body. To work around this, the team engineered that strain of Lp to bind to N-acetyl heparan sulfate (NaHS, a long chain of sugar molecules that plays important roles in cell signalling, structural support, and protein interaction) in the olfactory epithelium. This binding enables the localised and sustained release of medication, which minimises systemic absorption and enhances bioavailability in the brain. The engineered Lp strain was able to produce appetite-regulating hormones, which the team used to demonstrate potential in treating brain-related disorders. In preclinical studies, intranasal administration of the modified bacteria resulted in reduced appetite, lower body weight gain, improved glucose metabolism, and decreased fat accumulation. The medication, after being released at the olfactory mucosa, successfully reached and accumulated in the brain.

By bypassing the BBB, this approach offers a more efficient way to deliver treatments for neurological conditions, including neurodegenerative diseases and conditions requiring peptides or proteins that typically do not cross the BBB. This targeted delivery method leverages the unique anatomical and biological properties of the olfactory mucosa, overcoming key barriers that have historically limited the effectiveness of brain-targeted therapies.

“This study illustrates the potential of engineered bacteria to serve as precise delivery vehicles for brain-targeted therapies,” said Dr Shen. “Our findings could pave the way for novel treatments of neurological diseases, leveraging the underexplored connection between nasal microbiota and brain function.”

According to Dr Shen, the next phase of research will focus on optimising dosing regimens and conducting human clinical trials to confirm the efficacy and safety of the approach. Researchers will also investigate additional therapeutic applications, particularly in the treatment of neurodegenerative diseases such as Parkinson’s and Alzheimer’s.

Professor Matthew Chang, Director of the Synthetic Biology Translational Research Programme, NUS Medicine and SynCTI, added, “Our research highlights the potential of nasal bacteria as non-invasive vehicles for brain drug delivery, and also underscores the importance of further exploring the relationship between the olfactory microbiome and brain health. By utilising bacteria with natural affinities for key areas in the nasal cavity, we may unlock new strategies for managing neurological disorders.”

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About National University of Singapore (NUS)

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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, 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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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 2025 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2024).

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