

# **PRESS RELEASE**

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# Repurposed antibiotic shows promise against Central Nervous System Tuberculosis in NUS Medicine study

Researchers at the NUS Yong Loo Lin School of Medicine have discovered that combining doxycycline with standard Tuberculosis (TB) treatment may protect the brain from damage caused by excessive immune activity. The research highlights a new approach of suppressing the body's harmful immune response rather than targeting bacteria alone to minimise adverse effects of standard TB treatment.

Singapore, 12 November 2025 — Researchers at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), have demonstrated that doxycycline, a commonly available and inexpensive antibiotic, can improve survival rates and neurological outcomes in Central Nervous System Tuberculosis (CNS-TB) in a preclinical non-human study. Published in the <u>Journal of Neuroinflammation</u>, the study offers a promising adjunctive therapy for this severe and often fatal disease.

The study, led by Associate Professor Catherine Ong Wei Min, Principal Investigator from the Infectious Diseases Translational Research Programme at NUS Medicine, together with colead authors Dr Poh Xuan Ying and Dr Loh Fei Kean, who are from the same programme, studied the prognostic factors of CNS-TB. They analysed cerebrospinal fluid samples collected from 72 children with tuberculous meningitis and control patients and found elevated levels of tissue- damaging matrix metalloproteinases (MMPs) proteins and immune cell traps known as neutrophil extracellular traps (NETs), which drives the severity of CNS-TB, in the cerebrospinal fluid of children with CNS-TB.

While TB is generally associated with pulmonary TB which affects the lungs, CNS-TB is a more severe form of TB that affects the brain and spinal cords and occurs more commonly among children and the immunocompromised.

To investigate targeted treatment, the researchers developed a CNS-TB laboratory model that exhibited the brain pathology and neurological symptoms similar to those observed in humans, and contained TB bacteria. An RNA sequencing platform optimised for old and small archived tissue was used to analyse gene expression changes from TB infections in human and research tissue samples.

Their research found that treating the CNS-TB laboratory models with doxycycline alongside standard TB drugs suppressed MMPs and NETs, significantly improved survival and outcomes. The addition of doxycycline lowered inflammation, preserved brain tissue, and improved vascular integrity, leading to better drug penetration and outcomes.

Assoc Prof Ong said, "Our study suggests that doxycycline, when paired with standard TB drugs, curbs excessive immune activity that leads to brain damage and improve survival rates in preclinical studies. Doxycycline is inexpensive, widely available and has a well-established safety record. If these findings are confirmed in Phase II studies, its use could eventually be rapidly scaled across national TB programmes without the long delays typical of new drug development."

Collaborators of the study include Assistant Professor Joshua Tay from the Department of Otolaryngology, NUS Medicine; Associate Professor Andres F. Vallejo from the University of Southampton, UK; and Professor Tchoyoson Choie Cheio Lim from the Department of Neuroradiology at the National Neuroscience Institute, Singapore.

TB is a global health threat with more than 10.8 million cases of active TB recorded in 2023<sup>1</sup>. Singapore continues to see endemic transmission, with about 1,100 new active cases in 2024<sup>1</sup>. CNS-TB represents about 1 to 2 per cent of all global TB cases, with patients continuing to face neurological damage and high mortality despite receiving standard TB treatment<sup>2</sup>. This work underscores the potential of repurposing an inexpensive, well-tolerated drug such as doxycycline to improve treatment of CNS-TB and possibly other inflammatory brain infections. The study results have led to a Phase II clinical trial funded by the National Medical Research Council (NMRC) at the Ministry of Health, Singapore, that is currently ongoing in Singapore, Malaysia and Indonesia, to assess if adding doxycycline to standard TB treatment can safely improve survival and reduce brain damage in patients.

"As our study proceeds to the next phase, we aim to create a robust clinical dataset that enables us to develop more targeted and effective TB treatment, ultimately offering patients a better chance at a fuller recovery," said Assoc Prof Ong.

This research is supported by the Singapore Ministry of Health through the National Medical Research Council (NMRC) Office, MOH Holdings Pte Ltd under the NMRC Transition Award (NMRC/TA/0042/2015), as well as the National University Health System Research Office (NUHSRO/2016/066/NPCseedfunding/01).

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<sup>&</sup>lt;sup>1</sup> https://www.moh.gov.sg/newsroom/update-on-tuberculosis-situation-in-singapore-2025

<sup>&</sup>lt;sup>2</sup> https://pmc.ncbi.nlm.nih.gov/articles/PMC8789671/#s2

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For media enquiries, please contact:

#### Olivia CHOO

Communications Executive Yong Loo Lin School of Medicine, National University of Singapore

DID: +65 9056 7410

Email: medv4000@partner.nus.edu.sg

## **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 15 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 more than 20 NUS Overseas Colleges entrepreneurial hubs 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.

For more information on NUS, please visit <a href="http://www.nus.edu.sg/">http://www.nus.edu.sg/</a>

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

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

# **About the National Medical Research Council (NMRC)**

The NMRC was established in 1994 to oversee research funding from the Ministry of Health and support the development and advancement of biomedical research in Singapore, particularly in the public healthcare clusters and medical schools. NMRC engages in research strategy and planning, provides funding to support competitive research grants and core research enablers, and is responsible for the development of clinician scientists through awards and fellowships. The council's work is supported by the NMRC Office which is part of MOH Holdings Pte Ltd. Through its management of the various funding initiatives, NMRC promotes healthcare research in Singapore, for better health and economic outcomes.