



PRESS RELEASE

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A promising vaccine approach to induce longer-lasting protective immunity against COVID-19: NUS Medicine-Monash University study

04 June 2024, Singapore – A scientific team from the Yong Loo Lin School of Medicine at the National University of Singapore (NUS Medicine) and Monash University, Australia, has engineered a COVID-19 vaccine that induced – in pre-clinical models – very long-lasting, protective immunity against SARS-CoV-2 virus with a single-shot immunisation.

In an on-going, four-year collaboration, the team leveraged on a novel vaccine platform to fuse the receptor-binding domain (RBD) from the spike protein of the SARS-CoV-2 virus to the Clec9A antibody. The Clec9A antibody targets a specific subset of dendritic cells, a specialised type of immune cells found in tissues such as the skin, which are responsible for initiating immune responses in our body.

Upon a single shot immunisation of the Clec9A-RBD antibody construct, the team monitored the immune responses in pre-clinical models over 21 months, and found no signs of declined immunity. In contrast, it observed that the quality of the immune response (the neutralising antibody response, in particular), was associated with increased protection over time.

The study was published in *Molecular Therapy*, which is part of *Cell Press*.

This new Clec9A targeting technology may potentially address the issue of waning COVID-19 vaccine immunity, and eliminate the need for repeated booster jabs, particularly for people aged 60 and over, medically vulnerable individuals and their caregivers.

"The results that we see in this study are very promising, and we are confident that the work performed in pre-clinical models is highly translatable to humans," said Associate Professor Sylvie Alonso, Principal Investigator of this study. "Indeed, a human equivalent of this immune cell subset exists, and our collaborator, <u>Associate Professor Mireille Lahoud</u>, at Monash University is developing this approach towards future human application.

Associate Professor Lahoud said: "This study demonstrates the strength of our platform targeting specialised immune cells for vaccine improvement, and exemplifies the power of international research collaborations spanning basic discoveries to translational studies."

Current Messenger RNA (mRNA) COVID-19 vaccines have been reported to demonstrate peak effectiveness of ¹62% after three weeks, post-jab, before declining to nine per cent after

nine months. Protection from booster doses has been reported to wane, dropping from ²60 per cent one month after the booster dose to 13 per cent at nine months.

"Our teams in NUS Medicine and Monash University foresee that the exceptional durability of the immune responses induced by the Clec9A targeting technology, when used as a booster vaccine strategy, may address the shortcoming of current mRNA vaccines, chief of which is the rapid waning of immune responses," Associate Professor Alonso, who is also co-Director of the Infectious Diseases Translational Research Programme at NUS Medicine said.

"We are now evaluating our vaccine candidate as a booster vaccine in mRNA-vaccinated preclinical models. We hope to demonstrate that this booster approach will induce long-term protective immunity, and avoid the need of multiple (annual) booster shots.

"Beyond COVID19, this versatile, rapidly-deployable vaccine platform shows promising potential to be part of the pandemic response against Disease X caused by an unknown pathogen in the future."

This latest breakthrough follows closely on the heels of the team's 2022 research, published in the <u>Proceedings of the National Academy of Sciences of the United States of America</u> (PNAS). Back then, it leveraged on the Clec9A targeting vaccine platform to deliver the universal influenza vaccine candidate M2e.

M2e is notoriously known to be unable to induce strong and durable immune responses. The team demonstrated that a single-shot immunisation of the Clec9A-M2e construct triggered long-lasting immune responses to effectively protect against multiple strains of the flu. It effectively removes a major bottleneck in the clinical development of M2e-based vaccine candidates.

Read the new paper in *Molecular Therapy*, titled: Single-shot dendritic cell targeting SARS-CoV-2 vaccine candidate induces broad, durable and protective systemic and mucosal immunity in mice.

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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 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 nus.edu.sg.

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 2024 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/.

About the Monash Biomedicine Discovery Institute at Monash University

Committed to making the discoveries that will relieve the future burden of disease, the newly established Monash Biomedicine Discovery Institute at Monash University brings together

² Here's how long COVID-19 Vaccine Immunity Really Lasts https://time.com/6276552/covid-19-vaccine-immunity-wanes/.

more than 120 internationally-renowned research teams. Spanning seven discovery programs across Cancer, Cardiovascular Disease, Development and Stem Cells, Infection, Immunity, Metabolic Disease and Obesity, and Neuroscience, Monash BDI is one of the largest biomedical research institutes in Australia. Our researchers are supported by world-class technology and infrastructure, and partner with industry, clinicians and researchers internationally to enhance lives through discovery.