



PRESS RELEASE

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Mother's antibodies may worsen dengue infection in children

Vaccines inducing T-cell response can better fight dengue

Singapore, 24 January 2018 — A dengue vaccine that stimulates a strong T cell response in babies has been found to provide better and broader protection than vaccines which induce the production of mainly antibodies. An NUS research team that made this finding also found that a mother's antibodies which help to protect her babies against dengue virus infection can also be detrimental in some situations, as these maternal antibodies can enhance the severity of dengue infection in babies or interfere with their immunisation.

These discoveries were made by a team led by Associate Professor Sylvie Alonso from the Department of Microbiology and Immunology at the NUS Yong Loo Lin School of Medicine (NUS Medicine). The study was published in the scientific journal *JCI Insight* (<https://insight.jci.org/articles/view/94500>) on 21 December 2017.

The researchers' findings show that maternal antibodies which circulate in babies born to dengue vaccinated mothers can protect against dengue only if the infecting dengue strain is very similar to the strain that is present in the vaccine. However, maternal antibodies will not be able to protect against a dengue strain that is different from the strain used in the vaccine. And in fact, they may make the disease even worse.

In addition, the team has generated experimental evidence which indicates that maternal antibodies can interfere with the baby's vaccination. That is when antibody production will be completely prevented (a phenomenon known as "maternal antibody interference").

However, vaccination of babies born to dengue vaccinated mothers will still be able to induce a T cell response, the other arm of our immune system. A/Prof Alonso and her team showed that this T cell response is able to protect against dengue, even when the infecting strain is different from that used in the vaccine.

These findings therefore show that a dengue vaccine which induces an effective killer T cell response could provide better and broader protection for children born to vaccinated mothers, than vaccines which rely mainly on antibodies, such as Dengvaxia, the only dengue vaccine that is currently on the market.

The impact of these findings on vaccination strategies in humans is significant, as more children are born to mothers who have been vaccinated against dengue infection.

“We hope that our work will further convince the dengue vaccine community that it is of utmost importance to include a protective T cell response in their vaccine design. Too many efforts are currently being devoted to looking at an antibody-mediated protection while the T-cell responses are being overlooked,” said A/Prof Alonso.

She added, “We hope that the team currently taking care of the clinical development of the DENVax candidate will measure the T cell responses in the vaccines. Lastly, we hope that our work will entice clinical trial teams to include monitoring of children born to vaccinated mothers as well as vaccination efficacy in these children.”

Commenting on the importance of these findings, Professor Paul Anantharajah Tambyah, Senior Consultant at the National University Hospital’s Division of Infectious Diseases said, “These findings are very interesting because they help us to better understand the role that the different parts of our immune system play in our response to dengue and other viral infections. They emphasise the fact that we cannot just look at one measure (for example the antibody levels) but need to comprehensively ensure that individuals who are vaccinated by any candidate vaccine are truly protected from infection. It would be unfortunate if a vaccine actually made the situation worse by triggering off one part of the immune system to over-react instead of completely eliminating the virus.”

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A leading global university centred in Asia, the National University of Singapore (NUS) is Singapore's flagship university, which offers a global approach to education and research, with a focus on Asian perspectives and expertise.

NUS has 17 faculties and schools across three campuses. Its transformative education includes a broad-based curriculum underscored by multidisciplinary courses and cross-faculty enrichment. Over 38,000 students from 100 countries enrich the community with their diverse social and cultural perspectives. NUS also strives to create a supportive and innovative environment to promote creative enterprise within its community.

NUS takes an integrated and multidisciplinary approach to research, working with partners from industry, government and academia, to address crucial and complex issues relevant to Asia and the world. Researchers in NUS' Schools and Faculties, 30 university-level research institutes and centres, and Research Centres of Excellence cover a wide range of themes including: energy, environmental and urban sustainability; treatment and prevention of diseases common among Asians; active ageing; advanced materials; risk management and resilience of financial systems. The University's latest research focus is to use data science, operations research and cybersecurity to support Singapore's Smart Nation initiative.

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

Established in 1905, the NUS Yong Loo Lin School of Medicine is the first institution of higher learning in Singapore and the genesis of the National University of Singapore.

The School offers one of the finest undergraduate medical programmes in the Asia Pacific region and enjoys international recognition and respect. The Times Higher Education World University Rankings 2016 by subject and Quacquarelli Symonds (QS) World University Rankings by Subject 2017 list NUS Medicine as a leading medical school in Asia.

It admits 300 students to the MBBS degree programme annually and its principal missions are to educate and train the next generation of healthcare professionals, and foster research that will help to advance the practice of medicine.

The 18 NUS Medicine departments in the basic sciences and clinical specialties work closely with the Centre for Medical Education, the Centre for Biomedical Ethics, the Centre for Healthcare Simulation as well as the restructured public hospitals to ensure that teaching and research are aligned and relevant to Singapore's healthcare needs. The School is a founding institutional member of the National University Health System.

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