



PRESS RELEASE

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NUS scientists crack mystery of flu transmission

Virus hijacks respiratory cell proteins to incubate and multiply

Singapore, 28 March 2018 — New and more effective flu medicines may be in the offing, thanks to the National University of Singapore (NUS) scientists' discovery of how the virus is able to infect people.

The finding by the multidisciplinary team from the NUS Yong Loo Lin School of Medicine was published online in the December 2017 issue of the *Journal of Allergy and Clinical Immunology*. The team showed that flu viruses can hijack a unique class of proteins which are part of the body's (host) respiratory cellular machinery. Using the protein called CD151, the viruses clone and multiply before invading and colonising new victims. Along the way, they promote their own survival and multiply further in the bodies of infected individuals.

The work that led to the uncovering of flu viruses' modus operandi was led by Assistant Professor Thai Tran from the Department of Physiology, Professor Wang De Yun from the Department of Otolaryngology and Associate Professor Vincent Chow from the Department of Microbiology and Immunology. It takes medical science a step closer to the holy grail of influenza research – the development of a potent prevention and treatment strategy that works against a broad spectrum of virus strains, and whose effectiveness and potency overwhelm viral resistance through all flu seasons.

Fighting the flu – current approaches today

According to the World Health Organization, the flu affects approximately 1 billion people annually, three to five million of these severely. As many as 650,000 people die from the flu each year. Like other viruses, the flu virus relies on the host's resources or machinery for its infection, replication (making more copies of the virus), export and transmission.

Currently, because the virus changes its outer coat frequently, vaccine developments are based on predicting the key proteins on the outside of the flu virus months in advance and blocking (neutralising) these proteins so they cannot bind to host cells. In other words, current strategies try to find the "best match" for a particular flu season. However, since the flu virus may mutate frequently every few months, the "best match" strategy has obvious limitations.

Other treatment strategies such as oseltamivir (Tamiflu) work by inhibiting replication of the virus. However, they are only effective if given early in the infection. Worse, if these agents are overused, the flu virus can become resistant to them.

Fighting the flu – the next wave

This is why an approach which involves shifting the focus away from the virus and towards its host has enabled the NUS team to home in on the host elements critical for the virus life cycle. In doing so, the researchers believe they may have found a way to stop the flu bug in its tracks.

Using this approach, the NUS team found that the virus hijacks a protein on the nucleus of host respiratory cells called CD151 and uses it to export newly made viral material out of the nucleus, in order to form new viruses that can then infect other cells.

Using both human cells and preclinical models of the flu, the NUS investigators showed that blocking CD151 slows down the formation of new flu viruses, allowing the host sufficient time to mount a strong immune response to fight and recover from the infection more effectively. At the same time, this approach does not provoke an overly exaggerated immune response, which could trigger complications such as asthma or respiratory failure. CD151 blockers could thus act as broad-spectrum antivirals to complement current approaches against the flu virus.

“This newly discovered signalling pathway is conserved across H1N1 and H3N2 flu strains, which are the most prevalent circulating subtypes in humans, making this finding exciting as the development of CD151 blockers to stop the virus life cycle would negate the need for surveillance of circulating viruses each year,” explained Asst Prof Tran, the lead investigator of the study. The research was supported by grants from the Ministry of Education and the National Medical Research Council.

The finding spells fresh hope for flu fighters like Professor Paul Tambyah, Senior Consultant at the National University Hospital’s Division of Infectious Diseases. “This is a very promising discovery as our current range of drugs available for the treatment of influenza is very limited. If this leads to a new class of drugs which can be used to treat influenza and its complications, it will be a great step forward in efforts to not only treat common (seasonal) flu but also prepare for a flu pandemic,” he said.

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About the National University of Singapore (NUS)

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.

For more information on NUS, please visit www.nus.edu.sg.

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.

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