PRESS RELEASE

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Nano-sized cell particles are promising intervention tool in treating infectious diseases

In a study led by researchers at the NUS Yong Loo Lin School of Medicine, extracellular vesicles were found to inhibit the viral infection of COVID-19 and potentially other infectious diseases

Singapore, 28 November 2023—The COVID-19 pandemic demonstrated the importance of being prepared with drug interventions to contain viral outbreaks that can otherwise have devastating consequences. In preparing for the next pandemic—or Disease X, there is an urgent need for versatile platform technologies that could be repurposed upon short notice, to combat infectious outbreaks.

A team of researchers, led by **Assistant Professor Minh Le from the Institute for Digital Medicine (WisDM) and Department of Pharmacology at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)**, discovered that nano-sized particles released by cells, termed "extracellular vesicles" (EVs), can curb the viral infectivity of SARS-CoV-2—its wild type and variant strains—and potentially other infectious diseases. Asst Prof Le said, "Our study showed that these cell-derived nanoparticles are effective carriers of drugs that target viral genes precisely. These EVs are therefore an efficient tool for therapeutic intervention in patients who are infected with COVID-19 or other infectious diseases."

The study, conducted in collaboration with NUS Medicine's Biosafety Level 3 (BSL3) Core Facility, the Cancer Science Institute of Singapore, and the School of Physical and Mathematical Sciences at Nanyang Technological University (NTU), demonstrated potent inhibition of COVID-19 infection in laboratory models using a combination of EV-based inhibition and anti-sense RNA therapy mediated by *antisense oligonucleotides* (ASOs). A versatile tool that can be applied to any gene of interest, ASOs can recognise and bind to complementary regions of target RNA molecules and induce their inhibition and degradation.

In the study, published in *ACS Nano*, the authors utilised human red blood cell-derived EVs to deliver ASOs to key sites infected with SARS-CoV-2, resulting in efficient suppression of SARS-CoV-2 infection and replication. The researchers also discovered that EVs exhibited distinct antiviral properties, capable of inhibiting phosphatidylserine (PS) receptor-mediated pathways of viral infection—a key pathway utilised by many viruses to facilitate viral infection. These viral inhibitory mechanisms were applicable to multiple variants of SARS-CoV-2, including the Delta and Omicron strains, ensuring their broad effectiveness against SARS-CoV-2 infection.

The results from the study point to anti-sense RNA therapy with ASOs as a potentially effective approach that could serve to combat future viral outbreaks. The platform that was developed to deliver ASOs through EVs to target the SARS-CoV-2 viral genes can be readily applied to treat other viral infections by replacing the ASO sequences with those complementary to the target viral genes. Asst Prof Le and her graduate students Migara Jay and Gao Chang, the first authors of the study, are currently developing more potent combinations of ASOs with the help of artificial intelligence prediction models to achieve enhanced viral inhibition. This collaborative effort includes partnership with the research teams of Associate Professor Edward Chow from WisDM, NUS Medicine, and NUS Medicine's BSL3 Core Facility.

Associate Professor Justin Chu, Director of the BSL3 Core Facility at NUS Medicine, and co-author of the study, added, "This remarkable extracellular vesicle-based delivery platform technology coupled with anti-viral therapy is highly promising to combat a broad range of viruses and even Disease X." The latter is a general description for emerging and unknown infectious threats, such as novel coronaviruses. The term was used to alert and encourage the development of platform technologies, including vaccines, drug therapies and diagnostic tests, which could be quickly customised and then deployed against future epidemic and pandemic outbreaks. Assoc Prof Chu is also from the Infectious Diseases Translational Research Programme at NUS Medicine.

Professor Dean Ho, Provost's Chair Professor and Director of WisDM at NUS Medicine, said, "This work brings the scalable and well-tolerated extracellular vesicle-based drug delivery platform an important step closer towards clinical validation studies."

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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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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 Asia's leading medical schools 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 2023).

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