

PRESS RELEASE

Particles released by red blood cells are effective carriers for anti-cancer immunotherapy: Singapore study

A study demonstrated that vesicles released by red blood cells are a viable platform for delivering immunotherapeutic RNA molecules to suppress breast cancer growth and metastasis

Singapore, 19 April 2022— In the fight against cancer, the development of efficacious drugs is only half the battle; equally important is how drugs may be delivered efficiently and safely to the diseased sites in the body. The challenge of drug delivery is especially pertinent for RNA therapeutics which target an important immuno-modulatory receptor, RIG-I. When activated by certain types of RNAs, the receptor can initiate immune responses to kill cancer cells. As RNAs are unstable and fragile by nature, RNA-based drugs must be packaged in suitable carriers to prevent degradation, and promote efficient uptake by target cancer tissues.

A study led by researchers at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine)—in collaboration with the Lee Kong Chian School of Medicine, Nanyang Technology University, Singapore (LKC Medicine, NTU Singapore) and A*STAR's Genome Institute of Singapore (GIS)—demonstrated that nano-sized vesicles released by red blood cells are a viable platform for delivering immunotherapeutic RNA molecules to suppress breast cancer growth and metastasis. Published in the *Journal of Extracellular Vesicles*, the study successfully delivered RIG-I-activating RNAs using small, lipid membrane-bound particles released by red blood cells, called red blood cell extracellular vesicles (RBCEVs), to suppress cancer progression. The team had also discovered in earlier studies that these vesicles are ideal therapeutic carriers with a natural ability to deliver bioactive molecules to many cell types.

Assistant Professor Minh Le from the Institute for Digital Medicine (WisDM) and Department of Pharmacology at NUS Medicine, who led the study, explained, “With the discovery of these vesicles’ ability to deliver therapeutics effectively to targeted receptors, we hope that our research can lead to better treatment outcomes for cancer patients. The correct homing of the therapeutics to diseased cells is also critical in minimising off-target effects that can result in toxicity.”

For the study, two novel RNA molecules were developed at LKC Medicine, and packaged into RBCEVs to activate the RIG-I pathway, induce cell death in breast cancer cell cultures, and suppress tumour growth in laboratory models with breast cancer. The team also engineered RBCEVs to improve their specificity of homing towards metastatic cells that took hold in the

lungs. Associate Professor Luo Dahai, Associate Professor of Infection and Immunity at LKCMedicine, said, “Asst Prof Le’s RBCEV technology can overcome several hurdles related to therapeutic RNA delivery and unleash the anticancer potential of our immunomodulatory RNA (immRNA). I am thrilled to see the success of our collaboration.”

Dr Tam Wai Leong, Group Leader and Associate Director at GIS, one of the collaborators of the study, added, “The promising results highlight two key strengths of this innovative platform—the capacity for efficient delivery of different therapeutic cargoes, as well as the possibility for genetic modifications to enhance targeting to more cancer types.”

To further examine the function of RBCEVs in carrying a broader range of therapeutics to more cancer cell types, the team plans to conduct further research in collaboration with the National University Cancer Institute and Cancer Science Institute of Singapore. Concurrently, RBCEV technologies are under intensive research at Carmine Therapeutics, an EVX Ventures company which aims to develop the next generation of gene therapy based on RBCEVs for treatments of rare diseases and cancer. “We hope to expand the therapeutic value of the RBCEV platform to more cancer types and increase the reach of such novel forms of therapy to benefit more cancer patients,” said Asst Prof Minh Le, who is also one of the co-founders of the company.

Professor Dean Ho, Director of WisDM, added, “Our team at WisDM is committed to bridging medical innovation with clinically-relevant impact. The findings by Asst Prof Le and collaborators represent major advances in RNA-based therapy and nanomedicine that can be realised through multidisciplinary ecosystems.”

WisDM is one of ten Translational Research Programmes at NUS Medicine aimed at creating a strong and coherent scientific base to deliver impactful and meaningful research outcomes for the School and Singapore’s health system.

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About the 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 17 faculties 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 our NUS Overseas Colleges programme in more than 15 cities 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, 30 university-level research institutes, research centres of excellence and corporate labs 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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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, 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 2022 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2021).

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