

PRESS RELEASE

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Modified nano-sized cell particles boost cancer immunotherapy, reduce side effects: NUS Medicine study

Singapore, 16 September 2024—Immunotherapy is a type of cancer treatment that uses the body's own immune system to help fight cancer. It works by stimulating the immune response to recognise and attack cancer cells more effectively. The treatment involves using substances that boost the immune system, teaching immune cells to target cancer, or using engineered cells to specifically target and kill cancer cells. While it is a key approach in cancer treatment, the effectiveness of immunotherapy is limited by the risk of immune-related side effects, because the immune system, while targeting cancer cells, may also attack normal, healthy tissues. These side effects include inflammation or damage to various organs and tissues, causing a range of symptoms or complications in health outcomes.

A team 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)** has unveiled a novel delivery platform that significantly enhances the effectiveness of cancer immunotherapy while reducing the associated side effects. This innovative approach, leveraging nano-sized particles released by cells, termed “extracellular vesicles” (EVs), represents a major advancement in the field of cancer immunotherapy.

In the study, the researchers developed a technique which modified EVs to carry multiple immune-boosting molecules called ‘immunomodulatory ligands’, for the treatment of in vivo models of metastatic pancreatic cancer and melanoma. The approach enhanced the therapeutic effectiveness of the ligands—particularly the subset Tumour Necrosis Factor Receptor Superfamily (TNFRSF) agonists, which are key in controlling immune responses against cancer. The team also found that the delivery method enhanced retention of the immune-boosting ligands in the tumour—allowing for better therapeutic effects to be achieved with lower drug doses, which in turn reduced the risk of side effects that are often seen in current immunotherapeutic treatments.

Published in *Molecular Therapy*, the study demonstrates that the new EV-based delivery approach can alter the tumour’s immune composition to improve treatment outcomes of patients with cancer. Notably, the approach was consistently proven to show better outcomes in terms of tumour-specific immune activation, suppression of tumour burden, overall survival and resistance to tumour rechallenge (or recurrence), compared to the current clinical standard of care, whereby the ligands are administered in their free soluble form without the EV-based delivery platform. This is remarkable as it indicates that the EV-based delivery

approach is able to enhance the treatment of existing tumours and prevent the recurrence of the same cancer in the future via the development of tumour-specific immune memory.

Asst Prof Minh Le said, “We are thrilled to present this novel EV-based delivery system that not only enhances the therapeutic efficacy of immunomodulatory ligands but also significantly reduces systemic toxicity. Our findings pave the way for safer and more effective cancer immunotherapies, potentially transforming the landscape of cancer treatment.”

The first author of the study, **Dr Migara Jayasinghe from WisDM and the Department of Pharmacology at NUS Medicine**, added, “This new delivery platform holds great potential to improve both the effectiveness and safety of current immunotherapies, which often have limited results and major side effects. It also enables the development of advanced treatments that can more precisely target cancer cells while protecting healthy tissues.”

The findings of this study have been patented and the research group is now working on advancing this technology to further enhance the broader application of immunotherapeutic ligand-based therapies. Alongside plans to establish a clinical stage start-up, the technologies developed through this study will be commercialised to facilitate access for other researchers in the field and related disciplines.

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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.

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

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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 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 2023).

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