PRESS RELEASE

Metastatic cancers: How targeting a protein that fuels treatment-resistant tumours may be key to better outcomes

Singapore, 4 February 2025—One of the biggest challenges in cancer treatment is addressing the ability of cancer cells to adapt and become resistant, reducing the effectiveness of therapies over time. While treatments like chemotherapy or targeted therapies may initially shrink tumours, they often lose their effectiveness after a period. This resistance often emerges in metastatic tumours, because cancer cells can evolve in ways that allow them to survive, such as developing new ways to communicate with one another.

Seeking ways to help patients whose cancers no longer respond to treatment, a team from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), researched how tiny particles released by cancer cells, known as tumour-derived extracellular vesicles (TDEs), communicate with surrounding cells and induce resistance in cancer cells. Led by Professor Goh Boon Cher, Deputy Director of the NUS Centre for Cancer Research (N2CR) at NUS Medicine, and Professor Shazib Pervaiz who is also from the N2CR, the team found that blocking a certain protein, SLC1A5, led to more effective treatment of lung cancer.

Prof Goh said, “The discovery offers a new way to tackle one of the biggest challenges in cancer treatment: resistance to therapy. By targeting the proteins which make it easier for cancer cells to survive when treatments are trying to kill them, doctors could improve existing treatments and create more personalised approaches for patients whose cancers have stopped responding.” Prof Goh is also Deputy Director of the Cancer Science Institute of Singapore (CSI Singapore) at NUS and a Senior Consultant in the Department of Haematology-Oncology at the National University Cancer Institute, Singapore (NCIS).

Published in the journal *Theranostics*, the study involved the use of 161 plasma samples, obtained from 103 patients with lung cancer of different stages, and 58 healthy individuals from the National University Hospital and NCIS. TDEs were isolated from these plasma samples, and their protein levels were analysed in the laboratory. Results showed that SLC1A5 levels are significantly higher in late-stage treatment-resistant tumours from the plasma samples of 62 patients, compared to early-stage sensitive tumours, with a p-value of less than 0.0001. These indicate that high levels of this protein in TDEs are associated with increased resistance to cancer treatment.

The protein is also a glutamine transporter that helps move glutamine into cells, providing them with the nutrients needed for growth and energy, especially in rapidly dividing cancer cells. In the laboratory experiments where the protein was blocked using pharmacological inhibitors or silencing SLC1A5 in the TDEs, treatment of the cancer cells was found to be significantly more effective. The experiments, led by Assistant Professor Eliza Fong, a collaborator from CSI Singapore, The N.1 Institute for Health, and Department of Biomedical Engineering under the College of Design and Engineering at NUS, showed that tumours resistant to treatment exhibit elevated levels of SLC1A5. As glutamine fuels cancer cells with energy, enabling their growth and resistance to treatment, blocking its intake can enhance the effectiveness of cancer treatments.

Prof Pervaiz added, “Our study highlights how tumour-derived extracellular vesicles contribute to cancer drug resistance by transferring proteins like SLC1A5, which alter energy use in cancer cells, making them harder to treat. By breaking the communication network through blocking SLC1A5, we could help patients regain the benefits of therapy—and potentially increase chances of recovery from cancer.”

SLC1A5 levels could thus be used as a potential biomarker to detect resistance early and guide treatment decisions, added the study’s first author, Dr Jayshree Hirpara from CSI Singapore. “We also hope to understand better how tumour-derived extracellular vesicles and the SLC1A5 protein affect different cancer types, to provide new insights for more effective treatments. Having this mechanism in place, we need to develop treatments to overcome the transfer of SLC1A5 in the laboratory before considering clinical trials.”

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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 the leading medical schools in Asia and ranks among the best in the world (Times Higher Education World University Rankings 2025 by subject and the Quacquarelli Symonds (QS) World University Rankings by subject 2024).

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About the National Medical Research Council (NMRC)

The NMRC was established in 1994 to oversee research funding from the Ministry of Health and support the development and advancement of biomedical research in Singapore, particularly in the public healthcare clusters and medical schools. NMRC engages in research strategy and planning, provides funding to support competitive research grants and core research enablers, and is responsible for the development of clinician scientists through awards and fellowships. The council's work is supported by the NMRC Office which is part of MOH Holdings Pte Ltd. Through its management of the various funding initiatives, NMRC promotes healthcare research in Singapore, for better health and economic outcomes.