PRESS RELEASE

NUS researchers discover protein that promotes chemotherapy resistance

Singapore, 27 April 2021 — Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cancer cells in the body. It is a systemic treatment where drugs travel throughout the body and destroy cancer cells that have spread (metastasized) to parts of the body far away from the original (primary) tumour. As such, chemotherapy remains the main treatment against various cancers. Thus, when cancer cells resist chemotherapeutic drugs, treatment failure results.

The resistance of cancer cells to chemotherapy is marked by changes and increased output of certain proteins. These altered proteins can help doctors to identify patients who will not respond well to chemotherapy and paves the way for the development of therapeutic intervention to "re-sensitise" their cancer cells to treatment.

In a *Nature Communications* article published mid-April, Associate Professor Zhang Yongliang from NUS Yong Loo Lin School of Medicine's Immunology Translational Research Programme reported the finding of one such altered protein in a study that identified how a molecule called DUSP16 plays an important role in a cancer patient's response to chemotherapeutic drugs.

Assoc Prof Zhang and his study team, in collaboration with clinical scientists including the team led by Professor Goh Boon Cher, Deputy Director of both the Cancer Science Institute of Singapore at NUS and NUS Center for Cancer Research (N2CR), found that an increased expression of DUSP16 led to resistance from cancer cells to chemotherapy in colorectal, nasopharyngeal, gastric and breast cancer. Prof Goh's team studies mainly cancers of the upper aerodigestive tracts (of the head and neck and lung), which are among the most frequent cancers, and seeks to understand these diseases.

These four cancers are among the most common and deadly ones affecting Singaporeans and Southeast Asians. Nasopharyngeal cancer has a high incidence rate in Southeast Asians, while colorectal cancer is the most frequently occurring cancer in Singapore. Breast cancer is the cancer with the highest incidence among women in Singapore and gastric cancer is among the top three cancers causing death worldwide. In addition, the fact that these four cancers manifest as solid tumours with chemotherapy being a common form of post-operative treatment meant that they made for good candidates for the study.

Analysis of head and neck cancer patients, and breast cancer patients showed that those with higher DUSP16 expression in their cancer cells lived for significantly shorter periods compared to patients with lower levels of DUSP16. DUSP16 expression can thus be used as a biomarker for sensitivity of cancer patients to chemotherapy, which will be important for clinicians seeking to design suitable treatment, said Assoc Prof Zhang. This molecule could also be targeted for the development of new therapies to improve the success of chemotherapy treatment. While

this discovery is not only relevant to these four types of cancer, more research would be needed to examine other cancer types.

The study also found that chemotherapy drugs are a factor in the increased expression of DUSP16. This means that once chemotherapy begins, the expression of DUSP16 will increase in patients, Assoc Prof Zhang added. In addition, other factors such as stress or infections have also caused increased expression of DUSP16.

While there are no alternative treatments that might be effective in cancer patients who test positive for the increased expression of DUSP16, Assoc Prof Zhang and his team are planning to conduct further research to identify molecules and drugs that can reduce DUSP16 levels in patients.

The NUS Medicine Immunology Translational Research Programme aims to understand the role of the immune system in health and diseases. The programme strives to enable the discovery and development of more effective immunotherapy, new treatment guidelines and diagnostic tests for patients with disease-specific problems such as autoimmune and airway diseases, cancer, chronic inflammation, infections and organ/ tissue transplantation. These goals are to be achieved by fostering collaborative research and advancing latest technologies to probe immunological mechanisms, and enhancing infrastructure for clinical translation.

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 common among Asians; active ageing; advanced materials; as well as risk management and resilience of financial systems. Our latest research focus is on the use of 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)

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 Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

For more information about NUS Medicine, please visit https://medicine.nus.edu.sg/