



PRESS RELEASE

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NUS Medicine study discovers potential for new colorectal cancer treatment

The possibility of a new therapy for colorectal cancer could be achieved by blocking DUSP6, a protein that is important for cell growth, survival, and repair.

Singapore, 15 January 2025 – Colorectal cancer (CRC) is a type of cancer that begins in the colon (large intestine) or rectum, which are parts of the digestive system. It typically starts as abnormal growths called polyps that form in the lining of the colon or rectum. Over time, some of these polyps can become cancerous if left untreated. CRC is one of the most common cancers in Singapore, with an average of about 2,540 cases a year, and it is also one of the top cancers contributing to cancer mortality in Singapore. It is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases according to the reports from World Health Organization (WHO). Issues including cancer recurrence and development of drug resistance pose a significant challenge in CRC treatment, highlighting the need for new therapeutic methods.

Researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) have made a discovery that could change how CRC is treated. Their study, published in [Nature Communications](#), has revealed that a molecule called Dual-Specificity Phosphatase 6 (DUSP6) plays a major role in helping CRC grow. The CRC cells with higher DUSP6 tested in this study proliferate approximately 40% more than those with lower DUSP6 levels. In patients with CRC, elevated DUSP6 levels are associated with a poorer prognosis and decreased survival compared to patients with lower DUSP6 levels (p value = 0.029).

DUSP6 is a type of protein called a phosphatase that acts like a "switch-off" mechanism for specific signalling pathways inside cells. Its main function is to control the ERK1/2 MAPK pathway, which is important for cell growth, survival, and repair. Under normal circumstances, DUSP6 deactivates ERK1/2, preventing excessive cell growth or signalling. In some cancers, such as lung and skin cancers, DUSP6 acts as a tumour suppressor, helping to stop cancer growth. In other cancers however, such as CRC, DUSP6 has the opposite effect and promotes tumour growth.

The research was led by Associate Professor Zhang Yongliang, from the Department of Microbiology & Immunology, and Immunology Translational Research Programme (TRP), NUS Medicine. A/Prof Zhang said, "In CRC, higher levels of DUSP6 have been found in tumours, where it helps cancer cells grow faster, spread more easily, and leads to poorer outcomes for patients. This unexpected role highlights why DUSP6 is now seen as a possible target for new treatments. Our research not only explains why some colon cancers are so aggressive, but also gives us a clear target to develop new treatments."

The study found that DUSP6 protects cancer cells by inhibiting a process that normally destroys a key growth protein called Notch1—a protein that acts like a cellular communicator, helping cells decide what to do, such as grow, divide, or take on specific roles. It is part of the Notch signalling pathway, which is crucial during early development and in maintaining healthy tissues. Notch1 becomes active when it interacts with specific proteins on neighbouring cells. This triggers a series of "cuts" in the protein, releasing the Notch1 intracellular domain (NICD). NICD travels to the nucleus, where it switches on genes that drive cell growth, division, and survival. When Notch1 is overactive or stabilised, it can cause uncontrolled cell growth and contribute to cancer. In CRC, high levels of active Notch1 are linked to a poorer prognosis because it drives tumour growth and helps cancer cells survive longer. To keep Notch1 activity in check, it must be *phosphorylated* (marked for destruction) and broken down by the cell's "recycling system." If this balance is disrupted, Notch1 can remain active for too long and promote cancer growth.

Associate Professor Veronique Angeli, Director of the Immunology TRP at NUS Medicine, and from the Department of Microbiology & Immunology, added, "In simpler terms, DUSP6 acts like a protector/controller for Notch1, stopping it from being broken down and allowing it to stay active for longer than it should. This leads to increased tumour cell growth, faster spread of cancer cells, and worse survival outcomes for patients with CRC."

The possibility of a new therapy for CRC could be achieved by blocking DUSP6. In laboratory models, researchers were able to significantly slow down tumour growth through blocking the protein. High levels of DUSP6 are linked to worse survival, so it could also be used to predict how aggressive a patient's cancer might be. While the study focused on CRC, the findings could also help in other cancers where DUSP6 plays a role.

The team will be looking at research to further understand the pathogenesis of CRC, and to develop DUSP6 targeted therapies for treatment of the cancer, to improve health outcomes for patients.

This research is supported by the National Research Foundation, Singapore under the National Medical Research Council (NMRC) Open Fund - Individual Research Grant (MOH-001218) and administered by the Singapore Ministry of Health through the NMRC Office, MOH Holdings Pte Ltd, and the National University Health System of Singapore (NUHSRO/2021/110/T1/Seed-Sep/03 to C.W.P.)

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About 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 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)

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 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).

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

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.