PRESS RELEASE

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NUS Medicine study identifies protein that could strengthen cancer-fighting T cells against colorectal cancer

NUS Medicine researchers found that DUSP4 helps immune cells retain their cancer-killing ability, and that increasing its activity improved CAR-T cell performance against colorectal tumours

Singapore, 4 November 2026 — The immune system has powerful cells that can recognise and destroy cancer, but this ability can gradually wane when the cells reside within a tumour. Researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), and their collaborators have identified a protein that could help keep these cancer-fighting immune cells active and potentially provide a new way to strengthen engineered T-cell therapies against colorectal cancer.

In a study published in *Nature Communications*, the research team led by Associate Professor Zhang Yongliang, Department of Microbiology and Immunology, and Immunology Translational Research Programme (TRP), NUS Medicine, found that a protein called dual-specificity phosphatase 4 (DUSP4) helps CD8+ T cells, a type of immune cell that can directly kill cancer cells, maintain their anti-tumour function. When DUSP4 was absent, these cells became less effective and showed more signs of exhaustion, while laboratory models developed a greater colorectal tumour burden.

The researchers also explored whether DUSP4 could improve CAR-T therapy, in which T cells are genetically engineered to recognise cancer cells. In laboratory models, increasing DUSP4 activity helped CAR-T cells multiply more readily and kill colorectal cancer cells more effectively. This is important because CD8+ T cells can become “exhausted” within tumours, gradually losing their ability to multiply and attack cancer—a major challenge for immunotherapies targeting solid tumours.

To investigate DUSP4’s role, the team combined clinical data from colorectal cancer patients with experiments using human cells and preclinical models. Models lacking DUSP4 developed more and larger colorectal tumours and showed weaker CD8+ T-cell responses. These cells produced fewer cancer-killing molecules and showed more signs of exhaustion, suggesting that DUSP4 helps preserve their anti-tumour function. They then analysed tumour tissue from 105 colorectal cancer patients. Lower DUSP4 levels were associated with poorer overall survival, with a similar trend seen in an independent dataset. The findings suggest that DUSP4 mainly supports immune cells rather than directly slowing cancer cell growth: removing DUSP4 from cancer cells had little effect, while its loss in blood-forming cells weakened CD8+

T-cell responses and increased tumour development in preclinical models. They were able to identify how DUSP4 works—it helps regulate a signalling pathway involving ERK2 and KLF2. Without enough DUSP4, increased ERK2 activity raises KLF2 levels, which suppresses the genetic programmes CD8+ T cells use to kill cancer cells. By keeping this pathway in check, DUSP4 helps T cells remain active.

Assoc Prof Zhang said, “CD8+ T cells are among the immune system’s main weapons against cancer, but prolonged exposure to tumours can gradually weaken their ability to function. Our findings suggest that DUSP4 helps keep these cells in a state where they can continue to multiply and attack cancer cells effectively.”

The researchers next explored whether this knowledge could be used to improve CAR-T therapy, in which a patient’s T cells are genetically engineered to recognise cancer cells. Using CRISPR activation, or CRISPRa, the team increased DUSP4 activity in human CAR-T cells. Compared with standard CAR-T cells, the DUSP4-enhanced cells multiplied more readily and showed greater cancer-killing activity against colorectal cancer cells in laboratory experiments. In laboratory models, treatment with these cells also resulted in smaller and lighter tumours than treatment with standard CAR-T cells.

Professor Nicholas R.J. Gascoigne, Department of Microbiology and Immunology, and Immunology TRP, NUS Medicine, said, “By increasing DUSP4 activity, we were able to improve both the growth and cancer-killing capacity of CAR-T cells in our experimental models. This gives us a potential strategy for engineering T cells that are better able to maintain their function in the difficult environment of solid tumours.” Prof Gascoigne is also a professor at the Immunology Center of Georgia and Georgia Cancer Center, Augusta University, USA.

While the results of the study are promising, the researchers cautioned that the CAR-T findings remain at a preclinical stage. The colorectal cancer cells used in the CAR-T model were engineered to carry CD19, the target recognised by the CAR-T cells, and further studies are needed to evaluate the approach clinically. The team will next investigate how DUSP4 itself is regulated within tumours, identify other molecules through which it controls T-cell function, and explore ways of enhancing DUSP4 activity in engineered T cells. Ultimately, they hope the work could contribute to new approaches for improving T cell-based immunotherapies for colorectal cancer and other solid tumours.

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For media enquiries, please contact:
Shaun YEE
Senior Executive, Communications
Yong Loo Lin School of Medicine,
National University of Singapore
Email: shaun.yee@nus.edu.sg

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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, 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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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 in 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 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 2026 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2026).

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