NEWS RELEASE

Singapore, 3 Sep 2026

NTU Singapore scientists develop microdroplets that can reduce colorectal tumour growth at potentially lower cost

Scientists from **Nanyang Technological University, Singapore (NTU Singapore)** have developed microscopic peptide droplets that deliver large amounts of gene-silencing molecules into cancer and immune cells, reducing the growth of hard-to-treat colorectal tumours by about 67 per cent in mice.

The **patent-pending system** uses small interfering RNA, or siRNA, to disrupt the production of two proteins that cancer cells exploit to evade attacks by the immune system.

In the animal study, the combined siRNA treatment suppressed tumour growth to a level comparable to a combination of anti-PD-1 and anti-PD-L1 antibody treatments used as a benchmark.

The researchers estimate that an siRNA-based approach could potentially cost five to 10 times less to produce than monoclonal antibody treatments if successfully developed and scaled up.

Published in the peer-reviewed scientific journal *Biomaterials*, the study was led by **Professor Ali Miserez**, from NTU's **School of Materials Science and Engineering (MSE)** and **School of Biological Sciences (SBS)**, in collaboration with **Assistant Professor Bertrand Czarny,** who holds a **joint** position at **MSE** and the **NTU Lee Kong Chian School of Medicine**.

Stopping cancer cells from giving a false "handshake"

Their unique approach targets two proteins called PD-1 and PD-L1. PD-1 sits on the surface of T cells, which are immune cells that can recognise and kill abnormal cells. Whereas PD-L1 is displayed by tumour cells to trick T cells into a 'false handshake'.

When PD-1 and PD-L1 meet and bind, it sends a stop signal to the T cell, telling it to hold back its attack, thus allowing cancer cells to exploit this natural immune checkpoint to protect themselves.

Existing checkpoint immunotherapies use monoclonal antibodies to block this interaction from outside the cells.

The NTU approach goes one step further by reducing the amount of PD-1 and PD-L1 that the cells make in the first place, thus lowering their chances of interaction.

Cells typically make proteins by reading working genetic instructions carried by messenger RNA. The researchers used siRNA to recognise and destroy the specific instructions used to make PD-1 or PD-L1.

Prof Miserez, senior author of the study, explained: “Our approach works from inside both types of cells. The siRNA destroys the instructions they need to make these proteins. It is a little like throwing a spanner into a production line, except the disruption is targeted at the recipe for PD-1 or PD-L1.

“What is important about our microdroplets is that they can carry large amounts of siRNA into the cells where it needs to act. By targeting both sides of this handshake at the same time, we can help the immune cells attack the tumour more effectively.”

Two droplets, each with a different target

The researchers used **two separate peptide microdroplet formulations** together as a combination therapy.

One formulation, known as **siPD-1@THC**, carried siRNA against PD-1. Its surface was fitted with anti-CD3 antibodies, which helped the droplets enter T cells.

The second, **siPD-L1@HC**, carried siRNA against PD-L1 into colorectal cancer cells.

Once inside their respective cells, the two siRNAs reduced production of the checkpoint proteins.

Laboratory experiments showed that this increased T-cell activation and immune signalling and helped the T cells kill more colorectal cancer cells.

Commenting independently on the findings, **Professor Javier Montenegro García**, **Oportunius Research Professor at the Centre for Research in Biological Chemistry and Molecular Materials (CiQUS), University of Santiago de Compostela, Spain**, said: “The work by Prof Miserez and his colleagues is very

exciting. Their use of peptide microdroplets to deliver siRNA, while simultaneously targeting PD-1 and PD-L1, could have significant potential for cancer immunotherapy.

“Unlike antibodies, which block these receptors only while they remain bound, this approach can suppress the production of both proteins for a longer period. It could also simplify manufacturing and the translation of the technology by using a relatively straightforward RNA-peptide formulation.

“In addition, the liquid nature and physicochemical properties of these peptide droplets could support sustained release at the tumour site and improve penetration through the tumour microenvironment,” added Prof Montenegro García, whose internationally recognised research focuses on the intracellular delivery of RNA and other biomolecules.

A difficult test for immunotherapy

The researchers deliberately tested their approach against a model of **microsatellite-stable colorectal cancer**, or MSS colorectal cancer.

MSS tumours account for about 85 per cent of colorectal cancers, but immune checkpoint inhibitors that have transformed treatment for some other cancers have limited clinical benefit against this form of the disease. One reason is that these tumours tend to have relatively few cancer-killing T cells within them.

First author of the study, **NTU PhD student Ms Chen Zilin**, said they wanted to test the system against a colorectal cancer model where conventional checkpoint immunotherapy is facing challenges, rather than choosing a tumour that already responds well to it.

“Seeing tumour growth reduced by about 67 per cent, with a response comparable to the antibody treatment used as our benchmark, was very encouraging. It gives us a basis to investigate our platform further and we now hope to reproduce it in larger studies next.”

The findings are particularly relevant because colorectal cancer is one of the world’s most common cancers.

More than **1.9 million people were diagnosed in 2022**, and the disease causes more than **900,000 deaths a year**[1], making it the second leading cause of cancer death worldwide.

[1] International Agency for Research on Cancer. (2025, February 28). *IARC marks Colorectal Cancer Awareness Month 2025*. World Health Organization. https://www.iarc.who.int/news-events/iarc-marks-colorectal-cancer-awareness-month-2025/

In Singapore, **12,950 colorectal cancer cases** were diagnosed between 2019 and 2023[2]. It was the second most commonly diagnosed cancer in both men and women, accounting for about 16 per cent of cancers in men and 13 per cent in women.

Potential alternative to costly antibody treatments

Monoclonal antibodies that block immune checkpoints are large biological medicines that require specialised production and purification.

siRNA, by comparison, can be chemically synthesised and its sequence altered to target different genes.

The NTU researchers estimate that, if successfully translated into a treatment and manufactured at scale, their approach could potentially reduce manufacturing costs by about **five to 10 times** compared with monoclonal antibody-based immunotherapy.

Prof Miserez said: “An important advantage of siRNA is its programmability. Once there is an effective way of getting it into the right cells, changing the disease target can potentially be as straightforward as changing the RNA sequence.

“This could pave the way for a more flexible and potentially lower-cost approach than developing a new monoclonal antibody for every target.”

Packaging different payloads for other diseases

The peptide microdroplets could potentially offer an alternative to lipid nanoparticles, or LNPs, which are widely used to deliver RNA medicines. A key limitation of conventional LNPs is that only about 1 to 3 per cent of their RNA cargo typically escapes into the cell where it can act.

The NTU coacervates are designed to carry large RNA payloads and release them efficiently inside cells.

The team plans to test the platform in larger animal models to assess safety, dosing and how long the gene-silencing effect lasts.

As the siRNA cargo can be changed, the same platform could potentially be adapted to target other cancers and diseases.

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[2] National Registry of Diseases Office. (2026). *Singapore Cancer Registry annual report 2023*. Ministry of Health, Singapore. https://www.nrdo.gov.sg/docs/librariesprovider3/default-document-library/singapore-cancer-registry-annual-report-2023.pdf

Potential commercialisation efforts for NTU's coacervate technology are being supported by the **NTU Innovation and Entrepreneurship** initiative, with patent applications filed through **NTUitive**, the University's innovation and enterprise company.

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Note to Editor:

The paper titled **"Peptide Coacervate-Mediated siRNA Delivery for Dual PD-1/PD-L1 Blockade to Enhance Colorectal Cancer Immunotherapy"** was first published online in *Biomaterials* on 29 June 2026.
DOI: 10.1016/j.biomaterials.2026.124415

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