PRESS RELEASE

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NUS Medicine scientists develop swallowable nanocage for targeted gastric cancer therapy

Oral delivery platform is designed to protect therapeutic enzymes in the stomach and activate treatment selectively at tumour sites.

Singapore, 20 July 2026 — Researchers from the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine), have developed a swallowable nanoscale delivery platform designed to transport therapeutic enzymes through the stomach's acidic environment and activate a cancer-killing reaction at tumour sites. Early preclinical findings suggest that the approach may offer a new strategy for treating gastric cancer more precisely while reducing damage to healthy tissue.

The preclinical study, published in the *Journal of Nanobiotechnology*, was led by Associate Professor Chester Lee Drum, Department of Medicine and the Cardiovascular-Metabolic Disease Translational Research Programme (TRP), NUS Medicine, together with co-first authors Dr Muthu Kumaraswamy Shanmugam and Dr Girish Vallerinteavide Mavelli, both Senior Research Fellows at the Department of Medicine, NUS Medicine.

A nanocage built for the hostile gut

According to the Global Cancer Statistics, gastric cancer is the fifth most common cancer worldwide and the fourth leading cause of cancer-related death globally[1]. It remains one of the hardest cancers to treat, as it is often found late, can spread quickly, and may not always respond well to surgery or chemotherapy. One longstanding challenge has been how to deliver treatment directly to tumours in the stomach without degrading the therapy or affecting surrounding healthy tissue.

The acid and digestive enzymes in the stomach can break down fragile protein-based treatments before they reach their target. To overcome this, the team engineered disulfide-linked thermostable exoshells, or DS-tES, which are hollow protein nanocages about 15 nanometres in diameter, strengthened with carefully designed chemical links.

These reinforced exoshells are designed to survive stomach acid and protect their cargo until they reach gastric cancer tissue. Inside each nanocage, the team loaded horseradish peroxidase, or HRP, an enzyme that can trigger a specific chemical reaction. Once delivered

[1] Yang WJ, Zhao HP, Yu Y, Wang JH, Guo L, Liu JY, et al. Updates on global epidemiology, risk and prognostic factors of gastric cancer. *World J Gastroenterol. 2023*; 29(16): 2452–68.
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to gastric cancer cells, HRP helps convert indole-3-acetic acid, or IAA, a naturally occurring plant-derived compound, into active molecules with anti-cancer effects. As IAA is largely inactive on its own, and HRP is protected inside the exoshell during delivery, the system is designed to produce its cancer-killing effect at the disease site while reducing unnecessary exposure to healthy tissue.

Killing cancer through an unexpected door

Many cancer treatments work by triggering apoptosis, a common form of programmed cell death. However, some tumours can develop ways to resist this process. The team's approach instead activates necroptosis, another regulated form of cell death that may help overcome some forms of treatment resistance. In laboratory studies using two types of human gastric cancer cells, including HER2-positive and HER2-negative cells, the combined treatment system, known as DTHI, reduced cancer cell growth in a dose- and time-dependent manner. The treatment also activated key proteins involved in necroptosis, including RIP1, RIP3, and MLKL, and caused damage to the cancer cells' mitochondria, which are the energy-producing parts of cells.

"We found that the reactive metabolites generated by our system trigger a form of cell death that bypasses the resistance mechanisms commonly seen with standard chemotherapy," said Assoc Prof Drum. "By targeting the necroptotic pathway, we open a new avenue for treating gastric cancers that have become unresponsive to conventional drugs."

The team further tested the platform in a laboratory model of chemically induced gastric cancer. Laboratory models treated with DTHI for six weeks showed significantly reduced stomach inflammation and tumour polyp growth compared with control groups. Tissue analysis also showed fewer polyps and reduced tumour development. The researchers also analysed blood plasma samples and confirmed that IAA had been converted into its active metabolites in the body. These active metabolites, including indole-3-carboxaldehyde and indole-3-carbinol, were detected only in laboratory models that received the full DTHI treatment, supporting the team's proposed mechanism of local drug activation after oral administration.

Beyond its direct anti-cancer effects, the treatment was also linked to increased levels of antioxidant metabolites, including vitamin E and glutathione, in plasma. This suggests that the platform may also help influence oxidative stress and tumour-related inflammation, although further studies are needed to better understand these effects.

A versatile platform for gastrointestinal cancers

The exoshell platform is modular and adjustable, meaning doses can be fine-tuned and, in principle, different enzymes or inactive drug compounds could be paired for different treatment uses. The nanocage was also shown to enter gastric cancer cells through transferrin receptors, which are found on the surface of tumour cells and may help give the platform an added degree of tumour selectivity.

"What makes this platform exciting is its versatility," said Dr Shanmugam. "The exoshell system is designed to be adapted — different enzymes and prodrugs can be paired to tailor the therapy to specific cancer types and patient needs, while maintaining the oral delivery advantage that is so important for patient quality of life."

The team's next steps include further investigation into the safety profile of necroptosis-based therapy, optimisation of the platform, and additional studies to assess its potential for future clinical translation.

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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 15 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 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; 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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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 12,0000 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).

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

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