PRESS RELEASE

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Anti-cancer drug carriers

NUS Medicine Researchers Engineer Bacteria for Targeted Chemotherapy Delivery

6 June 2024, Singapore – Traditional chemotherapy often poses significant challenges, including severe side effects, damage to healthy tissue and limited efficacy.

Now, researchers at the Yong Loo Lin School of Medicine, National University of Singapore (NUS Medicine) have developed a revolutionary approach to cancer treatment — one that is a more targeted, effective, and less toxic alternative to traditional chemotherapy. This new approach not only improves treatment effectiveness but also significantly reduces the required drug dosage for cancer treatment.

Led by Associate Professor Matthew Chang, researchers at the NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI) and the Synthetic Biology Translational Programme (Syn Bio TRP) at NUS Medicine identified a new method of drug delivery that offers hope for the development of a new clinical treatment for cancer patients. The findings, published in *Nature Communications*, showcase a novel method for delivering chemotherapy drugs directly to tumour sites by utilising the natural interactions between bacteria and cancer cells.

Prodrugs are inactive molecules that transform into active drugs within the body, particularly in tumour environments, by leveraging unique tumour conditions, such as low oxygen or high acidity, to activate the drug precisely at the cancer site, minimising damage to healthy tissues. However, current prodrug strategies exhibit limited target specificity and frequently depend on macromolecular carriers, which complicates both drug distribution and clearance.

To overcome these limitations, NUS Medicine researchers developed a prodrug delivery method that utilises a commensal *Lactobacillus* strain that binds specifically to cancer cells via a surface molecule called heparan sulfate. These engineered bacteria carry a prodrug that converts to the chemotherapy drug SN-38 at the tumour site. In preclinical models of nasopharyngeal cancer, the engineered bacteria localised specifically in the tumour and released the chemotherapy drug directly at the cancer site, reducing tumour growth by 67% and increasing the effectiveness of the chemotherapy drug by 54%.

One of the most promising aspects of this research is the potential broader applications across various types of cancer therapy, as the *Lactobacillus* strain identified by the researchers binds specifically to cancer cells. Lead Researcher Dr Shen Haosheng, Research Fellow at SynCTI said: “By harnessing the affinity between bacteria and cancer cells, we aim to revolutionise chemotherapy delivery. We are evaluating the binding affinity of several microbial strains to multiple cancer cell lines with the aim of developing a versatile delivery system using microbial strains to target chemotherapy drugs to various mucosal cancers, such as colorectal, bladder, stomach, oral, lung, and nasal cancer.”

“Cancer treatment often takes a tremendously heavy toll on patients. Our research represents a significant step toward developing a more targeted and less toxic approach to fighting cancer. We hope this can pave the way for therapies that are both mild and effective,” added A/Prof Chang, Dean’s Chair in Medicine and Director of SynCTI and NUS Medicine Syn Bio TRP.

The study, titled ‘*Prodrug-conjugated tumor-seeking commensals for targeted cancer therapy*’ was published in *Nature Communications* on 21 May 2024.

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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.

For more information on NUS, please visit 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 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 2024).

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