

PRESS RELEASE

NUS researchers discover a dependency of glioblastoma on biotin distribution

Further research hopes to find a successful combination of drugs that would cripple the growth of glioblastoma cells in patients

Singapore, 15 September 2021 — Glioblastoma is the most lethal and malignant adult brain cancer that may arise from neuroglial stem or progenitor cells. Certain gene mutations or those with a known history of other cancers and radiation therapy may predispose patients to develop brain cancer. Tumour relapse is invariably inevitable due to the resistance of glioblastoma towards standard therapies. Additionally, the infiltrative nature of these tumour cells means it is often not possible to surgically remove them completely.

Researchers from NUS Yong Loo Lin School of Medicine have discovered that the FDA-approved anti-fungal drug, sulconazole, exhibits anti-cancer properties towards glioblastoma cells. This was published in the latest issue of *Science Advances*. An in-depth investigation of this compound revealed that it competes with biotin (Vitamin H), an important co-factor for metabolic enzymes and modifier of histones, allowing it to inhibit the normal function of biotin-dependent metabolic enzymes and specific histone modification-associated gene expression. This compromises glioblastoma metabolism and epigenetics, thereby impairing the tumour growth and invasiveness of glioblastoma cells.

In mammalian cells, holocarboxylase synthetase, or HLCS, is the enzyme that serves to distribute biotin to the biotin-dependent proteins. Gene silencing of HLCS mitigates the glioblastoma's tumorigenicity – its tendency to develop tumours – in mouse models. High HLCS expression is also associated with glioblastoma and inferior glioma patient outcome. While HLCS is present in healthy patients, its expression increases in the tumours of glioblastoma patients. Glioblastoma cells with higher HLCS expression will be able to better supply biotin to the biotin-dependent metabolic enzymes and histones, which results in a more proliferative and invasive glioblastoma. Thus, the dependency of glioblastoma on biotin distribution suggests that the rational co-targeting of biotin-dependent metabolism and epigenetic pathways may be explored for glioblastoma eradication.

“Since biotin is found in various food sources, including legumes, egg yolk and offal, and commonly consumed as a supplement, these findings raise an important consideration of regulating biotin consumption in glioblastoma patients. This discovery would also lay the foundation for the development of drug combinations from existing or new small molecule inhibitors against some of the biotin-dependent metabolic enzymes and histone modifications to cripple glioblastoma; some of these are already being actively explored in cancer treatment,” said Assistant Professor Derrick Ong from the Department of Physiology and Principal Investigator of this study.

About the 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 17 faculties 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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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 Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2020 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2020).

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