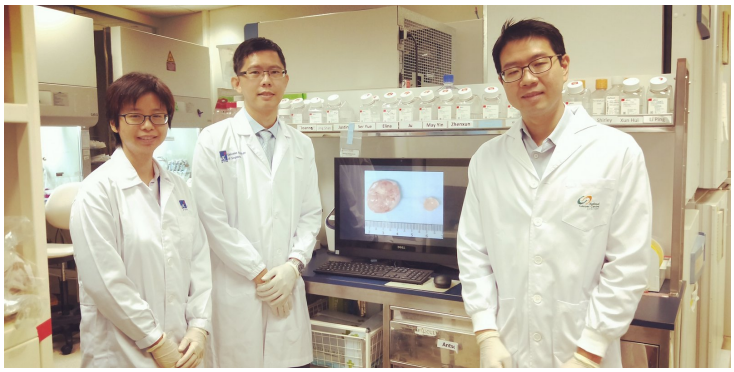
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A Nutrition Pathway to Stamp out the Start of Cancer

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Blocking 'methionine' dependency of cancer stem cells with potential anti-cancer therapeutics to reduce the cancer relapse and propagation rate



In a landmark study, scientists at the Agency of Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS), Bioprocessing Technology Institute (BTI) and oncologists at the National Cancer Centre Singapore (NCCC), have discovered that cancer stem cells, the founder cells of a tumour, have unique nutrient requirements. Unlike the rest of the tumour cells, cancer stem cells are addicted to a type of dietary amino acid -methionine- which is linked to its ability to form a tumour. The breakthrough innovation was announced by Dr Daniel S.W. Tan, Senior Clinician-Scientist, GIS and Dr Tam Wai Leong, Group leader, Precision Oncology, GIS on 27th May 2019 at A*STAR in Singapore.

Cancer stem cells are addicted to methionine which is derived from the diet and are absorbed by tumour cells. High methionine cycle activity drives the production of S-adenosylmethionine (SAM) that is essential for tumour formation and is involved in the regulation of critical gene functions in cancer stem cells. This methionine metabolism pathway is controlled by a critical metabolic enzyme – MAT2A (methionine adenosyltransferase 2A) that converts methionine to SAM. Thus, MAT2A is an important therapeutic candidate for cancer.

Tumours start from cancer stem cells and are able to resist multiple therapies, leading to drug resistance and relapse in the patient. Thus, there is an expeditious need for more precise methods to eliminate these recalcitrant cells. Through the integration of advanced genomics and metabolomics technologies housed at A*STAR, scientists are able to accurately recognise the unique nutritional requirements of cancer stem cells. The research has given the new insight and procedures on efficient application of cancer stem cells to overcome the problems associated with resistance in cancer therapies.

This remarkable discovery can inspire the development of high potential anti-cancerous drugs. Laboratory models of tumours are more effectively targeted by specifically drugging this metabolic pathway. The findings were published on online medical journal, Nature Medicine, on 6 May 2019. The research is supported by A*STAR, and the National Medical Research Council's Large Collaborative Grant for fighting lung cancer.

Dr Tam Wai Leong, the senior author of the study, Group Leader at the GIS and faculty member at Cancer Science Institute of Singapore, explained, "Cancer cells within a tumour are quite different from one another and have different dietary preferences. Through this study, we discovered that the cancer stem cells are addicted to a particular nutrient-methionine. By blocking the ability of the cancer stem cells to use this amino acid with potential anti-cancer therapeutics,

we are able to effectively halt the growth of the tumour".

"MAT2A is an interesting enzyme that controls the metabolism of cancer cells. From our findings, this enzyme represents an important new drug target, as its inhibition led to the ablation of cancer stem cells. This paves the way for the development of next-generation drugs that target this dependence on methionine," said Dr Wang Zhenxun, the first author of this study.