Novel discovery paves the way for more effective treatment of cancers

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A team of scientists from the National University of Singapore's (NUS) Department of Biological Sciences and Mechanobiology Institute have discovered how a drug-led compound – a compound that is undergoing preclinical trials as a potential drug – can deprive cancer cells of energy and stop them from growing into a tumour. This drug-led compound is named BPTES.

This is the first time a research group has provided evidence showing how a drug-lead compound suppresses tumour formation.

Building on the new findings, the NUS team also derived positive results for a novel dual-drug treatment regime involving BPTES that kills kidney and breast cancer cells more effectively.

The team led by Associate Professor Low Boon Chuan and Associate Professor Jayaraman Sivaraman first published their findings in the journal of *Proceedings of the National Academy of Sciences (PNAS)* on 26 April 2012.

Killing cancer cells by 'starving' them of energy

Classic experiments in cancer biology have demonstrated that cancer cells feed off the breakdown of the amino acid glutamine to gain energy and grow into a tumour. While it is known that human glutaminase is the first enzyme in catalysing this series of biochemical reactions, little is

known about how its activity is controlled, and how it can be manipulated.

The NUS research team has successfully identified the mechanism in which the BPTES that can bind and inhibit glutaminase, can effectively starve the cancer cells of their energy source, and hence, could potentially prevent tumour growth.

In addition, the team has also found that the glutaminase activity can be activated upon the addition of phosphate by epidermal growth factor signaling a pathway that controls cancer cells proliferation. By using another inhibitor to block the kinase Mek2 within this cancer-causing pathway, coupled with the use of BPTES, the combined therapeutic effect is more potent and less toxic. This raises the hope of offering a new dual-drug cancer treatment regime for cancers such as lymphoma, prostate, glioblastoma, breast and kidney cancer cells that is more effective and with fewer side-effects.

Armed with structural insights into the binding and signaling pathway that activates glutaminase, the NUS research team is conducting more studies to determine whether a combination of drugs would be even more effective in inhibiting glutaminase activity and hence, tumour formation.

Using the knowledge that they gained through their current studies, the research team will also look into optimising the tumour suppression property of BPTES to increase its efficiency and lower its side-effects.

Provided by National University of Singapore

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