Researchers at the Institute of Molecular and Cell Biology (IMCB) under the Agency for Science, Technology and Research (A*STAR) have recently found a method to trigger apoptosis in intestinal stem cells with cancer-causing properties, thereby preventing the development of cancer.

These findings, published in Cell Press’s recently launched journal *Cell Stem Cell*, explore an uncharted yet potentially powerful method of cancer prevention.

The team of researchers led by Dr Dmitry Bulavin, Principal Investigator at IMCB, studied the behavior of intestinal stem cells in Wip1-deficient mice.

Wip1 is a protein belonging to a class of phosphatases and a known regulator of several tumor suppressor genes. Following up on last year’s discovery by Dr Bulavin’s team that this strain of mice is generally resistant to cancer, the team investigated the behavior of intestinal stem cells under different conditions. They found that when a stem cell is converted into a tumor-initiating/cancer stem cell by acquiring cancer-promoting genetic changes, inactivation of Wip1 phosphatase sets off a chain reaction resulting in self-elimination of the errant stem cell.

The research team at IMCB had chosen to focus on stem cells in this particular study as evidence from recent research strongly supports the theory that cells with cancer-causing properties may have originated from stem cells. In turn, targeting stem cells during their conversion into tumor-initiating/cancer stem cells represented a powerful yet previously unexploited cancer prevention tool.

Work is still underway to find small molecules or compounds that could target and inactivate Wip1 phosphatase and this could form a new approach in cancer prevention and treatment.

“We have been investigating the effects of Wip1 on cancer for more than five years and our current
results show that inactivation or depletion of Wip1 can prevent the formation of cancer in the intestine. It is exciting to see that modulation of Wip1-dependent signaling pathways represents a powerful way of preventing cancer at its very birth,” said Dr Bulavin.

Professor Sir David Lane, executive director of IMCB, added: “The concepts that cancers contain a critical population of cells with stem cell-like properties, and that cancers may arise from stem cells may help explain why tumors that appear to respond well to chemotherapy can often recur. This in turn suggests that determining the particular pathways that act in cancer stem cells could lead to a new generation of more effective therapies. The IMCB team’s results point to the Wip1 phosphatase as a prime target for this approach and demonstrate the power of genetic mouse models to reveal critical insights into human cancer.”

Colorectal cancer is one of the world’s leading causes of death. In Singapore, it is the second most common form of cancer among males and females with more than 1000 cases of colorectal cancer diagnozed each year. This form of cancer is very curable if early screening and diagnosis is done. The research on Wip1 phosphatase initiated by the IMCB team may eventually result in potential applications and therapies in the prevention of colorectal cancer and other kinds of cancers, such as breast cancer, lymphomas and intestinal cancer.

About the Institute of Molecular and Cell Biology (IMCB)

The Institute of Molecular and Cell Biology (IMCB) is a member of Singapore’s Agency for Science, Technology and Research (A*STAR) and is funded through A*STAR’s Biomedical Research Council (BMRC). It is a worldclass research institute in biomedical sciences with core strengths in cell cycle, cell signaling, cell death, cell motility, protein trafficking, developmental biology, structural biology, genomics and infectious diseases. Established in 1987, the institute currently has 38 independent research groups with more than 400 staff members.

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The research findings described in this article can be found in Cell Stem Cell “Wip1 Phosphatase Regulates p53-Dependent Apoptosis of Stem Cells and Tumorigenesis in the Mouse Intestine” published on 15th August 2007.
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