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Potential new therapeutic molecular target to fight cancer

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Researchers at the Virginia Commonwealth University Massey Cancer Center have identified the enzyme sphingosine kinase 2 as a possible new therapeutic target to improve the efficacy of chemotherapy for colon and breast cancer.

In the Nov. 1 issue of the journal Cancer Research, researchers examined human colon and breast cancer cells and established a role of sphingosine kinase 2 (SphK2), an enzyme that forms the potent lipid mediator sphingosine-1-phosphate in the death of cancer cells mediated by the chemotherapeutic drug, doxorubicin.

Doxorubicin is able to kill cancer cells by working with p53, one of the most protective anti-cancer proteins in the human body. However, doxorubicin also relies on p53- independent mechanisms to induce death in colon and breast cancer cells.

“Understanding how doxorubicin kills in a p53-independent manner is a major goal of cancer researchers because most cancer cells have mutated p53,” said lead author Sarah Spiegel, Ph.D., chair and professor in the VCU Department of Biochemistry and Molecular Biology and co-leader of the cancer center's cancer cell biology program.

According to Spiegel, the study demonstrated that SphK2 is important for p53-independent induction of expression of p21, a cyclin-dependent kinase inhibitor. This p21 regulates the cell cycle, and apoptosis or programmed cell suicide, mediated by doxorubicin. Human colon and

breast cancer cells were killed more efficiently by doxorubicin when SphK2 was removed from the cells.

“Therefore, the findings suggest that SphK2 influences the balance between cytostasis, and apoptosis of human cancer cells,” Spiegel said. Cytostasis refers to the stoppage of cellular growth and multiplication.

Spiegel said that cell death was induced by doxorubicin and decreased p21.

Spiegel, who is internationally recognized for her pioneering work on new lipid mediators that regulate cell growth and cell death, and her colleagues, first discovered the role of sphingosine-1-phosphate in cell growth regulation nearly a decade ago. Spiegel and her team are continuing this work to better understand the functions of these enzymes.

Source: Virginia Commonwealth University