TOP

Breast Cancer Breakthrough at Mizzou

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Submitted by
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Columbia, Missouri - Researchers at the University of Missouri have proven that a compound initially developed as a cholesterol-fighting molecule not only halts the progression of breast cancer, but also can kill the cancerous cells.

“Cholesterol is a molecule found in all animal cells and serves as a structural component of cell membranes,” said Salman Hyder, the Zalk Endowed Professor in Tumor Angiogenesis and professor of biomedical sciences in the College of Veterinary Medicine and the Dalton Cardiovascular Research Center at MU. “Because tumor cells grow rapidly they need to synthesize more cholesterol. Scientists working to cure breast cancer often seek out alternative targets that might slow or stop the progression of the disease, including the elimination of the cancerous cells. In our study, we targeted the production of cholesterol in cancer cells leading to death of breast cancer cells.”

Previous studies suggest that 70 percent of breast cancers found in women are hormone dependent and can be treated with anti-hormone medicines such as **tamoxifen**. Although tumor cells may initially respond to therapies, most eventually develop resistance, which causes breast cancer cells to grow and spread. Cholesterol also can contribute to the development of anti-hormone

resistance because cholesterol is converted into hormones in tumor cells. Therefore, these cholesterol-forming pathways are attractive therapeutic targets for the treatment of breast cancer.

Using compounds initially developed by Roche Pharmaceuticals for the treatment of high cholesterol, which reduces cholesterol in a different manner than the widely used statins. Hyder and his team administered the molecule to human breast cancer cells. They found that the compound was effective in reducing human breast cancer cell growth and often caused cancer cell death. Most interestingly they found that the cholesterol lowering drug they tested destroyed an estrogen receptor, a protein which encourages the tumor cells to grow.

Equipped with this information, Hyder and the team tested the results in mice with breast cancer. Following injection of the compound, Hyder found that the molecule was effective at killing breast cancer cells by reducing the presence of estrogen receptors in tumor cells, Hyder said.

“The compound exhibited anti-tumor properties in both human samples, which were outside the body, and in samples that were administered by injection into the mice,” Hyder said. “In both cases, the proteins that cause tumors to grow were eliminated, leading to more aggressive cell death.”

Hyder believes that further clinical testing can lead to a drug that has the dual purpose of fighting high cholesterol and cancer.

Researchers involved with the study included Yayun Liang, research associate professor at Dalton Cardiovascular Research Center; Cynthia Besch-Williford, professor of veterinary pathobiology at MU; Benford Mafuvadze, post-doctoral fellow at Dalton Cardiovascular Research Center; Matthew Cook, pre-doctoral fellow in Biomedical Sciences; and Xiaoqin Zou, associate professor of physics and biochemistry and a researcher at the Dalton Cardiovascular Research Center. Johannes Aebi from Roche Pharmaceuticals also contributed to the research.

The study, “Cholesterol biosynthesis inhibitors as potent novel anti-cancer agents: suppression of hormone-dependent breast cancer by the oxidosqualene cyclase inhibitor RO 48-8071,” was published in Breast Cancer Research and Treatment and was funded by a grant from the Department of Defense Breast Cancer Program.

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