Novel approach to treating breast cancer shows great promise

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In a novel therapeutic approach to treating breast cancer, Loyola University Medical Center researchers are reporting positive results from a clinical trial of a drug that targets tumor stem cells.

Existing cancer drugs are effective in killing mature cancer cells. But a handful of cancer stem cells are resistant to such drugs. They survive and go on to develop into new tumor cells.

A pilot study at Loyola found that an experimental drug known as a "notch inhibitor" appears to block this process by turning off key genes. Kathy Albain, MD, who led the study, presented findings Dec. 7 during the 2011 CTRC-AACR San Antonio Breast Cancer Symposium.

Albain collaborated with scientists from Loyola, University of Mississippi Cancer Center, Baylor Breast Center and Merck Oncology.

"Our results suggest a potential role that notch inhibitors could play in optimizing existing therapies and in overcoming resistance to cancer drugs," Albain said.

The so-called notch protein promotes tumor growth and survival. The protein is present on the surface of cancer stem cells. The protein latches on to other cells, and the resulting "molecular handshake" activates various genes in the stem cells. Activating these genes, in effect, makes the stem cells resistant to common cancer drugs.

The study included 20 patients who finished all therapy. The women all had early-stage, estrogen-receptor-positive breast cancer.

Prior to surgery, the patients received one of two commonly used drugs, tamoxifen or letrozole. These drugs work by blocking estrogen stimulation of breast cancer cells. In addition to tamoxifen or letrozole, patients also received the experimental notch-inhibitor drug, MK-0752.

Following treatment with the notch inhibitor, patients underwent biopsies to provide tumor specimens. Researchers found that the drug turned off the key genes that in effect would have kept the tumor stem cells resistant to conventional drugs.

"The notch inhibitor appears to be doing what it is intended to do," said Clodia Osipo, PhD, a breast cancer scientist in Loyola's Cardinal Bernardin Cancer Center.

There were minimal side effects from either the notch inhibitor or the estrogen-blocking drugs. One patient experienced puffy eyes and coughing and four patients experienced facial acne. No patients experienced diarrhea or surgical complications

The purpose of the study was to determine how well the notch inhibitor is tolerated and how it affects the expression of critical genes in cancer stem cells. The next step is to determine how effective the drug would be in treating breast cancer.

Researchers proposed a randomized clinical trial, in which patients who received estrogen-blocking drugs before surgery would be compared to patients who received estrogen-blocking drugs plus a notch inhibitor.

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