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Possible new weapon found for fighting some types of breast cancer

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Researchers believe they have discovered one reason why some women with estrogen receptor-positive breast cancer may respond poorly or only temporarily to estrogen-blocking drugs such as tamoxifen. Results of a new study, which was presented Saturday at the joint meeting of the International Society of Endocrinology and the Endocrine Society: ICE/ENDO 2014 in Chicago, point to a previously unrecognized role of the androgen receptor.

Although this receptor (protein) is expressed in nearly all prostate cancers, it also is expressed in most breast cancers. Now scientists have found that estrogen receptor alpha—a main driver of estrogen-fueled breast cancer—may rely on the androgen receptor for its function.

In a study funded by the U.S. Department of Defense Breast Cancer Research Program, Jennifer Richer, PhD, from the University of Colorado Anschutz Medical Campus in Aurora, and her colleagues studied 192 women with estrogen receptor-positive breast cancers. They found that women were 4.4 times more likely to have a cancer recurrence during tamoxifen treatment when their main tumor had a high ratio (2:1 or greater) of androgen receptor-positive cells to estrogen receptor-positive cells.

"Women with breast cancer do not routinely receive testing for the androgen receptor," Richer commented.

The investigators hypothesized that maximal estrogen receptor activity

depends on the androgen receptor's nuclear localization. This process, Richer said, involves the receptor moving itself and the hormone molecule, to which it is bound, inside the nucleus of a cell, where the receptor "does its important business."

Richer and her co-workers then tested a new anti-androgen drug called enzalutamide, which is approved for treatment of prostate cancer. Unlike older anti-androgen drugs, which allow the androgen receptor to go to the cell's nucleus, enzalutamide inhibits the ability of androgen receptors to enter the nucleus, Richer said.

"If the androgen receptor is outside the nucleus, both estrogen and androgen driven tumor growth is inhibited," she explained.

In preclinical models (human cells and mice) of estrogen receptor-positive breast cancers that also were positive for the androgen receptor, enzalutamide treatment inhibited both androgen- and estrogen-controlled tumor growth, Richer reported. Further, the combination of enzalutamide and tamoxifen decreased estrogen-driven tumor growth better than either drug alone.

Another study by Richer's team, to be presented Monday (OR38-2), found that breast cancers that are estrogen receptor negative ("triple negative") can also rely on the androgen receptor for growth. In preclinical models of estrogen receptor-negative tumors, enzalutamide treatment decreased tumor growth by 85 percent, according to the abstract.

"Our research suggests that the androgen receptor may serve as a therapeutic target in both estrogen receptor-positive and negative breast cancers," Richer said.

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