Androgen receptor stops tumor growth in the most common form of breast cancer

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Researchers say they have found a viable new therapeutic strategy for estrogen receptor-positive (ER+) breast cancer, even cancers that are resistant to current standard of care treatments. Their new preclinical study was accepted for presentation at ENDO 2020, the Endocrine Society's annual meeting, and publication in a special supplemental section of the *Journal of the Endocrine Society*.

In various models of ER+ breast cancer, the most common form (about 75% of cases) of breast cancer, the researchers found that activating the androgen receptor decreased tumor growth, said Wayne Tilley, Ph.D., the study's principal investigator and a professor at the University of Adelaide in Australia. The androgen receptor is a protein in cells in men and women to which testosterone and other "male" reproductive hormones called androgens bind to elicit their effects, he explained. Importantly, androgens are found in women as well as men.

"There is a prevailing assumption that the androgen receptor promotes malignancy in breast cancer, as it does in prostate cancer," Tilley said. "Our study demonstrates that this is not the case for ER-driven breast cancer. Rather, the androgen receptor acts as a tumor suppressor."

ER+ breast cancer needs new drug treatments because as many as 35% of women with this type eventually become resistant to current hormone therapies, Tilley said. He noted that androgen receptor-stimulating drugs are under investigation for various diseases. The researchers tested one of these drugs, enobosarm, from a drug class called selective androgen receptor modulators, or SARMs, in models of ER+ breast cancer. These studies used ER+ breast cancer cell lines that are commercially available as well as tissues taken from breast cancer patients, including those resistant to current therapies. Some cell lines and human tissues were grown in culture dishes, and other cell lines and patient tumors were transplanted into mice to create patient-derived models.

In all models, the researchers found evidence that stimulating androgen receptor activity with enobosarm stopped tumor growth. From the different breast cancer models, they derived a gene "signature" of androgen receptor activity, which predicted cancer survival in participants in large studies of ER+ breast cancer. This androgen receptor signature outperformed other breast cancer prognostic signatures, he said.

When the investigators treated ER+ breast cancer tissues with enobosarm combined with current standard of care breast cancer drugs such as tamoxifen that target the estrogen receptor, Tilley said they observed better reduction in tumor growth than with the standard drug alone. Enobosarm is nonsteroidal and, according to Tilley, other researchers have found it to be safe in patients. Importantly, it does not cause women to develop male characteristics.

"Treatment of ER+ breast cancer with an androgen

receptor activator drug could be immediately tested in women," Tilley said.

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