

Researchers identify potential new treatment for subset of women with triple-negative breast cancer

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Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

Mayo Clinic researchers have identified the drug estradiol as a potential new treatment for a subset of women with triple-negative breast cancer. Their findings are published in the *Proceedings of the National Academy of Sciences*.

"Triple-negative [breast](#) cancer is a form of breast cancer that lacks expression of [estrogen receptor](#) alpha, progesterone receptor, and human epidermal growth factor receptor 2, also known as HER2. And it exhibits high rates of disease recurrence," says John Hawse, Ph.D., a molecular biologist at Mayo Clinic and senior author. "So far, there have been few drugs other than chemotherapy that appear to work effectively for the treatment of this disease."

In previous research, Dr. Hawse and his colleagues discovered that a second form of the [estrogen](#) receptor, known as estrogen receptor beta, is expressed in approximately 25 percent of triple-negative breast cancer tumors. In this study, Dr. Hawse's laboratory demonstrated that estradiol, a naturally occurring female hormone, effectively inhibits the growth of triple-negative breast cancer tumors expressing estrogen receptor beta.

"Remarkably, we discovered that estradiol, which normally stimulates growth of cancer cells in tumors that express [estrogen receptor alpha](#), has the opposite effect in triple-negative breast cancer," says Dr. Hawse.

"However, estradiol was only able to inhibit the growth of triple-negative breast cancer when estrogen receptor beta was present."

Dr. Hawse and his colleagues discovered one potential mechanism of how estradiol exerts its anticancer effects. They determined that when estradiol binds with estrogen receptor beta in triple-negative breast cancer, it stimulates the expression of a group of proteins called "cystatins," which exhibit tumor suppressing effects on neighboring and distant cancer cells.

Based on these data, researchers at Mayo Clinic and the Translational Breast Cancer Research Consortium will soon open a phase II clinical trial to test the effectiveness of estradiol as a treatment for women with metastatic triple-negative breast cancer that expresses estrogen receptor beta.

"Estradiol is FDA- [Food and Drug Administration] approved as a treatment for women with breast cancer; however, its use is typically limited to women with estrogen receptor alpha positive breast [cancer](#) that has become resistant to standard therapies," says Matthew Goetz, M.D., a medical oncologist and co-investigator with Dr. Hawse. "We are excited to study whether estradiol can be repurposed as a new treatment for [triple-negative breast cancer](#) that expresses estrogen receptor beta."

More information: Jordan M. Reese et al. ER β -mediated induction of cystatins results in suppression of TGF β signaling and inhibition of triple-negative breast cancer metastasis, *Proceedings of the National Academy of Sciences* (2018). [DOI: 10.1073/pnas.1807751115](https://doi.org/10.1073/pnas.1807751115)

Provided by Mayo Clinic

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