Estrogen and PARP inhibitor combination for advanced ER+ breast cancer shows promise in preclinical models

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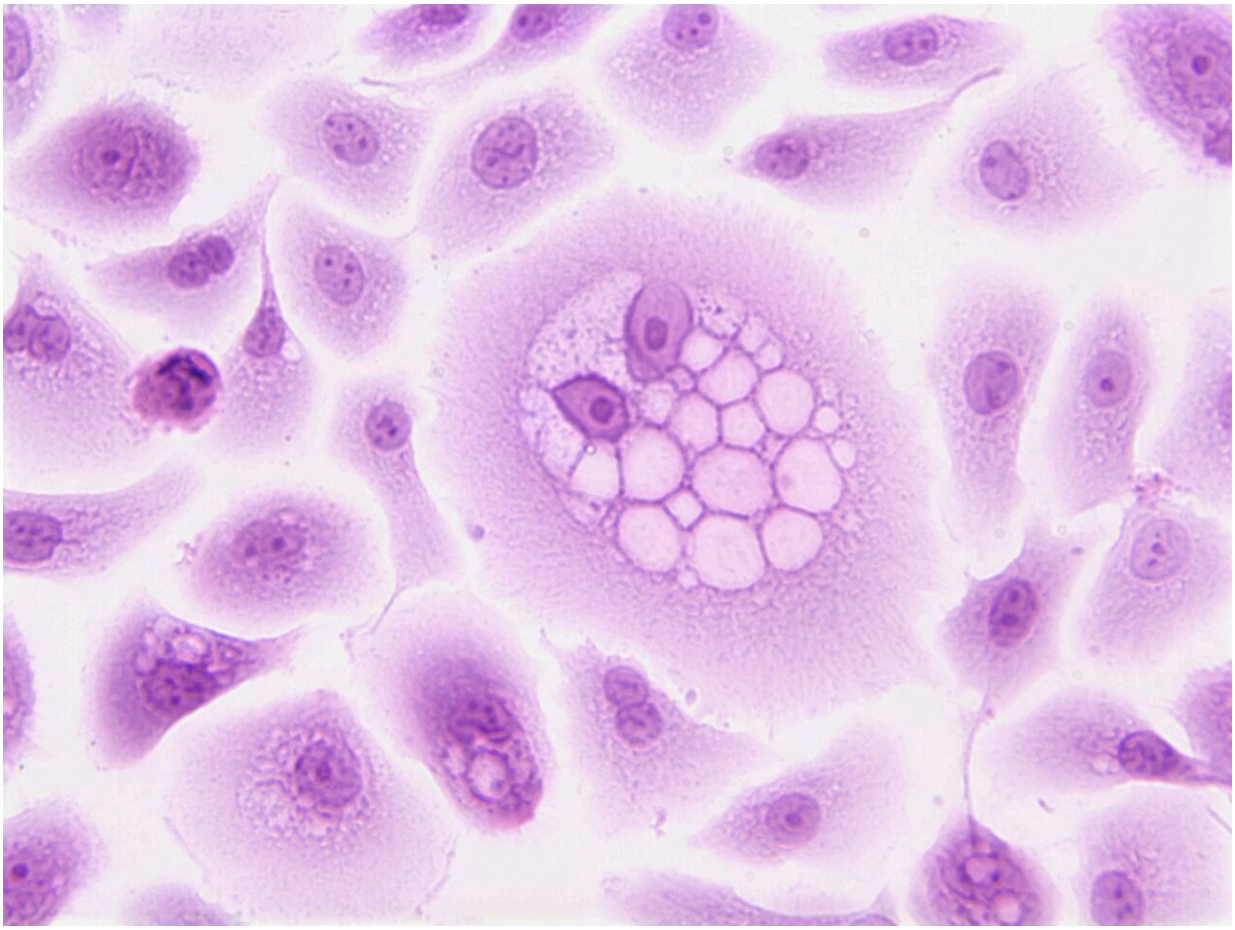

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Advanced estrogen receptor-positive (ER+) breast cancer can be especially difficult to treat. A new study by researchers at Dartmouth Cancer Center led by Todd W. Miller, Ph.D., shows promise in using a combination of estrogen and a PARP inhibitor (a drug that suppresses DNA damage repair), to treat this type of cancer.

Estrogen has been used for over 50 years to treat breast cancer. Clinical evidence has shown that treatment with estrogens elicits anti-cancer effects in about 30% of patients with advanced endocrine-resistant ER+ breast cancer. Despite the proven efficacy of estrogen therapy, its mechanism of action is unclear and the treatment remains under-utilized.

Miller's team found that estrogen can cause damage to cancer cells by re-engaging the estrogen receptor in the cells. This damage can be enhanced by using a PARP inhibitor, which prevents the cancer cells from repairing their DNA. Their study, "Estrogen therapy induces receptor-dependent DNA damage enhanced by PARP inhibition in ER+ breast cancer," is newly published ahead of print in *Clinical Cancer Research*.

"The combination of estrogen and PARP inhibitors has also been shown to be effective in treating advanced ER+ breast cancer regardless of whether the patient has a BRCA1 or BRCA2 genetic mutation," says Miller.

This new treatment strategy will be tested in a clinical study to ensure its safety and effectiveness for patients. If successful, the approach could provide a new option for patients with advanced ER+ breast cancer. "Our finding that PARP inhibitors can enhance the therapeutic effects of estrogen have the potential to greatly expand the clinical application of PARP inhibitors to more patients," says Miller.

More information: Nicole A. Traphagen et al, Estrogen therapy induces receptor-dependent DNA damage enhanced by PARP inhibition

in ER+ breast cancer, *Clinical Cancer Research* (2023). DOI: 10.1158/1078-0432.CCR-23-0488