

Researchers solving treatment resistance in most common breast cancer

February 7 2018



Mammograms showing a normal breast (left) and a breast with cancer (right).
Credit: Public Domain

At Magee-Womens Research Institute (MWRI) and UPMC Hillman Cancer Center, a large team of clinical and laboratory researchers dedicated to understanding treatment resistance in the most common form of breast cancer have identified a new genetic change in the estrogen receptor (ER) that contributes to therapy resistance. ER-positive breast cancer, diagnosed in two-thirds of breast cancer patients,

is fueled by the presence of estrogen in the body. Anti-estrogen therapy is usually successful in treating the disease initially, but ER-positive breast cancers will often recur because tumors develop a resistance to treatment.

Published in the *Annals of Oncology*, the research identifies the presence of ER gene (ESR1) fusion proteins in treatment-resistant [breast cancer](#). This is the first time that recurrent ESR1 fusion proteins have been identified in human breast [cancer](#), and understanding how they function could lead to improved treatments for the disease.

"We first identified this change in a patient who had ER-positive breast cancer, received anti-estrogen therapy, had her breast cancer recur and eventually passed away from the disease," said senior author Adrian Lee, Ph.D., director of the Women's Cancer Research Center at MWRI and UPMC Hillman Cancer Center, and professor of Pharmacology & Chemical Biology at the University of Pittsburgh. "A member of our lab noticed the mutation while performing posthumous genetic analysis from tissue in our organ donation program, and over time we were able to identify many more cases of this mutation in patients with recurrent disease." This work was performed in collaboration with Foundation Medicine Inc., a genomic testing company that examined ESR1 fusions in close to 10,000 breast cancers sequenced with the FoundationOne CDx test.

According to Lee, ESR1 fusion proteins "outsmart" traditional [treatment](#) by splitting in half and eliminating the binding site that anti-estrogen therapy targets.

"Physicians will continue administering anti-estrogen therapy, not realizing this genetic mutation has occurred," said Lee. "Now that we understand the change, though, we can detect it with a blood test and help improve treatments for this form of the disease."

According to Lee, genetic analysis will soon be the dominant field of ER-positive [breast cancer research](#), eventually leading to improved treatments and patient outcomes.

"Genomic sequencing is telling us so much about breast cancer. I believe the research we are doing in the laboratory will have a significant clinical impact in the near future, and the work we are doing will play a large part in improving patient care and survival," said Lee.

Provided by University of Pittsburgh Schools of the Health Sciences

Citation: Researchers solving treatment resistance in most common breast cancer (2018, February 7) retrieved 12 May 2024 from <https://medicalxpress.com/news/2018-02-treatment-resistance-common-breast-cancer.html>

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