

# Newly discovered genetic marker predicts breast cancer patients' treatment outcomes

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A multidisciplinary team of researchers from Roswell Park Comprehensive Cancer Center and Kaiser Permanente Northern California have identified the first pharmacogenomic marker for

anthracyclines and HER2-targeting drugs, two commonly used breast cancer chemotherapies. The results of the large genetic analysis were published today in *npj Breast Cancer*.

Advances in genetic technology open up the possibility of selecting the safest and most effective treatment for an individual patient based on their unique genetic characteristics. In the case of cancer treatment, uncovering these differences can allow oncologists to determine how each patient is likely to respond to a specific cancer drug before it is given, which results in both decreased toxicity and increased effectiveness. However, the ability to accurately predict a patient's response to treatment is an enormous challenge given the vast differences between patients and tumor types.

"Hundreds of genetic variants have been linked to [breast cancer](#) risk, but very few have been robustly linked with outcomes," says Qianqian Zhu, Ph.D., Associate Professor of Oncology in the Department of Biostatistics and Bioinformatics and Co-Director of the Biostatistics and Statistical Genomics Resource at Roswell Park. "Our study uncovered a gene that strongly associates with a patient's outcome after treatment with anthracyclines and anti-HER2 therapy, which may help oncologists formulate appropriate treatment strategies for patients with breast cancer based on their [genetic makeup](#)."

To make this discovery, the cancer researchers analyzed the DNA of 3,973 breast cancer patients from the Pathways Study, a large, multiethnic study of women undergoing treatment for breast cancer at Kaiser Permanente Northern California. Dr. Zhu, together with joint corresponding author Song Yao, Ph.D., Professor of Oncology and Director of Molecular Epidemiology at Roswell Park, and colleagues, in collaboration with the Kaiser Permanente Division of Research, evaluated millions of genetic variants for their association with breast cancer outcomes and found that the UACA gene, a key regulator of

[tumor suppressor](#) Par-4, was associated with overall survival in patients taking anthracyclines and anti-HER2 therapy.

"The opportunity to examine genetic factors with detailed treatment information can result in new information that may have clinical implications," says Lawrence Kushi, ScD, a Senior Research Scientist at the Division of Research who leads the Pathways Study and is senior author of the paper.

To test the strength of their discovery, the researchers conducted genetic analyses in three additional independent cohorts of women with breast cancer and confirmed the association.

The identified genetic variants are common in the general population, and consistent associations were observed across patients from diverse populations. If further replicated in other studies of breast cancer, these findings will make it possible to design a genetic test that will enable clinicians to personalize treatment plans by determining which patients will best respond to anthracycline or anti-HER2 therapy before treatment begins. The findings also highlight the potential of targeting both the UACA gene and the Par-4 pathway as new approaches to improving outcomes of patients with breast cancer

"It is amazing that we started with an agnostic search across the genome for [genetic markers](#) associated with breast cancer outcomes and identified UACA as a promising gene predictive of treatment outcomes for two commonly used agents for breast cancer," adds Dr. Yao.

**More information:** Qianqian Zhu et al, UACA locus is associated with breast cancer chemoresistance and survival, *npj Breast Cancer* (2022). [DOI: 10.1038/s41523-022-00401-5](https://doi.org/10.1038/s41523-022-00401-5)

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