

Gene Variants and Breast Cancer Risk in Black Women

Study findings could help improve risk prediction in this population and lead to more targeted therapies and prevention strategies.

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Breast cancer is the most often diagnosed cancer in many parts of the world, including the U.S. More than 310,000 new cases are expected nationwide this year.

Black women tend to develop breast cancer at a younger age than White women. Black women are also more likely than Whites to die from the disease, and they are twice as likely to develop an aggressive subtype called triple-negative breast cancer. But despite the increased risks faced by women of African descent, most large-scale genetic studies of breast cancer to date have focused on women of European ancestry.

To better understand their unique genetic risks, a research team led by Dr. Wei Zheng of Vanderbilt University analyzed genetic data from over 40,000 females of African descent. About 18,000 had been diagnosed with breast cancer. The data were gathered as part of the NIH-funded African Ancestry Breast Cancer Genetic consortium, which combined data from 26 studies. Most participants (85%) were African Americans. The rest were from Barbados or Africa.

The researchers conducted a genome-wide association study (GWAS) to look for genetic variants that are found more often in participants with breast cancer than in those without. This is believed to be the largest GWAS study to date of breast cancer in this population. Results were reported in [Nature Genetics](#) on May 13, 2024.

The analysis pinpointed 12 genetic regions, or loci, associated with breast cancer. Three of these loci were linked to the aggressive triple-negative cancer. About 8% of the women carried two genetic copies of risk variants in all three of these loci. Such women, the researchers found, were 4.2 times more likely to be diagnosed with triple-negative breast cancer than women who had only one or no copies of the variants.

Because this type of cancer lacks specific cell receptors often seen with breast cancer (like estrogen or HER2 receptors), there are fewer targeted options for treatment. These findings may help researchers identify new treatment targets.

The researchers also confirmed many breast cancer risk variants that were found earlier in other populations. And they identified an uncommon risk variant in the gene ARHGEF38, which had been previously linked to aggressive prostate and lung cancers.

The scientists used their findings to create polygenic risk scores (PRS) for breast cancer risk in females of African descent. PRS use genomic data to gauge the chance that a person will develop a certain medical condition. PRS created previously, using results from other populations, tend to perform poorly at predicting breast cancer risk for Black women. The new PRS, based on genomic data from African descendants, outperformed previous PRS at predicting breast cancer risk in this population.

The findings and data could lead to improved detection of breast cancer in this at-risk population and provide clues for potential treatment targets. Studies with even larger, more diverse populations will be needed to further improve the prediction of breast cancer risk.

“We have worked with researchers from more than 15 institutions in the U.S. and Africa to establish this large genetic consortium,” Zheng says. “Data put together in this consortium have been and will continue to be used by researchers around the world.”

This [research summary](#) was published by the Food and Drug Administration/National Institutes of Health on June 4, 2024.