

Researchers discover genetic variants modifying breast cancer risk

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Individuals with disrupting mutations in the BRCA1 gene are known to be at substantially increased risk of breast cancer throughout their lives. Now, discoveries from an international research team led by Mayo Clinic researchers show that some of those persons may possess additional genetic variants that modify their risk. These new findings enhancing individualized medicine appear in the current *Nature Genetics*.

"These findings should be useful in helping determine individual risk for [breast cancer](#) in BRCA1 carriers," says Fergus Couch, Ph.D., Mayo investigator and senior author of the study. "It also provides insights into hormone-receptor-negative breast cancer in the general population."

[Genetic mutations](#) in the BRCA1 gene give carriers of these mutations an increased risk for developing breast cancer. To determine if any genetic variations would modify or alter this risk among large populations of the mutation carriers, the researchers conducted genome-wide association studies (GWAS) that ultimately spanned 20 research centers in 11 different countries.

They first studied 550,000 [genetic alterations](#) from across the human genome in 1,193 carriers of BRCA1 mutations under age 40 who had [invasive breast cancer](#) and compared the alterations to those in 1,190 BRCA1 carriers of similar age without breast cancer. The 96 single nucleotide polymorphisms (SNPs) discovered were subsequently studied in a larger sample population of roughly 3,000 BRCA1 carriers with breast cancer and 3,000 carriers without cancer. Researchers found five

SNPs associated with breast cancer risk in a region of chromosome 19p13.

Further studies of those SNPs in 6,800 breast cancer patients without BRCA1 mutations showed associations with estrogen-receptor-negative disease, meaning cancer in which tumors don't possess estrogen receptors. In another GWAS involving 2,300 patients, the five SNPs also were associated with triple-negative breast cancer, an aggressive form of the disease accounting for about 12 percent of all breast cancer. Triple-negative tumors don't express genes for estrogen or progesterone receptors or Her2/neu. The researchers also found that these SNPs were not related to risk for ovarian cancer in BRCA1 mutations carriers.

By locating these risk-modifying SNPs, the researchers have provided a target for better understanding the mechanisms behind the development of breast cancer. Furthermore, when combined with other risk-modifying SNPs that remain to be identified in ongoing studies by this group, it may be possible to identify certain BRCA1 carriers who are at lower risk of cancer and, also, carriers at particularly elevated risk of cancer who may decide to change their approach to cancer prevention.

More information: Paper online: www.nature.com/ng/journal/vaop...rent/abs/ng.669.html

Provided by Mayo Clinic

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