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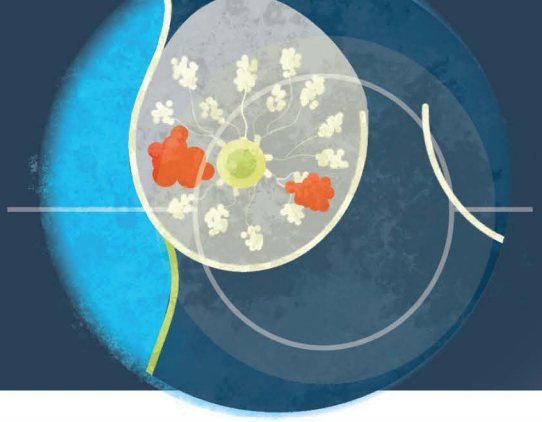
IN BREAST CANCER



The Importance of Genes in Breast Cancer

Family history and genetic mutations both play a part in disease risk

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An estimated 13% of women in the U.S. will develop breast cancer during their lifetime, but the risk increases for those who carry a genetic mutation known to increase breast cancer risk.

Mutations are changes to your DNA sequence that happen during cell division, or when your cells make copies of themselves. The term "risk" refers to factors and characteristics that appear to have some relationship to the development of a disease. If the risk factors are present, there is an increased chance — but not a certainty — that the disease will develop.

It's important to share your family history of cancer with your primary healthcare provider. For example: Were your parents or siblings ever diagnosed with cancer? Are there any known cancer diagnoses on either your mother's or father's side of the family? It is important to note that your medical team wants to know about any family members that have had cancer – for example: aunts and uncles, grandparents, cousins, etc. Information about a family cancer history will help your provider determine if genetic testing may be right for you.

Genetic testing for breast cancer is typically considered when there is a family history of the disease, specifically in cases of early-onset breast cancer (diagnosed before age 50), or when multiple family members have been diagnosed with cancer.

It's important to remember that not everyone with a genetic mutation that increases breast cancer risk will develop breast cancer, or another type of cancer. For example, a woman with a breast cancer genetic mutation has a 45-65% increased risk for the development of breast cancer, but that does not mean a breast cancer diagnosis is inevitable. In contrast, a person who does not carry a genetic mutation may be diagnosed with breast cancer. A key point is that only about 5-10% of breast cancers are hereditary.

Genetic testing can provide valuable information about your potential risk for breast cancer, treatment options, and potential implications for other members of your family.

Mutations

There are a variety of gene mutations that can increase your breast cancer risk. The most common of these are *BRCA1* and *BRCA2*, which are associated with an increased risk of breast cancer in both women and men and can be inherited from both sexes on either side of a family. *BRCA1* and *BRCA2* mutations occur at a higher incidence in individuals of Ashkenazi Jewish descent, and mutations in these genes substantially elevate the risk of breast and ovarian cancers. People with *BRCA1* or *BRCA2* gene mutations are also at higher risk of pancreatic cancer, melanoma, and prostate cancer.

In people expressing the *BRCA1* mutation, 55-72% have a greater chance of developing breast cancer. For those with the *BRCA2* mutation, 45-69% have a greater chance of developing breast cancer, according to the National Cancer Institute.

The following are high-risk inherited mutations for breast cancer:

- Women: *BRCA1, BRCA2, TP53, PTEN, STK11, ATM, BARD1, BRIP1, CHEK2, CDH1, NF1, PALB2, RAD51C, RAD51D*
- Men: *BRCA1, BRCA2, CHEK2, PALB2*

Types of Testing

If your healthcare provider is considering genetic testing for you, they may refer you to a genetic counselor who can provide detailed information about the testing process, the implications of test results, and potential management options.

If you have undergone prior genetic testing for breast cancer and tested negative for either *BRCA1* or *BRCA2* mutations before 2006, share this information with your healthcare provider. They may suggest you be retested, since the testing has improved since then. Testing assays are now capable of detecting mutations involving a larger area of each gene. Patients are now getting panel testing (testing for multiple genetic mutations at one time) and in the past, most patients were only getting single gene testing.

Depending on your personal and family history of cancer, your healthcare provider may order a limited or multigene panel test for you. The costs for multigene or limited panel tests are similar.

Before you undergo genetic testing, be sure your healthcare provider or genetic counselor checks with your insurance provider and communicates the results to you, to ensure that all parties know the costs that will be covered and what out-of-pocket costs, if any, will be your responsibility.

Managing Test Results

Your test results should be thoroughly discussed by your genetic counselor and healthcare provider so that you understand the significance of the results and what they mean for you and your family.

If the testing results indicate the presence of a genetic mutation that increases your risk of breast cancer, your provider should refer you to a breast cancer specialist to assess your overall risk profile and develop an appropriate management plan. This could include surveillance, prophylactic surgery, or in occasional cases, medications to reduce cancer risk (known as "chemoprevention").

A positive result for a "variant of unknown or uncertain significance" (VUS) indicates that a gene change was found, but how it applies to cancer risk is unknown. A negative result means a genetic mutation was not detected. It is important to note that the absence of a genetic mutation does not eliminate cancer risk.

Your healthcare provider or genetic counselor may encourage you to share the results of your genetic testing with other family members as this may help determine whether they need to pursue genetic testing.

Receiving a positive test indicating a breast cancer gene mutation is often emotionally and psychologically challenging, as can sharing the results with family members. You may want to access additional counseling and support services for help in coping with these things.