What's the Difference Between BRCA1 and BRCA2?

People who inherit pathogenic mutations in either one of these genes have an increased risk of developing certain cancers.

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BRCA1 and BRCA2 are cancer-susceptibility genes, meaning that people who inherit pathogenic* mutations in either one have an increased risk of developing certain cancers. Hereditary (or "germline") mutations in BRCA1 or BRCA2 cause Hereditary Breast and Ovarian Cancer Syndrome.

Having a pathogenic mutation in BRCA1 or BRCA2 doesn't mean you will definitely develop cancer, but it does increase one's risk. Individuals with hereditary BRCA1/2 mutations should seek proper genetic counseling and care to be aware of their risks and to take steps to reduce those risks.

How are mutations in BRCA1 and BRCA2 linked to cancer?

BRCA1 and BRCA2 are both DNA-repair genes. They hold the code for BRCA1 and BRCA2 proteins, which repair DNA damage in cells. When the BRCA1/2 genes are mutated or abnormal, they create malfunctioning BRCA1/2 proteins, which result inadequate repair of DNA damage. This can cause normal cells to turn cancerous.

How common are BRCA1 and BRCA2 mutations?

In the overall U.S. population, inherited BRCA1 or BRCA2 mutations are quite rare — estimated to affect one in 400 people, or 0.25%. The rate is higher in some racial/ethnic groups. In the Ashkenazi Jewish population, 2.5% harbor a pathogenic mutation in BRCA1 or BRCA2. There are also high rates of cancer-related BRCA1/2 mutations in individuals of other ancestries, including French Canadian, Bahamian, Middle Eastern, and Latin American.

Among patients with breast cancer but no family history of cancer, about 5% of cases are associated with BRCA1/2. In women with ovarian cancer, cancer-related germline mutations in BRCA1/2 are detected about 15% of the time. For this reason, guidelines recommend germline BRCA1/2 testing for all women with a diagnosis of ovarian cancer. Current guidelines consider whether an individual has personally had a cancer diagnosis (and the cancer type), a family history of cancer, or a known BRCA1/2 mutation in the family. For example, if an individual is diagnosed with cancer at a young age and has a family history of cancer, cancer genetic testing could be considered regardless of race, ethnicity, or ancestry.

What cancers are associated with BRCA mutations and how do BRCA mutations affect one's cancer risk?

Germline mutations in BRCA1 or 2 increase the risk of breast, ovarian, pancreatic, and prostate cancer, as well as melanoma.

The average lifetime risk of breast cancer is 12% until age 80. In women with BRCA1/2 mutations, the lifetime risk of breast cancer is 50-85%. In women with BRCA1 mutations, 69% of breast cancers are hormone receptor-negative cancers or "triple negative." In contrast, BRCA2 mutations are associated with hormone-receptor positive breast cancers (77%). Ten percent of all BRCA1 breast cancers are HER2-positive, and 13% of all BRCA2 breast cancers are HER2-positive. Women with BRCA1/2 mutations have a higher likelihood of developing breast cancer in both breasts.

Women with BRCA1/2 mutations have a higher risk of developing ovarian cancer or other related cancers of the fallopian tube or peritoneum. The average lifetime risk of ovarian cancer is 1-2%. This increases to 20-40% with BRCA1 and 10-20% with BRCA2.

For both men and women with BRCA mutations, the lifetime risk of pancreatic cancer increases from less than 1% to 2-5%, and these individuals have a higher risk of skin cancer like melanoma.

In addition to a higher risk of pancreatic cancer and melanoma, men with BRCA1/2 mutations have higher risks of breast and prostate cancer. When men with BRCA1/2 mutations develop prostate cancer, it tends to occur at a young age and is more aggressive.

How do I know if I need to get tested for BRCA1 or BRCA2? Do genetic tests cover both?

Genetic testing covers both BRCA1 and BRCA2 and is recommended for people with a high risk of having a mutation in either gene. This includes those who have:

- A family member with a BRCA1/2 mutation
- Anyone with Ashkenazi Jewish ancestry
- A personal history of breast cancer at age 45 or younger
- A personal history of triple negative breast cancer at age 60 or younger
- A personal history of breast cancer and a family history of breast cancer
- Anyone with cancer in both breasts
- Metastatic breast cancer
- A personal or family history of ovarian cancer, pancreatic cancer, aggressive prostate cancer, or metastatic prostate cancer
- A personal or family history of male breast cancer
- Anyone with genetic testing prior to 2013 who would like to consider additional genetic testing

- Anyone with more than 5% probability of BRCA mutation based on any model
- Anyone with cancer who underwent tumor genetic testing and was found to have a BRCA mutation in their tumor

What happens if I test positive for BRCA1 or BRCA2?

At Dana-Farber's Cancer Risk and Prevention Clinic, genetic counselors and physicians help individuals who test positive for BRCA1 or BRCA2 to understand the nature of their cancer risk, how it can be managed, and whether other family members should consider testing.

Genetic terminology

*__Pathogenic mutation__ in BRCA1 or BRCA2 increases an individual's risk of cancer. A pathogenic mutation is a positive result and determines that an individual has the Hereditary Breast and Ovarian Cancer Genetic Syndrome.

__Hereditary cancer__ syndromes occur when an individual inherits a genetic mutation(s) that predispose them to develop cancer. Hereditary cancer syndromes are caused by pathogenic germline or hereditary mutations.

__Germline/hereditary__ mutations are mutations in genes that are passed on from parents to offspring.

__Somatic mutations__ are mutations acquired by any cell in the body after birth and are not inherited or passed to offspring. These mutations are often detected in tumors and are of interest to developing new therapeutics to treat cancer.

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