



Cancer Genetics Summary

Breast Cancer

Breast cancer is considered common, affecting approximately 11 to 12.5 percent of women. About 90 to 95 percent of breast cancers are not related to a person's genetics. They are "sporadic" cancers that can happen to anyone. The remaining 5 to 10 percent are thought to be connected to heredity, with the BRCA1 and BRCA2 genes (BRCA1/2) accounting for two-thirds of those. Women in families with a known change in one of these genes have an increased likelihood of developing breast, ovarian and other forms of cancer. However, inheriting the hereditary factor is not enough to cause a cancer to develop. All breast cancers result from many factors, including age, lifestyle, gene changes acquired over a lifetime, environment, etc.

BRCA1 and BRCA2 are called "cancer predisposing genes" because they have mutations that are known to increase an individual's susceptibility to developing certain cancers. These mutations in BRCA1/2 account for about 65 percent of the hereditary cases of breast cancer in the United States. (This is 65 percent of the 5 to 10 percent of breast cancers that are due to a hereditary mutation.) In addition, BRCA1 and BRCA2 are estimated to be involved in causing 50 percent of hereditary ovarian cancer.

There are other known genes that predispose to the development of breast and/or ovarian cancer, but mutations in these genes are not as common. All the genes that predispose a person to developing cancer have not been identified; therefore, gene testing cannot identify all mutations that may contribute to breast and/or ovarian cancer.

BRCA1/2 cancer-predisposing mutations are inherited in an autosomal dominant manner. Every father or mother who inherits the altered gene has a 50 percent chance of passing it on to each of his or her children. The sons and daughters have an equal chance of inheriting a cancer-predisposition gene mutation.

Families with BRCA1/2 gene mutations often have several family members affected with breast and/or ovarian cancers, and the cancers tend to occur at an earlier age than in the general population. Breast cancer typically occurs in women after menopause. In families with BRCA1/2 gene mutations, women with breast cancer are often diagnosed prior to the onset of menopause; ovarian cancers may occur in women in their 30s or 40s, especially in those with BRCA1 mutations.

Individuals with a BRCA1/2 gene mutation have approximately a 65 percent likelihood of developing breast cancer, compared to 11 to 12.5 percent in the general population. Their risk of ovarian cancer is 20 to 40 percent, compared to 1.4 to 2 percent in the general population.

In addition, individuals who have had breast cancer and who have a BRCA1/2 mutation can have as much as a 65 percent chance of a recurrence of breast cancer and about a 40 percent risk of developing ovarian cancer. (In comparison, those with breast cancer who do not have a BRCA1/2 gene mutation have about a 10 percent chance of recurrence of breast cancer and a 2

percent risk for ovarian cancer.) Of course, some individuals with a BRCA1/2 mutation never develop cancer.

Men with these gene mutations may have an 8 percent higher risk for prostate cancer. Both men and women have a 6 percent increase in their risk for colon cancer. Increased risks for breast cancer in men, and an increased risk for pancreatic cancer and melanoma in both men and women, have also been associated with BRCA1/2 mutations.

Testing Process and Options

The gene testing available today for the BRCA1/2 mutation is “direct sequence analysis” and can detect 90 to 95 percent of mutations, with 98 percent accuracy. If direct sequencing does not detect an alteration, then most, but not all, mutations in BRCA1 and 2 will have been ruled out. If a cancer predisposing alteration is found, it indicates an increased predisposition for developing cancer. Following testing, an office visit with a cancer genetics counselor involves reviewing the test results, screening and early detection recommendations, as well as prophylactic surgery possibilities, if appropriate.

Receiving a negative test does not guarantee that a gene mutation is not present. Testing is not 100 percent accurate and testing is not yet available for all cancer predisposing genes. Sometimes test results are considered “uninformative,” meaning that either a gene change is detected, but it is not known if it predisposes to cancer, or no mutation is found in a family, but the family history strongly suggests an inherited predisposition.

Of course, choosing not to be tested is always an option.

One alternative to individual testing is to collect DNA samples from multiple family members and store them frozen in a banking laboratory. In this way, the family preserves the option of testing in the future. Having DNA samples from family members who may subsequently develop cancer will ensure that future generations have family genetic information available to help in the interpretation of their DNA testing.

Another alternative to testing is for a person to assume he/she has inherited the predisposition running in the family and to take steps to decrease the risk of developing cancer by more frequent screenings and/or prophylactic surgeries, when appropriate. These measures, of course, do not guarantee a 100 percent reduction in the risk of developing cancer.

For more information or questions, call 503-413-6534.

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