Yale NewHaven Health
Smilow Cancer Hospital

Yale CANCER CENTER
A Comprehensive Cancer Center Designated by the National Cancer Institute

Hereditary breast cancer

Smilow Cancer Genetics and Prevention Program

While most cases of breast cancer are not hereditary, an estimated 5 to 10 percent of breast cancer is due to an inherited cause. In some families, even when there is a high suspicion for an inherited risk, the underlying genetic cause for the breast cancer is still unknown.

Finding a hereditary explanation for breast cancer can help to:

- Guide the course of cancer treatment including decisions about surgery
- Provide a reason for why you or your relatives were diagnosed with cancer
- Alert you and your providers about possible risks for other cancers to offer guidance about additional screening or surveillance

The importance of genetic testing

Genetic testing is one way to understand if a person has a hereditary risk for breast cancer. If a person has genetic testing and finds they have a pathogenic variant (sometimes called a mutation) linked to hereditary breast cancer, it means he or she was born with an increased risk to develop breast and possibly other types of cancers. The risk for breast and other cancers associated with pathogenic variants in these genes can vary (see tables on next pages for details). Genetic testing can look for several hereditary cancer syndromes by testing a panel of genes (including *BRCA1* and *BRCA2*) that are related to hereditary breast cancer. Some of these genes have not been studied as long as other genes and some genes only have a *possible* association with breast cancer risk. For these less-studied genes, information about cancer risks and screening recommendations may change over time.

It is important to share the results of genetic testing with relatives because they may have also inherited the same increased risk to develop cancer. When a hereditary explanation is found in a family, relatives can also have genetic testing to better understand their risks. This will guide their own decisions about cancer screening, prevention and management.

High Risk Breast Cancer Genes	Lifetime Risk of Breast Cancer	Increased Risk for Other Cancers
BRCA1 ***BRCA2***	Female risk:60 percent or higher Male risk: up to 7 percent	– Ovarian cancer – Pancreatic cancer – Prostate cancer – Melanoma
CDH1	41 - 60 percent	– Diffuse stomach cancer – Possible increased risk for colorectal cancer
PALB2	41 - 60 percent	– Pancreatic cancer – Ovarian cancer – Possible increased risk for male breast, and prostate cancer
PTEN	40 -60 percent but may be higher in some families	– Thyroid, uterine, colorectal, kidney cancer, and melanoma
STK11	32 - 54 percent	– Colorectal, stomach, pancreatic, small intestine, lung, ovarian, endometrial, and cervical cancer – Increased risk for multiple polyps in small intestine
TP53	60 percent or higher	– Lifetime risk for developing cancer is approximately 90% in women and 73% in men – Risk to develop multiple different types of cancer

Low to Moderate Risk Breast Cancer Genes	Lifetime Risk of Breast Cancer	Increased Risk for Other Cancers
ATM	20 - 30 percent	– Pancreatic cancer – Ovarian cancer (slightly increased) – Possible increased risk for prostate cancer
CHEK2	20 - 40 percent	– Colorectal cancer – Possible increased risk for prostate cancer and melanoma
NF1	20 - 40 percent	– Causes Neurofibromatosis Type 1 – Nervous system tumors including benign and cancerous brain, spine, and eye tumors – Gastrointestinal Stromal Tumors (GIST)
BARD1	17-30 percent	– Unknown or limited evidence for other cancers at this time
RAD51C, RAD51D	17-30 percent	– Ovarian cancer – Possible risk for other cancers

Genes with Possible Breast Cancer Association	Lifetime Risk of Breast Cancer
BRIP1	Not well understood or defined at this time
Lynch syndrome **Genes:** ***MLH1, MSH2, MSH6, PMS2, EPCAM***	Slightly elevated above the 12 percent risk in the general population, for some but not all genes

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