Hereditary Breast Cancer
Information for Patients

What is hereditary breast cancer?
Breast cancer is the most common cancer in women. One in eight women will develop breast cancer in their lifetime. Breast cancer occurs when the cells in the breast begin to grow abnormally into a malignant tumor. About 5-10% of cases are inherited (hereditary breast cancer), while most are not. Hereditary breast cancer (HBC) occurs when a person has a genetic change (mutation) that causes their cells to be more likely to become cancerous. The mutation can be passed through generations in a family. Women and men with HBC have a higher risk of developing breast, and sometimes other cancers or health problems, as well.

How is hereditary breast cancer inherited?
Our genes, or DNA, tell the cells in our body how to work correctly. Cancer-risk genes can impact whether a cell will begin to grow uncontrollably into cancer. We have two copies of every gene, one from our mother and the other from our father. Hereditary breast cancer is most commonly inherited in an autosomal dominant way. For dominant conditions, having only one copy of a gene mutation is enough to cause symptoms. In the case of HBC, having one mutation leads to an increased risk for cancer. If a person has a mutation in one gene for HBC, there is a 50% risk that each of their children will inherit this mutation. Siblings, parents, and potentially other relatives could also have the mutation. Importantly, not everyone who has a mutation in a cancer-risk gene will develop cancer, but their chances are higher.

While rare, it is possible for a person to have a mutation for a dominant condition that is absent from both of their parents. In this situation, the mutation arose early before they were conceived or born. This is called de novo inheritance. Even after de novo inheritance, if a person has a mutation in one gene for hereditary breast cancer, each of their children will have a 50% risk to inherit the mutation.

Less commonly, HBC can be inherited in an autosomal recessive way. For recessive conditions, both copies of a person's gene must have a mutation before they will have an increased risk for cancer. Typically, an individual with a recessive condition will have inherited one mutation from their mom and one from their dad. Because the mom and dad have another copy of the gene without the mutation, they will usually not show symptoms. For these parents, there is a 25% risk with each pregnancy that the child will inherit both the mom's and the dad's mutations, and therefore, will have the recessive condition.

What are the most common breast cancer-risk genes?
Two genes, named BRCA1 and BRCA2, are common causes of hereditary breast cancer. Mutations in these two genes are also associated with a significant risk for ovarian cancer, as well as prostate and pancreatic cancer. A mutation in BRCA2 also confers a higher risk for breast cancer in men, and melanoma for both men and women. (Recommend inserting chart with specific risks from information here: https://www.ncbi.nlm.nih.gov/books/NBK1247/).
Besides BRCA1 and BRCA2, there are other cancer-risk genes associated with HBC and each one leads to a different set of cancer risks. Learn more about the genes included in Fulgent's Breast Cancer Comprehensive Panel and Breast Cancer Focus Panel (add hyperlink to panel descriptions).

What are hereditary breast cancer syndromes?
Hereditary breast cancer syndromes are conditions that impact other areas of an individual's body in addition to increasing their risk for breast cancer. A syndrome can be inherited in a dominant, de novo, or recessive manner. Some examples of hereditary breast cancer syndromes are listed below.
**Cowden syndrome (CS)**
People with Cowden syndrome often have large heads (macrocephaly) and are at an increased risk for different types of benign and malignant tumors, including endometrial, thyroid, and breast cancer. CS is caused by a mutation in the PTEN gene. The lifetime risk for breast cancer in women with Cowden syndrome can be as high as 85%.

**Ataxia telangiectasia (AT)**
Ataxia telangiectasia is a condition that usually presents in childhood with movement difficulties and frequent infections, in addition to a higher risk for cancer. AT is caused by a mutation in the ATM gene.

**Fanconi anemia (FA)**
Fanconi anemia can be caused by having two mutations in a number of different genes, and can lead to physical anomalies and progressive bone marrow failure. An increased risk of breast cancer is seen in some individuals with one mutation in a FA-associated gene.

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**Who might need genetic testing for hereditary breast cancer?**
Hereditary breast cancer testing is indicated if you or a close relative meet certain criteria. Your physician will make the final decision about testing based on your clinical and family history, but some “red flags” suspicious for HBC are listed below:

- Breast cancer diagnosed before age 50 years
- Known cancer-risk gene mutation in the family
- Triple negative (ER-, PR-, HER2-) breast cancer before age 60 years
- Two primary breast cancers in a single individual
- Breast cancer and either ovarian or pancreatic cancer in a single individual
- Ovarian cancer
- Male breast cancer
- Ashkenazi Jewish ancestry
- A family history of 3 or more individuals with breast, pancreatic, prostate, melanoma, or other cancers, especially if early onset or if multiple cancers occurred in a single individual

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**What will genetic testing tell me?**
There are three possible results from genetic testing:

- **POSITIVE:**
  A positive result means that a genetic mutation causing an increased risk for breast cancer was identified. Your risk for other cancers or health conditions may also be increased, depending on the gene involved. Your doctor can use this information to customize your care, which could include increased screening, preventative surgery, medication, and other steps. A positive result is also important for your family. Your parents, siblings, and children could have as high as a 50% chance to also have the mutation. As a result, sharing your genetic testing results with your relatives is important for their health.

- **NEGATIVE:**
  A negative result indicates that a genetic mutation was not identified. A negative result may indicate that there is not a cancer-risk gene mutation in you or your family. However, it can also mean that the gene increasing the risk in you or your family was not included on the ordered test, or that it may not be currently known. Your doctor can use a negative result to continue your treatment and screening based on your clinical and family history, or they may consider another type of genetic testing.

- **VARIANT OF UNCERTAIN CLINICAL SIGNIFICANCE (VUS):**
  The third possible test result is called a Variant of Uncertain Clinical Significance. A gene variant is a genetic difference that could be disease-causing (mutation) or could be a normal finding (benign). More research is needed to determine whether the variant is important or not, and it should be treated as a negative result until more information is available. Your doctor may follow up with the laboratory in the future to see if more has been learned. If you are interested in participating in research, many studies are listed at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).
Can family members be tested?
YES. Targeted testing (Familial Mutation Test) is available through Fulgent. The cost is much lower than the cost of a genetic panel testing.

How long does it take to receive my results?
Results are usually available in 3 to 4 weeks after the laboratory receives the sample.

Will insurance cover the cost of genetic testing?
Fulgent accepts all commercial insurance plans. Most insurance companies have specific criteria that they use to determine coverage for genetic testing. Whenever possible, Fulgent will obtain the required prior authorizations. Prior to testing, Fulgent’s insurance specialists will contact the patient if the anticipated out of pocket cost exceeds $100.

Can an employer or health insurance company use the genetic test results to discriminate against a patient or their family?
NO. The Genetic Information Nondiscrimination Act (GINA) was signed into law in 2008. It protects Americans from discrimination by an employer or a health insurance company based on genetic information. Importantly, GINA does not offer protections for disability, long term care, or life insurance. It also does not apply to members of the U.S. military or employees of the Federal government, Indian Health Service, or Veterans Health Administration.

Where can I learn more?
Bright Pink | www.brightpink.org
FORCE (Facing Our Risk of Cancer Empowered) | www.facingourrisk.org/index.php
PTEN Hamartoma Tumor Syndrome Foundation (Cowden Syndrome) | www.ptenfoundation.org