GENES

***Quick Summary* of Section**

Tumor Suppressor Gene	• Any of a class of genes that are normally involved in regulating cell growth but that may become cancer-causing when damaged.
BRCA1 and BRCA 2	• BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. These proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of each cell's genetic material.
PALB2	• The PALB2 gene is called the partner and localizer of the BRCA2 gene.
CHEK 2	• A tumor suppressor gene that encodes a serine/threonine kinase, the CHK2.
ATM	• Inherited mutations in the ATM (Ataxia-Telangiesctasia mutated) gene are associated with increased risk of certain cancers.

Tumor Suppressor Gene, *AKA* **Anti-oncogene** *and* **Inherited Gene Changes**	Any of a class of genes that are normally involved in regulating cell growth but that may become cancer-causing when damaged. • Tumor suppressor genes encode for proteins that are involved in inhibiting the proliferation of cells, which is crucial to normal cell development and differentiation. • Because of this ability, tumor suppressor genes can also act to stem the uncontrolled growth of cancer cells. Genetic damage, or mutation, that occurs to these genes contributes to the development of a cancerous tumor. *Britannica: Tumor suppressor gene* **Inherited gene changes** Certain inherited DNA mutations (changes) can dramatically increase the risk for developing certain cancers and are linked to many of the cancers that run in some families. For instance, the BRCA genes (BRCA1 and BRCA2) are tumor suppressor genes. When one of these genes changes, it no longer suppresses abnormal cell growth, and cancer is more likely to develop. A change in one of these genes can be passed from a parent to a child. *American Cancer Society: How Does Breast Cancer Start?* Other examples of inherited genes include PALB2, ATM and CHEK2.

BRCA1 and BRCA 2	BRCA1 and BRCA2 are human genes that produce tumor suppressor proteins. These proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of each cell's genetic material. • When either of these genes is mutated, or altered, such that its protein product is not made or does not function correctly, DNA damage may not be repaired properly. • As a result, cells are more likely to develop additional genetic alterations that can lead to cancer. • Specific inherited mutations in BRCA1 and BRCA2 most notably increase the risk of female breast and ovarian cancers, but they have also been associated with increased risks of several additional types of cancer. • People who have inherited mutations in BRCA1 and BRCA2 tend to develop breast and ovarian cancers at younger ages than people who do not have these mutations. • A harmful BRCA1 or BRCA2 mutation can be inherited from a person's mother or father. Each child of a parent who carries a mutation in one of these genes has a 50% chance (or 1 chance in 2) of inheriting the mutation. • About 12% of women in the general population will develop breast cancer sometime during their lives. By contrast, a recent large study estimated that about 72% of women who inherit a harmful BRCA1 mutation and about 69% of women who inherit a harmful BRCA2 mutation will develop breast cancer by the age of 80. • There also is a higher risk of developing a new primary cancer in the opposite (contralateral) breast in the years following a breast cancer diagnosis. **Who should get tested:** Several screening tools are available to help health care providers with this evaluation: • Breast cancer diagnosed before age 50 years • Cancer in both breasts in the same woman • Both breast and ovarian cancers in either the same woman or the same family • Multiple breast cancers in the family • Two or more primary types of BRCA1- or BRCA2-related cancers in a single family member • Cases of male breast cancer • Ashkenazi Jewish ethnicity *NHI – NCI (7) - BRCA Mutations*
PALB2	The PALB2 gene is called the partner and localizer of the BRCA2 gene. • Women with an abnormal PALB2 gene had a 14% risk of developing breast cancer by age 50 and a 35% risk of developing breast cancer by age 70. • Inheriting two abnormal PALB2 genes causes Fanconi anemia type N, which suppresses bone marrow function and leads to extremely low levels of red blood cells, white blood cells, and platelets. In women with an abnormal PALB2 gene, breast cancer risk was: • 8 to 9 times higher than average in women ages 20 to 39 • 6 to 8 times higher than average in women ages 40 to 60 • 5 times higher than average in women older than 60 • By age 70, women with an abnormal PALB2 gene: with no family history of breast cancer had a 33% risk of developing breast cancer. With two or more first-degree relatives (sister, mother, daughter) with breast cancer had a 58% risk of developing the disease "On the basis of our estimates, the breast-cancer risk for a PALB2 mutation carrier, even in the absence of a family history of breast cancer, would be classified as high according to various guidelines. *BreastCancer.org: Abnormal PALB2*

CHECK 2 **ATM**	**CHEK2** is a tumor suppressor gene that encodes a serine/threonine kinase, the CHK2. This gene is involved in pathways such as DNA repair, cell cycle regulation and apoptosis in response to DNA damage. Mutations of CHEK2 have been implicated in various types of cancer including breast cancer. *NCBI: Current perspectives on CHEK2 mutations in breast cancer* Women with mutations in the CHEK2 gene have an increased risk for breast cancer, sometimes at relatively young ages. This increase in risk is not as high as what is seen in women with mutations in the BRCA1 and BRCA2 genes, but it is high enough to consider ways to reduce cancer risk and to increase screening in an attempt to find any breast cancers that do develop as early as possible. A woman who has a CHEK2 mutation, and who has already had breast cancer, has a high risk of developing a second breast cancer within the next 5 to 25 years. *My support 360: CHEK2 Gene Mutations*
ATM	Inherited mutations in the ATM (Ataxia-Telangiesctasia mutated) gene are associated with increased risk of certain cancers. People who inherit a mutated copy of ATM from one parent are at increased risk of female breast cancer (up to 52% lifetime risk), and possibly pancreatic, prostate and other cancers. Ongoing research may identify other cancer risk, such prostate and pancreatic cancer in people with inherited ATM mutations. *FORCE-Facing Our Risk of Cancer Empowered, Inc: No one should face hereditary cancer alone*
HER2/neu gene	***See Prognosis Markers***

American Cancer Society: How Does Breast Cancer Start? *https://www.cancer.org/cancer/breast-cancer/about/how-does-breast-cancer-form.html*

American Cancer Society: Understanding Your Pathology Report: Breast Cancer *https://www.cancer.org/treatment/understanding-your-diagnosis/tests/understanding-your-pathology-report/breast-pathology/breast-cancer-pathology.html*

BreastCancer.org: Abnormal PALB2 Gene Increases Breast Cancer Risk More Than Previously Thought *https://www.breastcancer.org/research-news/abnormal-palb2-gene-increases-risk*

Britannica: Tumour suppressor gene *https://www.britannica.com/science/tumor-suppressor-gene*

FORCE-Facing Our Risk of Cancer Empowered, Inc: No one should face hereditary cancer alone *https://www.facingourrisk.org/understanding-brca-and-hboc/information/hereditary-cancer/other-genes/basics/atm.php*

My support 360: CHEK2 Gene Mutations *https://mysupport360.com/associations/genes/chek2-gene-mutations/*

NCBI: Current perspectives on CHEK2 mutations in breast cancer *https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5439543/*

NHI – NCI (7)- BRCA Mutations *https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet#what-are-brca1-and-brca2*