



Fact Sheet

PALB2 Mutations

Brought to you by the *National Society of Genetic Counselors, Cancer Special Interest Group*

What you should know about *PALB2* Mutations

People with a single *PALB2* mutation are at an increased risk to develop certain cancers, such as female breast cancer, male breast cancer, ovarian cancer, and pancreatic cancer. Individuals with two mutations in the *PALB2* gene (one from each parent) have Fanconi Anemia (FA). FA is a childhood onset genetic condition that is characterized by progressive bone marrow failure, short stature, microcephaly, and eye and genitourinary tract anomalies. Individuals with Fanconi Anemia also have an increased risk for some cancers, such as leukemia, head and neck cancers, skin cancers, and gastrointestinal and genitourinary tract cancers.

Cancer Risks and Features Associated with *PALB2* Mutations

Cancer Type	Lifetime Risk	General Population risk
Female Breast Cancer	33-58%	12%
Male Breast Cancer	1%	0.1%
Ovarian Cancer	Possibly increased	1.3%
Pancreatic Cancer	Increased	1.6%

Genetics and Inheritance of *PALB2* Mutations

Genes are our body's instructions. They provide our body with information about how to grow and develop. When there is a mutation in a gene it can cause the gene to no longer function correctly. Each person has two copies of every gene. One copy is inherited from their mother and the other copy is inherited from their father.

Cancer risks associated with mutations in the *PALB2* gene are inherited in an autosomal dominant manner. This means that children, siblings and parents of individuals with a *PALB2* mutation have a 50% (1 in 2) chance of having the mutation as well. Both males and females can inherit a *PALB2* mutation and can pass it on to their children.

If two individuals with *PALB2* mutations have a child together, there is a 25% (1 in 4) chance that the child will inherit both *PALB2* mutations. Individuals who inherit two mutations in the *PALB2* gene (one from each parent) have a different condition called Fanconi Anemia.

Managing Cancer Risks

Female Breast Cancer

- Starting at 30y (or 5-10 years before the youngest breast cancer diagnosis in the family)
 - Annual mammogram with consideration of tomosynthesis
 - Consider annual breast MRI with contrast
- Discuss option of risk-reducing mastectomy

Male Breast Cancer

- Currently there are no specific management recommendations for male breast cancer risk in *PALB2* carriers
- However, can consider clinical breast examinations and patient breast awareness education

To find a genetic counselor near you, go to www.nsgc.org



Managing Cancer Risks (Continued)

Ovarian Cancer

- Currently there are no specific management recommendations for ovarian cancer risk in *PALB2* carriers
 - Manage based on family history

Pancreatic Cancer

- If a close blood relative has a history of pancreatic cancer:
 - Annual screening with contrast-enhanced MRI/MRCP and/or endoscopic ultrasound starting at 50y OR 10 years younger than youngest pancreatic cancer case in family
- If no family history of pancreatic cancer:
 - No screening is currently recommended

Genetic Counseling

In many families, the cancer history may be due to a combination of genetic and environmental factors. In addition, other genetic conditions (i.e. other gene mutations) may appear clinically similar to *PALB2* mutations. For this reason, a detailed review of the family history by a genetics professional is important before pursuing genetic testing. A genetic counselor can help determine which, if any, genetic tests may be helpful for a family and review the benefits, risks and limitations of genetic testing. Genetic testing is usually performed through a blood or saliva sample.

Genetic test results can be complicated and are most useful when interpreted by a genetics professional in the context of an individual's personal and family history. To locate a genetic counselor near you, please visit www.nsgc.org and click on the 'Find a Genetic Counselor' link.

Genetic Discrimination

The Genetic Information Nondiscrimination Act (GINA) was signed into federal law in 2008. GINA prohibits health insurers and most employers from discriminating against individuals based on genetic information (including the results of genetic tests and family history information). According to GINA, health insurance companies cannot consider genetic information to be a preexisting condition, nor can they use it to make decisions regarding coverage or rates. GINA also makes it illegal for most employers to use genetic information in making decisions about hiring, firing, promotion, or terms of employment. It is important to note that GINA does not offer protections for life insurance, disability insurance, or long-term care insurance. More information about GINA can be found by contacting a local genetic counselor or by visiting www.ginahelp.org.

Resources

- My Support 360: <https://mysupport360.com/associations/genes/palb2-gene-mutations/>
- PALB2 Interest Group: <http://www.palb2.org/>
- FORCE: <https://www.facingourrisk.org/understanding-brca-and-hboc/information/hereditary-cancer/other-genes/basics/palb2.php>

References

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- Silvestri, V., Zelli, V., Valentini, V. et al. (2016). Whole-Exome sequencing and targeted gene sequencing provide insights into the role of *PALB2* as a male breast cancer susceptibility gene. *Cancer*, 123(2), 210–218.
- Rahman, N., Seal, S., Thompson, D., et al. (2007). *PALB2*, which encodes a *BRCA2*-interacting protein, is a breast cancer susceptibility gene. *Nature genetics*, 39(2), 165–167.
- Genetics Home Reference: <https://ghr.nlm.nih.gov/gene/PALB2#resources>
- "NCCN Clinical Practice Guidelines in Oncology Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic." NCCN, 4 Dec. 2019.