riscover®
HEREDITARY CANCER

Result Navigator

Positive Test Result: *CDKN2A*

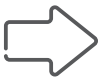
Positive test results identify a change, or "misspelling," of DNA that is known or predicted to cause an increased risk for cancer. DNA is the blueprint of life—it carries all of the genetic information needed for our bodies to function. A section of DNA with a specific job is called a gene. A pathogenic variant is a change in a gene that is known to cause increased risk for cancer. A likely pathogenic variant is a change in a gene that is very likely to cause increased risk for cancer.

After a positive test result, there can be many questions about what to do next.

This guide is a supplement to Riscover® Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

Navigate Your Results

Learn | *page 2*
Review the test results along with this guide, and discuss the meaning of these results with your healthcare provider.



Plan | *page 3*
Develop a healthcare plan for early detection and prevention of specific cancers.

Share | *page 4*
Understand the risks for other family members, and consider how to inform relatives of their risks.

Connect | *page 5*
Reach out to medical experts and find local and national groups that can provide more information and support.

Glossary of Terms

Gene: A section of DNA with a specific job.

Endoscopic ultrasound: Insertion of the tube into mouth down into the stomach/small intestine. At the base of the tube is an ultrasound probe that is used to visualize the internal organs (such as the stomach, small intestine, pancreas, liver or bile ducts).

Melanoma: Type of cancer that develops from the melanocytes, which are skin cells that contain pigment and are responsible for the color of the skin.

MRCP (Magnetic resonance cholangiopancreatography): Specific type of MRI that focuses on the pancreas, pancreatic duct, liver, gallbladder, and bile duct.

MRI: An abbreviation for magnetic resonance imaging, a test that provides detailed pictures of a specific part of the body.

Pathogenic: Causing or capable of causing disease.

Risk: The chance, or possibility, of developing a disease.

Variant: A change, or "misspelling," in the DNA sequence. Variants can be benign (not associated with disease), pathogenic (associated with disease), or of uncertain significance.

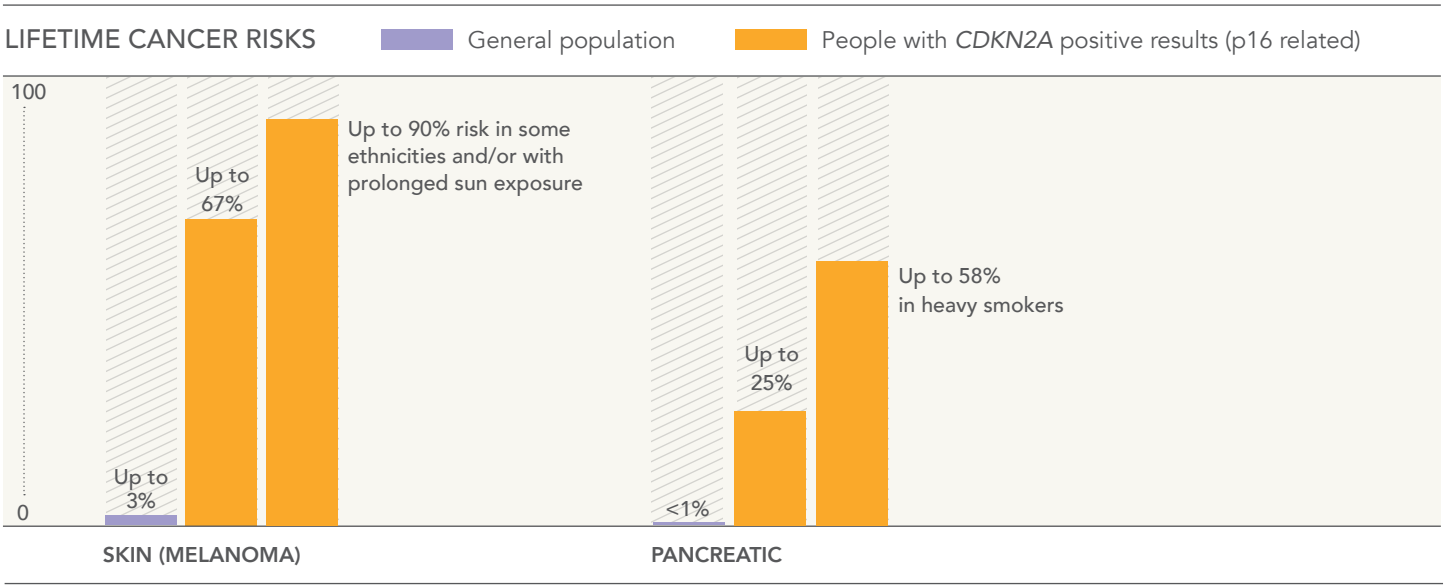
Your Diagnosis: Familial Atypical Multiple Mole Melanoma Syndrome

Familial atypical multiple mole melanoma syndrome (FAMM) is an inherited disorder caused by a pathogenic/likely pathogenic variant in the *CDKN2A* gene. FAMM is associated with an increased lifetime risk of melanoma and pancreatic cancer. FAMM has also been called hereditary melanoma- pancreatic cancer syndrome (M-PCS). Approximately 5 – 12% of all melanoma is associated with an inherited gene variant. Pathogenic variants in the *CDKN2A* gene account for about 20 – 40% of all hereditary cases.

It is unknown how many people in the general population have a *CDKN2A* pathogenic variant. Some individuals with a *CDKN2A* pathogenic variant will have a higher risk of cancer based on their specific variant, ethnicity, and level of sun exposure.

Your Risk

Not all people with positive test results will develop cancer, but the chance for cancer is higher than the general population risk. The graphs below show how much the risk for cancer increases when a pathogenic variant is found. The cancer risks are presented in ranges based on multiple studies of families who have a pathogenic variant. There is not enough evidence available to give a specific risk to a person or family.



Your Screening and Management Options

Listed below are the intervention options that are recommended by medical experts for individuals who carry this cancer gene variant. Your healthcare provider can explain these options in more detail, and together you can make a plan for cancer prevention and/or early detection.

MELANOMA

Whole body dermatologic (skin) examinations	Whole body dermatologic examinations are recommended every 6 – 12 months beginning at age 10, or earlier based on personal and family history of melanoma.
Self-skin examination	Self-skin examinations are recommended on a monthly basis beginning at age 10.
Sun protection	Sun protection is recommended.

PANCREATIC CANCER

Endoscopic ultrasound (EUS) and/or MRI/MRCP	No specific guidelines are available. Your healthcare provider can recommend screening options based on your personal and family history of pancreatic cancer.
Smoking avoidance	Smoking increases cancer risks and should be avoided.

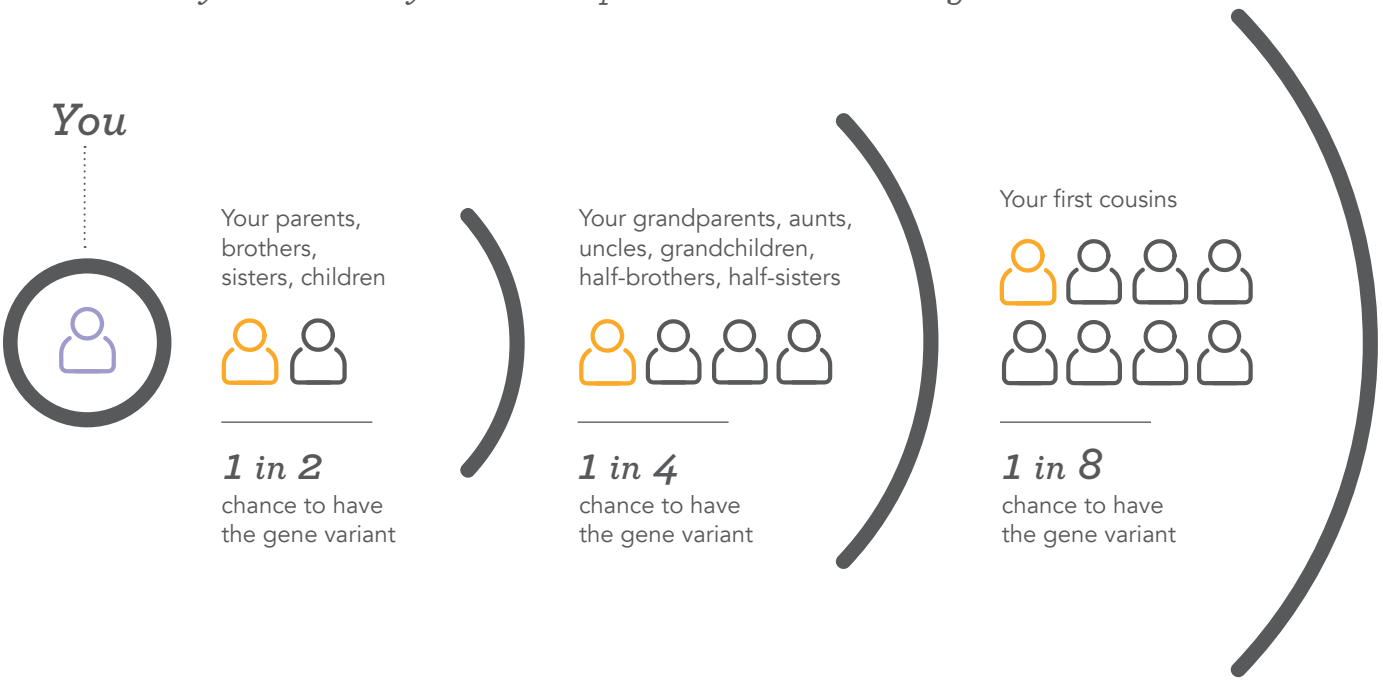
Your Family Matters

Cancer gene variants are inherited in an autosomal dominant manner. This means that when a parent tests positive, each child has a 1 in 2 chance to inherit the variant. Some people who inherit the variant will develop cancer, and some will not, but the risks are significantly increased compared to the average person. People in the same family may develop different types of cancers at varying ages, and the pattern of cancer and age of onset can differ from family to family.

Gene variants can be passed through families for many generations. When a gene variant is identified in one person in the family, relatives can be tested for just that variant. Sharing information about test results with family members is important, because it allows them to make informed choices about their healthcare and to decide whether they want genetic testing.

Some people who have pathogenic and likely pathogenic variants are interested in learning how to avoid passing these variants on to their children. If you are planning to have a child, you may wish to consult with a reproductive medicine specialist to discuss all of your reproductive options, including use of an egg or sperm donor, preimplantation genetic diagnosis, and prenatal genetic testing.

The likelihood for family members to carry the same gene variant depends on how closely related they are to the person with a known gene variant.



Your Expert Team

As you take your next steps, it can help to have a team of experts on your side. This team may include your primary care provider and a number of specialists who will help along the way.

If you haven't already done so, you may wish to speak with a genetic counselor. Genetic counselors are healthcare professionals with specialized training in medical genetics and counseling. They can help you understand your test results, discuss your healthcare plan, and connect to other resources in your area. Your healthcare provider may be able to provide a referral to a local genetic counselor. You can also find a genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

For questions about your test results, our genetic counseling team is available to help.
To reach a genetic counselor, call +1 855-293-2639 and select option 3.

Helpful Resources

American Cancer Society
cancer.org/cancer/cancercauses/sunanduvexposure/skincancerpreventionandearlydetection
National organization whose mission is to eliminate cancer and improve the lives of individuals with cancer through research, education, advocacy, and service.

National Comprehensive Cancer Network (NCCN)
nccn.org
Expert guidelines for cancer screening and treatment. Versions available for both providers and patients.

Skin Cancer Foundation
skincancer.org
International organization whose mission is to create public awareness and educational programs that help people understand the importance of skin cancer prevention, early detection and prompt, effective treatment.

REFERENCES

Mize DE, Bishop M, Resse E, Sluzevich, J. Familial Atypical Multiple Mole Melanoma Syndrome. In: Riegert-Johnson DL, Boardman LA, Hefferon T, et al., editors. Cancer Syndromes [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2009-2016. Available from: http://www.ncbi.nlm.nih.gov/books/NBK7030

National Comprehensive Cancer Network. Pancreatic Adenocarcinoma (Version 2.2018). Available from: http://www.nccn.org

Potrony M et al. Update in genetic susceptibility in melanoma. 2015. Annals of Translational Medicine, 3 (15), 1-12

Skin Cancer Prevention and Early Detection. American Cancer Society.
Available from: http://www.cancer.org/acs/groups/cid/documents/webcontent/003184-pdf.pdf