

## Result Navigator

### ⊕ Positive Test Result: CDK4

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. Another name for these types of variants is mutation.

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

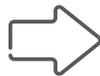
This guide is a supplement to Riscover™ Hereditary Cancer test results, helping patients and healthcare providers understand the results and together determine the best path forward.

## 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.

**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.

**Mutation:** A change in a gene that causes or is capable of causing disease. Another word for pathogenic/likely pathogenic variants.

**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: Hereditary Cutaneous Melanoma

Hereditary cutaneous melanoma is an inherited disorder associated with an increased lifetime risk of melanoma (skin cancer). Up to 5 – 12% of all melanoma is associated with an inherited gene variant. Pathogenic variants in the *CDK4* gene account for about 1 – 3% of all hereditary cases.

It is unknown how many people in the general population have a *CDK4* pathogenic variant. Some people with a *CDK4* pathogenic variant will have a higher risk of cancer based on their ethnicity and level of sun exposure.

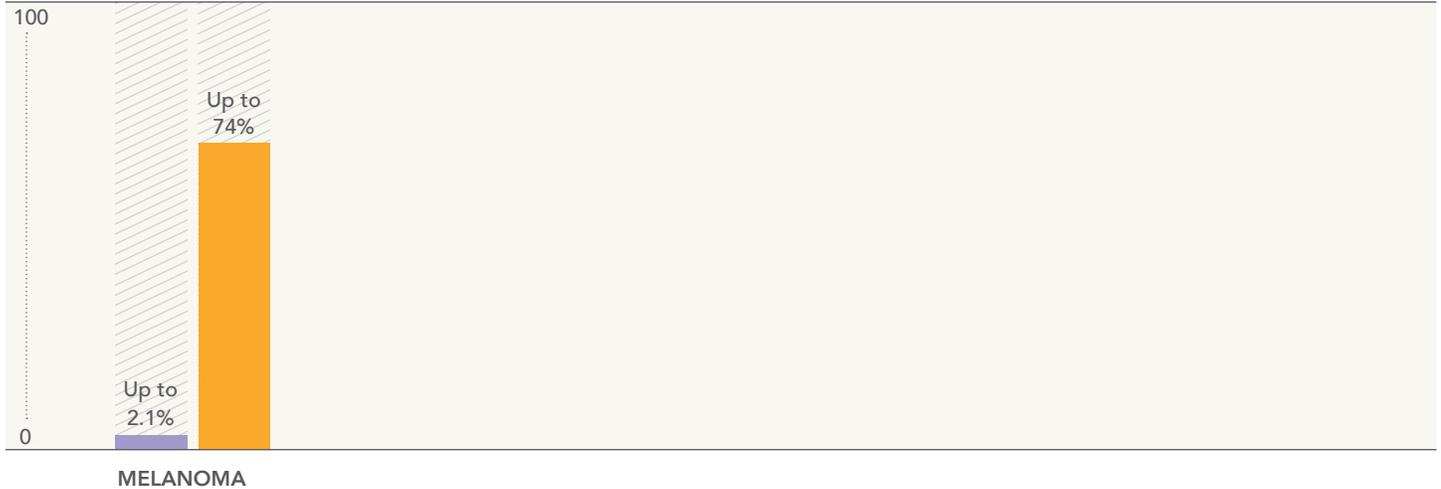
## Your Risk

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.

LIFETIME CANCER RISKS

■ General population

■ People with *CDK4* positive results



## 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 in childhood.

Self-skin examination

Self-skin examinations are recommended on a monthly basis beginning in childhood.

Sun protection

Sun protection is recommended.

---

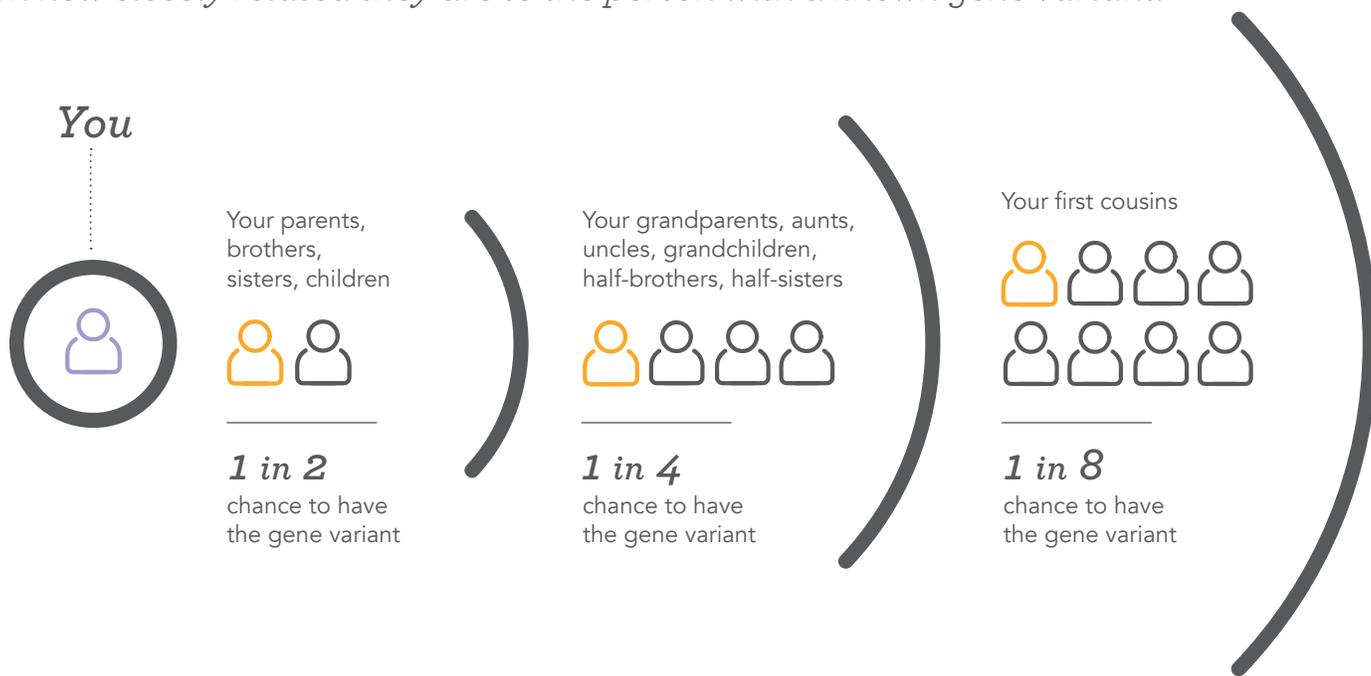
## Your Family Matters

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](http://www.nsgc.org).

For questions about your test results, Progenity's 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](http://cancer.org)

National organization whose mission is to eliminate cancer and improve the lives of individuals with cancer through research, education, advocacy, and service.

### REFERENCES

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

Puntervoll HE, Yang XR, Vetti HH, et al. "Melanoma prone families with CDK4 germline mutation: phenotypic profile and associations with MC1R variants." *J Med Genet*. 2013 Apr; 50(4):264-70. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3607098>

Skin Cancer Prevention and Early Detection. American Cancer Society.

Available from: <http://www.cancer.org/acs/groups/cid/documents/webcontent/003184-pdf.pdf>

5230 S. State Road, Ann Arbor, MI 48108 USA • Tel +1 855-293-2639 • [progenity.com](http://progenity.com)

Progenity is a CLIA-certified clinical laboratory and is accredited by the College of American Pathologists (CAP). The information contained in this document is provided by Progenity as an educational service for clinicians and their patients. © 2015, 2016 Progenity, Inc. All rights reserved. Progenity® is a registered service mark of Progenity, Inc. Riscover™ is a trademark of Progenity, Inc. WH-55010-01 REV 122016