

## **Familial Malignant Melanoma [1]**

### **What is familial malignant melanoma?**

Familial malignant melanoma is a term usually referring to families in which two or more first-degree relatives, such as a parent, sibling, and/or child, have a type of skin cancer called [melanoma](#) [2]. Cancer begins when healthy cells begin to change and grow uncontrollably forming a mass called a tumor. Overall, about 8% of people newly diagnosed with melanoma have a first-degree relative with melanoma. A much smaller percentage, about 1% to 2%, has two or more close relatives with melanoma.

Dysplastic nevi are large, flat, irregular, asymmetric, variably pigmented moles. They occur primarily on sun-exposed skin, but they also occur in areas that are not exposed to the sun. Individuals in melanoma-prone families frequently have these moles. The moles must be monitored very carefully for any change in size, shape, and color to watch for cancer. In the United States, the average age when melanoma is diagnosed in people with familial melanoma is in the 30s; the average age when melanoma is diagnosed in the general population is in the 50s.

### **What causes familial melanoma?**

Familial melanoma is a genetic or inherited condition. This means that the risk of melanoma can be passed from generation to generation in a family. To date, two genes have been linked to familial melanoma; they are called *CDKN2A* and *CDK4*. A mutation (alteration) in one of these genes gives a person an increased risk of melanoma. However, alterations in these two genes only account for a small percentage of familial melanoma.

*CDKN2A* is unusual because it affects two separate proteins that have different functions; one is called p16, and one is called p14ARF. Both *CDKN2A* and *CDK4* play important roles in controlling

when cells divide. Studies of families with mutations in *CDKN2A* from Europe, North America, and Australia have shown that the risk of melanoma varies by geographic area. The reasons for these differences are not fully understood. There may be differences in the amount of sun they receive, other individual or genetic differences, or a combination of these factors.

Within melanoma-prone families with known genetic mutations, dysplastic nevi (moles) and sun exposure are independent risk factors for melanoma. There is also growing evidence that variations in another gene, *MC1R*, alter the risk of melanoma, both in individuals with *CDKN2A* mutations and in individuals without *CDKN2A* mutations. *MC1R* is important in regulating pigment; variations have been associated with freckling and red hair.

Other inherited genes are associated with an increased risk of melanoma. For instance, [xeroderma pigmentosum](#) [3] (XP) is a rare disorder in which patients have a mutation in a gene needed for repair of ultraviolet radiation (sunlight) induced DNA damage. Patients with XP have an extremely high rate of skin cancer, including melanoma. A [hereditary breast cancer gene](#) [4] called *BRCA2* is also associated with a risk of melanoma. Scientists believe that there are other genes not yet identified that also increase the risk of melanoma. Learn more about the [risk factors of melanoma](#) [5]. Research is ongoing to learn more about familial melanoma.

## **How is familial melanoma susceptibility inherited?**

Normally, every cell has two copies of each gene: one inherited from the mother and one inherited from the father. Familial melanoma susceptibility follows an autosomal dominant inheritance pattern, in which case a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of his or her normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

Options exist for couples interested in having a child when they know that one of them carries a gene mutation that increases the risk for this hereditary cancer syndrome. Preimplantation genetic diagnosis (PGD) is a medical procedure done in conjunction with in-vitro fertilization (IVF). It allows people who carry a specific known genetic mutation to have children who do not carry the mutation. A woman's eggs are removed and fertilized in a laboratory. When the embryos reach a certain size, one cell is removed and is tested for the hereditary condition in question. The parents can then choose to transfer embryos which do not have the mutation. PGD has been in use for over a decade, and more recently has been used for several hereditary cancer predisposition syndromes. However, this is a complex procedure with financial, physical, and emotional factors for couples to consider before starting. For more information, talk with an assisted reproduction specialist at a fertility clinic.

## **How common is familial melanoma?**

Most cases of melanoma are sporadic, meaning it occurs by chance. The number of people who

have an inherited risk of melanoma is unknown, but the number is thought to be low. It is estimated that about 8% of people with melanoma have a first-degree relative with melanoma and that 1% to 2% of people with melanoma have two or more close relatives with melanoma.

## **How is familial melanoma diagnosed?**

Familial melanoma is suspected when two or more close relatives have invasive melanomas, meaning the melanoma has spread to other parts of the body. In areas of higher sun exposure, like the southern United States or Australia, the frequency of sporadic melanoma is higher, so familial melanoma is not diagnosed unless three or more close relatives have invasive melanoma. Familial melanoma may also be suspected if a single family member has multiple melanomas.

Genetic testing for mutations in the *CDKN2A* gene is commercially available. However, genetic test results are unlikely to change screening recommendations or clinical care for people who have had melanoma or people who have a strong family history of melanoma. Most families with familial melanoma will not even have a genetic mutation identified.

## **What are the estimated cancer risks associated with familial melanoma?**

A person with a hereditary risk of melanoma has a greatly increased risk of developing melanoma during his or her lifetime.

There is also an increased risk of [pancreatic cancer](#) [6] in families with familial melanoma and *CDKN2A* mutations, but this is relatively rare. Brain tumors have also been reported in a few families. In people with XP, there is also an increased risk of other skin cancers, such as squamous and basal cell carcinomas. In people with the *BRCA2* mutation, there is also an increased risk of breast and ovarian cancer in women, prostate cancer in men, and pancreatic cancer in both men and women.

## **What are the screening options for familial melanoma?**

Anyone with a parent, sibling, or child who has had melanoma should be carefully monitored. In people that have had melanoma, thorough skin exams should initially be performed every three to six months by a dermatologist, a doctor who specializes in skin problems, a nurse specializing in dermatology, or another specially trained health care provider to monitor any pigmented lesions (mole or spot). It is important to [watch moles closely for any signs of change in shape, size, or color](#) [5]. Dermatologists may take pictures of the skin and moles, known as mole mapping, or view moles with a hand-held device known as a dermatoscope. This may be helpful to show changes over time. Any suspicious moles or other skin changes should be removed by a doctor so the tissue can be analyzed under a microscope.

In families known or strongly suspected to have familial melanoma, children should begin screening by age 10. Family members should also perform regular self-examinations to look for

skin changes. Due to the high risk of multiple melanomas, people with familial melanoma should avoid sun exposure unprotected. Learn more about [protecting your skin from the sun](#) [7].

Screening recommendations may change over time as new technologies are developed, and more is learned about familial melanoma. It is important to talk with your doctor about appropriate screening tests.

Learn more about [what to expect when having common tests, procedures, and scans](#) [8].

## Questions to ask the doctor

If you are concerned about your risk of melanoma, talk with your doctor. Consider asking the following questions of your doctor:

- What is my risk of melanoma?
- What can I do to reduce my risk of cancer?
- What are my options for cancer screening?

If you are concerned about your family history and think that you or other family members may have familial melanoma, consider asking the following questions:

- Does my family history increase my risk of melanoma?
- Does it suggest the need for a cancer risk assessment?
- Will you refer me to a genetic counselor or other genetics specialist?
- Should I consider [genetic testing](#) [9]?
- What preventive measures do you recommend?

## More Information

[The Genetics of Cancer](#) [10]

[Genetic Testing](#) [9]

[What to Expect When You Meet With a Genetic Counselor](#) [11]

[Collecting Your Family Cancer History](#) [12]

[Sharing Genetic Test Results with Your Family](#) [13]

## Additional Resources

**National Cancer Institute**

[www.cancer.gov](http://www.cancer.gov) [14]

**American Cancer Society**

[www.cancer.org](http://www.cancer.org) [15]

## **CancerCare**

[www.cancercare.org](http://www.cancercare.org) [16]

To find a genetic counselor in your area, ask your doctor or visit these websites:

## **National Society of Genetic Counselors**

[www.nsgc.org](http://www.nsgc.org) [17]

## **National Cancer Institute: Cancer Genetics Services Directory**

[www.cancer.gov/cancertopics/genetics/directory](http://www.cancer.gov/cancertopics/genetics/directory) [18]

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### **Links**

[1] <http://www.cancer.net/cancer-types/familial-malignant-melanoma>

[2] <http://www.cancer.net/node/31265>

[3] <http://www.cancer.net/node/19727>

[4] <http://www.cancer.net/node/18922>

[5] <http://www.cancer.net/node/19254>

[6] <http://www.cancer.net/node/31388>

[7] <http://www.cancer.net/node/24659>

[8] <http://www.cancer.net/node/24959>

[9] <http://www.cancer.net/node/24895>

[10] <http://www.cancer.net/node/24897>

[11] <http://www.cancer.net/node/24907>

[12] <http://www.cancer.net/node/30761>

[13] <http://www.cancer.net/node/24906>

[14] <http://www.cancer.gov/>

[15] <http://www.cancer.org/>

[16] <http://www.cancercare.org/>

[17] <http://www.nsgc.org/>

[18] <http://www.cancer.gov/cancertopics/genetics/directory>