Genetic Risk for Melanoma

Most cases of melanoma are sporadic and related to environmental exposure. However, there are cases that are hereditary. 10-15% of patients with melanoma have a positive family history.  

Only a minority of these cases represent true hereditary melanoma. A discussion of important genes and other genetic risk factors is below.

CDKN2A

This is the most common mutated gene associated with melanoma. It is a tumor suppressor gene and is also known as p16. A mutation results in loss of cell cycle control and inappropriate cell growth and division. Families with this mutation have multiple affected members, individuals with melanomas at an early age, and multiple melanomas per person. Additionally, there is an association between this mutation and pancreatic cancer.

CDK4

This is a less common mutated gene associated with familial melanoma. A mutation in CDK4 results in a very similar clinical picture as CDKN2A.

Familial atypical mole and melanoma (FAMM) syndrome

This is an autosomal dominant syndrome that carries an estimated lifetime risk of developing malignant melanoma of up to 100%. It may also be referred to as dysplastic nevus syndrome or atypical mole syndrome. It is estimated to be responsible for about 5.5% of all melanoma cases. Afflicted family members present with multiple dysplastic nevi. These nevi are not considered premalignant, but rather separate markers for genetic susceptibility to the development of melanoma later on. Patients with this syndrome are more likely to develop multiple melanomas as well as melanoma at a younger age.

Xeroderma pigmentosum

Xeroderma pigmentosum is an autosomal recessive disease with mutations in the nucleotide excision repair enzymes responsible for DNA repair after damage from UV radiation. Patients with xeroderma pigmentosum have an increased risk of developing all types of skin cancer, including melanoma, often developing cancer before age 10. One study found the risk of developing melanoma to be 22%, or 1000 times the risk of the general population.

References:


