

Family members without inherited mutation have increased risk of melanoma

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In families who carry certain inherited mutations that increase the risk for melanoma, members who do not carry the mutation also have an increased risk of melanoma, a study from Karolinska Institutet published in *Genetics in Medicine* reports. The phenomenon, which is called phenocopy, could result from other shared risk-enhancing genes or environmental factors within the families.

Malignant [melanoma](#) of the skin is one of the fastest increasing cancer types in the West. The main risk factors for melanoma are UV light exposure and hereditary factors. It is therefore relatively common for the afflicted to have family members with the disease. Inherited [mutations](#) of the tumour suppressor gene CDKN2A are the strongest known risk factors for familial melanoma and mutations in this gene also increase the risk of other cancers. Children, siblings or parents of mutation carriers have a 50-50 chance of also having the mutation, which can be identified with a gene test.

The present study included Swedish and American families with inherited CDKN2A mutations. The researchers studied whether family members who

have not inherited the mutation have any higher than normal risk of developing melanoma or other cancers.

Melanoma, but no other cancers, was more common in the non-carriers in these families compared to the normal population. The phenomenon whereby non-carriers of a specific mutation copy the phenotype (in this case melanoma) from their mutation-carrying relatives is known as phenocopy.

"Phenocopy can be caused by other risk-modifying [genes](#) or exposure patterns that increase the probability of the specific phenotype manifesting itself," says the study's first author Hildur Helgadóttir, researcher at Karolinska Institutet's Department of Oncology-Pathology, Stockholm, Sweden.

Previous studies have shown that people with the mutation who also have certain pigmentation variants run an even higher risk of melanoma. Even though the CDKN2A mutation should be present in all populations, it has almost exclusively been identified in families with a Caucasian heritage.

"This suggests that dark-skinned people with this mutation probably don't develop melanoma as often and are therefore not tested for this specific mutation, presumably because they lack the risk-modifying pigmentation variants that increase the risk of melanoma," says Dr Helgadóttir.

The researchers believe that such pigmentation variants also contribute to a higher melanoma risk in the family members who do not carry the mutation.

"Our results suggest that [family members](#) that test negatively for their family's CDKN2A mutation should be informed that they still can have an increased risk of developing melanoma. They should be advised to avoid sunburn, be aware of

any change in their moles, and some might even need to be monitored by a dermatologist," says Dr Helgadóttir.

More information: Hildur Helgadóttir et al. Phenocopies in melanoma-prone families with germ-line CDKN2A mutations, *Genetics in Medicine* (2017). DOI: [10.1038/GIM.2017.216](https://doi.org/10.1038/GIM.2017.216)

Provided by Karolinska Institutet

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