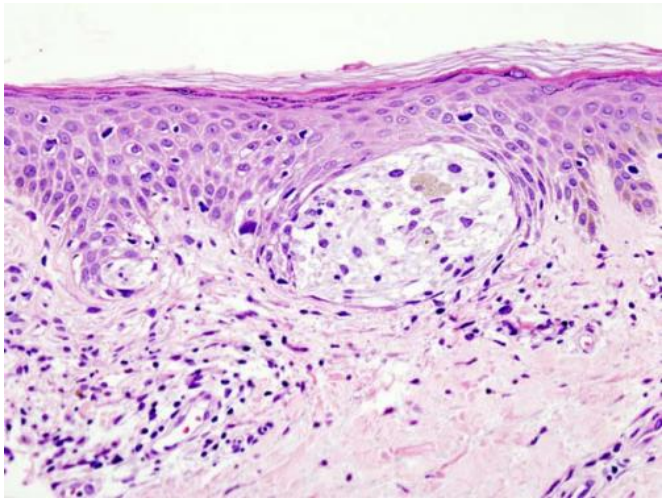
Inherited mutation doubles the risk of death from malignant melanoma

14 June 2016



Melanoma in skin biopsy with H&E stain — this case may represent superficial spreading melanoma. Credit: Wikipedia/CC BY-SA 3.0

People with malignant melanoma with an inherited mutation in a certain gene are twice as likely to die of the disease, according to a new study carried out by researchers at Karolinska Institutet and Lund University in Sweden. The finding, which is published in The *Journal of the National Cancer Institute*, suggests that individuals with familial melanoma who have the mutation should be monitored particularly closely.

Exposure to the sun is a key risk factor of malignant melanoma, one of the fastest growing cancers in the West. Often, however, heredity plays an important part as well. Roughly one in ten people with familial melanoma has a mutation in a gene called CDKN2A, a so-called tumour-suppressor gene, which prevents cancer cells from developing in the body.

Increase risk

It has been known since the mid-1990s that mutations in this gene greatly increase the risk of developing malignant melanoma. Researchers have previously shown that people with a CDKN2A mutation also have an elevated risk of smoking-associated cancer in the airwaves and upper digestive organs. In the present study, the researchers show for the first time that mutations in the gene also affect survival rates for melanoma.

"We found that the individuals who had an inherited CDKN2A mutation were on average ten years younger when diagnosed with melanoma than those with familial melanoma but no mutation," says co-author Hildur Helgadottir at Karolinska Institutet's Department of Oncology-Pathology. "However, despite the fact that lower age at diagnosis usually is a protective factor, they run more than twice the risk of dying from their melanoma. They are also seven times more likely to die of another cancer than non-carriers of the gene mutation."

The shorter survival time amongst mutation-carriers remains when adjusted for other examined factors that might affect the progression and survival from the disease, including thickness of the skin melanoma.

Undiscovered factors

The researchers argue that this suggests the presence of still undiscovered biological factors in the tumours of individuals with CDKN2A mutations that make them more aggressive than those of non-carriers.

"These findings emphasize the importance of including CDKN2A mutation-carriers in preventive health programmes. The aim is to prevent the development of tumours by giving advice on healthy sun-habits and promote abstinence from tobacco use and also to identify tumours at as early stages as possible and to discover any relapses

before they become untreatable," says Dr Helgadottir.

Since the 1980s, Swedish families with multiple cases of malignant melanoma have been included in a preventive programme. In this study, the researchers linked data on CDKN2A mutations in these family members to data from Swedish health and population registries. In this way comprehensive information on all cancer types that had been diagnosed along with information on all registered deaths was obtained to ascertain if there is a link between the mutation and survival.

More information: Hildur Helgadottir et al. GermlineMutation Status and Survival in Familial Melanoma Cases, *Journal of the National Cancer Institute* (2016). DOI: 10.1093/jnci/djw135