

Gene discovery may explain female melanoma survival advantage

August 13 2020

Centenary Institute scientists have discovered that genes on the X chromosome may be key to the improved survival rates of females with melanoma—as compared to their male counterparts. The findings could ultimately lead to more effective treatments for what is an aggressive and potentially deadly form of skin cancer.

We know that survival from [melanoma](#) is strongly related to gender with females having a survival rate almost twice that of males," said Dr. Abdullah Al Emran, researcher in the Melanoma Oncology and Immunology Program at the Centenary Institute and lead author of the study.

"Many explanations such as behavioral differences in sun exposure and other factors have been previously proposed for this gender difference but none had withstood critical scrutiny. We believed that further examination of the role of the X chromosome was warranted."

What the researchers explored were a number of genes on the X chromosome—and more specifically those genes that had been found to escape a [cellular process](#) called 'X-inactivation'.

A normal regulatory process in the body, X-inactivation is where one of a female's two X [chromosomes](#) is inactivated or silenced during embryonic development. Only one functional copy of the X chromosome is required in each body cell.

This 'silencing' process is not perfect however—between 10-20% of the genes on the silenced X chromosome are still able to be expressed. As a result of this phenomena females have a double expression of many genes involved in immune responses when compared to males.

"Our study found that two of these genes on the X chromosome that manage to escape inactivation—the [genes](#) KDM6A and ATRX—were both associated with improved survival rates for women with melanoma. We believe that their high expression levels aid the body's [immune system](#) in helping to fight cancer," said Dr. Emran.

Notably, the researchers were also able to show a clear link of the gene KDM6A to components of the immune system believed to be important in the killing of melanoma. This was particularly so in the production of interferon gamma, a key protein activated by the immune system to help kill cancer cells.

Professor Peter Hersey, Head of the Melanoma Oncology and Immunology Program at the Centenary Institute, together with co-senior study author Dr. Jessamy Tiffen, also from the Centenary Institute, believe the research findings are significant in pointing to KDM6A as a major regulator of immune responses. The focus will now be on how KDM6A is regulated.

"We want to fully know how KDM6A is regulating immune responses and boosting the production of interferon gamma. Understanding these processes will potentially allow the translation of this knowledge into more effective treatments for all melanoma patients," said Professor Hersey.

More information: Abdullah Al Emran et al. Study of the Female Sex Survival Advantage in Melanoma—A Focus on X-Linked Epigenetic Regulators and Immune Responses in Two Cohorts, *Cancers* (2020).

[DOI: 10.3390/cancers12082082](https://doi.org/10.3390/cancers12082082)

Provided by Centenary Institute

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