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Triggering melanoma cell death

Scientists at the Centenary Institute have reported a new strategy to battle melanoma, the most dangerous form of skin cancer, responsible for approximately 1,700 deaths in Australia each year.

Using drugs to inhibit two separate proteins, the researchers found that they could effectively kill melanoma cells by inducing apoptosis (the process of cellular self-destruction that takes place when a cell is no longer needed).

This new treatment strategy has the potential to benefit a subgroup of melanoma patients who do not respond to targeted therapies or immunotherapy.

“Provoking apoptosis has proven extremely difficult due to the high expression of anti-apoptotic or ‘protector’ proteins found in melanoma cancer cells,” said lead author of the study, Dr Hsin-Yi Tseng, Research Officer in the Melanoma Oncology and Immunology Program at the Centenary Institute.

“These protector proteins help the melanoma cell to survive, thrive, and in some cases to aid resistance against advanced medical drug treatments,” she said.

In the study, the researchers inhibited, in combination, the protein MCL1, together with proteins from the bromodomain and extra-terminal (BET) family. Both are known to have key roles in protecting and supporting melanoma cancer cells inside the body.

“Our research showed that combining BET and MCL1 inhibitors is highly effective at killing melanoma. The protective abilities of the BET and MCL1 proteins are decreased by the drug inhibitors and also induce the cancer cells to self-destruct,” said Dr Hsin-Yi Tseng.

Senior co-author on the study, Dr Jessamy Tiffen also from the Centenary Institute’s Melanoma Oncology and Immunology Program says the team’s research is highly significant and offers up a potential new treatment strategy for melanoma patients.

“Up to one half of melanoma patients do not respond to immunotherapy and a majority of patients tend to develop acquired resistance to targeted therapies. Our research examined a large number of human melanoma cell lines as well as use of mouse models. We saw extensive melanoma reduction in both cases which bodes well for the translation of this research into the next stage of development,” said Dr Tiffen.

The study was reported in the International Journal of Cancer.

Melanoma is the most common form of cancer affecting young Australians, those individuals aged from 15 to 39 years old.

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Publication: Co-targeting BET proteins and MCL1 induces synergistic cell death in Melanoma. International Journal of Cancer.

<https://onlinelibrary.wiley.com/doi/abs/10.1002/ijc.33000>

Images:

Dr Jessamy Tiffen, Centenary Institute and Dr Hsin-Yi Tseng, Centenary Institute
<https://drive.google.com/file/d/1zUGYi9Ss1UxcZvNEGdbDRsE3fB4h9rd4/view?usp=sharing>

Dr Jessamy Tiffen, Centenary Institute
https://drive.google.com/open?id=16ovlj2PmT_-xI3QnRicMPOeTT7B01KoB

For all media and interview enquiries, please contact

Tony Crawshaw, Media and Communications Manager, Centenary Institute on 0402 770 403 or email: t.crawshaw@centenary.org.au

About the Centenary Institute

The Centenary Institute is a world-leading independent medical research institute, closely affiliated to the University of Sydney and the Royal Prince Alfred Hospital. Our research focuses on three key areas: cancer, inflammation and cardiovascular disease. Our strength lies in uncovering disease mechanisms and applying this knowledge to improve diagnostics and treatments for patients.

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