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## Dual drug approach to treat deadly melanoma

Research from the Centenary Institute has found that a new dual drug approach could offer up a highly effective treatment strategy for melanoma, the most serious form of skin cancer responsible for more than 1,700 deaths each year in Australia.

Reported in the 'Journal of Investigative Dermatology' the findings have the potential to benefit melanoma patients who do not respond favourably to current therapeutic treatments.

In the study, the research team found that the combined use of inhibitors targeting two specific proteins markedly reduced the growth of melanoma both in cellular experiments as well in models with mice. The two proteins targeted were the bromodomain and extra-terminal domain (BET) family of proteins and cyclin-dependent kinase 9 (CDK9). High expression of BET and CDK9 proteins are associated with an adverse prognosis in melanoma patients and also regulate melanoma cellular activity.

According to Dr Abdullah Al Emran, researcher in the Melanoma Oncology and Immunology Program at the Centenary Institute and lead author of the study, a key finding from the study was that the combination BET and CDK9 inhibitor treatment demonstrated significantly increased melanoma killing benefits when compared to use of the same inhibitor drugs when tested alone.

"Co-targeting BET and CDK9 proteins with inhibitors killed high numbers of melanoma cells regardless of type or status including melanomas exhibiting both BRAF and NRAS genetic mutations. The inhibitors worked by disrupting separate signalling pathways found within the melanoma cells—those responsible for cell communication and growth and this may explain the effectiveness we saw," he said.

"We also found molecular gene signatures suggesting biomarkers of which melanoma patients were most likely to respond to this BET and CDK9 inhibitor treatment," he added.

Dr Jessamy Tiffen, Head of the Centenary Institute's Melanoma Epigenetics Laboratory and senior author on the research paper believes that use of combination drug treatments may offer up a new strategic approach in the fight against the often fatal skin cancer.

"Over half of all melanoma patients do not respond to current therapies and new treatment approaches are urgently required. We've now seen that drugs working in combination are able to produce a synergistic effect when it comes to the killing of melanoma cells. This strategy could lead to higher survival rates for patients and as a result we will be further exploring this exciting avenue of research," she said.

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### Publication:

A combination of epigenetic BET and CDK9 inhibitors for treatment of human melanoma.

[https://www.jidonline.org/article/S0022-202X\(21\)01121-0/fulltext](https://www.jidonline.org/article/S0022-202X(21)01121-0/fulltext)

### Images:

Dr Abdullah Al Emran:

[https://drive.google.com/file/d/1JIKkLDCpk2dqOZBQb17KUxXcS\\_BunqOi/view?usp=sharing](https://drive.google.com/file/d/1JIKkLDCpk2dqOZBQb17KUxXcS_BunqOi/view?usp=sharing)

Dr Jessamy Tiffen:

<https://drive.google.com/file/d/1Vx8G7YN1rcubj4WdRLOoa7SpVV7iGqC-/view?usp=sharing>

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**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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