Study shows new strategy to boost immune system to fight melanoma

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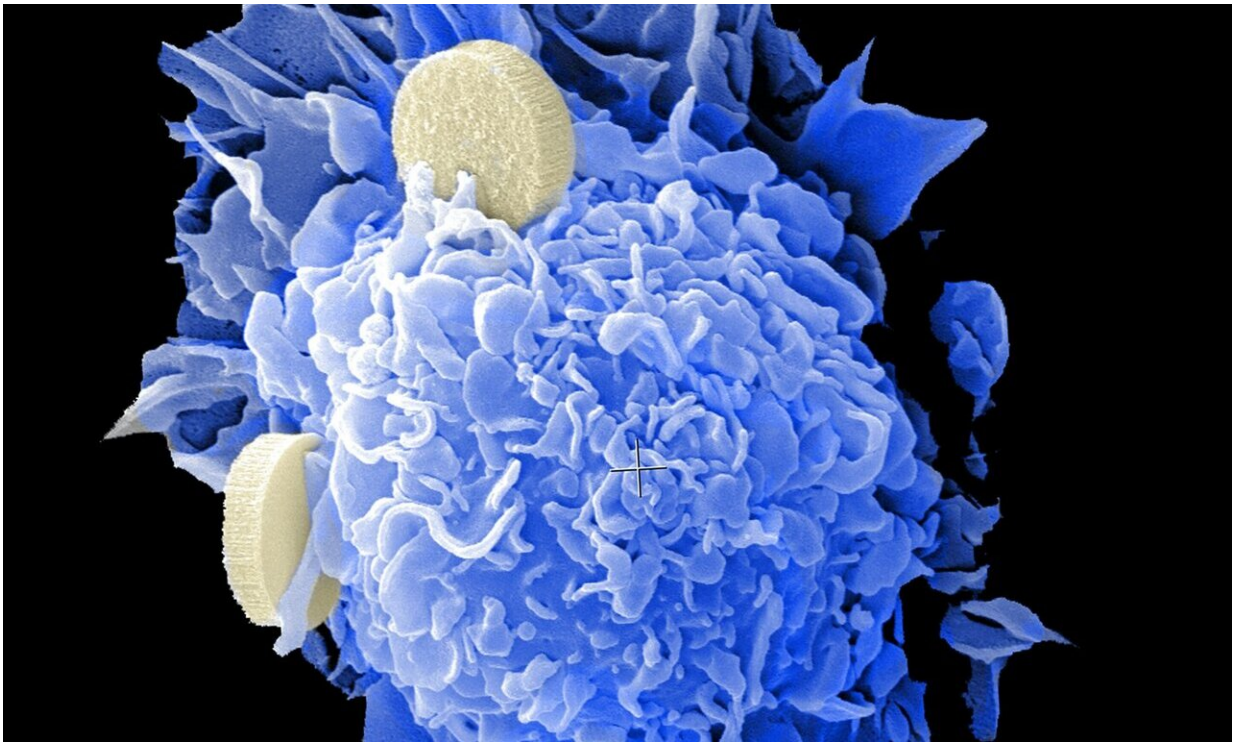

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A new study led by Yale Cancer Center researchers shows that the enzyme KDM5B suppresses anti-melanoma immunity. These findings could help develop a new treatment strategy to benefit patients with melanoma and other cancers, especially those who do not respond to current therapies. The research is published online today in the journal

Nature.

"These results are exciting as we discovered fundamental roles of some poorly studied genetic elements in immune responses and identified a new way to stimulate the ability of our immune system to fight cancer," said Qin Yan, Ph.D., Associate Professor of Pathology and Director of the Epigenetics Program in the Department of Pathology and a member of Yale Cancer Center. "In addition, we showed that this method can be used to overcome the resistance to current cancer immunotherapies."

In the study, researchers show depletion of the protein KDM5B, which is critical for melanoma maintenance and drug resistance, induces robust adaptive immune responses, and enhances responses to immune checkpoint blockade. KDM5B partners with SETDB1, a protein coding gene, to repress the expression of certain genetic elements such as MMVL30. Expression of these genetic elements stimulates RNA and DNA sensing pathways and subsequent interferon responses, leading to tumor rejection and immune memory.

Yan and his team have been working on the roles of KDM5 proteins in development and cancer for many years. These studies began when researchers sought to understand the roles of KDM5B in melanoma in close collaboration with the lab of fellow Yale researcher Marcus Bosenberg, MD, Ph.D., a co-corresponding author of the study. Resources and expertise provided by the Yale Center for Immuno-Oncology and the Yale SPORE in Skin Cancer were critical for this research.

"It is urgent to find new strategies to render immunotherapies effective to help treat patients with cancer," said Bosenberg. "We're encouraged as now we're working on dissecting how these genetic elements contribute to cancer and developing specific cancer drugs based on our discovery," added Yan.

More information: Qin Yan, KDM5B promotes immune evasion by recruiting SETDB1 to silence retroelements, *Nature* (2021). DOI: 10.1038/s41586-021-03994-2.

Provided by Yale Cancer Center