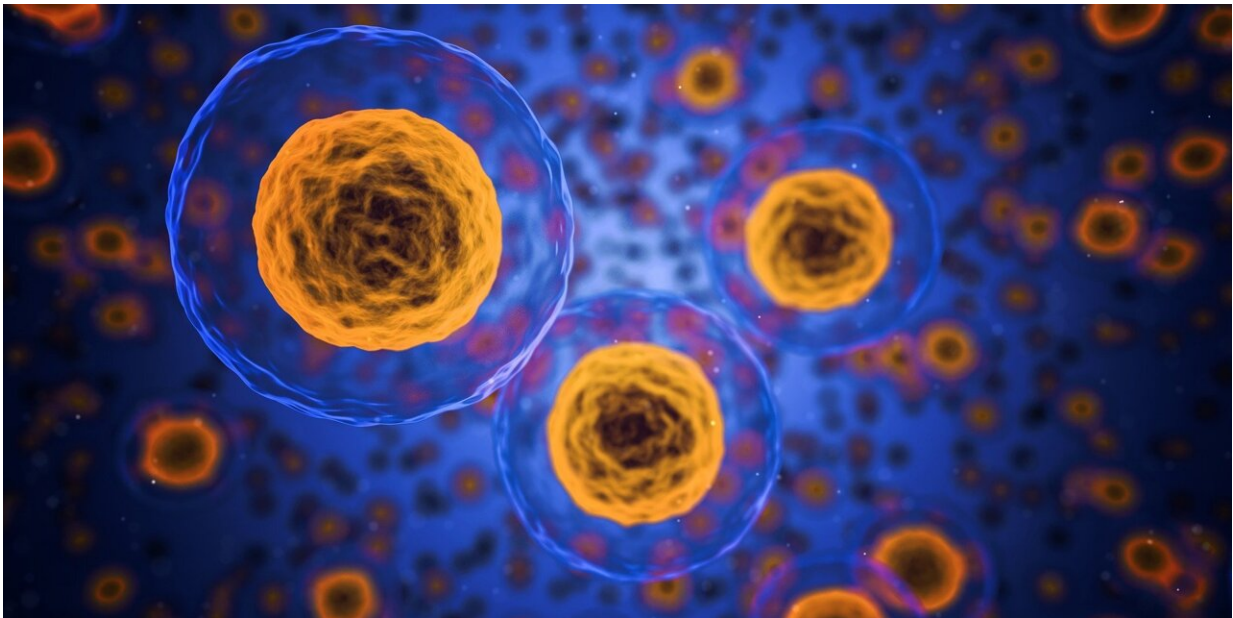


Study reveals hidden immune defense against cancer

November 28 2023, by Denise Heady



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Researchers at the UCLA Jonsson Comprehensive Cancer Center have found certain immune cells can still fight cancer even when the cancer cells lack an important protein that the immune system relies on to help track down cancer cells.

The team discovered the absence of the crucial protein B2M seems to activate an alternative immune response involving natural killer (NK)

cells and CD4⁺ T cells in both animal studies and patient tumor biopsies, indicating a potential backup mechanism in the [immune system](#) to recognize and attack cancer cells.

Immunotherapies, such as [immune checkpoint blockade](#), rely heavily on reactivating CD8⁺ T cells, which recognize tumor antigens through specific surface molecules on cancer cells. B2M proteins play a key role in this process to help CD8⁺ T cells identify the cancer cells. However, the researchers noticed that in cases where the B2M protein is missing or significantly reduced, some patients' cancers can still respond positively to immune checkpoint blockade.

To understand this better, the researchers edited the genes of mice with melanoma using CRISPR/CAS9 to make them lose the B2M protein, similar to how some [cancer cells](#) lose it. They discovered that in these mice, [immune cells](#)—specifically CD4⁺ T cells and NK cells—could still fight cancer when given the immunotherapy treatment.

Similarly, a large cohort of patients with melanoma found that tumors lacking proper B2M often displayed an increased presence of activated NK cells, suggesting that these cells might play a vital role in combating cancer when the usual recognition markers are missing.

The study shows that the immune system can still fight certain cancers, like melanoma, even when they lack B2M, and thus, CD8⁺ T cells are rendered less efficient. Understanding these mechanisms could pave the way for developing more effective combination cancer immunotherapy treatments.

"The unexpected critical role of NK and CD4⁺ T cells may be yet another way the immune system can combat certain types of tumors with the help of immune checkpoint blockade drugs," said Mildred Galvez, an MD/Ph.D. student at the David Geffen School of Medicine at UCLA-

Charles R. Drew Medical Education Program and co-first author of the study. "This paper is another example of how we can naturally exploit the body's immune system to figure out which players we need to retarget cancer."

The [study was published](#) in the journal *Cancer Immunology Research*.

More information: Davis Y. Torrejon et al, Antitumor Immune Responses in B2M-Deficient Cancers, *Cancer Immunology Research* (2023). [DOI: 10.1158/2326-6066.CIR-23-0139](https://doi.org/10.1158/2326-6066.CIR-23-0139)

Provided by University of California, Los Angeles

Citation: Study reveals hidden immune defense against cancer (2023, November 28) retrieved 28 April 2024 from <https://medicalxpress.com/news/2023-11-reveals-hidden-immune-defense-cancer.html>

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