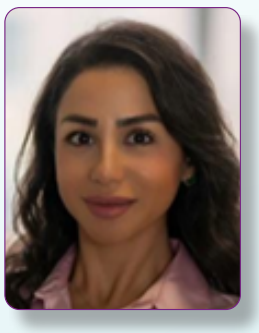
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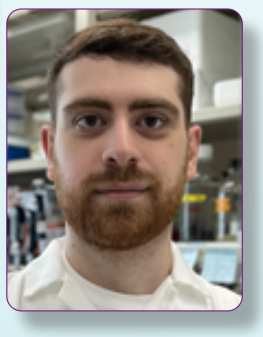
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PAPER OF THE MONTH • OCTOBER 2026



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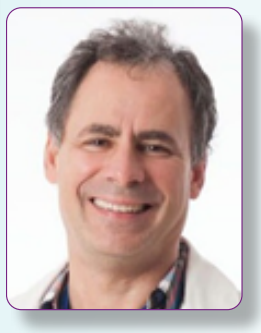
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nature communications

PRMT7 restricts CD8+ T cells expansion via the NF-KB pathway

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Immunotherapies, particularly immune checkpoint inhibitors (ICI) like anti-PD-1 and anti-CTLA-42 and adoptive cell therapies (ACT), such as chimeric antigen receptor (CAR)-T cells, T cell receptor (TCR)-engineered T cells and tumor-infiltrating lymphocyte (TIL) therapy, have shown revolutionary survival outcomes in patients with metastatic melanoma. However, immune resistance and T cell dysfunction remain major challenges.

Successful cellular immunotherapy for cancer utilising cytotoxic T lymphocytes (CTL) requires efficient expansion while maintaining effector function. Understanding how CTL expansion and function are regulated during the cell preparation process is thus important.

We have identified PRMT7 as a protein that acts like a brake on the immune system's cancer-fighting T cells. In this study, we show that T cell-specific deletion of Prmt7 using CD4-Cre increases CD8+ T cell effector differentiation, cytokine secretion, cytolytic activity and anti-tumor responses. Prmt7 deficiency transcriptionally reprograms CD8+ T cells by activating the NF-κB pathway, boosting proliferation, and facilitating the production of effector molecules such as CD25, CD69 and IFNγ.

We also developed a new drug-like compound called MS54, which removes PRMT7 from T cells. Treating mouse and human T cells with MS54 boosted their growth, activation and ability to attack melanoma cells. In mice, T cells treated with MS54 controlled tumors more effectively, especially when combined with an existing immunotherapy drug. Mechanistically, PRMT7 associates with RelA and restricts RelA nuclear translocation. In vitro, MS54 similarly activates the NF-κB pathway as in Prmt7-deficient CTL. In vivo, adoptive cell transfer of MS54-treated OT-I CTLs improves tumor control in a mouse syngeneic melanoma model. In human CTL, MS54 enhances proliferation, activation markers (CD69, CD137) expression, IFNγ production and cytotoxicity toward melanoma.

Our findings thus identify PRMT7 as a negative regulator of CD8+ T cell immunity and highlight MS54 as a potential strategy to improve adoptive T cell therapy.

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