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 Cell Reports

PRMT7 ablation stimulates anti-tumor immunity and sensitizes melanoma to immune checkpoint blockade

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Despite the success of immune checkpoint inhibitor (ICI) therapy for cancer, resistance and relapse are frequent. Combination therapies are expected to enhance response rates and overcome this resistance.

As protein monomethyl arginine methyl transferase 7 (PRMT7) is over expressed in cancer and in melanoma in particular, we hypothesized that the PRMT7 epigenetic regulator promotes immunosuppression in melanoma.

In this publication, we identify PRMT7 as a regulator of immunotherapy sensitivity for melanoma B16.F10 cells. Our findings show a trend toward a correlation between PRMT7 expression, immune infiltration, and clinical response. More specifically, our findings demonstrate that PRMT7 loss elicits anti-tumor immunity associated with increased immunogenicity and T cell infiltration *in vivo*. PRMT7 deficient cells had increased expression of transcripts derived from repetitive elements and resulting double-stranded RNAs (dsRNAs), mimicking a viral response. Thus, PRMT7 inhibitors may be effective in cases of ICI resistance.

Our data provides the impetus for further drug development for more effective PRMT7 inhibitors, as these can potentially be combined with immune-based therapies to achieve synergy. Future studies will be directed at ascertaining the use of PRMT7 inhibition across different cancer types and to examine if PRMT7 could be used as a biomarker for ICI responsiveness, which could ultimately lead to new forms of combination therapy.

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