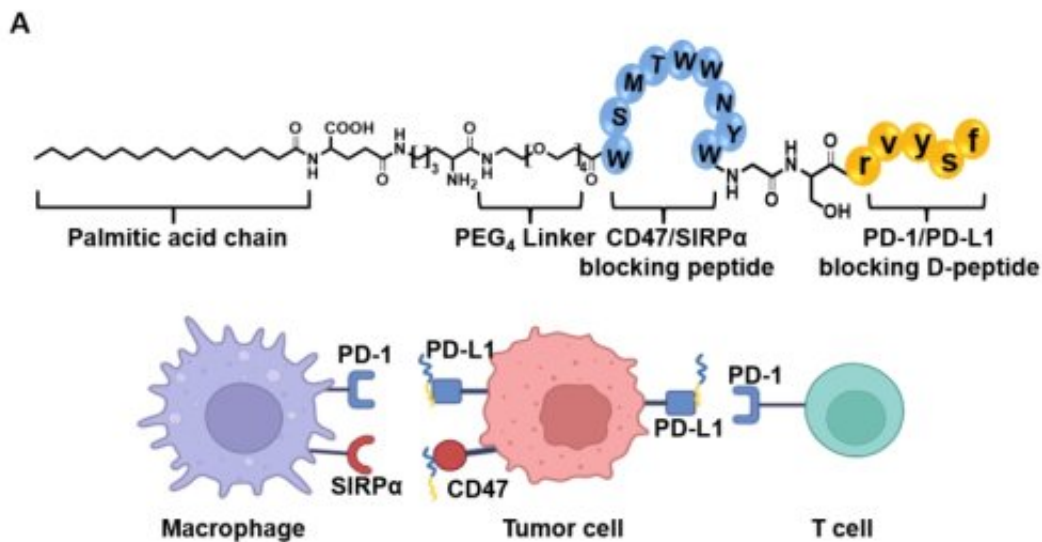


Researchers synthesize chimeric peptide that elicits antitumor activity for cancer immunotherapy

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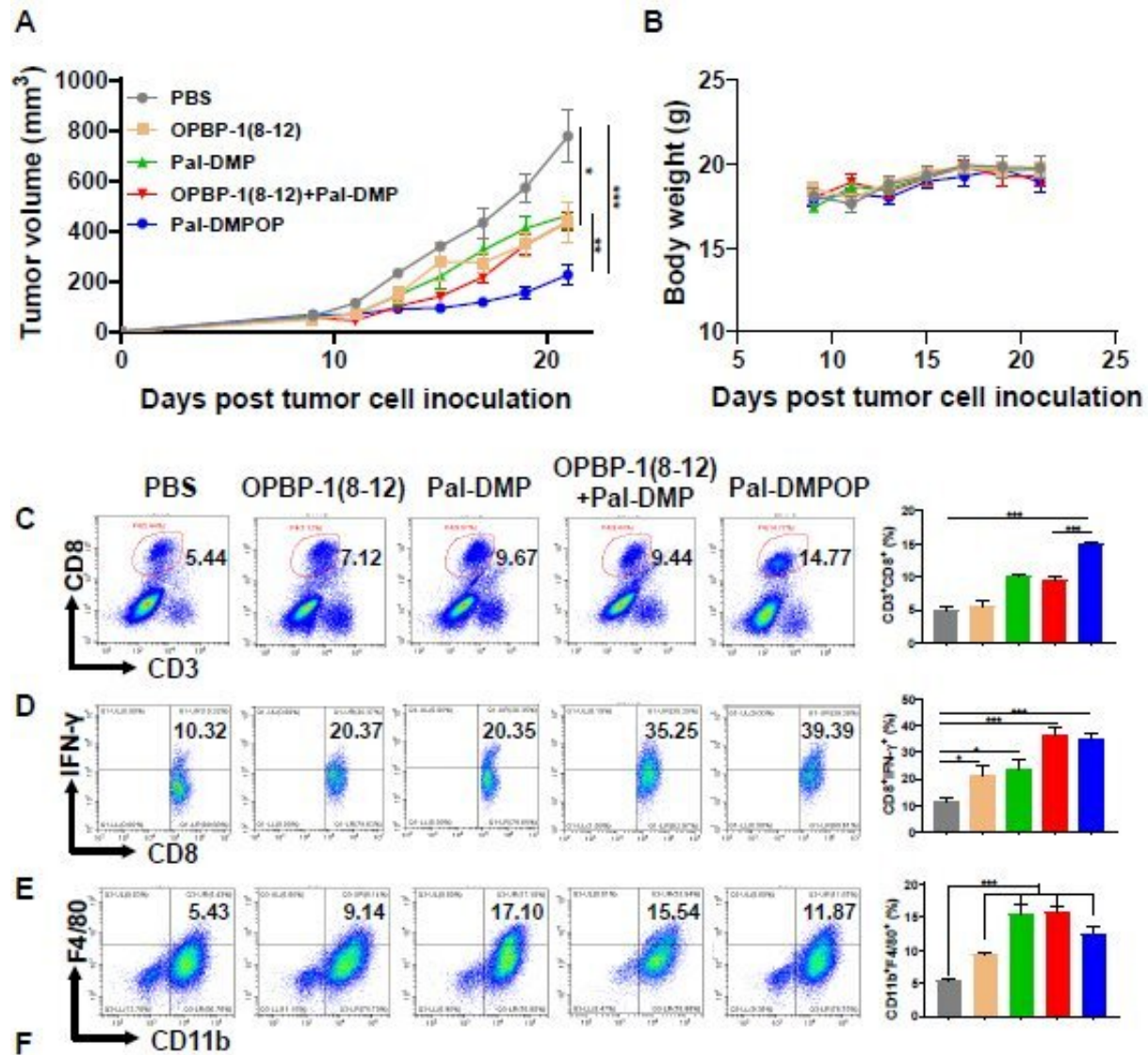
The peptide Pal-DMPOP consists a peptide inhibitor of CD47/SIRP α , a D-peptide inhibitor of PD-1/PD-L1, and a palmitic acid tail conjugated at its N-terminal through a PEG₄ linker. This design made this peptide resistant to serum proteolysis and accumulated in the tumor tissues. It can block CD47/SIRP α and PD-1/PD-L1 to enhance the phagocytosis of macrophage, and block PD-1/PD-L1 to restore the function of T cell. Credit: ©Science China Press

Professor Yanfeng Gao's team from the School of Pharmaceutical Sciences (Shenzhen), Sun Yat-sen University have designed and synthesized Pal-DMPOP, a chimeric peptide that can simultaneously

block CD47/SIRP α and PD-1/PD-L1. This bispecific peptide elicits synergistic antitumor activity by enhancing macrophages phagocytosis and activating CD8⁺ T cells. The findings are published in the journal *Science China Life Sciences*.

Although immune checkpoint inhibition has been shown to effectively activate antitumor immunity in various [tumor](#) types, only a small subset of patients can benefit from PD-1/PD-L1 blockade. CD47 expressed on [tumor cells](#) protects them from phagocytosis through interaction with SIRP α on macrophages, while PD-L1 dampens T cell-mediated tumor killing.

Also, it was reported that macrophages can also express PD-1 to mediate a "don't eat me" signal through interaction with PD-L1 on tumor cells. Compared with antibodies, peptides have better tumor penetration ability and easy to be synthesized. Therefore, design of peptides dual-targeting blockade of both PD-1/PD-L1 and CD47/SIRP α may improve the efficacy of cancer immunotherapy.



Pal-DMPOP (1 mg/kg, i.p., daily) significantly inhibits the tumor growth (A), has no impact on body weights (B), enhances CD8⁺ T cell infiltration (C) and its IFN-γ secretion in the tumor tissue (D). The infiltration of intratumoral macrophages (CD45⁺CD11b⁺F480⁺) (E) and the M1/M2 ratio (F) in the tumor tissue were elevated. Credit: ©Science China Press

In this article, the authors designed a chimeric peptide Pal-DMPOP. It consists of the smallest fragment of the D-peptide inhibitor of PD-1/PD-

L1 (OPBP-1) and the optimized peptide inhibitor of CD47/SIRP α (Pep-20). Also, the palmitic acid tail was modified at its N-terminal to improve its anti-enzymatic ability and in vivo half-life.

The research team verified that Pal-DMPOP can improve the phagocytosis of macrophages on tumor cells, and can also restore the killing effect of CD8⁺T cells on tumor cells in vitro. The effect of tumor immunotherapy in vivo has been determined in MC38 and CT26 mouse models. The tumor volume in Pal-DMPOP administration group is significantly reduced compared with the [control group](#), and Pal-DMPOP has no obvious toxic effect in the tumor-bearing mice.

More information: Zheng Hu et al, Design of a novel chimeric peptide via dual blockade of CD47/SIRP α and PD-1/PD-L1 for cancer immunotherapy, *Science China Life Sciences* (2023). [DOI: 10.1007/s11427-022-2285-6](https://doi.org/10.1007/s11427-022-2285-6)

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