Cleveland Clinic Innovations

PRODUCT
Tip as CAR-T co-stimulatory domain

INDICATION
CAR-T, Oncology

VALUE PROPOSITION
Tip CAR-T's have higher anti-tumor activity compared to traditional CAR-T constructs.

DEVELOPMENT STAGE
Approach validated in murine study.

INTELLECTUAL PROPERTY
Patent Pending.

RELATED PUBLICATIONS
Chung, K et al. "Signaling Role of Viral Protein Motif and Its Application in CAR T Cell Therapy." Blood vol. 142, 1 (2023): 4815.

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Novel Tip Co-stimulatory Domain for CAR-T Therapy

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UNMET NEED

Chimeric antigen receptor T-cell (CAR-T) therapy involves modification of isolated human T-cells with a chimeric antigen receptor (CAR) which confers tumor specific antigen recognition, T-cell proliferation, and cytokine secretion that leads to tumor killing. While CAR-T therapy is the gold standard to treat B-cell malignancies following failure of first-line treatments, challenges still remain with the modality as current CAR-T therapies are unable to elicit a 100% response rate in patients. This is attributed to a multitude of factors including poor T-cell survivability in the patient as well as insufficient T-cell activation and cytokine secretion.

SOLUTION

Cleveland Clinic researchers have developed a CAR which includes a novel 37-amino acid co-stimulatory domain derived from Herpesvirus saimiri tyrosine-protein kinase-interacting protein (Tip). Tip interacts with the major T-cell kinase Lck, promoting Lck-CAR interactions which result in increased early-stage T-cell activation by native T-cell receptors as well as enhanced CAR-antigen mediated activation upon exposure to the tumor. When compared to a standard CAR construct (WT/CAR), Tip/CAR T-cells show greater persistence, antigen recognition, and cytokine secretion. Tip/CAR T-cells also exhibit higher antitumor activity in mice bearing human tumor xenografts, demonstrating the advantages of the Tip derived CAR compared to current CAR constructs.