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Abstract Title:
MxV Glycoproteins: A Novel Fusogen for In Vivo CAR-T Generation

Category:
Cell Therapy: H2 – In-Vivo Editing of HSPCs and Immune Cells

Are you Interested in being Selected for a Poster Talk?:
Yes

Abstract Body:

Chimeric antigen receptor (CAR) T-cell therapies have revolutionized cancer treatment, yet their widespread use is hindered by complex manufacturing processes and high costs. To overcome these challenges, we developed a novel lentiviral vector pseudotyped with MxV glycoprotein (MxV-G), demonstrating promising efficacy for in vivo CAR-T generation. First, we observed that MxV-G significantly outperformed the traditional VSV-G pseudotyped vectors, achieving 2-5 fold higher viral titers, both for reporter gene construct GFP and CAR constructs. Additionally, the MxV-G pseudotyped vector exhibited superior CAR-T transduction efficiency at equivalent multiplicities of infection (MOI). We next utilized this vector, incorporating a T-cell targeting module, to generate CAR-T cells in vivo. In a MHCI/II knockout NSG mouse model bearing Nalm6-Luc tumors, intraperitoneal injection of the vector one day after peripheral blood mononuclear cell (PBMC) infusion resulted in complete tumor eradication. Notably, high levels of CAR-T cells were detected post-virus administration. To abolish natural tropism and enhance specificity of MxV-G, we

designed a number of mutants with single and multiple amino acid mutation based on an AI-Driven protein model and a Large Language Model. Our results showed that a mutant with multiple AAs mutation diminished infectivity in non-T cells, while the T-cell targeting module restored comparable transduction efficiency on T cells, similar to the wild-type MxV-G vector. These findings collectively highlight mutated MxV-G as a novel fusogen for in vivo CAR-T generation, offering a potentially more efficient and cost-effective approach for CAR-T therapy.