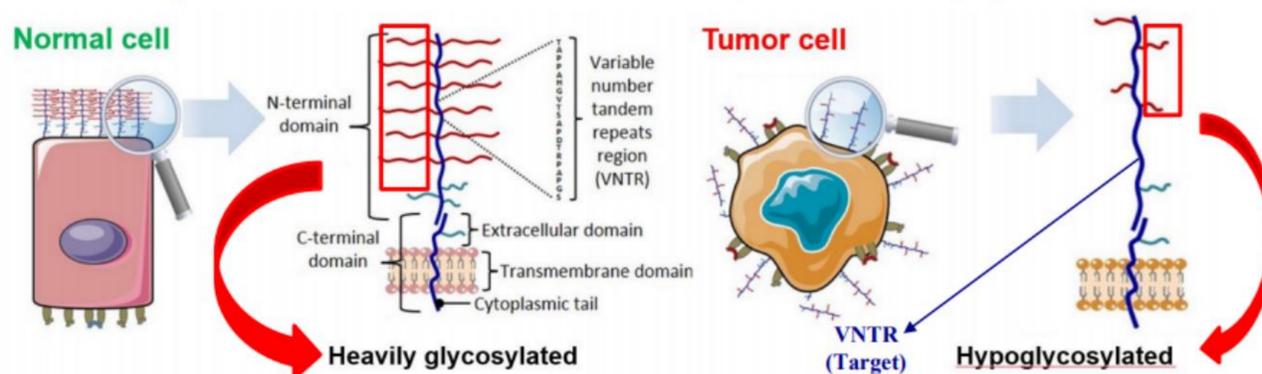


Lead Optimization of Solid tumor-targeting MUC1-CAR-T Cell Therapy Candidate Utilizing AviCLIP-CAR Technology

TiCARos. Inc

Disease Area	<i>Solid Tumor</i>
Product Type	CGT: CAR-T
Indication	Stomach, breast, ovarian, and pancreas cancer
Target	MUC-1 (Mucin-1).
Mechanism of Action	Targeting backbone of MUC-1's VNTR(variable number of tandem repeats) region where about 20 amino acids are repeated 25 to 125 times, allowing overall binding avidity by having multiple CAR molecules to bind with numerous repeated exposed epitopes.
Competitiveness	The competitive advantage of targeting VNTR peptides with MUC1-CAR-T cells has the capability of avoiding on-target off-tumor toxicity while significantly enhancing CAR avidity by allowing CAR molecules to bind to multiple repetitive targets in the VNTR(backbone of MUC-1 peptide). So far, this avidity-tuned strategy has not yet been investigated for MUC1 CAR-T cell therapy. Therefore, TiCARos aims to use a new VNTR-targeting antibody in MUC1 CAR-T cell therapy to establish a foundation for a CAR-T cell therapy that is both low in toxicity and enhanced in efficacy
Development Stage	<i>Pre-Clinical</i>
Route of Administration	<i>i.v</i>

Muc-1: overexpressed in various solid tumors (breast, ovary, pancreas, liver, lung, etc.)



MUC1 protein has **VNTR binding regions** at its N-terminal, repeating 25 to 125 times

In normal condition, heavily **hyperglycosylated Muc-1** is widely expressed in the mesh-like structure in epithelial region, acting as **physical barrier** for VNTR (*Int. J. Mol. Sci. 2021 22 6567*)

However, in **Tumor Condition**, significant **decrease** in MUC1 glycosylation (**hypoglycosylation**) occurs, enabling **wider exposure** of binding domains **VNTR** (*Vaccines 2020 8 659*).

Thus, CAR-T cells against MUC1 peptide backbone can overcome **On-Target Off-Tumor Toxicity**

- After subcutaneously injecting tumor cells into NSG mice, on the 13th day (with a tumor size of 120.18 mm³), groups of MUC1 CAR-T cells with a CAR expression rate of 60% were administered in two doses of 1×10⁶ and 5×10⁶

Key Data