4. Tumor-Associated TAG72 (Glycoprotein-72)

(City of Hope)

5TH KDDF GLOBAL C&D TECH FAIR

Asset Overview

Product Type	Cell therapy
Diseases Area	Oncology
Indication	Ovarian cancer
Current Stage	Phase I
Target	Tumor-Associated Glycoprotein-72(TAG72)
MoA	TAG72-CAR T cells target ovarian cancer peritoneal metastasis
Brief Description	• This asset has demonstrated that aberrantly glycosylated cell surface proteins on tumor cells are amenable CAR targets. • Tumor-associated glycoprotein 72 (TAG72) antigen is the sialyl-Tn found on multiple O-glycoproteins expressed at high levels on the surface of several cancer types, including ovarian cancer. Here, we developed a humanized TAG72-specific CAR containing a 4-1BB intracellular co-stimulatory signaling domain (TAG72-BBz). • TAG72-BBz CAR T cells showed potent antigen-dependent cytotoxicity and cytokine production against multiple TAG72+ ovarian cancer cell lines and patient-derived ovarian cancer ascites. • Using in vivo xenograft models of peritoneal ovarian tumors, regional intraperitoneal delivery of TAG72-BBz CAR T cells significantly reduced tumor growth, extended overall survival of mice, and was further improved with repeat infusions of CAR T cells. However, reduced TAG72 expression was observed in early recurring tumors, which coincided with a lack of T cell persistence. • Inventors demonstrate efficacy with TAG72-CAR T cells in ovarian cancer, warranting further investigations as a CAR T cell therapeutic strategy for this disease.
Intellectual Property	US20210308184A1 / WO2020028721A1
Publication	Effective Targeting of TAG72+ Peritoneal Ovarian Tumors via Regional Delivery of CAR-Engineered T Cells, Front Immunol (2018)
Inventors	Saul J. Priceman, John P. Murad, Stephen J. Forman, Jack SHIVELY, Paul YAZAKI, David Colcher, Anna Kozlowska, Hee Jun Lee

Highlights

A second-generation TAG72-specific CAR-T cell with a 4-1BB intracellular co-stimulatory signaling domain in preclinical models of ovarian cancer

- TAG72-CAR T cells demonstrated significant anti-tumor activity against peritoneal ovarian tumors
- While CD28-containing CAR T cells exhibit potent anti-tumor activity in solid tumors, undesirable increases in T cell exhaustion markers, limited persistence, and targeting of tumor cells that express very low levels of antigen may potentiate off-tumor toxicity
- Repeat therapy with TAG72-BB CAR T cells increased both maximal therapeutic responses as well as disease control in the OV90 model

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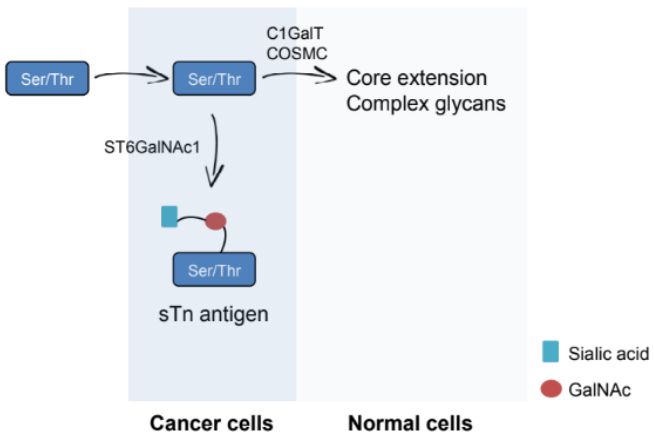
Key Data

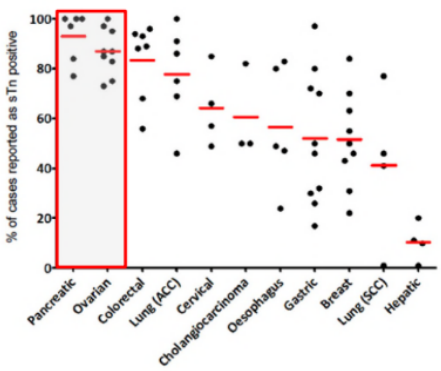
Tumor-Associated Glycoprotein-72(TAG72) as a CAR target

Cancer Specific Glycosylation:

- Tn - O-glycans
- **STn – truncated O-glycans (e.g., TAG72)**

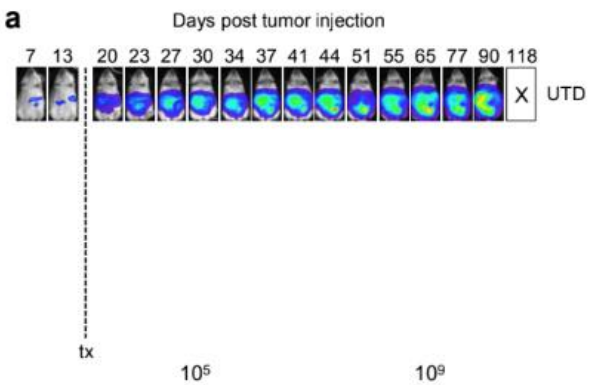


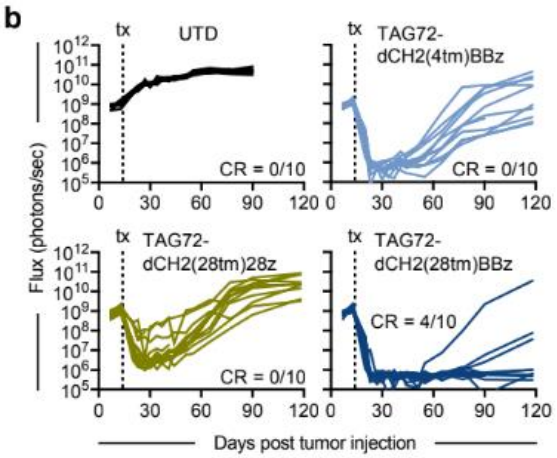
Reported TAG72 expression:



Adapted from Arabi et al., *Exp. Cell Research*, 2018

Repeat regional administration of TAG72BBtmBBz CAT T cells





- TAG72-CARs with CD28 transmembrane domain with 4-1BB costimulation greatly improves *in vivo* anti-tumor efficacy