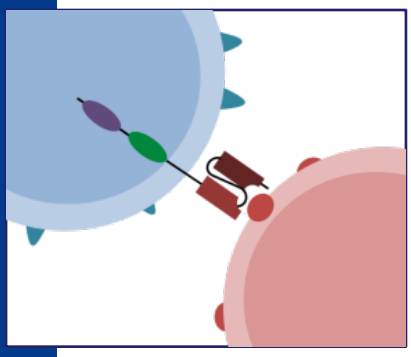
TAG72 Targeting Chimeric Antigen Receptor Expressing T cell (CAR-T) for Cancer Immunotherapy



The technology is a chimeric antigen receptor-expressing T cell (CAR-T) specific for the pancarcinoma marker TAG-72. The construct of our CAR works by using a TAG-72 scFv region to enable T cell targeting of the tumor and T cell activation through the incorporation of several costimulator and intracellular signaling regions in the CAR-T construct. Second generation TAG-72 scFv regions with improved, nanomolar binding affinities have the potential to increase tumor killing activity of the CAR-T cells.

COMMERCIAL OPPORTUNITY

- Tumor associated glycoprotein 72 (TAG-72) is a pancarcinoma marker expressed in several cancers including those of the breast, prostate, ovary, endometrium, stomach, esophagus, and pancreas. According to the American Cancer Society, an estimated 606,230 new diagnoses of patients having any one of these cancers occurred in the United States during 2016.
- The marketplace is attractive for CAR-T development, as there are 27 current CAR-T clinical trials being carried out by companies including Kite Pharma (market cap $2.3B), Juno Therapeutics (market cap $2.0B), Cellectis (market cap $614.4M), and Bluebird Bio (market cap $2.9B). Several of these CAR-T therapies have received breakthrough therapy designation allowing priority review by the FDA.
- A first generation Tag72 CAR-T construct had been made and tested by Cell Genesys Inc over a decade ago. The TAG-72 CAR-T cells showed anti-tumor activity in murine tumor xenograft models with TAG-72-positive human tumor cells. The construct was also used in a phase 1/2 trial for stage 4 colorectal cancer with liver metastases. Safety was demonstrated by there being no dose limiting toxicity at doses of 10^{10} TAG-72 CAR-T cells, and there was a reduction in TAG-72 serum markers. Anti-tumor activity was evidenced by one patient exhibiting stable disease; however, no tumor responses were observed in these advanced-stage patient cohorts. It is expected that newer later generation CAR-T constructs in combination with TAG-72 scFv regions with higher binding affinities will perform better in the clinic.

TECHNOLOGY

Two novel antigen binding scFv regions against the pancarcinoma tumor antigen TAG72 were generated, Ab3890 and Ab3891. Ab3891 demonstrated a superior phage binding profile, and was chosen for further affinity maturation study. A standard mutagenesis library was prepared and screened to identify 3 unique clones with complementarity determining region (CDR) mutations, Ab4116, Ab4117, and Ab4118. All three clones demonstrated improved binding with K_Ds of 15.3nM, 9.9nM, and 21.3nM, respectively, compared to Ab3891 with a K_D of 64.4nM.

PUBLICATION/PATENT

- Provisional patent application filed for Dr. Hatem Soliman and Dr. Marco Davila in December 2016.

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