

**Promab Biotechnologies' CAR-T new product development programs are being designed for pre-clinical and future clinical applications.**

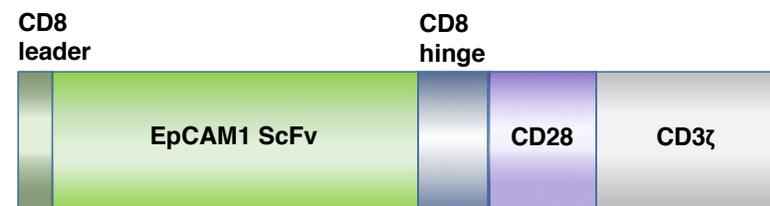
**CAR-T cells can be used for:**

1. Compound screening
2. Antibody screening
3. Co-stimulatory and activation domain comparison
4. Personalized medicine and donor variations for CAR-T screening
5. Checkpoint inhibitors
6. Safety switches and regulators of CAR-T functions
7. Pre-clinical in vivo models
8. Treg and T memory cells in CAR-T setting
9. CAR-T signaling, tumor microenvironment
10. Proof of concept studies for clinical trials

**The structure of CAR from Promab's available CAR-T cells targeting EpCAM antigen**

**Epithelial cell adhesion molecule (EpCAM)** is a transmembrane glycoprotein mediating Ca<sup>2+</sup>-independent cell-cell adhesion functions in epithelia. EpCAM is also involved in cell signaling, migration, proliferation, metastasis and differentiation. Additionally, EpCAM has oncogenic functions such as upregulation of c-myc, e-fabp, and cyclins A & E. Since EpCAM is expressed exclusively in epithelia and epithelial-derived neoplasms, EpCAM can be used as diagnostic marker for various cancers. It appears to play a role in tumorigenesis and metastasis of carcinomas, so it can also act as a potential prognostic marker and as a potential target for immunotherapeutic strategies.

In addition, EpCAM is expressed in circulating tumor cells and can be used as marker of circulating metastatic cells. EpCAM-expressing circulating tumor cells are predictors of short survival and serve as a liquid biopsy marker to guide therapy.

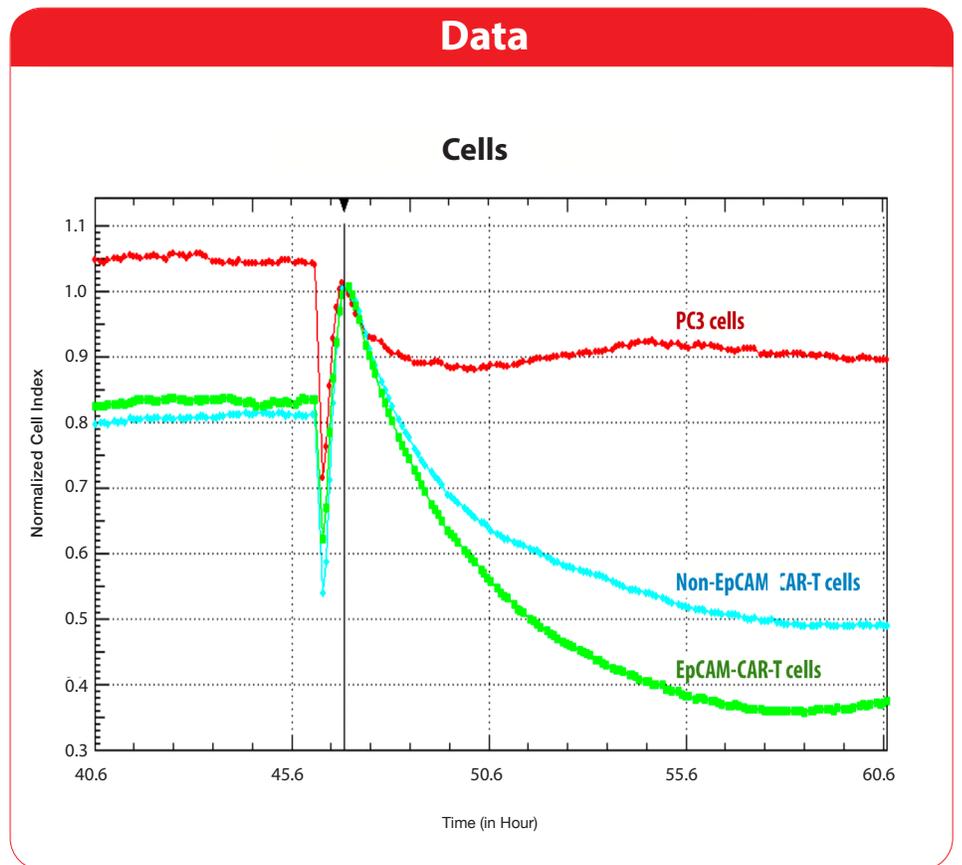


**Figure 1.** CAR-T cells expressing the above constructs are available from Promab targeting EpCAM antigen. ScFv, single chain variable fragment. These CAR-T cells are generated with EPCAM1 ScFv-CD28-CD3ζ CAR construct.



To date Promab generated 2nd or 3rd generation CAR and CAR controls (2nd generation of CAR is shown in Figure 1), CAR-T cells and CAR-Natural Killer (NK) effector cells against cancer target cells that show excellent functionality, including dose-dependent and target cell-specific cytotoxic activity (Figure 2).

These cells can be tested with CAR-T in cytotoxic assays and used for testing modulators of immune checkpoint inhibitors (PD-1, CTLA-4 pathways) or activators of immune response, small molecules affecting T cell or Treg activity.



**Figure 2.** Real-time cytotoxic activity of EpCAM ScFv-CAR-T effector cells against EpCAM-positive target PC3 prostate cancer cells. The ratio of effector cells to target cells is 10:1.