



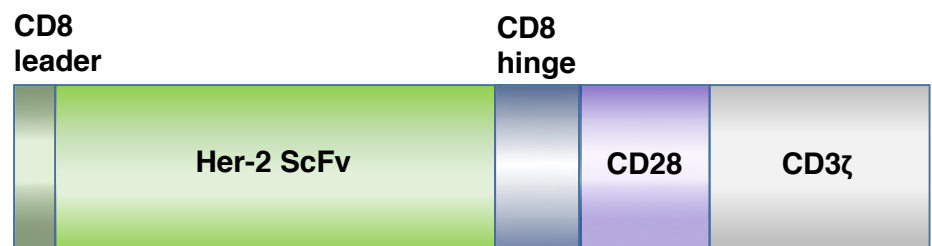
**Promab Biotechnologies' CAR-T new product development programs are being designed for pre-clinical and future clinical applications.**

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

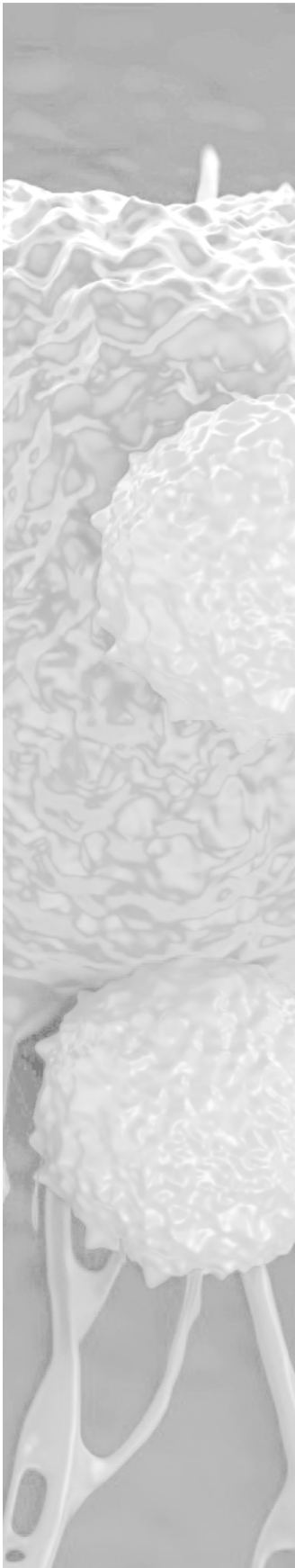
1. Compound screening
2. Antibody screening
3. Co-stimulatory and activation domain comparison
4. Personalized medicine and donor variations for CAR-T screening
5. Checkpoint inhibitors
6. Safety switches and regulators of CAR-T functions
7. Pre-clinical in vivo models
8. Treg and T memory cells in CAR-T 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 Her-2 antigen**

Receptor tyrosine-protein kinase erbB-2, also known, as proto-oncogene Neu, ErbB2 (rodent), or ERBB2 (human). It is encoded by the ERBB2 gene, which is also frequently called HER2 (from human epidermal growth factor receptor 2) or HER2/neu. HER2 is a member of the human epidermal growth factor receptor (HER/EGFR/ERBB) family. Amplification or over-expression of this oncogene has been shown to play an important role in the development and progression of certain aggressive types of breast cancer. In recent years the protein has become an important biomarker and target of therapy for >25% of breast cancer patients. Her-2 can be used as a tumor antigen for CAR-T immunotherapy.

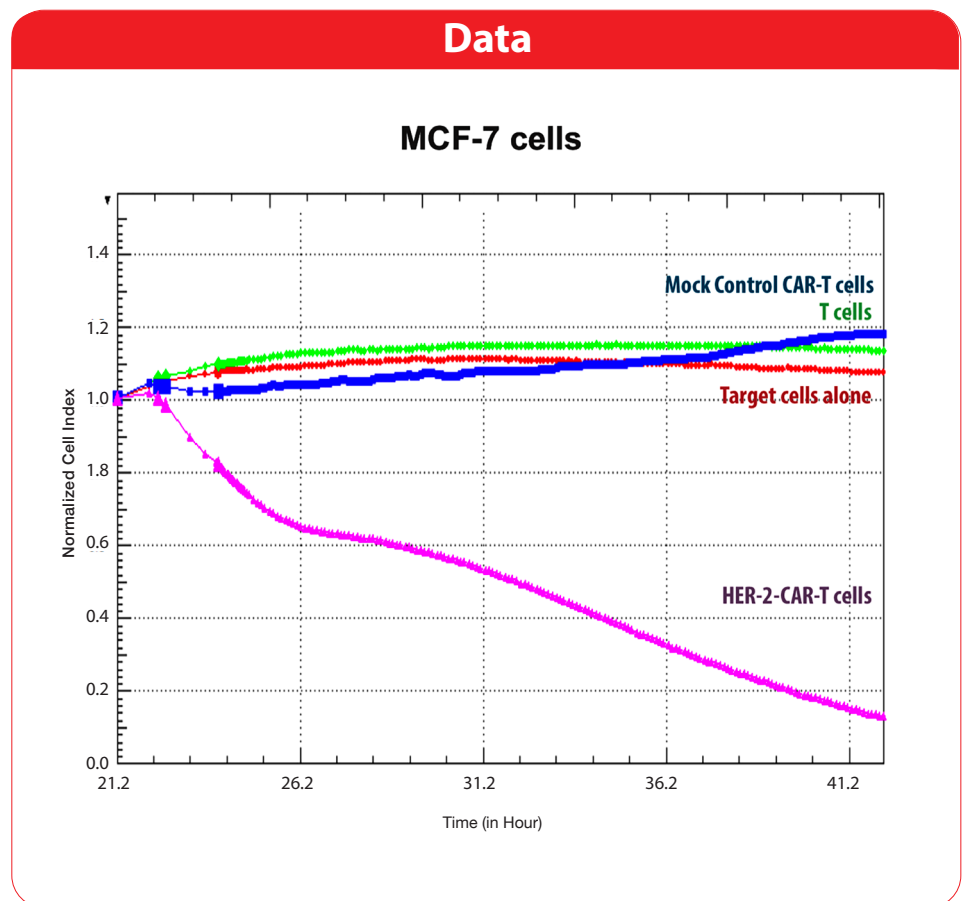


**Figure 1.** CAR-T cells expressing the above constructs are available from Promab targeting HER-2 antigen. ScFv, single chain variable fragment. These CAR-T cells are generated with HER-2-CD28-CD3 zeta construct.



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.

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 T reg activity.



**Figure 2.** High cytotoxic activity of HER-2scFv-CD28-CD3zeta-CAR-T cells against Her-2-positive MCF-7 cells by RTCA assay. Effector:target cell ratio is 10:1.