Washington University in St. Louis
Office of Technology Management

ENGINEERING OF T CELL REGULATORY GENES TO IMPROVE CAR T CELL THERAPY

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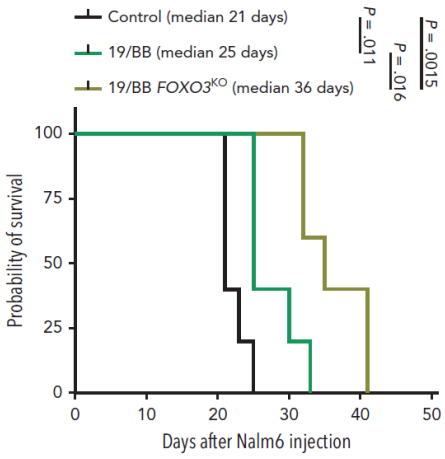
Value proposition: *Improved method using edited CAR-Ts to reduce T cell exhaustion and enhance cancer treatments.*

Technology Description

High tumor burden and repeated antigen stimulation are often associated with the lack of durable remission from CAR-T therapy. Researchers at Washington University have found that T cell exhaustion in 4-1BB-based CARs has a different genetic manifestation from CD28-based CARs, and ultimately results in the reactivation of FOXO3 signaling. Reprogramming of 4-1BB CAR-T by FOXO3 knockout prolongs the persistence of T cells and enhances the elimination of cancer.



Above Figure: In vivo mouse data showing survival improvements between unmodified 4-1BB CAR-T and reprogrammed CAR-T possessing FOXO3 knockout.

Publications

Selli, Mehmet Emrah, et al. "Costimulatory domains direct distinct fates of CAR-driven T-cell dysfunction." Blood, The Journal of the American Society of Hematology 141.26 (2023): 3153-3165.

Stage of Research

In vitro and in vivo proof-of-concept experiments performed, which show improved, durable response over the standard of care CAR-T. Target validated using clinical samples from a patient treated with tisagenlecleucel (Kymriah®, a CD19-directed 4-1BB CAR).

Key Advantages

- Enhances T cell fitness without compromising efficacy
- Can rescue already exhausted T cell functions
- Simple to implement method

Patents

Patent application filed

Related Web Links – Nathan Singh Profile**;** Singh Lab