Partnerships & Innovation | University of Manitoba

TECHNOLOGY LICENCING OPPORTUNITY

T cells engineered to express precise levels of CAR

Technology Details

Researchers at the University of Manitoba have developed microRNA silencing-mediated-fine-tuners (misFIT) to control the stepwise expression of CD19 CAR transgene expression in T cells. Cytokine release syndrome and excessive inflammation occur in ~60% of CAR-T recipients and can be life-threatening. The researchers have created a library of viral vectors to transduce a CD 19 CAR and miSFIT sequence into human T cells. miSFITs are engineered target sites that recruit endogenous microRNA, thereby controlling the expression of a gene of interest. They demonstrated it is possible to reduce CD19 CAR expression with miSFITs without hampering tumor-killing capacity.

Background

Chimeric Antigen Receptor (CAR) T therapy has revolutionized the immunotherapy landscape, especially for leukemia and lymphoma. Majority of the patients administered with CAR T achieved complete remission and have been living disease-free for years. Despite its clinical success, suboptimal durability and safety continue to delimit the advancement of CAR T as a first-line treatment for cancers. Such limitations lie in the overly high levels of CAR expression on the transduced T cells, resulting in two major challenges: T cell exhaustion renders them dysfunctional, and causes excessive inflammation. Utilizing miSFIT technology, a library of lentiviruses was established for the stepwise control of CD19 CAR transgene expression in human T cells to mitigate the challenges of CAR-T therapies.

Technology Benefits

Stepwise control of CAR expression with miSFIT to find a goldilocks level of CAR expression to mitigate T cell exhaustion while maintaining tumor-killing capacity.

Development Stage

Technology Readiness Level: 2-3

This technology is seeking a licensing, development or commercial partner.

Publications:

(1) Michaels et al. Precise tuning of gene expression levels in mammalian cells. *Nature Communications.* 2019. *10.*

Patent Status: Provisional Patent in Progress

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