**Docket #:** S17-182

# Method to direct T-cell fate towards T stem cell memory phenotype

Researchers at Stanford have developed a method to direct T cell fate toward the T stem cell memory (TSCM) phenotype during ex vivo expansion for adoptive cell transfer (ACT) therapies. During ACT, tumor-specific lymphocytes are expanded ex vivo and then administered to the patient as a therapeutic to treat cancer. Sometime these T cells are also engineered with chimeric antigen receptors (CAR) that enable these cells to specifically recognize and kill cancer cells. TSCM cells are a subset of memory lymphocytes that have a stem cell-like ability to self-renew and the multipotent capacity to differentiate into memory and effector T cell subsets. Increasing the numbers of TSCM cells has been suggested as a way to improve the efficacy of ACT therapies. Current approaches to do so, however, are limited as TSCM cells constitute a very rare subset of T cells that are hard to obtain and culture. Thus, new methods are needed to enhance the TSCM population. To help meet this need, the inventors have developed a method that uses drugs to disrupt specific signaling pathways during T cell activation to skew T cell differentiation to the TSCM phenotype. This technology provides a simple non-genetic method for the expansion of T cells ex vivo in a manner that greatly enhances the number of TSCM cells. It has the potential to improve clinical outcomes for cancer immunotherapy patients.

**Stage of research**
Preliminary data shows that culturing CAR-T cells in the presence of ibrutinib can endow a more TSCM phenotype, reduce expression of inhibitory receptors, and enhance functionality.

## Applications

- Adoptive cell transfer therapies, including:
    - Expanded tumor-infiltrating lymphocytes

    - Chimeric antigen receptor (CAR)-engineered T lymphocytes

## Advantages

- Steers T cell fate toward the TSCM phenotype and improves the quality of T cells transferred
- TSCM cells are clinically favorable for ACT therapies due to their excellent engraftment, persistence, and efficacy against cancer cells
- Potential to improve clinical outcomes for cancer immunotherapy patients

## Publications

- Z. Good, L Borges, N. Gonzalez, B. Sahaf, N. Samusik, R. Tibshirani, G. Nolan, S. Bendall "Proliferation tracing with single-cell mass cytometry optimizes generation of stem cell memory-like T cells." Nature Biotechnology February 2019.

## Patents

- Published Application: WO2019140137
- Published Application: 20220186184
- Published Application: 20240309324
- Issued: 12,024,716 (USA)

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