Docket #: S23-342

Chimeric transcription factors for engineering exhaustion-resistant CAR-T and other cell therapies

Stanford researchers have developed a strategy for generating chimeric transcription factors that enables exhaustion-resistant CAR-T cells and can be generalized to a wide range of cell therapies.

Chimeric Antigen Receptor (CAR) T-cells have revolutionized the treatment of blood cancers. However, a major barrier to CAR-T efficacy, particularly against solid tumors, is T-cell exhaustion, a dysfunctional state caused by repeated exposure to cancer antigens. While many approaches have been tried that involve knocking down or overexpressing certain T-cell genes, this results in a T-cell phenotype that exists along the continuum of natural T-cell states, from "stem-like" (capable of renewing and differentiating into other types of T-cells) to "cytotoxic" T-cells (capable of tumor cell killing). Unfortunately, these natural cell states are similarly prone to exhaustion as their unmodified counterparts.

Instead, Stanford researchers therefore engineered T-cells that exist in a completely synthetic, exhaustion-resistant state. To accomplish this, they created a library of chimeric synthetic transcription factors (TFs), which regulate gene expression in T-cells. By repeatedly stimulating CAR-T cells expressing these transcription factors, they identified a subset that rendered CAR-T cells resistant to exhaustion better than overexpression of endogenous TFs. Beyond CAR-T therapy, this strategy for engineering chimeric transcription factors could better enable a wide range of cell therapies.

Stage of Development

In vitro

If interested in this technology, please reach out to us by March 30, 2025.

Applications

- Exhaustion-resistant CAR-T therapy
- Improved cell therapies including TIL, TCR, and NK cell therapies

Advantages

- Renders CAR-T cells resistant to exhaustion
- Induces a synthetic, exhaustion-resistant transcriptional state (beyond endogenous "stem-like" or "cytotoxic" states)
- Expands the engineering space for cell therapy engineering beyond endogenous transcription factors
- Strategy is applicable to engineering a wide range of cell therapies

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