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# Enhancing CAR T-Cell Therapy for Solid Tumors with Multi-Specific Engineering and Exhaustion Resistance

Stanford researchers have developed a novel, multi-specific chimeric antigen receptor (CAR) T-cell therapy designed to overcome the key challenges of treating solid tumors, including tumor heterogeneity, immune evasion, and CAR T-cell exhaustion. Current CAR T therapies have demonstrated remarkable success in hematologic cancers but struggle in solid tumors due to limited tumor infiltration, suppressive microenvironments, and rapid T-cell exhaustion.

This technology leverages a multi-specific CAR approach that simultaneously targets multiple tumor-associated antigens to enhance tumor recognition and therapeutic efficacy; notably, the inventors' facile T-cell engineering strategy enables flexible targeting of diverse, clinically promising combinations of tumor antigens. Additionally, their technology integrates an shRNA-based knockdown of genes involved in transcriptional regulation, a unique strategy that improves CAR T-cell persistence and function by reducing exhaustion while maintaining therapeutic potency. This approach eliminates the need for CRISPR-mediated knockout, enabling a more streamlined and scalable manufacturing process without sacrificing effectiveness.

With promising preclinical validation in *in vivo* models, this therapy represents a major step forward in adoptive cell therapy for difficult-to-treat malignancies, including brain cancers and other solid tumors.

**Stage of Development**
Proof of concept — *in vitro* and *in vivo* data

## Applications

- Adoptive T-cell therapy for solid tumors, including brain tumors, that are resistant to existing CAR-T therapies
- Multi-specific recognition and targeting of tumor antigens
- Scalable, engineered T-cell platforms with high persistence for clinical use

## Advantages

- Multi-specific CAR design enhances cancer cell recognition and response for superior tumor targeting
- Engineering approach reduces T-cell exhaustion, improving persistence and efficacy
- Enables more scalable manufacturing by eliminating the need for CRISPR-based gene knockouts
- Overcomes immune evasion in solid tumors for enhanced therapeutic potency

## Innovators

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