Docket #: S24-327

Constitutively Active IL-9R Signaling for Engineered T Cell Therapy

Researchers at Stanford have developed a novel T cell engineering platform that leverages constitutively active interleukin-9 receptor (IL-9R) signaling to improve the efficacy and scalability of immunotherapies for solid tumors.

Traditional T cell therapies have struggled with treating solid tumors due to their reliance on intensive conditioning regimens, high cell doses, and systemic cytokine delivery. This innovative approach overcomes these challenges by integrating a constitutively active IL-9R signaling directly into engineered T cells, eliminating the need for external cytokine support.

By linking the wild-type IL-9 cytokine to its receptor via a flexible amino acid linker, the engineered T cells maintain continuous IL-9R signaling, enhancing their stemness, in vivo engraftment and persistence, and tumor-killing ability. The construct is compatible with both viral and non-viral gene delivery systems and adaptable across CAR-T and TCR-T platforms.

This innovation offers a potent, scalable, and clinically translatable solution for adoptive cell therapy, with potential applications in in vivo gene editing and next-generation cancer immunotherapies.

Applications

- Solid tumor immunotherapy: improves CAR-T and TCR-T therapies in hard-to-treat solid tumors
- In vivo gene editing
- Scalable clinical therapies: supports cost-effective, off-the-shelf T cell therapy development

Advantages

- Increased efficacy: continuous IL-9R signaling enhances T cell survival and tumor-killing capacity.
- Lower dose requirements: fewer engineered cells needed per treatment
- No conditioning required: eliminates lymphodepletion and systemic cytokine support
- Scalable and adaptable: compatible with diverse delivery platforms and T cell types

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