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Synthetic JAK/STAT Signaling Domains to Program Cell Function

Stanford researchers have developed a modular system of Synthetic cytokine receptors (SCRs), which are customizable receptors that mimic cytokine signals to precisely control immune cell behavior without the need for external cytokines.

Immune cells, such as T cells and NK cells, depend on constant cytokine signals to survive and function. However, natural cytokine signaling is imprecise, expensive to maintain in vitro, and difficult to control in therapeutic settings. Conventional methods offer limited flexibility and can lead to unwanted or excessive immune responses. This lack of fine-tuned control undermines the effectiveness and safety of advanced immune cell therapies, including CAR T cells.

To overcome these limitations, Stanford researchers have developed Synthetic Cytokine Receptors (SCRs), which are engineered surface proteins composed of programmable combinations of peptide signaling motifs. Each SCR mimics cytokine receptor signaling in a modular and tunable way, enabling precise control over immune cell behavior. Using this system, researchers can program immune cells and precisely control immune cell behavior without the need for external cytokines. SCRs can be integrated into a variety of immune cells and constructs, offering a plug-and-play platform to design immune responses tailored to specific diseases. Collectively, this system provides precise control over immune cell fate, improving the efficacy, safety, and scalability of immune cell therapies.

Stage of Development
Research - *in vivo*. Ongoing *in vivo* research has demonstrated that certain SCRs can improve NK cell anti-tumor function, however, additional development is necessary before their full utility in NK cells can be achieved.

Applications

- Cancer therapy
- Autoimmune diseases
- Infectious diseases
- Research tools

Advantages

- Modular and programmable
- Precise control with broad utility
- Cytokine-free
- Scalable platform

Publications

- Wansang Cho, Jenny Y Liu, Alex N Beckett, Judith C Lunger, Peng Xu, Katie Ho, Ethan E Chen, Antonio Salcido-Alcántar, Lucas E Sant'Anna, Kamal Obbad, Nakoa Po, Elena Sotillo, Crystal L Mackall, Kyle G Daniels (2025). A continuous landscape of signaling encodes a corresponding landscape of CAR T cell phenotype. bioRxiv 2025.06.05.658149.

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