Docket #: S21-402

Surrogate Cytokine Agonists

Researchers at Stanford have developed engineered IL-2 "surrogate" mutant agonists with varying patterns of STAT1/3/5, ERK, and PI3K signaling, as well as preferential induction of memory T cell differentiation and NK cell cytotoxicity relative to native IL-2. Notably, the team has created a bispecific ligand that brings the IL-2 receptor (IL-2R) and IL-10 receptor (IL-10R) into proximity, generating an entirely new heterodimeric signaling entity active on NK and T cells that is not found in nature.

These novel compositions have broad applications as anti-tumor therapeutics.

Stage of Development
The researchers have used the surrogate platform to create a ligand that induces proximity between IL-2R and IL-10R, creating an entirely new heterodimeric signaling entity, not found in nature, with activity on NK and T cells. This result shows that the approach is not limited to signals through natural cytokine receptor dimers, but can create new agonist signals that deliver synthetic signals on natural cells without gene editing.

Applications

- Development of anti-tumor IL-2 therapeutics
- Development of cytokine therapeutics for wide range of diseases

Advantages

- Transformational advance beyond the conventional engineering of natural cytokines

Publications

- Yen, Michelle, Junming Ren, Qingxiang Liu, Caleb R. Glassman, Timothy P. Sheahan, Lora K. Picton, Fernando R. Moreira et al. (2022). Facile discovery of surrogate cytokine agonists. Cell, 185(8), 1414-1430.

Patents

- Published Application: WO2023150733
- Published Application: WO2023150735

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