Docket #: S17-190

Engineered proteins to enhance the sensitivity of immune cells to IL-2

Researchers at Stanford have engineered proteins to selectively sensitize T cells to IL-2. The ability to manipulate immune cells for therapeutic use is of great clinical interest. Cytokines are signaling molecules that can be used to alter cellular behavior. IL-2 is a cytokine that plays a key role in the adaptive immune response as its signaling regulates T cell homeostasis by controlling the balance of immunostimulatory and immunosuppressive responses. For this reason, it is an appealing target for therapeutic development. However, at clinically relevant doses it is highly toxic. Thus, new methods that would allow IL-2 therapeutic use with decreased toxicity are needed. To help meet this need the inventors have engineered the IL-2 receptor, IL-2Ra (CD25) to have increased affinity for IL-2. They have also developed methods to use IL-13Ra2 as a surrogate high affinity receptor for an IL-2/IL-13 fusion protein. These engineered proteins can be used to increase the affinity of IL-2 to its receptor thus enabling lower doses, or endogenous amounts, of IL-2 to be used. This technology has the potential to increase the safety of adoptive cell therapy applications by reducing the amount of IL-2 needed.

Stage of research
In vivo validation studies are ongoing. *In vitro* experiments show increased expansion with the engineered IL-2Ra (CD25).

Applications

- Cell therapy for indications including:
  - Cancer
  - Autoimmunity

Advantages

- Increase safety of cell therapy applications by allowing administration of lower doses of IL-2 that are not toxic
- Selectively sensitize cells to IL-2

Patents

- Published Application: [WO2019113221](WO2019113221)
- Published Application: [20200385438](20200385438)
- Published Application: [20240092855](20240092855)
- Issued: [11,780,899 (USA)](11,780,899)
- Issued: [12,466,868 (USA)](12,466,868)

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