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Co-agonists of Transforming Growth Factor Beta and Cytokines

Researchers from Stanford developed recombinant polypeptide-cytokine conjugates and methods to induce antigen-specific regulatory T cells (Treg) for the treatment of inflammatory and autoimmune diseases.

Transforming growth factor beta (TGF-?) is a cytokine important in the maturation and differentiation of different lymphocytes including Tregs. TGF-? binding to TGF-? receptor in concert with other signals from other cytokines can initiate and determine lymphocyte maturation and/or differentiation. However, TGF-? is toxic at high doses, limiting its potential clinical use in the differentiation of cells and treatment of diseases by differentiating cells.

To address these issues, the inventors conjugate a low affinity TGF-? receptor agonist to a cytokine for controlled downstream signal activation. In vitro and in vivo experiments have been conducted and confirm this surrogate agonist to robustly induce antigen-specific, functional peripheral Tregs with high stability within peripheral lymphoid organs. Treatment with the surrogate agonist in mice effectively suppressed airway inflammation, demonstrating its potential as a new therapeutic modality against inflammatory and autoimmune diseases.

Stage of Development: Methods have been demonstrated in vitro and in vivo

Applications

- Inflammatory and autoimmune diseases

Advantages

- Enhanced Treg durability

- Induction of antigen-specific Tregs
- Establishing long-lasting and precise immune tolerance for autoimmune and inflammatory diseases.

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