

Docket #: S25-276

Immune silencing with targeted TGF β surrogate agonists

Stanford researchers have developed recombinant polypeptides targeting growth factor beta (TGF- β) receptor 1 and TGF β receptor 2 conjugated to a targeting moiety that binds to various target immune cells to induce suppression and silencing of target immune cells which may be useful for therapeutic applications.

Transforming growth factor beta (TGF- β) is a cytokine important in the maturation and differentiation of different lymphocytes. TGF- β binding to TGF- β receptor can lower proliferation and suppression of immune cells. However, TGF- β is toxic at high doses and does not have drug-like properties, limiting its potential clinical use in the suppression of immune cells and treatment of diseases.

To address these issues, the inventors developed TGF- β receptor agonists conjugated to antibodies for cell-specific targeting. In vitro and in vivo experiments have been conducted and show these conjugates are capable of independently and specifically silencing B cells, T cells, and all immune cells. These TGF- β agonist-antibody conjugates establishes a completely new immunotherapy modality that allows for selective inhibition of different immune cells without depletion.

Applications

- Autoimmunity, inflammation, blood cancers

Advantages

- Reduced systemic toxicity
- Targeted delivery and silencing function
- No cell depletion
- Novel approach for immune modulation

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