Docket #: S22-214

Multivalent SIRP-alpha Fusion Polypeptides

Stanford researchers have developed multivalent SIRP-alpha fusion polypeptides that selectively block the CD47–SIRP-alpha immune checkpoint with enhanced potency, enabling next-generation immunotherapies that promote immune clearance of cancer and diseased cells while minimizing off-target toxicity.

Cancer and diseased cells evade immune clearance by overexpressing CD47, a "don't-eat-me" signal that binds SIRP-alpha on macrophages and blocks phagocytosis. Current CD47-targeting antibodies show limited efficacy and safety, as CD47 is also found on healthy cells, particularly red blood cells, leading to anemia and off-target toxicity. Achieving potent, selective blockade without harming normal tissue remains a major therapeutic challenge.

To address this issue, Stanford researchers have developed multivalent SIRP-alpha fusion polypeptides that overcome these limitations through enhanced selectivity and potency. By incorporating multiple engineered SIRP-alpha domains within a single fusion molecule, the design achieves high-avidity CD47 binding on diseased cells while minimizing interaction with normal tissue. These constructs can be fused to effector domains, enabling precise immune activation and tissue-specific delivery. This modular architecture supports customization for diverse therapeutic applications with improved safety and efficacy.

Stage of Development:
Preclinical

Applications

- Cancer immunotherapy
- Fibrosis and degenerative diseases
- Diagnostics

Advantages

- Potent, selective CD47 checkpoint blockade
- Low toxicity
- Tunable, multivalent fusion format
- Compatible with antibody or conjugate platforms

Patents

- Published Application: WO2023183890
- Published Application: 20250257113

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