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Antibody-Cytokine Fusions for Targeted Activation of Macrophages in Local Tumor Environment

Researchers from Stanford developed antibody-cytokine fusions and methods to provide targeted recognition of tumors, controlled cytokine release, and localized immune activation.

Cytokine therapy has the potential to stimulate potent antitumor immune responses; however, systemic cytokine exposure can cause significant toxicity and limit the therapeutic window. Furthermore, insufficient localization of cytokine activity to the tumor microenvironment may limit therapeutic efficacy

To address these issues, the inventors link a tumor-specific antibody to an immunologically active cytokine with a cleavable linker activated by a protease highly enriched in tumor tissue, with the goal of concentrating immune stimulation at tumor sites while limiting systemic exposure. In vitro and in vivo experiments have been conducted to assess cleavage efficiency, macrophage recruitment and activation, tumor targeting, therapeutic efficacy, and systemic toxicity. This antibody-cytokine conjugate establishes a new therapeutic strategy to treat tumors with high efficacy and low toxicity in a controlled and targeted manner.

Stage of Development

Methods have been demonstrated in vitro and in vivo

Applications

- Cancer immunotherapy

Advantages

- Enhanced efficacy
- Reduced systemic toxicity
- Targeted delivery and activation

Innovators

- Jie Liu
- Irving Weissman
- Ravindra Majeti

Licensing Contact

Minxing Li

Licensing and Strategic Alliances Manager

Email