Docket #: S23-254

RBC Toxicity Mitigation in Anti-CD47 Antibody Cancer Therapies and Autoimmune Conditions

Researchers at Stanford have discovered a therapeutic strategy to overcome off-target red blood cell (RBC) toxicity associated with anti-CD47 antibody cancer therapies and possibly antibody-mediated autoimmune anemia and thrombocytopenia.

Anti-CD47 drugs that promote the destruction of cancer cells by blocking the "don't eat me" signal look promising as cancer treatments, but off-target RBC toxicity associated with anti-CD47 antibody cancer therapies may hinder the efficacy of the treatment and contribute to failed clinical trials.

Here, Stanford researchers discovered that this off-target toxicity is likely caused by anti-CD47 antibodies flagging erythrocytes for Fc-mediated macrophage phagocytosis. The researchers find several possible routes to mitigation of this off-target toxicity via reducing the Fc receptor-mediated phagocytic activity of macrophages against RBCs. They found a priming dose of CD47 antibody therapy decreases RBC clearance through inhibition of phagocytic capacity of macrophages, and provides red blood cells protection against subsequent greater dosing. Additionally, they proposed that modifying or blocking the Fc region of anti-CD47 antibodies to reduce binding to high-affinity Fc receptors can similarly ameliorate off-target RBC effects by lowering the phagocytotic activity of macrophages. Targeting Fc? receptors and their interaction with the Fc region of anti-CD47 could enhance cancer treatments without causing anemia and could also potentially be leveraged against autoimmune anemia and thrombocytopenia, whose pathology is related to autoantibody-mediated macrophage phagocytosis.

Stage of Development
Pre-clinical

Applications

- Therapeutic anti-CD47 cancer treatment without anemia associated with off-target RBC toxicity
- Treatment for off-target RBC toxicity associated with CD47 antibody cancer therapies
- Therapeutic for treating autoimmune conditions impacting RBC and platelets, and conditions characterized by defective phagocytosis

Advantages

- Provides a potential path to successful anti-CD47 cancer therapies
- Effective treatment without causing anemia – Mice treated with a loading dose saw a less than 10% reduction in RBC count even after subsequent dosing
- Cheaper and more accessible than existing therapeutic strategies like patient-derived immunoglobulin (IVIG) to treat autoimmune diseases affecting red blood cells and platelets

Publications

- Markovic, M., Banuelos, A., Nolan, G., & Weissman, I. (2023). 506 CD47 antibody therapy protects circulating red blood cells and platelets from immune destruction. *Journal for ImmunoTherapy of Cancer, 11*(Suppl 1), A569–A569.

Patents

- Published Application: WO2025024309

Innovators

- Maxim Markovic
- Garry Nolan
- Irving Weissman

- Allison Banuelos

Licensing Contact

Minxing Li

Licensing and Strategic Alliances Manager

Email