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Targeted Multi-Specific Antibody for Safer Blood Stem Cell Transplant Conditioning

Researchers at Stanford have developed a novel multi-specific antibody construct that precisely targets and eliminates diseased blood stem cells, offering a less toxic alternative to the chemotherapy and radiation currently used to prepare patients for stem cell transplantation.

Blood stem cell transplantation (HSCT) can cure a wide range of life-threatening blood disorders, from sickle cell disease and leukemia to chronic autoimmune conditions. Yet fewer than 5% of patients who could benefit actually receive it. The main barrier is toxicity: the conditioning regimens used today to clear out diseased stem cells also damage healthy tissues throughout the body, making the procedure too risky for many patients.

Stanford researchers have engineered a multi-specific antibody that simultaneously engages two surface markers found on diseased blood stem cells and recruits the immune system's own cells to destroy them. Preclinical studies show potent clearance of leukemia-generating stem cells, with even deeper results when combined with donor natural killer (NK) cell therapy. This construct has the potential to improve outcomes across a range of blood cancers and disorders, both as a standalone therapeutic and in combination with cell-based therapies.

Stage of Development: Pre-clinical

Applications

- Targeted conditioning agent for blood stem cell transplantation across a broad range of blood disorders

- Standalone immunotherapy for blood cancers unresponsive to standard treatment
- Combination immunotherapy platform deployable with cell-based therapies for enhanced efficacy

Advantages

- Targeting diseased cells while leaving healthy tissue unharmed
- Novel dual-targeting approach, opening a new treatment avenue not previously explored
- When combined with NK cell therapy, carrying a safer side effect profile than T cell-based approaches

Publications

- Shiraz, P., Rodriguez Santiago, C.J., Fonseca, S.M., Le, K.P., Poyser, J., Yan, H., & Shizuru, J.A. (2026). Multimodal immunotherapy for high-risk acute myeloid leukemia and myelodysplastic syndrome. Journal of Clinical Oncology, 44(16_suppl), 6569.

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