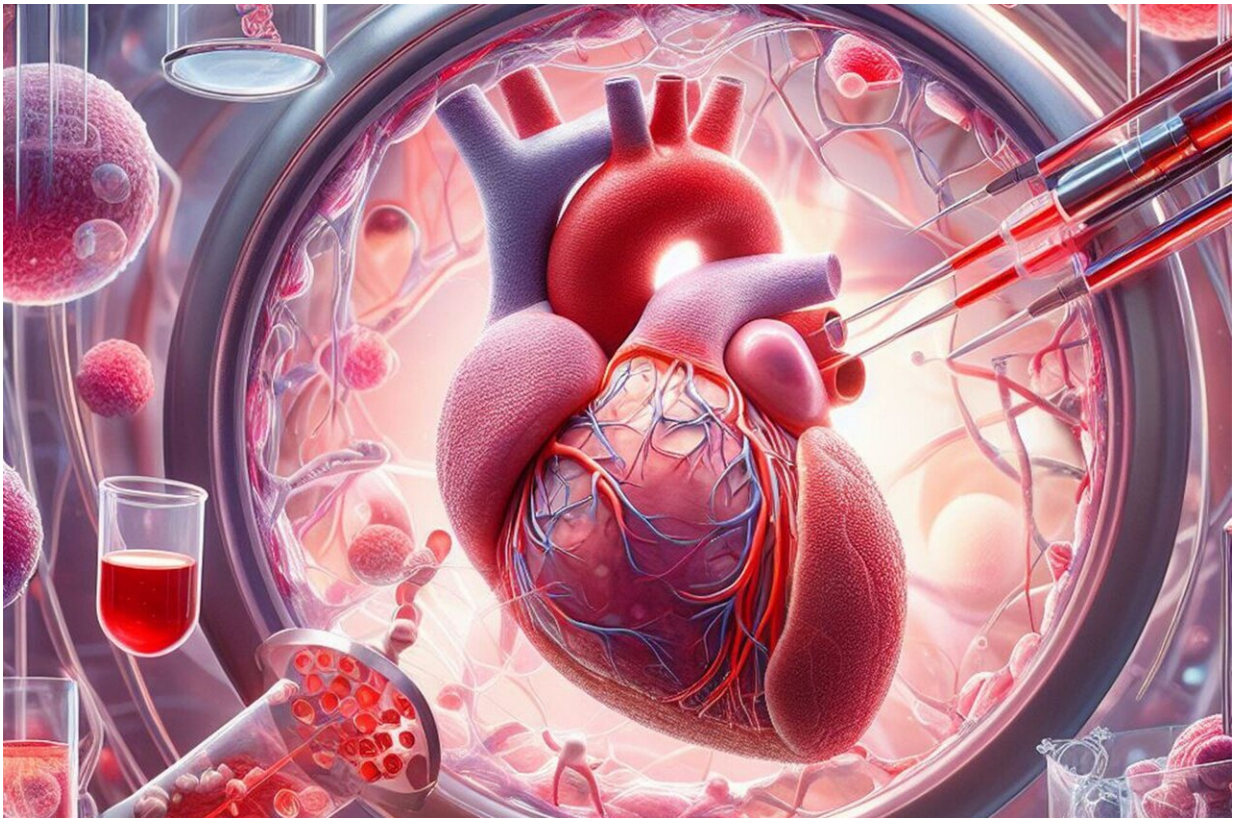


# Potential new approach to enhancing stem-cell transplants

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A discovery by a three-member Albert Einstein College of Medicine research team may boost the effectiveness of stem-cell transplants, commonly used for patients with cancer, blood disorders, or

autoimmune diseases caused by defective stem cells, which produce all the body's different blood cells.

The findings, made in mice, were [published](#) in the journal *Science*, in a paper titled "Regulation of the hematopoietic stem cell pool by c-Kit-associated trogocytosis."

"Our research has the potential to improve the success of stem-cell transplants and expand their use," explained Ulrich Steidl, M.D., Ph.D., professor and chair of cell biology, interim director of the Ruth L. and David S. Gottesman Institute for Stem Cell Research and Regenerative Medicine, and the Edward P. Evans Endowed Professor for Myelodysplastic Syndromes at Einstein, and deputy director of the National Cancer Institute-designated Montefiore Einstein Comprehensive Cancer Center (MECCC).

Dr. Steidl, Einstein's Britta Will, Ph.D., and Xin Gao, Ph.D., a former Einstein postdoctoral fellow, now at the University of Wisconsin in Madison, are co-corresponding authors on the paper.

## **Mobilizing stem cells**

Stem-cell transplants treat diseases in which an individual's hematopoietic (blood-forming) stem cells (HSCs) have become cancerous (as in leukemia or [myelodysplastic syndromes](#)) or too few in number (as in [bone marrow failure](#) and severe autoimmune disorders). The therapy involves infusing healthy HSCs obtained from donors into patients.

To harvest those HSCs, donors are given a drug that causes HSCs to mobilize, or escape, from their normal homes in the bone marrow and enter the blood, where HSCs can be separated from other blood cells and then transplanted. However, drugs used to mobilize HSCs often don't

liberate enough of them for the transplant to be effective.

"It's normal for a tiny fraction of HSCs to exit the bone marrow and enter the blood stream, but what controls this mobilization isn't well understood," said Dr. Will, associate professor of oncology and of medicine, and the Diane and Arthur B. Belfer Faculty Scholar in Cancer Research at Einstein, and the co-leader of the Stem Cell and Cancer Biology research program at MECCEC.

"Our research represents a fundamental advance in our understanding, and points to a new way to improve HSC mobilization for clinical use."

## **Tracking trogocytosis**

The researchers suspected that variations in proteins on the surface of HSCs might influence their propensity to exit the bone marrow.

In studies involving HSCs isolated from mice, they observed that a large subset of HSCs display surface proteins normally associated with macrophages, a type of immune cell. Moreover, HSCs with these surface proteins largely stayed in the bone marrow, while those without the markers readily exited the marrow when drugs for boosting HSCs mobilization were given.

After mixing HSCs with macrophages, the researchers discovered that some HSCs engaged in trogocytosis, a mechanism whereby one cell type extracts membrane fractions of another cell type and incorporates them into their own membranes.

Those HSCs expressing high levels of the protein c-Kit on their surface were able to carry out trogocytosis, causing their membranes to be augmented with macrophage proteins—and making them far more likely than other HSCs to stay in the bone marrow.

The findings suggest that impairing c-Kit would prevent trogocytosis, leading to more HSCs being mobilized and made available for transplantation.

"Trogocytosis plays a role in regulating immune responses and other cellular systems, but this is the first time anyone has seen stem cells engage in the process. We are still seeking the exact mechanism for how HSCs regulate trogocytosis," said Dr. Goa, assistant professor of pathology and laboratory medicine at the University of Wisconsin-Madison, Madison, WI.

The researchers intend to continue their investigation into this process. "Our ongoing efforts will look for other functions of trogocytosis in HSCs, including potential roles in blood regeneration, eliminating defective stem cells and in hematologic malignancies," added Dr. Will.

The study originated in the laboratory of the late Paul S. Frenette, M.D., a pioneer in hematopoietic [stem cell research](#) and founding director of the Ruth L. and David S. Gottesman Institute for Stem Cell Biology and Regenerative Medicine Research at Einstein.

Other key contributors include Randall S. Carpenter, Ph.D., and Philip E. Boulais, Ph.D., both postdoctoral scientists at Einstein.

**More information:** Xin Gao et al, Regulation of the hematopoietic stem cell pool by c-Kit-associated trogocytosis, *Science* (2024). [DOI: 10.1126/science.adp2065](https://doi.org/10.1126/science.adp2065).  
[www.science.org/doi/10.1126/science.adp2065](https://www.science.org/doi/10.1126/science.adp2065)

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