

HSCI Fighting Disease

Blood Program

Beyond bone marrow



When do you think stem cells were first successfully used to treat patients? This year? Five years ago? A decade ago? Try 43 years ago.

That's right. The first successful stem cell transplant was announced in 1968, but it wasn't called a stem cell transplant—it was called a bone marrow transplant. And in the four decades since, bone marrow transplantation has become a mainstay in the battle against leukemia, lymphoma, and other blood-borne cancers.

Harvard Stem Cell Institute

- 225 Faculty
- 20 Institutions
- 1 Promising Scientific Field

Collaborative stem cell science speeding the development of safer, more effective treatments for disease

But what are commonly called bone marrow transplants are actually blood stem cell transplants. Dispersed among millions of cells in the bone marrow are a comparatively minute number of hematopoietic—blood-forming—stem cells. These self-renewing cells are working constantly to keep us supplied with three main types of blood cells essential to sustain life: oxygen-carrying red cells, white blood cells which fight infection and platelets which help the blood to clot. All these cells originate from a rare hematopoietic stem cell population which resides in the bone marrow.

The Harvard Stem Cell Institute's Blood Program is focused on explicating the molecular mechanisms that allow these stem cells to self-renew and on developing ways to

increase their population and survival rate in order to improve the success of transplants. Since the blood is one of the best understood systems in the human body, the Blood Program is also looking at how a detailed understanding of the self-renewal process can be applied to other organs—both when it works well and also when it goes awry, as in the case of leukemia, for example.

Coaxing and taming blood cells

Under the leadership of Daniel Tenen, MD, an HSCI Principal Faculty member based at Beth Israel Deaconess Medical Center, HSCI investigators at Massachusetts General Hospital (MGH), Children's Hospital Boston, and Dana-Farber Cancer Institute are studying the molecular and genetic mechanisms of both normal and leukemic blood cells. These five independent laboratories are coordinating their efforts using complementary research tools and model systems to answer two key questions:

- How can we manipulate blood stem cells to increase their numbers?
- How can we limit the self-renewal properties of cancerous blood cells to prevent or at least slow their replication?

One of the Principal Investigators in our Blood Program is David Scadden, MD, co-director of HSCI and a hematologist-oncologist at MGH. Scadden's team has greatly expanded our understanding of the behavior of blood stem cells during the transplantation process, and has shown with real-time video how these cells migrate and settle into their niche—their developmental environment. This has led his group to test drugs that improve the odds that blood stem cells will survive transplantation and adjust to their new home.

As part of the Program we began a clinical trial of a drug designed to expand the population of blood stem cells and which could have widespread applicability: in bone marrow failure syndromes, anemias, and other diseases of normal blood cell production; in patients receiving chemotherapy for other tumors, especially solid tumors, in which their low blood counts are often the dose-limiting toxicity; and, in treatment of blood diseases in which the entire blood system of the patient is replaced with that of a donor.

Targeting leukemia stem cells

In addition to learning how to turn on self-renewal when we need it, we're also trying to block self-renewal when it's harmful. To figure out how to control self-renewal in the case of cancer, we're focusing on leukemia stem cells, which are among the best-characterized cancer stem cells. We hope that understanding how to break the self-renewal cycle of these cancerous cells will not only help us cure leukemia but also prevent further spread of malignant cells, making other therapies more effective. Furthermore, many of the targets identified in our studies are applicable to many other tissues and cancers—including, but not limited to, lung, colon, and breast cancer—adding to the substantial breadth of the clinical problems we address.

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