A scientific breakthrough could be the first step in a better treatment for leukemia patients

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A discovery made by Dr. Tarik Moroy, President and Scientific Director and Director of the Hematopoiesis and Cancer research unit at the Institut de recherches cliniques de Montréal (IRCM), and his team was recently published in *Blood*, the official journal of the American Society of Hematology. The researchers found that a protein can regulate certain characteristics of blood stem cells, which could lead to a better treatment for leukemia patients. Dr. Cyrus Khandanpour, medical doctor and postdoctoral fellow in Dr. Moroy's laboratory, is the study's first author.

The transplantation of blood stem cells in used worldwide as a therapy for patients suffering from leukemia and other blood diseases. "The blood stem cells given to leukemia patients are capable of renewing the entire blood producing system and all its blood cells, including white cells, red cells and platelets," explains Dr. Moroy.

Patients with leukemia or a blood disease are initially treated with chemotherapy, which destroys their entire blood forming system along with the disease. *Blood* stem cells can then be used in two different ways. The first is to harvest them from the patient before chemotherapy, and give the patient his/her own stem cells back after the treatment so they can rebuild blood cells. "One of the problems with this therapy is that blood stem cells normally reside in a niche between the bone and surrounding cells, and are in a dormant state," explains Dr. Khandanpour. "To obtain a sufficient number of stem cells, they have to

be mobilized from their bone marrow niche so they can enter the bloodstream where they can be readily collected."

The second possibility is to harvest blood stem cells from a healthy donor and give them to a patient following the chemotherapy treatment. These foreign cells will then rebuild the patient's blood system and regenerate its blood cells. "However, this therapy still fails in about 10% to 20% of cases," adds Dr. Khandanpour. "Among other reasons, these patients die because the transplanted stem cells do not generate new blood cells quickly enough, which leads to infection and death."

"We have found a protein (called Gfi1b) that seems to regulate the stem cells' activity level and where they reside in the bone," says Dr. Khandanpour. "In our mouse model, we were able to turn off the gene coding for Gfi1b. When we did this, the stem cells became activated, started expanding drastically, left their bone marrow niche and entered the bloodstream without losing their function. The ability to manipulate blood stem cells in this manner would significantly increase the efficiency of stem cell therapy."

According to the researchers, the inactivation of Gfi1b in the transplanted stem cells could accelerate the production of new blood cells, thus making stem cell therapy more efficient and less dangerous for the patient. However, the mechanisms regulating stem cell dormancy and mobilization are not well understood.

"Our next goal is to investigate the precise molecular mechanisms achieved by the ablation of Gfi1b, and to study in more detail how Gfi1b regulates the location and activation of blood stem cells," adds Dr. Möröy. "Our project will contribute to a better understanding of the biology of stem cell mobilization and dormancy, which could lead to the design of better treatment regimens for transplant donors and patients."

According to The Leukemia & Lymphoma Society of Canada, one person is diagnosed with a blood cancer every four minutes and someone dies from a blood cancer every 10 minutes. This statistic represents over 54,000 people per year. Leukemia causes more deaths than any other cancer among children and young adults under the age of 20.

More information: *Blood* paper: bloodjournal.hematologylibrary …ood-2010-04-280305v1

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