Protein key to control, growth of blood cells

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New research sheds light on the biological events by which stem cells in the bone marrow develop into the broad variety of cells that circulate in the blood. The findings may help improve the success of bone marrow transplants and may lead to better treatments for life-threatening blood diseases.

"As we better understand the biological pathways that regulate the growth of stem cells, we may identify new approaches for treating blood disorders," said study leader Wei Tong, Ph.D., a hematology researcher at The Children's Hospital of Philadelphia. Her study appeared online July 10 in the *Journal of Clinical Investigation.*

Hematopoietic stem cells (HSCs) develop into all types of blood cells: red blood cells, platelets and immune cells. HSCs, like other stem cells, have the ability to self-renew: each can give rise to more mature, developed cells with more specific functions, as well as a new stem cell. (Everyone carries HSCs in their bone marrow, unlike embryonic stem cells, which exist only in embryos.)

In her study, conducted in mice, Tong focused on a protein called Lnk that helps control HSC expansion. When a growth factor in the blood called thrombopoietin (TPO) acts on its cell receptor, it triggers signals along a pathway that includes another protein, JAK2. JAK2, in turn, causes stem cells to increase their numbers.

Tong's group and others previously found that Lnk is a negative regulator for HSCs, acting as a brake on stem cell expansion. In the current study, they found that mice genetically engineered to lack the Lnk protein had 10 times the normal amount of HSCs in their bone marrow. Without Lnk to directly interact with JAK2 and inhibit its activity, TPO made stem cell production go into overdrive.

However, there was an unexpected potential benefit-- the expanded population of stem cells had a higher proportion of quiescent cells, those in a resting stage in the cell cycle. Quiescent stem cells, said Tong, are more likely to succeed in a recipient when they are used in bone marrow transplantation.

Although much research remains to be done, added Tong, other researchers might build on this knowledge to manipulate HSCs for more effective bone marrow transplants for cancer patients after high-dose chemotherapy or radiotherapy. It might also improve treatments for particular blood disorders. For example, aplastic anemia, severe combined immunodeficiency disorders and hemoglobin disorders involve deficiencies of specific immune cells in the blood. Using a drug to inhibit Lnk could potentially produce larger numbers of HSCs for a successful bone marrow transplant.

Myeloproliferative disorders (MPDs), on the other hand, entail the opposite danger—a sometimes-fatal overproduction of certain bone marrow cells. Clinicians might use Tong's research on Lnk and its associated signaling pathway to curtail stem cell production and control MPDs.

Source: Children's Hospital of Philadelphia