Researchers decipher blood stem cell attachment, communication

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Researchers at the National Institutes of Health have deciphered a key sequence of events governing whether the stem cells that produce red and white blood cells remain anchored to the bone marrow, or migrate into the circulatory system.

An understanding of the factors that govern migration of blood stem cells might lead to improved treatment of leukemia, a cancer that affects circulating white blood cells. The findings also have implications for culturing infection-fighting immune cells outside the body, where they could be temporarily held in storage during chemotherapy and other treatments which suppress the immune system. Moreover, the findings could contribute to a strategy for growing large quantities of red blood cells in laboratory dishes outside the body, to reduce the need for blood donations.

Previously, researchers thought that the cellular environment in which the stem cells reside produced the chemical signals that determined whether the cells would be stationary or free-floating. The current study provides evidence that the stem cells produce chemical signals of their own that may, in turn, influence the chemical signals they receive from their environment.

"This important discovery will advance our understanding of how blood cells and immune cells are generated," said Duane Alexander, M.D., director of the NIH's Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

The findings were published on line in Nature Cell Biology. The study was conducted in the laboratory of Jennifer Lippincott-Schwartz, Chief of the NICHD Section on Organelle Biology. The study's first author was Jennifer Gillette, also of the Section on Organelle Biology. Other authors were Andre Larochelle and Cynthia E. Dunbar of the Hematology Branch of NIH's National Heart, Lung, and Blood Institute.

Dr. Gillette explained that hematopoetic progenitor stem cells—the cells which give rise to red blood cells and immune cells—travel between the bloodstream and the bone marrow. Within the bone marrow, they anchor themselves in place by attaching to bone marrow cells called osteoblasts.

Other studies have shown that osteoblasts secrete a substance that acts as a chemical signal that regulates the attachment of the stem cells. Large amounts of the chemical, which is known as SDF-1 (stromal cell derived factor-1), cause the stem cells to leave the bone marrow and enter the bloodstream. A small, continuous pulse of SDF-1, however, attracts the stem cells and results in their attachment to the osteoblasts.

In laboratory cultures, Dr. Gillette and her coworkers incubated unattached stem cells with osteoblasts. As the stem cells approached the osteoblasts, they developed long, tentacle-like projections, called uropods. The uropods attached to the surface of the osteoblasts. Then, a small portion of a uropod was absorbed inside an osteoblast. The uropod material was eventually sealed inside an endosome—a tiny balloon-like structure within the cell. After the osteoblasts absorbed the uropod material, they began producing SDF-1.

Dr. Gillette noted it appeared to be the stem cell material that stimulated the osteoblast to produce SDF-1, the substance that causes the stem cell to remain attached to the osteoblast or migrate into the blood.

"Our study indicates that stem cells may actually be able to manipulate

the signals that they receive from their environment," Dr. Gillette said. "Stem cells seem to have a little more control than we thought."

Next, the researchers plan to study the influence of SDF-1 on leukemia cells—free floating cancer cells that originate from stem cells, in hopes of learning how leukemia cells communicate with their cellular environment.

"One lead we hope to pursue is determining whether the cancer cells stimulate the cells in their environment to produce substances that help them grow in a similar manner," she said. "Perhaps we could disrupt these signals and inhibit the cancer cells."

Moreover, by learning more about the binding process itself, researchers may one day be able to duplicate the factors that stimulate stem cells to remain stationary and begin producing blood cells. The ability to culture blood in the laboratory could decrease the need for blood donations.

Source: NIH/National Institute of Child Health and Human Development (news : web)