Studying marrow, researchers accelerate blood stem cells

December 5 2012

(Medical Xpress)—University of Rochester Medical Center scientists are testing a new approach to speed a patient's recovery of blood counts during a vulnerable period after a stem-cell transplant, according to a study published in the journal *Stem Cells*.

Laura M. Calvi, M.D., and Rebecca L. Porter, an M.D./Ph.D. student in Calvi's lab, reported that prostaglandin E2 (PGE2), a drug previously used to treat stomach ulcers, boosts blood production following an assault on the bone marrow from radiation or chemotherapy. Although their study was done in mice, Calvi believes it has significance for patients in the future.

"Our research suggests exciting potential to remedy myelosuppression," said Calvi, an associate professor of Medicine at URMC, with a special interest in endocrine/metabolism and the way blood stem cells behave. "During the first six weeks or so after a transplant, patients can easily acquire serious infections due to low blood counts. It's during this window that we're investigating new opportunities for replenishing cells in the bone marrow, and understanding the mechanisms by which this occurs."

Stem cell transplants, also known as bone marrow transplants or peripheral blood transplants, can be life-saving therapies for people with leukemia, other blood cancers, or blood disorders. The James P. Wilmot Cancer Center at URMC performs about 120 transplants a year, making it the largest program in western New York.

Blood stem cells mostly live in the bone marrow (spongy center of bones) where they divide or stay quiet, mature, and then enter the blood stream, or die. Many things influence the behavioral choices of these cells. And when leukemia, certain types of lymphoma, or injury from chemo and radiation destroys blood stem cells, a transplant offers a fresh replacement.

However, wiping out blood cells (healthy cells and cancer) during the transplant process also presents grave risks for the patient. Transplant success is partly determined by whether the body can remake adequate numbers of new hematopoietic stem cells by spurring them from their usual, quiet state.

Calvi's research discovered that early treatment with PGE2 not only accelerated blood cell recovery, but protected the surrounding microenvironment to stimulate production of the newly transplanted cells. In fact, one of the most promising aspects of the research was the observed activity in the marrow microenvironment, she said.

Prostaglandin is a hormone normally produced in the body, and during radiation or chemotherapy the hormone rushes in to mediate the inflammatory response. Prostaglandin usually remains elevated for about six days. During this time, the bone marrow begins to recover slowly on its own. However, Calvi's research also showed that feeding the PGE2 drug compound to mice seemed to offer an additional benefit during this time, by changing the marrow's environment to make it more supportive of faster and better blood cell production.

In fact, early treatment with PGE2 expanded blood cells in several different ways: Not only did the drug increase proliferation of new, healthy blood cells, but it slowed the death of cells being rapidly killed off during the response to radiation injury.

"Having the ability to manipulate the function of hematopoietic stem cells in this context offers new and meaningful approaches for the clinic," Calvi said. "Patients face very serious consequences when the bone marrow doesn't make enough platelets and other blood cells, and few options are currently available to aid the recovery."

More information: onlinelibrary.wiley.com/doi/10 … 2/stem.1286/abstract

Provided by University of Rochester Medical Center