UT SOUTHWESTERN MEDICAL CENTER NEWS

Media Contact: Jeff Carlton
214-648-3404
jeffrey.carlton@utsouthwestern.edu

EMBARGOED UNTIL NOON, CST, SUNDAY, FEB. 24, 2013

Scientists identify bone-marrow environment that leads to production of infection-fighting T and B cells

DALLAS – Feb. 24, 2013 – The Children's Medical Center Research Institute at UT Southwestern has deepened the understanding of the environment within bone marrow that nurtures stem cells, this time identifying the biological setting for specialized blood-forming cells that produce the infection-fighting white blood cells known as T cells and B cells.

The research found that cells called early lymphoid progenitors, which are responsible for producing T cells and B cells, thrive in an environment known as an osteoblastic niche. The investigation, published online today in *Nature* and led by Dr. Sean Morrison, also establishes a promising approach for scientists to map the entire blood-forming system.

Scientists already know how to manufacture large quantities of stem cells that give rise to the nervous system, skin, and other tissues. But they have been unable to make blood-forming stem cells in a laboratory, in part because of a lack of understanding about the niche in which blood-forming stem cells and other progenitor cells reside in the body.

"We believe this research moves us one step closer toward the development of cell therapies in the blood-forming system that don't exist today," said Dr. Morrison, director of the Institute and professor of pediatrics at UT Southwestern Medical Center. "In understanding the environments for blood-forming stem cells and those of different kinds of progenitor cells, we can work toward reproducing those environments in the lab and growing cells that can be transplanted to treat a host of medical conditions."

These findings eventually may help increase the safety and effectiveness of bone-marrow transplants, such as those needed after healthy marrow is destroyed by radiation or chemotherapy treatments for childhood leukemia, Dr. Morrison said. The findings also may have implications for treating illnesses associated with loss of infection-fighting cells, such as HIV and severe combined immunodeficiency disease, better known as bubble boy disease.

The *Nature* study augments earlier work by Dr. Morrison and his team that showed endothelial cells and perivascular cells lining the blood vessels in the bone marrow create the environment that maintains haematopoietic stem cells, which produce billions of new blood cells every day. The latest study shows that bone-forming cells create the environment that maintains early lymphoid progenitors.

"Our research documents that there are different niches, or microenvironments, for blood-

(MORE)

forming stem cells and restricted progenitors in the bone marrow," Dr. Morrison said. "One way that bone marrow makes different kinds of blood-forming cells is by compartmentalizing them into different neighborhoods within the marrow."

The researchers identified niches for stem cells and early lymphoid progenitors by determining which cells are the sources of a growth factor (CXCL12) necessary for the proliferation of those two populations of blood-forming cells. By taking the same approach for other growth factors in the bone marrow, researchers should be able to map the niches for every kind of blood-forming progenitor cell in the bone marrow, Dr. Morrison said.

The UTSW paper's first author is Dr. Lei Ding, a former postdoctoral research fellow at the Children's Research Institute and the Howard Hughes Medical Institute (HHMI) at UT Southwestern. Dr. Ding is now an assistant professor at Columbia University.

Research support came from the HHMI and the National Heart, Lung, and Blood Institute.

About the Children's Research Institute

Children's Medical Center Research Institute at UT Southwestern (CRI) is a joint venture positioned to build upon the comprehensive clinical expertise of Children's Medical Center and the internationally recognized scientific environment of UT Southwestern Medical Center. CRI's mission is to perform transformative biomedical research to better understand the biological basis of disease. Established in 2011, CRI is creating interdisciplinary groups of exceptional scientists and physicians to pursue research at the interface of regenerative medicine, cancer biology, and metabolism, which together hold unusual potential for discoveries that can yield groundbreaking advances in science and medicine.

###