Study unlocks origins of blood stem cells

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This is a mouse fetus shortly after hematopoietic stem cells appear. Credit: Nancy Speck, Ph.D., Perelman School of Medicine, University of Pennsylvania

A research team led by Nancy Speck, PhD, professor of Cell and Developmental Biology at the Perelman School of Medicine at the University of Pennsylvania, has discovered a molecular marker for the immediate precursors of hematopoietic (blood) stem cells (HSCs) in the developing embryo, which provides much-needed insights for making these cells from engineered precursors.

Because HSCs, found in the bone marrow of adult mammals, generate all of the blood cell types of the body, unlocking the secrets of their origin may help researchers to better manipulate embryonic stem cells to generate new blood cells for therapy. Speck is also an Investigator with the Abramson Family Cancer Research Institute at Penn. The work was published this week in *Cell Stem Cell*.

"The ultimate goal for stem-cell therapies is to take precursor stem cells and push them down a particular lineage to replace diseased or dead cells in human adults or children," says Speck. First things first, she says: "You have to understand how this happens in the embryo."

Previous studies indicated that HSCs originated from a small population of cells lining blood vessels, called endothelial cells. But, it was unclear precisely which endothelial cells transitioned to blood stem cells during early development.

In the embryo, there are multiple waves of blood-cell development. The first wave gives the embryo a quick oxygen source and the final wave sets up the development of HSCs that ultimately reside in adult bone marrow. The first wave of progenitors can be generated in the lab from embryonic or induced pluripotent stem cells, but efforts to produce hematopoietic stem cells have failed, says Speck.

"Understanding the developmental origins of hematopoietic stem cells is important for learning how to produce them in the lab from embryonic or induced pluripotent stem cells," says Speck.

How much closer does this study take hematologists to be able to make HSCs successfully? Scientists can make blood cells from endothelial cells now and can monitor these in the embryo. But not all endothelial cells give rise to HSCs. The team used a special marker to follow the development of HSCs. Progenitor cells in the first wave of embryo blood-cell development and the HSCs of later waves of development differentiate from distinct populations of blood-producing endothelial cells. The marker, called Ly6a, is expressed in the endothelial cells that lead to HSCs, and it is not expressed in endothelial cells that make the first wave of blood cells.

Knowing more about the development of HSCs and its distinct markers will be helpful in making HSCs in the lab for stem-cell therapies so leukemia patients, for example - many of whom are unable to find suitable donors - could use their own cells to make HSCs and eventually blood cells depleted by blood cancers and some of its treatments.