Researchers identify granddaddy of human blood cells

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Researchers at the Stanford University School of Medicine have isolated a human blood cell that represents the great-grandparent of all the cells of the blood, a finding that could lead to new treatments for blood cancers and other blood diseases.

This cell, called the multipotent progenitor, is the first offspring of the much-studied blood-forming stem cell that resides in the bone marrow and gives rise to all cells of the blood. It's also the cell that's thought to give rise to acute myelogenous leukemia when mutated.

Isolating this cell, which is well known in mice but had yet to be isolated in human blood, fills in an important gap in the human blood cell family tree. The work will be published in the Dec. 13 issue of the journal *Cell Stem Cell*.

Irving Weissman, MD, director of Stanford's Institute for Stem Cell Biology and Regenerative Medicine, spent his early career identifying each cell in the mouse blood family tree. The progression went from the stem cell through the progenitor cell through progressively more specialized cells, ending up with the red blood cells, platelets and immune cells that make up the bulk of the blood.

This detailed information has helped researchers understand the origins of blood diseases and cancers and has led to advances in bone marrow transplantation. But studies in mice are never a perfect substitute for understanding those same cells in humans, said Ravindra Majeti, MD,

PhD, an instructor in hematology and co-lead author of the paper.

Majeti isolated the human progenitor cell by grouping human blood cells according to proteins on their cell surface. He and co-lead author Christopher Park, MD, PhD, an instructor in pathology, then looked for a pool of cells that could form all the final cells of the blood, but lacked the ability to constantly renew their own supplies - a trait that is unique to the stem cell. Those characteristics are what distinguish the mouse progenitor cell, and, they thought, would likely be shared by the human equivalent.

One pool of cells fulfilled those requirements. Knowing the proteins on the surface of that cell, researchers can now reliably identify, isolate and study the cell in the lab.

Being able to isolate and study this cell has many implications for human disease, according to Majeti. First, this progenitor cell is also thought to be the cell that, after a number of mutations, eventually becomes the acute myelogenous leukemia stem cell. That's the cell that lies at the heart of the leukemia and that must be destroyed in order to cure the disease.

"We can compare the leukemic stem cell to this progenitor cell and from that find out what makes the leukemic stem cell different," Weissman said. That difference could very well be a target for leukemia treatments.

Another use for this cell could be in bone marrow transplantation, according to Majeti. Having the human progenitor cell means researchers can then produce all the cells of the blood in a lab dish. They can then take their pick of which cells would be most beneficial for possible transplantation.

Source: Stanford University