Targeting Blood Stem Cells

A team of bioengineers at the University of Toronto (U of T) has discovered a way to increase the yield of stem cells from umbilical cord blood, to an extent that could broaden therapeutic use of these cells.

In a paper published in *Experimental Hematology,* researchers working in the U of T's stem cell bioengineering laboratory have identified an important component blocking the growth of stem cells. U of T scientists discovered stem cells in 1961, and for about two decades, researchers around the world have been searching for a way to expand the number of stem cells harvested from umbilical cord blood, which can be used instead of bone marrow for transplantation into patients with blood cancers.

"It's been very hard to grow blood stem cells at all," says Peter W. Zandstra, MCIC, of the University of Toronto's Institute of Biomaterials and Biomedical Engineering, and head of the laboratory in which the research was conducted. "We've tried to understand how those cells talk to each other, and by controlling that, trying to get the ones we want to grow better."

In any culture, blood stem cells are very rare, Zandstra explains—typically less than one in 100 cells. "If you want to grow that one cell among the other cells that are more aggressive, you have to target that cell."

The research team developed a way to remove the non-stem cells—differentiated cells, or "lineage-positive" cells—to create an environment that allows stem cells to grow better. "A mature (lineage-positive) cell expresses markers of differentiated lineages, and a stem cell is typically negative for these markers," Zandstra says. "So we removed the lineage-positive cells. They secrete molecules, or cytokines, which inhibit growth of stem cells. So, by removing them, we're making the environment better for stem cells."

Typically, the umbilical cord does not yield a large volume of stem cells—perhaps enough to treat a child, but rarely an adult. The new research findings may allow new cord-blood stem cells to be developed in the laboratory—enough to treat adult patients as well as children. The major use of blood stem cells is for transplantation into patients with leukemia and other blood-borne cancers.

From their studies in mice, the researchers know that new stem cells obtained through their expansion technology can engraft in bone marrow and maintain special properties such as the ability to migrate in the body. The researchers have further refined their system by developing a "bioreactor"—a vessel in which to grow the stem cells in a closed and controlled environment, away from environmental contaminants.

"The hope is that very soon, if the results are the same with the bioreactor as they were with our experiments to date, we will move to clinical trials," says Zandstra—ideally within the next year.

University of Toronto