Cord Blood Stem Cell Expansion: Increasing the Yield of a Valuable Resource

Cord blood stem cells can be collected only once - immediately following birth. This means that the number of genetically unique cord blood stem cells is limited to the quantity obtained at this single point in time. To allow for multiple uses and also to increase their capacity for transplantation in adolescents and adults, researchers are developing methods to stimulate stem cells to divide and increase in number while retaining their primitive state. This process is known as stem cell expansion.

Stem cell expansion is an important tool both for improving transplant outcomes and enabling individuals to use their own cord blood samples for more than one treatment. This is particularly important given advances in regenerative medicine - the science of using the body's own cells to repair or replace damaged tissues and organs - which will likely increase the number of diseases that cord blood stem cells are able to treat as a result.

While expanded stem cells are not yet approved for medical use in humans, several expansion studies and clinical trials are underway. An emerging number of expansion techniques succeeding in vitro and in animal models suggest that one or many of these methods will eventually be available.

In fact, published research indicates that cord blood stem cells can be successfully expanded with reproducible results. In one study, researchers isolated primitive embryonic-like stem cells from cord blood and expanded the number of stem cells in culture 389-fold.[1] In another study, researchers expanded the number of stem cells in culture up to 723-fold by isolating stem cells from cord blood using cell surface markers.[2]

According to the National Marrow Donor Program (NMDP), more than 6,000 men, women and children are searching the NMDP registry on any given day. Expanding the volume of stem cells available in a cord blood unit would allow even more patients to be treated, including adults. It would also allow those families who have privately banked their cord blood stem cells to use them for multiple treatments and even potentially donate a portion of their cord blood sample to patients in need.

Leading Researchers are Evaluating Expanded Cord Blood Stem Cells in Human Patients

The use of expanded cord blood stem cells in humans is currently being assessed in a number of clinical trials.

In November, the Gamida Cell/Teva Joint Venture announced that the first patient in its international, multi-center trial received a transplant of stem/progenitor cord blood stem cells in combination with non-expanded cells from the same unit. The trial will assess the efficacy and safety of expanded cord blood transplantation as a treatment for hematological malignancies, including leukemia and lymphoma.[3]

Below are three additional clinical studies that show the applicability of stem cell expansion in human cord blood transplants:

> At Hackensack University Medical Center in Hackensack, New Jersey, two adults with chronic myelogenous leukemia exhibited rapid engraftment after receiving expanded cord blood transplants. These results show the promising role cell expansion may hold in adult transplantation.[4]
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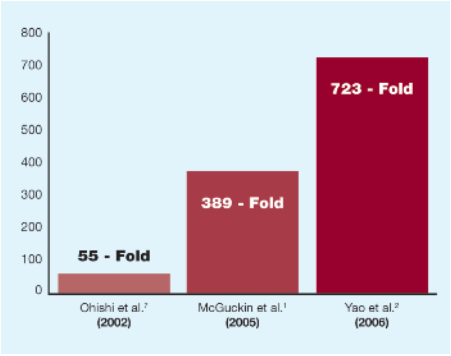
> Thirty-seven patients with blood or breast cancer received expanded cord blood transplants in a study at the University of Colorado. This trial demonstrates the feasibility and safety of using ex-



Umbilical cord blood cells' ultimate versatility, their abundance, and their high proliferative potential make them choice targets for the future cell expansion procedures.

Cord blood stem cells have the ability to differentiate into nearly any cell type and tissue in the body, a capability called pluripotency. These stem cells are easily and painlessly acquired from a child's umbilical cord immediately following birth. Since they are not subject to the complex ethical issues that have brought embryonic stem cell research to a standstill, and because they offer many advantages when compared to bone marrow stem cells, cord blood is becoming the preferred stem cell source in transplant therapy.

panded cord blood stem cells to treat patients with high-risk malignancies.[5]

Investigators at Duke University Medical Center administered cord blood stem cells expanded by the Aastrom Replicell System (developed by Aastrom Biosciences) to 27 patients with malignant and nonmalignant disorders. The recipients exhibited durable long-term engraftment and demonstrated the safety of this cell expansion technique for clinical use.[6]

The increasing number of institutions that are actively pursuing these new technologies is an indication of the scientific importance of stem cell expansion. The positive results seen in studies thus far suggest that expansion technologies may be available to more patients in the future. Although further study is needed to determine just how cord blood yields benefits in treating diabetes in humans, it is just one of a growing number of regenerative stem cell therapies that are moving from the lab into the clinic. Regenerative medicine studies are underway for a variety of conditions including heart disease, stroke, Parkinson's disease, spinal cord injury, amyotrophic lateral sclerosis, muscular dystrophy and liver disease.

References

1. McGuckin et al. Production of stem cells with embryonic characteristics from human umbilical cord blood. *Cell Prolif.* 2005;38:245-255. **2.** Yao CL, et al. Characterization of serum-free ex vivo-expanded hematopoietic stem cells derived from human umbilical cord blood CD133+ cells. *Stem Cells and Development.* 2006;15:70-78. **3.** First Patient Undergoes Expanded Cord Blood Transplant in the ExCell Registration Study of StemEx® for Leukemia and Lymphoma. Available at: http://home.businesswire.com/portal/site/google/index.jsp? ndmViewId=news_view&newsId=20071106005916&newsLang=en. **4.** Pecora AL, et al. Prompt and durable engraftment in two older patients with high risk chronic myelogenous leukemia (CML) using ex vivo expanded and unmanipulated umbilical cord blood. *Bone Marrow Transplantation.* 2000;25:797-799. **5.** Shpall E, et al. Transplantation of ex vivo expanded cord blood. *Biology of Blood and Marrow Transplantation.* 2002;8:368-376. **6.** Jaroscak J, et al. Augmentation of umbilical cord blood (UCB) transplantation with ex vivo expanded UCB cells: Results of a phase I trial using the Aastrom Replicell system. *Blood.* 2003;101:5061-5067. **7.** Ohishi K, varnum-Finney B, and Bernstein I. Delta-1 enhances marrow and thymus repopulating ability of human CD34+CD38-cord blood cells. *The Journal of Clinical Investigation.* 2002;110(8):1165-1174.