The Anatomy of the Umbilical Cord

Newborn Stem Cells, Issue 1

Stem Cells Are Now Being Collected From More of the Umbilical Cord

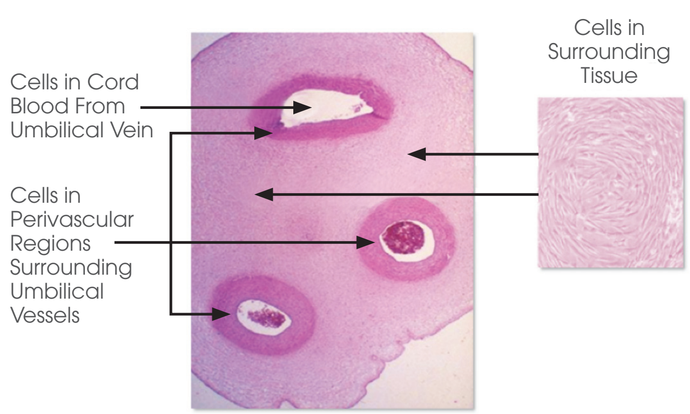
Stem cells are naive cells that have the ability to replicate themselves and to differentiate into a range of diverse cell types, each specialized to carry out a specific function. Stem cell transplants are currently being used to treat life-threatening conditions and chronic diseases such as leukemias, severe aplastic anemia, sickle cell disorders, and thalassemias.[1] Stem cells needed for transplants can be harvested from bone marrow, peripheral blood, and umbilical cord blood. Newborn stem cells are increasingly being used as a noncontroversial, noninvasive source for patients in need of transplantation or autologous infusion.[2] These are valuable cells that can be harvested from umbilical cords, which were once regarded as medical waste.[3]

The umbilical cord contains valuable stem cells in the blood, tissue, and perivascular regions

Stem cells can be extracted from three main sources in the umbilical cord. The most widely known and used source, which is commonly referred to as cord blood, comes from the blood in the umbilical vein. It has recently been discovered that the connective tissue of the cord contains stem cells. The perivascular regions of the umbilical cord are also a source. These are the spaces directly surrounding the vessels, including both arteries and one vein (**Figure 1**).[4-6]

Umbilical cords contain different types of stem cells that can be distinguished by the cell lineages they can become. Cord blood is an excellent source of both hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs). Cord tissue and the perivascular regions of the umbilical cord are especially abundant sources of MSCs, the highest overall concentration of which can be found in the perivascular regions. HSCs and MSCs are readily accessible at birth from the umbilical cord and can be collected and stored for future use.[4,7]

Figure 1. Sources of Stem Cells in the Umbilical Cord



HSCs are capable of generating all of the different types of blood cells found in the bloodstream, including red blood cells, white blood cells, and megakaryocytes that become platelets.[7] Unlike HSCs, MSCs do not generate blood cells. Instead, MSCs readily differentiate into a range of cells,[8] such as osteoblasts, chondrocytes, and adipocytes.[9] MSCs maintain their multipotency throughout their self-renewal. These MSCs also can be successfully isolated and expanded in culture.[10]

Because newborn stem cells have such varied and growing therapeutic potential, it is crucial that expectant parents be made aware of what these life-saving stem cells can do. Although almost all of the transplants performed to date with the use of newborn stem cells have been with cord blood–derived HSCs, preclinical research being performed with the use of MSCs (such as in Parkinson's disease,[11] stroke,[12] and myocardial infarction[13]) points to a future that could be full of therapeutic possibilities for MSCs from the umbilical cord. Even the uses of HSCs from cord blood are expanding as the body of research grows, and these may possibly include therapeutic applications for cerebral palsy[14,15] and type 1 diabetes; the use of HSCs from cord blood has yet to demonstrate efficacy in type 1 diabetes but may still be promising with further study.[16]

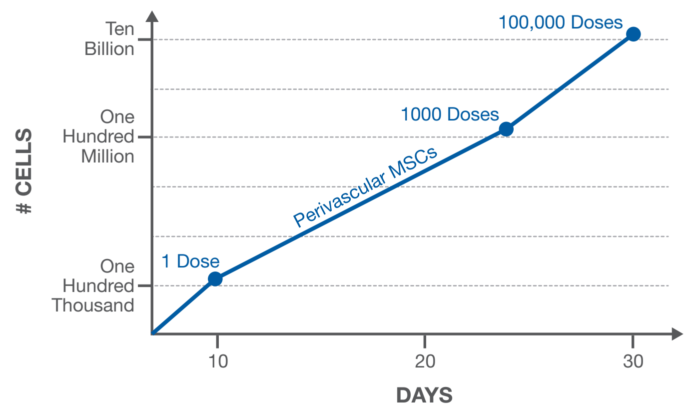
Umbilical Cord Perivascular Regions Contain Mesenchymal Stem Cells That Are Rapidly Expandable

Scientists have now determined that mesenchymal stem cells (MSCs) can be obtained from the perivascular regions surrounding umbilical cord blood vessels. There is such a dense population of MSCs in this space that isolating them is an important step to being able to realize their full potential. It has been shown that these cells can be successfully and rapidly expanded, so the number of MSCs with therapeutic potential is exponentially greater than the number originally extracted.

Perivascular MSCs can be rapidly expanded into billions of cells

Sarugaser and colleagues published their experience with the isolation and expansion of human umbilical cord perivascular cells. After 30 days of cell culturing, the number of cells increased from 6.6×10^3 to 1.4×10^{10}. The authors reasoned that if approximately 2×10^5 MSCs are considered to be a therapeutic dose, then a single therapeutic dose derived from perivascular MSCs can be achieved within 10 days of harvest. Furthermore, it would take 24 days to produce 1000 doses and 30 days to produce 100,000 doses (**Figure 2**). These figures reflect a decrease in the expansion time by almost half compared with multipotent progenitor cells from adult bone marrow, which can produce one dose in 22 days and 1000 doses in 42 days.[5]

Figure 2. Cell Expansion and Translation Into Therapeutic Doses by Day of Cell Culture



In addition, this study shows that the umbilical cord perivascular cell populations possess a high concentration of colony-forming unit-fibroblast–deriving cells; this concentration is much higher than that in the bone marrow of newborns. These perivascular cells proliferate rapidly in culture, with a shorter average doubling time than has been seen with embryonic stem cells and stem cells derived from adult bone marrow.[5]

The rapid expansion of potent MSCs from umbilical cord perivascular regions may be clinically relevant in the future, based on the clear therapeutic potential that bone marrow–derived MSCs have demonstrated through clinical trials aimed at treating a number of conditions, including

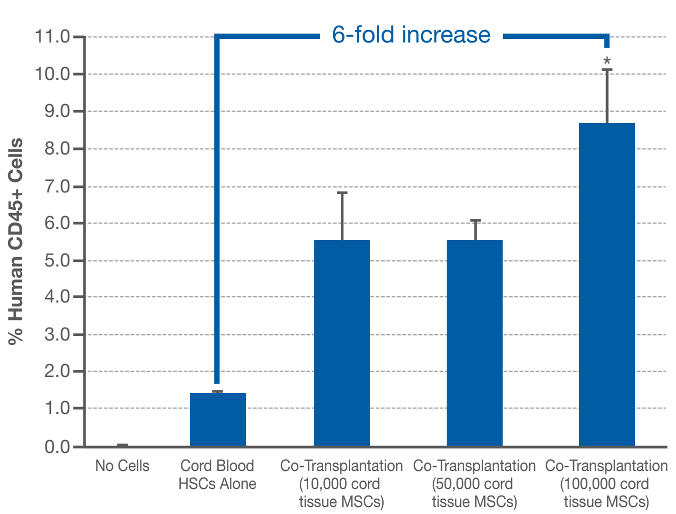
- acute myocardial infarction,[17,18]
- ischemic cardiomyopathy,[19]
- Parkinson's disease,[20]
- multiple sclerosis,[21,22]
- degenerative disc disease,[23]
- osteogenesis imperfecta,[24]
- and spinal cord injury.[25]

Combining Cord Blood and Cord Tissue Stem Cells Can Improve Engraftment

In order to discover the effects of combining hematopoietic stem cells (HSCs) with mesenchymal stem cells (MSCs), Dr. Rouzbeh Taghizadeh and colleagues studied the effects of co-transplanting cord blood HSCs with cord tissue–derived MSCs in a preclinical model that used non-obese diabetic/severe combined immunodeficient mice.[26]

Approximately 24 hours after total body irradiation the mice received an injection of mononuclear HSCs from human cord blood only, human cord blood HSCs plus 3 varying amounts of human MSCs from cord tissue, or a diluent as a negative control. The extent of the success of human engraftment in murine bone marrow was measured by the presence of human CD45+ cells. The authors observed a 6-fold increase in human CD45+ cell expression when 10 x 10^4 MSCs from human cord tissue were combined with 10^6 HSCs from human cord blood compared with 10^6 HSCs transplanted alone (P=0.03). Human CD45+ cell expression also increased when fewer MSCs were used in the co-transplantation, although not to a statistically significant degree (**Figure 3**).[26]

Figure 3. Engraftment Following HSC and MSC Co-Transplantation



Extent of successful human cell engraftment (%) following co-transplantation of human cord blood HSCs and human cord tissue MSCs in a mouse model.
*P<0.05.

Cord tissue and cord blood cells can work together to enhance engraftment

The authors' findings suggest that engraftment may increase when MSCs from cord tissue are combined with HSCs from cord blood during the transplantation process. Although studies like the one conducted by Taghizadeh et al are in experimental preclinical stages, results such as these point to the potential future advantages of preserving cord tissue MSCs today. Further research will need to be done to confirm and expand on these results and to make the link between preclinical findings and actual clinical benefits in transplant recipients.

The Latest in Stem Cell Research

Wu et al published the first reported use of umbilical cord tissue–derived mesenchymal stem cells (MSCs) in the human clinical setting, paving the way for future clinical trials. The authors found that cord-derived MSCs were able to dramatically improve two patients' severe steroid-resistant acute graft-versus-host disease after each of four infusions, with no adverse events.[27] This is an exciting step in the transition from preclinical experiments to future therapeutic use of cord-derived MSCs.

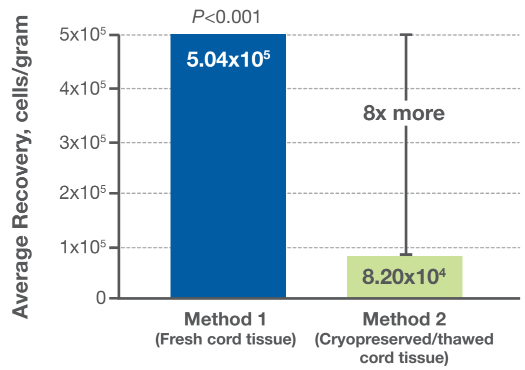
Transplants involving cord tissue cells were recently performed in humans

Did You Know?

Processing Cord Tissue Before Cryopreservation Has a Significant Impact on the Recovery of Viable Cells

Briddell et al tested two methods of cryopreservation to determine the optimal method for storing mesenchymal stem cells (MSCs) from cord tissue: cryopreserving MSCs that have already been isolated from fresh cord tissue versus cryopreserving the intact cord tissue and isolating the cells later. The authors found that 8.4-fold more viable cells were able to be recovered when MSCs were harvested prior to cryopreservation as opposed to when the MSCs were isolated later, after the cord tissue was cryopreserved and then thawed.[28]

MSC Isolation From Fresh Cord Tissue = 8x Isolation From Cryopreserved Cord Tissue



Newborn Stem Cell Collection Tip

Clean the Umbilical Cord

Following the delivery, reprep the perineum by swabbing the area with ***Betadine*** and ***water*** to help reduce the chance of inadvertent microbial contamination.

Using the cleaning product included in the collection kit, make sure to clean the umbilical cord using an up and down motion starting just above the clamp.

After cleaning the site, take care not to allow secretions, nonsterile items, or maternal blood to contaminate the intended venipuncture site.

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