



Cord Blood Stem Cells and Cardiovascular Disease

Cardiovascular disease is the leading cause of death for both men and women in the U.S. Approximately one million people die of cardiovascular disease annually despite medical intervention, with coronary artery disease claiming 50 percent of those lives.¹ Although heart disease impacts an older population whose heart muscle, arteries and pumping function have deteriorated over time, heart ailments also strike the very young. According to the National Institutes of Health, congenital heart disease is responsible for more deaths in the first year of life than any other birth defect.²

To date, there is no proven “off-the-shelf” therapy to repair or regenerate the heart after acute myocardial infarction (heart attack) or congestive heart failure. Because heart cells have a limited capacity to regenerate, researchers are exploring potential therapies using various stem cell sources to repair or replace damaged tissue including vascular endothelial cells, which form the inner lining of new blood vessels, and cardiomyocytes, the heart muscle cells that contract to pump blood into and out of the heart.³

The stem cells found in a newborn’s umbilical cord blood are one type of stem cell holding great promise in cardiovascular repair. Stem cells from cord blood may have an advantage over those found in bone marrow or peripheral blood because they are immunologically “younger” and appear to be more versatile. They also demonstrate an important characteristic with embryonic stem cells: they are able to differentiate into nearly all cell types in the body. However, cord blood stem cells offer important advantages: 1) they do this in a safe and controlled manner;

2) they have been used in clinical practice to treat humans for more than 20 years; and 3) there is no controversy involved in their collection.

Researchers are noting several positive observations in pre-clinical animal studies. Thus far, in animal models, cord blood stem cells have shown the ability to selectively migrate to injured cardiac tissue, improve vascular function and blood flow at the site of injury, and improve overall heart function.¹

Repairing Blood Vessels and Improving Ventricular Function

The heart demands a large volume of blood flow in order to bring nutrients and oxygen to the muscle tissue after it has been damaged. Research demonstrates that cord blood stem cells are capable of giving rise to vascular endothelial-like cells, which are believed to aid in the repair of heart tissue damage due to myocardial infarction. Several pre-clinical studies of induced myocardial infarction in rats have shown that cord blood stem cells have the ability to:

- Migrate and engraft to damaged heart muscle^{4,5}
- Contribute to the formation and proliferation of new blood vessels^{4,6}
- Improve left ventricular remodeling, structural damage and function⁷
- Decrease the size of infarction⁸

These animal studies may lay the foundation for future human clinical trials testing cord blood stem cell treatment for patients with heart damage due to myocardial infarction.

Cardiomyocytes and Cord Blood: In Vitro Studies Show Promise

Permanent loss of cardiomyocytes (heart muscle cells) and the formation of scar tissue following a heart attack result in irreversible damage to cardiac function. Human cord blood contains several different types of stem cells including hematopoietic, endothelial and mesenchymal stem cells. Although still in early stages, four in vitro studies have shown that under certain treatment conditions, cord blood mesenchymal stem cells differentiate into cardiomyocyte-like cells⁹⁻¹² and were able to induce regeneration of healthy cells from damaged cardiomyocytes.¹² This suggests that cord blood stem cells have a high potential to differentiate into cardiomyocytes and aid the regeneration of cardiomyocytes lost due to heart damage.

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.

Cord Blood and Congenital Heart Defects

Although more research needs to be done, scientists believe cord blood stem cells may have the most immediate benefit for children born with congenital heart defects — or problems with the heart's structure that are present at birth.

According to one in vitro study, cord blood endothelial stem cells demonstrated excellent growth potential for tissue-engineered vascular grafts that could replace human heart defects. These findings offer a compelling reason why parents with a child diagnosed intrauterinely with congenital defects should consider preserving their child's cord blood, since it may offer a treatment option in the future.¹³

Advances in Peripheral Vascular Disease

The ability of cord blood stem cells to become vascular endothelial-like cells

and thus, blood vessels, indicates they will likely have potential applications beyond the heart.

Peripheral vascular disease (PVD) is a restriction of blood flow outside of the heart usually occurring in the legs and arms. Restricted blood flow is caused by blood vessel narrowing from fatty plaque formation on vessel walls (atherosclerosis) or blockage due to blood clots. If the blockage is severe enough, tissue death can occur. If left untreated, the limb may need to be amputated.¹⁴ In animal models, cord blood stem cells have been able to significantly reverse the effects of ischemia, or loss of blood flow in the blood vessels. In models of hind limb ischemia, transplantation of cord blood stem cells appeared to reverse surgery-induced ischemia resulting in limb salvage.^{15,16} These observations may lead to future human clinical trials using cord blood stem cells to treat patients with peripheral vascular disease.

The Future of Cord Blood Stem Cell Therapy

As science advances, so do the number of preserved cord blood units being used in regenerative medicine applications. If expectant parents store their baby's cord blood in a family bank, the stem cells are immediately available for use in medical treatments, including future therapies to repair or replace damaged heart tissues. As a result, an infant's cord blood could prove to be a life-saving treatment option if that child is born with a congenital heart defect, or later in life following a sudden and serious heart attack. In regenerative medicine, the latest scientific evidence suggests that using one's own stem cells likely delivers more favorable outcomes.

References

1. Harris DT, Badowski M, Ahmad N, Gaballa MA. The potential of cord blood stem cells for use in regenerative medicine. *Expert Opinion on Biological Therapy*. 2007;7(9):1311-1322.
2. U.S. National Library of Medicine and National Institutes of Health. Medline Plus. Congenital Heart Disease page. <http://www.nlm.nih.gov/medlineplus/ency/article/001114.htm>. Accessed January 2008.
3. National Institutes of Health. Stem Cell Information Page. <http://stemcells.nih.gov/info/scireport/chapter9.asp>. Accessed January 2008.
4. Ma N, Stamm C, Kaminski A, Li W, et al. Human cord blood cells induce angiogenesis following myocardial infarction in NOD/scid-mice. *Cardiovascular Research*. 2005;66(1):45-54.
5. Hu CH, Wu GF, Wang XO et al. Transplanted human umbilical cord blood mononuclear cells improve left ventricular function through angiogenesis in myocardial infarction. *Chin Med J (Engl)*. 2006;119(18):1499-506.
6. Ma N, Ladilov Y, Kaminski A, Piechaczek C, Stamm C. Umbilical cord blood cell transplantation for myocardial regeneration. *Transplant Proc*. 2005;38(3):771-3.
7. Leor J, Guetta E, Feinberg MS et al. Human umbilical cord blood-derived CD133+ cells enhance function and repair of the infarcted myocardium. *Stem Cells*. 2006;24(3):772-80.
8. Henning RJ, Abu-Ali H, Balis JU, Morgan MB, Willing AE, Sanberg PR. Human umbilical cord blood mononuclear cells for the treatment of acute myocardial infarction. *Cell Transplant*. 2004;13(7-8):729-39.
9. Cheng F, Zou P, Handong Y. Induced differentiation of human cord blood mesenchymal stem/progenitor cells into cardiomyocyte-like cells in vitro. *J Huazhong Univ Sci and Tech*. 2003;23(2):154-157.
10. Nishiyama N, Miyoshi S, Hida N, et al. The significant cardiomyogenic potential of human umbilical cord blood-derived mesenchymal stem cells in vitro. *Stem Cells*. 2007;25(8):2017-24.
11. Bonanno G, Mariotti A, Procoli A, et al. Human cord blood CD133+ cells immunoselected by a clinical-grade apparatus differentiate in vitro into endothelial- and cardiomyocyte-like cells. *Transfusion*. 2007;47(2):280-9.
12. Yamada Y, Yokoyama S, Fukuda N, et al. A novel approach for myocardial regeneration with educated cord blood cells cocultured with cells from brown adipose tissue. *Biochem Biophys Res Commun*. 2007;353(1):182-8.
13. Schmidt D, Breymann C, Weber A, Guentert CI, Neuenschwander S, Zund G, Turina M, Hoerstrup SP. Umbilical cord blood derived endothelial progenitor cells for tissue engineering of vascular grafts. *Ann Thorac Surg*. 2004 Dec;78(6):2094-8.
14. U.S. National Library of Medicine and National Institutes of Health. Medline Plus. Peripheral Vascular Disease page. <http://www.nlm.nih.gov/medlineplus/peripheralvascular diseases.html>. Accessed January 2008.
15. Ikeda Y, Noboru F, Wada M, Matsumoto T, Satomi A, Yokoyama SI, Saito S, Masumoto K, Katsuo K, Mugishima H. Development of angiogenic cell and gene therapy by transplantation of umbilical cord blood with vascular endothelial growth factor gene. *Hypertens Res*. 2004;27(2):119-128.
16. Cho S-W, Gwak S-J, Kang S-W, et al. Enhancement of angiogenic efficacy of human cord blood cell transplantation. *Tissue Eng*. 2006;12(6):1651-1661.