EMBARGOED FOR RELEASE
Sunday, March 12, 12:00 PM EST

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POTENTIAL HEART BENEFIT FOUND IN STEM CELLS

Researchers Find Viable New Sources for Stem Cell Transplants to the Heart

ATLANTA, GA (March 12, 2006) — Stem cell transplantation is among one of the most exciting and hotly debated areas of medical research today. While the promise of personalized medicine and effective treatments for debilitating diseases drive progress in this area, moral and ethical dilemmas about embryonic cells continues to cloud the field. In research presented today at the American College of Cardiology's 55th Annual Scientific Session, scientists continue to explore mature stem cell sources for potentially significant cardiovascular benefits. ACC.06 is the premier cardiovascular medical meeting, bringing together over 30,000 cardiologists to further breakthroughs in cardiovascular medicine.

"We hope that the exploration of stem cells derived from new sources may bypass some of the debate that is preventing research progress right now," said Sharon A. Hunt, M.D., Stanford University. "The research presented here is extremely promising, and should be followed by more in-depth and patient-focused studies to determine the true feasibility of this treatment method."

Human Menstrual Blood Derived Stem Cell Has a High Cardiomyogenic Potential; Possible New Cell Source for Cardiac Stem Cell Therapy (Abstract 921-105) /
Human Umbilical Cord Blood Derived Mesenchymal Stem Cell Has A Powerful Cardiomyogenic Potential in Vitro; A Novel Cell Source for Cardiac Stem Cell Based Therapy (Abstract 921-107)

Some previous research on the efficacy of stem cell therapy for heart repair has shown benefit from mesenchymal stem cells (often found in bone marrow), but mostly because they

— more —

assist in the growth of new blood vessels. The true benefit of stem cells to heart function, however, may be in promoting cardiomyogenesis (CM, the growth of cardiac muscle). To achieve CM, the source of the cells needs a high rate of cardiac activity and similar gene and protein expression. In two studies presented from researchers at the Keio University School of Medicine in Japan, new sources from menstrual blood-derived endometrial cells and umbilical cord blood-derived mesenchymal cells show significant promise in this function.

In the first study, the team collected menstrual blood from six women to obtain a sample of endometrial cells (E-DOM). The researchers found that approximately half of the E-DOM cells contracted simultaneously, suggesting an electrical communication between the cells. Further analyses of the cells revealed appropriate cardiac gene expression and action potential, as well as sustained and significant positive cardiac troponin-1, a calcium-regulated protein in muscle tissue, and connexin 43, a protein that assists in intracellular interactions. The *in vitro* data suggests that stem cells from this source have significant CM potential and are potentially valuable not only because they can be easily collected from young volunteers, but also because of their collection-efficacy. A single sample of the menstrual blood returns a large number of stem cells.

In a second study, the same team collected human umbilical cord blood-derived mesenchymal stem cells (UCB-MSC). In reviewing these cells, nearly all of the UCB-MSC contracted simultaneously, indicating a significant electrical communication between the cells. Again the extended analysis showed cardiac gene expression, as well as significant positive cardiac troponin-1 and connexin 43. In this study, approximately half of the stem cells were successfully transformed into cardiomyocytes (premature cardiac functioning cells) *in vitro*.

"We believe that by looking at these new sources for stem cells, we will eventually be able to use our own stem cells to repair our own heart dysfunctions," said Sunichiro Miyoshi, M.D., of the Keio University in Japan, and one of the lead authors of the study. "The value of finding new sources is in finding younger and stronger stem cells."

<u>Effect of Stem Cells on Left Ventricle Wall Thickness and Capillary Density in Pigs Following Myocardial Infarction (Abstract 829-3)</u>

Stem cell transplantation is a controversial, yet promising option for a number of areas of the body that need repair or replacement. In fact, adult autologous (as in, using one's own cells) stem cells may be a novel approach for cardiac regeneration after heart attacks. In a closer look at

their regenerative function, researchers from Tulane University in Louisiana evaluated the stem cell transplant's effect on the thickness of the heart wall following a heart attack.

To test the hypothesis, the researchers induced heart attacks in 17 pigs by way of an angioplasty balloon and harvested stem cells from the animals' subcutaneous fat tissues (ADSC, adipose derived stem cells). After repairing the hearts, a suspension including the ADSC was injected through the balloon into the heart. After eight weeks, the animals were euthanized and the hearts were removed to measure the left ventricle wall thickness and the density of the corresponding capillaries in four areas: the damaged or infarct area, the healthy myocardium (cardiac muscle), and in two parts of the border zone.

As predicted, the infarct areas of the heart walls in the ADSC group were thicker than in the animals not receiving the injection (5.9 vs. 3.6 millimeters), and the same difference was seen in the border zones (11.2 vs. 8.6 mm). Capillary density in the border zones of the ADSC group was also significantly increased compared to the control group. The healthy myocardium areas showed no significant differences.

"We feel that these results help explain the positive impact of stem cell transplants for heart patients, demonstrating that they do, in fact, work to thicken the heart wall," said Eckhard Alt, M.D., of Tulane University and lead author of the study. "We believe that stem cells from the adipose tissues may be a valuable novel alternative source for helping support cardiac regeneration after a heart attack."

Beneficial Effect of Combined Intramyocardial and Intracoronary Administration of Autologous Stem Cells on Global and Regional Left Ventricular Function and Myocardial Perfusion in Patients with Ischaemic Cardiomyopathy (Abstract 934-173)

Yet another potential new source for stem cells to be used for cardiac therapy is the bone marrow. To improve global left ventricular ejection fraction (EF, the volume of blood pumped out of the heart's main chamber during a single beat) and regional left ventricular wall motion, which is related to ejection fraction, researchers evaluated a treatment with bone marrow-derived cells, attempting to clarify the extent of stress-induced or rest perfusion defect (scar tissue) in patients with ischemic cardiomyopathy, or blockages in the arteries leading to the heart infarction.

In the study, 17 patients with ischemic cardiomyopathy were treated with a combined percutaneous injection (both intramyocardial and intracoronary, either the heart muscle or the

heart's artery) of bone marrow-derived mononuclear cells. At baseline and follow-up evaluation, the investigators reviewed the myocardial viability and local wall motion abnormalities, as well as the size of resting and stress-induced perfusion defects. They also measured the global EF and the wall motion score index, which measures the percentage of normal functioning muscle tissue in the heart wall.

The combined stem cell injection resulted in an increase in global EF, (from 34.8 to 39.5 percent), as well as a significant increase in wall motion at the six-month follow up. The team noted a trend to smaller stress-induced defects, and found that the number of bone-marrow stem cells injected was positively related to the follow-up EF levels, and negatively correlated to the stress-induced and resting perfusion defects.

"In at-risk patients, combined treatment with bone-marrow derived stem cells may offer an effective alternative to improving cardiac function," said Helmut Glogar, M.D., of the Medical University of Vienna, and lead author of the study.

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