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## Cell transplantation and cardiac repair

### EUREKALERT

Contact: Hans Dohman

[Directoria.cientifica@procardiaco.com.br](mailto:Directoria.cientifica@procardiaco.com.br)

55-212-131-1584

Cell Transplantation Center of Excellence for Aging and Brain Repair

Tampa, Fla. (July 1, 2009) The frontiers of cell transplantation for cardiac repair are discussed in the current issue of *Cell Transplantation* (Vol. 18 No.3), now available on-line without charge at <http://www.ingentaconnect.com/content/cog/ct>.

Two studies are highlighted, one by a Brazil-based research team who looked at two different bone marrow cell delivery methods following myocardial infarction, and a second study from a team of researchers in Germany who used bone marrow stem cell transplants to repair limb ischemia with a goal of preventing amputations.

#### Two delivery techniques for stem cells

With evidence mounting that cell-based therapies can repair the injured myocardium following acute infarction, a Brazil-based research team addressed questions of the best way to safely deliver bone-marrow mononuclear cells (BMMNC) derived from the same patient (autologous cells) to the heart, following a heart attack caused by a prolonged interruption of blood flow leading to changes in the electrocardiogram (ST elevation myocardial infarction). They compared two different delivery techniques through the anterograde intra-coronary (ICA) or via the retrograde intra-coronary artery vein (ICV). Researchers used radiolabeled cells to evaluate cell distribution patterns in the heart and their relationship with left ventricle function improvement.

"BMMNC retention by damaged heart tissue was apparently higher when the anterograde approach was used, although further studies are required to confirm this data," said corresponding author Dr. Hans Dohman of the Hospital Pro-Cardiaco in Rio de Janeiro, Brazil.

While previous reports observed that microvascular obstruction impairing cell uptake by the heart could be an issue, the team hypothesized that an intravenous approach may overcome that potential.

"We hypothesized that an intravenous approach might overcome this issue since the passage (diapedesis) of circulating cells into the adjacent cardiac tissue occurs on the venous side of microcirculation," added Dr. Dohman. "In addition, we found that the grade of obstruction of microcirculation does not correlate with the efficiency of cell delivery to the infarcted tissue."

The research team also found that higher cell retention correlated with better changes in observed ejection fraction from baseline to a six-month follow-up.

"Our data point toward a causal relationship between the total number of cells that participate in infarct repair and the final enhancement of cardiac function," concluded Dr. Dohman.

Contact: Hans Dohman, Hospital Pro-Cardiaco, Rua Dona Mariana 219, Botafogo, Rio de Janeiro, Brasil. CEP: 22280-000 Tel. (55) 21-21311584 [Directoria.cientifica@procardiaco.com.br](mailto:Directoria.cientifica@procardiaco.com.br)

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## Bone marrow cell transplants for limb ischemia

Bone marrow cell transplantation has been shown to induce new blood vessel growth (angiogenesis) and foster improvements in patients with ischemic artery disease. This study, conducted by a Berlin-based group, evaluated the long-term effects of intermuscular, autologous bone marrow cell (aBMC) transplants in patients at major risk for amputation due to the loss of blood flow to a limb (limb ischemia) and who have failed or who are not candidates for surgical techniques to remove or bypass blockages. Patients who have failed surgical steps have high rates of amputation. In this study, 90 percent of patients participating in the study had been scheduled for major amputations; their long-term limb salvage rate was 53 percent.

"Our results suggest that aBMC transplants have the potential to treat severely ischemic limbs," said corresponding author Dr. Berthold Amann of the Franziskuskrankenhaus Berlin-Vascular Center. "Among the patients in whom limb salvage was successful and amputation avoided, the leg was also pain-free and usable."

Dr. Amann noted that the patients with limb salvage had better baseline perfusion than the eventually amputated patients. Among the limb-salvaged group, analgesic consumption was reduced by 62 percent and their total walking distance improved from zero to 40 meters.

"This study found that after aBMC, in addition to being spared amputation, a critically ischemic leg can have increased blood flow and support wound healing while patients have reduced pain," concluded Dr. Amann.

Researchers suggested that their results are yet to be confirmed, but a double-blind, placebo controlled study is currently underway.

"Should ours and other studies prove this therapy to be effective, adoption by hospitals other than large academic centers will require a simple method for processing the bone marrow," added Dr. Amann.

Contact: Dr. Berthold Amann, Dept. of Internal Medicine, Franziskuskrankenhaus, Berlin Vascular Center, 10787 Berlin, Germany. Tel: (49) 30-2638-3601 [amann@franziskus-berlin.de](mailto:amann@franziskus-berlin.de)

"The use of bone marrow derived cells for improvement in ischemic muscle in the heart or leg is very promising," said Amit N. Patel, associate professor of surgery at the University of Utah School of Medicine and the cardiovascular, skin, other tissue section editor of *Cell Transplantation*. "Both articles demonstrate that the route of delivery is one of the key determinants in having positive outcomes in the early clinical trials."

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The editorial offices for *CELL TRANSPLANTATION* are at the Center of Excellence for Aging and Brain Repair, College of Medicine, the University of South Florida and the Diabetes Research Institute, University of Miami Miller School of Medicine. Contact, David Eve, PhD at [celltransplantation@gmail.com](mailto:celltransplantation@gmail.com) or Camillo Ricordi, MD at [ricordi@miami.edu](mailto:ricordi@miami.edu).

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