Adult bone marrow stem cells injected into skeletal muscle can repair heart tissue

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University at Buffalo researchers have demonstrated for the first time that injecting adult bone marrow stem cells into skeletal muscle can repair cardiac tissue, reversing heart failure.

Using an animal model, the researchers showed that this non-invasive procedure increased myocytes, or heart cells, by two-fold and reduced cardiac tissue injury by 60 percent.

The therapy also improved function of the left ventricle, the primary pumping chamber of the heart, by 40 percent and reduced fibrosis, the hardening of the heart lining that impairs its ability to contract, by up to 50 percent.

"This work demonstrates a novel non-invasive mesenchymal stem cell (MSC) therapeutic regimen for heart failure based on an intramuscular delivery route," said Techung Lee, Ph.D., UB associate professor of biochemistry and senior author on the paper.

Mesenchymal stem cells are found in the bone marrow and can differentiate into a variety of cell types.

"Injecting MSCs or factors released by MSCs improved ventricular function, promoted myocardial regeneration, lessened apoptosis (cell death) and fibrotic remodeling, recruited bone marrow progenitor cells and induced myocardial expression of multiple growth factor genes," Lee said.

"These findings highlight the critical 'cross-talks' between the injected MSCs and host tissues, culminating in effective cardiac repair for the failing heart."

The paper reporting this development appears online in the Articles-in-Press section of the *American Journal of Physiology -- Heart Circulation Physiology* at ajpheart.physiology.org/cgi/reprint/00186.2009v1

The heart disease death rate has dropped significantly in the last three decades due to better treatments, resulting in large numbers of people living with heart failure. This advance has lead to another health hurdle: The only therapy available to reverse the decline in cardiac function is heart transplantation, and donor hearts are very scarce.

Clinical trials of myocardial stem cell therapy traditionally have relied on surgery -- infusing the stem cells directly into the heart or injecting them into the myocardium, the heart muscle -- invasive methods that can result in harmful scar tissue, arrhythmia, calcification or small vessel blockages.

"In our research with a swine model of heart failure," said Lee, "we've found that only 1-to-2 percent of MSCs infused into the myocardium grafted into the heart, and there was no evidence that they differentiated into heart muscle cells. In addition, diseased tissue is not a healthy environment for cell growth.

"For these reasons, and because patients with heart failure are not good surgical risks, it made sense to explore a non-invasive cell delivery approach," said Lee. "An important feature of MSCs is their ability to produce a plethora of tissue healing effects, known as "tropic factors," which can be harnessed for stem cell therapy for heart failure.

Lee noted that the multiple trophic factors produced by MSCs have been

shown in the literature to be capable of reducing tissue injury, inhibiting fibrosis, promoting angiogenesis, stimulating recruitment and proliferation of tissue stem cells, and reducing inflammatory oxidative stress, a common cause of cardiovascular disease and heart failure.

"Since skeletal muscle is the most abundant tissue in the body and can withstand repeated injection of large number of stem cells, we thought it would be a good method to deliver MSCs," Lee said. "We hypothesized that MSCs, via secretion of these functionally synergistic trophic factors, would be able to rescue the failing heart even when delivered away from the myocardium.

"This study proves our hypothesis," said Lee. "We've demonstrated that injecting MSCs, or trophic factors released by MSCs, into skeletal muscle improved ventricular function, promoted regeneration of heart tissue, decreased cell death and improved other factors that cause heart failure.

"This non-invasive stem cell administration regimen, if validated clinically, is expected to facilitate future stem cell therapy for heart failure."

Lee said the next step is to use genetic and pharmacological engineering to make the stem cells more active, so good therapeutic effects can be achieved with fewer cells.

"That is our goal. It would reduce the cost of stem cell therapy and make it more affordable for patients in the future."

Source: University at Buffalo (news : web)