MedicalXpress

Youthful stem cells from bone can heal the heart

September 4 2013

Many people who survive a heart attack find themselves back in the hospital with a failing heart just years later. And the outcome often is unfavorable, owing to limited treatment options. But scientists at Temple University School of Medicine's Cardiovascular Research Center (CVRC) recently found hope in an unlikely source – stem cells in cortical, or compact, bone. In a new study, they show that when it comes to the regeneration of heart tissue, these novel bone-derived cells do a better job than the heart's own stem cells.

According to the study's senior investigator, Steven R. Houser, Ph.D., FAHA, Chairperson of Temple's Department of Physiology and Director of the CVRC, it is early days for cortical bone-derived stem cells (CBSCs). Nonetheless, his team's findings, featured on the cover of the August 16th issue of *Circulation Research*, have considerable implications for stem cell therapy for the heart.

A major challenge in the treatment of heart attack is early intervention, which is key to reducing the chances for long-term complications, such as heart failure. When it comes to stem cells, Houser said, "The strategy is to inject the cells right after [a heart attack]." Currently, though, that approach works only in animal studies. To make it work in humans, Houser explained, "we need cells right off the rack and ready to go clinically."

CBSCs could be those cells. Stem cells are youthful by degrees, and CBSCs are considered some of the most pluripotent – like human

newborns, naïve and ready to become anything. But while CBSCs and similarly pluripotent stem cells retain the ability to develop into any cell type needed by the body and sometimes bring their youthful energy to the aid of mature cells – making them especially appealing for therapeutics – they also have the potential to wander off course, possibly landing themselves in unintended tissues. Cardiac stem cells, on the other hand, are a little more capable and a little more set in their ways, like toddlers. While they may need some coaxing into action, they are more likely to stay in their resident tissue.

To figure out how CBSCs might behave in the heart in the first place, Houser's team, led by Temple graduate student Jason Duran, began by collecting the cells from mouse tibias. The particular mice used had been engineered with green fluorescent protein (GFP), which meant that the CBSCs carried a green marker to allow for their later identification. The cells were then expanded in petri dishes in the laboratory before being injected directly into the hearts of non-GFP mice that had suffered heart attacks. Some mice received cardiac stem cells instead of CBSCs.

In the following weeks, as the team monitored the progress of the mice, they found that the youthfulness of the CBSCs had prevailed. The cells had triggered the growth of new blood vessels in the injured tissue, and six weeks after injection, they had differentiated, or matured, into heart muscle cells. While generally smaller than native heart cells, the new cells had the same functional capabilities, and overall they had improved survival and heart function. Similar improvements were not observed in the subset of mice treated with cardiac stem cells. Nor was there evidence in those mice that the cardiac cells had undergone differentiation.

The findings challenge the general assumption that cardiac stem cells, because they reside in the heart, are the cells most capable of repairing damaged heart tissue. For that reason, according to Houser, the new

paper likely will be controversial.

"What we did generates as many questions as it does answers," he said. "Cell therapy attempts to repopulate the heart with new heart cells. But which cells should be used, and when they should be put into the heart are among many unanswered questions."

To address at least some of those questions, Houser's team plans next to investigate CBSCs in a large-animal heart attack model. If that study yields similar results as the first, the cells could be ushered into a small-scale clinical trial of human patients. In humans, CBSCs would be collected from bone using techniques akin to those employed for bone marrow aspiration, a much simpler process than that used to isolate cardiac stem cells. While the cells would originate from a different person, raising the risk of rejection by the patient's immune system, it may be possible to have them at the ready in hospital settings, allowing for their injection immediately after a heart attack.

The cell therapy work by Houser's team represents just one of several forms of heart therapy being explored at Temple's CVRC. According to Houser, "Temple has made a commitment to cardiovascular research, with a clinical enterprise focused on treating patients. We're trying anything and everything to repair the heart [safely]." Other avenues of research include gene therapy, drug therapy, and the use of novel biomaterials to more effectively deliver drugs.

Provided by Temple University