# Stem cells boost heart's natural repair mechanisms

30 January 2013

Injecting specialized cardiac stem cells into a patient's heart rebuilds healthy tissue after a heart attack, but where do the new cells come from and how are they transformed into functional muscle?

Researchers at the Cedars-Sinai Heart Institute, whose clinical trial results in 2012 demonstrated that stem cell therapy reduces scarring and regenerates healthy tissue after a heart attack, now have found that the stem cell technique boosts production of existing adult heart cells (cardiomyocytes) and spurs recruitment of existing stem cells that mature into heart cells. The findings, from a laboratory animal study, are published in *EMBO Molecular Medicine* online.

"We're finding that the effect of stem cell therapy is indirect. It stimulates proliferation of dormant surviving host heart tissue, and it attracts stem cells already in the heart. The resultant new heart muscle is functional and durable, but the transplanted stem cells themselves do not last long," said Eduardo Marbán, MD, PhD, director of the Heart Institute. Marbán, the article's senior author, invented the experimental stem cell procedures and technology tested in humans.

Consistent with previous studies, the researchers found that the heart's native stem cells are not responsible for the normal replenishment of lost heart cells, but they do contribute to rebuilding heart tissue after heart attack.

This study shows that existing heart cells contribute to formation of new heart cells in the normal heart: Through a gradual cycling process, dying heart cells are replaced by new ones. The researchers found that this cycling process escalates in response to heart attack, enabling existing heart cells to assist in the development of new ones. Further, these effects can be amplified through stem cell therapy.

The investigational therapy turns on genes that bolster cell production from both sources – existing heart cells and existing stem cells – essentially boosting the heart's normal means of cell replacement and its natural responses to injury. The injection of stem cells also improves heart structure and function.

Marbán and his clinical and research teams in 2009 performed the first procedure in which a heart attack patient's own heart tissue was used to grow specialized stem cells that were injected back into the heart. Earlier this year, they reported results of a clinical trial that found significant reduction in the size of heart attack-caused scars in patients who underwent the experimental stem cell procedure, compared to others who did not.

Although the preliminary results are positive, the researchers do not know precisely how the research treatment works.

"Understanding the cellular sources and mechanisms of heart regeneration is the first step toward refining our strategies to more effectively regenerate healthy tissue after heart attacks," said Marbán, the Mark S. Siegel Family Professor.

**More information:** *EMBO Molecular Medicine*, "Cardiomyocyte proliferation and progenitor cell recruitment underlie therapeutic regeneration after myocardial infarction in the adult mouse heart," Dec. 19, 2012.

Provided by Cedars-Sinai Medical Center