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Mayo's 'smart' adult stem cells repair hearts

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Mayo Clinic investigators, with Belgian collaborators, have demonstrated that rationally "guided" human adult stem cells can effectively heal, repair and regenerate damaged heart tissue. The findings -- called "landmark work" in an accompanying editorial -- appear in today's *Journal of the American College of Cardiology*.

Stem cells isolated from patients have normally a limited capacity to repair the heart. This innovative technology boosts the regenerative benefit by programming adult stem cells to acquire a cardiac-like profile. Primed by a cocktail of recombinant cardiogenic growth factors, mesenchymal stem cells (MSCs) harvested from the bone marrow of a cohort of patients with coronary artery disease showed "superior functional and structural benefit without adverse side effects" over a 1-year follow-up in a model of heart failure according to the study.

"These findings provide proof-of-principle that "smart" adult stem cells have added benefit in repairing the heart, providing the foundation for further clinical evaluation," says Andre Terzic, M.D., Ph.D., Mayo Clinic researcher and senior investigator of the study. "The successful use of guided "lineage specified" human stem cells is based on natural cardiogenic cues" adds Atta Behfar, M.D., Ph.D. first author of the study. The pre-clinical data reported in this seminal paper have cleared the way for safety and feasibility trials in humans, which were recently conducted in Europe.

In their editorial, Eduardo Marban, M.D., Ph.D., and Konstantinos Malliaras, M.D., of Cedars-Sinai Heart Institute, in Los Angeles describe

the Mayo approach as a "boot camp" for stem cells and also write that the study "… provides the first convincing evidence that MSCs, at least in vitro, can in fact become functional cardiomyocytes (heart cells) …"

The long-term potential of the findings include development of an effective regenerative medicine therapy for patients with chronic heart failure.

How It Was Done

Researchers obtained bone marrow-derived stem cells from heart disease patients undergoing coronary bypass surgery. Testing of these stem cells revealed that cells from two of 11 individuals showed an unusual capacity for heart repair. These rare cells demonstrated upregulated genetic transcription factors that helped identify a molecular signature identifying highly regenerative stem cells. The cardiogenic cocktail was then used to induce this signature in non-reparative patient stem cells to program their capacity to repair the heart. Mouse models with heart failure, injected with these cells, demonstrated significant heart function recovery along with improved survival rate after a year, compared to those treated with unguided stem cells or saline.

Specifically, researchers found that the heart tissue healed more effectively; that human cardiac and vascular cells were found participating in the regeneration, repair and strengthening of heart structures within the area of injury; and that scars and vestiges of heart damage appeared to fade away.

Provided by Mayo Clinic