Transplanted muscle cells may help heal failing hearts

The first direct evidence that muscle cells transplanted from within a heart patient's body could help heal their damaged heart muscle was recently reported by a team from the University of Michigan Health System, Massachusetts General Hospital and Diacrin, Inc.

The results come from three patients who had cells from their thigh muscles injected into their heart muscle while they awaited a heart transplant, then allowed their old, damaged hearts to be examined for signs of cell growth after they got a new heart.

The detailed examinations, the first of their kind, showed that the injected cells not only survived in their new environment, but began to form muscle fibers. The areas where cells were injected also had an increase in the formation of small blood vessels.

None of the patients experienced immune reactions to the cell transplants.

"These results give us the first indication that muscle cell transplants, even from an entirely different kind of muscle, could one day be used to help repair damaged, failing hearts without danger of rejection," says U-M cardiac surgeon Dr. Francis Pagani, who will presented the results the Nov. 18 meeting of 75th Scientific Sessions of the American Heart Association. "We have much further to go, but we're very encouraged."

THE STUDY

The detailed findings come from a two-part Phase I study sponsored by Diacrin, designed to see if transplanted skeletal muscle cells might be a feasible option for repairing hearts damaged by heart attack and other diseases.

The study relies on the premise that certain kinds of cells can be expanded in culture and maintain their functional characteristics. Though similar to the concept of "stem cells" that can become any kind of cell in the body, the study uses "satellite cells," which occur naturally in muscle and help repair damage by dividing and moving to injured areas.

The arm of the study conducted at UMHS and Temple University involves patients awaiting a heart transplant to replace their scarred, failing hearts, and scheduled to receive an implanted heart-assisting device called an LVAD to help them survive until a new heart becomes available. Because their old heart can be removed for tests after the transplant, detailed analysis of the injected cells is possible.

The other arm of the study, led by the Arizona Heart Institute, looked at how well patients tolerate different doses of transplanted skeletal muscle cells injected during heart bypass surgery. It assessed the safety of the cell injection, and found indirect evidence of scar tissue regeneration. But it could not examine the hearts directly.

In both arms of the study, sample cells were removed from the quadriceps muscle, and treated with enzymes to isolate the satellite cells. They were then grown in a laboratory under carefully controlled conditions, to give the original handful of cells time to divide and produce 300 million cells.

Then, surgeons injected the cells into the wall of the heart's pumping chamber during an open-heart surgical procedure – either the LVAD implantation surgery or a coronary artery bypass graft (CABG) operation.

In LVAD patients, the new cells were placed in cardiac muscle tissue that had been severely scarred and hardened to the point that it can no longer contract sufficiently to help pump blood. (The LVAD helps boost the patient's pumping power, by feeding blood into a battery-powered metal pump and out through a tube connected to the main artery.)

When the patient got a heart transplant, the old heart was removed and sent for a series of histological tests at Diacrin headquarters in Charlestown, Mass.

THE RESULTS

The new results come from an analysis of two UMHS patients and one Temple patient. Two other U-M LVAD patients have received cell injections but are still awaiting heart transplants.

"The results show direct evidence of skeletal muscle cell survival and differentiation into mature muscle fibers, measured using antibodies that specifically target skeletal muscle cells," says Pagani. "Because cardiac muscle and skeletal muscle are two distinct types of tissue, the antibody test shows conclusively that the transplanted skeletal muscle satellite cells survived."

The transplanted cells also appear to have begun forming vascular muscle cells, which make up the walls of blood vessels. In areas where cells had been injected, there was a significant increase in small blood vessels compared with areas that had not received injections.

In addition to the encouraging finding that the injected cells "grafted" into their new environment, the results show on a molecular level that the heart muscle did not reject the newcomers. No evidence of an immune reaction or lymphocytes was seen in either grafted or non-grafted areas, using a test specific for the T-cells that usually respond to "invasions" of foreign cells.

"Because the skeletal muscle cells are from the patient's own body, we don't expect the kind of immune reaction and rejection that we often see in transplants of whole hearts from donors," says Pagani, an associate professor of surgery at the U-M Medical School and head of the Heart Transplant Program at the U-M Cardiovascular Center. "If further study bears this finding out, we may have a new option for repairing hearts without putting the patient at risk of dying from rejection, or needing lifelong anti-rejection medications.

Pagani stresses that these early results, while encouraging, are merely the first steps in evaluating skeletal muscle cell transplants. Combined with the results from the safety wing of the study, the initial results may help the researchers determine how to proceed toward evaluations of whether cell transplants can actually help heal patients' hearts.

"The promise of this line of research is immense, but we must be careful not to overstate what we have found thus far," says Pagani. "Only through further research and the cooperation of more LVAD and bypass patients can we see whether we can get a clinically significant effect."