Stem cell patch may result in improved function following heart attack

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University of Cincinnati (UC) researchers have found that applying a stem cell-infused patch together with overexpression of a specific cell instruction molecule promoted cell migration to damaged cardiac tissue following heart attack and resulted in improved function in animal models.

The researchers also found that function improved more so than when stem cells were directly injected in heart tissue—a therapy that is being studied elsewhere.

These findings are being presented for the first time at the American Heart Association's Scientific Meeting in Chicago on Nov. 15.

Researchers in the department of pathology and laboratory medicine led by Yi-Gang Wang, PhD, found that when a tri-cell patch, made up of cardiomyocytes (to restore heart contractility), endothelial cells (to build new blood vessels) and embryonic fibroblasts (to provide support to the cell structure), was applied to the surface of the damaged area of the heart, better outcomes in overall heart function resulted.

"Following myocardial infarction, better known as heart attack, tissue becomes damaged and scarred, cardiomyocytes die and heart pump function is reduced," Wang says. "There are therapies being tested by other researchers where stem cells are injected directly into damaged heart muscle to see if contractile function can be restored.

"In our current study, we wanted to determine if the amplified instructions from overexpressed miR-29, a microRNA, in animal models would enhance the effectiveness of the cell patch by reducing barriers in the infarcted area, leading to enhanced regeneration of heart tissues and resulting in the restoration of heart function after myocardial infarction."

Researchers first generated cardiac progenitor cells—cells that can become various cardiac tissue cell types—from induced pluripotent stem cells (iPSC). These stem cells can differentiate into any type of cell in the body and are artificially derived from non-pluripotent cells by inducing a forced expression of a number of desired genes.

The iPSC were then combined with specific heart tissue promoters to generate the desired cells. These cells were also labeled with green fluorescent protein (GFP) and firefly luciferase (a glowing laboratory reagent) to help with tracing cell migration and proliferation into the animal's system.

Researchers injected either the virus-mediated miR29b or a control material into the heart of the animal model and then experimentally induced a heart attack.

"These models allowed us to determine the possible benefits of miR29b and outcomes observed in two different control groups," Wang says.

Three days following the heart attack, researchers placed a cell patch on the damaged region and measured the expression of cardiac-related transcription factor A (a protein that binds to specific DNA sequences, controlling the movement of genetic information from DNA to mRNA), collagen levels in the damaged tissue and scar formation-related signaling pathways.

One month after the cell patch implantation, echocardiograms were

performed to evaluate heart function.

"The mobilization of cells into the infarcted region of the heart was then analyzed by counting the number of GFP cells and by bioluminescence imaging (BLI) of cells with firefly luciferase, an imaging technology where the ongoing biological processes are visualized," Wang says.

Researchers found the number of GFP cells, BLI signals and heart function as a whole significantly increased in animals with the viral transfer that overexpressed miR-29b and were treated with the tri-cell patch.

"These findings show that an overexpression of miR-29 results in heart tissue changes that favor enhanced mobilization of desired cell types into infarct regions after heart attack, leading to improved heart function," he says. "Hopefully, one day such treatments will restore cardiac function in patients who have experienced a heart attack, leading to a longer and better quality of life."

Provided by University of Cincinnati Academic Health Center