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Combination of cells and genes repairs damaged heart tissues in animal models of myocardial infarction

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Researchers at the University of Utah compared the therapeutic potential of umbilical cord-derived sub-epithelial cells (UC-SECs), bone marrow-derived mesenchymal stem cells (BM-MSCs) and induced pluripotent stem cell-derived cardiomyocytes (iPSC-CMs)—all derived from human tissue—along with genes (S100a1 and SDF-1a) and growth factor (VEGF165) to evaluate how injected biologics might enhance cardiac function in mice modeled with myocardial infarction (MI; commonly referred to as heart attack). The study revealed a range of beneficial results.

According to study co-author Dr. Amit N. Patel, director of cardiovascular regenerative medicine at the University of Utah and section editor for *Cell Transplantation*, the use of cell—and gene-based therapeutics to preserve cardiac function have made considerable advancements over the past several years, with a variety of genes and cells proposed as therapeutic options because they possess multi-potency and therapeutic potential.

"Our goal was to simultaneously compare cells and genes in a pre-clinical ischemic heart model," said Dr. Patel. "The study was a unique approach to using multiple human cell and gene-based therapies and demonstrated that, depending on which aspect of cardiac recovery is being evaluated—scar remodeling, improvement in contractile function, angiogenesis (new blood vessel growth) or inflammation—a different

biological may be best suited. There were no safety issues related to the biologics, and no gross tumors or other abnormalities on histology."

The study investigated which cells or biologics demonstrated the best results for a number of cardiac-related problems, including cardiac function and scarring. Scarring was of interest, said the researchers, because there is currently no approved therapy to reverse scar formation in the damaged heart or to replace scar tissue with new cardiac muscle cells (cardiomyocytes).

The authors noted that scar remodeling was best addressed by using UC-SECs, yet both S100a1 and SDF1a also demonstrated significant scar reduction when compared to controls and other biologics. Contractile function was most significantly improved by injecting hiPSC-CMs or S100a1 followed by UC-SECs. Angiogenesis was most significant in the group treated with growth factor (VEGF).

"The current study demonstrated that multiple cell types and genes, injected into a mouse model of MI, can positively alter various aspects of cardiac function and scarring for up to 12 weeks post-MI," concluded the researchers. "Future studies should aim to evaluate dose and combination therapies in order to decipher the most clinically applicable treatment."

More information: Evaluation of Multiple Biological Therapies for Ischemic Cardiac Disease, *Cell Transplantation* (2016). DOI: 10.3727/096368916X691501

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