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Effect of Human Mesenchymal Stem Cells Derived From Epicardial Fat on Ischemic Hind Limb in Mouse

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Background:
Despite the recent advance in cardiovascular regenerative medicine, clinical trials did not replicate stem cell use benefits recorded in preclinical studies. Thus, there is a need for new cell sources. The epicardium has been recently suggested as the source of cardiac progenitors in heart development. In this study, we aimed to determine the regenerative potential of mesenchymal stem cells derived from human epicardial fat tissue, in mice with hind limb ischemia.
Methods and Results:
Epicedial fat tissue was extracted from patients undergoing open/ closed heart procedures. Cells were isolated with an enzymatic digestion cocktail. Cell phenotype was defined by flow cytometry and immunocytochemistry. Mice (n=20) were subjected to moderate limb ischemia by permanent legation of the left femoral artery. Legation was verified by Laser Doppler and Animals were randomized to 2 treatment regimens: Cell implantation group (n=10) and placebo group (n=10). 10 days from legation, a functional test was performed, limb perfusion was assessed by Laser Doppler, animals were euthanized and immunohistochemical examination performed. Functional tests depicted a significantly better improvement in the cell implantation group (mean functional test score of 0.6±0.1 VS 3.4±0.1). Mean flow improvement by Laser Doppler was significantly higher in the cell implantation group (304.9±33.3 VS. 57.5±27.9, p=0.0001). Using human mitochondrial stain, human implanted cells were located in mice limb tissue 10 days after implantation.
Conclusions
Human epicardial fat tissue is a viable source of mesenchymal stem cells. These cells can be used to improve perfusion in ischemic limbs.