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Micro-Review Article
Honors Option

At the Heart of It: Mesenchymal Cells in Cardiovascular Therapy

As cardiovascular disease climbs above cancer and infections as the leading cause of death around the world, demands for treatments have increased (Taylor and Zenovich 2008). Dr. Doris Taylor of the Texas Heart Institute is confident the cure lies in stem cell research and regenerative medicine. She proposes that cardiovascular disease is a result of decreases in stem cell count and function; progression of the disease, then, is a result of inefficient endogenous cellular repair. Proposed therapies include delivering mesenchymal stem cells, pluripotent cells isolated from either adult bone marrow or adipose tissue (Madonna et al. 2013), to sites of myocardial injuries and other areas expressing failures in repair (Taylor and Robertson 2009). This research also lends itself to finding the cure for aging as it pertains to cardiovascular disease.

In a study by Dixon et al. (2009), intramyocardial injections of mesenchymal precursors cells (MPCs) in sheep after induced myocardial infarctions showed significant decreases in myocardial infarction expansion, the spreading of the infarct region into areas of normal myocardium. The greatest effects from this study were shown in samples treated with lower MPC content, hinting at a threshold for effective cellular therapy. In untreated cells, the infarct length was 9.20 ± 0.32 cm. In cells treated with 25×10^6 MPCs, that number was reduced to 7.48 ± 0.331 cm and 7.88 ± 0.16 cm in the line treated with 75×10^6 MPCs. The infarct length rose in 225×10^6 and 450×10^6 MPCs injected cells to 8.23 ± 0.22 cm and 8.62 ± 0.27 cm, respectively (Dixon et al. 2009). As infarct expansion is a predictor of cell death after myocardial infarction (Dixon et al. 2009), MPCs may prove to be a valuable treatment.

A study by Houtgraaf et al. (2013) supports these conclusions: MPCs led to a 40% decrease in infarct size in sheep with MI and showed improved cardiac function. They speculate that the threshold for effectiveness is due to possible vascular obstruction by high doses of MPCs. In addition, they found that the number of apoptotic cardiomyocytes decreased from $1.31 \pm 0.15\%$ of total cardiomyocytes to $0.77 \pm 0.12\%$ when treated with MPC. These results strongly support MPC as a means of reducing unfavorable changes to ventricular structure and function after a heart attack (Houtgraaf et al. 2013).

Lastly, a study by Madonna et al. (2013) showed that mesenchymal stem cells engineered to overexpress telomerase reverse transcriptase (TERT) and myocardin (MYOCD) can be used

to restore regenerative and myogenic properties in aged MSC from adipose tissue. Telomerase promotes cell survival while myocardin regulates myogenic development in cardiovascular tissue. They showed that TERT and MYOCD work together to increase proliferation and the amount of smooth muscle cells (Madonna et al. 2013). Additionally, they found that transplantation of the MSCs into ischemic mouse limbs showed improved blood flow and formation of new arteries. This finding is especially important for prolonging cell life of newly regenerated muscle cells.

Data presented by Dixon et al. (2009), Houtgraaf et al. (2013), and Madonna et al. (2013) reinforces the use of mesenchymal stem cells in regenerative medicine to not only treat known diseases but also to use as a preventative measure against aging. While more studies need to be done, a clinical phase done by Houtgraaf et al. (2013) showed that MPC injections were safe, feasible, and effectively decreased cardiac mortality. As explained by Dr. Doris, efforts towards stem cell research has great potential to provide insight into curing cardiovascular disease as well as the age-old struggle with aging.

Citations

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