**Healing the Heart with Mesenchymal Stem Cell-Derived Exosomes**

Author: Milan Mckenna

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**Key Words: [Stem Cell, Mesenchymal, Exosomes, Therapeutic, Cardiovascular Disease]**

Abstract: Mesenchymal stem cell-derived exosomes (MSC-Exos) have emerged as a therapeutic strategy for cardiovascular disease with an unprecedented amount of opportunities for growth. This paper reviews the cardioprotective efficacy and clinical potential of mesenchymal stem cell-derived exosomes (MSC-Exos). Mesenchymal stem cell-derived exosomes (MSC-Exos) have shown key pieces and functional properties not unlike their parent cell the mesenchymal stem cell. These properties include regulation of cell health and viability, inflammation, angiogenesis, and tissue remodeling. Mesenchymal stem cell-derived exosomes (MSC-Exos) mitigate myocardial ischemia-reperfusion injury, myocardial infarction, heart failure, and many more heart conditions in preclinical trials and models. Compared to stem cells, mesenchymal stem cell-derived exosomes (MSC-Exos) have the advantages of lower immune recognition and their cardioprotective effects can be further enhanced with the use of a multitude of different administration tools. The paper discusses local and systemic delivery strategies along with other bioengineered approaches to improve retention and targeting. Ongoing studies are focused on elucidating molecular mechanisms, scaling production, developing cardiac-specific targeting moieties, and testing safety and efficacy in large animal models. While significant progress has been made in demonstrating the therapeutic potential of MSC-Exos for cardiac repair, clinical translation remains limited owing to gaps in understanding therapeutic dosing, biodistribution, optimizing delivery vehicles, and long-term impact in humans. Addressing these limitations through multi-disciplinary efforts can pave the way for harnessing the potential power of exosomes. Mesenchymal stem cell-derived exosomes (MSC-Exos) have the potential to be a very viable therapy for a variety of heart conditions in the future.

**Introduction**

The struggle of heart diseases all around the world is ever-growing and in parallel to that problem so is the need for treatments that are able to address this overarching problem. Mesenchymal stem cells derived exosomes (MSC-Exos) potentially hold many answers to an array of heart diseases that include, but are not limited to cardiovascular diseases (CVDs), myocardial ischemia-reperfusion injury (myocardial I/R injury), amelioration of myocardial inflammation and ventricular remodeling, heart failure (HF), ischemic heart disease (IHD), and atherosclerosis (AS). The use of mesenchymal stem cell-derived exosomes (MSC-Exos) to treat the many heart complications listed is promising in regard to a multitude of factors. One of the major factors that different types of mesenchymal stem cell-derived exosomes (MSC-Exos) help treat is inflammation which is a symptom of most heart diseases and can be a complication in most heart surgeries. The cardioprotective effects of mesenchymal stem cell-derived exosomes (MSC-Exos) involve some underlying molecular mechanisms that help provide mesenchymal stem cell-derived exosomes (MSC-Exos) with the ability to regulate cardiomyocyte viability, inflammatory levels, angiogenesis, and ventricular remodeling after a heart injury. By using mesenchymal stem cell-derived exosomes (MSC-Exos) instead of just mesenchymal stem cells that do not have exosomes, also recognized as extracellular debris by scientists of the past, there has been a large decrease in the possibility of tumor formation and in immune rejection by the patient. These reduced risks have helped to formulate more of a drive for scientists to continue research using mesenchymal stem cell-derived exosomes (MSC-Exos) in future studies and treatments. Hypoxia preconditioning of mesenchymal stem cells is also one of the modification methods used to change exosomes because it enhances the cell’s cardioprotective functions that are overexpressed in a multitude of genes and with treatments that utilize certain drugs on the market. There has been much research about the best way to administer exosomes into the heart for clinical use as each heart issue would be treated differently depending on how the organ is ultimately affected. So far, scientists have come up with an array of techniques that range from intramyocardial injections to cardiac patches to even injections of hydrogels that contain exosomes into the pericardial cavity. All of the preclinical and clinical trials using mesenchymal stem cell-derived exosomes (MSC-Exos) and the ones that use different forms of exosomes to treat the heart have not completed clinical trials as of now, but this is mostly due to the lack of sufficient transportation and accurate targeting methods of exosomes to the ischemic myocardium. In terms of recent progress, there are a few progressions that have developed as of late due to the ever-growing need to help treat a multitude of heart conditions. One is that new ways of administration and extraction of mesenchymal stem cell-derived exosomes (MSC-Exos) continue to emerge, one being ultrasound-guided injection to target exosomes into infracted rat hearts. Another piece of recent progress has been through the use of peptides, which are covalent bonds with additional amino acids that are the building block of proteins within the human body, that can be modified to enhance the targeting of exosomes to the necessary areas of the heart. The most relevant progression in correlation to this study is the identification of new mechanisms and miRNA cargo in mesenchymal stem cell-derived exosomes (MSC-Exos) that are believed to contribute directly to the cell’s cardioprotective effects that have been reported across many different works of research. With each step into the future, the therapeutic potential of mesenchymal stem cell-derived exosomes (MSC-Exos) used to treat the heart gets more obtainable, and with just a good foundation laid down by both human and animal trials, it is only a matter of time until it becomes a more established part of the medical reality involving heart conditions.

**Discussion**

There were multiple valid results reported with the use of mesenchymal stem cell-derived exosomes (MSC-Exos) being used to treat the heart. One valid result involved mesenchymal stem cell-derived exosomes (MSC-Exos) ability to inhibit apoptosis, inflammation, and fibrosis in mice with MI, also known as myocardial infarction or heart attack that tends to lead to a diagnosis of coronary artery disease (CAD), meaning that part of the mouse’s heart muscle is unable to receive a regulatory about of blood to properly function. This result is considered valid because not only has the study been replicated numerous times. Another result that is considered valid is that mesenchymal stem cell-derived exosomes (MSC-Exos) promote angiogenesis in both cell culture models and in the mouse hindlimb ischemia models. The increase of capillary density and higher expression of angiogenic proteins is represented in both models with the use of mesenchymal stem cell-derived exosomes (MSC-Exos). There are three other results that are also considered valid in the main research publication. One of the three left consists of the valid results are that mesenchymal stem cell-derived exosomes (MSC-Exos) reduced infarct size paired with improved cardiac function in both rat and mouse myocardial infarction models. The validity of this was due to reduced scar size and improved echocardiographic parameters of cardiac contractility, also known as an improved heart rate and depth of contraction of the organ’s muscles. The tests done involving the delivery method of mesenchymal stem cell-derived exosomes (MSC-Exos) in a hypoxia also showed statistical significance in regards to reducing myocardial infarction injury in rat models due to the exosomes anti-apoptotic and angiogenic qualities. The last valid result is that the overexpression of MIF, miR-146a in mesenchymal stem cells (MSCs) improves the mobility of the cells secreted exosomes with constructs overexpressing certain miRNA and proteins that lead to enhanced cardioprotective effects in myocardial models. All valid results aside, there are still many questions and concerns that remain unanswered. For example, the safety data in large animals and humans is greatly lacking sufficient testing and approval. Not to mention that the potential long-term risks, or lack thereof, involved with the use of mesenchymal stem cell-derived exosomes (MSC-Exos) in the treatment of the heart are still a large unknown. On top of that with the issues that surround the processing and harvesting of mesenchymal stem cell-derived exosomes (MSC-Exos) not being yet accessible to most would be a treatment that is supposed to help a large portion of the would even be able to with such restrictions. That said, the more time, effort, and money that are invested into different ways the treat the heart with mesenchymal stem cell-derived exosomes (MSC-Exos) the more that unknowns turn into knowns and knowns can turn into certainties.

**References**

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