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MINI REVIEW

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The emerging role of exosomes derived from induced pluripotent stem cells (iPSCs) in cardioprotection: Potential applications in ischemic heart disease

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ABSTRACT

Coronary artery blockages that restrict blood flow to the heart are the main cause of ischemic heart disease (IHD), the world's largest cause of death. Traditional treatments are ineffective at repairing damaged cardiac tissue; instead, they concentrate on managing symptoms. In cardiovascular therapy, exosomes produced from induced pluripotent stem cells (iPSCs) have lately become a safer option since they provide regenerative advantages without the concerns of tumor growth or immune rejection that come with whole-cell therapies. iPSCs release these nanosized vesicles, which contain bioactive compounds with pro-angiogenic, anti-inflammatory, and anti-apoptotic qualities that aid in tissue repair and enhance cardiac function. Preclinical research demonstrates that exosomes produced from iPSCs promote heart regeneration by increasing angiogenesis, decreasing fibrosis, and improving myocardial cell survival. This mini-review addresses the cardioprotective mechanisms and therapeutic prospects of iPSC-derived exosomes in treating IHD. Research on exosomes may pave the way for improved cardiovascular regenerative therapy.

KEYWORDS

Induced pluripotent stem cells; Exosomes; Myocardial ischemia; Coronary vessels; Cell survival; Neoplasms

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Introduction

Ischemic heart disease (IHD) is the main cause of cardiovascular diseases (CVDs), which continue to be the leading cause of death worldwide, accounting for around 18 million deaths each year [1]. Reduced blood flow to the heart muscle because of coronary artery narrowing or blockage, often brought on by atherosclerosis, is the cause of coronary artery disease or IHD. This results in myocardial ischemia, which can lead to heart failure, myocardial infarction, and reduced cardiac function if left untreated. Although they do not repair damaged heart tissue, traditional treatments include medication, angioplasty, coronary artery bypass, and lifestyle modifications to try to increase blood flow and lessen symptoms [2].

Regenerative medicine has presented fresh possibilities for treating CVD in recent years. Because induced pluripotent stem cells (iPSCs) can develop into smooth muscle, endothelium, and cardiomyocyte cells, they hold promise for use in stem cell therapy [3]. Because iPSCs are made from a patient's cells, they avoid the moral dilemmas surrounding embryonic stem cells and reduce the possibility of immunological rejection. However, tumorigenesis risks and cell integration issues restrict the clinical use of iPSCs. Exosomes made from iPSCs have drawn interest as a cell-free treatment alternative to overcome these drawbacks. Small extracellular vesicles called exosomes contain bioactive substances like proteins and RNAs that affect the behavior of receiving cells [4]. Without the dangers of cell transplantation, iPSC exosomes have shown cardioprotective benefits such as decreased inflammation, improved tissue repair, and greater angiogenesis [5]. This mini-review explores the mechanisms, cardioprotective benefits, recent preclinical findings, and future research directions for iPSC-derived exosomes in regenerative cardiovascular therapy, particularly for IHD.

Exosomes: Nature and Function

Definition and characteristics

Exosomes are extracellular vesicles (EVs), usually with a diameter of 30 to 150 nm, that are released by a range of cell types, including stem cells, in both healthy and diseased states [6]. These endosomal-derived vesicles, which contain bioactive substances such as proteins, lipids, RNA, and microRNAs, are released into the extracellular space [7]. By delivering their chemical contents to recipient cells and modifying several biological functions, exosomes facilitate intercellular communication.

Role of exosomes in cardiovascular diseases

Exosomes have been demonstrated to be important in the control of inflammatory reactions, apoptosis, and tissue repair in the setting of cardiovascular disorders [8]. They also contribute to the improvement of heart function after injury, the promotion of angiogenesis, and the reduction of oxidative stress. They are therefore a potentially effective treatment option for diseases like IHD, where tissue destruction is a serious issue.

Induced Pluripotent Stem Cells (iPSCs) and their Exosomes

iPSCs: Revolutionizing regenerative medicine

Reprogramming adult somatic cells into a pluripotent state, which allows them to differentiate into any type of cell, produces induced pluripotent stem cells, or iPSCs [9]. Shinya Yamanaka invented this ground-breaking approach, which has transformed regenerative medicine by enabling the creation of patient-specific cell lines without the moral dilemmas surrounding embryonic stem cells (ESCs) [10].

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iPSCs have enormous promise for drug development, disease modeling, and tissue regeneration.

Exosomes derived from iPSCs

The capacity of iPSC-derived exosomes to replicate the therapeutic effects of iPSCs without the dangers of cell-based therapies such as immunological rejection or tumorigenicity has drawn attention to them [11]. The proteins, lipids, and nucleic acids carried by these exosomes demonstrate the regenerative potential of iPSCs [12]. Research has indicated that exosomes produced from iPSCs increase angiogenesis, decrease apoptosis, and boost cell survival, making them a viable option for the management of ischemic heart disease [13].

Mechanisms of Cardioprotection by iPSC-Derived Exosomes

iPSC-derived exosomes exhibit various mechanisms that contribute to cardioprotection in IHD. These mechanisms include anti-inflammatory, anti-apoptotic, pro-angiogenic, and anti-fibrotic effects, as summarized in Table 1 [13].

Table 1. Properties and Therapeutic Effects of iPSC-Derived Exosomes in Ischemic Heart Disease.

Property	Description	Therapeutic Effect in IHD
Anti-inflammatory	Contains microRNAs like miR-21 that modulate immune responses and reduce inflammation	Reduces inflammation, promoting tissue repair
Anti-apoptotic	Delivers molecules like miR-146a and heat shock proteins that inhibit apoptotic pathways in cardiomyocytes	Enhances cardiomyocyte survival and reduces cell death
Pro-angiogenic	Contains VEGF, angiopoietin-1, and miR-126 that promote endothelial cell migration and proliferation	Supports the formation of new blood vessels, restoring blood flow
Anti-fibrotic	Carries miR-29 and miR-133 that suppress fibroblast activation and collagen deposition	Limits fibrosis, aiding in better tissue remodeling
Cell-free approach	Lacks viable cells, reducing the risk of immunogenic response and tumor formation	Minimizes clinical risks associated with cell-based therapies

Current Research and Clinical Applications

Preclinical studies

The therapeutic potential of iPSC-derived exosomes in animal models of IHD has been shown in multiple studies of preclinical investigations. For example, a study by Khan et al. (2015) demonstrated that, in comparison to controls, giving iPSC-derived exosomes to a mouse model of myocardial infarction markedly improved cardiac function, decreased infarct size, and increased angiogenesis [14]. In a rat model of ischemia injury, Nasser et al. (2021) showed that exosomes loaded with certain microRNAs enhanced heart regeneration [15].

Challenges and limitations

Despite encouraging preclinical evidence, several kinds of obstacles must be overcome before iPSC-derived exosomes may be used in clinical treatments. Consistent therapeutic results depend on the scale and standardization of exosome synthesis, which is a significant challenge. Exosome-based medicines' biodistribution, safety, and long-term impacts also require careful research [16].

Future Directions

The potential applications of iPSC-derived exosomes in the therapy of ischemic heart disease are numerous, although several areas warrant further investigation. Optimizing exosome isolation and characterisation, as well as comprehending their pharmacokinetics and biodistribution in vivo, should be the main goals of future studies [17]. Furthermore, the therapeutic efficacy of exosome treatment may be increased by combining it with other regenerative techniques like tissue engineering or gene editing [18]. Additionally, developing targeted delivery methods for exosome-based therapies could improve precision, maximizing the cardioprotective benefits of iPSC-derived exosomes while minimizing off-target effects [19].

Conclusions

iPSC-derived exosomes are a potentially effective treatment option for ischemic heart disease. They are a desirable option for regenerative medicine because of their capacity to control inflammation, lower apoptosis, encourage angiogenesis, and prevent fibrosis. Our knowledge of exosome biology and its therapeutic potential is expanding quickly due to continuing research, even if there are still obstacles in the way of bringing this therapy to the clinic. Exosomes produced from iPSCs may be crucial to cardiovascular treatment in the future with further development.

Disclosure Statement

The authors declare that there are no conflicts of interest that could affect the results or conclusions of this study.

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