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Insights on Nanovesicle Production from Human-Induced Pluripotent Stem Cells for Cardiovascular Repair

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Introduction

"Scalable Generation of Nanovesicles from Human-Induced Pluripotent Stem Cells for Cardiac Repair" is a research article published in the journal ACS Nano. The article describes a method for generating nanovesicles from human-induced pluripotent stem cells (hiPSCs) that have potential applications for cardiac repair. The researchers used a microfluidic system to culture hiPSCs and generate nanovesicles from them. The nanovesicles were then tested for their ability to promote the growth and survival of cardiac cells in vitro and in vivo. The results showed that the nanovesicles had a positive effect on cardiac cell growth and survival, and could potentially be used for cardiac repair in the future. The researchers also demonstrated the scalability of their method by generating large quantities of nanovesicles using a continuous-flow microfluidic system.

This could be important for future clinical applications, as a large number of nanovesicles would be needed for treating patients with cardiac disease [1-3]. Overall, the article provides evidence that nanovesicles derived from hiPSCs have potential as a therapeutic approach for cardiac repair. Further research is needed to determine the safety and efficacy of this approach in human patients. The need for effective strategies to promote cardiac tissue protection and subsequent regeneration in the heart following a major cardiac event (e.g., myocardial injury, ischaemia) remains unmet. Given the human heart's limited regenerative capacity, stem cell therapies have emerged as a promising strategy for cardiac repair and restoring heart function. Clinical trials involving cell-based therapy, on the other hand, report a low engraftment rate and are associated with the risk of arrhythmia and teratomas. Importantly, the poor engraftment of stem cells following transplantation suggests that secreted factors may have mediated the observed cardiac repair.

Description

Extracellular vesicles (EVs) have emerged as an important component of secreted factors that regulate cardiac repair. EVs are membranous vesicles with sizes ranging from 30 to 1000 nm that are released by cells and are involved in intercellular signalling in physiological and pathological processes. EVs transport a variety of packaged proteins and nucleic acids that can be transferred to target cells and used to regulate functional response. EVs derived from various stem cell sources have been studied for their ability to regulate key cardioprotection and repair processes such as cardiomyocyte survival, revascularization, and regulating fibroblast activation (scar tissue formation), as well as their regenerative properties in other tissues [4,5].

Furthermore, in an in vivo acute injury ischemia-reperfusion model, iPSC-derived EVs reduced cell death and oxidative stress while attenuating macrophage infiltration and preserving renal function. EVs derived from human iPSCs inhibited fibrosis in hepatic stellate cells (in response to TGF-) by decreasing expression of -smooth muscle actin (-SMA), collagen I1 (COL1A1), and tissue inhibitor of metalloproteinases-1. (TIMP-1). However, scalable EV generation (particularly from stem cells) remains a technical challenge, limiting their clinical utility. Thus, in recent years, therapeutic interest has been generated by technologies that directly generate particles that mimic EVs (nanovesicles, NVs) from stem cells due to their high yield and reparative function. For example, NVs have been generated in large numbers from mesenchymal stem cells (MSCs) and have been shown to have myocardial protective effects in vitro (pro-angiogenic, pro-survival) and in vivo (scar size reduction, cardiac function preservation) settings. MSCs, on the other hand, are notoriously difficult to isolate and keep in large quantities.

Conclusion

This limitation can be overcome by using pluripotent stem cells (iPSCs), which are easy to generate autologously from individual somatic cells (easily sourced from skin, hair, peripheral blood, and bodily fluids such as urine), have unlimited proliferative capacity, and can be cultured indefinitely. As a result, iPSCs are recommended as a preferred alternative source for scalable NV generation. However, it is unknown whether iPSC-derived NVs have cardiac repair function. We described a reproducible strategy for efficiently generating functional NVs from various human iPSCs and demonstrated their therapeutic potential as a functional surrogate for natural EVs for tissue repair.

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