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Insights on Cellular Reprogramming Based Strategies for Heart Regenerative Repair

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Introduction

The heart is a vital organ that pumps blood throughout the body, providing oxygen and nutrients to the cells. However, heart disease is a leading cause of morbidity and mortality worldwide. The heart has limited regenerative capacity, and the loss of cardiomyocytes (heart muscle cells) due to injury or disease often results in irreversible damage. Traditional therapies for heart disease focus on managing symptoms rather than repairing the damage. However, recent advances in cellular reprogramming-based approaches offer promising avenues for heart regenerative repair. Cellular reprogramming is a technique that converts one type of cell into another type without passing through a pluripotent state. Pluripotent cells have the ability to differentiate into any cell type in the body, whereas reprogrammed cells can only differentiate into specific cell types. Cellular reprogramming can be achieved through various methods, including transcription factor-based approaches and small molecule-based approaches.

Transcription factor-based approaches involve the forced expression of specific transcription factors in cells to induce their reprogramming. One of the most well-known transcription factor-based approaches is the induction of pluripotency in somatic cells through the overexpression of four transcription factors: Oct4, Sox2, Klf4, and c-Myc. This technique, known as induced pluripotent stem cell (iPSC) reprogramming, was first described in 2006 and has since revolutionized the field of regenerative medicine [1-3].

Description

In addition to iPSC reprogramming, transcription factor-based approaches can also be used to directly reprogram cells into specific cell types, bypassing the pluripotent state. For example, cardiomyocytes can be directly reprogrammed from fibroblasts (a type of connective tissue cell) through the forced expression of specific transcription factors. This technique, known as direct cardiac reprogramming, was first described in 2010 and has since been refined to produce functional cardiomyocytes in vitro and in vivo. Small molecule-based approaches involve the use of chemical compounds to induce cellular reprogramming. These approaches are attractive because they are generally less invasive and more scalable than transcription factor-based approaches.

One of the most promising small molecule-based approaches for heart regenerative repair is the use of epigenetic modifiers, which can alter the expression of genes without changing the underlying DNA sequence. For example, a recent study used a combination of small molecules to reprogram fibroblasts into cardiomyocytes. The small molecules included an inhibitor of the Wnt signaling pathway, which is involved in cell fate determination, and a histone deacetylase inhibitor, which promotes gene expression by removing acetyl groups from histones (proteins that package DNA). The resulting cardiomyocytes exhibited functional and structural properties of mature cardiomyocytes. Cellular reprogramming-based approaches offer promising avenues for heart regenerative repair [4,5].

These approaches can potentially replace damaged or lost cardiomyocytes with new ones, restoring the heart's function. Here, we highlight some recent advances in cellular reprogramming-based approaches for heart regenerative repair. Direct cardiac reprogramming involves the conversion of non-cardiac cells into cardiomyocytes without passing through a pluripotent state. This approach has several advantages over iPSC reprogramming, including a shorter reprogramming time and fewer safety concerns associated with the use of pluripotent cells. However, direct cardiac reprogramming is still a relatively new technique, and several challenges need to be addressed before it can be used clinically. One challenge is the low efficiency of reprogramming. The efficiency of direct cardiac reprogramming varies depending on the cell type and reprogramming factors used.

Conclusion

IPSC-derived cardiovascular cells hold enormous promise for the field of regenerative heart repair research. iPSC-CMs have made the most contributions to the functional improvement of the damaged heart among iPSC-derived cardiovascular cells. Several optimised protocols with relatively high cardiomyocyte derivation efficiencies and functional biological characteristics have been published. The three major approaches for converting iPSCs into CMs are monolayer-based differentiation protocols, inductive coculture protocols, and spin-embryoid body (Spin-EB) protocols.

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