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Opinion Article

Exploring Cardiac Progenitor Stem Cells as a Treatment for Heart Restoration

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DESCRIPTION

The adult heart is mainly composed of cardiomyocytes, which are the contractile cells that generate the pumping force of the heart. Cardiomyocytes are terminally differentiated cells that have lost their ability to divide and renew themselves. Therefore, when cardiomyocytes are injured or die due to various causes, such as myocardial infarction (heart attack), ischemia (lack of blood supply), infection, or aging, they are not replaced by new cardiomyocytes, but by scar tissue that impairs the function and structure of the heart. To overcome this problem, researchers have been exploring different strategies to restore the lost or damaged cardiomyocytes and regenerate the injured heart. One of these strategies is stem cell therapy, which involves using stem cells to generate new cardiomyocytes or other cardiac cells. Stem cells are undifferentiated cells that have the potential to develop into many different types of cells in the body and can also renew themselves by dividing. Stem cell therapy aims to harness this potential and use stem cells as a source of new cardiac cells that can integrate into the existing heart tissue and improve its function.

Different types of cardiac progenitor stem cells

Endogenous CPCs are the CPCs that are naturally present within the adult heart and can be isolated by using specific markers or genetic tracing techniques. ECPCs are responsible for maintaining the homeostasis and turnover of cardiac cells throughout life and can also respond to injury by increasing their proliferation and differentiation.

Exogenous CPCs are the CPCs that are derived from other types of stem cells by using various methods of induction or reprogramming. For example, xCPCs can be generated from embryonic stem cells (ESCs) or Induced Pluripotent Stem Cells (iPSCs) by using specific growth factors or transcription factors that direct their differentiation towards a cardiac lineage. Alternatively, xCPCs can be generated from adult somatic cells by using direct reprogramming techniques that convert them into CPCs without passing through a pluripotent state. However, not all stem cells are equally suitable for cardiac regeneration. Some stem cells, such as Embryonic Stem Cells (ESCs) or induced Pluripotent Stem Cells (iPSCs), have the ability to differentiate into any cell type in the body, including cardiomyocytes. However, these stem cells also pose some challenges, such as ethical issues, immunological rejection, tumorigenicity, and low efficiency of differentiation. Therefore, researchers have been looking for alternative sources of stem cells that are more specific and compatible with the cardiac tissue. One of these sources is Cardiac Progenitor Stem Cells (CPCs), which are tissue-specific stem progenitor cells harboured within the adult mammalian heart. CPCs are proliferative and committed to cardiac fate, capable of generating cells of all the cardiac lineage, cardiomyocytes, smooth muscle cells, and endothelial cells. CPCs express several markers of stemness (such as Oct3/4, Bmi-1, Nanog) and cardiac identity (such as c-kit, Sca-1, Isl-1, Nkx2.5). CPCs have significant regenerative potential *in vivo* and can improve cardiac function after transplantation into animal models of myocardial infarction. CPCs can be derived from various sources within or outside the heart. One source is the endogenous CPCs (eCPCs), which are resident within the adult heart and can be isolated by using specific markers or genetic tracing techniques. ECPCs are responsible for maintaining the homeostasis and turnover of cardiac cells throughout life and can also respond to injury by increasing their proliferation and differentiation. However, eCPCs are rare and difficult to obtain from human hearts without invasive procedures.

Another source is the exogenous CPCs (xCPCs), which are derived from other types of stem cells by using various methods of induction or reprogramming. For example, xCPCs can be generated from ESCs or iPSCs by using specific growth factors or transcription factors that direct their differentiation towards a cardiac lineage. Alternatively, xCPCs can be generated from adult somatic cells (such as skin or blood cells) by using direct reprogramming techniques that convert them into CPCs without passing through a pluripotent state. XCPCs offer some advantages over eCPCs, such as higher availability, scalability, and genetic manipulation. However, both eCPCs and xCPCs face some challenges for clinical applications. Some of these

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challenges include optimizing their isolation, expansion, characterization, differentiation, delivery, engraftment, survival, integration, maturation, functionality, safety, and efficacy in human hearts. Moreover, there is still a lack of consensus on the definition, identity, origin, and heterogeneity of CPCs, as different studies have used different markers and methods to identify and characterize them.

Therefore, more research is needed to understand the biology and potential of CPCs and to overcome the obstacles for their clinical translation. CPCs represent a promising source of stem cells for cardiac regeneration, as they are more specific and compatible with the cardiac tissue than other types of stem cells. CPCs could offer a novel therapeutic option for patients with heart failure, by providing new cardiac cells that can repair the injured heart and restore its function.