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Research paper

Genetic engineering and stem cell therapy for the treatment of heart failure

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Abstract

Endogenous cardiac stem cells (eCSCSs) are defined as tissue specific progenitor cells concealed within human heart. Adult heart was thought primarily as a post mitotic organ devoid of any regenerative capacity. But eCSCSs proves the existence of immature cycling myo-cytes in adult myocardium which promotes regeneration after infarction. In addition to the restocking ofheart tissue, eCSCs put up in turn marks major and paramount role in growth and development of heart tissue.

Myocardial infarction has become a major cause of death of a very large population per year and those who outlast live with heart stoppage. The permanent dropping of cardiomyocytes at the time of infarction makes a healthy body susceptible to irregular heartbeat called arrhythmia as electro-mechanically dysfunctional tissues are fabricated. Under this condition, heart becomes unable to pump sufficient amount of blood to the body including heart, lungs, brain leading to cardiovascular collapse. Brain and other organs can't work properly and may shut down or will be damaged when heart doesn't pump blood productively.

Due to arrhythmia, as heart doesn't pump blood effectively to various vital organs of the body, they can't function properly and eventually wear off. To reinstate cardiac function in heart failure, potential therapeutic approaches via cell based therapies using multipotent (adult) and pluripotent (embryonic) stem cells are used.

Keywords: *Arrhythmia; Embryonic Cardiac Stem Cells (ECSCSS); Heart Failure (HF); Myocardial Infarction (MI); Multipotent and Pluripotent Stem Cells.*

1. Introduction

Myocardial injuries causes them is laying of cardiomyocytes, predominantly due to MI which is the prime cause of mortality worldwide. In patients with awful ischemic heart failure, Intra myocardial skeletal muscle transplantation has improved heart function after infarction. During coronary artery bypass grafting of remote myocardial areas, autologous skeletal myoblasts are lodged into the post infarction scar.

During aging and after heart in injury CSCs proves to be a major mechanism of myocardial repair. But, they are ineffective for myocardial regeneration in mammalian heart. Exogenous stem cells are transplanted into injured heart thereby succor in heart regeneration.

- Stem Cells

The major stem cells employed for regeneration of heart are multipotent (adult) and pluripotent (embryonic) stem cells (ESCs or iPSCs).Diverse regenerative capabilities are exhibited by pluripotent nature of stem cells. To site as an example, bone marrow derived mesenchymal stem cells (MSCs) becomes fat, muscle, bone, cartilage; but only first of these four types would be worthwhile. Tumors are manifested as a result of the injection of highly proliferated uncommitted embryonic stem cells. Hence, for the safety and efficacy of cardiac cell therapies, the selection and isolation of pure population of stem cells with cardiogenic characteristics are diametric.

- Episode Of Cardiogenic Stem Cells

Human embryonic stem cells derived from embryonic bodies constitute for less than 10% of total population of cells. Proliferation, differentiation, or cardiac regeneration of stem cells isn't impaired by the genetic expression of enhanced green fluorescent proteins (EGFPs). Genetically acquired resistance to antibodies are selected and driven by the activation of cardiomyocytes, which enabled 99% in vitro purification of rat embryonic stem cell derived myocyctes. At early cardiogenic transcription stages, genetically engineered stem cells are selected at the time of cardiomyogenic activation.

- Mesenchymal Stem Cells

Genetic selection and isolation of cardiogenic cells as well as the removal of potentially tumorogenic undifferentiated stem cells requires a large amount of stem cells for implantation. To increase the efficiency of stem cell differentiation into cardiac or non-cardiac cells, new genetic engineering techniques are employed. To express myocardin, a cardiogenic transcription factor, genetically engineered human MSCs are used. These MCSs are isolated and expanded from bone marrow (BM) or other sources easily due to their ability to adhere to culture dishes. Cardiomyoytes, smooth muscle cells and endothelial cells are differentiated to cells belonging to mesenchymal lineage. They fuel angiogenesis in ischemic myocardium thereby outstripping myocardial function. Due to scant level of expression of class II major histocompatibility complex II antigen,t hey show low potential for immune rejection.

- Detection Of Fate Of Injected Cells

Through in vivo and ex vivo stalking of location and destiny of injected cells, the structural and functional integration and differ-

entiation of implanted cells in the heart are assessed properly. The fluorescent proteins which allow the localisation and imaging of live implanted cells are expressed through genetically engineered stem cells.

In recent times, a receptor promoting integrin-mediated cell adhesion improvised retention of MSCs in the heart of rats at the site of injection using genetically engineered cells. This shows that cell implantation therapies fail when donor cells remain at the injury site.

- Myocardial Resurrection

Ischemic event and cardiac repair can be vanquished and initiated at the border of infarct or within the infarct as a result of the identification of human CSCs. The regenerated myocytes were not the product of fusion between CSCs and spared myocytes as male heart possess one X and one Y chromosome while female heart possess two X chromosomes. Hence proves that the dead myocardium objective of cell fusion is repaired as heart has an intrinsic growth reserve.

- Stimulation Of Myocardial Function Through Stem Cell Integration

The functional improvements within an infarcted heart followed by the stem cell injections are defined by the host-donor electromechanical coupling, which harmonizes the broad spectrum of pancreatic factors secreted by donor cells. The extraneously lodged cells have to be both myogenic and must functionally integrate within the syncytium of the heart. The implantation of skeletal muscle promoter banished arrhythmias. While on the other hand upon comparing with skeletal myoblasts, MSCs when coupled to host myocyctes reduced arrhythmogenesis.

Abnormal heart rhythm is regulated by genetically engineered stem cells which act as biological pacemakers. After cryoablation of AV node activity, cardiomyocytes can integrate within myocardium and pace ventricles with the aid and abet of green fluorescent protein labeled human embryonic stem cell. Engineering targeted multi actions within ion channel genes in implanted cells are attained by customized pace making functions which is a subject of future scope.

2. Future scope of stem cell therapy

One of the brightest approaches for the treatment of HF is to restore lost or impaired heart by implanting stem cells in to it. The limitations of current stem cell therapies include cell death and apoptosis, dearth of cell augmentationetc. Both adult and embryonic stem cells have their own pros and cons. Side effects like risk of proarrythmia and tumour formation have to be survived properly. Ideal cell source for cardiac repair may be the one genetically designed rather than discovered. Genetic engineering is overcoming limitations in stem cells and exogenous cell implantation. Stem cell like properties can be obtained by using genetically engineered adult heart fibroblasts. The most effective treatment for HF is made by employing the combined effect of genetic engineering and stem biology. Cardiac implantation therapies involving the use of genetic engineering to exalt selection, survival along with the integration of stem cells proves to be a major advancing field. The understanding of genetic mechanism governing cardiogenic stem cell demarcation as well as host-settler integration and affluent and usable mend of vandalized heart tissue provides further slot by employing genetic mechanisms for cardiac cell research.

3. Conclusion

Several subsets of progenitor cells having a significant ability by which they differentiate themselves into major heart cells are concealed within adult myocardium. But the growth of CPCs in infracted and scarred tissues poses a major challenge in this area. CPCsdifferentiation towards an adult cardiac phenotype is very compound as it involves surrounding cells and matrix reckoning on cell surface interaction, intercellular connections and paracrine factors which is impossible in vitro cell culture. Cardiac progenitor cell is the best method of cardiac cell therapy. To ensure sufficient blood supply to cell transplantations, different subtypes of stem cells inclined for angiogenesis is appertained. Myocardial regeneration by stem cells is expected to be curative for most of the deadly diseases around the world.

In cardiac cell research, genetic manipulations give more opportunities to the successful functional repair of damaged heart tissue and safe host- donor integration via genetic mechanisms, which governs cardiogenic stem cell differentiation along with cellular properties. Genetic engineering promises to be a great scope to the selection, survival and integration of stem cells in cardiac cell therapy.

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