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Review Article

PLURIPOTENT STEM CELLS FOR VASCULAR DISEASE THERAPY

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ABSTRACT

Vascular regeneration for ischemic disease represents an unmet clinical need. The ability to derive and expand homogenous populations of human vascular endothelial cells from either human embryonic stem (hES) cells or human induced pluripotent stem (iPS) cells creates an opportunity to develop novel treatments for patients with peripheral and myocardial ischemic conditions. The review focuses on pluripotent stem cells and their capacity to differentiate vascular endothelial cells.

Keywords: Endothelial cells, Myocardial ischemic, Human embryonic stem, human induced pluripotent stem, Vascular therapy etc.

INTRODUCTION

After Globalization, there is no proper treatment for many chronic diseases like diabetes, Parkinson's disease, Alzheimer's disease etc. Stem cells are giving a light hope for the treatment of these incurable diseases. Now-a-days research on stem cells is advancing. This scientific investigation is given the possibility of cell-based therapies to treat disease, which is referred as regenerative (or) reparative medicine.
Stem cells are the raw material for development of differentiated cells in the body. Stem cells are given rise to brain cells, nerve cells, heart cells, pancreatic cells, etc.

Definition: A cell that has the ability to continuously divide and differentiate (develop) into various other kind(s) of cells/tissues.

Properties of stem cells: Regardless of their source all the stem cells have three general properties.

- They are capable of dividing and renewing themselves for long periods.
- They are unspecialized.
- They can give rise to specialized cell types.

This is unlike muscle, billd (or) nerve cells which do not normally replicate themselves. These cells are capable of long-term self-renewal.Stem cells are unspecialized and do not have any tissue-specific structures that allow for specialized function.

Stem cell Types
Totipotent: The ability to differentiate into all types and can form any cell of the embryo as well as the placenta.
Ex: Morula
Pluripotent: The ability to differentiate into almost all types except placental tissue.
Ex: Cells from inner cell mass of blastocyst.
Multipotent: The ability to differnetiate into multiple specialized cells of a closely related family of cells.
Ex: Hematopoietic stem cells

Embryogensis & Differntiation: Specific regions of the embryo give rise to the specific organ systems.
Ectoderm: It generates the outer layer of the embryo and produces the surface layer (epidermis) of the skin and forms the nerves.
Endoderm: It becomes the innermost layer of the embryo and produces the digestive tube and its associated organs (including the lungs

Mesoderm: It becomes sandwiched between the ectoderm and endoderm and genrates the blood, heart, kidney, gonads, bones & connective tissues.

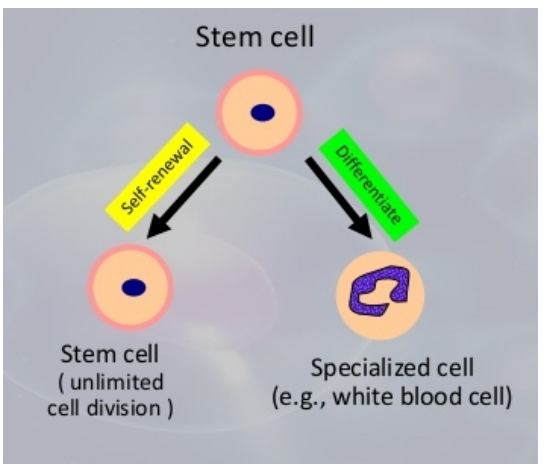

Figure 1. Diagramatic representation of stem cell divisions.

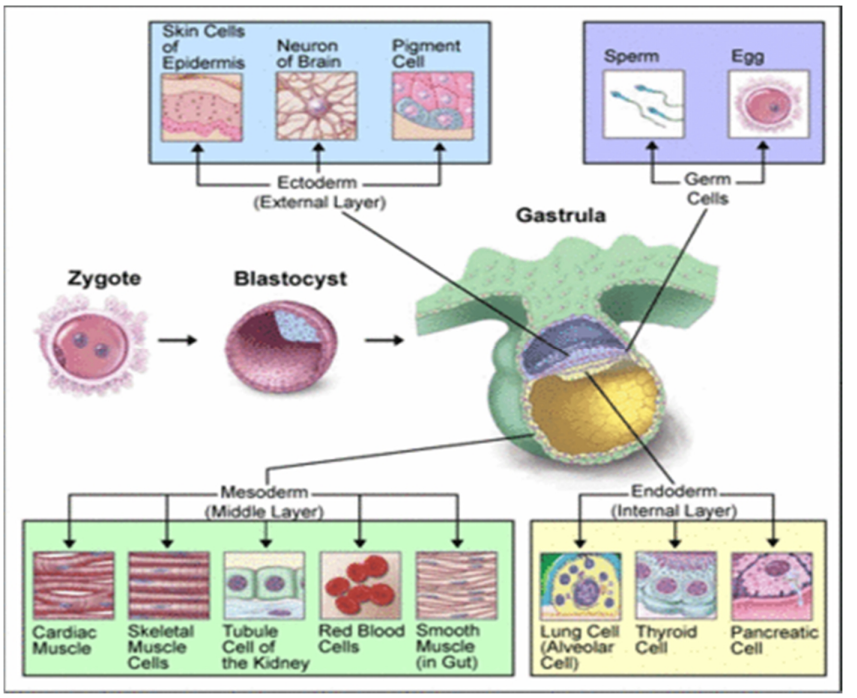

Figure 2. Embryogensis & Differntiation of Embryo

Stem cell therapy: It is introduction of new adult stem cells into damaged tissue in order to treat disease (or) injury. The ability of stem cells to self-renew and give rise to different cells, that can potentially replace diseased and damaged areas in the body, with minimal risk of rejection and side effects. A number of stem cell therapies exist, but most are at experimental stages, costly (or) controversial.

There are two distinctly different types of self replication.
1.**Symmetrical Replication** – Here a single "parent" stem cells divides into two identical "daughter cells " which is identical to the parent and possess all the same replicative and potency characteristics.
2. **Asymmetrical Replication** - In this type of replication there are two different products from the dividing stem cell. The first is an exact copy of the parental stem cell with all characteristics and the second has limits on replication.

PLURIPOTENT STEM CELLS

- Pluripotent stem cells have the capacity for exponential scale up and differentiation into any cell type in the body including vascular cells expressing functional characteristics, genes and proteins.
- Therapeutic pluripotent stem cells may promote neovasculogenesis (origin of vessels from progenitor cells) and support angiogenesis (formation of capillary and arteriole vessels from pre-existing vascular structures) in clinical ischemic conditions.

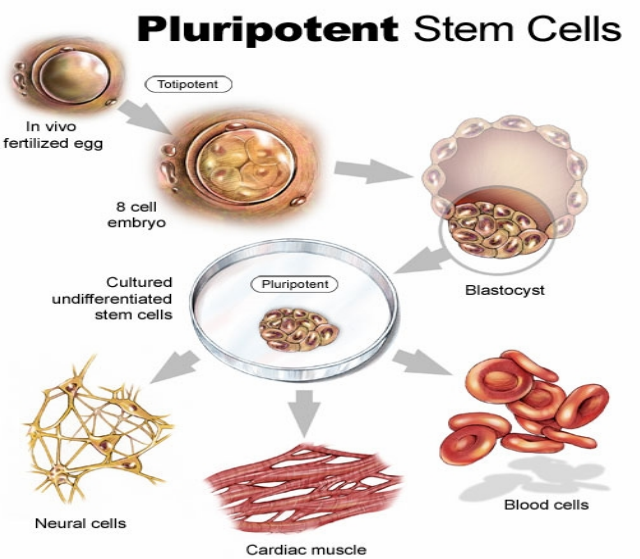

Figure 3. Types of stem cell and cell formations.

DIFFERENTIATION STRATEGIES

In vitro derivation of vascular cells from pluripotent SCs, involves culturing the pluripotent stem cells as embryoid bodies (EB), which closely resemble early in vivo embryogenesis with differentiation to all three germ layers (including vascular development).
During differentiation it is possible to monitor the progression from pluripotency to mature vascular endothelial cell as cells acquire morphology indicative of vascular cells concomitant with expression of differentiation markers and functionalities.
The combinations of multiple endothelial-specific markers and functional assays such as Dil-labeled acetylated low density lipoprotein (Dil- Ac-LDL) uptake and in vitro angiogenesis assays are classic hallmarks in identifying and characterising hES-derived ECs. hES-derived ECs acquire cobblestone morphology and many of the ECmarkers, such as endothelial nitric oxide synthase (eNOS), which are functionally important for endothelial formation, maintenance and remodelling. VEGF-R2 is one of the earliest endothelial linage development markers, however, VEGF-R2 is also expressed by pluripotent stem cells, angioblasts and mature ECs.

FUTURE PERSPECTIVE

Initial preclinical studies using pluripotent stem cell-derived vascular endothelial cells show encouraging results in small animal models of myocardial infarct, limb ischemia, vein graft and atherosclerosis.
Prior to clinical applications, pluripotent stem cell derivatives must be subject to governing differentiation and translation research in large animals to ensure eventual production of a safe and efficient cellular product for clinical use.
In addition to cell transplantation for vascular regeneration, it is also predicted that vascular derivatives of pluripotent stem cells will be incorporated into biotissues for tissue replacement therapy.
Additionally, and more likely in the immediate future, vascular endothelial cells derived from pluripotent stem cells will facilitate patient-tailored drug screening (iPS cells), efficient and rapid in-vitro screening platforms for novel pharmaceutical therapeutic interventions such as angiogenic or anti-angiogenic small molecules, and toxicology studies.

The derivation of vascular endothelial cells from pluripotent stem cells creates exciting and realistic possibilities for innovative therapies for peripheral and myocardialischemic conditions.

CONCLUSION

Preclinical studies for vascular endothelial cells show encouraging results in animal models of myocardial infarct, limbischemia, vein graft and atherosclerosis. It is concluded that vascular derivatives of pluripotent stem cells will be incorporated into biotissues for tissue replacement therapy.

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