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Stem Cell Technology in Organogenesis

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Abstract: ***Stem cell therapy is a promising strategy for overcoming the limitations of current treatment methods. The modification of stem cell properties may be necessary to fully exploit their potential. Stem cells are cells that can differentiate into other types of cells, and can also divide in self-renewal to produce more of the same type of stem cells. Telomerase is active in normal stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts in early embryonic development, and adult stem cells, which are found in various tissues of fully developed mammals. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues and other organs.***

Keywords: Repair, Progenitor, Embryo, Specialized, Regenerative, Promising, Turnover

1. Introduction

The development of individual organs in animal embryos involves the formation of tissue-specific stem cells that sustain cell renewal of their own tissue for the lifetime of the organism. Although details of their origin are not always known, tissue-specific stem cells usually share the expression of key transcription factors with cells of the embryonic rudiment from which they arise, and are probably in a similar developmental state. On the other hand, the isolation of pluripotent stem cells from the postnatal organism has encouraged the formulation of models of embryonic and postnatal development that are at variance with the conventional ones. Possible explanations for the existence of such cells, and the issue of whether they also exist in vivo, are discussed. Pluripotent stem cells (PSCs) have the ability to spontaneously generate structured tissues in vitro reminiscent of embryonic tissue development. Recently, complex organoids such as cortical tissues, cerebral brain organoids, optical cups, intestinal tissues, and liver buds have been generated from PSCs derived from healthy individuals and patients with genetic diseases, providing powerful tools to understand morphogenesis and disease pathology.

2. Organogenesis by stem cells

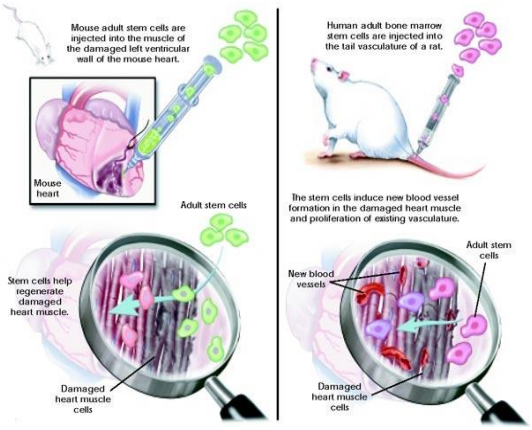
Over the last decade, stem cell research has made significant progress in various aspects of controlling cellular differentiation, including cell-type specification and reprogramming. For example, pluripotent stem cells can be steered to differentiate into specific somatic cell lineages by providing cultured cells with positional information corresponding to signals presented during embryogenesis. In the embryo, these patterning signals typically emanate from special signalling centres. For example, an “organizer” is a region that has strong inductive effects on a relatively wide area of embryonic tissues and plays a crucial role in pattern formation by creating morphogen gradients. Spemann’s organizer specifies the DV pattern of the gastrula embryo and the isthmic organizer in the midbrain-hindbrain boundary induces the AP pattern in this brain region. Besides their morphogen-mediated patterning activity, organizers have an important shared characteristic: they robustly maintain their identity regardless of external environmental influences.

Researchers are currently focusing heavily on the therapeutic potential of embryonic stem cells, with clinical use being the goal for many laboratories. Potential uses include the treatment of diabetes and heart disease. The cells are being studied to be used as clinical therapies, models of genetic disorders, and cellular/DNA repair. However, adverse effects in the research and clinical processes such as tumours and unwanted immune responses have also been reported.

The most important potential application of human stem cells is the generation of cells and tissues that could be used for cell-based therapies. Today, donated organs and tissues are often used to replace ailing or destroyed tissue, but the need for transplantable tissues and organs far outweighs the available supply. Stem cells, directed to differentiate into specific cell types, offer the possibility of a renewable source of replacement cells and tissues to treat diseases including macular degeneration, spinal cord injury, stroke, burns, heart disease, diabetes, osteoarthritis, and rheumatoid arthritis.

For example, it may become possible to generate healthy heart muscle cells in the laboratory and then transplant those cells into patients with chronic heart disease. Preliminary research in mice and other animals indicates that bone marrow stromal cells, transplanted into a damaged heart, can have beneficial effects. Whether these cells can generate heart muscle cells or stimulate the growth of new blood vessels that repopulate the heart tissue, or help via some other mechanism is actively under investigation. For example, injected cells may accomplish repair by secreting growth factors, rather than actually incorporating into the heart. Promising results from animal studies have served as the basis for a small number of exploratory studies in humans (for discussion, see call-out box, "Can Stem Cells Mend a Broken Heart?"). Other recent studies in cell culture systems

Indicate that it may be possible to direct the differentiation of embryonic stem cells or adult bone marrow cells into heart muscle cells



3. Can Stem Cells Mend a Broken Heart?

Stem Cells for the Future Treatment of Heart Disease.
Cardiovascular disease (CVD), which includes hypertension, coronary heart disease, stroke, and congestive heart failure, has ranked as the number one cause of death in the United States every year since 1900 except 1918, when the nation struggled with an influenza epidemic. Nearly 2,600 Americans die of CVD each day, roughly one person every 34 seconds. Given the aging of the population and the relatively dramatic recent increases in the prevalence of cardiovascular risk factors such as obesity and type 2 diabetes, CVD will be a significant health concern well into the 21st century.

Cardiovascular disease can deprive heart tissue of oxygen, thereby killing cardiac muscle cells (cardiomyocytes). This loss triggers a cascade of detrimental events, including formation of scar tissue, an overload of blood flow and pressure capacity, the overstretching of viable cardiac cells attempting to sustain cardiac output, leading to heart failure, and eventual death. Restoring damaged heart muscle tissue, through repair or regeneration, is therefore a potentially new strategy to treat heart failure.

The use of embryonic and adult-derived stem cells for cardiac repair is an active area of research. A number of stem cell types, including embryonic stem (ES) cells, cardiac stem cells that naturally reside within the heart, myoblasts (muscle stem cells), adult bone marrow-derived cells including mesenchymal cells (bone marrow-derived cells that give rise to tissues such as muscle, bone, tendons, ligaments, and adipose tissue), endothelial progenitor cells (cells that give rise to the endothelium, the interior lining of blood vessels), and umbilical cord blood cells, have been investigated as possible sources for regenerating damaged heart tissue. All have been explored in mouse or rat models, and some have been tested in larger animal models, such as pigs.

A few small studies have also been carried out in humans, usually in patients who are undergoing open-heart surgery. Several of these have demonstrated that stem cells that are injected into the circulation or directly into the injured heart tissue appear to improve cardiac function and/or induce the formation of new capillaries. The mechanism for this repair remains controversial, and the stem cells likely regenerate heart tissue through several pathways. However, the stem cell populations that have been tested in these experiments vary widely, as do the conditions of their purification and application. Although much more research is needed to assess the safety and improve the efficacy of this approach, these preliminary clinical experiments show how stem cells may one day be used to repair damaged heart tissue, thereby reducing the burden of cardiovascular disease.

1) Survey showing knowledge of population about stem cell in India and Perm (Russia)

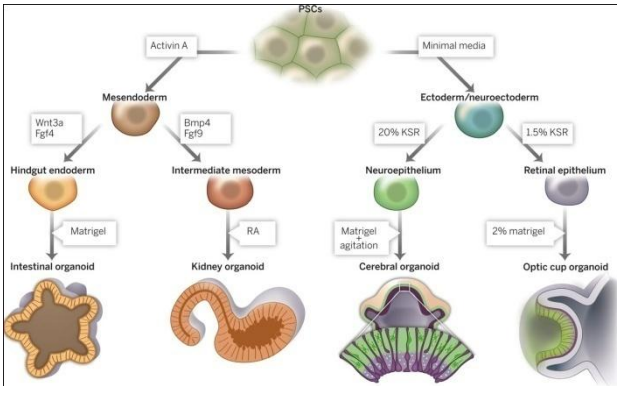
Questions	*Delhi (n%)*		*Perm (Russia) (n%)*	
	Yes	No	Yes	No
Have you heard of the term stem cells?	148 (18.3)	661 (81.7)	50 (25)	150 (75)
Do you know what stem cells are?	144 (17.8)	665 (82.2)	49 (24.5)	151 (75.5)
Are you aware stem cells are potentially beneficial?	132 (91.7)	12 (8.3)	46 (93.9)	3(61)

2) Survey showing time of extraction of stem cell

Timings	Delhi (%)	Perm (%)
Umbilical cord as a source	141 (100)	49(100)
Immediately after delivery	120 (85.1)	40 (81.6)
1 day after delivery	3 (2.1)	0
2 days after delivery	0	0
1 month after delivery	18 (12.8)	9 (18.4)

4. Overview of Organoid methodologies

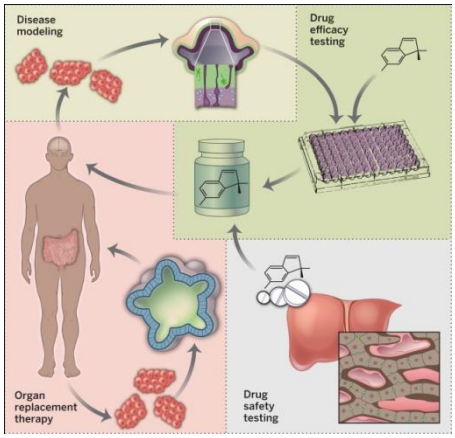
Organoid differentiation strategies developed so far from human PSCs. Conditions and growth factors are indicated for the derivation of progenitor identities. For neuroectoderm, minimal medium without serum is used. KSR is knockout serum replacement, a serum-free growth-promoting alternative. Limiting its use, along with a low concentration of Matrigel dissolved in the medium, promotes retinal neuroepithelium, whereas higher KSR and embedding in pure Matrigel promotes the formation of various brain regions. Renal organoids have been generated several ways, but growth factors in common are shown.



5. Therapeutic potential of organoids

Organoids can be used to model diseases (beige box), for example modelling neurodevelopment disorders with cerebral organoids. These types of disease models can then be used for testing drug efficacy in vitro before moving to animal models (green box). Drug compounds can be tested for toxicity and metabolic profile in liver organoids (gray

box). And finally, organoids could be made from patient cells to provide autologous transplant solutions (pink box).



6. Conclusion

Stem cell technology is not a new concept having been popular since last decade. Stem cells are auto-generative cells which have the capability of indefinite division. They can easily be maintained in laboratories as cell lines. Since they can divide and differentiate to form different cells of the body, they have vast scope in medical realm with respect to repair and replacement of human tissues and a probable cure for many conventional and non-conventional diseases.

To realize the promise of novel cell-based therapies for such pervasive and debilitating diseases, scientists must be able to manipulate stem cells so that they possess the necessary characteristics for successful differentiation, transplantation, and engraftment. The following is a list of steps in successful cell-based treatments that scientists will have to learn to control to bring such treatments to the clinic. To be useful for transplant purposes, stem cells must be reproducibly made to:

- Proliferate extensively and generate sufficient quantities of cells for making tissue.
- Differentiate into the desired cell type(s).
- Survive in the recipient after transplant.
- Integrate into the surrounding tissue after transplant.
- Function appropriately for the duration of the recipient's life.
- Avoid harming the recipient in any way.

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