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Stem Cells: A New Direction

Mahind Pavitra Kashinath, Adate Rupesh D.
College of Pharmacy, Medha, Satara, Maharashtra, INDIA

ABSTRACT

Stem cell therapy is the use of Stem cells to treat or prevent disease or condition. Stem cell therapy is emerging as potent new way to treat disease and injury with wide range medical benefits. Research is underway to develop various sources for stem cells and to apply stem cell treatment for neurodegenerative diseases and conditions diabetes, heart diseases and other conditions. However stem cells therapy produce many ethical and scientific questions that are to be solved. Nevertheless, stem cells therapy, a preamble to research of cell based therapeutics, will one day restore the functionality of the formerly un abled people, is yet to be unveiled.

Keywords: SC- stem cell, MSCs- multi potent mesenchymal stromal cells, ES cells- embryonic stem cells, HIV -human immunodeficiency virus type-1.

*Corresponding Author Email: mahipavitra@gmail.com

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INTRODUCTION

Stem cell therapy is the use of stem cells to treat or prevent a disease or a condition. Stem cell therapy has become controversial following development such as ability of scientists to isolate and culture embryonic cells, to create stem cells using somatic cell nuclear transfer and their use of techniques to create induced pluripotent stem cells.⁷

Stem cells are distinctive and versatile type of cells that can divide indefinitely and have unique capacity to renew themselves and to give rise to specialized cell types⁵. Researchers, for years have looked for a way to use stem cells to replace damaged cells.

Thus, human stem cells hold the promise to repair and replace cells that were once destroyed or diseased and also help the disabled to be abled again.

History

The history of stem cells had a benign, embryonic beginning in the 1800's with the discovery that some cells could generate other cells. In early 1900's the first real stem cells were discovered. It was seen that some cells generated blood cells. The term 'STEM CELLS' was proposed by Russian histologist Alexander Maximov in 1908⁶.

Bone marrow transplant between two siblings successfully treated SCID in 1968⁹. James Thomson and co-workers derived the first human embryonic stem cell line at university of Wisconsin in 1998⁹. More recently, in 2005, scientists at Kingston University in England were purported to have found another category of stem cells. These were named cord blood embryonic-like stem cells, which originate in umbilical cord blood. Korean researcher Hwang Woo-Suk (2004–2005) claimed to have created several human embryonic stem cell lines from unfertilized human oocytes¹⁰.

Stem cells:

A stem cell is a cell that has the ability to divide (self-replicate) for indefinite periods often throughout the life of the organism. Under the right conditions, or given the right signals, stem cells have the potential to develop into mature cells that have characteristic shapes and specialized functions, such as heart cells, skin cells, or nerve cells^{11,12}.

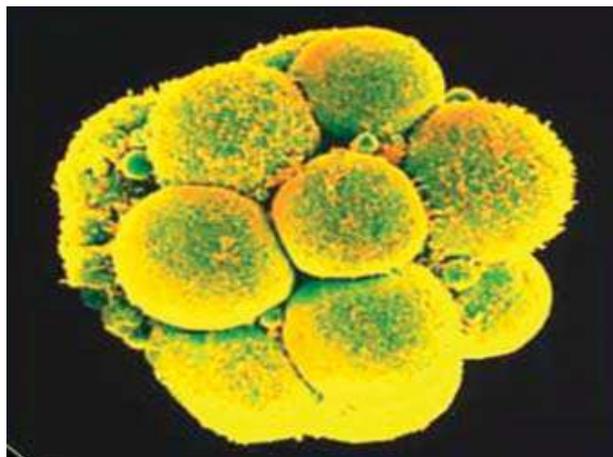


Figure 1: stem cell as a pluripotent cell

A stem cell is a non-specialized, generic cell which can make exact copies of it self indefinitely and can differentiate and produce specialized cells for the various tissues of the body¹³.

Stem cells are cells found in most, if not all, multi-cellular organisms. They are characterized by self-renewal and potency i.e. the ability to renew themselves through mitotic cell division and differentiating into a diverse range of specialized cell types¹³. They are vital to the development, growth, maintenance, and repair of our brains, bones, muscles, nerves, blood, skin, and other organs¹⁴.

CLASSIFICATION OF STEM CELLS ON BASIS OF SOURCE:

- 1) Embryonal stem cell
- 2) Adult stem cell

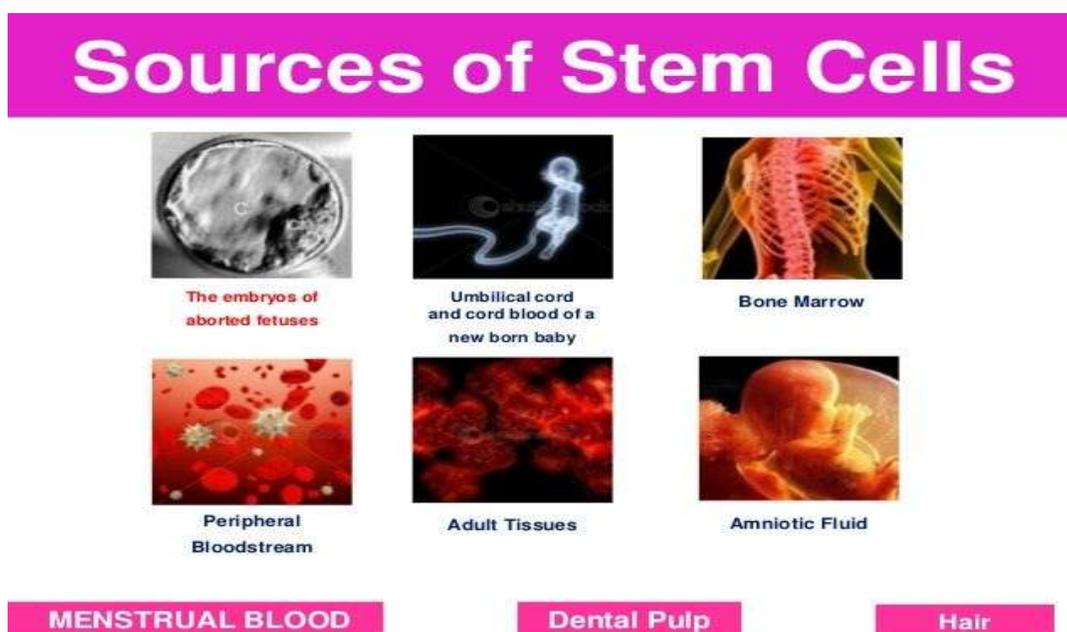


Figure 2: sources of stem cells

EMBRYONIC STEM CELLS

They are derived from embryos (blastocyst) that develop from eggs that have been fertilized in vitro—in an in vitro fertilization clinic—and then donated for research purposes with informed consent of the donors^{15,16}.

Embryonic stem cells are self-replicating pluripotent cells that are potentially immortal¹⁷. They are derived from embryos at a developmental stage before the time of implantation would normally occur in the uterus¹³. The embryos from which human embryonic stem cells are derived are typically four or five days old and are a hollow microscopic ball of cells called the blastocyst⁸.

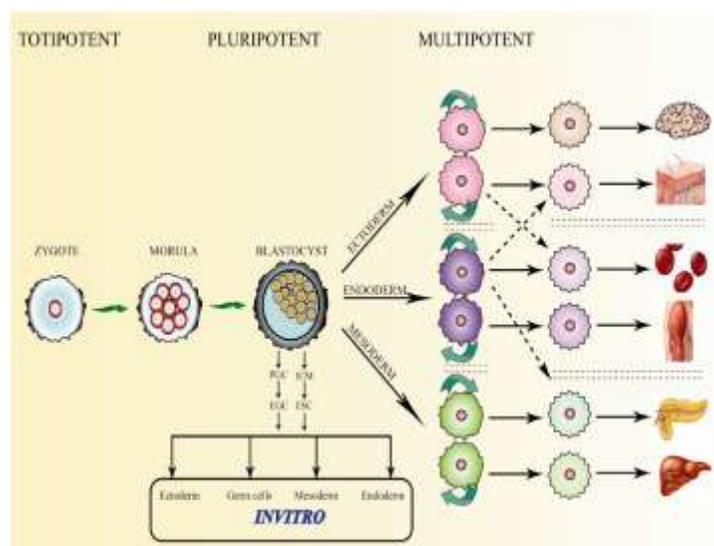


Figure 3: General hierarchy for the stem cell niche

ADULT STEM CELLS

Adult stem cells are undifferentiated totipotent or multi potent cells, found throughout the body after embryonic development, that multiply by cell division to replenish dying cells and regenerate damaged tissues. (Fig.-4). The primary roles of adult stem cells in a living organism are to maintain and repair the tissue in which they are found. Unlike embryonic stem cells, which are defined by their origin (the inner cell mass of the blastocyst), the origin of adult stem cells in some mature tissues is still under investigation³.

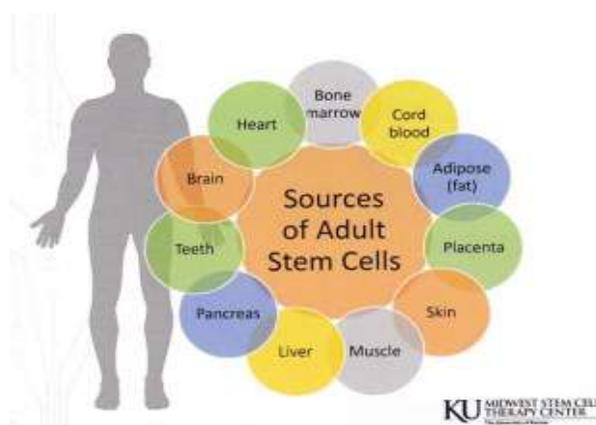


Figure 4 : Sources of adult stem cells

Adult stem cells have been identified in many organs and tissues, including brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, teeth, heart, gut, liver, ovarian epithelium, and testis. They are thought to reside in a specific area of each tissue called a “stem cell niche”. In many tissues, current evidence suggests that some types of stem cells are pericytes, cells that compose the outermost layer of small blood vessels. Stem cells may remain quiescent (non-dividing) for long periods of time until they are activated by a normal need for more cells to maintain tissues, or by disease or tissue injury⁷.

CLASSIFICATION OF STEM CELLS ON THE BASIS OF POTENCY

Stem cells can be classified by the extent to which they can differentiate into different cell types. These four main classifications are totipotent, pluripotent, multi potent, or unipotent.

Totipotent

The ability to differentiate into all possible cell types. Examples are the zygote formed at egg fertilization and the first few cells that result from the division of the zygote.

Pluripotent

The ability to differentiate into almost all cell types. Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation. Scientists have engineered these induced pluripotent stem cells (iPS cells) by manipulating the expression of certain genes -'reprogramming' somatic cells back to a pluripotent state¹⁸⁻¹⁹.

Multipotent

The ability to differentiate into a closely related family of cells. Examples include hematopoietic (adult) stem cells that can become red and white blood cells or platelets.

Oligopotent

The ability to differentiate into a few cells. Examples include (adult) lymphoid or myeloid stem cells.

Unipotent

The ability to only produce cells of their own type, but have the property of self-renewal required to be labeled a stem cell. Example include (adult) muscle stem cells.

PROPERTIES OF STEM CELL

1. They are unspecialized,
2. They are capable of continuous self-renewal,
3. They can give rise to specialized cell types^{20,21}.
4. Stem cells can divide either symmetrically (allowing the increase of stem cell number) or asymmetrically. Asymmetric divisions keep the number of stem cells unaltered and are responsible for the generation of cells with different properties.

These cells can either multiply (progenitors or transit amplifying cells) or be committed to terminal differentiation. Progenitors and transit amplifying cells have a limited lifespan and therefore can only

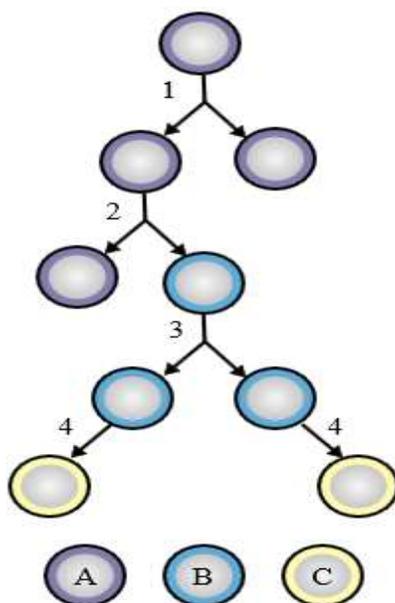


Figure 3: Process of Stem Cell Division

(A: Stem cell; B: Progenitor cell; C: Differentiated cell .1: Symmetric division-give rise to two stem cells; 2: Asymmetric division- forms one stem and one progenitor cell ; 3:Progenitor division: gives rise to progenitor cells ; 4:Terminal differentiation)

Reconstitute a tissue for a short period of time when transplanted. In contrast, stem cells are self-renewing and thus can generate any tissue for a lifetime. This is a key property for a successful therapy and use in Regenerative medicine. Fig.no. 5 shows the process of stem cell division and differentiation where A is the Stem cell, B is the Progenitor cell and C is the Differentiated cell. First symmetric division gives rise to two stem cells, second asymmetric division forms one stem and one progenitor cell, third progenitor division gives rise to progenitor cells while the fourth is the terminal differentiation²².

Adult stem cells are believed to reside in a specific area of each tissue, i.e., a “stem cell niche”. Many types of adult stem cells reside in several mesenchymal tissues, and these cells are collectively referred to as mesenchymal stem cells or multipotent mesenchymal stromal cells (MSCs)²².

APPLICATIONS OF STEM CELLS RECENT & FUTURE:

Knowledge about stem cell science and their potential applications has been accumulating for more than 30 years. Limited types of stem cell therapies are already in use.

The most well-known therapy is the stem cell transplant (a form of a bone marrow transplant) for cancer patients. But it has been only recently that scientists have understood stem cells well enough to consider the possibilities of growing them outside the body for long periods of time. Today stem cells have found applications in varying area of Medicine ranging from therapeutics to replacement of lost tissues²³.

1. SKIN REPLACEMENT

The knowledge of stem cells has made it possible for scientists to grow skin from a patient’s plucked hair. Skin (keratinocyte) stem cells reside in the hair follicle and can be removed when a hair is plucked²⁴. These cells can be cultured to form an epidermal equivalent of the patients own skin and provides tissue for an autologous graft, by passing the problem of rejection.

2. BRAIN CELL TRANSPLANTATION

Stem cells can provide dopamine – a chemical lacking in victims of Parkinson’s disease. It involves the loss of cells which produce the neurotransmitter dopamine. The first double-blind study of fetal cell transplants for Parkinson’s disease reported survival and release of dopamine from the transplanted cells and a functional improvement of clinical symptoms²⁵. However, some patients developed side effects, which suggested that there was an over sensitization to or too much dopamine. Although the unwanted side effects were not anticipated, the success of the experiment at the cellular level is significant.

3. STEM CELLS AND DIABETES

For decades, diabetes researchers have been searching for ways to replace the insulin-producing cells of the pancreas that are destroyed by a patient's own immune system.²⁷ Recently, hope for a permanent cure of diabetes has appeared, namely, the transplantation of islets isolated from donor pancreata into the livers of diabetic patients.

Some promising results have already been obtained with embryonic stem cells (ES cells) of both rodent and human origin.²⁷ However, the potential use of ES cells for the treatment of diseases in humans is be clouded in controversy because of the ethical issues. In theory, embryonic stem cells could be cultivated and coaxed into developing into the insulin-producing islet cells of the pancreas. It is concluded that stem cells offer the greatest potential for the development of an abundant source of pancreatic islets, although specific obstacles must be overcome before this can become a reality.^{28,29}

4. STEM CELL THERAPY FOR HIV

The hematopoietic stem cell has long been hypothesized to be a target of human immunodeficiency virus type-1 (HIV) infection that limits the potential for compensatory immune cell production.

Data have recently emerged documenting stem cell dysfunction in HIV disease and indicating that immune recovery from potent antiretroviral therapy is partly driven by new T-cell generation. Effects of HIV on stem cell physiology, however, appear to be indirect, as stem cells are highly resistant to HIV infection. Despite the presence of surface receptors for HIV, the hematopoietic stem cell is not infectible with HIV and can serve as a resource for cellular therapies for AIDS³⁰.

5. TREATMENT OF HEART DISEASE

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 capillaries³³. 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 application³¹. 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 disease⁷.

CONCLUSION:

We conclude that ongoing research on stem cell therapies gives hope to patients who would normally not receive treatment to cure their disease. The stem cell data presented raise the hope that important

medical progress can be made in several fields: neuro-degenerative diseases, those linked to cellular deficit, some aspects of aging linked to cellular degeneration.

A silhouette of the potential use of stem cells for the treatment of human disease is now perceptible. Documentation of complete history of the cells, and their characterization, for use in therapy is essential to safeguard against potential risks of biological therapy. This is particularly important when human Embryonic/somatic Stem Cells are used for this purpose. The field of medicine caters to wide range of diseases, disorders and congenital defects along with cases of trauma which may result in single or multi-organ failures.

Current alternative approaches to treatment of these diseases and defects incorporate the use of stem cells from the patient himself. More recently use of stem cells have been found to be useful in the research area allowing the scientists to develop models for studying human biology, pathology and genetics.

The coming years will undoubtedly user in new developments and technologies that would translate the envisioned therapeutic potential of stem cells to bedside medicine for patients suffering from devastating and debilitating diseases.

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