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Stem Cells – A General Study

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Abstract: **All multicellular organisms contain some basic stem cells that have the potential to differentiate into a variety of adult cells. Regeneration and self-renewal assign a unique trademark to these special types of cells. Although stem cell research is highly debatable on life creation/destruction issue, these specialized cells tend to open new horizons in clinical research and treatment. Here, in this paper, we aim to provide a general overview on stem cells, its properties and types along with its various harvest procedures. Highlights are made on potential uses of stem cells in biomedical research along with the challenges and future perspectives of work at the crossroads of biology and computer science.**

Keywords**: Apheresis, Biomedical Research, Cloning, Stem Cells**

I. INTRODUCTION

Modern research work possesses a great hope from stem cell research in the field of organ transplantation and replacement of damaged tissues. With the ability of self-renewal and potency, stem cells can generate various types of tissue cells. There can be two sources of stem cells – autologous and allogenic. Autologous embryonic stem cells are generated through therapeutic cloning and highly plastic adult cells are obtained from the umbilical cord blood or the donor's bone marrow. Allogenic stem cells can be derived from marrow, peripheral blood and cord blood of both family donors and unrelated donors. With the help of in-vitro fertilization, the stem cells can be proliferated in the culture medium. Here, in this paper, we aim to carry out a generic analysis on stem cells, its harvest procedure, challenges in stem cell research followed by answers to some ethical questions.

II. DEFINITION OF STEM CELLS:

Stem cells are undifferentiated or unspecialized primal cells that have the remarkable ability to produce specialized cell types in the body. They occur at all stages of human development from embryo to adult but the number and the variety of the cells tend to decrease with age. Replication of stem cells can give rise to other stem cells or specialized cells like muscle cells, nerve cells or RBC. [1][4]

III. PROPERTIES OF STEM CELLS:

Stem cells are a unique type of cells in the body. They differ from other types of cells by certain properties. Mainly, three general properties are found in basic stem cells. Such properties are as below.

1. Self-Renewal**:** This is a process where a stem cell divides to generate at least one daughter cell that remains undifferentiated by the process of mitosis. Through this property, stem cell population can be expanded and maintained throughout the life-span of an organism.

2. Being Undifferentiated**:** Stem cells are unspecialized and basic cells. They don't have any tissue-specific structures, so they don't function like nerve cells, muscle cells or any other specific body cell.

3. Differentiation**:** Differentiation is the process through which unspecialized cells acquire specific cellular traits which transform them into specialized cell types. The stem cell can give rise to any specialized cell in the body. The number of different specialized cell types that a stem cell can give rise to defines the potency of the stem cell.

IV. TYPES OF STEM CELLS:

In mammals, stem cells are broadly classified into two categories as below.

1. Embryonic Stem Cells (ES Cells): ES cells are the primitive pluripotent stem cells derived from the inner cell mass of blastocyst of a 4 to 5 days preimplant embryo. ES cells have the unique potential to produce three primary germ layers: ectoderm, mesoderm and endoderm. These three types of germ layers can develop into a variety of organs, tissues and cell types. The embryonic stem cell can develop into more than 220 different cell types of the adult body.

Fig 1. Embryonic Stem Cells

***1. Sources of ES Cells*:** Normally, embryonic stem cells are obtained by growing human embryo in a cluster of cells that contain an inner cell mass. After the inner cell mass is removed, the embryo is ultimately destroyed. This process is called Somatic Cell Nuclear Transfer (SCNT). [8] In this procedure, the nucleus is removed from a somatic cell and then it is implanted into a donor egg from which the nucleus was previously removed. The egg cell has its own DNA and after stimulation, it divides just as a normally fertilized egg would before forming an embryo. Inner cell mass is extracted, thus destroying the embryo and cultured in a culture medium containing nutrients for embryonic stem cells.

2. Adult Stem Cells (ASC): The undifferentiated stem cells that reside in bone marrow and fat along with the other tissues and organs of the body, are called adult stem cells or somatic stem cells. They are found throughout the body. They divide to replenish the dying cells and repair the damaged tissues in which they are found. They are found both in children and adults. [2][3]

3. Sources of ASC: Recent discoveries establish that adult stem cells are present in many organs and tissues including, brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin, teeth, heart, gut, liver, ovarian epithelium and testis. Per the different sources, adult stem cells are classified as below.

- ***Hematopoietic Stem Cells*:** Hematopoietic stem cells are present in the bone marrow and umbilical cord blood. They produce all types of blood cells – RBC, B lymphocytes, T lymphocytes, natural killer cells, basophils, neutrophils, eosinophils, monocytes and macrophages.
- ***Mammary Stem Cells*:** Mammary stem cells give rise to the source of cells for growth of mammary gland during puberty and gestation, and play an important role in breast cancer. Such single cells generate both the luminal and the myoepithelial cell types of the gland.
- ***Mesenchymal Stem Cells:*** They are present in various tissues. Those from bone marrow (of stromal stem cells, skeletal stem cells) produce various types of cells – bone cells (osteoblasts and osteocytes), cartilage cells (chondrocytes), fat cells (adipocytes) and stromal cells that support blood formation. [6]
- ***Neural stem cells*:** They can give rise to three types of cells in the brain – nerve cells or neurons & two categories of non-neuronal cells – astrocytes and oligodendrocytes.
- ***Olfactory Adult Stem Cells*:** They are harvested from the human olfactory mucosa cells, present in the lining of the nose.
- ***Epithelial Stem Cells*:** They are present in the lining of the digestive tract and produce a variety of cell types – absorptive cells, goblet cells, Paneth cells and enteroendocrine cells.
- ***Skin Stem Cells*:** They reside in the basal layer of the epidermis and hair follicles. The epidermal cells give rise to keratinocytes which migrate to the skin surface and form a protective layer.

V. DIFFERENCES BETWEEN EMBRYONIC AND ADULT STEM CELLS:

Parameter	Embryonic Stem Cells	Adult Stem Cells
Flexibility and Versatility	High	Low
Differentiation Potential	High	Low
Development Outcome	Can develop into almost every cell in human body	Can develop only into a limited number of cell types
Ease in Growing	Can be grown easily in culture	Isolation of these cells from adult tissue is challenging
Ethical Background	Creates huge controversy among public for the abortion debate	No ethical dilemma, as such cells are collected with donor's consent

VI. HARVEST PROCEDURE OF STEM CELLS:

The process of collecting stem cells for transplant depends on the source of stem cells. There are two different methods to collect stem cells. Both the methods apply equally to autologous or allogenic donations.

***1. Bone Marrow Harvest*:** The hip bone (pelvic) contains the largest amount of active marrow in the body, and henceforth, the largest number of stem cells. Here comes up the process to extract stem cells from bone marrow.

a. At first, the person will be given a spinal or general anesthetic.

b. The doctor then makes several punctures in the skin over the pelvic bone.

c. Marrow and blood are extracted through the punctures by syringe. This process is repeated multiple times to ensure

enough stem cells are collected for the transplant. It usually takes 1 to 2 hours.
d. 0.5 to 1.5 liters of bone marrow are removed from the iliac crest. The specific amount of marrow and blood varies from person to person depending on the donor's weight and concentration of stem cells in the marrow.
e. About 500-1000ml of marrow is removed from an adult individual, which is about 3% to 5% of the marrow.
Few risks are associated with the bone marrow donation. The body usually replaces these cells within a few weeks. The doctor may suggest iron supplements until blood cell count increases.

2. Stem Cells from Peripheral Blood: This technique does not require surgery. Harvesting stem cells from peripheral blood follows the below mentioned steps.
a. Prior to collection, the donor is given a medication to promote the growth and release of stem cells from bone into blood. It is reported that blood usually contains very few stem cells. So, before 4 to 5 days, a drug is injected once or twice. This hematopoietic growth factor drug is known as GCSF (Granulocyte Colony Stimulating Factor). It causes movement of more stem cells from bone marrow into blood stream.
b. After a few days, when there are enough stem cells in blood, blood sample is taken from vein in one arm and passed along a tube into a special centrifuge called apheresis machine.
c. The blood is returned to the body through another tube into a vein of another arm. Apheresis (the process of separating stem
cells from blood) takes about 2-3 hours. This technique has a great popularity over last 10 years as it has no surgical risks and anesthetic requirement. But, it may have a side-effect of growth factor drug like temporary joint pains, head aches, bone pain, etc.

***Stem Cells from Umbilical Cord Blood*:** Stem cells are collected from umbilical cord blood shortly after a baby is born. With the parent's consent, collected stem cells are frozen and stored by cord blood banks until they are needed.

VII. STEM CELLS IN BIOMEDICAL RESEARCH:

Stem Cells have potential uses in many different areas of research and medicine. [9]

1. Replacement of Damaged Tissues: Human stem cells are used in the generation of cells and tissues for cell based therapies. Stem cells can be used to treat heart failure, spinal injuries, diabetes, Parkinson disease, etc. for their remarkable ability to replenish damaged cells.
***2. Brain Damage and Spinal Cord Injury*:** Neural stem cells can regenerate nerve tissue damaged by spinal injury. Recent discoveries reveal that stroke patients see signs of recovery in stem cell trial, in which stem cells are injected in the brain of stroke patients.
***3. Wound Healing*:** Stem Cells can also be used to stimulate the growth of human tissues. Their ability of tissue regeneration helps in healing wounds.
***4. Muscle Damage*:** Adult stem cells repair muscle damage after heart attacks. Researchers found that injecting bone marrow stem cells into patient who is going to have heart attack, resulted in 33% improvement in heart functionality and 68% tissue regrowth. [11]
***5. Cure from Leukemia*:** Hematopoietic stem cells are transplanted into leukemic patients to generate new blood cells.

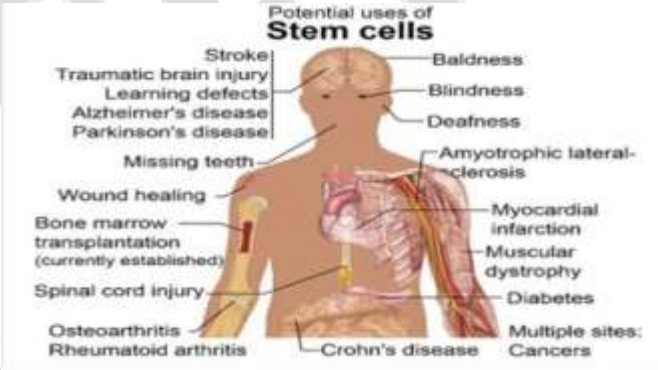

Fig 2. Potential Uses of Stem Cells

6. Cancer Treatment: Adult stem cells cure certain cancers through bone marrow transplants. This is a vital and often, life-saving treatment because, chemotherapy destroys not only the cancer cells, but also the bone marrow cells.
***7. Testing New Drugs*:** Laboratory grown stem cells are useful for testing chemicals and drugs before they are trialed in people. The cells are directed to differentiate into cell types for screening of the drug. These cells mimic the response of human tissue to the drug being tested. This makes drug testing safer, cheaper and more ethically acceptable to those who oppose the use of animals in pharmaceutical testing. [10]
***8. Testing Gene Therapy Methods*:** Stem cells are used to study development of new methods for gene therapy that may help people suffering from genetic diseases. [5]
***9. Human Development Study*:** Stem cells are used to study the pathway of human development, differentiation of cell types and their functions. This may help to realize why stem

cells become malignant and how certain genetic diseases developed.

VIII. CHALLENGES IN STEM CELL THERAPY:

Researchers face several challenges as they study stem cells. Some such technical hurdles include:

1. Though stem cells exist in adult tissues, they are not present in large numbers. So, it is difficult to find and extract stem cells for growth.
2. It is also difficult to grow cells into large batches of unspecialized cells in laboratory.
3. Acceptance of the implanted stem cell by the native body cell is dependent on effective integration into the patient's body systems and other cells. [2]
4. Immunological rejection is a major hurdle to successful stem cell transplants. When patient's immune system views the transplanted cells as foreign, it wages an attack on the newly transplanted cells. To reduce the changes of rejection, the patient must take strong immunosuppressive drugs, which in turn leave the patient vulnerable to infection.

IX. ETHICAL CONTROVERSY WITH STEM CELLS:

Embryonic stem cells are derived from embryos created outside of a woman's body (in vitro) using donated eggs fertilized in laboratory, and not from the eggs fertilized inside the body. The collection of embryonic stem cells requires destroying the embryo. So, a great controversy occurs if the process involves the destruction of human life or not. [7]

Some scientists have obtained embryonic stem cells through therapeutic cloning. During this process, scientists replace the nucleus of an egg cell with the nucleus of some other body cell to grow an embryo from which stem cells with specific properties can be harvested. This raises a wider range of objection in that saying, a potential life is created for a specific purpose. Despite of such challenges, stem cells still hold promise for treating many diseases.

X. CONCLUSION:

Stem cell therapies would give a great hope to the patients who suffers from the diseases which are considered as incurable nowadays. At present, more trials and researches are required to realize the appropriate role of stem cell therapy in world of regenerative medicine. Current study on stem cell therapy has illuminated the aspects of clinical practice for regeneration in muscular dystrophy, intervertebral disc degeneration, cerebral infarcts and transplantation medicines.

XI. FUTURE WORK:

We look forward to merge statistical pattern recognition and computer vision to cell imaging, thus achieving cell sorting. Multiple cell image processing and feature (like – morphology, structure, cell size, etc.) extraction from the same may help to pave the path towards stem cell's status determination. Such status in turn will have a vital role in specific stem cell based therapies.

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