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Review Research Paper

Stem Cells: An Update

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Abstract

Stem cells are unspecialized cell. They are capable of continuous self-renewal. They can give rise to specialized cell types. Since the discovery of stem cells till now, for years scientists have been working on the numerous possibilities that the stem cells have and studies carried out to channelize their sources to the best for benefit of mankind. Starting from the knowledge of only embryonic stem cells as the source of stem cells, now it is known that they can be extracted from cord blood and mature adult tissue. Likewise, their applications earlier limited to restoration of diseased and damaged tissue or organs have also found their place in Forensic science investigations as well. More recently use of stem cells have been found to be useful in the research arena allowing the scientists to develop models for studying human biology, pathology and genetics. This article is a general update on stem cells, their properties, sources and current applications in Medicine.

Key Words: Stem cells, Embryonic stem cells, Adult stem cells, Mesenchymal stem cells

Introduction:

Stem cells are unspecialized cells in the human body that are capable of becoming specialized cells, each with new specialized cell functions. [1] The term stem cell was proposed for scientific use by Russian histologist Alexander Maksimov in 1908. [2] Fluorescent markers can be used to identify stem cells hidden among ordinary adult cells. [3] Human embryonic stem cells are recognized by the marker proteins they express (green). (Fig.1)

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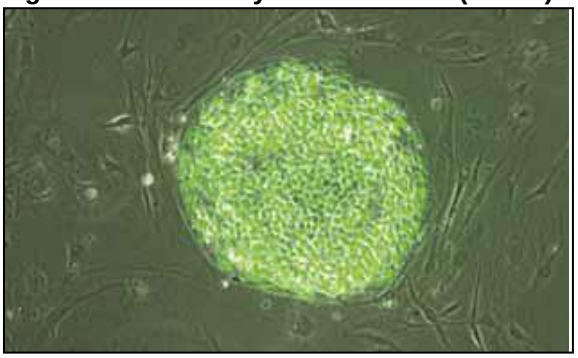
Fig. 1: Human Embryonic Stem Cell (Green)



Terms Related to Stem Cells: [3]

Adult Stem Cell: A stem cell derived from the tissues or organs of an organism after birth (in contrast to embryonic or fetal stem cells).

Embryonic Stem Cell: Embryonic stem cells are derived from the inner cell mass up to the stage of blastocysts. These cells can be cultured indefinitely under in vitro conditions that allow proliferation without differentiation, but have the potential of differentiating into any cell of the body.

Fetal Stem Cell: a stem cell derived from fetal tissue, including placenta. A distinction is drawn between the fetal germ cells, from which the gametes develop, and fetal somatic cells, from which rest of the organism develops.

In Vitro and In Vivo: outside and inside the body; in vitro (literally, in glass) generally means in the laboratory.

Mesenchymal Stem Cells: Stem cells present in human bone marrow and umbilical cord that

have been shown to differentiate into a variety of cell types.

Multipotent: Multipotent stem cells are those which are capable of giving rise to several different types of specialized cells constituting a specific tissue or organ. For example, blood-forming (hematopoietic) stem cells are single multipotent cells that can produce all cell types that are normal components of the blood.

Oligopotent: Stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.

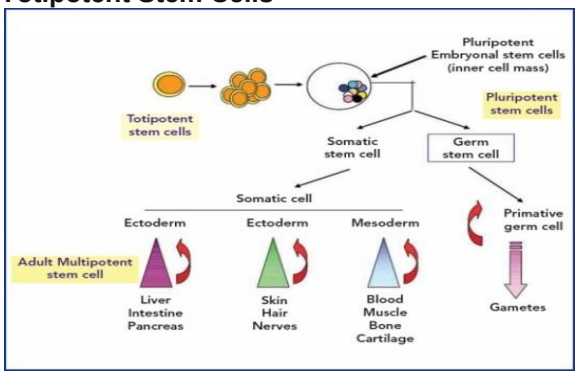
Pluripotent: Pluripotent stem cells have the ability to give rise to various types of cells that develop from the three germ layers (mesoderm, endoderm and ectoderm). They have the potential to generate into every cell type in the body, but cannot develop into an embryo on its own.

Somatic stem cell: an undifferentiated cell found among differentiated cells in a tissue or organ, which can renew itself and can differentiate to yield the major specialized cell types of the tissue or organ.

Totipotent: Capable of giving rise to all tissues and organs, including placenta.

Unipotent: Cells can produce only one cell type, their own, but have the property of self-renewal. They have the lowest differentiation potential.

Fig. 2: Stem Cell Lineage Starting From Totipotent Stem Cells



Properties of Stem Cells:

Stem cells have three general properties:

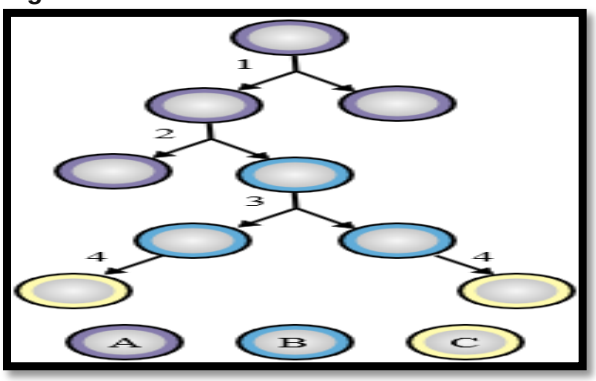
1. They are unspecialized,
2. They are capable of continuous self-renewal,
3. They can give rise to specialized cell types. [4, 5]
4. Stem cells can divide either symmetrically (allowing the increase of stem cell number) or asymmetrically. Asymmetric divisions keep the number of stem cells unaltered 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 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. [6]

Fig. 3 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 differentiation.

5. 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). [7]

Fig. 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)

Classification of Stem Cells:

Stem cells can be divided into two categories: **Embryonic and Adult**. [4, 5]

Embryonic Stem Cells are totipotent cells capable of differentiation into virtually any cell type, as well as being propagated indefinitely in an undifferentiated state. The use of embryonic stem cells generates several ethical concerns regarding the consumption of blastocysts. This makes postnatal stem cells a more feasible approach for translation into clinical practice. [8]

Adult Stem Cells: are not totipotent, and they can be further classified depending on their origin and differentiation potential.

These are further classified as follows: [2, 4-11]

- **Embryonic Stem Cells (ECS):** They are derived from the inner cell mass of the blastocyst. They can make all the cell types in the body and can self-renew (copy themselves) almost forever, so large supplies can be made. However, they have ethical issues associated with their use and their rate of differentiation is difficult to control and they might as well form tumors after injection.
- **Embryonic Germ Cells:** Human embryonic germ (EG) cells share many of the characteristics of human ES cells, but differ in significant ways. Human EG cells are derived from the primordial germ cells, which occur in a specific part of the embryo/fetus called the gonadal ridge, and which normally develop into mature gametes (eggs and sperm).

Their isolation requires the generation of embryoid bodies from EG cells, which consists of an unpredictable mix of partially differentiated cell types. The embryoid body-derived cells resulting from this process have high proliferative capacity and gene expression patterns that are representative of multiple cell lineages. Advantages of these cells are that they are non-tumorigenic unlike embryonic stem cells but at the same time their isolation requires destruction of foetuses thus limiting their use till now on mice experiments.

Also, they have less population doubling (70-80 cells doublings) as compared to Embryonic stem cells which cam make 200-300 cell doublings per sample.

- **Amniotic Fluid / Fetal Stem Cells:** They are derived from aspirates of amniocentesis during genetic screening without any damage to embryo. They are used to make adipocytes, chondrocytes, osteoblasts, myocytes, endothelial cells, neuron-like and live cells. They are easier to obtain than other embryonic cells and have the same pluripotency as embryonic stem cells but are not tumorigenic. Their therapeutic value remains to be discovered and at times their retrieval can lead to loss of pregnancy and risk to unborn child (0.06% cases).
- **Induced Pluripotent Stem Cells (iPS):** They refer to adult or somatic cells that have been coaxed to behave like embryonic cells. They can make all types of cells in the body.

They could provide patient specific treatment but they can have a carcinogenic / tumorigenic potential. Also, it has not yet been established how reprogramming works in these cells and their need further comparison with embryonic stem cells.

- **Umbilical Cord Blood Stem Cells:** They are taken from cord blood after the birth of the baby. They can differentiate into several cell types like liver cells, skeletal muscle, neural tissue and immune cells and can be frozen and stored. Their limitations lies in fact that there is still a need to know how to them and a limited number of cells can be procured from umbilical cord. Also, graft reaction/rejection is a possibility. They are only proven of use in blood disorders.
- **Adult Stem Cells/ Tissue Stem Cells / Mesenchymal Stem Cells (MSCs):** They are somatic /postnatal stem cells in several mesenchymal tissues. They are used to make only the types of cells that belong in their own tissue and they find application in transplantation therapy.

Since, they are already partly specialised, it makes more straightforward to obtain the particular specialised cell type required. But, customising these stem cells is not possible and tissues must be 'matched' or come from the patient's own body for use in treatments. Scientists are still learning how to multiply; control and use different types of tissue stem cells.

- **Bone Marrow Mesenchymal Stem Cells (BMMSC):** Their source is bone marrow of adult bones. They can make cells of the skeletal tissues: bone, cartilage, fat and support blood stem cells to make new blood cells. They are easily obtained from the bone marrow of patients used for efficient generation of skeletal tissues in the body. In vitro expansion capability appears to be lower. Donor age is important consideration for clinical efficacy of bone formation.

Applications of Stem Cells:

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 arena of Medicine ranging from therapeutics to replacement of lost tissues. [12]

Some of the Medical conditions where stem cells have found their use are as follows: [12-19]

- Type 1 Diabetes in Children
- Nervous system diseases like Parkinson's disease and Alzheimer's disease
- Immunological diseases like severe combined immunodeficiency disease (the "bubble boy" disease), Wiskott-Aldrich Syndrome, and the autoimmune disease lupus
- Diseases of bone and cartilage like osteogenesis imperfecta and chondrodysplasias
- Cancer, Cardiac diseases, Spinal cord injury
- Blindness
- Treatment of urological disorders like complicated bowel resection and possible complications, such as adhesions, mucus secretion, metabolic derangements and even malignant transformation
- Age -related functional defects
- Lung diseases like Pulmonary idiopathic arterial hypertension, chronic obstructive pulmonary disease
- Chronic liver injuries
- Digestive disorders like Crohn's disease
- Arthritis, Inflammatory skin diseases and Muscular diseases

Stem cells are also used in the field of Medical research: [12-19]

- Study of human developmental biology
- Models of human disease that are constrained by current animal and cell culture models
- Transplantation and Gene Therapy
- Forensic DNA profiling and Correlation and collection of Ante-mortem and Post-mortem data

Conclusion:

A silhouette of the potential use of stem cells for the treatment of human disease is now perceptible. [12] 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. [20] 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 (autologous sources).

This saves the need for the use of organ donations which are always short at the supply end and subsequently improves the patient acceptance of the replaced organ.

More recently use of stem cells have been found to be useful in the research arena allowing the scientists to develop models for studying human biology, pathology and genetics.

The coming years will undoubtedly usher 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. [21]

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