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Programme: M.Sc., Biochemistry
Course Title : Cell Biology
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Unit-5
STEM CELLS

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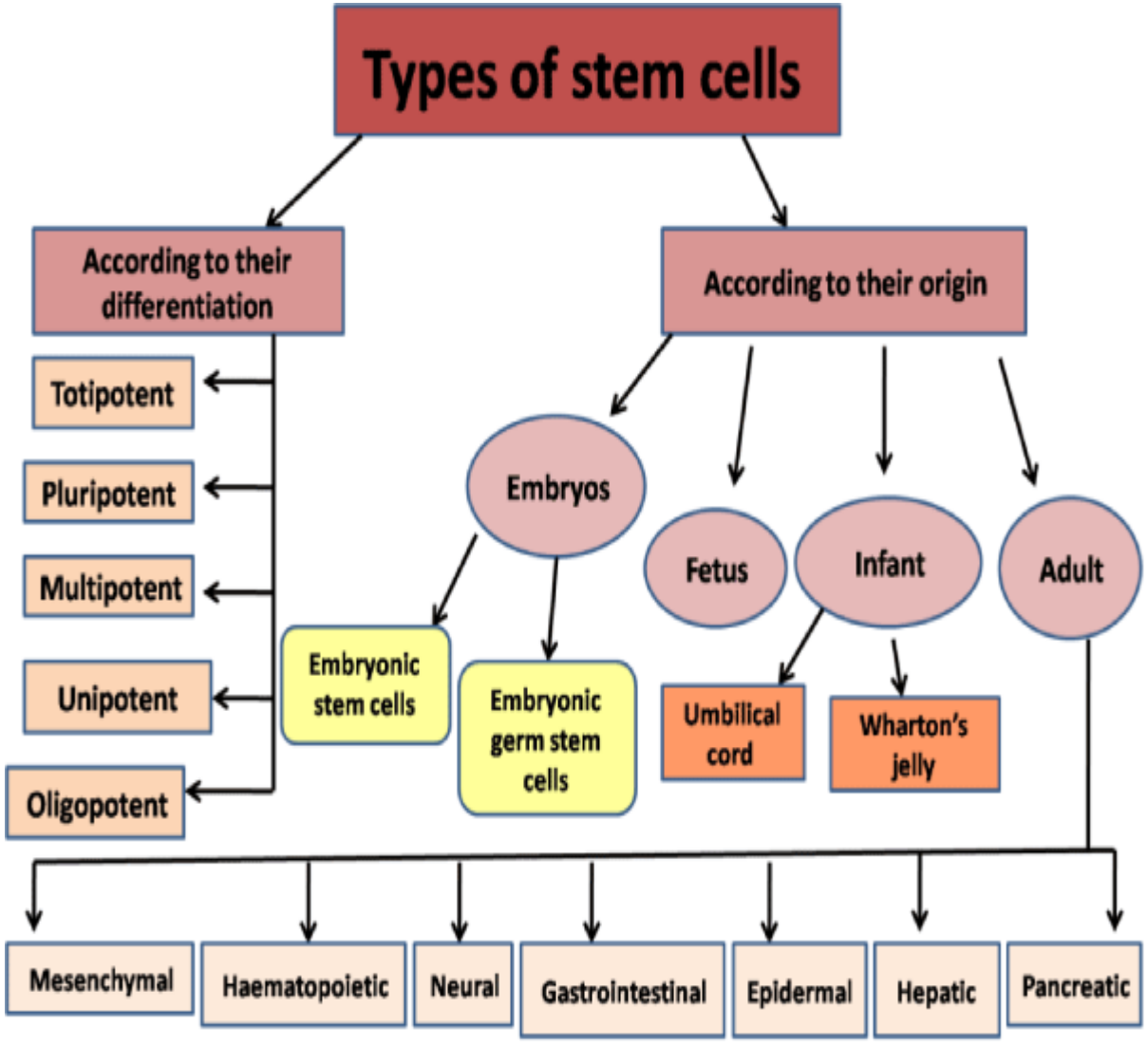
History

- The **history of stem cell therapy** and research began in the year 1902 when a Russian histologist Alexander M. Maximow referred to them (stem cells) as ‘polyblasts’ and ‘wandering cells at rest’
- From 1896 until 1902, Maximow authored documents, which identified his interest in the blood and connective tissues
- He confirmed the unitarian theory of hematopoiesis and proved that all blood cells mature from a precursor cell
- Since then, scientists from all over the world followed the study of stem cells, experimenting (on mice, plants and human patients) in search of a cure for various disorders, diseases, and injuries
- The history of stem cell therapy was successfully investigated in 1969 by *Edward Donnall Thomas*
- He performed the first bone marrow transplant with stem cells collected from another person

What are Stem Cells

- They are not specialized cell and have the ability of self replicating , differentiation according to suitable signals
- Stem cells can reproduce itself over and over again through asymmetric cell division, they can produce the newly produced offspring cells preserve the characteristics of the mother cell that has a different potency and lineage potential, such as a committed progenitor that transiently amplifies to make several offspring



Classification and Sources of Stem Cells:

Stem cells can be classified according to their origin into four broad types,

1. From Embryos
2. from the fetus
3. from the infants
4. from the adult.

Also, they can be classified according to their potency

Stem Cells Classification according to their Origin

Embryonic Stem Cells (ESCs)

- Embryonic stem cells are pluripotent, self-renewing cells that can be derived from both mouse or human blastocysts, they are taken from the very early stages of embryo development after 4-5 days after fertilization
- They can be stored in culture as undifferentiated cell lines and can be stimulated to differentiate into any cell line
- They can differentiate into endoderm, mesoderm, and ectoderm embryonic germ layers, and also any type of somatic cells
- They, therefore, hold a great capacity in tissue regeneration therapy

Embryonic Germ Stem Cells:

- Embryonic Germ (EG) cells are taken from the later stages of the embryo development cells. They are derived from Primordial Germline Cells (PGCs) in the early development. They are mainly isolated from the fetal tissue in narrow-window timing
- The PGC-derived cells were pluripotent, although, it was not possible to demonstrate pluripotency by generating the formation of teratomas in mice

Fetal stem cells:

- Fetal stem cells are primal cell types found in the organs of the fetuses. They are able to differentiate into two types of stem cells: pluripotent stem cells and hematopoietic stem cells
- Neural crest stem cells, fetal hematopoietic stem cells and pancreatic islet cells have been isolated in the fetuses
- Human fetal stem cells have been used by many people, children and adults that are suffering from many of mankind’s most devastating diseases

Infant stem cell

- Umbilical cord stem cells: Umbilical cord blood contains prevalent stem cells which differ from those of bone marrow and adult peripheral blood
- Cord blood stem cells have shown to be multipotent as it being able to differentiate into neurons and liver cells
- Wharton’s jelly: Wharton’s jelly, which is the umbilical cord matrix, is considered to be a source of mesenchymal stem cells
- These cells express typical stem cell markers, can be propagated for long times and can be induced to differentiate *in vitro* into neurons

Adult stem cell

- any stem cells taken from mature tissue; they are found in the tissues of a fully developed child (whole embryo) or adult and can only produce a limited number of cell types
- They have limited potential as compared to the stem cells that derived from embryos and fetuses because of the stage of development of these cells
- They play a vital role in tissue repair, regeneration; and they are referred to their tissue origin
- Bone marrow is an abundant source of adult stem cells
- Mesenchymal stem cells:
- Mesenchymal Stem Cells (MSCs) are a different population of cells with the potential to differentiate into various somatic lineages
- They were at first described as adherent cells with a fibroblast-like appearance that can differentiate into osteocytes, chondrocytes, adipocytes, tenocytes and myocytes

- MSCs can be isolated from the bone marrow and readily discreted from the hematopoietic stem cells due to their plastic adherence
- They are used in tissue engineering and regenerative medicine
- They are character by long-storage without major loss of their potency

Hematopoietic stem cells:

- cells having the self-renewing potential and the capacity to give rise to differentiated cells of all hematopoietic lineages
- Therefore, they transplanted for complete healing of hematologic disorders and after high-dose chemotherapy against malignant diseases

Neural Stem Cells:

- multipotent and self-replication cells, they are established in specialized molecular microenvironments in the adult mammalian brain
- They can display the potential role in cellular therapy of the brain

Gastrointestinal stem cells: The stem cells of the gastrointestinal tract reside in a “niche” in the intestinal crypts and gastric glands

- The mechanism and the direction of the diffusion of this converted clone in the gastrointestinal mucosa are hotly disputed, and the central to this case is the position and nature of the gastrointestinal stem cells

Epidermal stem cells:

- The mammalian epidermis is a rapidly rejuvenating tissue that consists of three types of keratinocytes with varying differentiation potential: epidermal stem cells, Transiently Amplified Cells (TA cells) and terminally differentiated cells
- The epidermal stem cells have free self-renewal power
- They are establishing in the basal layer and remarkable in maintaining homeostasis and cellular regeneration of normal skin; wound healing and neoplasm formation, whereas TA cells, progeny of the epidermal stem cells, undergo terminal differentiation after 3–5 divisions
- After division, TA cells leave the basal layer and move through the suprabasal layers to the tissue surface, where they are periodically shed as squames

Hepatic stem cells:

- The liver has a strong regenerative capacity, utilizing different modes of regeneration according to the type and extent of the injury. Mature liver cells can propagate to replace the damaged tissue permit the recovery of the parenchymal function
- Chronic liver injury gives rise to a potential stem cell compartment which is located in the smallest branches of the intrahepatic biliary tree being activated, which called oval cell ductular reaction
- These oval cells are derived from the canal of Hering, which amplifies this biliary populations prior to these cells differentiate into hepatocytes
- In the human liver, the organization of the biliary tree is different, with the canal of hering extending to the proximate third of the lobule and so apparently requiring a name change from oval cells to hepatic progenitor cells

Pancreatic stem cells:

- Insulin-producing cells previously generated from pluripotent stem cells.
- The generation of these cells would provide a novel cell source for drug discovery and cell transplantation therapy in people suffering from diabetes
- Insulin-producing beta-cells turnover every 40-50 days by processes of apoptosis and the propagation and differentiation of the newly islet cells from progenitor epithelial cells, which are located in the pancreatic ducts

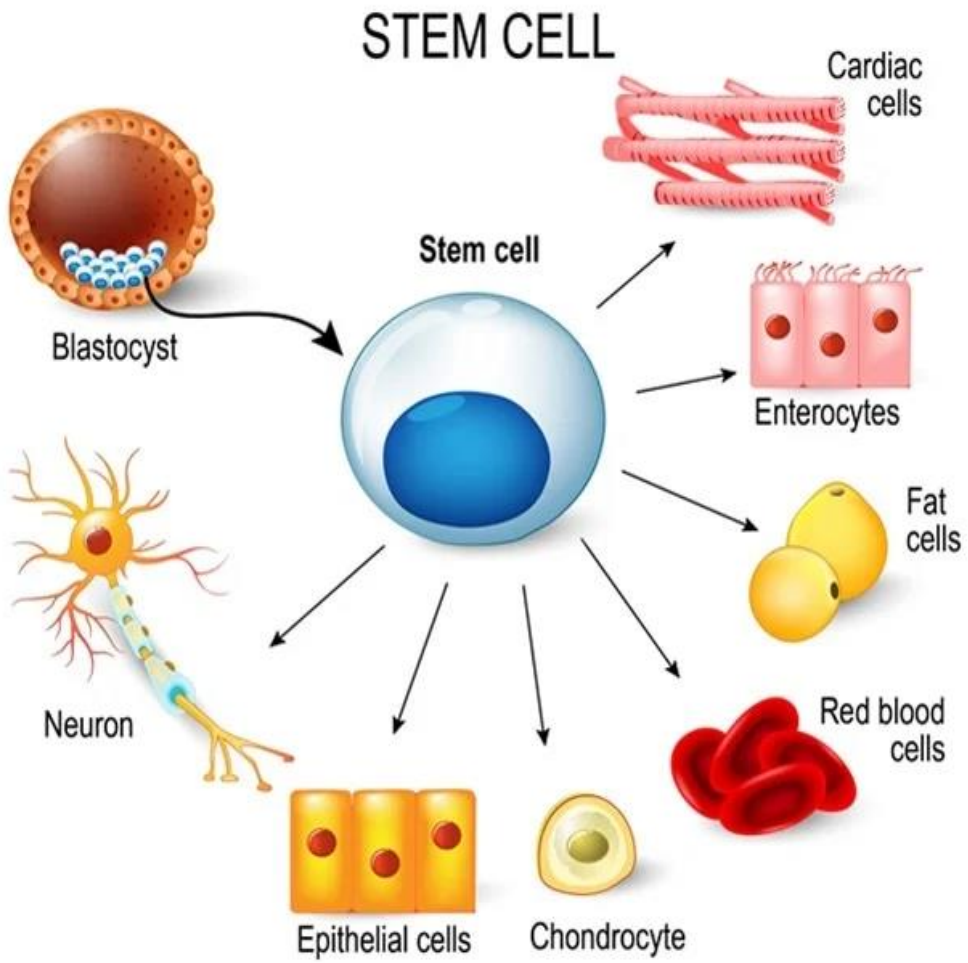


Fig. News Medical.net

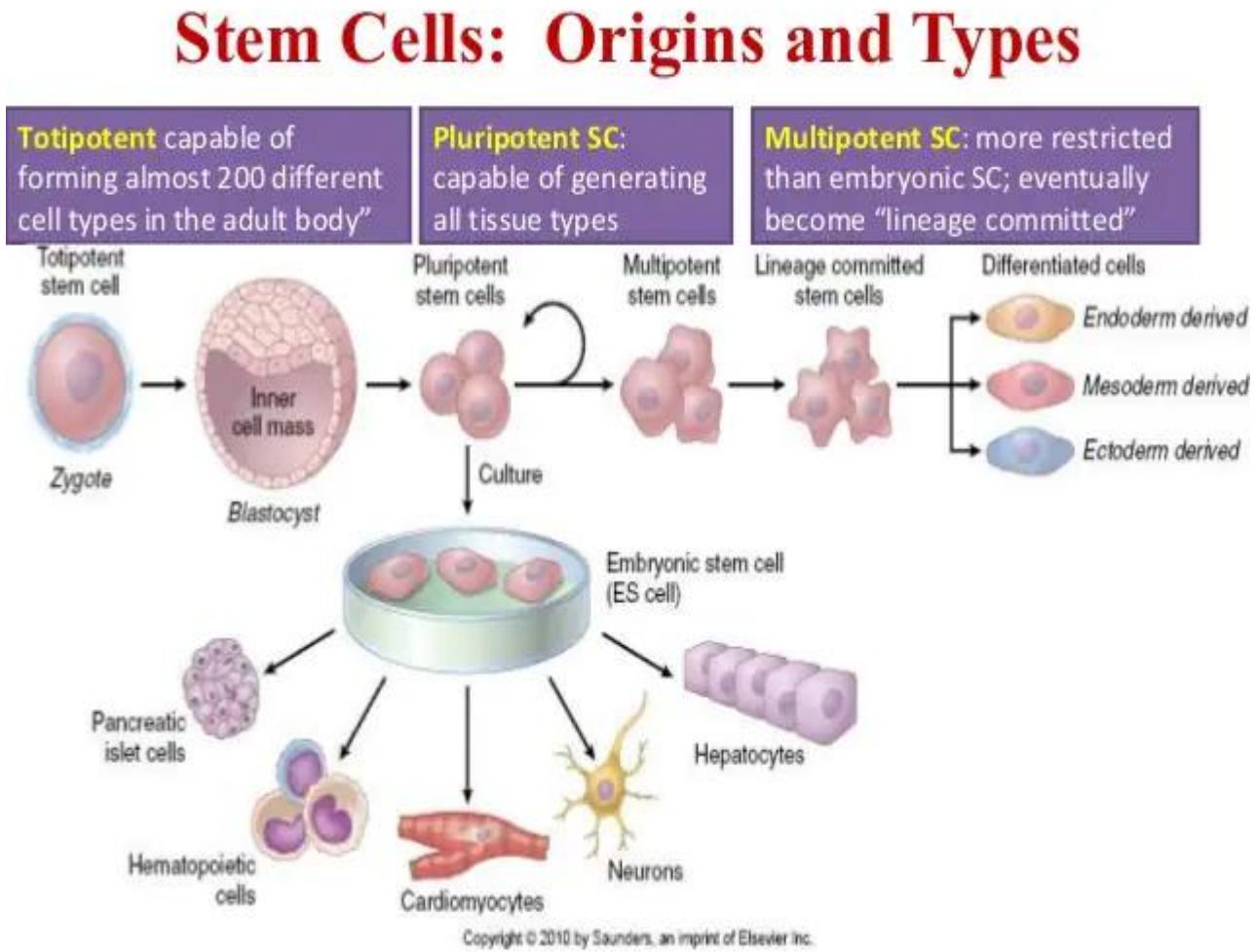


Fig. Elsevier

Types of stem cells according to their differentiation

- Stem cells can be classified according to their differentiation potential as a totipotent, pluripotent, multipotent, unipotent and oligopotent
- Totipotent stem cells: Totipotency means that it has the total potential to give rise to all types of cells
- Totipotent is the capacity of a single cell to divide and differentiate into all cell types in an organism and produce fertile offspring
- Oocytes and sperm are the best differentiated cells in our body and they are capable of forming any tissue in the body

Pluripotent stem cells:

- Pluripotency is the ability of the cells to produce any type of cells in the organism.
- They have been derived from the mouse embryo.

- All are capable of differentiating into cells representative of a variety of adult tissue types in various assays, including embryoid body, teratoma, and some can contribute to mouse development in chimeras.
- There are many differences being recognized among pluripotent stem cell types, such as their morphology, gene expression profiles and growth factor requirements

Multipotent stem cells:

- Multipotency means to those cells that can only give rise to cells of the tissue from which they are isolated

Unipotent stem cell:

- Adult stem cells are found in the tissues of the adults they produce a limited number of cell types and can repair damaged tissue by replacing specialized cells

- Because of their restricted lineage, they were thought to be either multipotent, with the ability to differentiate into a limited range of cells or unipotent, with the ability to produce only one cell type

Oligopotent stem cells:

- Oligopotency means to those cells that can differentiate into only a few cell types, like lymphoid or myeloid stem cells

Stem Cell Research

Scientists use different types of stem cells for this purpose:

- Neural stem cells (NSCs)
- Mesenchymal stem cells (MSCs)
- Embryonic stem cells (ESCs)
- Induced pluripotent stem cells (iPSCs)

Some of the clinical application of stem cells

1. Stem Cells and diabetes mellitus

- Stem cells have generated incredible interest for repairing failing tissues and organs
- Stem cell therapy has become a tantalizing idea to provide glucose-responsive insulin-producing cells to Type 1 diabetic patients as an alternative to islet transplantation
- Mesenchymal stem cells will grow and differentiate according to their environment
- When MSCs injected into the pancreas *in vivo*, it is expected that MSCs will differentiate into pancreatic cells that have both exocrine and endocrine functions.
- Thus, transplantation of MSCs from bone marrow stem cells can repair the pancreas in its role to provide paracrine effects and other cell differentiation effects

2. Parkinson’s Disease

- Parkinson’s disease (PD) is a widespread neurodegenerative disease that characterized by bradykinesia, rigidity, and tremor
- The pathological causes of PD are due to the Decrease of Nigrostriatal Dopamine (DA) neurons, but neuronal degeneration also occurs in non-DA-ergic systems
- MSCs are capable of differentiating into tyrosine hydroxylase-positive neurons and can ameliorate motor performance in mice Parkinson’s disease model
- Moreover, it has been demonstrated that cells with DA-ergic can be produced from both rat and human MSCs, and that transplantation of these cells showed an improvement of motor function in an animal model of PD

3. Heart Disease

- Cardiac transfer of stem and progenitor cells can have an adequate effect on tissue perfusion and contractile performance of the injured heart
- Stem cells have the potency to promote myocardial perfusion and contractile performance in patients who are suffering from acute myocardial infarction, advanced coronary artery disease, and chronic heart failure

4. Autoimmune diseases

- According to their ability to modulate immune responses, MSCs have also been proposed as a treatment for autoimmune diseases
- Patients who are suffering from severe autoimmune diseases do not respond to the standard therapy and often require autologous or allogeneic Hematopoietic Stem Cell Transplantation (HSCT)

5. Liver diseases

- Liver failure and cirrhosis occur as a result of a variety of chronic hepatic injuries
- MSCs have the potential to be used for the treatment of liver diseases due to their regenerative potential and immunom-odulatory properties
- They display sequential and overlapping severe pathogenic processes that include severe inflammation, hepatocyte necrosis, and fibrosis/ cirrhosis, and carry a high mortality rate
- MSCs have been demonstrated to play an immune-modulatory role through producing inhibitory cytokines or inducing the development of regulatory T cells
- MSC therapy appears to be effective in regulating the immune response in tissue injury, transplantation, and autoimmunity in both animal models of liver disease and patients in clinical trials

6. Kidney disease

- Mesenchymal stem cells can migrate to deteriorate kidney tissue where they can generate an array of anti-inflammatory cytokines and chemokines that can alter the course of the injury
- Mesenchymal stem cells are thought to elicit repair through paracrine and/ or endocrine mechanisms that mend the immune response resulting in tissue repair and cellular replacement

Reference

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- Mayoclinic.org