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# Stem cells and their potential therapeutic applications

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**Abstract**

Stem cells are undifferentiated biological cells that can differentiate into specialized cells. They can divide through mitosis to produce more stem cells. In mammals, there are two broad types of stem cells i) Embryonic stem cells ii) Adult stem cells. The classical stem cells possess two properties) Self-renewal ii) Potency. Diseases and conditions where stem cell treatment is being investigated include: Diabetes, Rheumatoid arthritis, Parkinson's disease Alzheimer's disease, Osteoarthritis, Stroke and traumatic brain injury repair, Learning defects, Spinal cord injury repair, Heart infarction, Anti-cancer, Baldness, Replace missing teeth, Repair hearing, Restore vision, Amyotrophic lateral sclerosis, Crohn's disease, Wound healing. Stem cell therapy is the use of stem cells to treat or prevent a disease or condition. Research is underway to develop various sources for stem cells. Stem cells are in treatments for neurodegenerative diseases and conditions, diabetes, heart disease, and other conditions. Stem cell therapy also has some disadvantages. Immunosuppression is required before treatment. Pluripotency in stem cells could also make it difficult to obtain a specific cell type. Some stem cells form tumors after transplantation. Stem cells have a very promising role and potential in therapeutic application of various human diseases and if researched and utilised in the correct way can prove to be a boon in medical field.

**Keywords:** pluripotent, self-renewal, Stem cells, therapeutic applications.

## Introduction

Stem cells are undifferentiated biological cells that can differentiate into specialized cells. They can divide through mitosis to produce more stem cells. They are found in multicellular organisms. In mammals, there are two broad types of stem cells:

a. Embryonic stem cells, which are isolated from the inner cell mass of blastocysts.
b. Adult stem cells, which are found in various tissues.

In adult organisms, stem cells and progenitor cells act as a repair system for the body. It helps in replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells like ectoderm, endoderm and mesoderm. They also maintain the normal turnover of regenerative organs like blood, skin, or intestinal tissues.

There are three sources of autologous adult stem cells in humans:

1. Bone marrow- It requires extraction by harvesting, i.e. drilling into bone. Usually the femur or iliac crests are used for this purpose.
2. Adipose tissue- It requires extraction by liposuction.
3. Blood-It requires extraction through apheresis. In this method, blood is drawn from the donor and passed through a machine that extracts the stem cells and returns other portions of the blood to the donor.

4. Stem cells can also be taken from umbilical cord blood just after birth.

## Properties:

The classical stem cells possess two properties:

1. Self-renewal- It is the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
2. Potency- It is the capacity to differentiate into specialized cell types. This requires stem cells to be either totipotent or pluripotent.

Types of stem cells:

## 1. Embryonic:

Embryonic stem cells are stem cells derived from the inner cell mass of a blastocyst. Blastocyst is an early-stage embryo[1]. Human embryos reach the blastocyst stage 4–5 days post fertilization. At this time they consist of 50–150 cells. Embryonic stem cells are pluripotent. They give rise during development to all derivatives of the three primary germ layers: ectoderm, endoderm and mesoderm. They do not contribute to the extra-embryonic membranes or the placenta. (Figure 1)

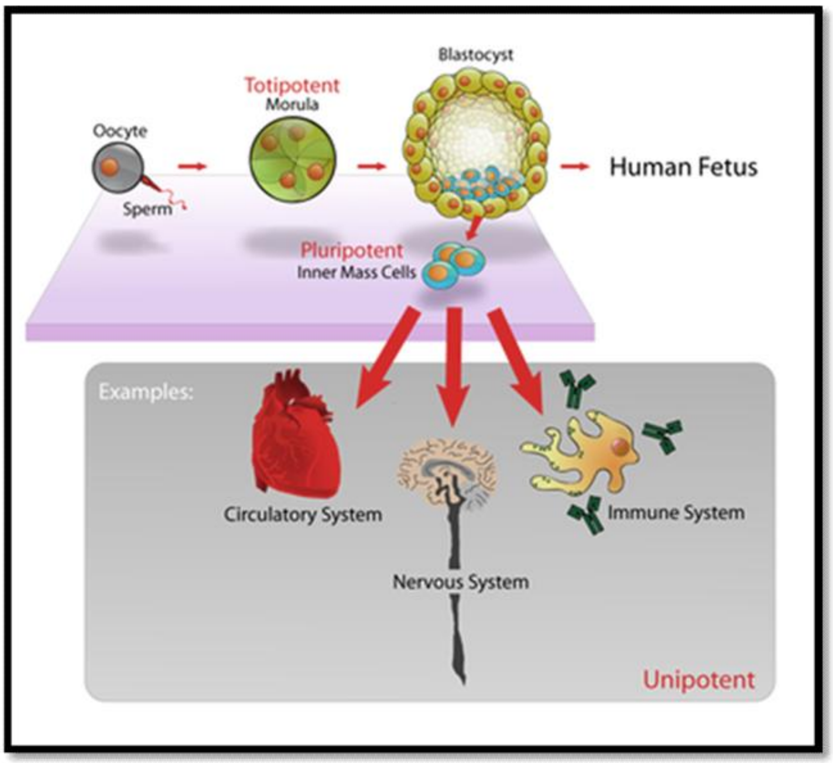


**Figure 1.** Pluripotent, embryonic stem cells originate as inner cell mass (ICM) cells within a blastocyst. These stem cells can become any tissue in the body, excluding a placenta. Only cells from an earlier stage of the embryo, known as the morula, are totipotent, able to become all tissues in the body and the extra embryonic placenta.

A human embryonic stem cell is also defined by the expression of several transcription factors and cell surface proteins. The transcription factorsOct-4, Nanog, and Sox2 form the core regulatory network. It ensures the suppression of genes that lead to differentiation and the maintenance of pluripotency[2].

## 2. Foetal:

The primitive stem cells located in the organs of foetuses are referred to as foetal stem cells [3]. There are two types of foetal stem cells:

a. Foetal proper stem cells come from the tissue of the foetus proper. They are obtained after an abortion. These stem cells are not immortal but have a high level of division and are multipotent.

b. Extra embryonic foetal stem cells come from extra embryonic membranes. They are not distinguished from adult stem cells. These stem cells are acquired after birth. They are not immortal but have a high level of cell division, and are pluripotent [4]. (Figure 2)

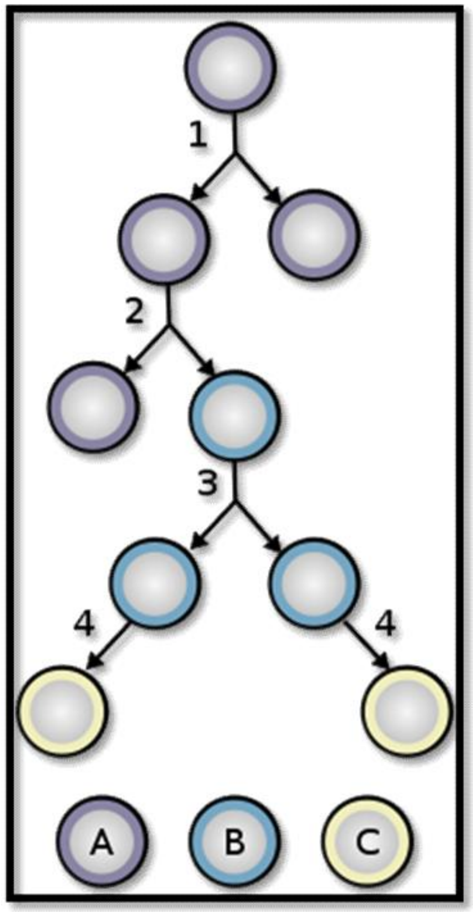


**Figure 2**. Stem cell division and differentiation. A: stem cell; B: progenitor cell; C: differentiated cell; 1: symmetric stem cell division; 2: asymmetric stem cell division; 3: progenitor division; 4: terminal differentiation

### 3. Adult:

Adult stem cells are also called somatic stem cells. They are stem cells which maintain and repair the tissue in which they are found. They can be found in children as well as in adults [5].

Pluripotent adult stem cells are rare and small in number. But they can be found in umbilical cord blood and other tissues[6]. Bone marrow is a rich source of adult stem cells [7].They have been used in treating several conditions including spinal cord injury [8], liver cirrhosis[9], chronic limb ischemia [10] and end stage heart failure[11]. The quantity of bone marrow stem cells declines with age and is greater in males than females during reproductive years [12].

### 4.Amniotic:

Multipotent stem cells are also found in amniotic fluid. These stem cells are very active. They expand extensively without feeders and are not tumorigenic. Amniotic stem cells are multipotent and can differentiate in cells of adipogenic, osteogenic, myogenic, endothelial, hepatic and neuronal lines [13].

### 5. Cord blood:

Cord blood stem cell (CB-SC) is multipotent and displays embryonic and hematopoietic characteristics. Phenotypic characterization demonstrates that (CB-SCs) display embryonic cell markers (e.g., transcription factors OCT-4 and Nanog, stage-specific embryonic antigen (SSEA)-3, and SSEA-4) and leukocyte common antigen CD45. CB-SCs display very low immunogenicity as indicated by expression of a very low level of major histocompatibility complex (MHC) antigens and failure to stimulate the proliferation of allogeneic lymphocytes[14-15]. They can give rise to three embryonic layer-derived cells in the presence of different inducers[14,16].

### 6. Induced pluripotent:

These are adult cells (e.g. epithelial cells) reprogrammed to give rise to pluripotent capabilities. Using genetic reprogramming with protein transcription factors, pluripotent stem cells equivalent to embryonic stem cells have been derived from human adult skin tissue[17-19].

### Treatments:

Diseases and conditions where stem cell treatment is being investigated include:

- Heart infarction
- Anti-cancer
- Baldness
- Replace missing teeth
- Repair hearing
- Restore vision
- Amyotrophic lateral sclerosis
- Crohn's disease
- Wound healing
- Diabetes
- Rheumatoid arthritis
- Parkinson's disease
- Alzheimer's disease
- Osteoarthritis
- Stroke and traumatic brain injury repair
- Learning defects
- Spinal cord injury repair

Stem cell therapy is the use of stem cells to treat or prevent a disease or condition. Research is underway to develop various sources for stem cells. Stem cells are in treatments for neurodegenerative diseases and conditions, diabetes, heart disease, and other conditions [20].

### Neurodegeneration:

Stem cells may be used to treat brain degeneration, such as in Parkinson's, Amyotrophic lateral sclerosis and Alzheimer's disease [21-22].Healthy adult brains contain neural stem cells which divide to maintain general stem cell numbers or become progenitor cells. In healthy adult animals, progenitor cells migrate within the brain and function primarily to maintain neuron populations for olfaction (the sense of smell). Pharmacological activation of endogenous neural stem cells has been reported to induce neuroprotection and behavioral recovery in adult rat models of neurological disorder [23-25].

### Brain and spinal cord injury:

Stroke and traumatic brain injury lead to cell death. It is characterized by loss of neurons and oligodendrocytes within the brain. A small clinical trial was underway in Scotland in 2013, in which stem cells were injected into the brains of stroke patients[26].

### Heart:

Stem cell therapy for treatment of myocardial infarction usually makes use of autologous bone marrow stem cells. Other types of adult stem cells may be used such as adipose-derived stem cells [27].

Possible mechanisms of recovery include:

- Generation of heart muscle cells
- Stimulation of growth of new blood vessels to regenerate damaged heart tissue
- Secretion of growth factors

It may be possible to have adult bone marrow cells differentiate into heart muscle cells.

Stem cell therapy has the potential for cardiac tissue regeneration to reverse the tissue loss underlying the development of heart failure after cardiac injury [28].

### Haematopoiesis (blood-cell formation):

The human immune-cell allows the human body to defend itself from rapidly adapting antigens. The immune system fights against the pathogenesis of disease. The immune system plays in defence. Degradation of immune system is fatal to the organism. Diseases of hematopoietic cells are diagnosed and classified by a subspecialty of pathology known as haematopathology. The immune cells recognize foreign antigens which cause challenges in the treatment of immune disease.

Mature human red blood cells may be generated ex vivo by hematopoietic stem cells (HSCs), which are precursors of red blood cells. In this process, HSCs are grown together with stromal cells. It helps in creating an environment that mimics the conditions of bone marrow, the natural site of red-blood-cell growth. Erythropoietin (growth factor) is added. It coaxes the stem cells to complete terminal differentiation into red blood cells [29].

**Baldness**:

Hair follicles also contain stem cells. These follicle stem cells may help in treating baldness through an activation of the stem cells progenitor cells. Baldness is treated by activating already existing stem cells on the scalp. Baldness treatments may be able to signal follicle stem cells to give off chemical signals to nearby follicle cells which have shrunk during the aging process. These follicles in turn respond to these signals by regenerating and once again making healthy hair.

**Missing teeth:**

The tooth regeneration technology can be used to grow live teeth in human patients. Stem cells taken from the patient could be coaxed in the lab into turning into a tooth bud which can be implanted in the gums. It will give rise to a new tooth and would be expected to be grown in a time over three weeks [30]. It will fuse with the jawbone and release chemicals that encourage nerves and blood vessels to connect with it. The process is similar to what happens when humans grow their original adult teeth.

**Deafness:**

Heller has reported success in re-growing cochlea hair cells with the use of embryonic stem cells [31].

**Blindness and vision impairment:**

Since 2003, researchers have successfully transplanted corneal stem cells into damaged eyes to restore vision. Sheets of retinal cells used by the team are harvested from aborted foetuses. When these sheets are transplanted over the damaged cornea, the stem cells stimulate renewed repair and help inrestoring vision [32].

**Diabetes:**

In Diabetes, there is loss of the function of insulin-producing beta cells within the pancreas [33].Embryonic stem cell can be coaxed to turn into beta cells in the lab. Transplanted beta cell will be able to replace malfunctioning in a diabetic patient [34].

**Transplantation:**

Human embryonic stem cells may be grown in cell culture and stimulated to form insulin-producing cells that can be transplanted into the patient.

Clinical success is highly dependent on the development of the following procedures:

- Transplanted cells should proliferate
- Transplanted cells should differentiate in a site-specific manner
- Transplanted cells should survive in the recipient
- Transplanted cells should integrate within the targeted tissue
- Transplanted cells should integrate into the host circuitry and restore function

**Orthopaedics:**

Mesenchymal stem cells play an important role in treatment of many orthopaedic conditions. It may increase cartilage and meniscus volume in individual human subjects[35-36].Their results show adequate safety and minimal complications associated with mesenchymal cell transplantation[37].

**Wound healing:**

Stem cells can also be used to stimulate the growth of human tissues. In an adult, wounded tissue is replaced by scar tissue. The scar tissue is characterized in the skin by disorganized collagen structure, loss of hair follicles and irregular vascular structure. In the case of wounded foetal tissue, wounded tissue is replaced with normal tissue through the activity of stem cells [38]. A possible method for tissue regeneration in adults is to place adult stem cell at the site of injured tissue and allow the stem cells to stimulate differentiation in the tissue bed cells. This method elicits a regenerative response more similar to fetal wound-healing than adult scar tissue formation [38].

**Infertility:**

Culture of human embryonic stem cells in mitotically inactivated porcine ovarian fibroblasts (POF) causes differentiation into germ cells (precursor cells of oocytes and spermatozoa), as evidenced by gene expression analysis [39]. It could potentially treat azoospermia. These cells have the potential to treat infertility.

**Disadvantages of stem cell therapy:**

- Stem cell treatments require immunosuppression because of a requirement for radiation before the transplant to remove the patient's previous cells. The patient's immune system also can target the stem cells.

- Pluripotency in stem cells could also make it difficult to obtain a specific cell type. It is also difficult to obtain the exact cell type needed, because not all cells in a population differentiate uniformly. Undifferentiated cells can create tissues other than desired types[40].
- Some stem cells form tumours after transplantation. Pluripotency is associated to tumor formation in embryonic stem cells, foetal proper stem cells, induced pluripotent stem cells. Foetal proper stem cells form tumors despite multipotency.
- Hepatotoxicity and drug-induced liver injury account for a substantial number of failures of new drugs in development and market withdrawal, highlighting the need for screening assays such as stem cell-derived hepatocyte-like cells, that are capable of detecting toxicity early in the drug development process[41].

## Conclusion and Future Perspective:

Stem cells have a very promising role and potential in therapeutic application of various human diseases and if researched and utilised in the correct way can prove to be a boon in medical field.

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