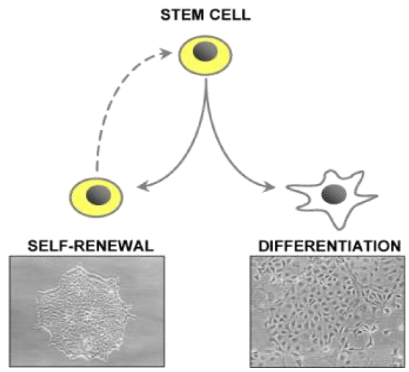
Stem cells: Unspecialized cell that has the ability to divide for indefinite periods of time, and can also give rise to specialized cell types in the body.
They are cells found in all multicellular organisms, characterized by:

- Self-renewal: the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.
- Potency: the capacity to differentiate into specialized cell types.



The unique properties of all stem cells

Stem cells differ from other kinds of cells in the body. All stem cells regardless of their source have three general properties:

1. **Stem cells are unspecialized**.

One of the fundamental properties of a stem cell is that it does not have any tissue-specific structures that allow it to perform specialized functions. For example, a stem cell cannot work with its neighbors to pump blood through the body (like a heart muscle cell), and it cannot carry oxygen molecules through the bloodstream (like a red blood cell). However, unspecialized stem cells can give rise to specialized cells, including heart muscle cells, blood cells, or nerve cells.

2. **Stem cells are capable of dividing and renewing themselves for long periods**.

Unlike muscle cells, blood cells, or nerve cells which do not normally replicate themselves, stem cells may replicate many times, or **proliferate**. If the resulting cells continue to be unspecialized, like the parent stem cells, the cells are said to be capable of **long-term self-renewal**.

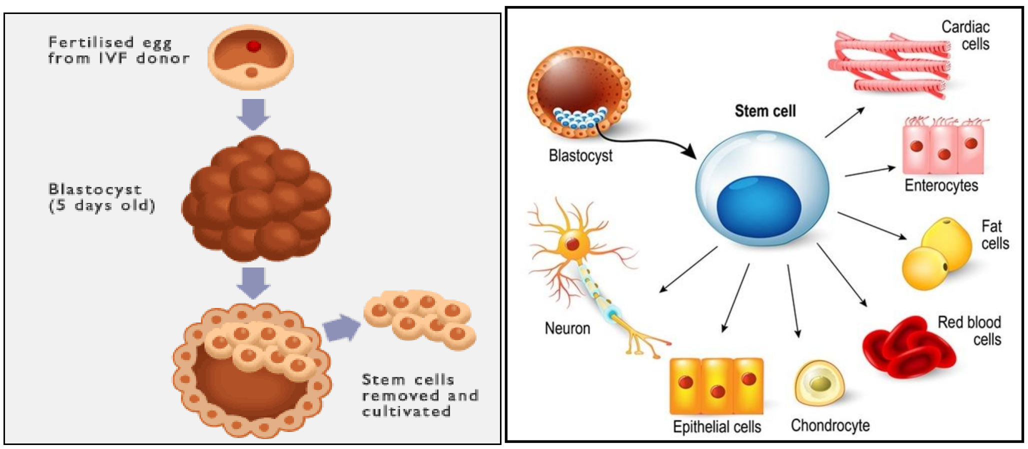
3. **Stem cells can give rise to specialized cells**.

When unspecialized stem cells give rise to specialized cells, the process is called **differentiation**. While differentiating, the cell usually goes through several stages, becoming more specialized at each step.

Types of Stem Cells: The two general types of mammalian stem cells are:

1-Embryonic stem cells: that are isolated from the inner cell mass of blastocysts, which derived from embryos typically four or five days old. Most embryonic stem cells are derived from embryos that develop from eggs that have been fertilized ***in vitro*** (***in vitro* fertilization**) clinic—and then donated for research purposes. They are *not* derived from eggs fertilized in a woman's body.

The blastocyst includes three structures: the **trophoblast**, which is the layer of cells that surrounds the **blastocoel**, a hollow cavity inside the blastocyst; and the **inner cell mass**, which is a group of cells at one end of the blastocoel that develop into the embryo proper. In a developing embryo, stem cells can differentiate into all of the specialized embryonic tissues.



2-Adult stem cells, An adult stem cell is thought to be an **undifferentiated** cell, found among differentiated cells in a tissue or organ that can renew itself and can differentiate to yield some or all of the major specialized cell types of the tissue or organ. The primary roles of **adult stem cells** in a living organism are to maintain and repair the tissue in which they are found.

Scientists use the term **somatic stem cell** instead of adult stem cell, where somatic refers to cells of the body (not the germ cells, sperm or eggs).

In adult organisms, stem cells act as a repair system for the body, replenishing specialized cells, but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.

A person's body contains stem cells throughout their life. The body can use these stem cells whenever it needs them.

Also called tissue-specific or somatic stem cells, adult stem cells exist throughout the body from the time an embryo develops.

The cells are in a non-specific state, but they are more specialized than embryonic stem cells. They remain in this state until the body needs them for a specific purpose, say, as skin or muscle cells.

Day-to-day living means the body is constantly renewing its tissues. In some parts of the body, such as the gut and bone marrow, stem cells regularly divide to produce new body tissues for maintenance and repair.

*Stem cells are present inside different types of tissue. Scientists have found stem cells in tissues, including:

-brain

-bone marrow

-blood and blood vessels

-skeletal muscles

-skin

-liver

However, stem cells can be difficult to find. They can stay non-dividing and non-specific for years until the body summons them to repair or grow new tissue.

Adult stem cells can divide or self-renew indefinitely. This means they can generate various cell types from the originating organ or even regenerate the original organ, entirely.

This division and regeneration are how a skin wound heals, or how an organ such as the liver, for example, can repair itself after damage.

Induced pluripotent stem cells (iPS)

Induced pluripotent stem cells (iPS cells or iPSCs) are a type of pluripotent stem cell that can be generated from adult somatic cells such as skin fibrobalsts or peripheral blood mononuclear cells (PBMCs) by genetic reprograming or the 'forced' introduction of reprogramming genes (Oct4, Sox2, Klf4 and c-Myc).

Epigenetic regulations in ESCs and reprogramming to iPSCs

The pluripotent state of ESCs is enforced by epigenetic factors closely linked to the pluripotency transcription factor network. Resetting the epigenetic state of somatic cells to that of ESCs is one of the ultimate tasks for the reprogramming factors in iPSC generation. The epigenetic factors involved in maintaining the pluripotency of ESCs must be activated through the reprogramming process. Furthermore, epigenetic modulating strategies must be used to overcome the inherent somatic epigenetic state. Therefore, some epigenetic factors may function specifically to erase somatic epigenetic statuses. In this section, we discuss the detailed roles of epigenetic modulations in iPSC generation by juxtaposing the functions of these modulations in maintaining ESC identity and in establishing iPSC pluripotency.

Epigenetics involves genetic control by **factors** other than an individual's DNA sequence. **Epigenetic** changes can switch genes on or off and determine which proteins are transcribed. **Epigenetics** is involved in many normal cellular processes.

How are the induced pluripotent stem (iPS) cells produced?

In 2006, Shinya Yamanaka produced the first iPS cells - from **mouse embryonic fibroblasts** (MEFs) and skin fibroblasts by inserting four transcription factor genes encoding Oct4, Sox2, Klf4, and c-Myc.

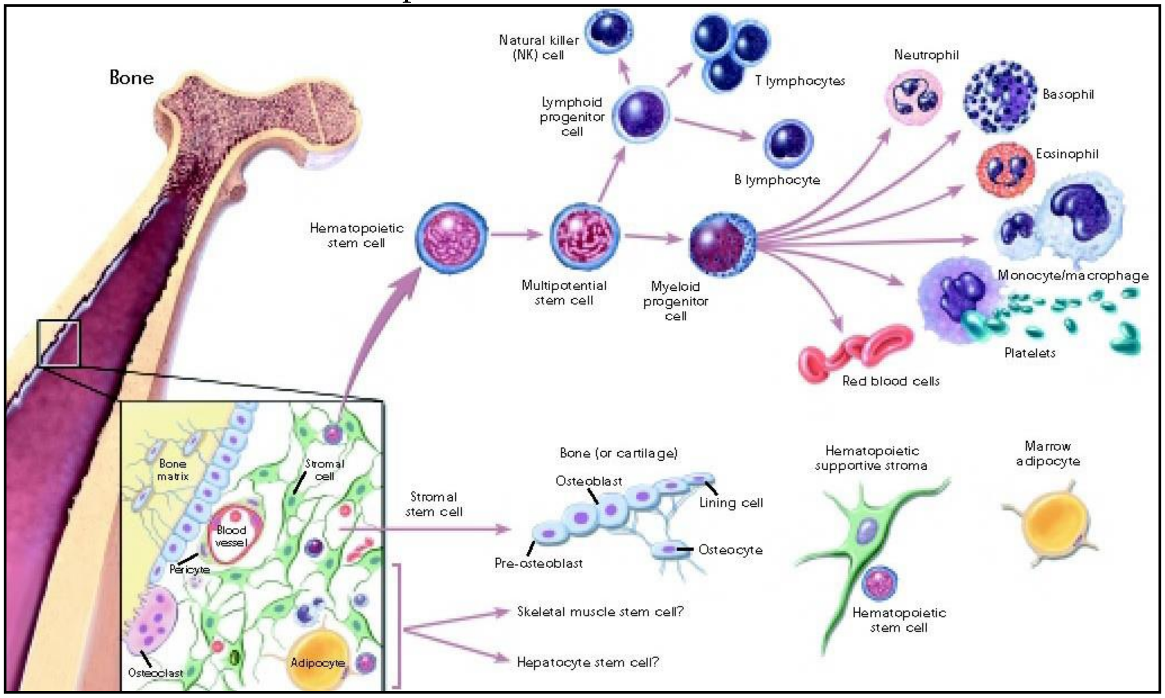
Another group of researchers identified two other genes, Nanog, and Lin28 as a replacement of Klf4, and c-Myc to reprogram human cells. The source of reprogramming genes could be generated from various origins, including neuronal progenitor cells, keratinocytes, hepatocytes, B cells, and fibroblasts of mouse-tail tips, kidneys, muscles, and adrenal glands. Fusion of two types of cells could convert specialized cell types from one lineage to another. These newly developed cells possess similar morphology and growth characteristics as parent ES cells by expressing ES cell-specific genes. The success of reprogramming iPS cell technology depends on the sources of cell lines. It has been reported that reprogramming of human keratinocyte cells withdrawn from skin biopsies to pluripotency proceed at much higher frequency and faster speed than fibroblasts.

Adult stem cell differentiation?

Adult stem cells occur in many tissues and that they enter normal **differentiation** pathways to form the specialized cell types of the tissue.
The following are examples of differentiation pathways of adult stem cells.

Hematopoietic stem cells give rise to all the types of blood cells red blood cells, B lymphocytes, T lymphocytes, natural killer cells, neutrophils, basophils, eosinophils, monocytes, and macrophages.
Mesenchymal stem cells give rise to a variety of cell types: bone cells (osteocytes), cartilage cells (chondrocytes), fat cells (adipocytes), and other kinds of connective tissue cells such as those in tendons.
Neural stem cells in the brain give rise to its three major cell types: nerve cells (neurons) and two categories of non-neuronal cells **astrocytes** and **oligodendrocytes.**
Epithelial stem cells in the lining of the digestive tract occur in deep crypts and give rise to several cell types: absorptive cells, goblet cells, paneth cells, and enteroendocrine cells.
Skin stem cells occur in the basal layer of the epidermis and at the base of hair follicles. The epidermal stem cells give rise to keratinocytes, which migrate to the

surface of the skin and form a protective layer. The follicular stem cells can give rise to both the hair follicle and to the epidermis.



Hematopoietic and stromal stem cell differentiation.

Types of stem cell according to the capacity of differentiation or their Potency:-

1- Totipotent - the ability to differentiate into all possible cell types. Examples are the zygote and the first few cells that result from the division of the zygote.

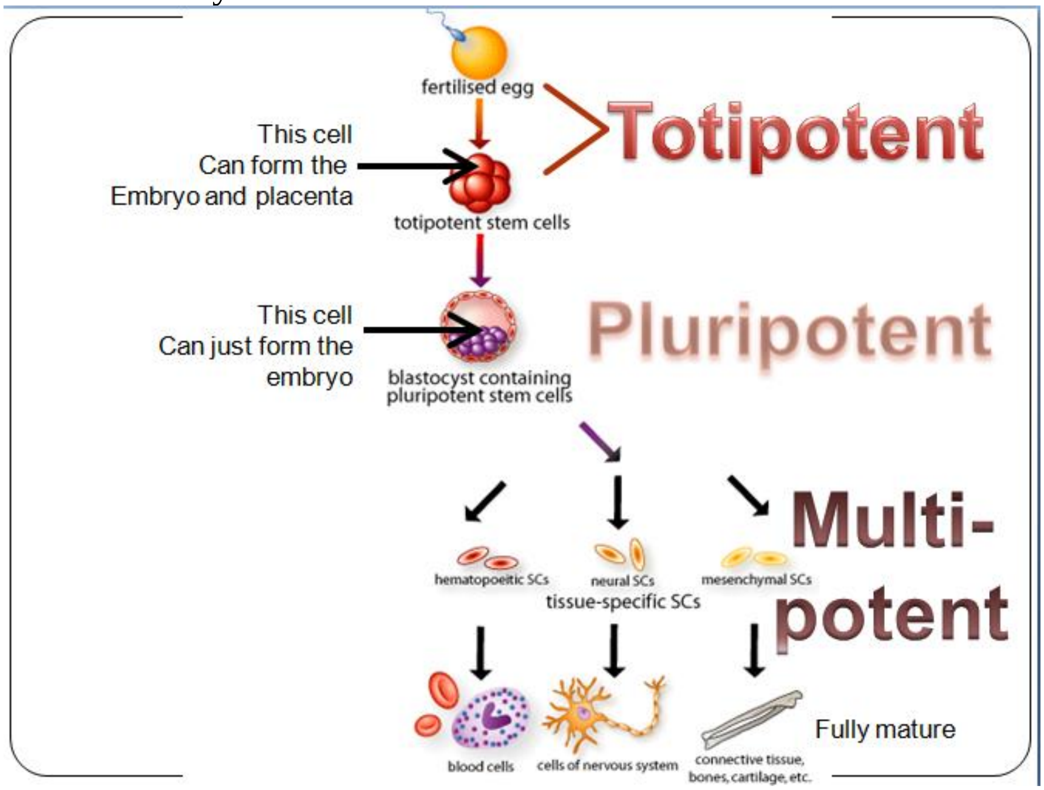
2- Pluripotent - the ability to differentiate into almost all cell types. Examples include embryonic stem cells and cells that are derived from the mesoderm, endoderm, and ectoderm germ layers that are formed in the beginning stages of embryonic stem cell differentiation.

3- 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.

4- Oligopotent - the ability to differentiate into a few cells. Examples include (adult) lymphoid or myeloid stem cells.

5- 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. Examples include (adult) muscle stem cells.

Embryonic stem cells are the most potent since they must become every type of cell in the body.



-Other types of stem cells

- Stem cells can also be taken from the umbilical cord of new babies.
- Like adult stem cells, these cells can differentiate into a limited range of specialised cells.

-The importance of umbilical stem cells:

1. **Plasticity**: Potential to change into other cell types like nerve cells
2. **Homing:** To travel to the site of tissue damage
3. **Engraftment:** To unite with other tissues

Why are scientists so excited about stem cells?

1- Stem cells provide an ideal model for studying the development of an organism

2- Stem cells have the ability to replace damaged cells in the body that would otherwise not be replenished.

3- Stem cells can be used to study disease processes, if directed to produce the specific cells that are damaged in those diseases.

4- Stem cells can be directed to produce specific cell types in the laboratory that can be used to test drugs on.

Difference between ES cells and AS cells:

ES cells	Adult stem cells
Proliferate very rapidly in the embryo	Quiescent or proliferate very slowly
Pluripotent stem cells (generate all tissues of the embryo)	Multipotent cells (committed to a particular lineage such as skin)
Occur only in the embryo	Found in fetal and fully developed tissues
Completely undifferentiated	Have partially differentiated into a more mature type of cell
Found in the inner cell mass (ICM) at the blastocyst stage of the embryo	Present in small numbers

Applications of stem cells:

Tissue regeneration

Tissue regeneration is probably the most important use of stem cells.
Until now, a person who needed a new kidney, for example, had to wait for a donor and then undergo a transplant.
There is a shortage of donor organs but, by instructing stem cells to differentiate in a certain way, scientists could use them to grow a specific tissue type or organ.
As an example, doctors have already used stem cells from just beneath the skin's surface to make new skin tissue. They can then repair a severe burn or another injury by grafting this tissue onto the damaged skin, and new skin will grow back.

Cardiovascular disease treatment

In 2013, a team of researchers from Massachusetts General Hospital reported that they had created blood vessels in laboratory mice, using human stem cells.
Within 2 weeks of implanting the stem cells, networks of blood-perfused vessels had formed. The quality of these new blood vessels was as good as the nearby natural ones.
The authors hoped that this type of technique could eventually help to treat people with cardiovascular and vascular diseases.

Brain disease treatment

For as long as anyone can remember, people have noticed that the brain has a limited ability to heal after injury. It was generally thought that this was in part due to the inability of the brain to make new cells. Then, researchers observed that there are two special regions of the brain that actually do produce new cells, even in adults. The cells from these two special regions are called neural stem cells and now scientists are working hard to determine how their special properties can be used to treat different types of damage in the brain.

The location of brain areas called the hippocampus and lateral ventricles are shown, deep inside the brain. Scientists have found neural stem cells in these two regions of the brain.

Doctors may one day be able to use replacement cells and tissues to treat brain diseases, such as Parkinson's and Alzheimer's.

In Parkinson's, for example, damage to brain cells leads to uncontrolled muscle movements. Scientists could use stem cells to replenish the damaged brain tissue. This could bring back the specialized brain cells that stop the uncontrolled muscle movements.

Researchers have already tried differentiating embryonic stem cells into these types of cells, so treatments are promising.

Cell deficiency therapy

Scientists hope one day to be able to develop healthy heart cells in a laboratory that they can transplant into people with heart disease.

These new cells could repair heart damage by repopulating the heart with healthy tissue.

Similarly, people with type I diabetes could receive pancreatic cells to replace the insulin-producing cells that their own immune systems have lost or destroyed.

The only current therapy is a pancreatic transplant, and very few pancreases are available for transplant.

Blood disease treatments

Doctors now routinely use adult hematopoietic stem cells to treat diseases, such as leukemia, sickle cell anemia, and other immunodeficiency problems.

Hematopoietic stem cells occur in blood and bone marrow and can produce all blood cell types, including red blood cells that carry oxygen and white blood cells that fight disease.