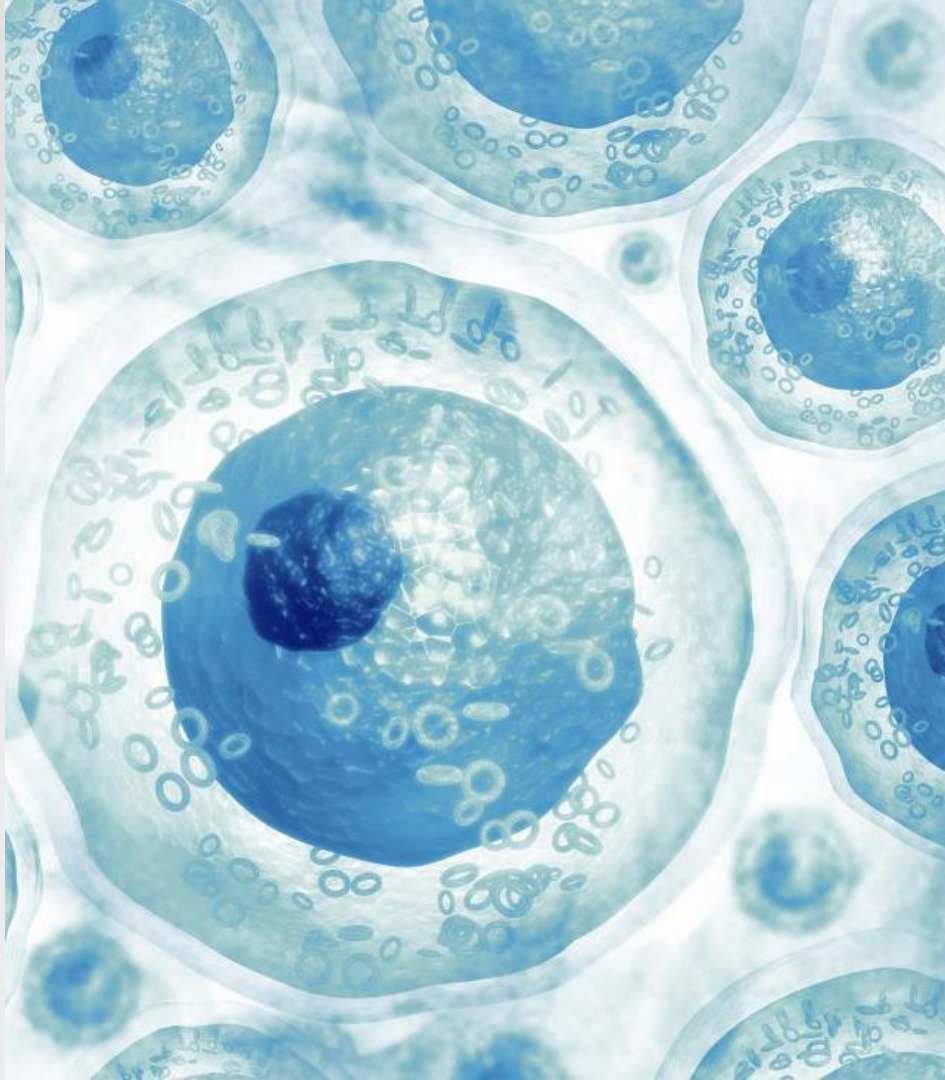
Chapter 4: Stem Cells

H2 Biology



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Introduction

For a multicellular organism to function properly, it must **diversify cell types**, **control their production**, and **eliminate aged/damaged cells.**

Differentiation is a process by which **a less specialised cell develops tissue-specific adaptation that enables it to become a more specialised cell type.**

Many differentiated cell types have limited life spans. Disease can also lead to their loss.

Since differentiated cells do not usually divide, their supply must be replenished and this is achieved through **stem cells.**

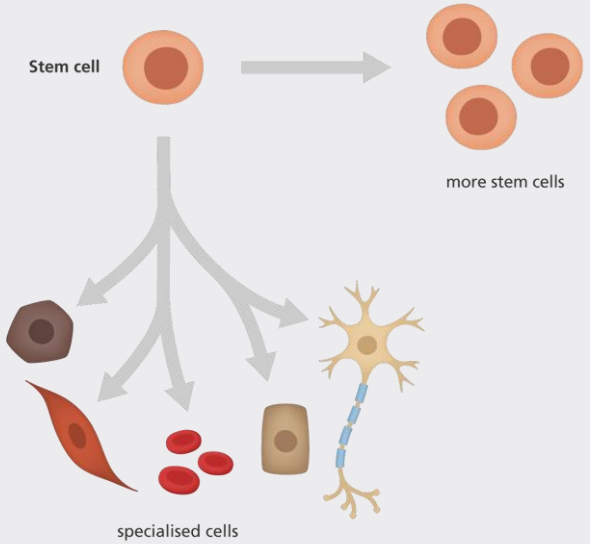
Introduction

All stem-cells have **three unique features**:

1. Stem cells are a group of **undifferentiated and unspecialised cells.**

2. Stem cells can undergo **extensive proliferation** and are **capable of self-renewal through mitosis.**

3. Stem cells can differentiate into various **specialised cell types** upon stimulation by the **appropriate molecular signals.**

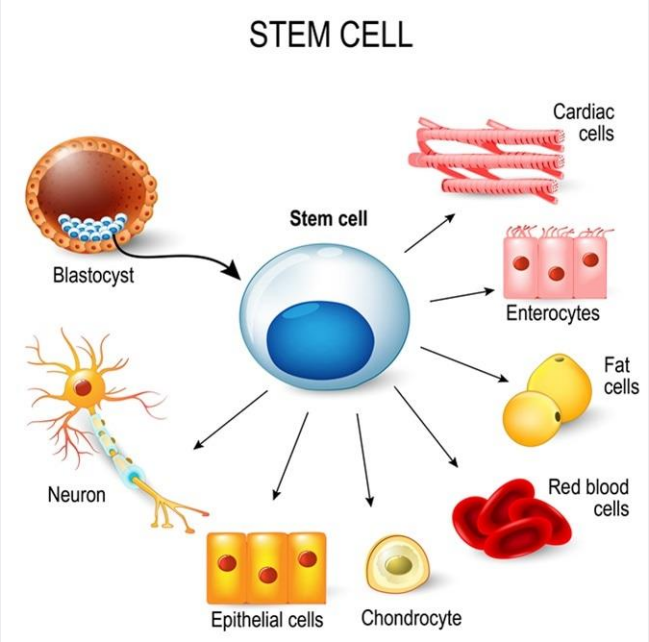


Introduction

Stem cells are a group of **undifferentiated and unspecialised cells:**

- **Specialised cells** in tissues are **differentiated** and have **tissue-specific structures** that allow them to be adapted to perform **unique roles**. e.g. of specialised cells include red blood cells, muscle cells and nerve cells.

- Stem cells, however, **do not have any tissue-specific structures** and **cannot perform tissue specific functions**.



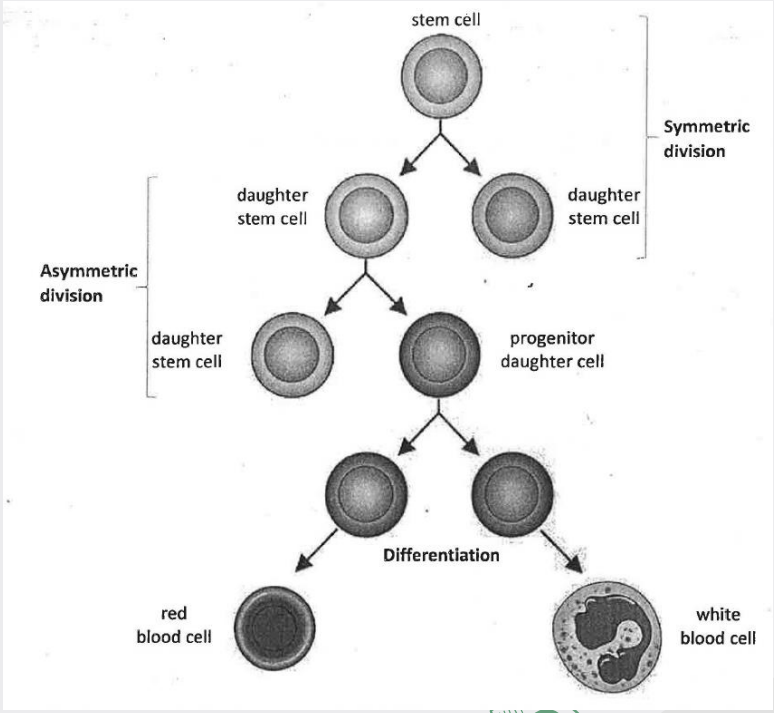
Introduction

Stem cells can undergo **<u>extensive proliferation</u>** and are **<u>capable of self-renewal through mitosis:</u>**

There are 2 possible types of cell division a stem cell can undergo:

i) **<u>Symmetrical Division</u>** – the stem cell divides to produce **2 daughter stem cells that have the same characteristics as parent cell** – i.e, same developmental and differentiation potential as the parent cell.

ii) **<u>Asymmetrical Division</u>** – the stem cell divides to produce **1 daughter stem cell that is identical to the parent cell and 1 progenitor daughter cell which is able to increase or renew population of specialized cells in a specific tissue.**

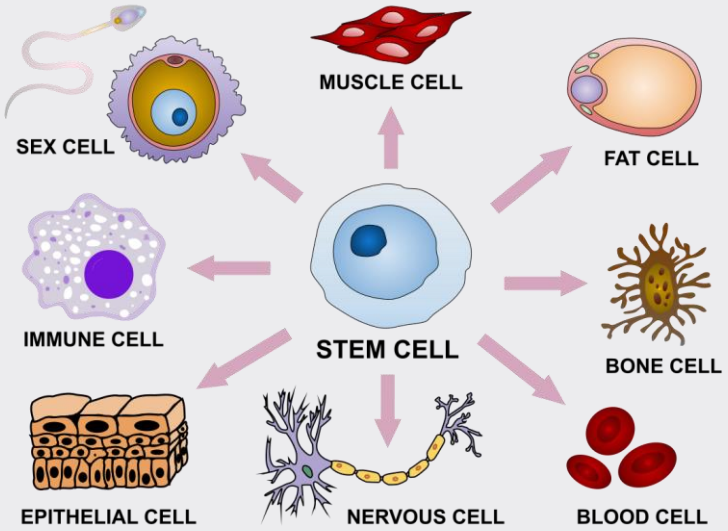


Introduction

Stem cells can differentiate into various **specialized cell types** upon stimulation by the **appropriate molecular signals:**

i) These molecular signals switch some genes on and others off

ii) E.g., Molecular Signals: Transcription factors, growth factors, hormones, cell-cell signals, properties of neighboring cells.



Types of Stem Cells

In mammals, stem cells are commonly categorised according to their ability to differentiate/differentiation potential, i.e. **totipotent, pluripotent or multipotent**.

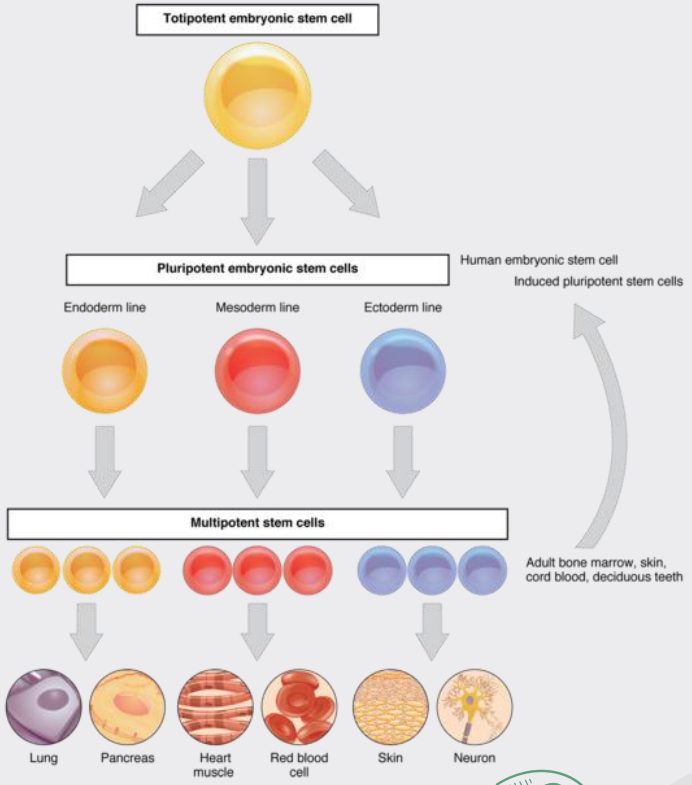
Totipotent Stem Cells:

Has the ability to differentiate into **all of the cell types** that make up an entire organism including extra-embryonic tissue such as placenta, which nourishes the embryo.

Via multiple cellular divisions, totipotent stem cells have the ability to give rise to an entire organism.

Totipotent cells are said to be also **pluripotent and multipotent.**

E.g., Zygotic stem cell that is derived from a fertilised egg, zygote, as well as cells that are produced within the first 3 mitotic divisions (i.e. up to 8 cell stage) after the egg is fertilized.



Types of Stem Cells

In mammals, stem cells are commonly categorised according to their ability to differentiate/differentiation potential, i.e. **totipotent, pluripotent or multipotent**.

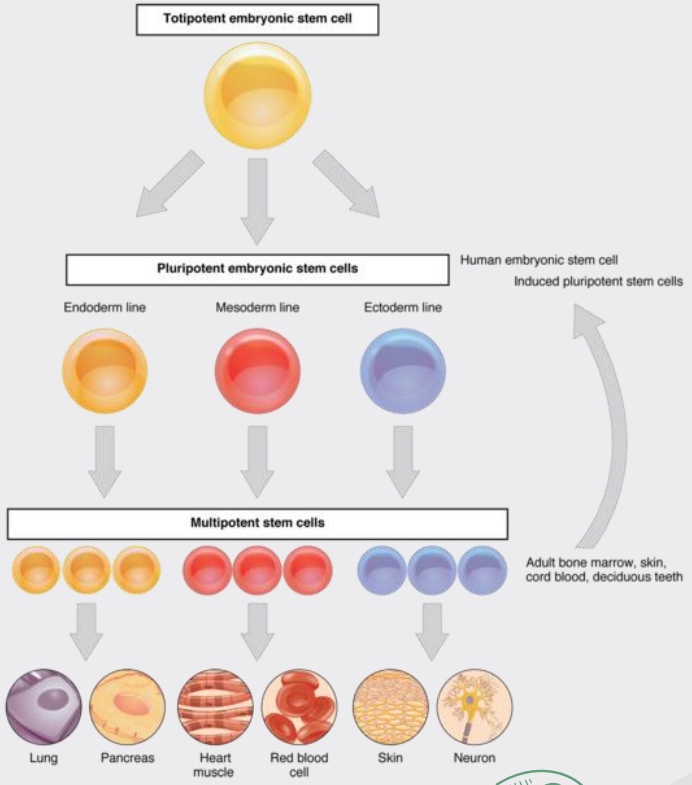
Pluripotent Stem Cells:

Has the ability to differentiate into **all of the cell types** that make up an organism **except extraembryonic tissue such as the placenta.**

Pluripotent stem cells alone cannot form the entire organism as extraembryonic tissues such as the placenta is required for foetal nourishment and development.

Pluripotent cells are also said to be multipotent.

E.g., Embryonic stem cells (ESCs) are derived from cells of inner cell mass of blastocyst (200-300 cells), which forms at about 4 to 5 days post fertilisation



Types of Stem Cells

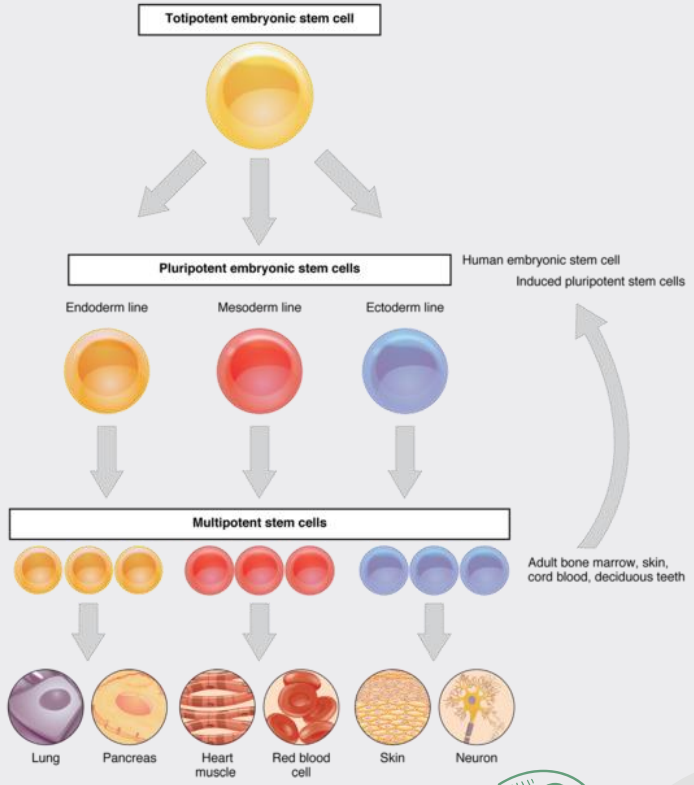
In mammals, stem cells are commonly categorised according to their ability to differentiate/differentiation potential, i.e. **totipotent, pluripotent or multipotent**.

Multipotent Stem Cells:

Has the ability to differentiate into **several related specialised cell types** but far fewer types than the pluripotent embryonic stem cell.

The main purpose of multipotent adult stem cells is to **produce specialized cells for growth and development**, and for **replacement of cells that are lost due to cell death and injury**.

E.g., Stem cells found in a juvenile or adult animal is usually multipotent adult stem cells. These stem cells are found in different tissues of an organism after embryonic development. They are found in small numbers in diverse tissues such as bone marrow, blood, cornea and retina, teeth, intestine, liver, muscles, nervous system and brain, pancreas and skin. Examples are blood/hematopoietic stem cells



Applications of Stem Cells

Multipotent and self-renewing nature of adult stem cells has been harnessed to provide **therapy and treatment** to a range of diseases.

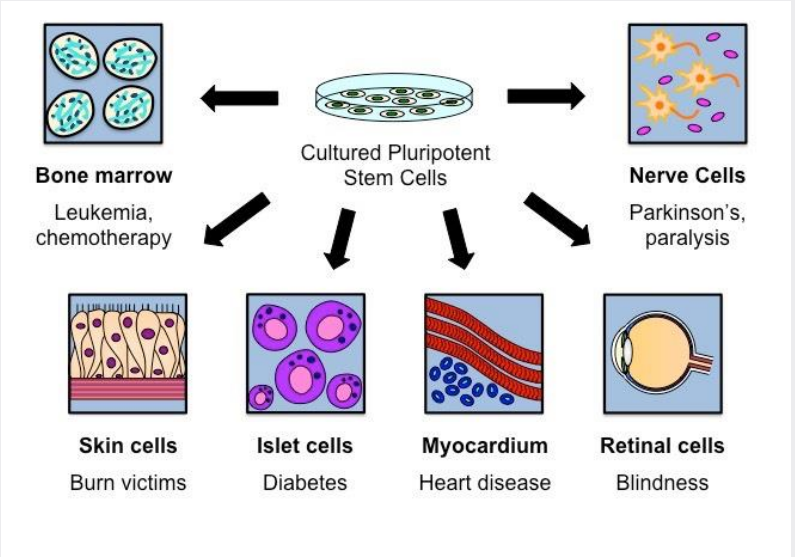
Stem cell therapy involving adult stem cells has **general advantages**:

- **Multipotent nature of adult stem cells** ensures that the adult stem cells **differentiates into the respective specialised cell type**, thus **restoring function of damaged or diseased tissue**.

- Self-renewing nature of stem cells ensures that transplanted stem cells constantly replicate in the patient to **maintain a constant pool of stem cells**. Hence, repeated stem cell transplants are not necessary to sustain the therapeutic effects.

There are two general approaches to stem cell therapies:

- **Stem cell transplant**
- **Genetically modified stem cell transplant**



Applications of Stem Cells

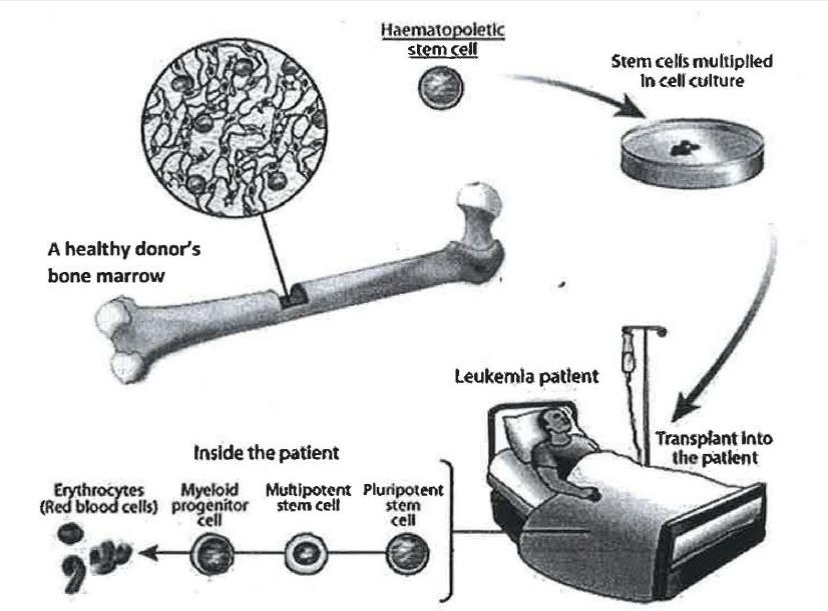
Stem Cell Transplant:

Adult stem cells can be obtained directly from the **donor organ or tissue** in which they are found and have provided **many different therapies for illnesses** such as Parkinson's disease, leukemia, multiple sclerosis, lupus, sickle-cell anaemia, and heart damage.

These treatments carry a risk that the **donated cells will be rejected.**

Also, unlike pluripotent embryonic stem cells which have the ability to differentiate into all cell types that make up an (except for extra-embryonic tissues), **adult stem cells are limited to differentiating into different cell types of their tissue of origin.**

Example:
Transplant of bone marrow haematopoietic stem cells from normal healthy bone marrow donors to leukaemia patients



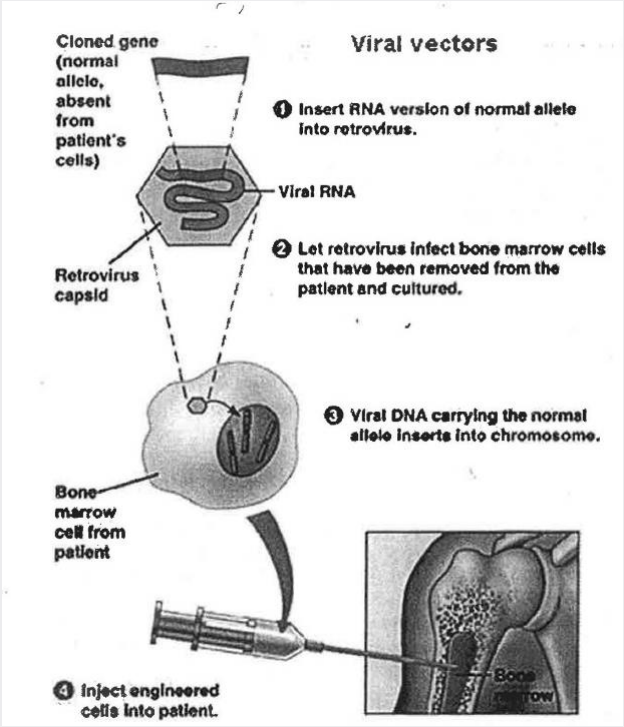
Applications of Stem Cells

Genetically Modified Stem Cell Transplant:

Genetically modified stem cells can be used in **gene therapy** to treat **genetic diseases**.

This strategy involves **removing stem cells** from the patient, **genetically modifying the genome** of the stem cells by **inserting a normal, functional allele** and then **reintroducing the modified stem cells back into the patient.**

The genetically modified stem cells are capable of **self-renewal**, and thus will **proliferate to form more genetically modified stem cells** that **contain the normal, functional allele.** These genetically modified stem cells will differentiate into specialized cell which restores the functions of the diseased tissues.

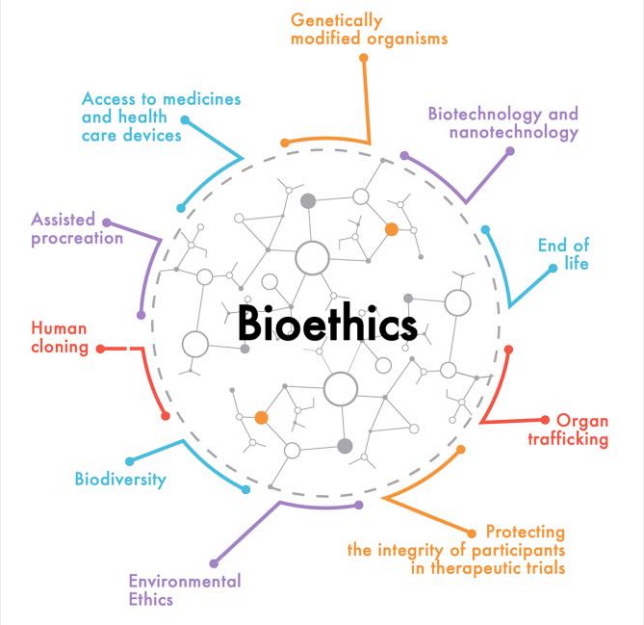


Bioethics

Ethics is a field of study that looks at the **moral basis of human behaviour** ("Why do we act as we do?") and attempts to determine the best course of action in the face of conflicting choices ("How do we decide what to do when people disagree about a complex issue?").

Bioethics is a subfield of ethics that explores ethical questions related to the life sciences. **Bioethical analysis helps people make decisions about their behaviour and about policy questions** that governments, organizations, and communities must face when they consider **how best to use new biomedical knowledge and innovations.**

Examples:
"How should we decide who receives organ transplants?" or,
"Should a terminally ill patient be allowed to end his/her life with physician prescribed medication?''



Bioethics

Ethical Implications of Stem Cell Therapy and Research
Argument against using embryonic stem cells

- Some assert that the **embryo has the status of a human being** as it has the potential to become one. They believe that embryonic stem cell research **violates the sanctity of life and is tantamount to murder.**

- Some object to extracting stem cells from an embryo to make replacement body cells is **treating the embryos just a source of spare parts.** Embryonic stem cell research takes a purely utilitarian view of the embryo.

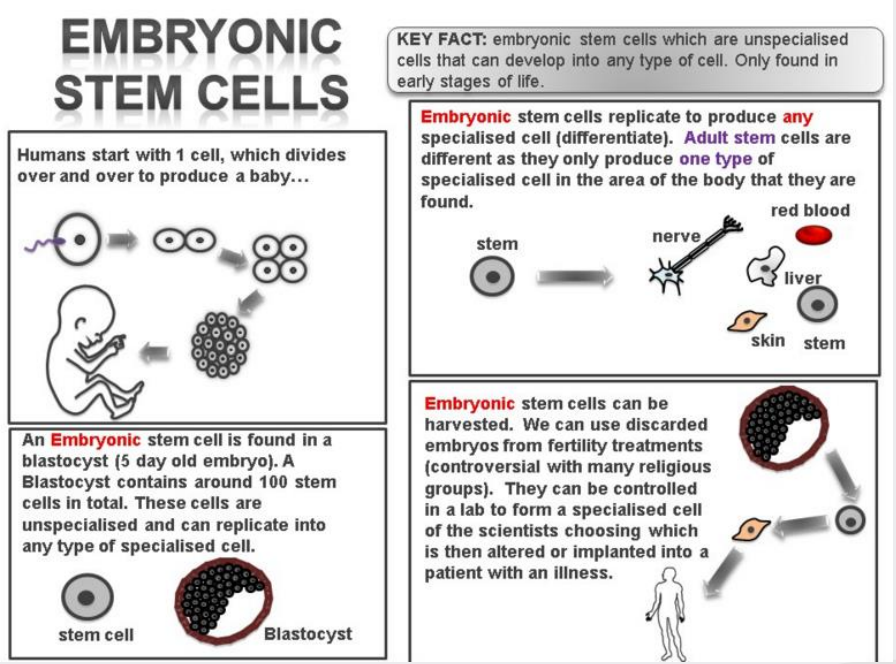
- Current benign applications may lead to **abuse in the future.** Once human status is denied to embryos, this precedent may extend to other categories of human beings such as the profoundly disabled or the elderly infirm.

Bioethics

Ethical Implications of Stem Cell Therapy and Research
Arguments for using embryonic stem cells

- Embryonic stem cells can **potentially treat a wide range of diseases** as they have the potential to grow indefinitely in a laboratory environment and can differentiate into almost all types of bodily tissue. Treatments that have been proposed include treatment for physical trauma, degenerative conditions (e.g. Parkinson's disease), and genetic diseases (in combination with gene therapy).

- **Embryos are not equivalent to human life**: something that can potentially become a person should not be treated as if it actually were a person. An early embryo therefore does not have any interests to be protected, and we can use it for the benefits of patients, who are people. **The embryo cannot develop into a child without being transferred to a uterus**. Some believe life only begins when the heartbeat develops (during the fifth week of pregnancy) or when the brain begins developing (at 54 days after conception).



Bioethics

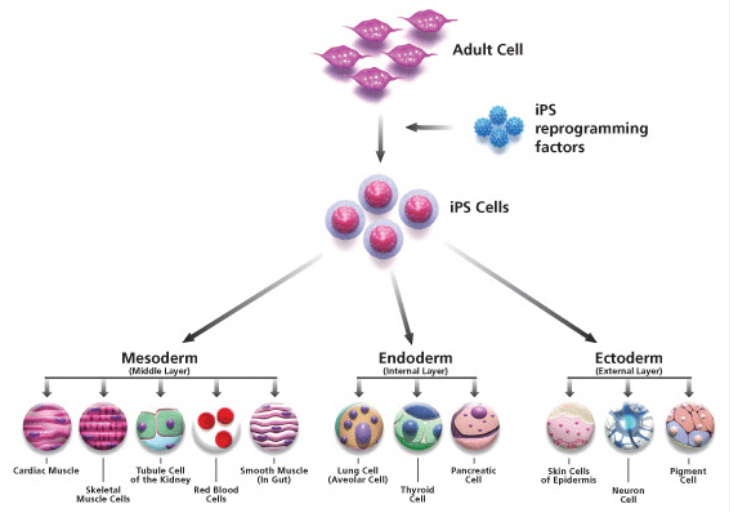
Induced pluripotent stem cells (iPSCs)
An **alternative** to ES Cells?

Differentiated and specialised adult somatic cells (e.g. skin cells) can be **reprogramed to become pluripotent stem cells** called **induced pluripotent stem cells (iPSCs)**.

The iPSC technology was pioneered by Shinya Yamanaka's lab in 2006; the introduction of four specific genes encoding transcription factors could 'reprogramme' some specialised cells to become pluripotent so that they lose their specialist functions and behave in virtually the same way as embryonic stem cells.

Advatanges:
- No destruction of embryos.
- If obtained from same patient, no chance of rejection by immune system.
- Easily obtained without risk to donor.

Disadvatanges:
- Low efficiency
- May pose cancer risk
- Ethical concerns



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