River Valley High School
2025 JC1 H2 Biology

Lecture Topic 13: Stem Cells

Name: _____ ( ) Class: 25J__ Date: _____

References

Title	Authors
Biology (9th Edition)	Campbell and Reece
Introduction to Biotechnology (2nd Edition)	Thieman and Palladino
Stem Cells for Dummies (2nd Edition)	Goldstein and Schneider

H2 Biology Syllabus 9477 (2025)
Candidates should be able to use the knowledge gained in the following section(s) in new situations or to solve related problems.

Related Topic	**Concepts**
Organelles and Cellular Structures	Cell Theory

Learning Outcomes

1D. Stem Cells

a. Describe the unique features of stem cells, including zygotic stem cells, embryonic stem cells and blood stem cells (lymphoid and myeloid), correctly using the terms:
   i. totipotency (e.g. zygotic stem cells)
   ii. pluripotency (e.g. embryonic stem cells)
   iii. multipotency (e.g. lymphoid and myeloid stem cells)

~~b.~~ Explain the normal functions of stem cells in a living organism, including embryonic stem cells and blood stem cells (lymphoid and myeloid).

Lecture Outline

I. Nature of Stem Cell
- A. Terminology
- B. Origin of Stem Cells

II. Types of Stem Cell
- A. Zygotic Stem Cells
- B. Embryonic Stem Cells
- C. Adult Stem Cells

III. Applications of Stem Cell
- A. Stem Cell Research
- B. Ethical Implications
- C. Human Induced Pluripotent Stem Cells

Websites

URL	Description
https://www.dnalc.org/resources/animations/stemcells.html	Numerous animations on stem cells
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7367472/	Review paper on stem cell-based therapies

I. NATURE OF STEM CELL

A. Terminology

Differentiation

- The gradual appearance of characteristic cellular specialisations during development as the result of gene activation or repression.

Stem cell

- A relatively unspecialised cell that can
  - divide and grow indefinitely
  - differentiate into specialised cells of one or more types under appropriate conditions
- Hence, stem cells are able to replenish their own population and to generate cells that travel down specific differentiation pathways.
- In some cases, stem cells also may undergo **asymmetric division,** in which one daughter cell retains its stem cell properties and the other undergoes differentiation and develop into a specialised cell.

Totipotency

- Describes a cell that can give rise to all parts of the embryo and adult, as well as extra-embryonic tissues in species that have them.
- Totipotent cells can differentiate into any cell type to form whole organisms.
- In mammals, only zygote and the first four cells derived from a zygote are totipotent.

  They give rise to all the cells in the adult as well as the cells that form the placenta and umbilical cord, without which no foetus can survive

Pluripotency

- Describes a cell that can give rise to many, but not all parts of an organism
- Pluripotent cells can differentiate into almost any cell type to form any organ in the organism.
- In mammals, embryonic stem cells are pluripotent.

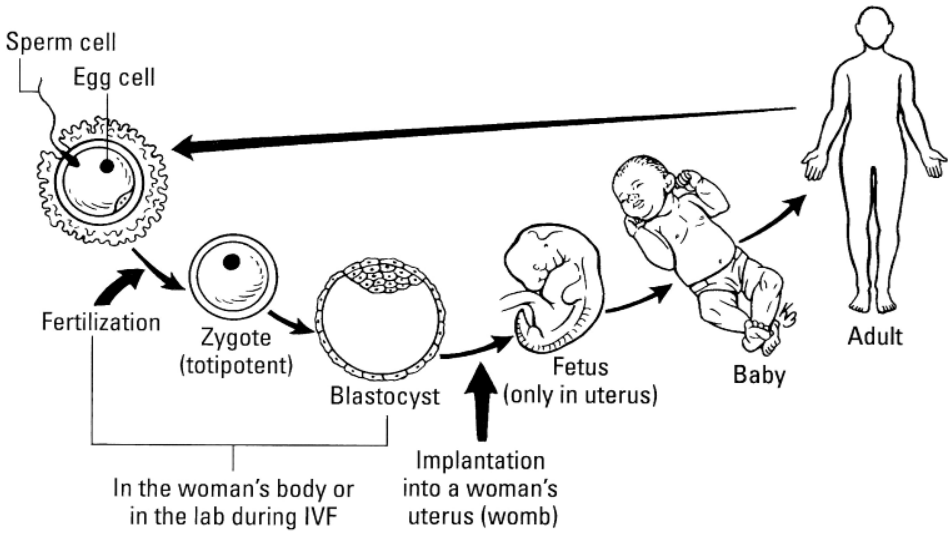
  They can give rise to any cell type except those that form the placenta and the umbilical needed to establish and maintain a pregnancy

Multipotency

- Describes a cell that can give rise to some parts of an organism
- Multipotent cells can differentiate into a limited range of cell types in a specific category of cell.
- In mammals, adult stem cells (e.g. lymphoid and myeloid stem cells) are multipotent.

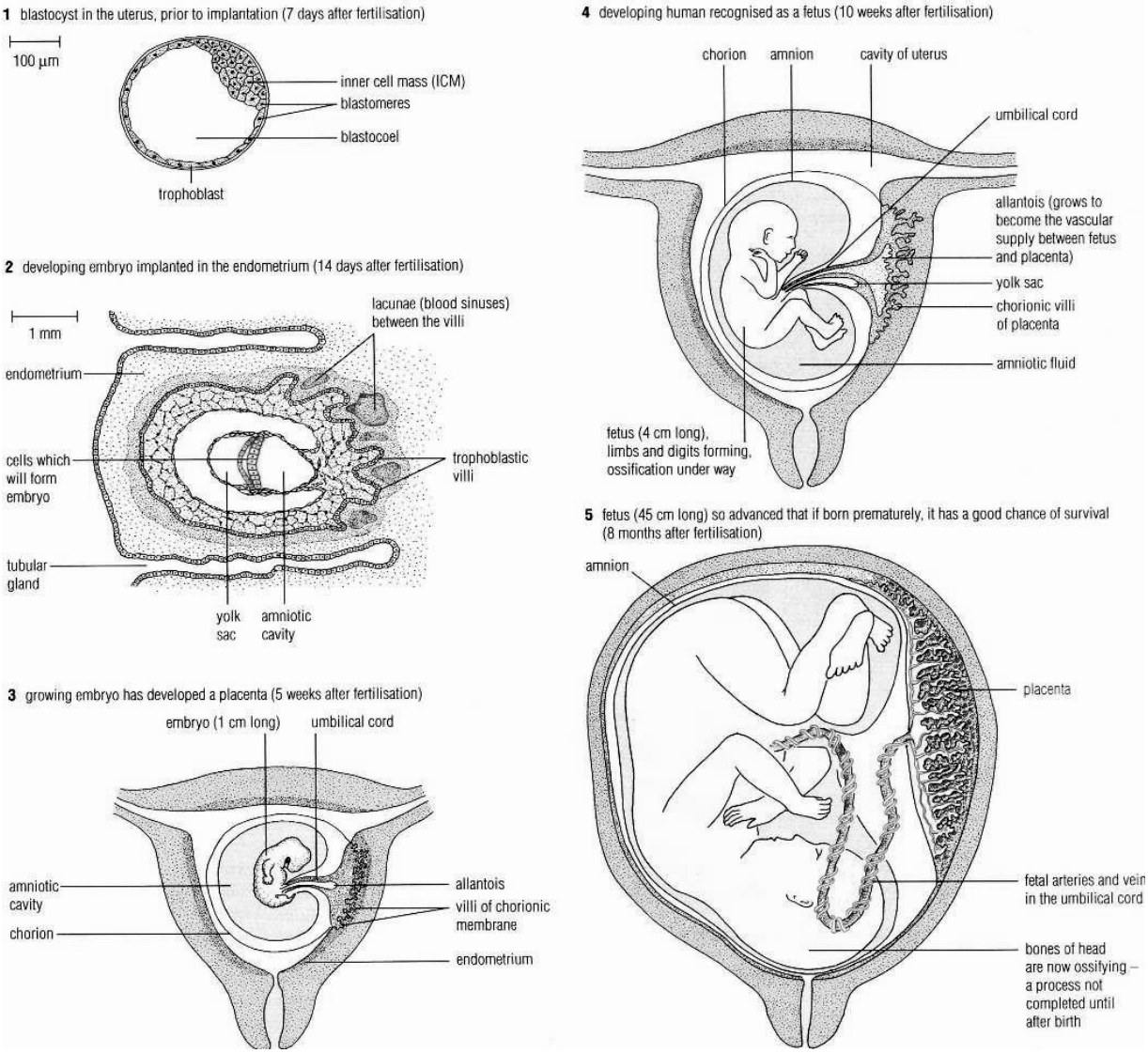
  They can give rise to lots of different cell types, but usually not all the cell types in an adult body.

B. Origin of Stem Cells



- In mere 40 weeks, what begins as a single cell (zygote) becomes an individual whose body contains trillions of cells organised into a complex array of highly specialised structures.
- All the tissues, organs and organs systems take shape and begin to function.
- The creation of different types of cells required by this process is called **differentiation**, which occurs through selective changes in genetic activity, during which some genes are turned on and others are turned off.
- Stages of development from fertilisation to maturity:
    - development begins at fertilisation / conception.
    - embryological development comprises events that occur during the first two months after fertilisation
    - foetal development begins at the start of the ninth week and continues till birth

Fertilisation to Embryological Development



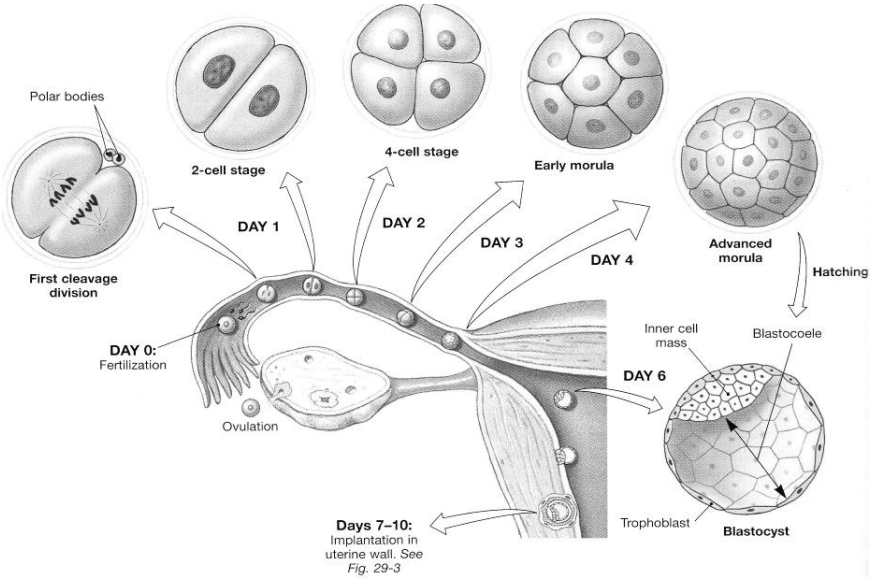
- At the moment of fertilisation, the fertilised ovum is <u>a single cell</u> (zygote) that has a diameter of about 0.135mm and a weight of approximately 150mg.
- By the end of the first trimester (12th developmental week), the foetus is almost 75mm long and weighs approximately 14g.
- Many important and complex developmental events occur during the first trimester.

  The four general processing include:

  1. **Cleavage**
     A sequence of <u>mitotic cell divisions</u> that begin immediately after fertilisation, ending at the first contact with the uterine wall.
     During cleavage, the zygote develops into a multicellular complex known as a **blastocyst**.
  2. **Implantation**
     Implantation begins with the attachment of the blastocyst to the uterine wall and continues as the blastocyst invades maternal tissues.
  3. **Placentation**
     Placentation occurs as blood vessels form around the periphery of the blastocyst and the placenta develops.
     The placenta is a complex organ that permits exchange between the maternal and embryonic circulatory systems.
  4. **Embryogenesis**
     Formation of a viable embryo.

II. TYPES OF STEM CELL

A. Zygotic Stem Cells



- A totipotent zygote cell is formed by the fusion of ovum and sperm.
- A series of mitotic cell divisions that subdivide the cytoplasm of the totipotent zygote.
- The first cleavage produces a pre-embryo consisting of two identical cells.
- The first four cells derived from a zygote are totipotent.

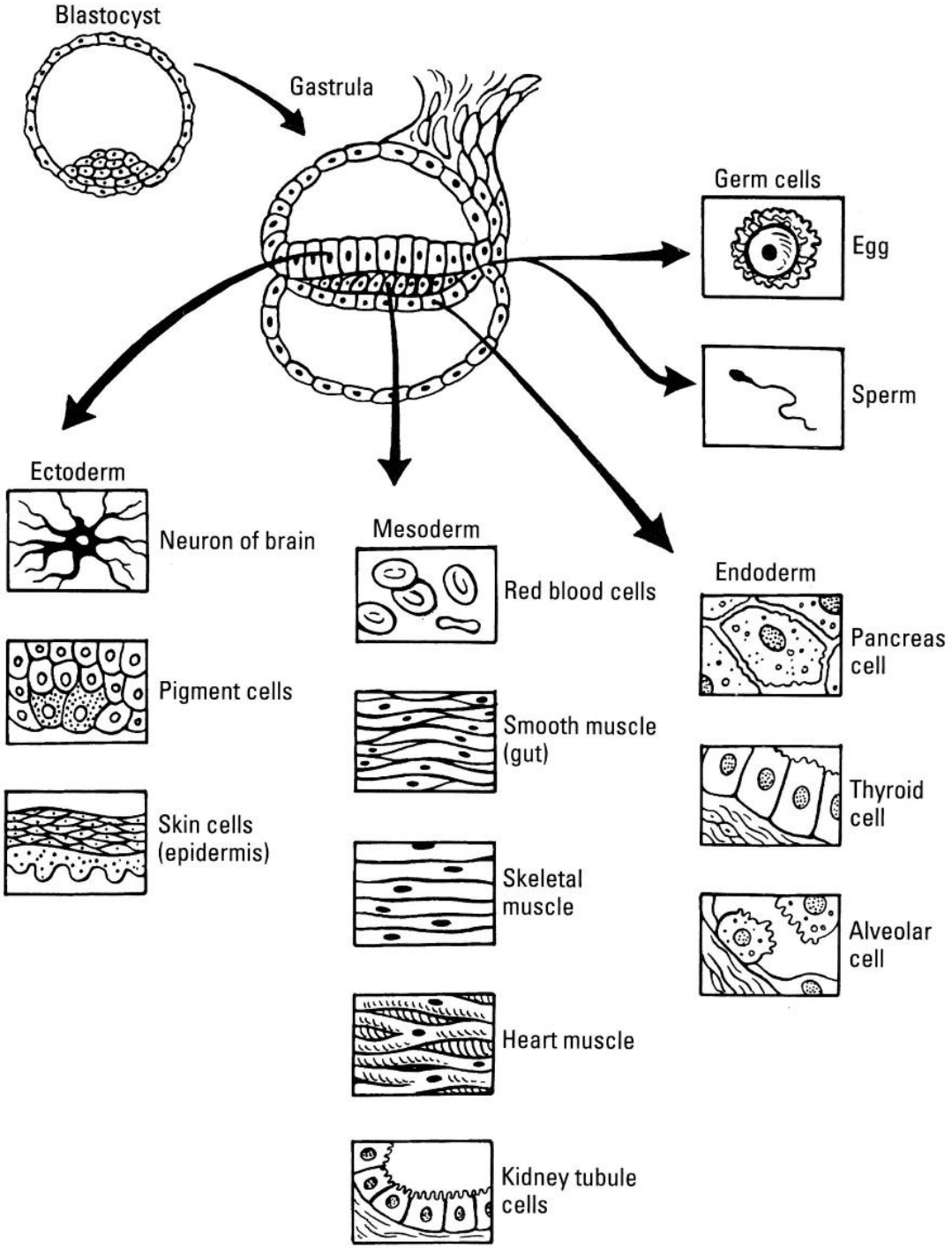
  Totipotent cells give rise to all the cells in the adult as well as the cells that form the placenta and umbilical cord, without which no foetus can survive
- Subsequent cell divisions produce identical cells called **blastomeres**.
- During the initial divisions, all the blastomeres undergo mitosis simultaneously.

  As the number of blastomeres increases, the timing becomes less predictable.
- After three days of cleavage, the pre-embryo is a solid ball of cells known as a **morula**.

  The morula typically reaches the uterus on day 4.
- **Blastocyst** formation

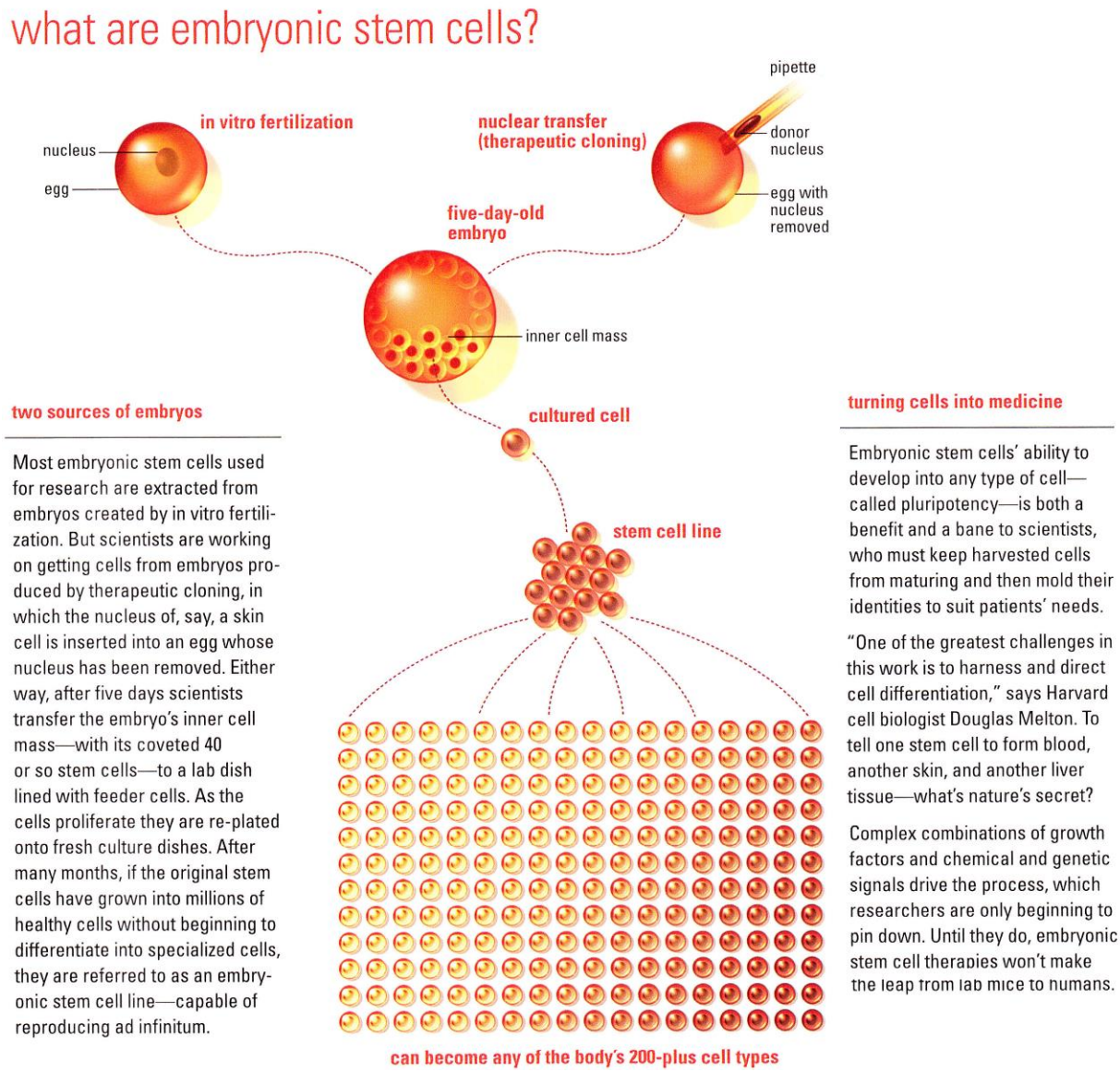
  Over the next two days, the blastomeres form a blastocyst, a hollow ball with an inner cavity known as the **blastocoel**.
- The blastomeres are no longer identical in shape and size.
- The outer layer of cells, called the **trophoblast**, provides nutrients to the developing embryo.
- The second group of cells, called the **inner cell mass** (**ICM**), lies clustered at one end of the blastocyst.
  The ICM will form the embryo.

B. Embryonic Stem Cells



- The group of cells inside the blastocyst inner cell mass, consists of **embryonic stem cells**
- These cells cannot be used to form whole cloned embryos as they cannot form a placenta if placed in a surrogate mother.
- However, they do still have the ability to divide repeatedly and to develop into any other kinds of tissue. This group of cells is described as **pluripotent**.
- The inner cell mass gives rise to the cells of the resulting three germ layers: **endoderm**, **mesoderm**, and **ectoderm** which eventually form all the highly specialised cells needed to produce an adult organism.

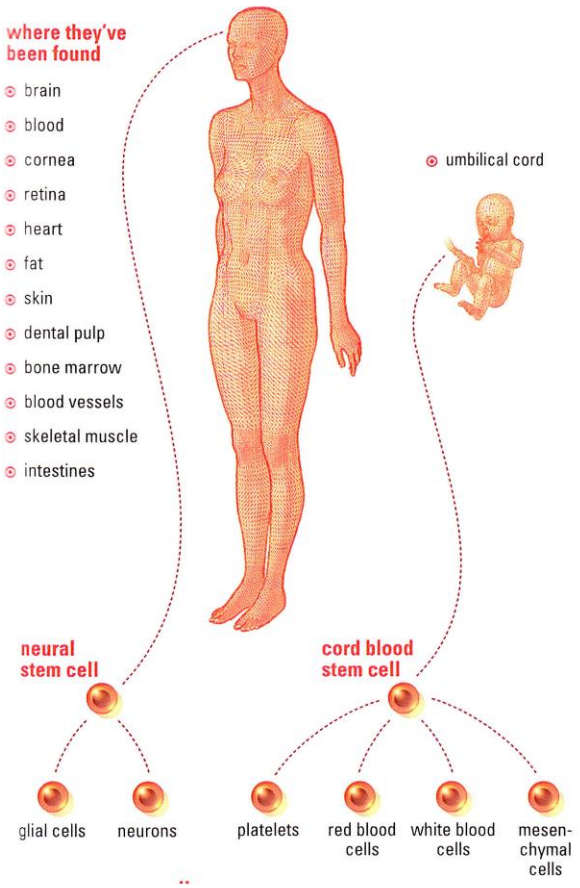
Application



- In culture, these embryonic stem cells divide indefinitely; and depending on culture conditions, they can be made to differentiate into a variety of specialised cells for treating human disease.
- For humans, embryonic stem cells are extracted from excess blastocysts produced during **in vitro fertilization** (**IVF**) procedures. Harvesting ES cells from human blastocysts is controversial because it destroys the embryo, which could have been implanted to produce another baby (but often was simply going to be discarded).

C. Adult Stem Cells

what are adult stem cells?



a more grown-up cell

The adult body has a small number of stem cells in many tissues and organs—where they lie low until activated by illness or injury. Unlike embryonic stem cells, adult stem cells haven't proved able to morph into every kind of cell and may be limited to becoming cell types within their tissue of origin. An adult stem cell in the brain, for example, can become a neuron or glial cell—both neural cells—but not a bone or liver cell.

So far only adult stem cells have been tested in humans, though research on both adult and embryonic cells progresses apace as scientists seek treatments for myriad diseases. "This is the century of cells," says Harvard biologist Douglas Melton. Results are preliminary, but they hint at a transformation in medicine. Some disease updates:

heart disease

Adult bone marrow stem cells injected into heart arteries are believed to improve cardiac function in victims of heart attack or heart failure.

leukemia and other cancers

In various studies leukemia patients treated with stem cells from bone marrow and umbilical cord blood emerged free of disease; donor blood stem cells have also reduced non-Hodgkin's lymphoma and pancreatic and ovarian cancer in some patients.

Similarly stem cells from a newborn's cord blood (considered adult cells because they aren't from embryos) produce only blood cells. Recently, though, cord tissue has been found to contain mesenchymal cells capable of generating bone and cartilage.

In general, adult stem cells are scarcer in the body and harder to culture than embryonic cells, yet large numbers are needed for therapies.

rheumatoid arthritis

Adult stem cells may be helpful in jump-starting repair of eroded cartilage. In human trials, joint pain lessened temporarily after donor stem cell therapy in some patients, and some then responded better to standard drug therapies.

parkinson's disease

Since fetal tissue implants had mixed success in reducing neurological symptoms, some researchers say the best hope is that a patient's own neural stem cells may eventually be coaxed to mature into the dopamine-producing cells needed to treat the disease.

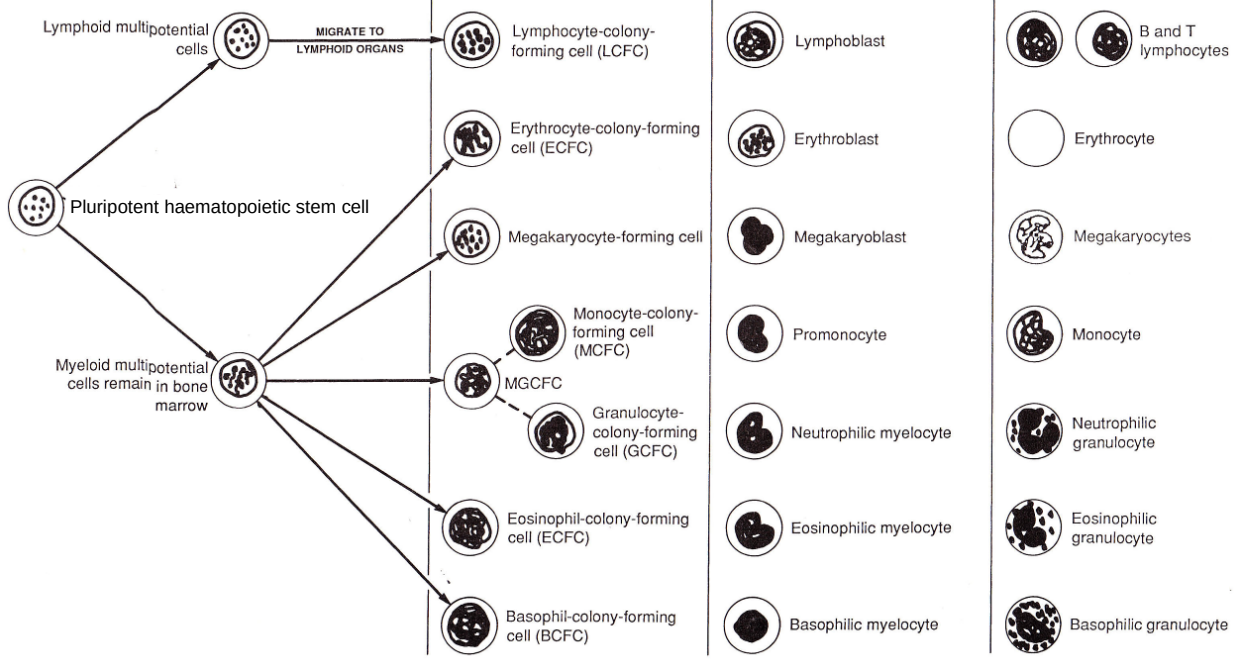
type I diabetes

Basic research is focused on understanding how embryonic stem cells might be trained to become the type of pancreatic islet cells that secrete needed insulin. Recent developments using proteins to spur cell differentiation may speed progress.

- **Adult stem cells** are undifferentiated cells found among differentiated cells in a tissue or organ.
- The primary role of adult stem cells is to maintain and repair the specific tissues where they reside.
- Adult stem cells occur within many differentiated tissues and they can enter normal differentiation pathways to form the specialised cell types of the tissue which they reside in. E.g. stem cells found in muscle will normally only give rise to muscle cells.
- Adult tissues containing stem cells include brain, bone marrow, peripheral blood, blood vessels, skeletal muscle, skin and liver.

PHASE	STEM CELLS Multipotential	PROGENITOR CELLS	PRECURSOR CELLS (BLASTS)	MATURE CELLS
Early morphologic	Not morphologically distinguishable; have general aspect of lymphocytes		Beginning of morphologic differentiation	Clear morphologic differentiation
Mitotic activity	Low mitotic activity; self-renewing; scarce in bone marrow	High mitotic activity; self-renewing; common in marrow and lymphoid organs; mono- or bipotential	High mitotic activity; not self-renewing; common in marrow and lymphoid organs; monopotential	No mitotic activity; abundant in blood and hematopoietic organs

*Figure 13-6 (shown in color at the beginning of this chapter) shows the morphologic differentiation of these cells.



- Hematopoietic stem cells, lymphoid stem cells and myeloid stem cells are blood stem cells.
- **Hematopoietic stem cells** can give rise to <u>all types of blood cells</u>: red blood cells and white blood cells (neutrophils, basophils, eosinophils, platelets, mast cells, monocytes, tissue macrophages, osteoclasts, platelets and the T and B lymphocytes). As such, they are **pluripotent**.
- These stem cells differentiate to give rise to **lymphoid stem cells** and **myeloid stem cells**. Each of which can only differentiate into <u>a limited range of cell types</u> (blood cell types). As such, lymphoid stem cells and myeloid stem cells are **multipotent**.
    - The <u>lymphoid stem cells</u> migrate to the lymph nodes, spleen and thymus, where they complete their differentiation into lymphocytes (T and B lymphocytes), contributing to the lymphatic system (e.g. immune defense).
    - The <u>myeloid stem cells</u> develop in the bone marrow to form granulocytes, monocytes, erythrocytes and megakaryocytes, contributing to the function of the blood circulatory system (e.g. gaseous exchange and immune defense).

III. APPLICATION OF STEM CELL

A. Stem Cell Research

- Stem cell research is not just about figuring out how cells work. Scientists are trying to solve practical problems through understanding how and why problems arise.
- Potential application of stem cell research includes
    1. Developing reliable ways to make different cell types such as motor neurones, pancreatic β-cells.

       Scientists seek to determine the extracellular factors (e.g. treatment with appropriate growth actors) that allow cells to thrive in culture and induce cells to develop into particular cell types
    2. Building disease models

       This allows for investigation on disease mechanism; gene expression; and drug testing.
    3. Studying stem cell transplants in animals.

       This serves as a basis for developing cell therapies for humans, where defined cells made from stem cells are generated in the lab and transplanted into a person to treat a given disease and / or replace cells lost to the disease.
- The ultimate aim of stem cell research is to supply cells to treat medical problem arising from damage to differentiated cells includes:
    - Type 1 diabetes mellitus where the β-cells of the pancreas have been destroyed by an autoimmune attack
    - Parkinson's disease where dopamine-secreting cells of the brain have been destroyed
    - Ischemic stroke where a blood clot in the brain has caused neurons to die from oxygen starvation

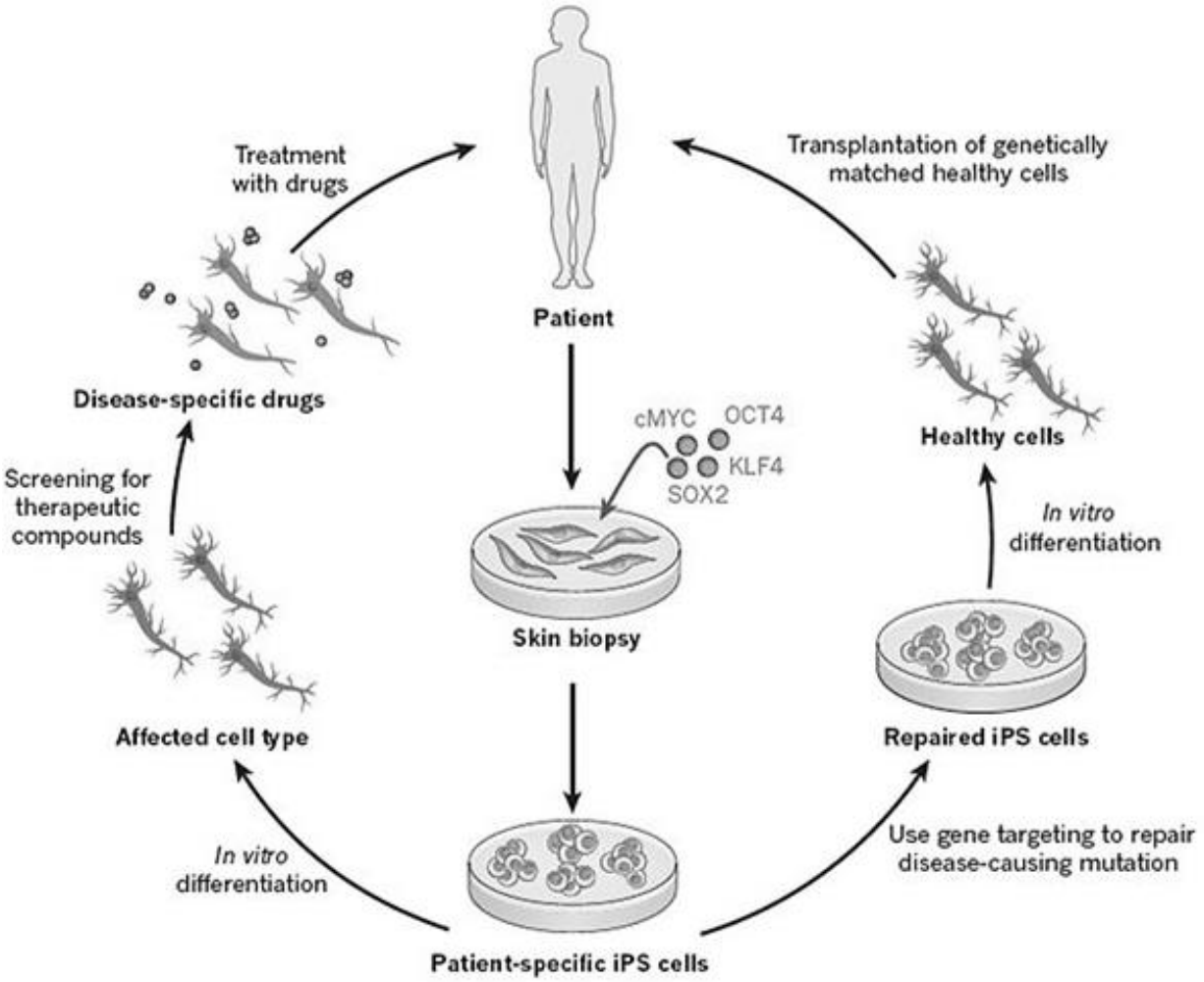
B. Ethical Implications

- Embryonic stem cells hold more promise than adult stem cells for medical applications because of their pluripotency. However, the only source of embryonic stem cells is from human embryos, which raises ethical and political concerns such as
    1. Harvesting embryonic stem cells from excess human blastocysts produced during *in vitro* fertilisation (IVF) procedures is controversial. The harvesting of embryonic stem cells will destroy the embryo, which could have been implanted to produce another baby, hence it is considered morally wrong. However, others argue that the excess blastocysts are often simply discarded, also embryos that are not implanted into the uterus does not have the psychological, emotional and physical characteristics to be associated as being a person. Hence, the criteria of personhood are unclear.
    2. Different religions define the moral status of embryos differently. Some religions believe that embryo has the full moral status of human from conception and no embryo research should be allowed. However, others believe that embryo does not have full human status before 40 days so they permit research on such embryos.
- Therefore, many countries have set up bioethics advisory board; and have laws and policies to regulate the use of embryos in stem cell research (e.g. use of excess embryos from IVF for research, creation of embryos).

- With increasing clinical knowledge of embryonic stem cells, stem cell therapy is fast becoming a viable treatment option for patients with genetic diseases. However, ethic aspects of stem cell therapy need to be carefully considered:

Benefits	Cost
Offers a possible cure to genetic diseases	May not result in therapeutic effect, and could worsen the condition
May bring about greater economic gain in the long run as recovered patients no longer need costly disease management.	An expensive procedure that is not affordable to the poor
Patients are using own cell instead of embryonic stem cells	Development of procedure involves trials with patients suffering from life-threatening diseases
Does not involve modification of germline cells, thus genetic changes will not be passed on to offspring	Alternative methods of disease management might be safer than the associated risk
	An invasive procedure that requires long recovery time, and may worsen patients' health condition

C. Human Induced Pluripotent Stem Cells



- Scientists have shown that differentiated adult cells can be reprogrammed to behave like undifferentiated human embryonic stem cells, producing **human induced pluripotent stem cells (iPSC)**
- Human iPSCs are adult cells that are reprogrammed genetically into an embryonic stem cell state by reactivating the genes that give rise to pluripotent characteristics.
- The use of human iPSCs can circumvent most of the ethical concerns associated with the use of embryonic stem cells. Besides, they have similar pluripotent characteristics as embryonic stem cell, thus can be used for medical research without destroying human embryos.
- To make iPSCs, four or more **master regulatory genes** (genes encoding transcription factors) are inserted into the DNA of an adult cell, such as a fibroblast skin cell. These genes act like a reset button, returning the cell to a 'blank' state. This reprogramming allows the former skin cell to behave like a pluripotent stem cell, giving rise to different types of tissue.
- Two major potential of human induced pluripotent stem cells are:
    - Cells from patients can be reprogrammed to become induced pluripotent stem cells, which can act as model cell for studying the disease and potential treatments.
    - In the field of regenerative medicine, a patient's own cells could be reprogrammed into induced pluripotent stem cells and then used to replace non-functional tissues.
- However, scientists are still working to find the best way to insert the master regulatory genes into the DNA of the adult cell. Retroviruses have been used but are problematics because random insertion of the gene into DNA can cause cancer.