Biochem_3 – stem cells

℘ What are stem cells?

Are primal cells that retain the ability to **renew** themselves through cell division and can be **differentiated** into a wide range of specialized cell types.

℘ Characteristics of stems cells:

- Unspecialized (undifferentiated) cells.
- Unlimited capability to divide.
- Self-renewal: The ability to go through numerous cycles of cell division while maintaining the undifferentiated state.(it divide to produces two different types of daughter cells, one of these is to regenerate the population of stem cells- self renewal)
- Asymmetric division; which is due to differential segregation of cell membrane proteins between the daughter cells- Important.

℘ progenitor cell

Stem cells generate an intermediate cell type or types before they achieve their fully differentiated state; it mean they won't become fully differentiated in a single step, they undergo multiple stages before they become fully differentiated, these stages are called progenitor cells.

℘ Stem cell niche; definition

A specialized microenvironment that surrounds any stem cell to provide the support needed for self-renewal.

℘ Stem cell niche; types

The niche is either made up of **cells alone** (either of the same type or of a different type), **ECM alone** or a **combination of both**.

℘ Stem cell niche; functions

1. To keep stem cell in a healthy situation and to keep their stemness.
2. To drive their differentiation (when needed).
3. For nutrition.
4. For coordination among tissue compartments; for example in the bone morrow we have several types of stem cells, they may act as niches for each other, so as one type activates the differentiation of another type or inhibits it, so there are some interchangeable signals in between them that may support their differentiation or regeneration.
5. Needed as a feedback control system: at some points we need to turn the stem cell on for division or differentiation, and we need to turn it off as well, so the niche works as a feedback system to stop this signal once we no longer need differentiation into a certain cell type.
6. They act as hubs for inter-lineage coordination: this is specifically important for populations of stem cells that are found in combination with other populations of stem cells (Just like the case in the bone morrow where the hematopoietic stem cell generates different types of blood cells and different progenitors, so there are many lineages and the niche works as a coordinator between them).

- Types of stem cells according to potency

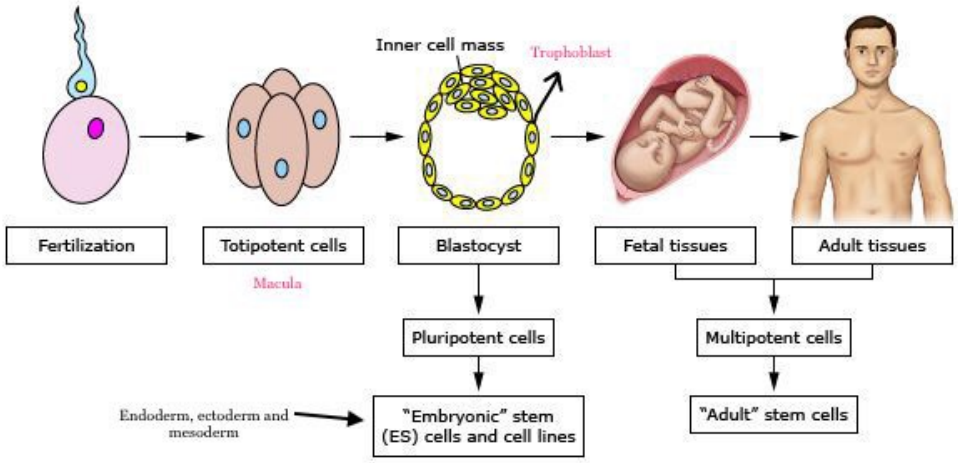
1. Totipotent : a stem cell that has the ability to differentiate into all cells of the embryo in addition to extraembryonic tissue cells (e.g: placenta), is found in a very early stage during development called **the Morula** (the 8-cell stage, التوتة).

2. Pluripotent: it can differentiate into all cell types of the embryo but not to extraembryonic tissues, It's found in the inner cell mass of the embryo.

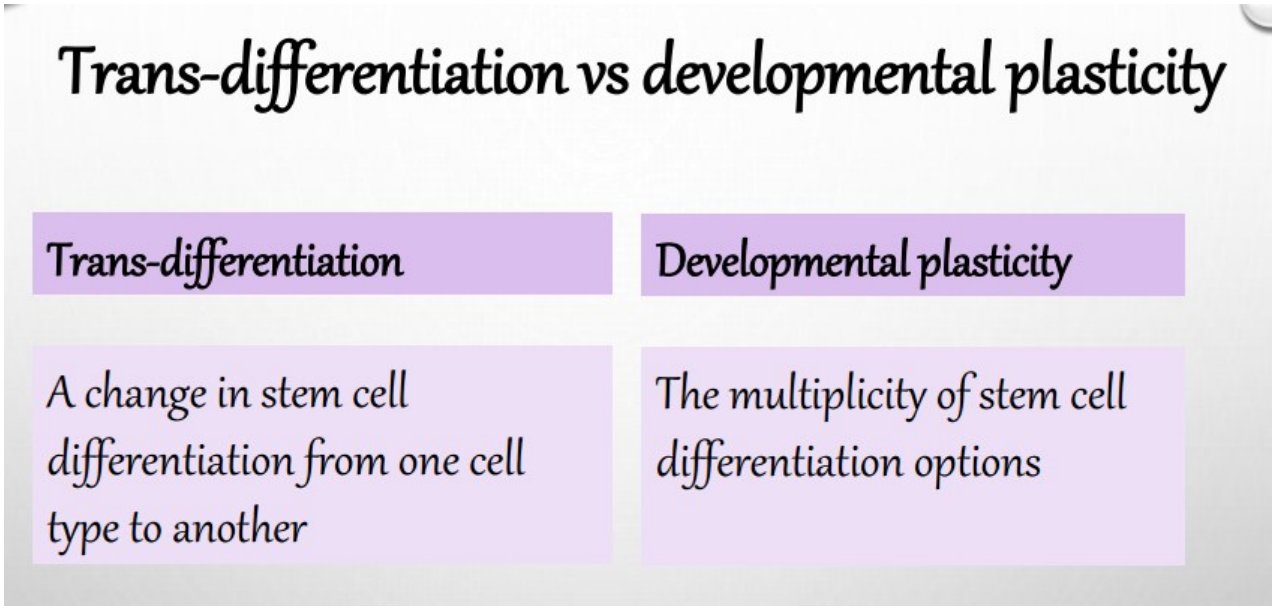
The Totipotent cell Inside the morula will keep dividing until they form a ball of cells which is hollow from the inside, the surrounding cells are known as ***Trophoblasts***, and at one side of this ball there is an aggregation of cells called the ***Inner cell mass*****,** and this whole structure is called ***"Blastocyst"*** - which is made of trophoblasts and an inner cell mass.

3. multipotent: these are present in adults not during fetal development and they can differentiate to several cell types

4. unipotent: it's the last stage which can differentiate into only one cell type.



- Read this slide, note: "**transdifferentiation**" is also known as **epithelial-mesenchymal transition**



℘ Types of stem cells; Embryonic & Adult stem cells

A- Embryonic stem cells

- These are pluripotent stem cells, they're found in the inner cell mass of the blastocyst, and they give rise to all types of cells in all three germ layers.
- Their pluripotency comes fromtheir expression of special factors called "pluripotency factors", these factors are important to keep the cells' pluripotency and their ability to divide and differentiate. Ex; Oct 4/ Nanog/ Wnt-β-catenin signaling / Other TFs.

- The limitations associated with the use of embryonic stem cells for treatment of diseases are: they're **not autologous** (cause rejection problems) & **Ethical issues**: when we isolate these stem cells form embryos we're basically killing the embryo.
- "**Induced pluripotent stem cells, iPSCs**":

✓ These cells are obtained by **de**differentiating fibroblasts form skin biopsies and reprogramming them to become pluripotent stem cells exactly like those found in the embryo.

✓ The advantages of iPSCs :

- **No ethical problems**.

-They should be safer since we're taking the cells form the recipient himself (they're **autologous**).

-They are **patient-specific**: this means that they're not just pluripotent, but also they contain the whole genetic material and epigenetic changes in that person. So if he has a specific mutation it would exist in the genetic material of this iPSC.

Fibroblasts normally are spindle-shaped, after their transformation into pluripotent stem cells they grew in colonies. They were similar to embryonic stem cells in terms of: **1**-morphology **2**-surface antigens **3**-gene expression (he compared gene expression by the technique of microarrays) **4**-telomerase activity (remember that adult cells are old compared to embryonic cells and they have shorter telomeres. After transformation, iPSCs had a similar telomerase activity to embryonic stem cells in keeping the length of the telomeres) **5**-the epigenetic status **6**-the promoters activity **7**-their ability to differentiate to the 3 embryonic stem cells layers (their potency) **8**-their ability to proliferate **9**-their ability to form teratomas (teratomas are embryonic tumors of the three germ layers).

✓ iPSCs are used for :

- modeling of diseases
- Drug screening
- Personalized medicine.

B- Adult stem cells

1. Bone marrow stem cells **Hematopoietic stem cell** & **mesenchymal** stem cells they give rise to osteoblasts, chondrocytes, myocytes, adipocytes and neuronal cells & mammary stem cells (the last two subtypes could be collectively called **somatic stem cells**
2. Neural stem cells responsible for adult neurogenesis in subventriculare zone, which lines the lateral ventricles of the brain, and the dentate gyrus of the hippocampal formations.
3. Adipose stem cells (ASCs). do NOT give rise to adipocytes (adipocytes are derived from mesenchymal
stem cells), instead they give rise to endothelial cells, fibroblasts, pericytes and smooth muscle cells
4. Umbilical cord stem cells
5. Olfactory adult stem cells: found in olfactory mucosal cells
6. Tissue stem cells in cornea, trabecular meshwork, etc

℘ USES OF STEM CELLS

- TO STUDY THE SPECIFIC SIGNALS AND DIFFERENTIATION
- GENETIC THERAPY
- DRUG TESTING
- CELL BASED THERAPIES
- STEM CELLS FOR CANCER TREATMENT BY ACTIVATION OF CHEMOTHERAPEUTIC AGENTS

℘ STEM CELL THERAPY LIMITATIONS

- CARCINOGENICITY
- IMMUNE REJECTION
- INFECTION
- Lack of markers: and this makes it difficult for stem cells to isolate, especially with the huge number of different types of stem cells.For example, there are many types of stem cells in the teeth so it's hard to find the specific marker that distinguishes the stem cell type from another.
- In vivo experiments differ from those in vitro because it’s hard to simulate the stem cell niche.
- The multipotency of stem cells could also be a problem. For example mesenchymal stem cells differentiate into bone cells if PMP2 is applied, if myodin is applied they differentiate into skeletal muscle cells. So if one molecule is altered this might change the resulting cells completely.

- Cancer stem cells:

These are not a distinct type of stem cells; but it was found recently that even cancer has its own stem cells that keep the formation and regeneration of the cancer. So cancer cells don't just lose the control systems over their division, but also have their own stem cells that keep them regenerated and keep their expansion. [*from the slides*: cancer stem cells Are tumor cells that have the essential properties of self-renewal, clonal tumor initiation capacity, clonal long term repopulation potential and plasticity].

- Why is it important to perform stem cell research?
  - Functional genomic studies to understand human embryonic gene expression, genomic data mining, and bioinformatics.
  - To study biological processes to understand human developmental disorders like birth defects, cancers, etc.
  - Creating human disease models for drug discovery and development.
  - For Cell-based therapy and regenerative medicine

THE END