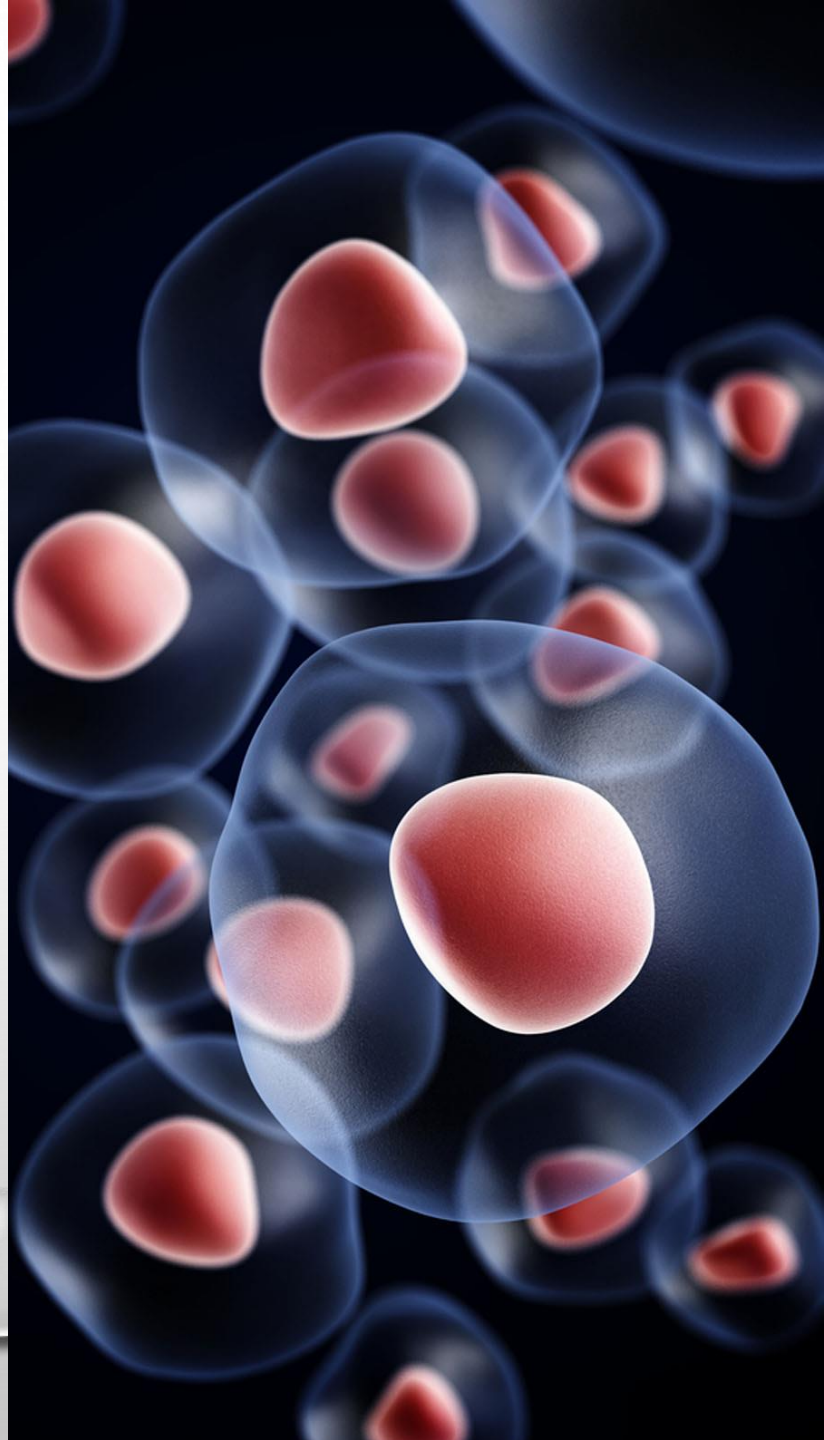
Stem Cells: The New Therapeutics Era

Dr. Diala Abu-Hassan, DDS, PhD

School of Medicine

dr.abuhassand@gmail.com

Central Nervous System

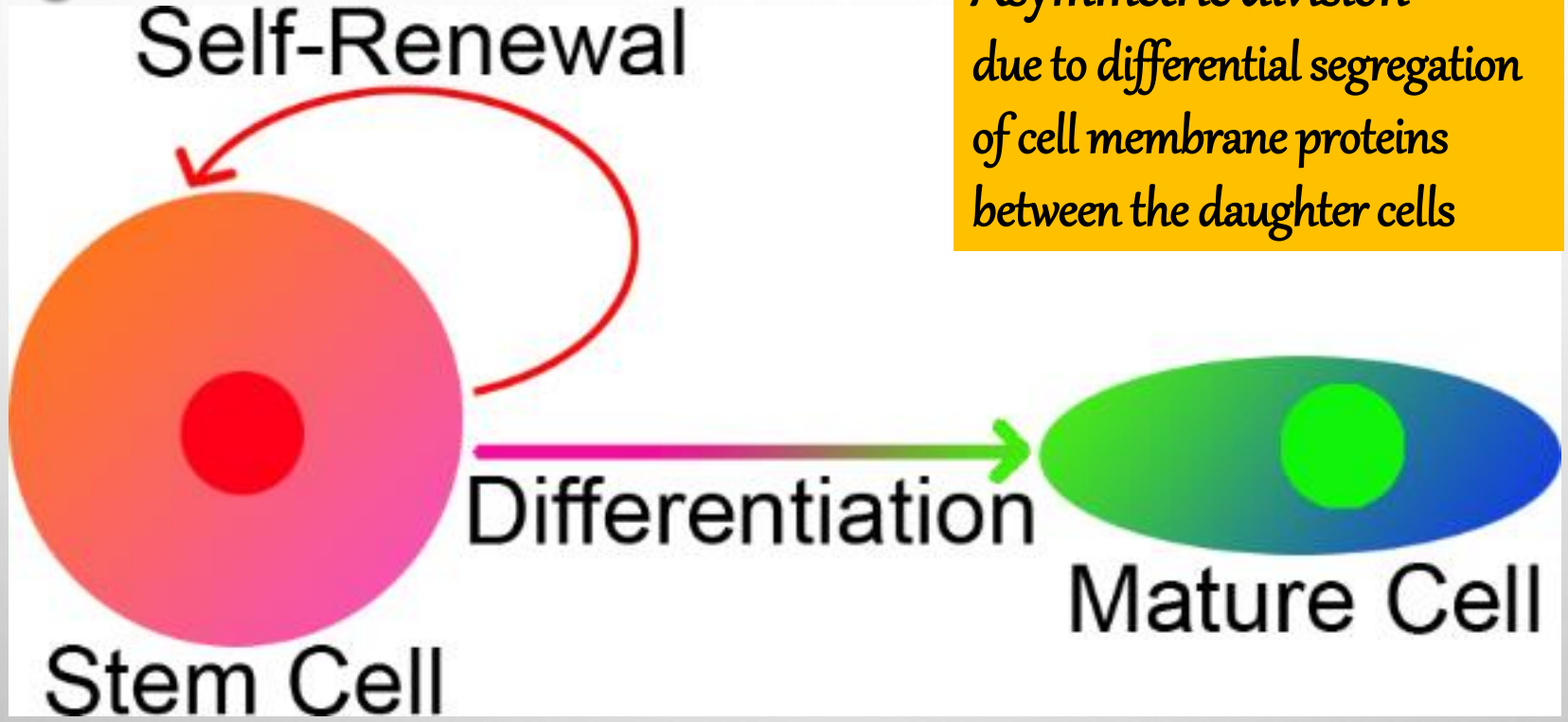


What do you know about stem cells?

What are stem cells?

- Are primal cells common to all multicellular organisms that retain the ability to **renew** themselves through cell division and can be **differentiated** into a wide range of specialized cell types.
- All stem cells are unspecialized (**undifferentiated**) cells that are of the same family type (**lineage**).

Differentiation vs self renewal



Asymmetric division
due to differential segregation of cell membrane proteins between the daughter cells

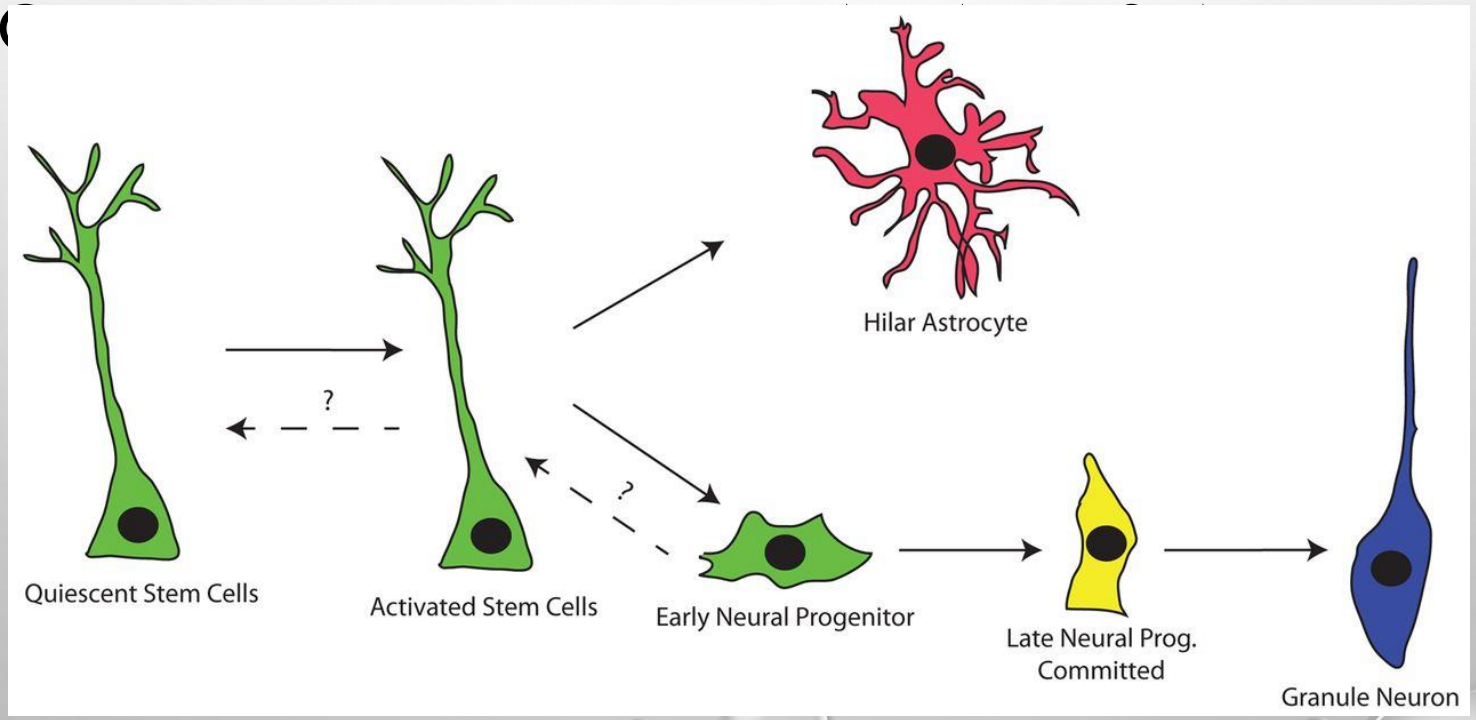
Self-renewal: The ability to go through numerous cycles of cell division while maintaining the undifferentiated state.

HOW DOES ASYMMETRIC DIVISION OCCUR?

- DIFFERENTIAL SEGREGATION OF CELL MEMBRANE PROTEINS (SUCH AS RECEPTORS) BETWEEN THE TWO DAUGHTER CELLS.

WHAT DOES STEM CELL DIVISION PRODUCE?

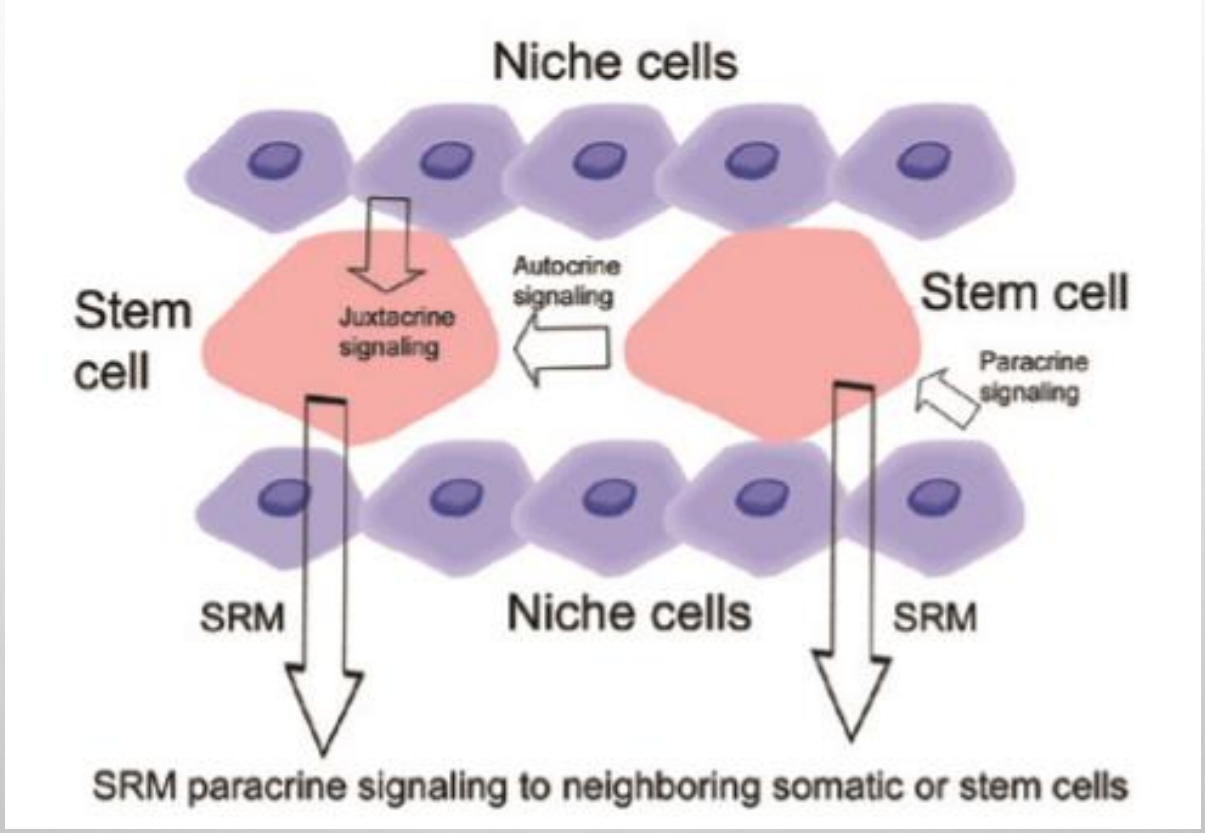
- **PROGENITOR CELL** :STEM CELLS GENERATE AN INTERMEDIATE CELL TYPE OR TYPES BEFORE THEY A



Venere et al 2012

Stem cell niche

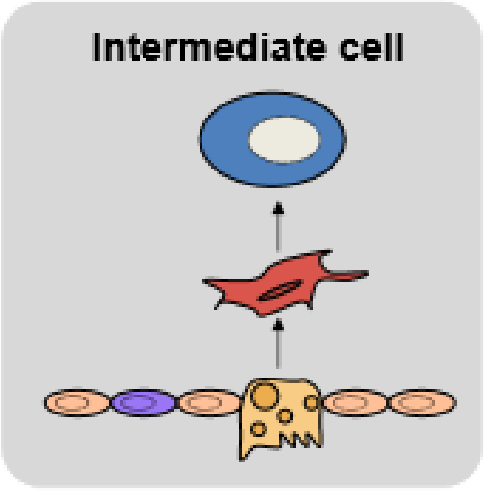
A specialized cellular environment that provides stem cells with the support needed for self-renewal.

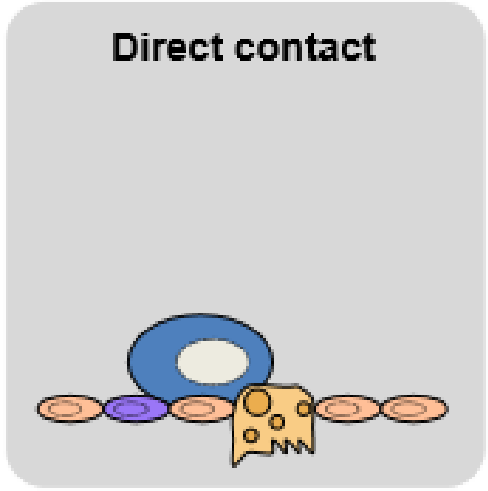


Stem cell niche

Cells only

A single cell type, or a whole host of interacting cells. Cells outside the stem cell's lineage, or they may derive primarily from the stem cell's own descendants.

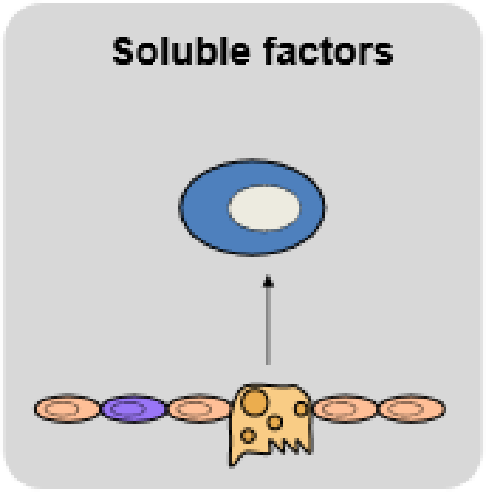




Cells & ECM

Secreted or cell surface factors

Notch, Wnt, FGF, EGF, TGF-β, SCF, and chemokine families



Why stem cells need a special environment?

- Demands on stem cells necessitate **special support for viability**.
- **Nutritive** function
- Niches might be agents of **feedback control (control of stem cell pool size)**.
- Niches are instruments of **coordination among tissue compartments**.
- Niches are **hubs of inter-lineage coordination**.

POTENCY OF STEM CELLS

- THE DIFFERENTIATION POTENTIAL OF THE STEM CELLS

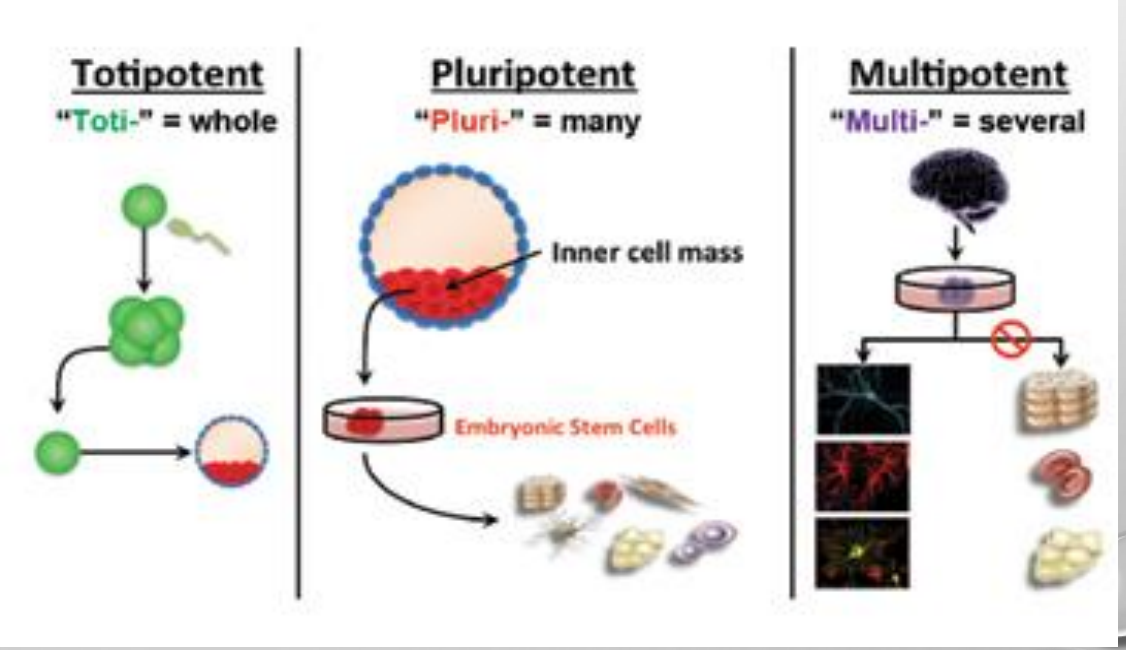
TYPE OF POTENCY :

1-TOTIPOTENT

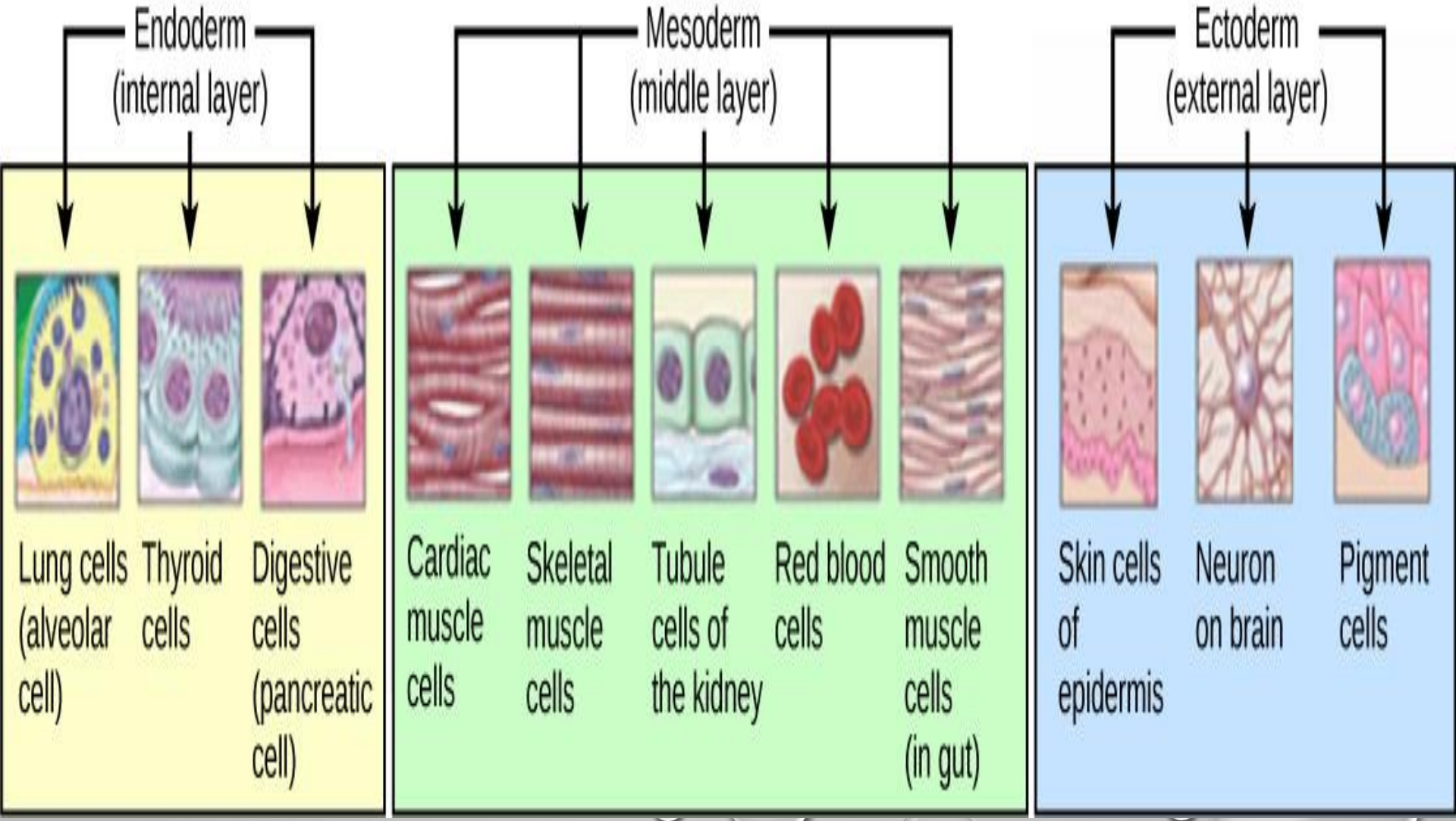
2-PLEURIPOTENT

3-MULTIPOTENT

4-UNIPOTENT



THREE GERM LAYERS



Trans-differentiation vs developmental plasticity

Trans-differentiation	Developmental plasticity
A change in stem cell differentiation from one cell type to another	The multiplicity of stem cell differentiation options

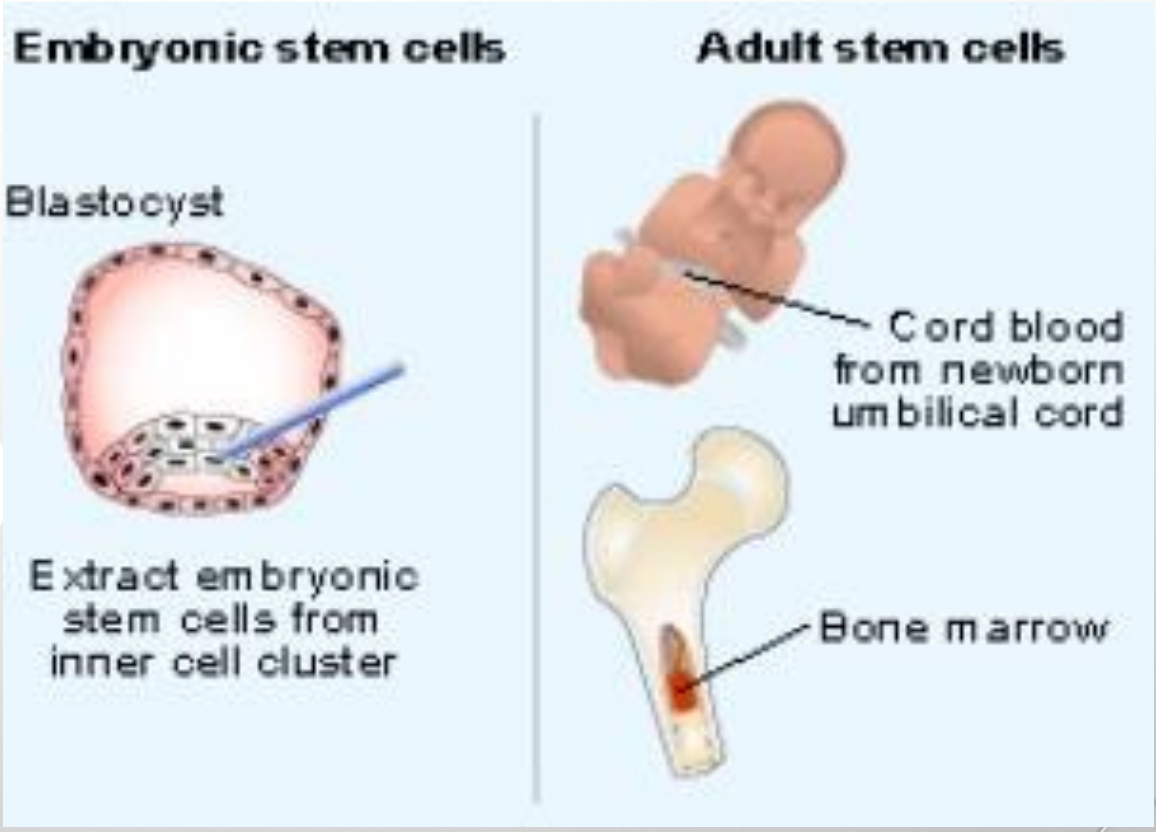
Types of stem cells

Embryonic stem cells

- Are able to differentiate into all the specialized embryonic tissue

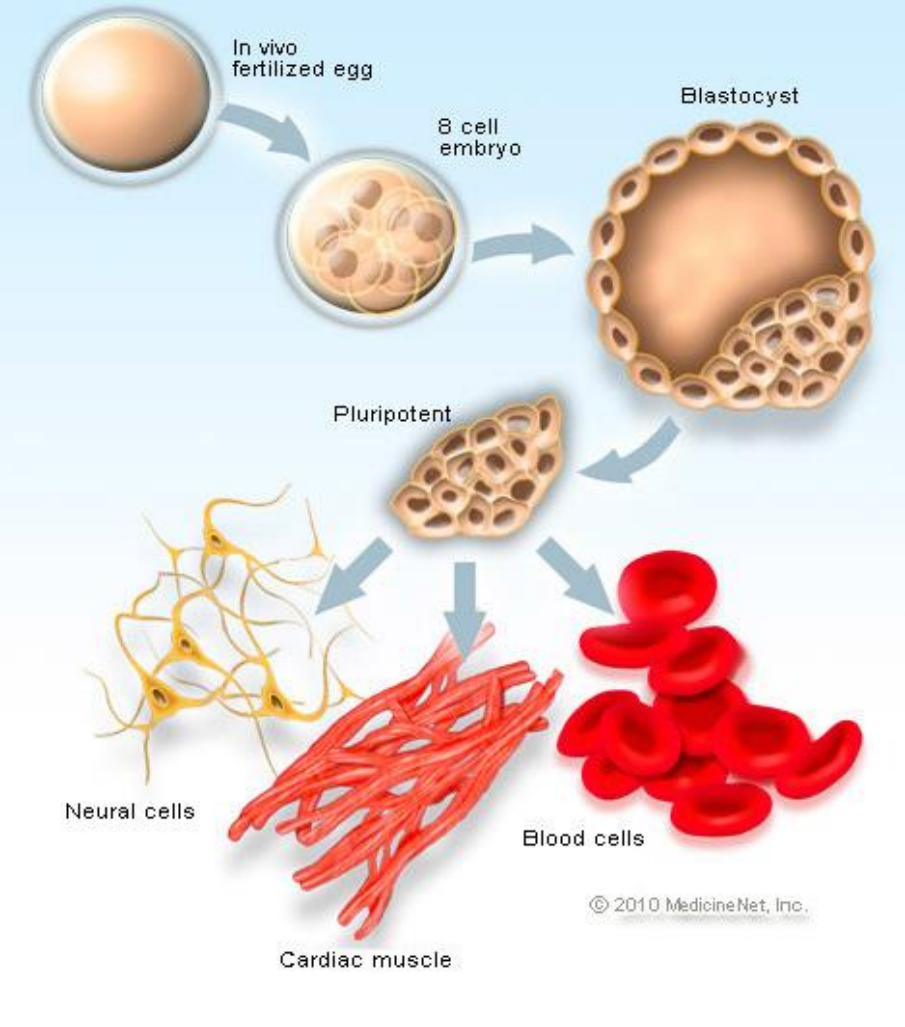
Adult stem cells

- Act as a repair system for the body replacing specialized damaged cells



Embryonic Stem Cells (ESCs)

- ✓ES cells are derived from inner cell mass of mammalian blastocysts
- ✓Develop before implantation in the uterus



Pluripotency of ESCs

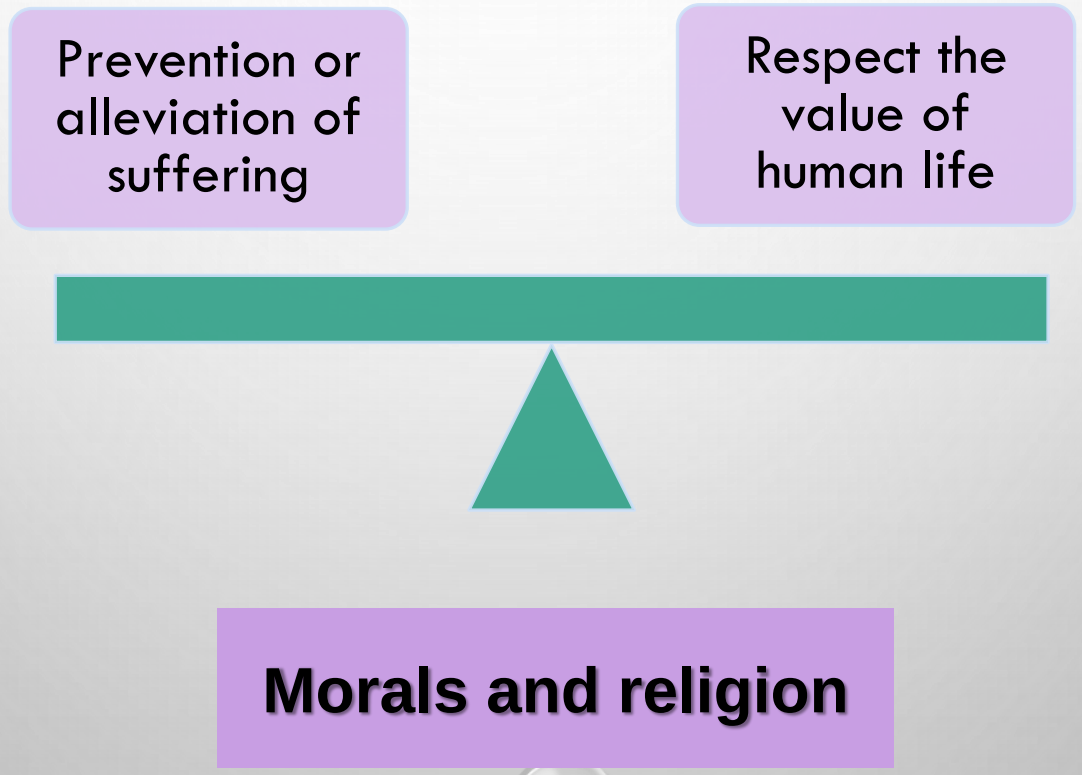
Pluripotency transcription factors:

1. Oct 4
2. Nanog
3. Wnt-β-catenin signaling
4. Other TFs

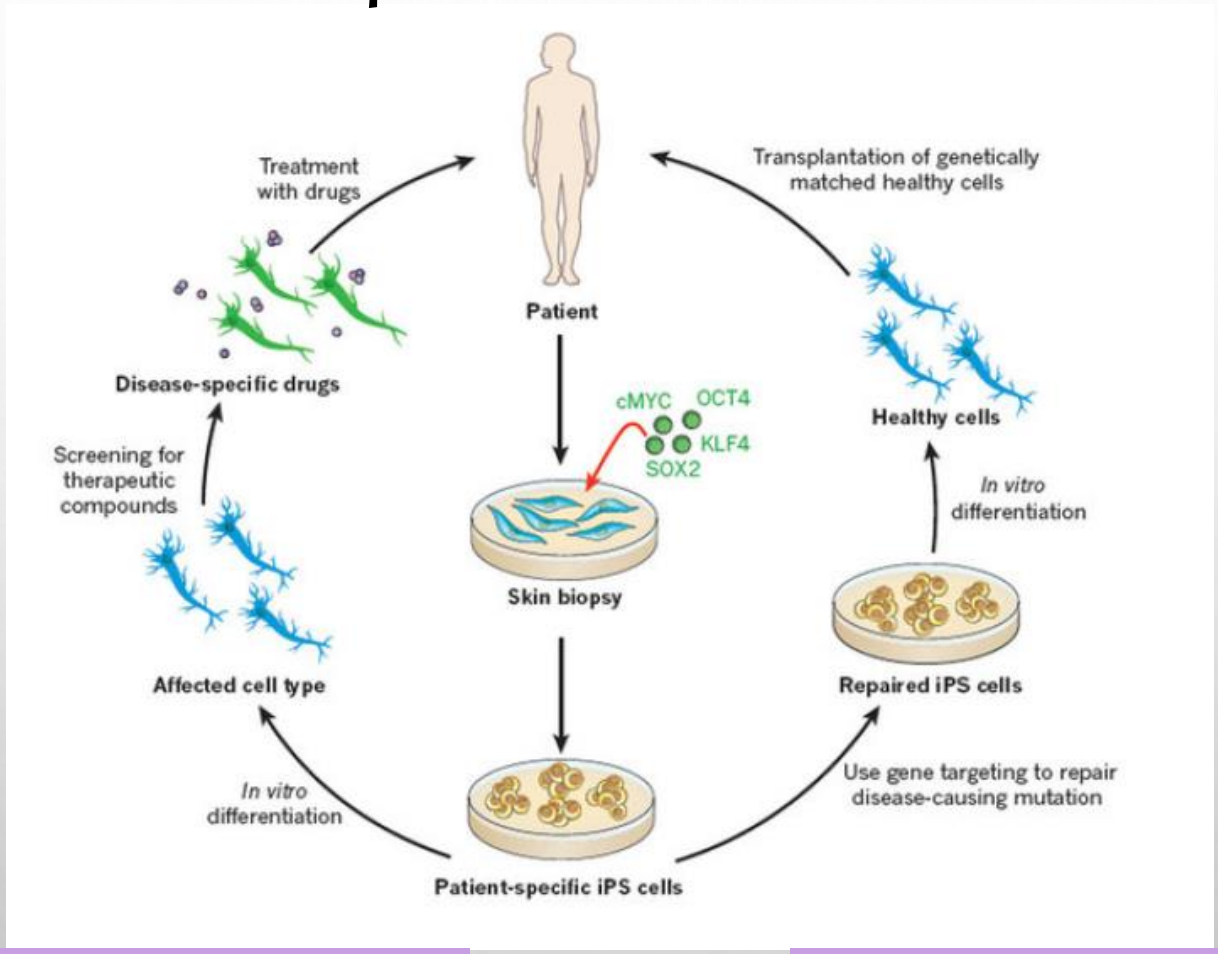
HUMAN EMBRYOS CLONING

- HWANG'S WORK WAS ABLE TO OFFER AN ALTERNATIVE TO USE OF ACTUAL HUMAN EMBRYO BY CLONING SEVERAL HUMAN EMBRYOS, HELPING TO ELIMINATE THE NEED FOR NEW EMBRYOS.
- HWANG CLAIMED HE HAD SUCCESSFULLY CLONED 30 HUMAN EMBRYOS, CLAIMS THAT HAVE NOW BEEN SHOWN TO BE LIES.

The Ethical Dilemma of ESCs



Induced Pluripotent Stem Cells (iPSCs)



Ethical

Autologous

Patient-specific

Safer

Generation of iPSCs

- **iPS cells were obtained by transducing embryonic and adult fibroblasts with defined transcription factors.**
  - **OCT3/4, SOX2, c-Myc, KLF4**

Takahashi K, Yamanaka S. 2006. *Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors.* **Cell 126:663–676.**

Takahashi K, Tanabe K, Ohnuki M, Narita M, Ichisaka T, Tomoda K, Yamanaka S. 2007. *Induction of pluripotent stem cells from adult human fibroblasts by defined factors.* **Cell 131:861–872.**

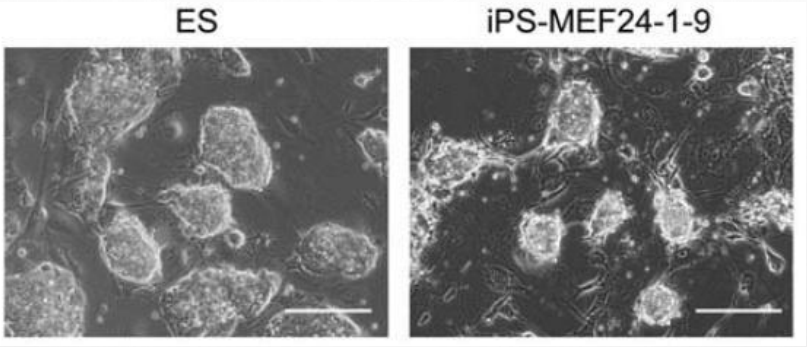
Yamanaka's comparison of iPS and ES cells

Surface antigens

Morphology

Gene expression

Telomerase activities



iPS cells are indistinguishable from ES cells in:

Epigenetic status of pluripotent cell-specific genes

In vitro differentiation

Proliferation

Teratoma formation

Promoter activities

Adult stem cells

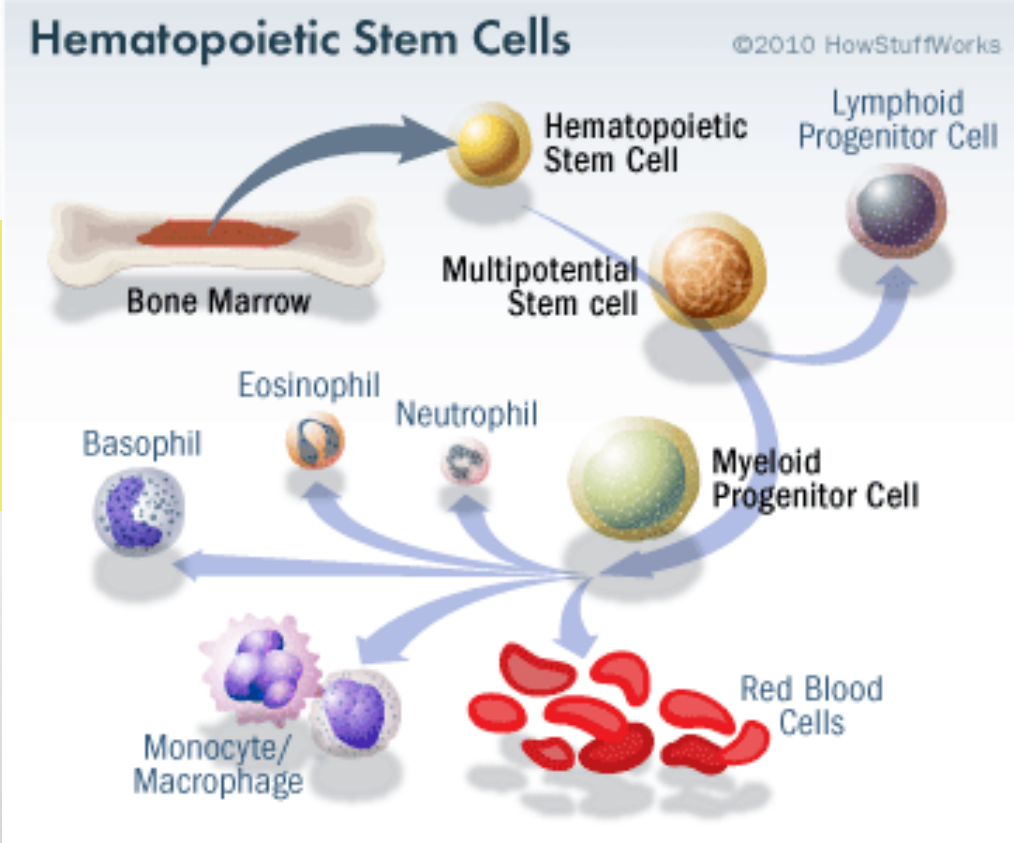
Undifferentiated cells found through out the body.

Function: they divide to replenish dying cells and regenerate damaged tissue

Types of adult stem cells

1. Bone marrow stem cells

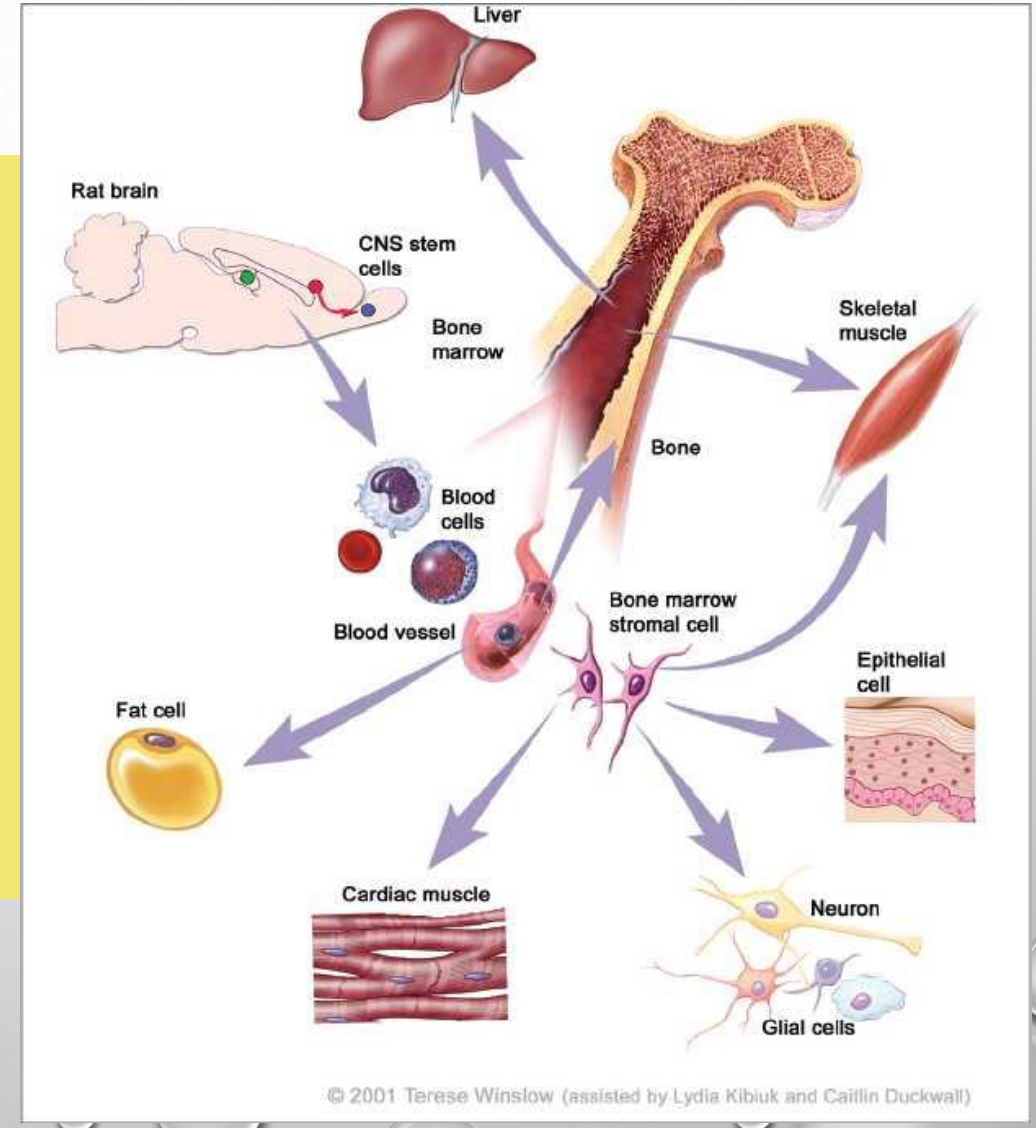
A. Hematopoietic stem cells



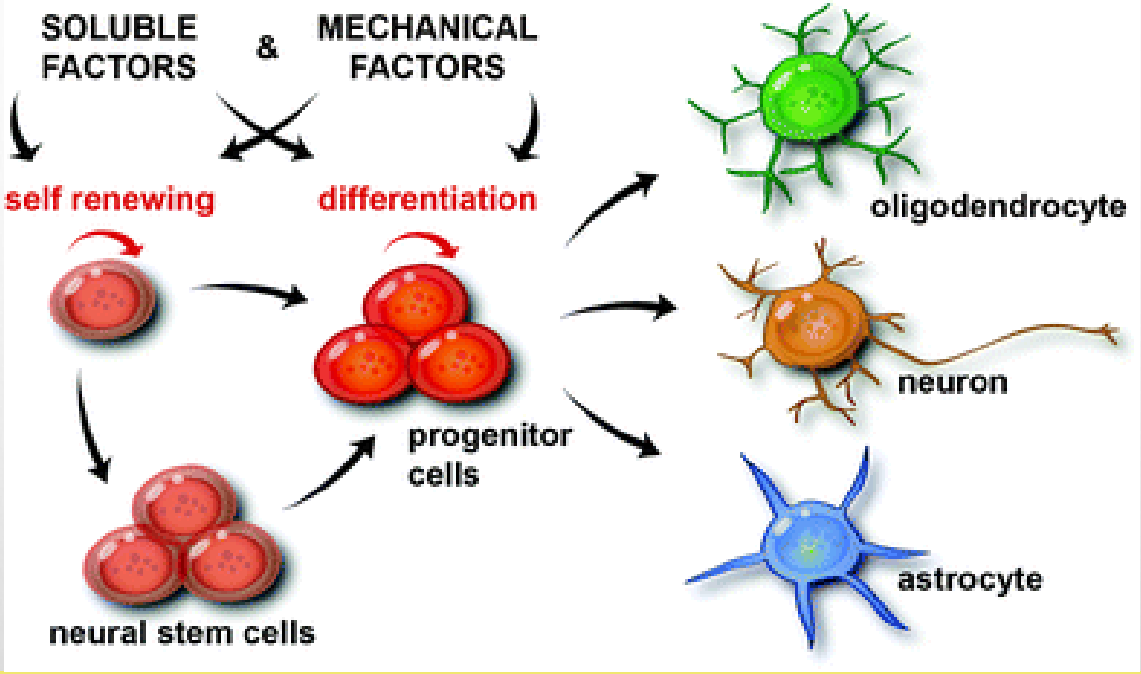
Types of adult stem cells

1. **Bone marrow stem cells**

B. **Somatic stem cells** such as mammary stem cells and mesenchymal stem cells (osteoblasts, chondrocytes, myocytes, adipocytes, neuronal cells).

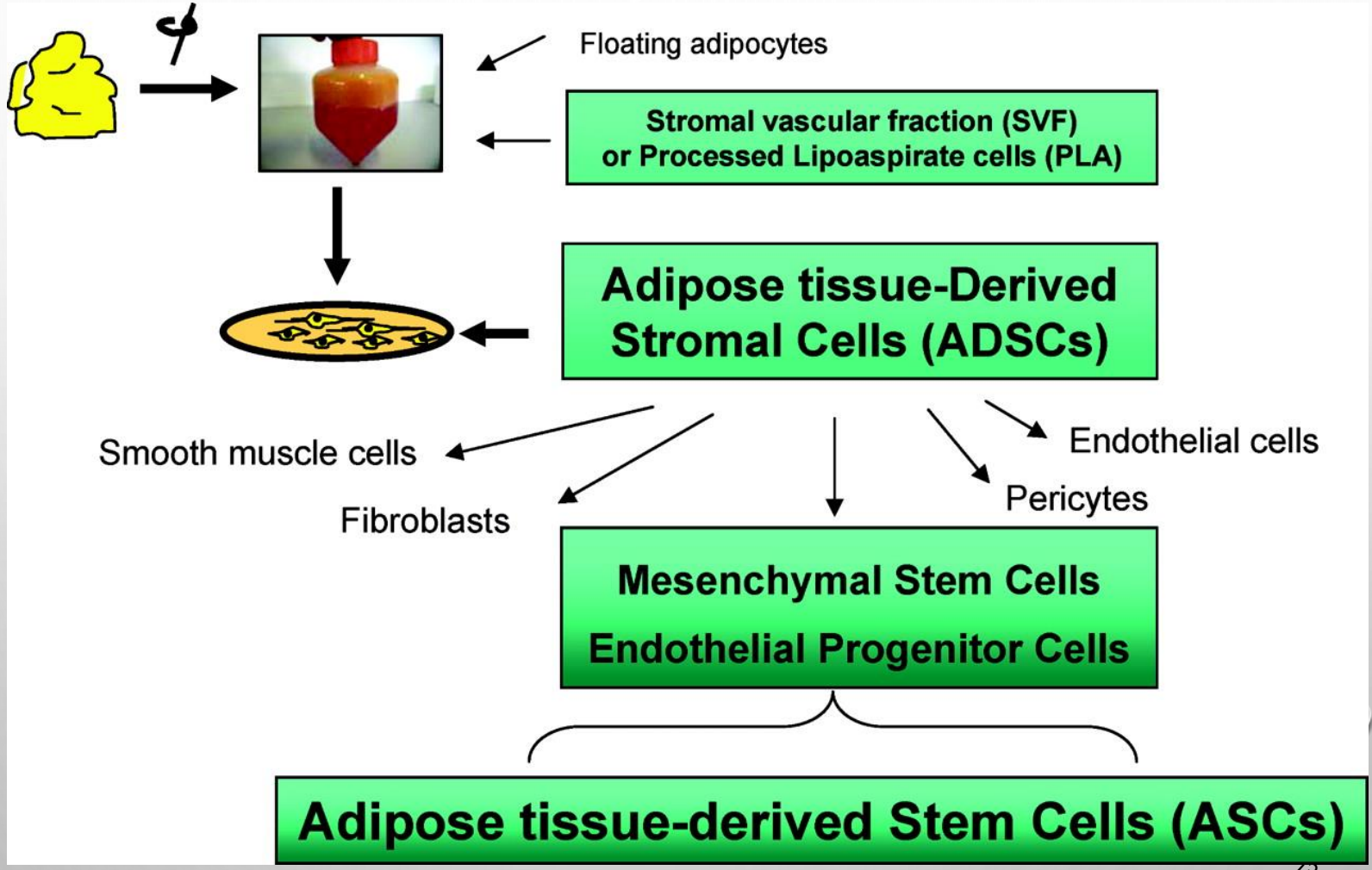


Types of adult stem cells



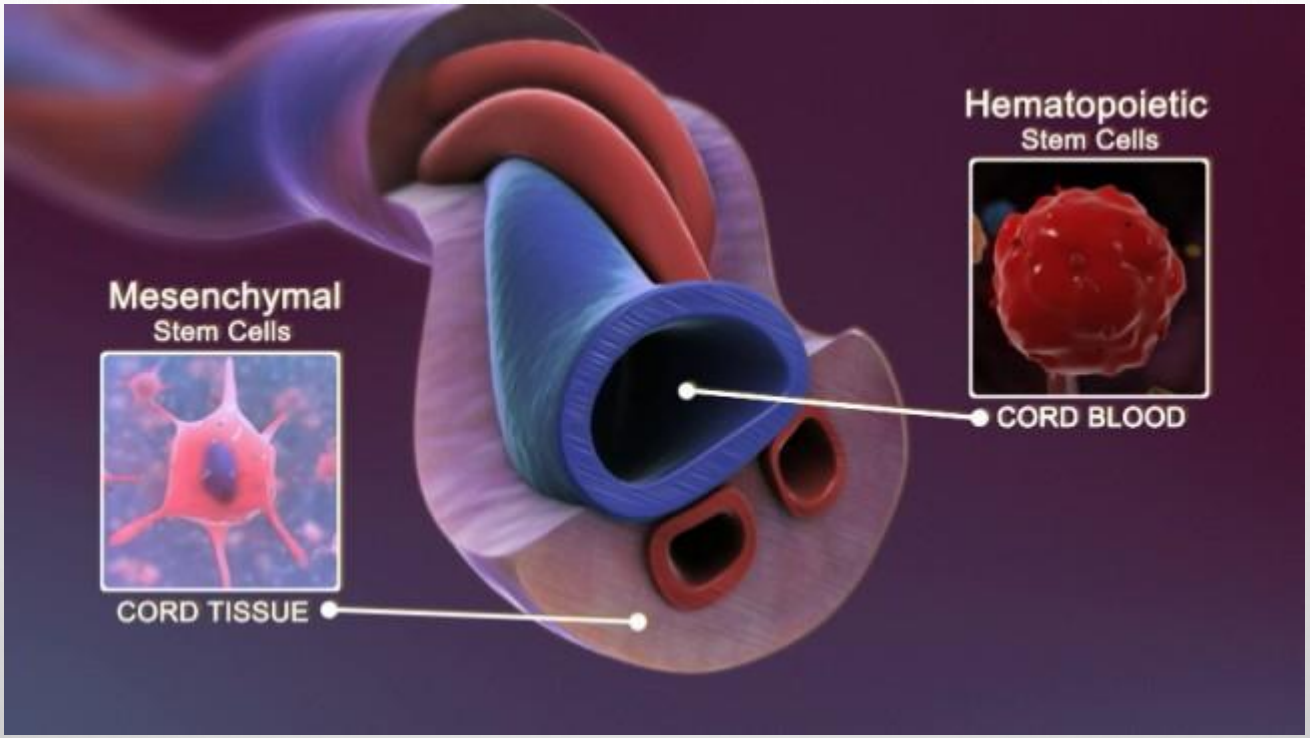
2. Neural stem cells : neurospheres – floating heterogenous aggregates of cells, containing a large proportion of stem cells responsible for adult neurogenesis in **subventriculare zone**, which lines the **lateral ventricles of the brain, and the dentate gyrus of the hippocampal formations**.

Types of adult stem cells



3. Adipose stem cells (ASCs).

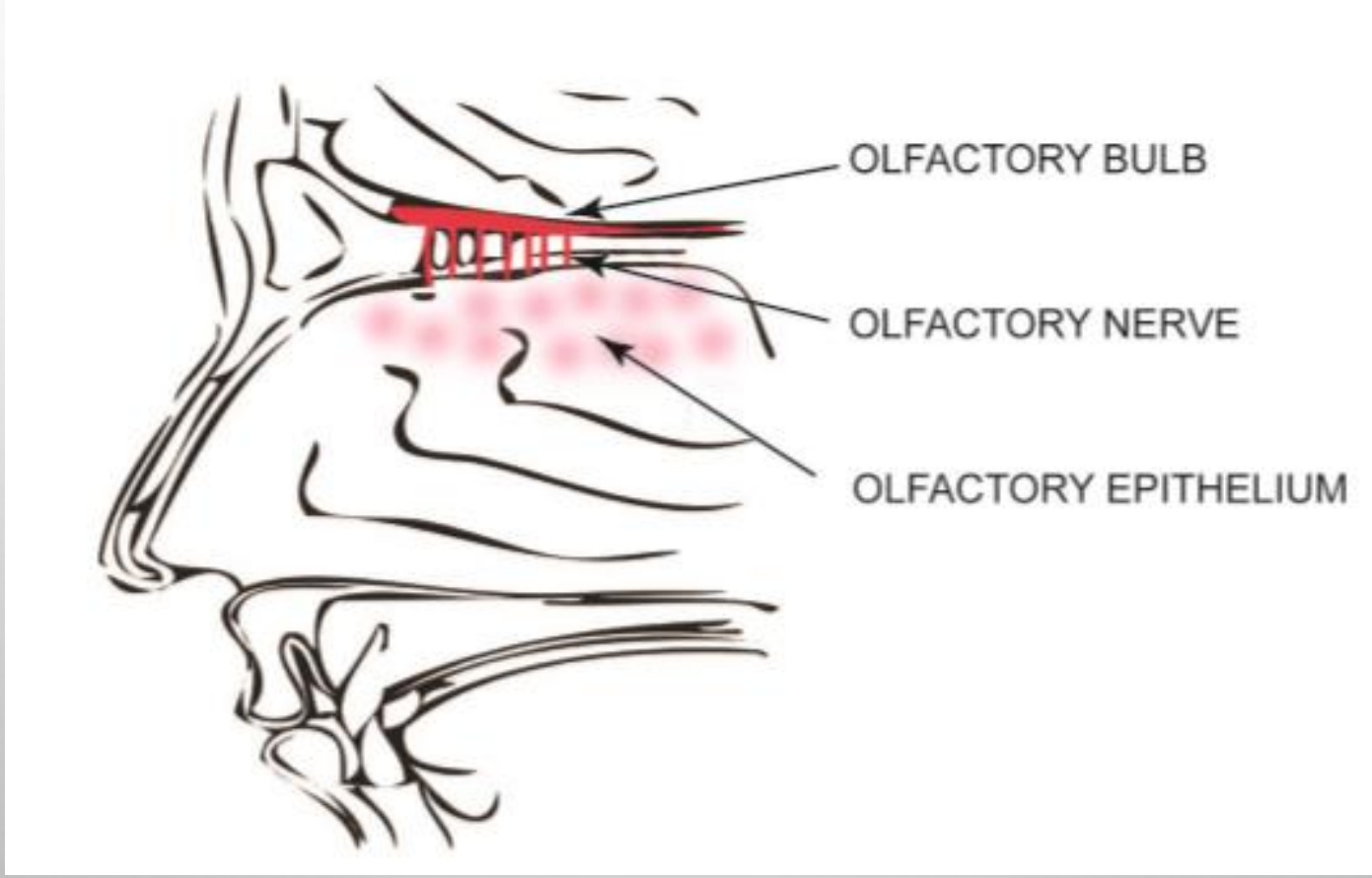
Types of adult stem cells



4. Umbilical cord stem cells

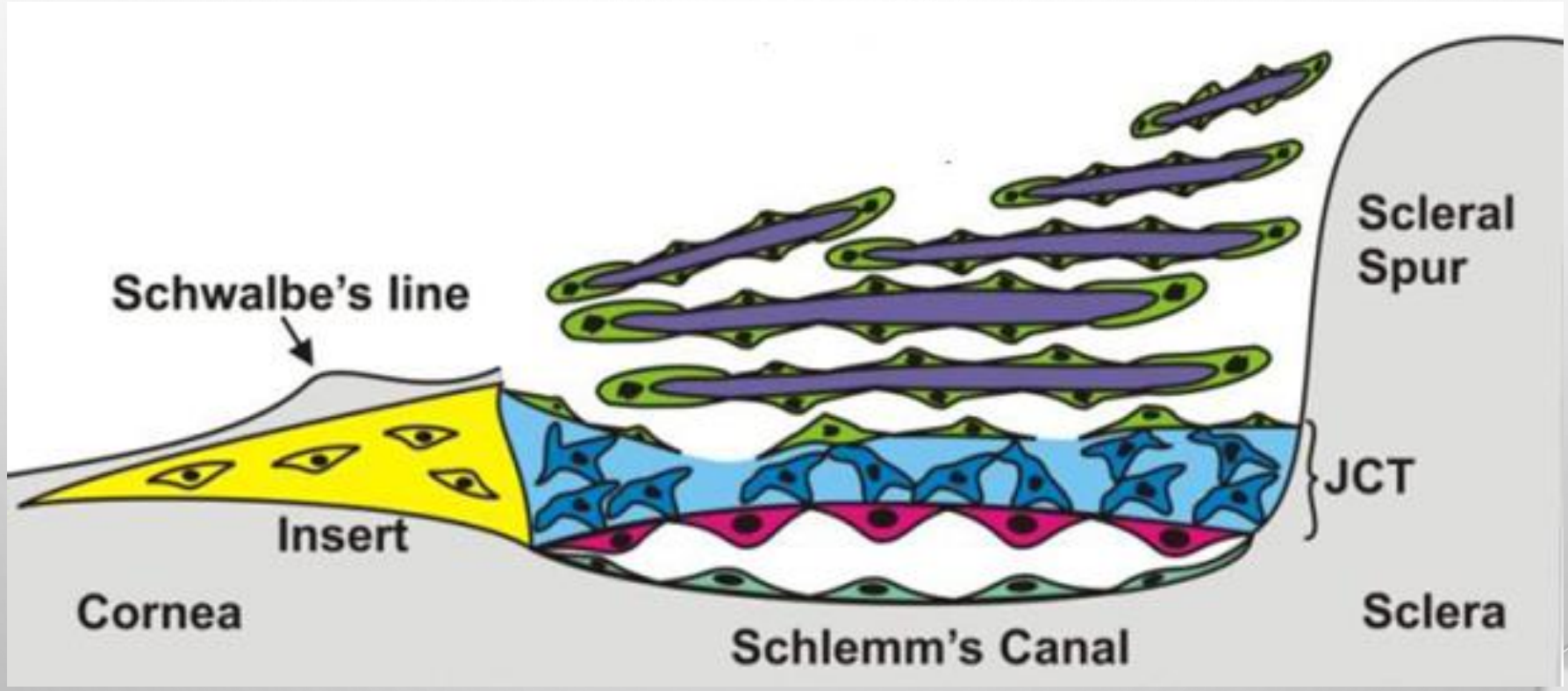
Types of adult stem cells

5. Olfactory adult stem cells: *found in olfactory mucosal cells*



Types of adult stem 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

- ✓ STEM CELL THERAPY HAS DISADVANTAGES SUCH AS

- ➢ CARCINOGENICITY
- ➢ IMMUNE REJECTION
- ➢ INFECTION

- ✓ THESE FACTORS MAKE THE USAGE OF STEM CELL LIMITED.

LIMITATIONS OF USING ADULT STEM CELLS

1-LACK OF STEM CELL MARKERS RESULTING IN DIFFICULTIES TO SEPARATE AND IDENTIFY CELLS.

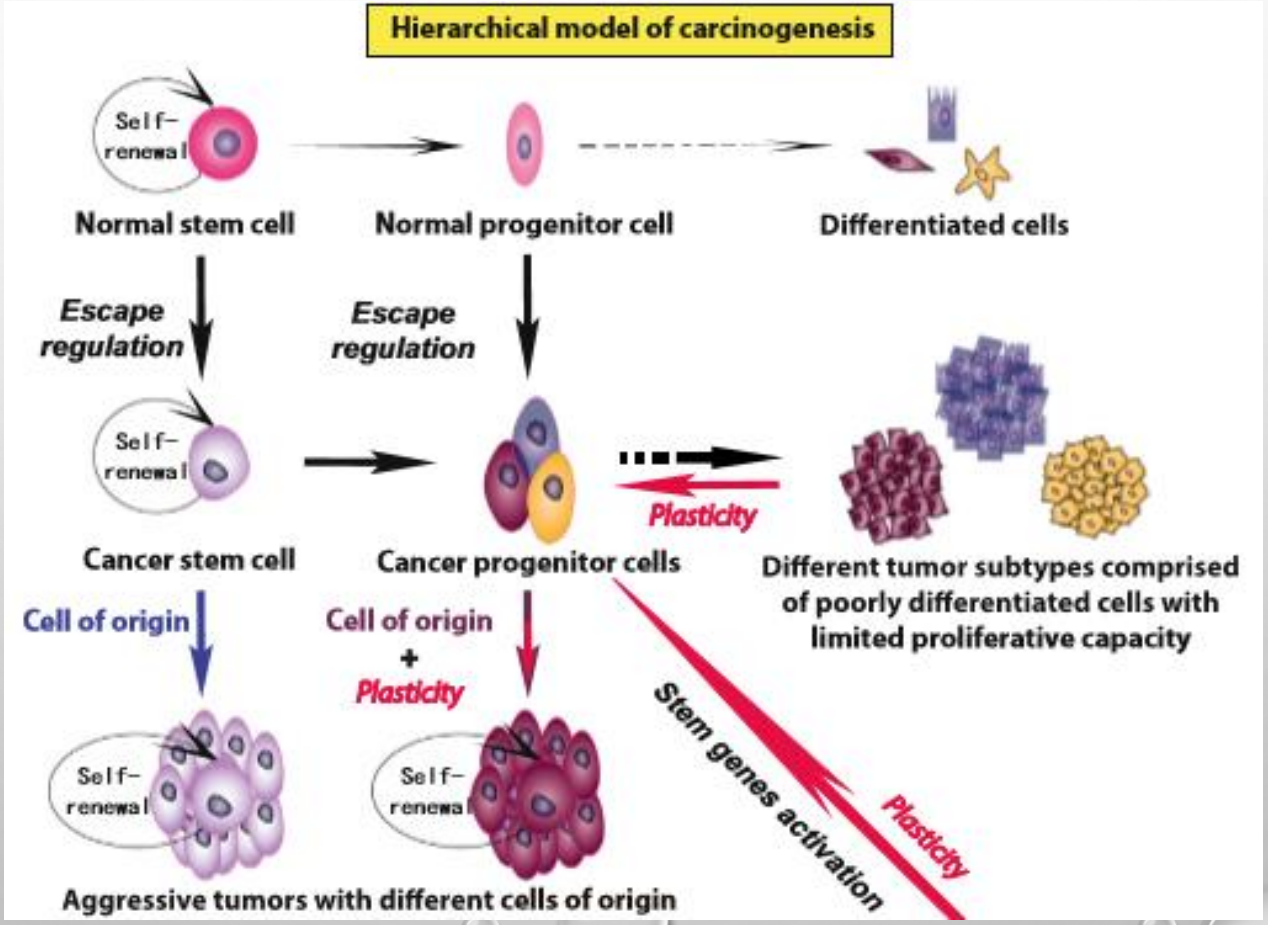
2-IN VITRO SYSTEMS FOR MANIPULATING ADULT STEM CELL POPULATIONS ARE OFTEN NOT WELL DEFINED

3-IN VIVO :OUR UNDERSTANDING OF HOW ADULT STEM CELLS ARE REGULATED WITHIN THEIR NICHE IS IN ITS INFANCY.

4-MULTIPOTENCY OF ASCS

Cancer stem cells (CSCs)

Are tumor cells that have the essential properties of self renewal, clonal tumor initiation capacity, clonal long term repopulation potential and plasticity



Why 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.

- **Cell-based therapy and regenerative medicine**.