Tissue Engineering & Regenerative Medicine

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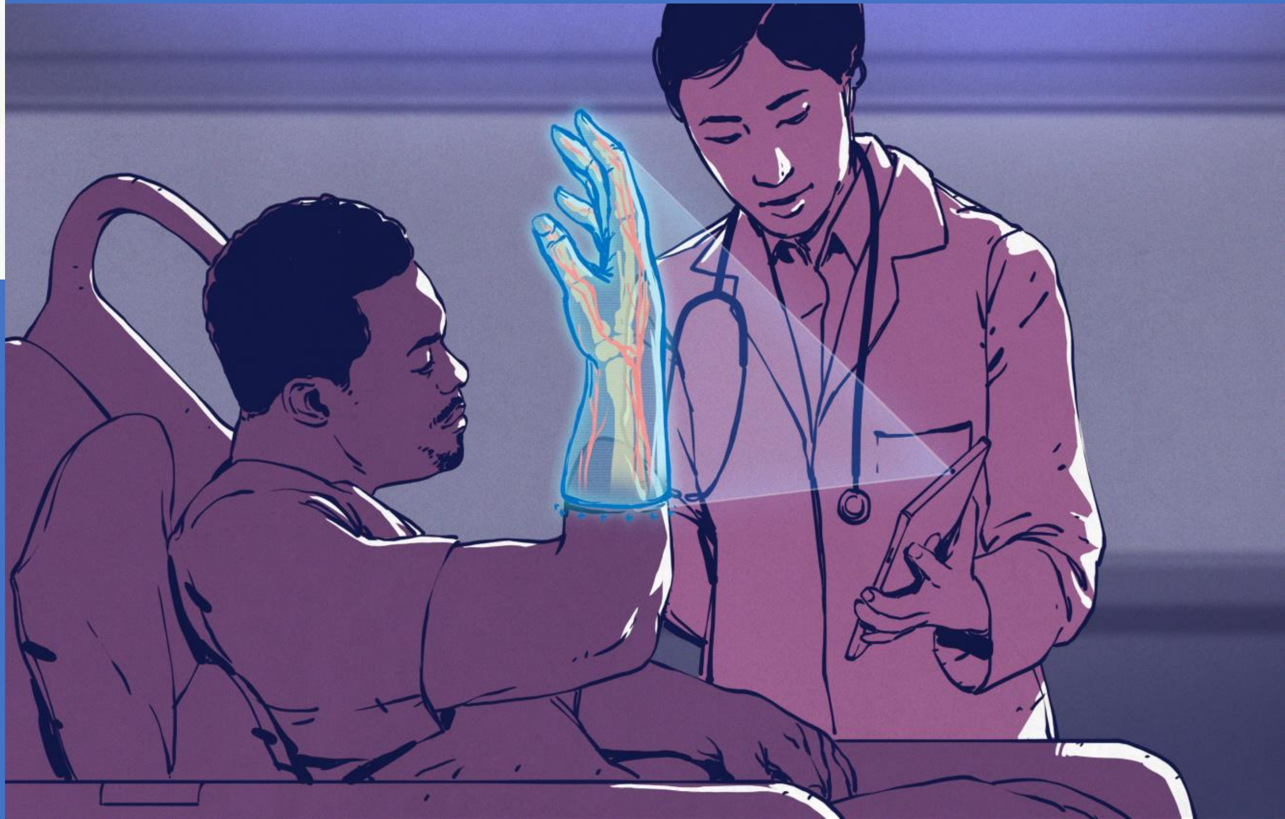
Human “Spare Parts Industry”



First Experiments

- The first of the experiments in 1993.

- They sprinkled chondrocytes with collagen in scaffolds with 3D pores and co cultured the two in a bioreactors.

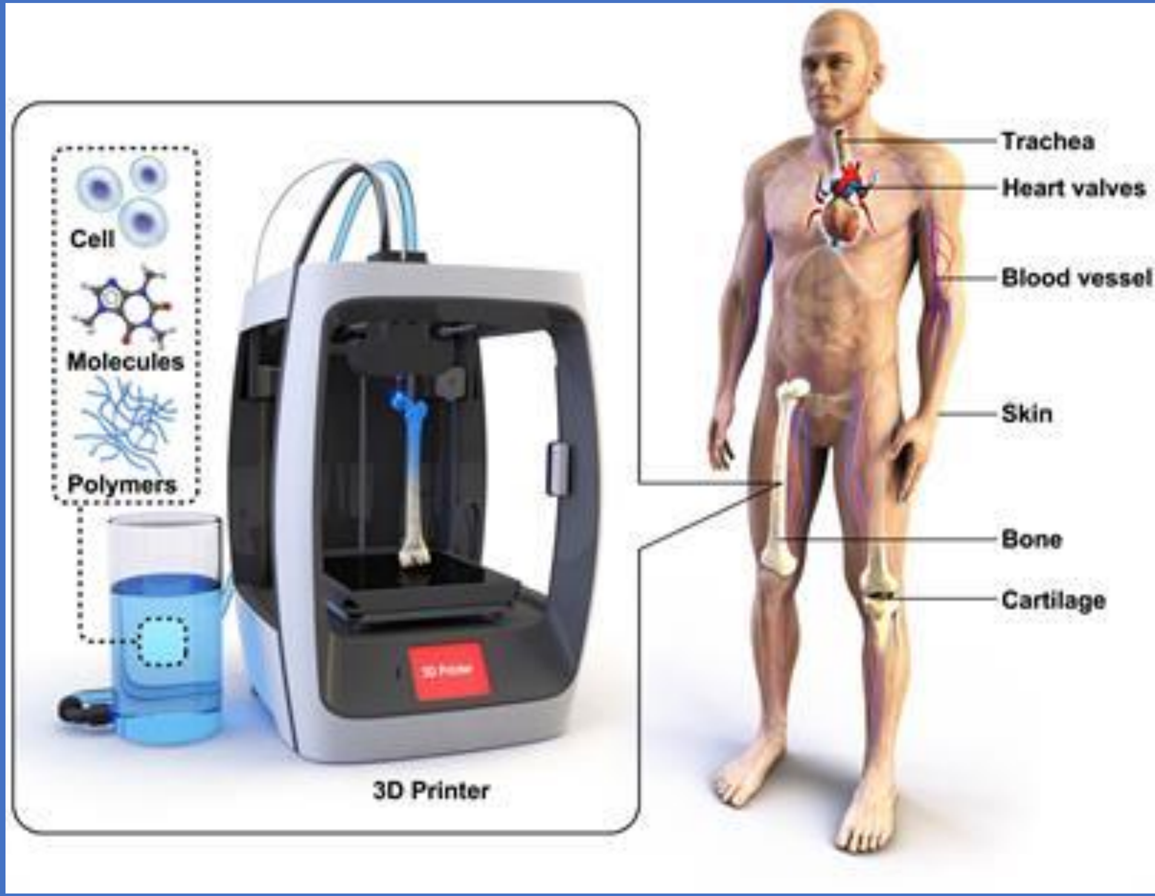
- The chondrocytes eventually replace the collagen & successfully develop an ear which was grafted and grown on the back of a laboratory mouse.

History of stem cell

- 1st successful human islets cell transfer from cadavers.
- 2001- 1st cloned human embryos (only to 6 cell stage) created by Advanced Cell Technology (USA).
- 2004- Harvard researchers grow stem cells from embryos.

Tissue engineering

- This is one type of technology.
- An amalgamation of biology, medicine and engineering.
- Similar to regenerative medicine.



Regenerative medicine

- RM means use of stem cells.

What is stem cell?

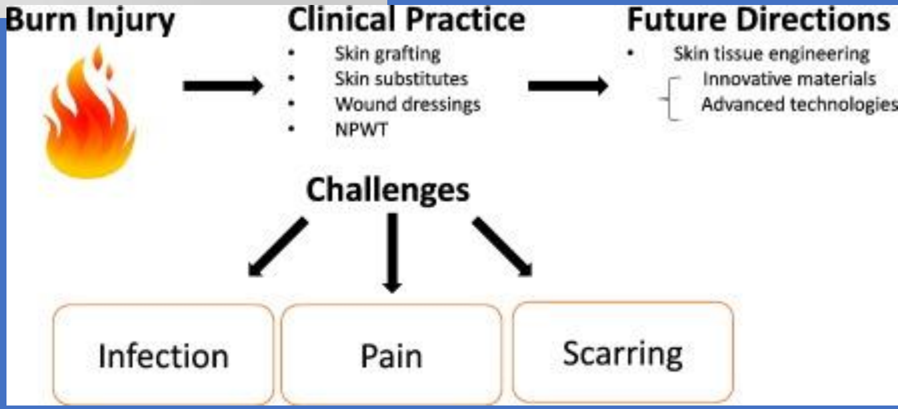
- All SC have 3 general properties-
  - Undifferentiated (unspecialized) biological cells.
  - Can differentiate into specialized cells.
  - Can divide to produce more stem cells for long periods.

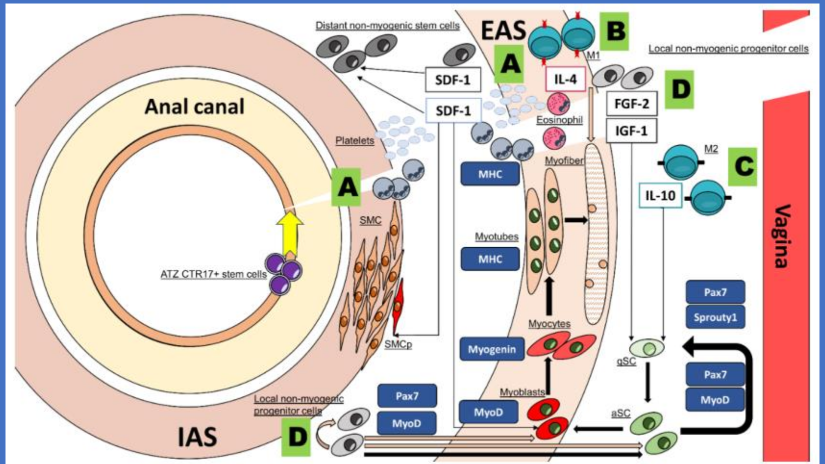
Ultimate goal-

Develop replacement tissues or organs for individuals.

- To replace or support the function of defective or injured body parts.

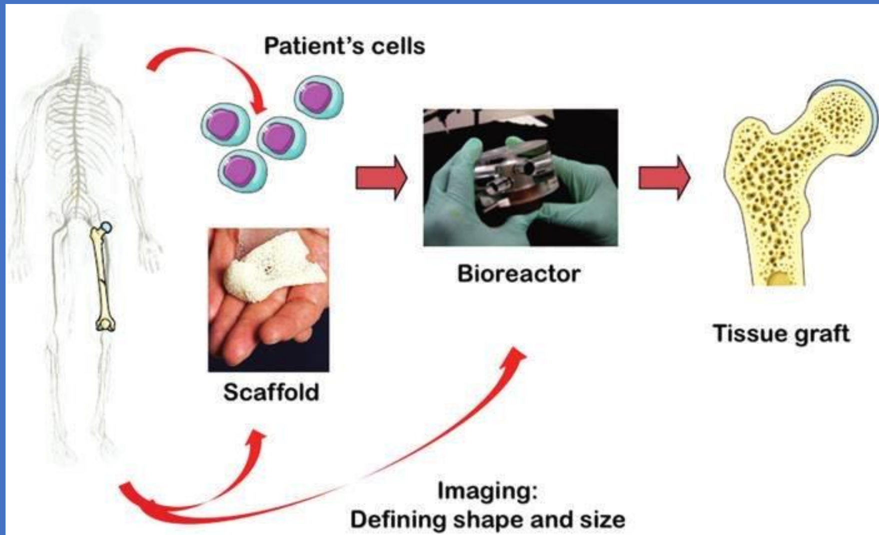
- Directed management of the repair of tissues within the body.





Cell sources

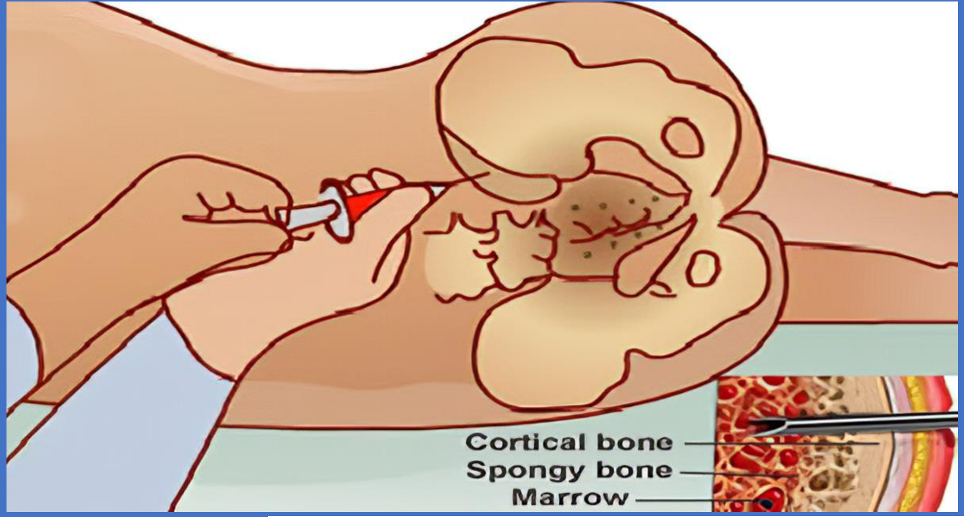
- Primary cells-
  - Differentiated cells harvested from pt (tissue biopsy).
  - Low cellular yields.
  - Potential age related problems.
- Passaged cells-
  - Serial expansion of primary cells(100-1000x).
  - Tendency to lose potency or de differentiation with too many passages.
- Stem cells-
  - Undifferentiated cells.
  - Self renewal capacity (unlimited).
  - Can differentiate into functional cell types.
  - Very rare.

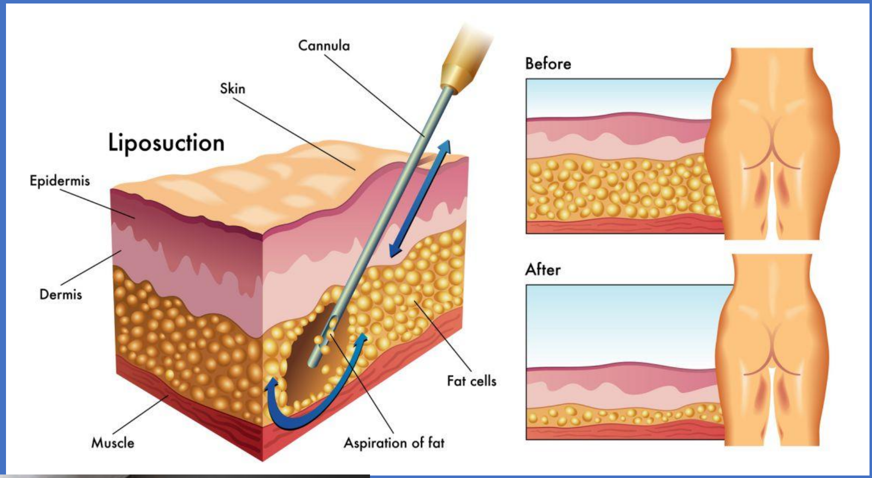


Stem cells sources

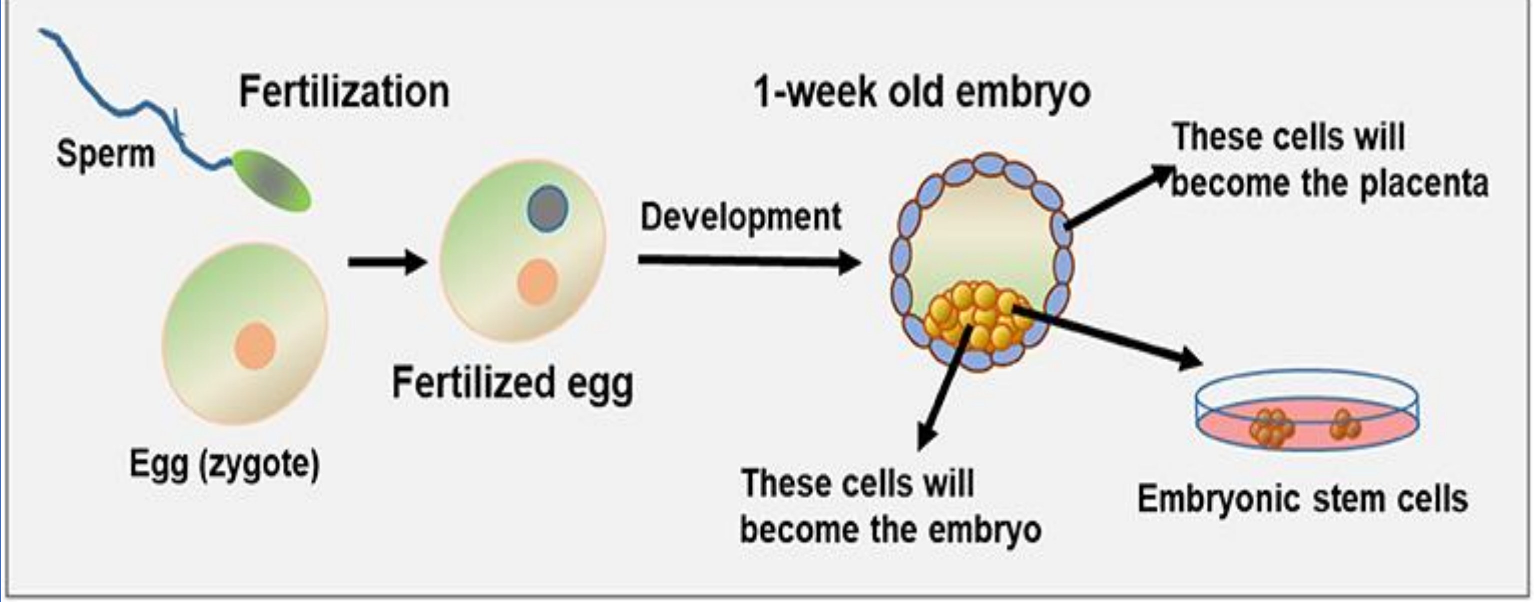
3 sources of autologous adult stem cells in humans:

- BM- femur or iliac crest.
- Adipose tissue (lipid cells)- by liposuction.
- Blood-
  - From the donor.

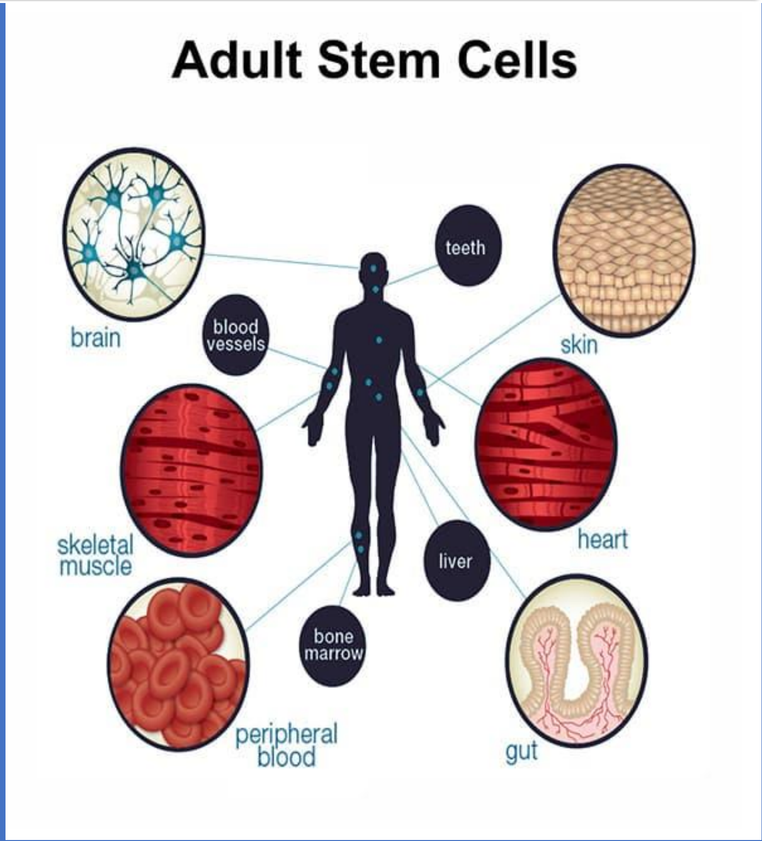




Types of stem cell

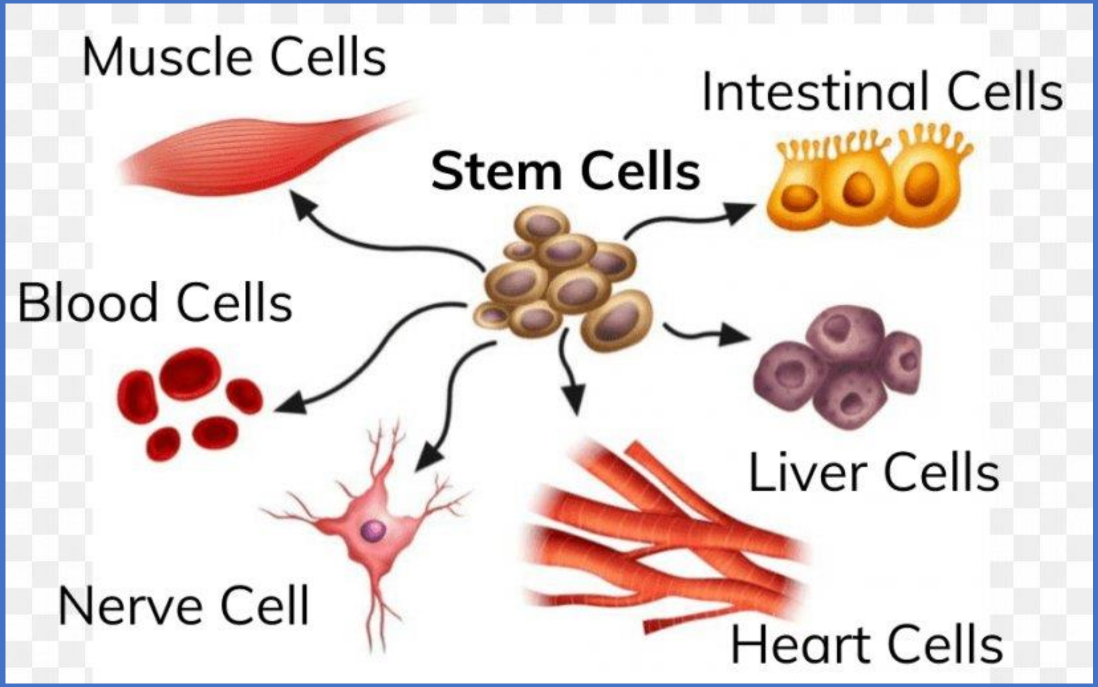


- Embryonic SC.
- Adult SC.



Adult stem cells

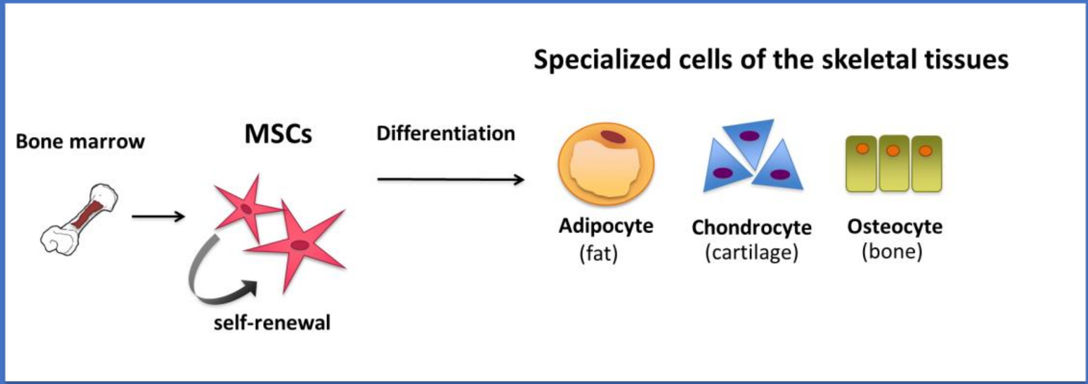
- Also called somatic stem cells.
- Can be found in children, as well.
- Mostly multipotent and are generally referred to by their tissue origin.
- To treat leukemia and related bone/blood cancers through BM transplants.
- Used in regenerative medicine to treat tendon and ligament injuries in muscle, joint and cosmetology.

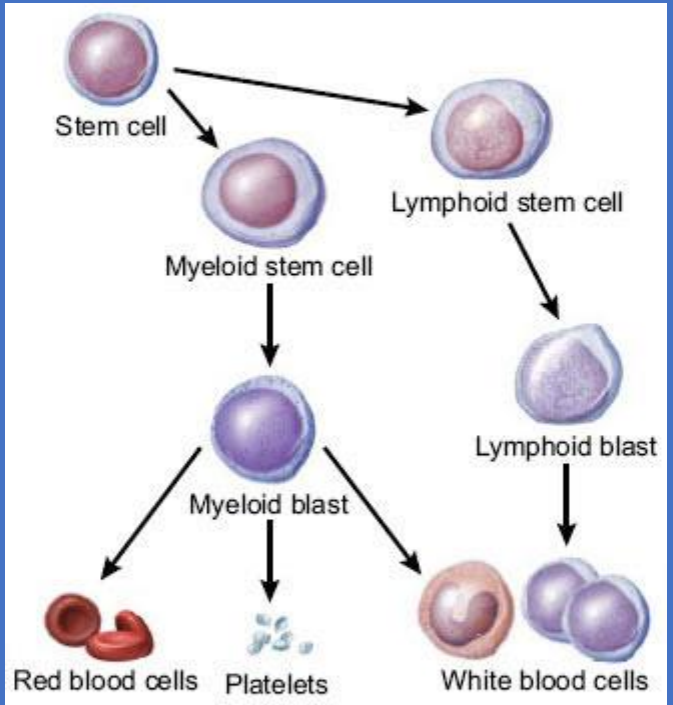


Stem cell types

2 types-

- Mesenchymal-
  - Connective tissue (bone, cartilage etc).
  - Typically isolated from BM.
- Haematopoetic-
  - Give rise to blood cells & lymphocytes.
  - Isolated from BM, blood (umbilical cord).



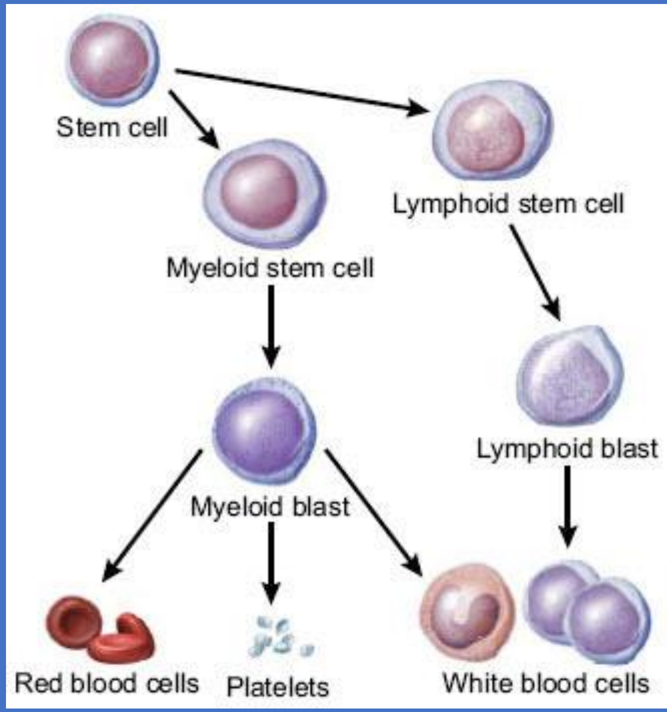


Terminology

Cell type	Potency	Example
Totipotent	Can differentiate into any embryonic cell.	Zygote. (---embryo, placenta).
Pluripotent	Can differentiate into almost any kind of cells.	Embryonal stem cells.
Multipotent	Can differentiate into only closely related cells.	Germ layer stem cell, HSC.
Bipotent	Makes 2 cell type.	Tissue determined stem cell.
Unipotent	Can form only 1 type of cell.	Terminal cell (muscle SC, cardiac SC).
Progenitor cell	Committed to certain cell types.	

Stem cell Availability

- Naturally exist in all tissues.
- Stem cells are rare.
- BM typically has-
  - Single MSC for every 10 lacs myeloid cells.
  - Single HSC for every 1 lac myeloid cells.



Uses

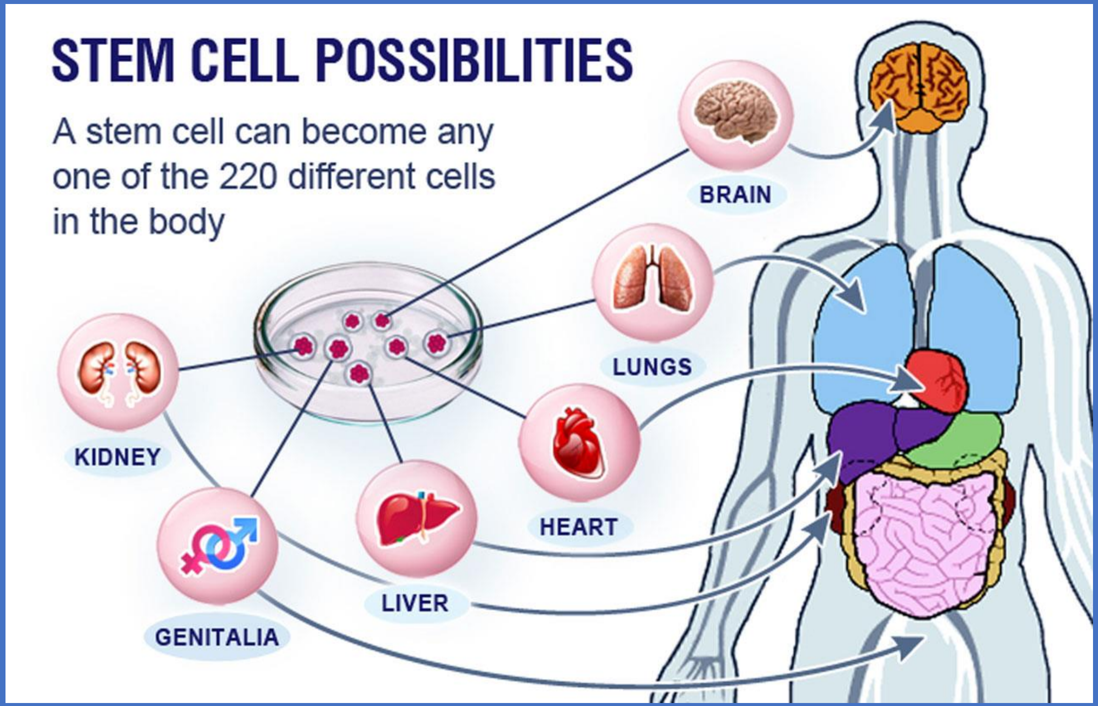
Treatments

1. Osteoarthritis
2. Rheumatoid arthritis
3. Baldness reversal
4. Spinal cord injury repair
5. Diabetes
6. Stroke and traumatic brain injury repair
7. Heart infarction
8. Amyotrophic lateral sclerosis
9. Crohn’s disease.
10. Wound healing.
11. Replace missing teeth.
12. Restore vision.
13. Parkinson’s disease
14. Repair hearing.

Tissue engineering

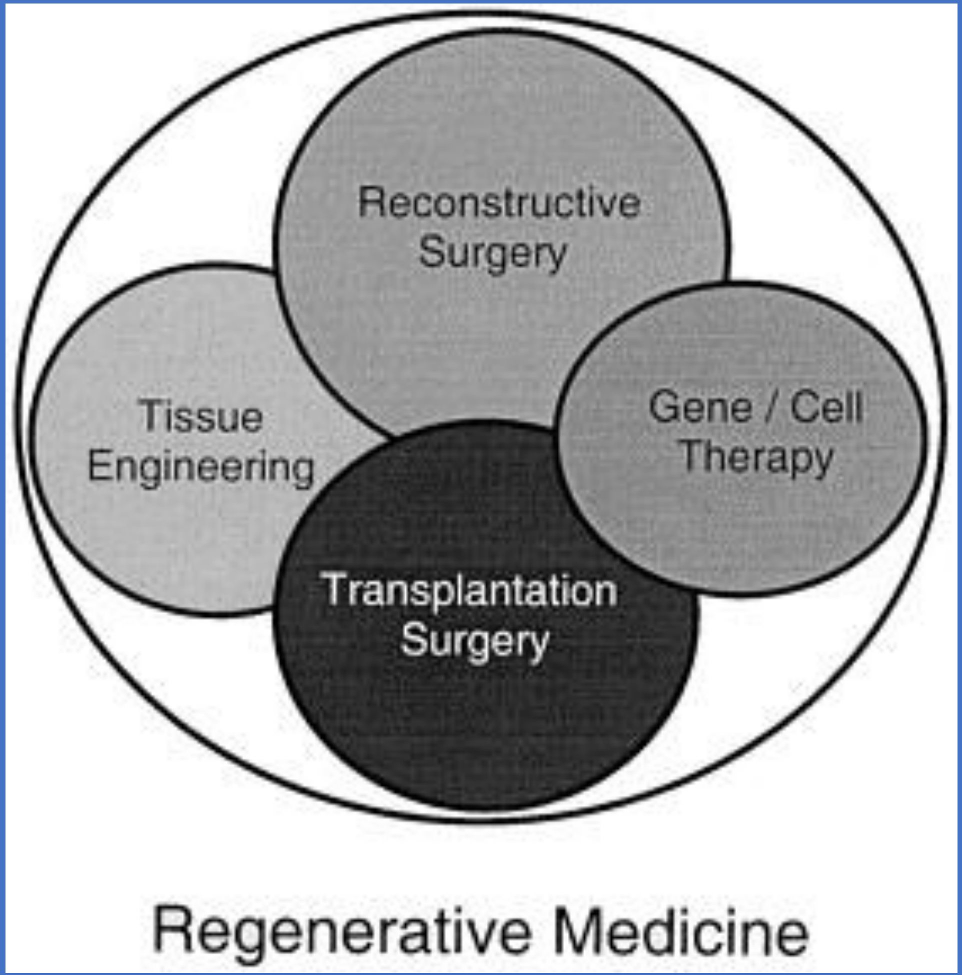
Research is going on for-

- Skin.
- Cartilage.
- Blood vessels.
- Bone.
- Muscle.
- Nerves.
- Liver.
- Kidney.
- Etc. etc. etc.



Tissue engineering in surgical disease

Tissue	Conditions treated
Skin	Burns & skin defects after excision or trauma.
Bladder	Congenital malformation & cystectomy.
Anal/bladder sphincter	Incontinence.
Oesophagus	Benign stenosis & resection for malignancy.
Small intestine	Intestinal failure after surgical resection for crohn's disease, cancer or ischaemia.
Trachea & bronchus	Cong. & acquired stenosis & resection for malignancy.
CRC	Gene therapy.



Gene therapy

Principle:

Transferring genetic material into target cells, which allow for-

Correction of genetic defects in tumor suppressor genes,

Inactivation of oncogenes.

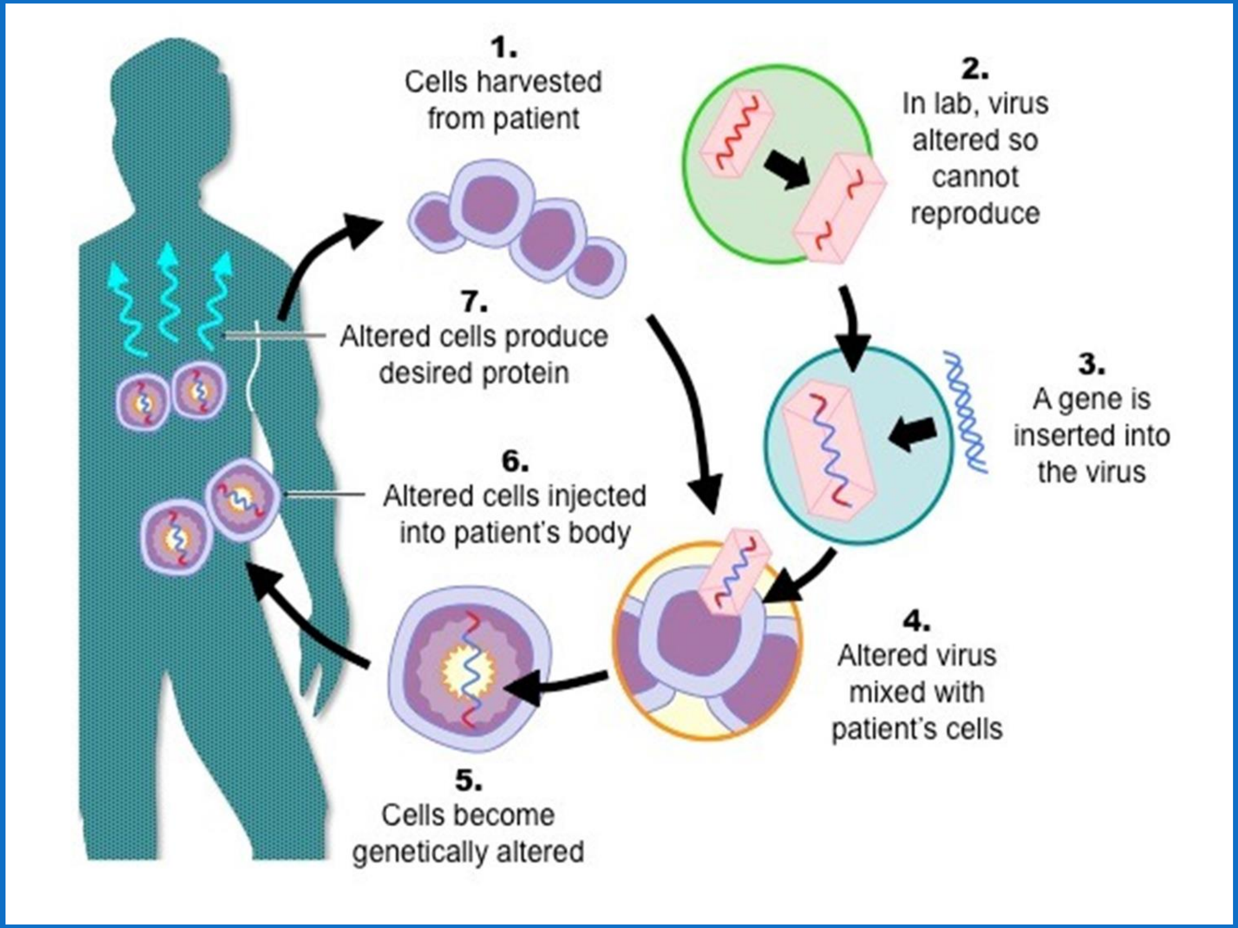
Insertion of “suicide genes” into the colorectal cells.

Example:

- Correction of p53 mutations,
- Inactivation of k-ras gene product.
- delivery of pro-drug-converting enzymes are currently being studied.

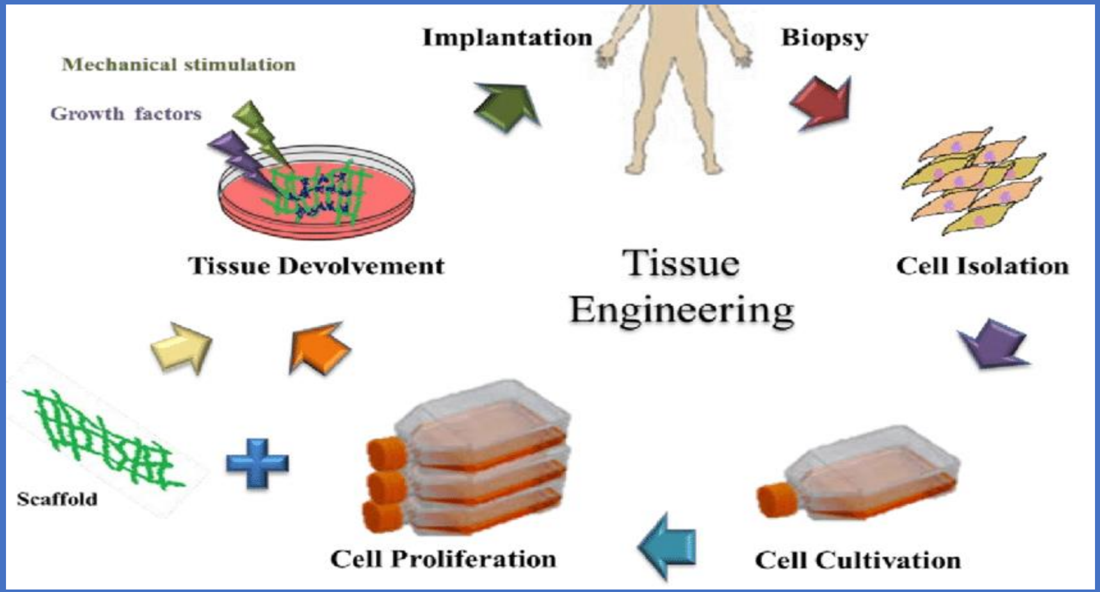
Future:

Long term clinical usefulness remains to be defined.



Steps for tissue engineering

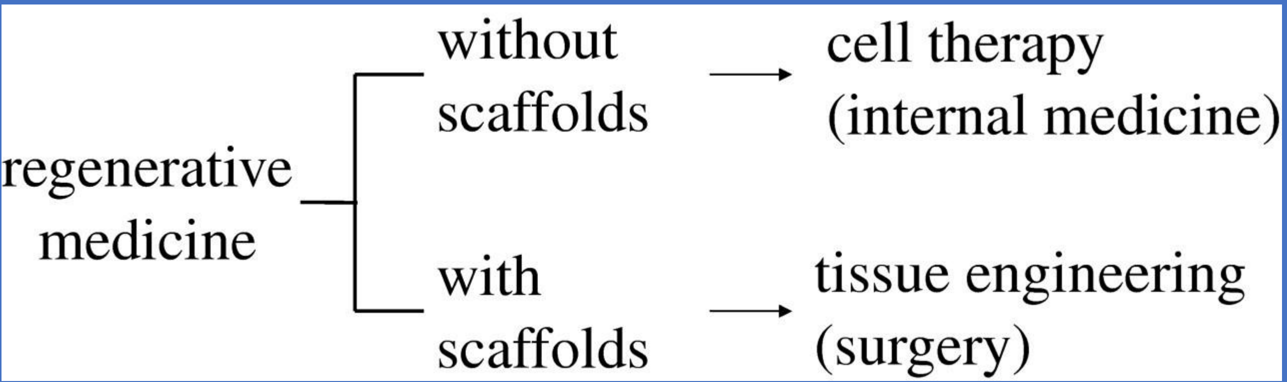
- Cell isolation & expansion from patient.
- Cell deposition into 3D scaffolds.
- Dynamic culture (bioreactor) of the scaffold + cell system.
- Incorporation into the patient.



Scaffolds

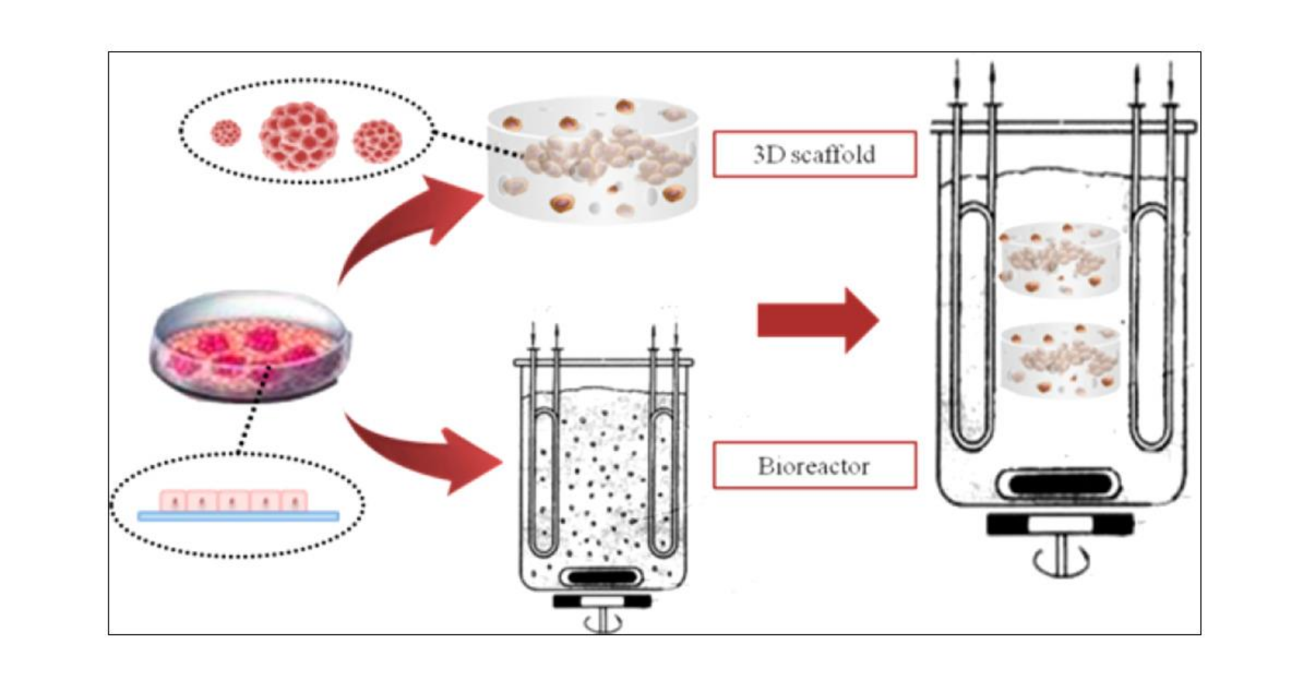
- Typically made of polymeric biomaterials,

- **Provide the structural support for cell attachment and subsequent tissue development**.



Bioreactor

- Used in vitro development of new tissue by-
  - Providing biochemical and physical regulatory signals to cells and
  - Encouraging them to undergo differentiation and/or to produce ECM prior to in vivo implantation.



Culture media

Appropriate chemical environment-

- pH.
- Osmolarity.
- Ionic strength.
- Buffering agents.

Appropriate nutritional environment-

- Nutrients.
- Amino acids.
- Vitamins.
- Minerals.
- Growth factors.

Growth conditions

Stimulate physiological environment.

- pH-7.4.
- 37 degree C.
- 5% CO_2.
- 95% relative humidity.
- Culture media replenished periodically.

Chemical environment

- O_2 concentration must be within a specific range-
    - Low O_2 – can retard growth.
    - High O_2- can be inhibitory or toxic.
- At 37 degree C contains only 21 mMO_2.

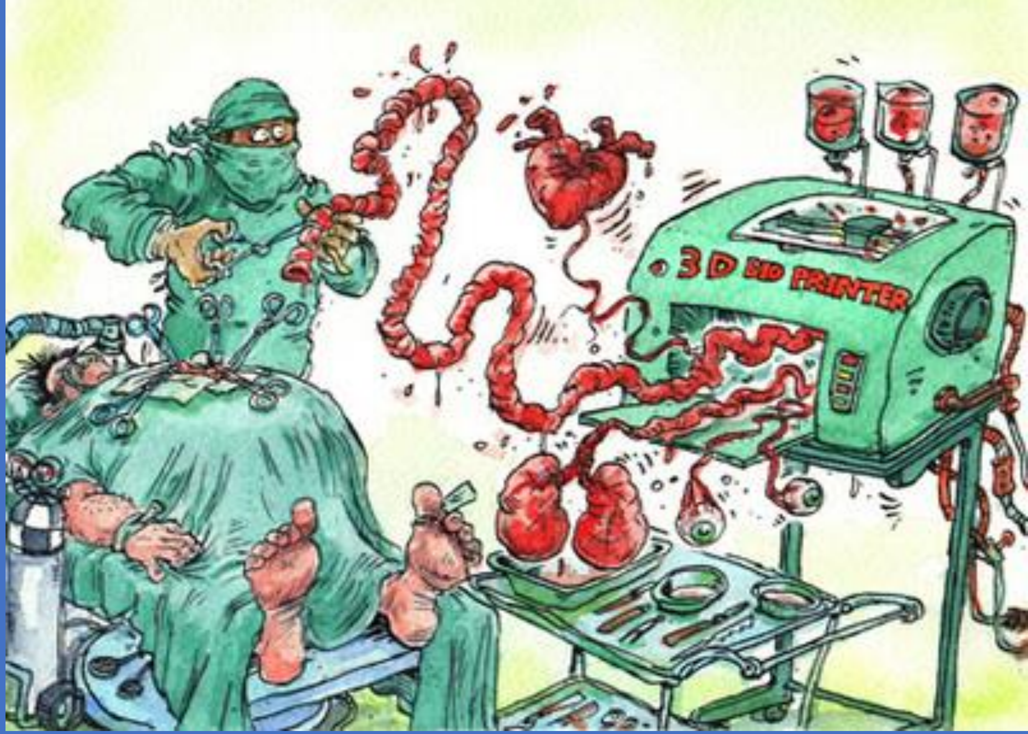
Culturing of cells

Sterilization-

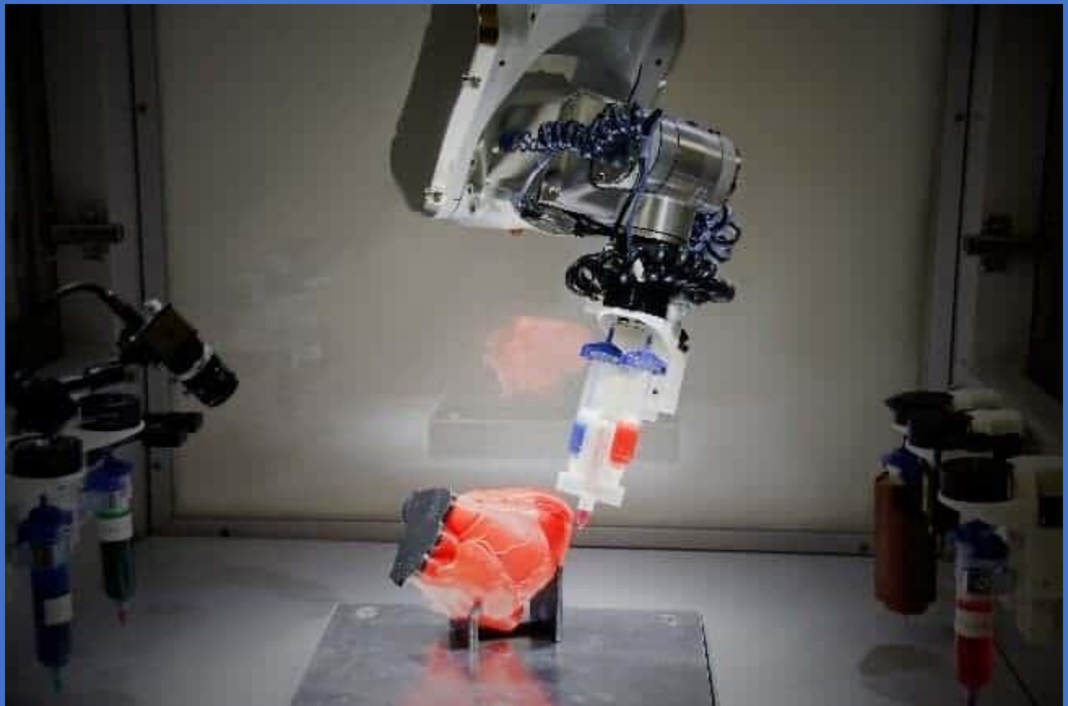
- UV light.
- 70% ethanol.
- Steam autoclave.
- Gamma irradiation.
- Ethylene Oxide gas.

Risk of cell based therapy

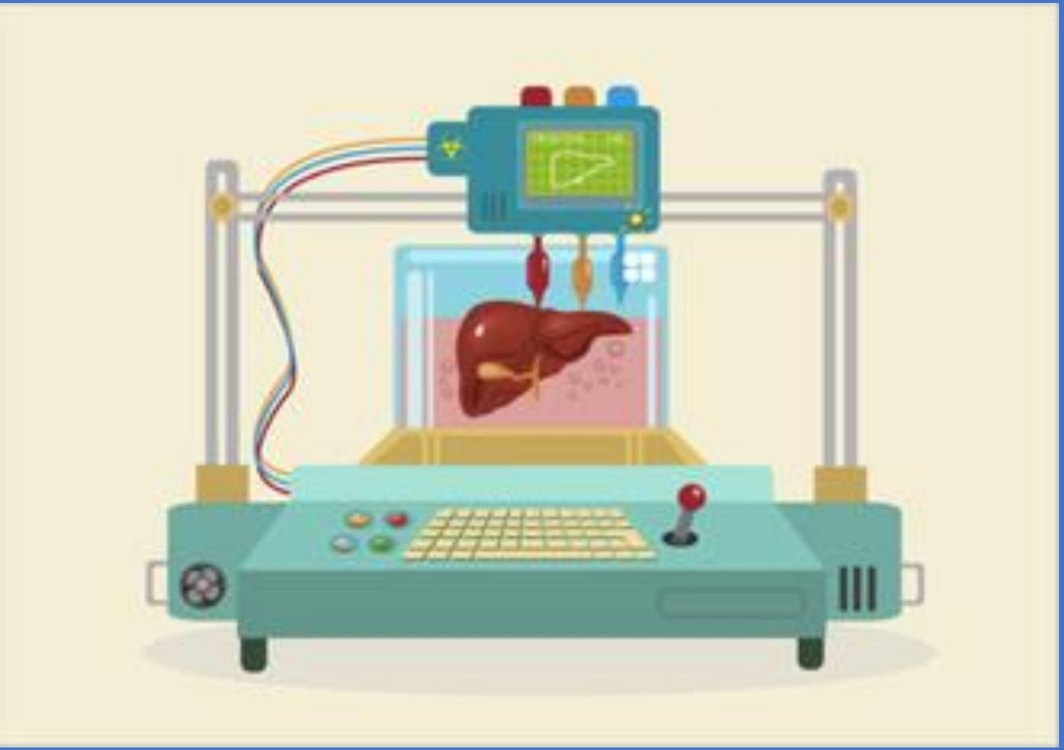
- Malignant transformation.
- Genetic & epigenetic abnormalities.
- Infection.
- Poor viability.
- Loss of function.
- Differentiation to undesired cell types.
- Rejection.
- S/E of immunosuppression.

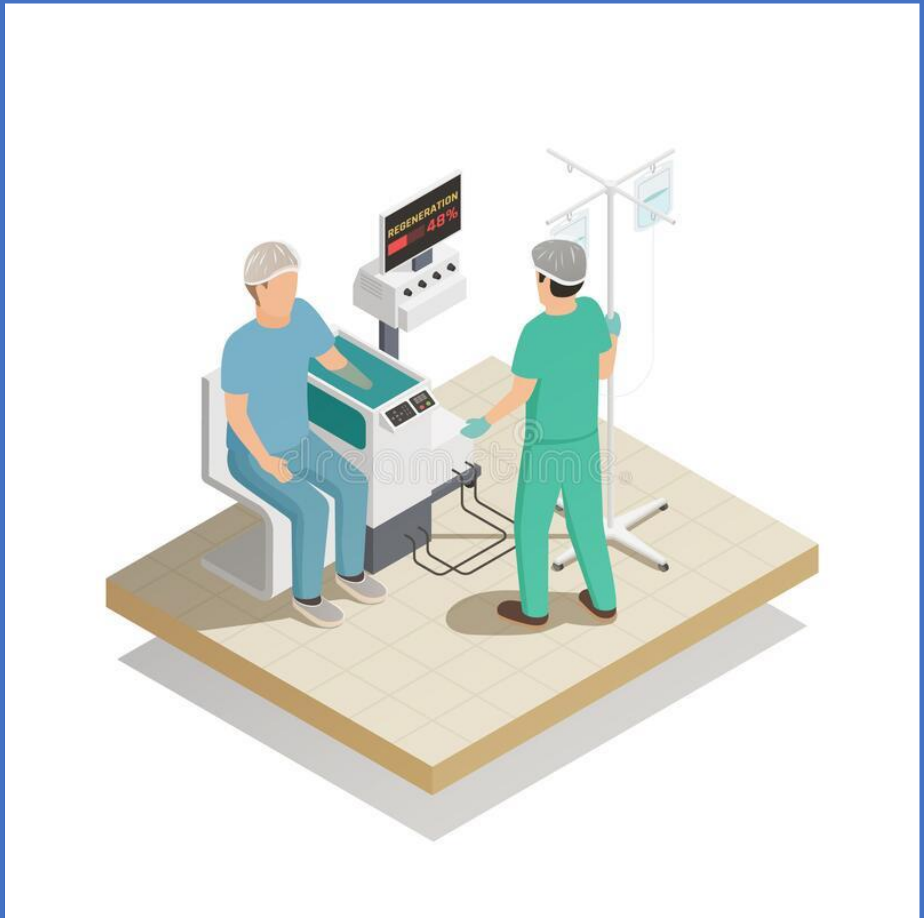


3 D bioprinting- Future tissue engineering

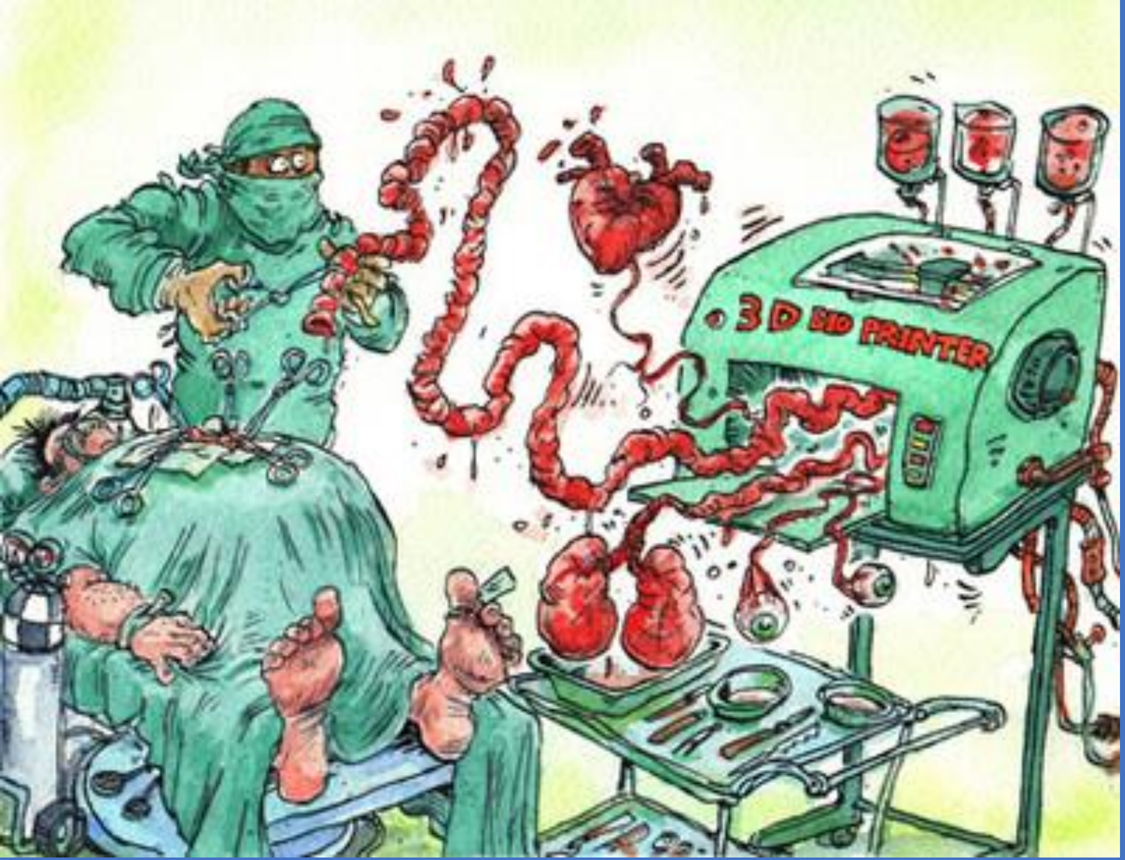


3- D bioprinting, future of tissue engineering





Future directions



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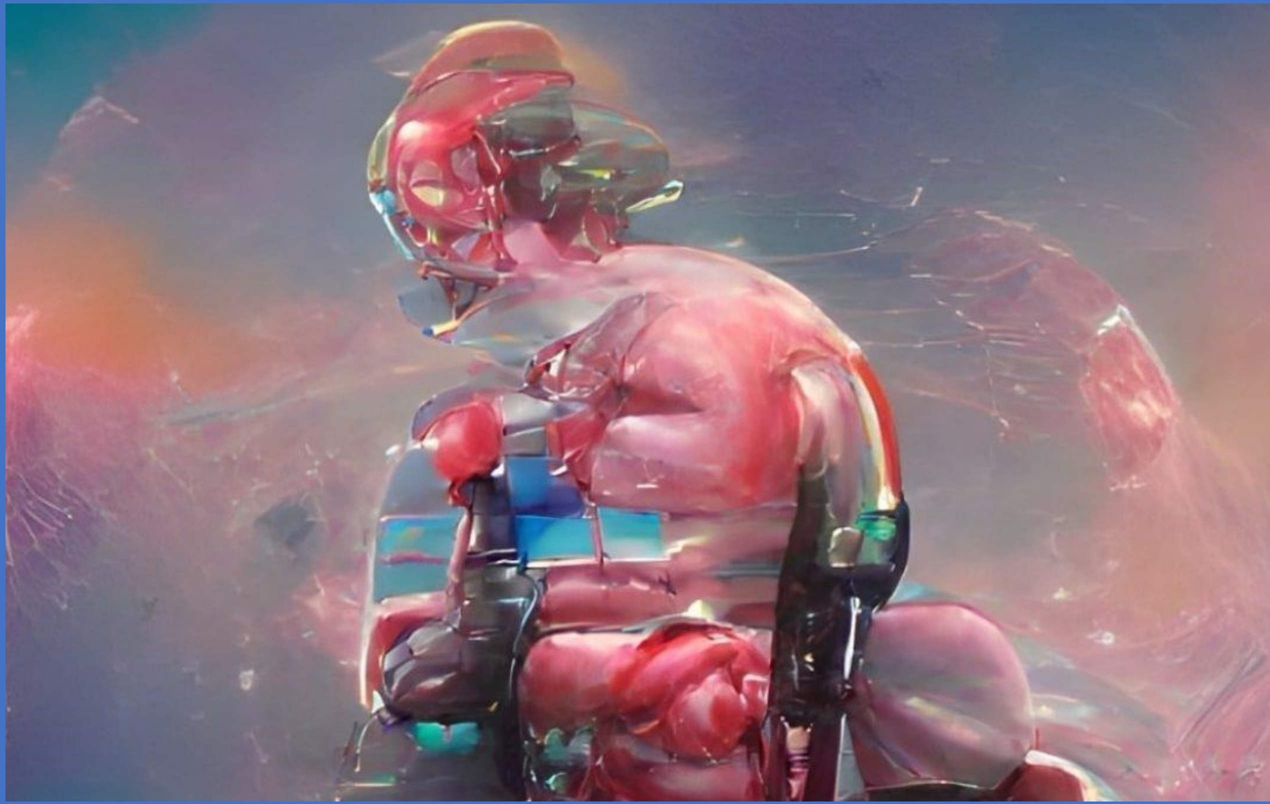

4 D bioprinting

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