General Applications of Mammalian Cell Cultures

by

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- **Important applications of mammalian cell cultures include:**

1- Virology and Vaccines Production.

2- Drug Discovery and Screening.

3- Toxicology Testing.

4- Cancer Research.

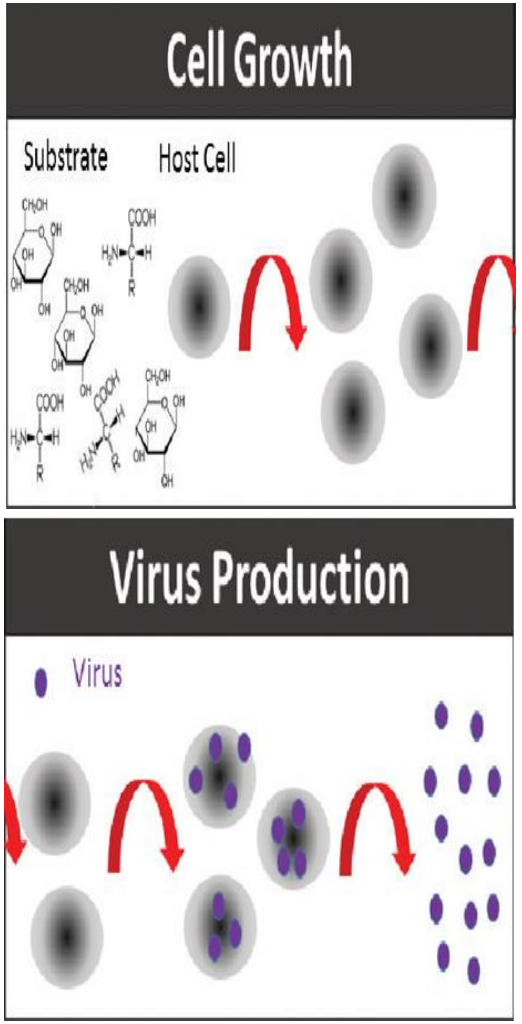
5- Biotechnology and Tissue Engineering.

6- Genetically Engineered Proteins.

1- Virology and Vaccines Production

- Cell cultures has become a very **useful** and **convenient** method for isolating viruses since **1949** when **Enders** successfully cultured **polio viruses** on neuronal cell culture.

- Since that time, cell culture still remains the "**gold standard**" for isolating many viruses.



- **This because:**

- A **single cell culture** can cultivate **a broad** spectrum of viruses.

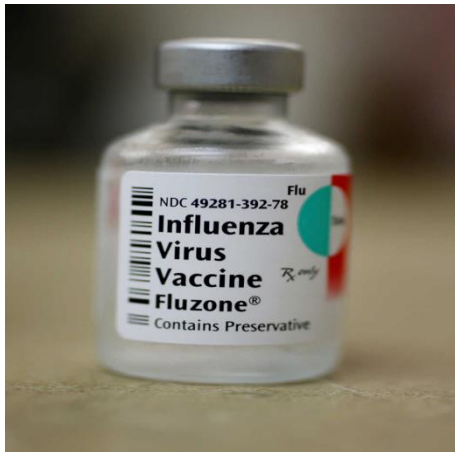
- Cultures facilitate production of **high tittered viruses** used in Abs **testing**, viral **characterization** and molecular **analysis**.

- Regarding vaccine production, cell cultures have been used to produce **virus-based vaccines** since early 1950s.

- Vaccine production is **the first industrial application** of animal cell culture technology.

- **Vaccine that have been produced by cell cultures:**

Polio	Measles
Rubella	Mumps
Chickenpox	Smallpox
Rabies	Hepatitis
Influenza	Rotavirus



2- Drug Discovery and Screening

- Cell cultures play an **initial** and **crucial** role in drug **development** and **screening**.

- They are **superior** to ***in vivo*** models **as they**:

1- More **efficient**.

2- **Costless** (low compounds requirement and short duration).

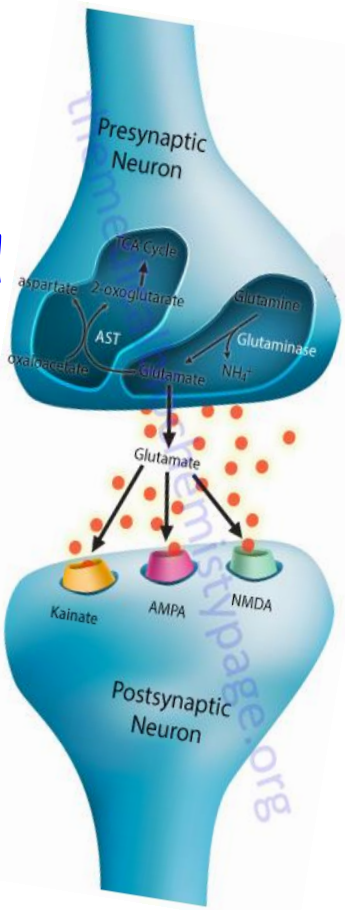
3- Escape **ethical** issues.

- **Testing the potential neuroprotective effect of rotigotine against Glu toxicity in primary mesencephalic cell culture (a PD *in vitro* model):**

  - **Concept:**

- Glu is an **excitatory** neurotransmitter released by **glutamatergic** neurons in the brain.

- Upon **elevation**, Glu can result in degeneration of **DAergic** neurons by stimulation of **NMDA** receptors which in turn increases IC Ca2+ burden and **mitochondrial damage**.

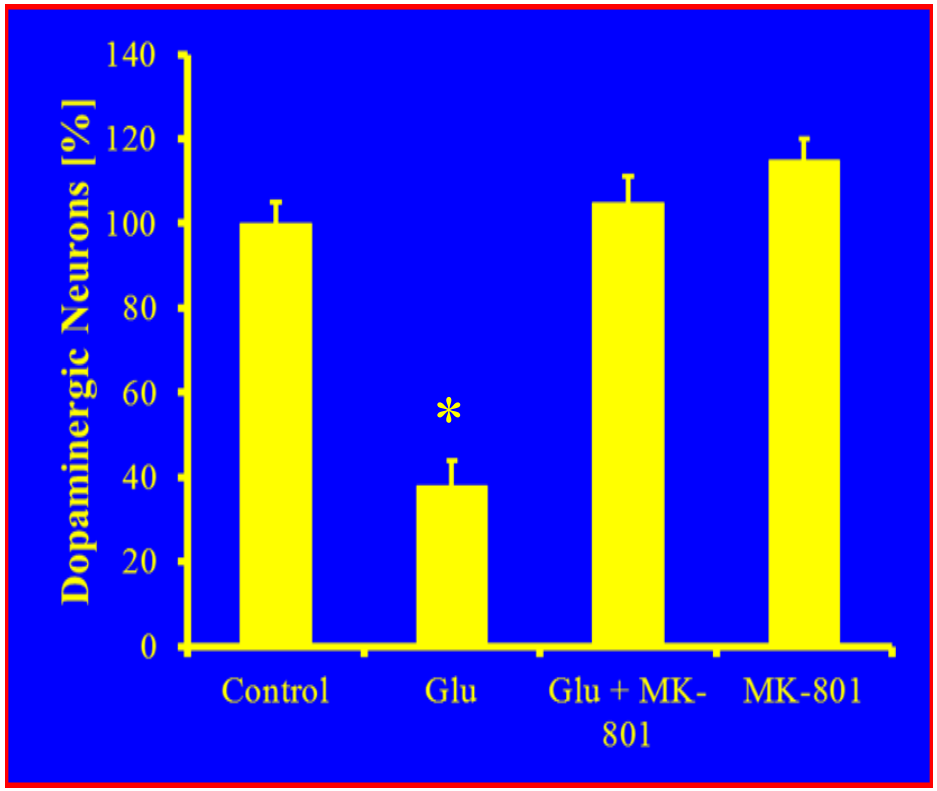


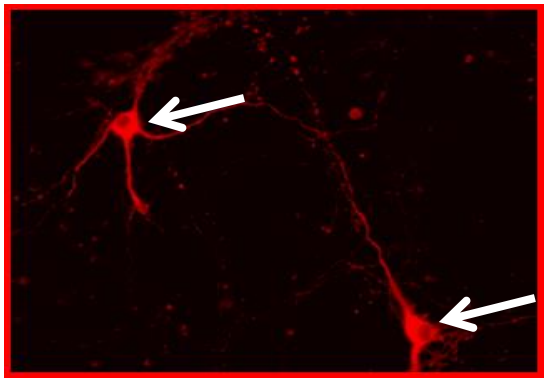
- **Steps**:

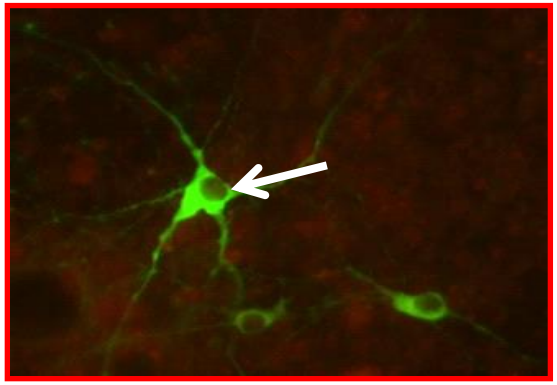
- **0.5 mM Glu** to the cultures on the 10th DIV for 9 min followed by a 2-day recovery period resulted in:

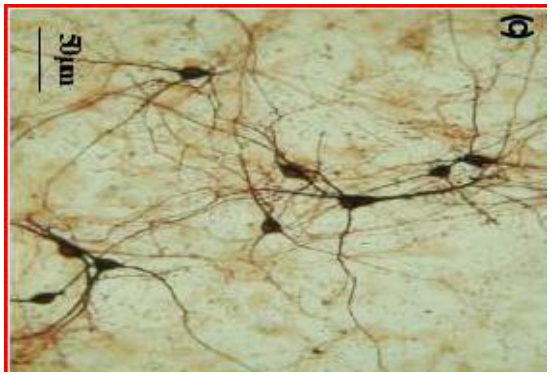
(1) Stimulation of

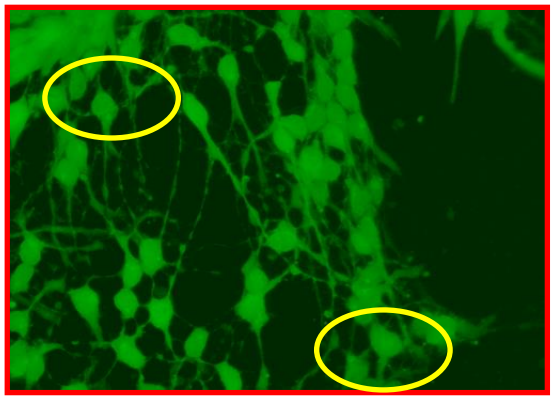
NMDA receptors

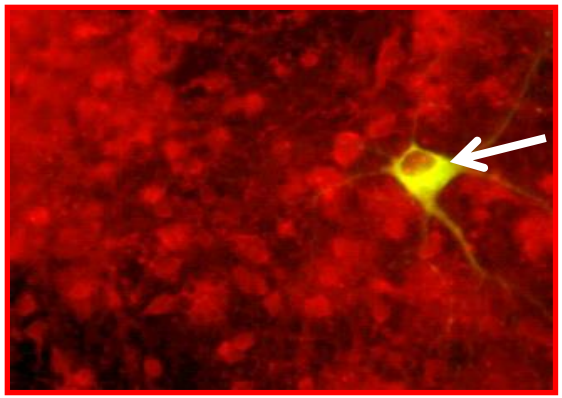


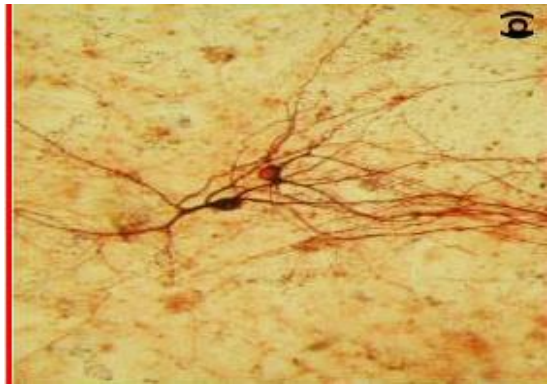












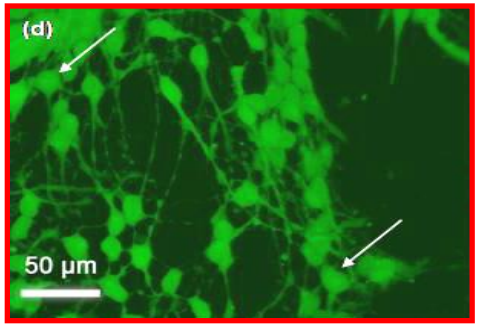
↑ Ca^{2+} **influx** into DAergic neurons as measured by **Fluo-4 dye**

↑ **$O2^{-\cdot}$** as measured by MitoSOX dye

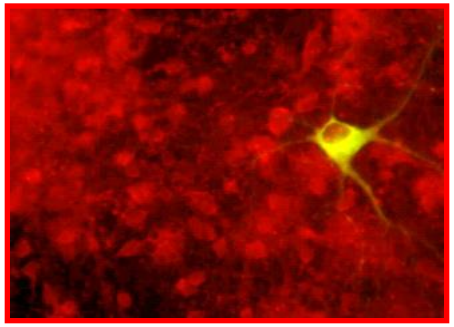
↓ **DAergic** neurons compared to untreated controls

Disease modeling

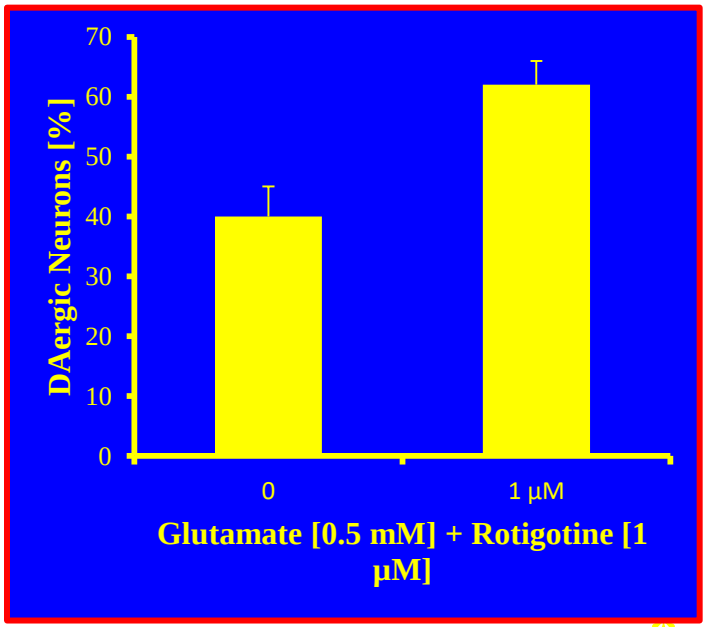
- **1 μM rotigotine** on the 9th DIV and **0.5 Glu** on the 10th DIV for 9 min. After two days recovery, **rotigotine caused**:



↓ Ca^{2+} influx into DAergic neurons



↓ O^{2-}· production



Protection of DAergic neurons against Glu toxicity

Target Identification & Drug Discovery

3- Toxicology Testing

• Cell cultures are considered **more superior** to animal models to test compounds for their potential toxicity **as:**

VS

- Efficient, **fast** and costless tool.

- Can investigate **precise** mechanisms.

- Escape **ethical** issues.

- **Two types of toxicology tests can be done on cell cultures:**

1- General toxicity tests:

- Carried out on **many cell types** (e.g. fibroblast, HeLa and hepatoma cells).
- **Measuring** viability, cytosolic enzyme release, cell growth etc.

2- Organ-specific cytotoxicity tests:

Done on **specialized cells** and measure specific cell functions (e.g. **glycogen** storage in primary hepatocyte cultures, **phagocytosis** in macrophages).

4- Cancer Research

- "Almost **all malignant tumor** cells have been established as **immortal cell lines**, and many of them are available commercially"……**This help in:**

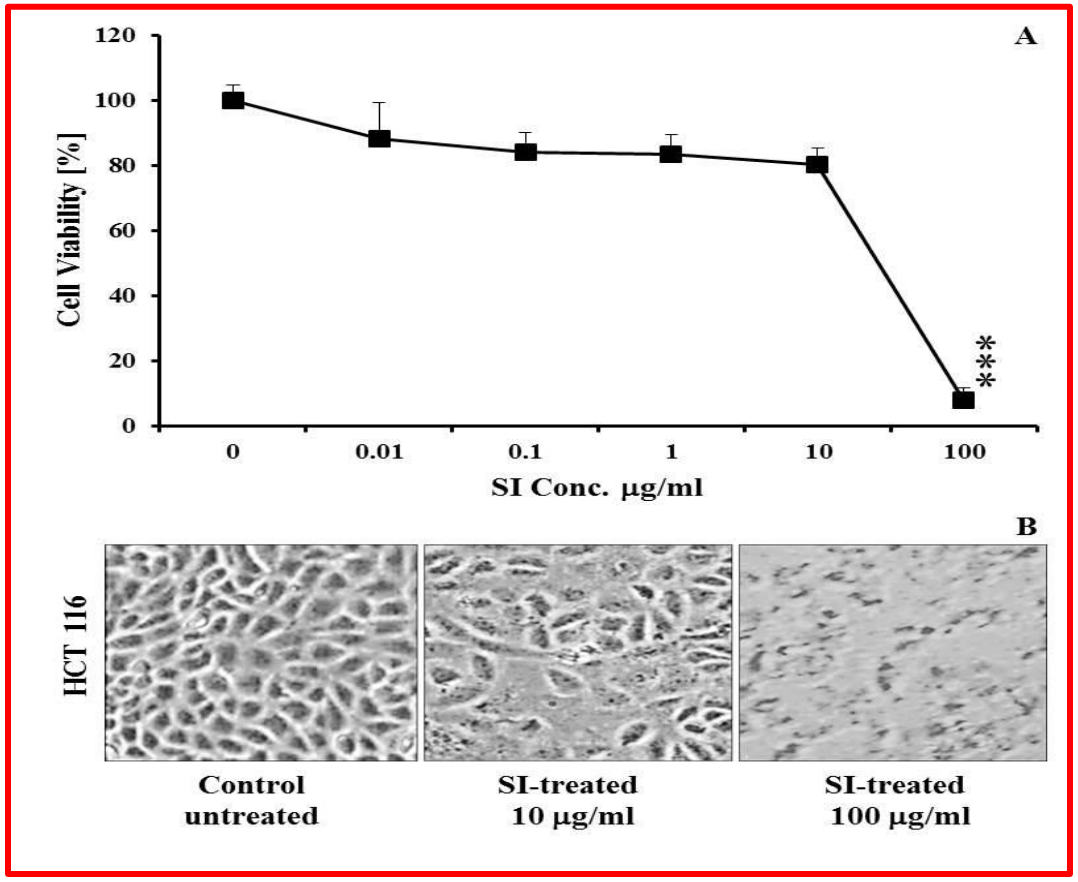
- Studying the **behavior** of different tumors.

- Evaluating **carcinogenic potentials** of different agents.

- Studying the **protective roles** of various natural and synthetic substances against cancer.

- **Anti-cancer activities of *Solanum incanum* aqueous extract on colon HCT 116 cell line:**

- ***S. incanum*** aqueous extract significantly reduced **cell viability** of cultured cells.



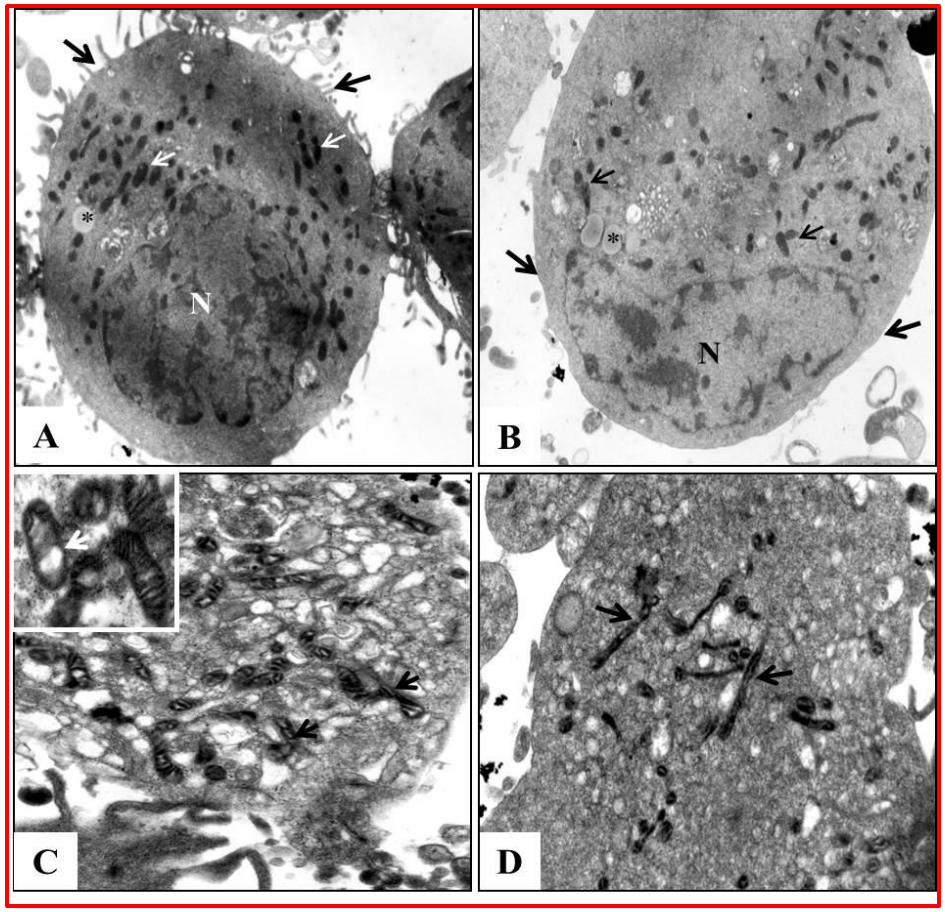
- ***S. incanum* aqueous**

extract caused:

- Loss of the surface

microvilli.

- **Mitochondrial** damage.
- Cytoplasmic **vacuolation**.

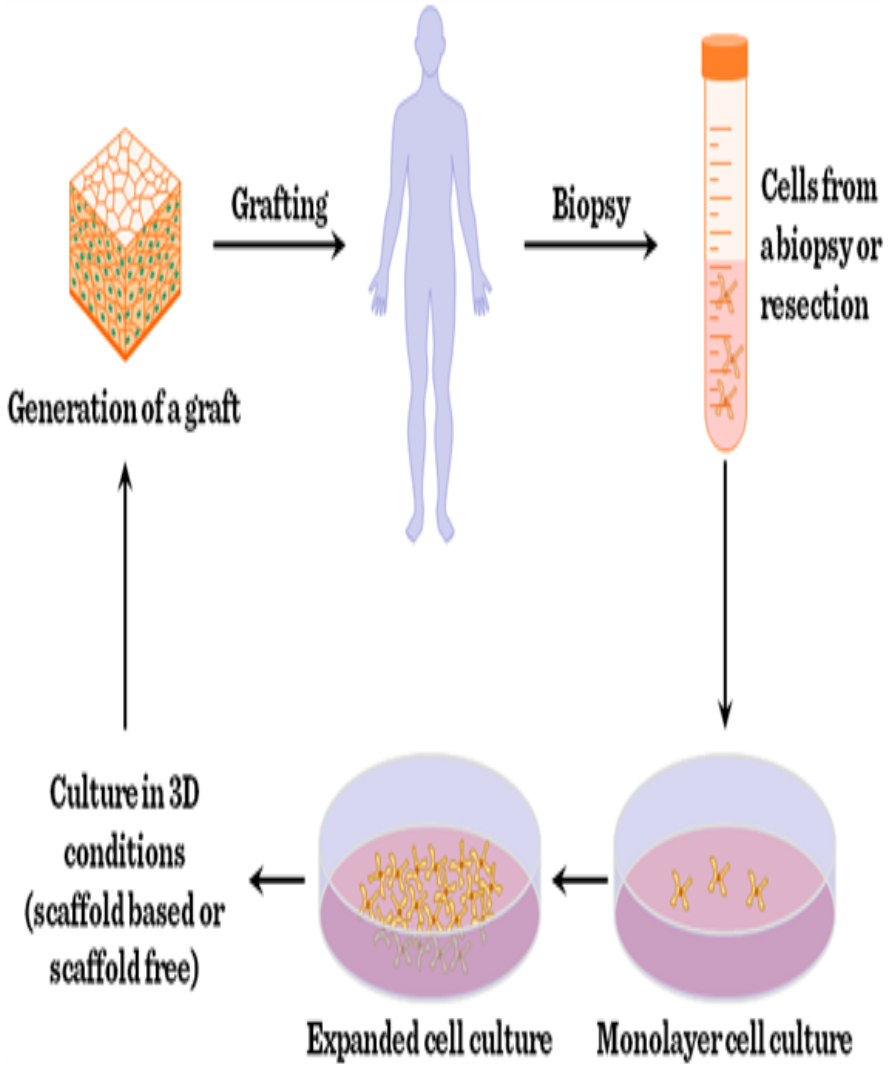


A) Untreated control . B) Loss of surface villi. C) Mitochondrial vaculation. D) Mitochondrial elongation.

5- Biotechnology and Tissue engineering

- Simply, **tissue engineering** means "the **re-constitution** of human tissues from the **combination of cell types** grown in culture".

- It is an **important prospect** for future therapeutic treatment with **organ failure**.

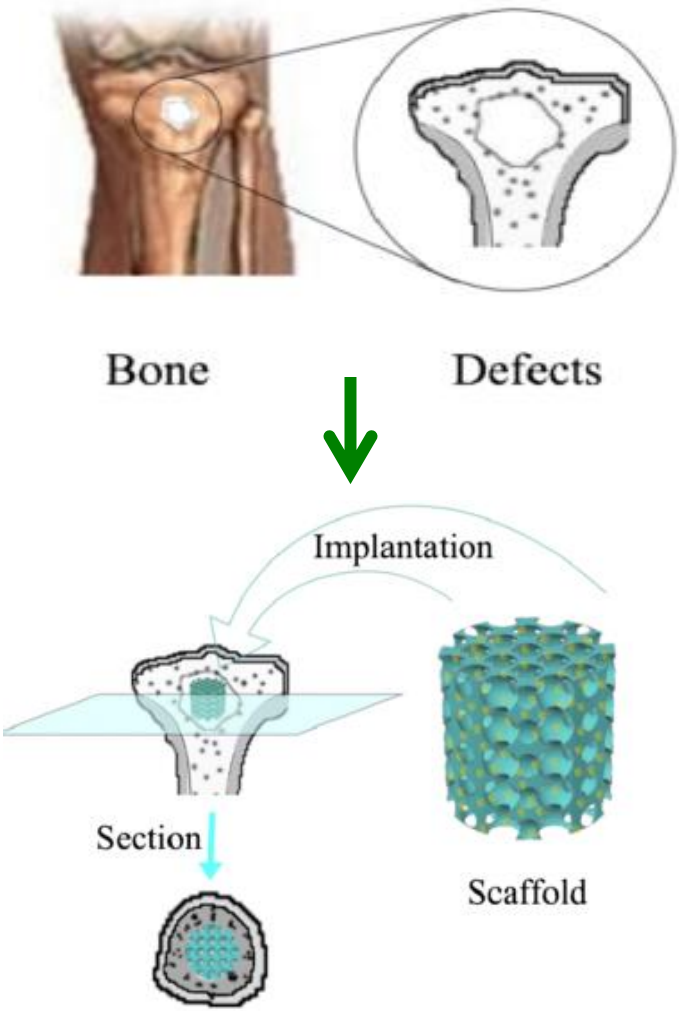


- **Two main approaches** are utilized to produce **engineered tissues**:

(1)

- Generating **scaffolds** as a cell **support device**, upon which cells are **seeded** *in vitro*.

- Then, cells are encouraged to lay down **matrix** to produce the foundation of a tissue for transplantation.

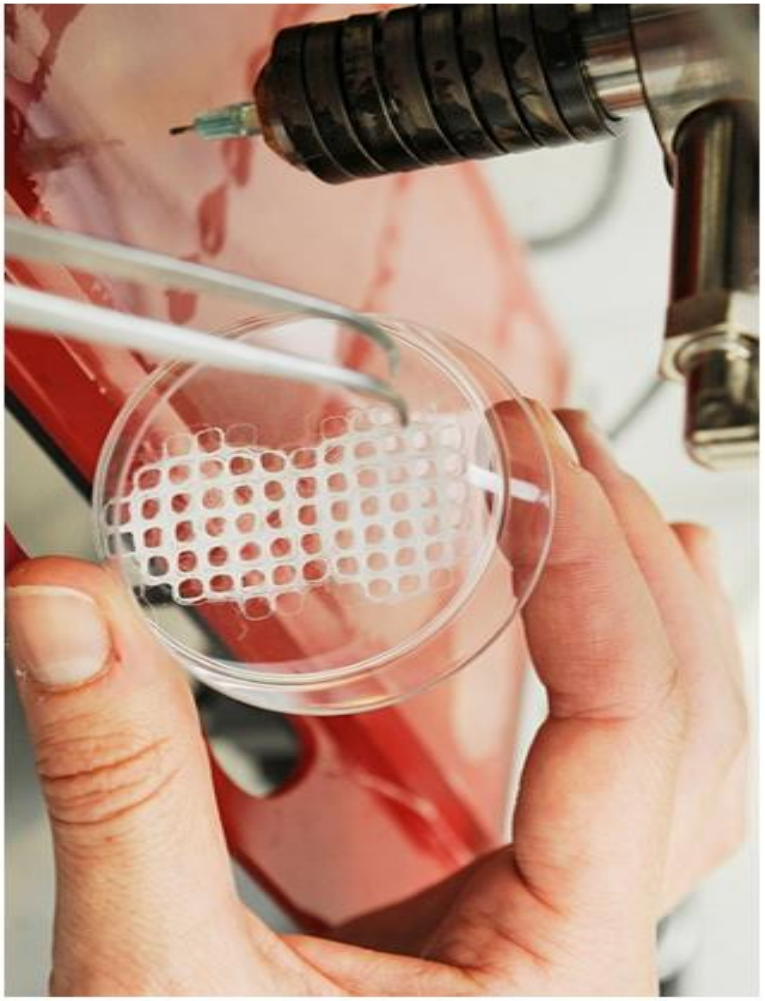


(2)

- Using the **scaffolds as a growth factor/drug delivery device**.

- In which, the scaffolds being **combined** with growth factors.

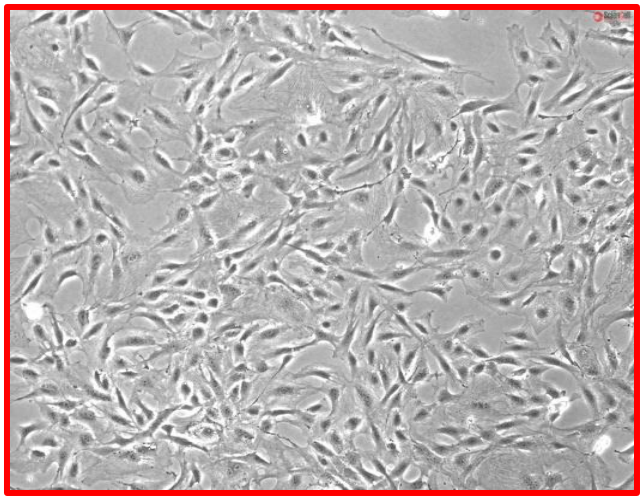
- **Upon implantation**, body cells **recruited** to the scaffold site and form a tissue.

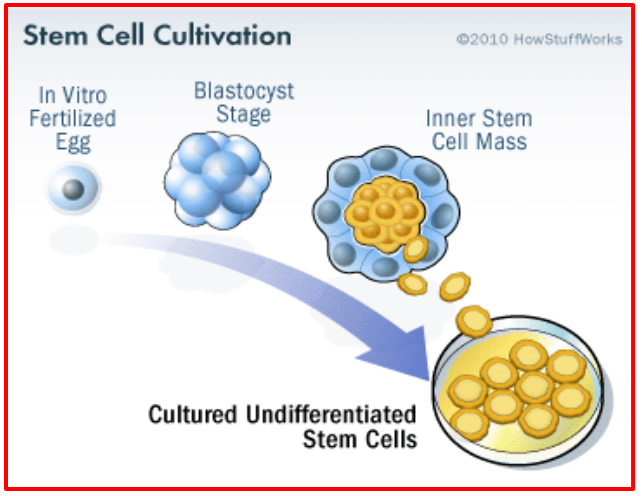


- **Sources of cells for tissue engineering :**

- **Primary cells** taken from the patients in conjunction with **scaffolds** to produce tissue for re-implantation

- **Stem cells** including **embryonic** stem cells, **mesenchymal** stem cells etc.

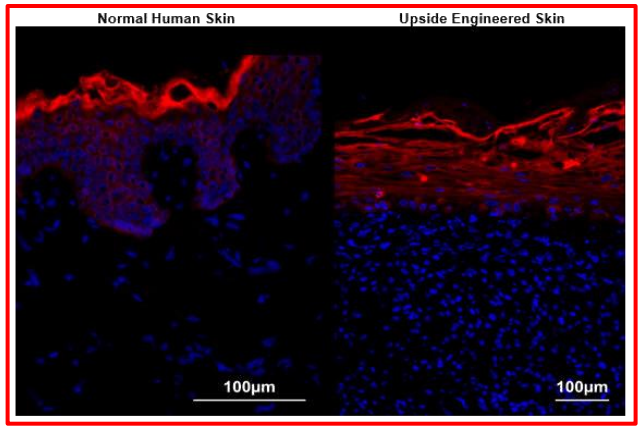




- **The more current successful approaches:**

- Using **primary chondrocytes** for the replacement of damaged cartilage.

- **Skin cell sheets** for damaged skin.



- **Reconstruction** of some **larger** and **complex** tissues, more notably, the **bladder**.

6- Genetically Engineered Proteins

Cell cultures can be used to produce **proteins** that have **medicinal** or **commercial** values such as mABs, insulin, hormones, cytokines etc.

1- **Production of monoclonal antibodies (mAbs):**

- **mAbs** are produced in large amount by using **hybrid cells**.

- **Hybrid cells** prepared by fusion of **Ab-producing cells** from immunized mouse with a **tumor cells** called **myeloma cells**.

i- Production of recombinant proteins:

- Based on **transfection** of cultured cells with an **isolated gene.**

- **Amplification** of this gene results in **expression** of high level of the corresponding **protein.**

- **e.g.,** interferone, tissue plasminogen activator and clotting factors.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謝謝
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Баярлалаа
teşekkür ederim
mersi
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спасибо
faafetai lava
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