Regnerative Medicine
Introductory course

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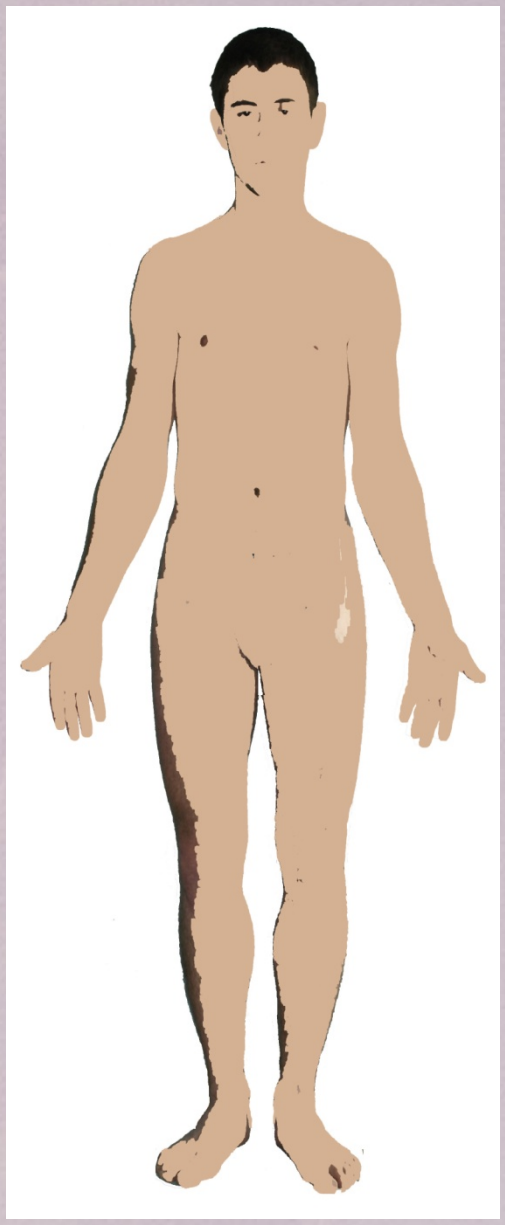
How to help the body heal itself

- Replace organs;
- *Tissue engineering organ transplant;*
- Repair by *microenvironment;*

regenerative “pill”, Cell signals, Local delivery to tissue.



Definition

Regenerative medicine refers to technologies that repair or replace diseased or defective cells, tissues or organs to restore the normal function.

Regenerative Medicine, 2008, 3(1), 1–5 [47]

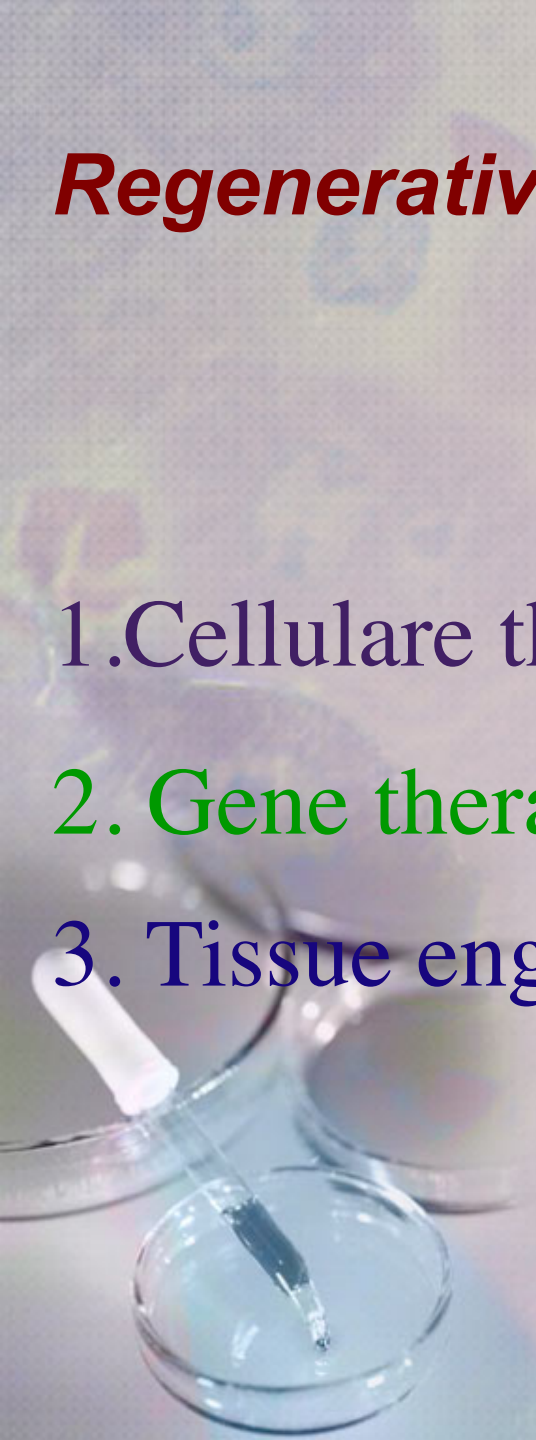
- **The main types of regenerative medicine utilize products:**
- **naturally occurring in the body;**
- **genes and proteins (antibodies, growth factors, hormones);**
- **embryonic stem cells,**
- **mature cells and tissues;**
- **Biomaterials (scaffolds etc.).**

Regenerative medicine:

1.Cellulare therapy

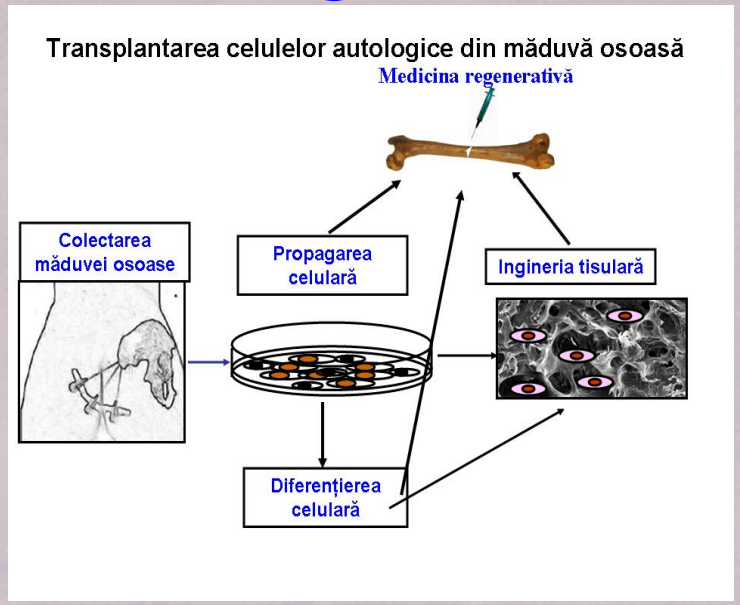
2. Gene therapy

3. Tissue engineering



Definition

Cellulare Therapy is transplantation of the human or animal cells to replace or repare of the damaged tissue or cells.

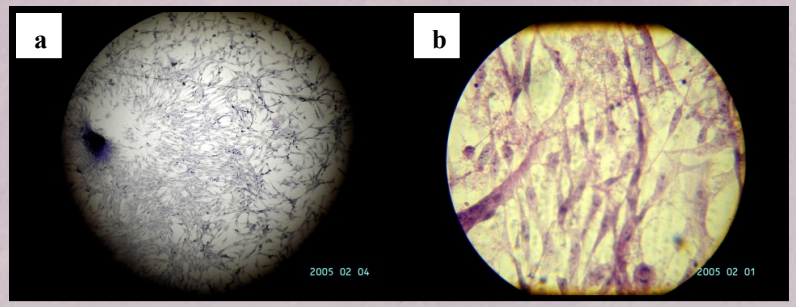


Definition

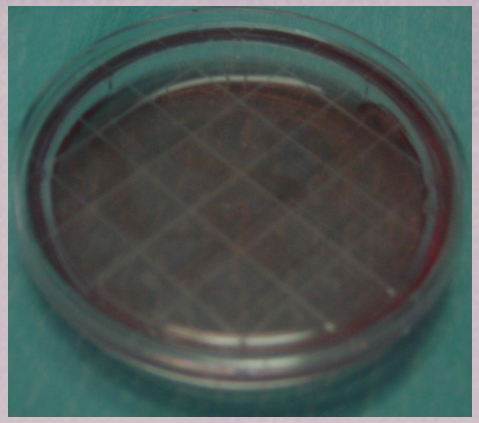
Gene therapy - is the insertion of genes into an individual's cell and biological tissues to treat disease, such as cancer where mutant alleles are replaced with functional ones.

Definition

Tissue engineering – is an multidisciplinary field which include biology, medicine, and enginery capable to restore, mentenance or improuve the function of the tissue and organs.



Colonii de celule mezenchimale cultivate pe lamă de sticlă. Ziua a 7-a de cultivare. Celule din măduva osoasă. Coloraţie hematoxilină: a) x 100; b) x 200.



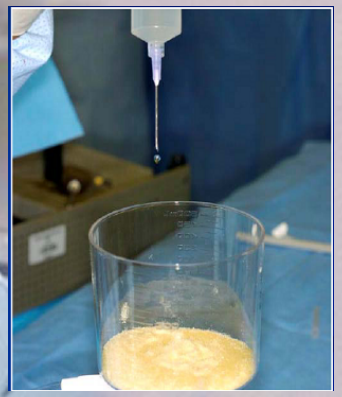
Alogenous demineralised bone matrix

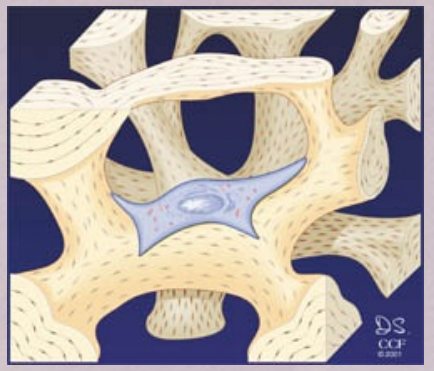
+

Cellulare culture

=

The combined graft






The national and international legislation in this field

- LAW NO. 42 of 06.03.2008, the transplantation of organs, tissues and cells. Published: 25/04/2008 in Monitorul Official Nr. Article No. 81: 273. Effective Date: 25.10.2008.
  In order to protect the rights of donors and recipients of organs, tissues and cells, to facilitate the transplantation of organs, tissues and cells, contribute to saving human life or significantly improve its quality and to prevent the sale of human body parts under art. 36 of the Constitution, the Parliament adopts the present law.

Moldova Government decision Nr. 386 of 14.05.2010 on establishing the Agency for Transplantation Published: 21/05/2010 in Official Gazette Nr. Article No. 78-80: 457

DIRECTIVE 2004/23/EU OF THE EUROPEAN PARLIAMENT COUNCIL of 31 March 2004 on setting standards of quality in donation, obtaining, testing, processing, preservation, storage of cells and tissues and distribution of human cells. (OJ L 102, 7.4.2004, p. 48)

Modification by Regulation (EC) no. 596/2009 of the European Parliament Council of 18 June 2009

- (1) Transplantation of cells and tissues is an area of medicine in strong growth, providing opportunities for the treatment of diseases considered incurable. Must ensure quality and safety of these substances, in particular to prevent disease transmission.

- (2) The availability of human tissues and cells used for therapeutic purposes depends on Community citizens who are willing to donate.
  To protect public health and prevent infectious disease transmission by human tissues and cells, to be taken all necessary security measures to the donation, processing, preservation, storage, distribution and use.

- International Legislation Embryonic Stem cell research is highly controversial not only in the United States but worldwide.

- In the past years, many nations have begun to tolerate, if not to support, the research.

- Australia - 20.3 M
  Belgium - 10.4 M
  Brazil - 188 M
  Canada - 33.1 M
  China - 1,314 M
  Czech Republic - 10.2 M
  Denmark - 5.4 M
  Estonia - 1.3 M
  Finland - 5.2 M
  France - 62.8 M
  Greece - 10.7 M
  Hong Kong - 6.9 M
  Hungary - 10 M
  Iceland - .3 M
  India - 1,045 M
  Iran - 69 M
  Israel - 6.4 M
  Japan - 127 M
  Latvia - 2.3 M
  The Netherlands - 16.5 M
  New Zealand - 4.1 M
  Portugal - 10.6 M
  Russia - 146 M
  Singapore - 4.5 M
  Slovenia - 2.0 M
  South Africa - 44 M
  South Korea - 40.4 M
  Spain - 40.4 M
  Sweden - 9 M
  Switzerland - 7.5 M
  Taiwan - 23 M
  Thailand - 65 M
  Turkey* - 70 M
  United Kingdom - 60.6 M
  United States - 306 M

History

- The late XXth century discoveries in molecular and cell biology, open broad prospects for the development of new biotechnologies.
- 1954 – John Enders received the Nobel Prize in medicine for growing polio virus in embryonic kidney cells;
- in 1968 was done the first bone marrow transplant used to treat leukemia and immunodeficiency.
- În 1998, John Gearhart (Johns Hopkins University) received germinative stem cells.
- În 1998, James Thomson (University of Wisconsin-Madison) izolated stem cells from blastocist and received first embryonic stem cells line.

History of Somatic Cell Nuclear Transfer (Cloning)

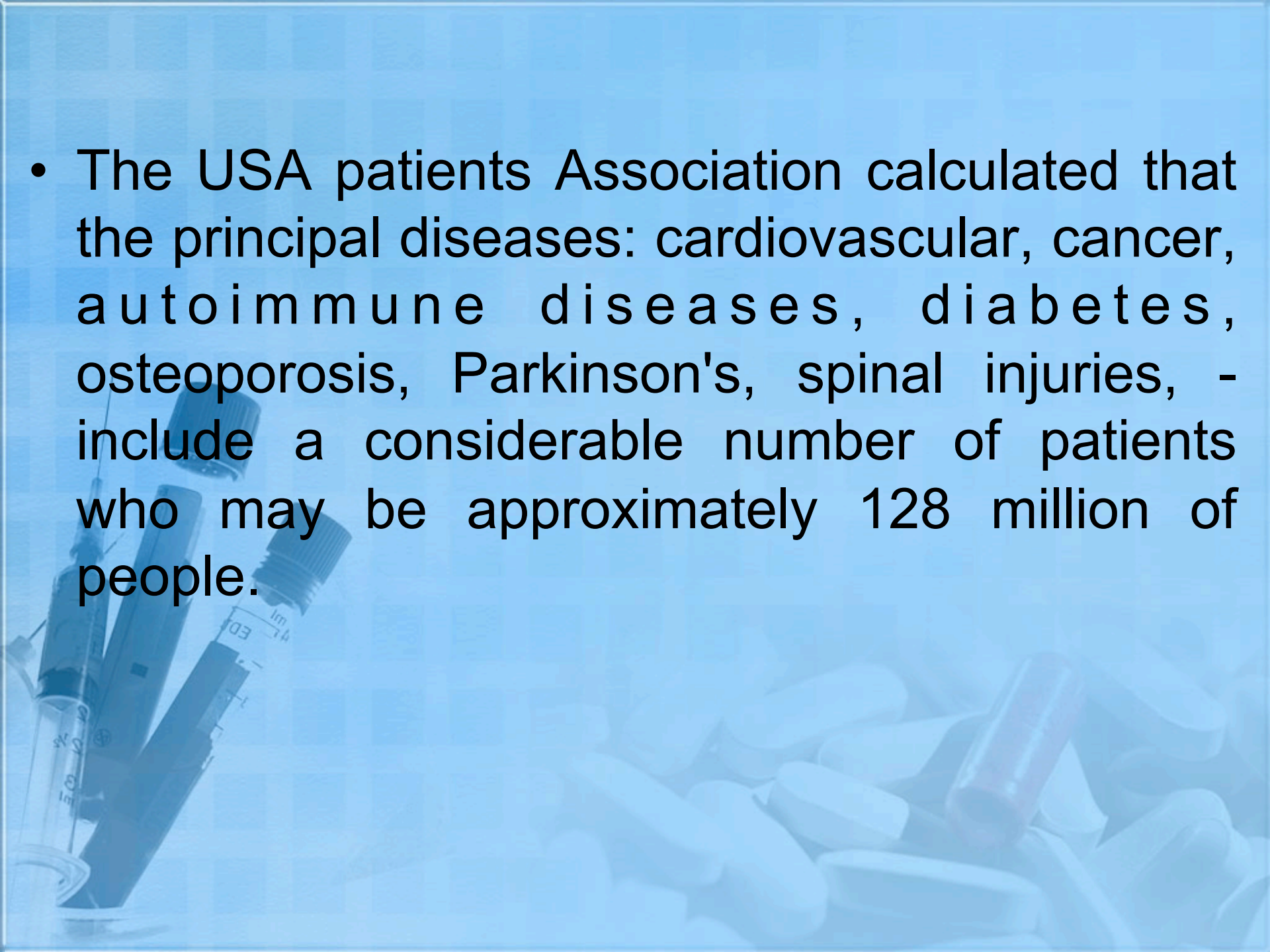
- 1952 –Briggs and King cloned tadpoles
- 1996 –The first mammal cloned from adult cells was Dolly, the sheep.
- 1998 – Mice cloned
- 1998 – Cows cloned
- 2000 – Pigs cloned
- 2001 – Cat cloned
- 2002 – Rabbits cloned
- 2003 – Mule cloned
- 2004 – Bull serial-cloned
- 2005 – Dog cloned

Cloning Dolly

1997 - 2003

(Roslin Institute http://www.roslin.ac.uk/library/)

- The USA patients Association calculated that the principal diseases: cardiovascular, cancer, autoimmune diseases, diabetes, osteoporosis, Parkinson's, spinal injuries, - include a considerable number of patients who may be approximately 128 million of people.



Moldova

1972 – Pavel Ciobanu and Nicolae Cereş proposed to use the fetal bone marrow cells for bone healing stimulation.

The professor V. Belousov, used the avian osteocytes.

- professor Sroit I. and all. Used for treatment of the inflammatory diseases activated limfocites
- our laboratory (V. Nacu and P. Ciobanu, F. Gornea, B. Topor, Gh. Croitoru, M. Darciuc) from 2002 used BMSC for treatment of non unions in 160.
- in 17 cases we used cellular grafts from umbilical cord.

In 2007 was created the Laboratory of tissue engineering and Celulare cultures

The directions of research in laboratory:

- stem cells in skeletal tissue discordies, (BMSC and UCBC)
- Stem cells in hepatic tissue regeneration,

In the tratament:

- Of combustional wounds,
- Type I diabetus,
- Stem cells in dermatology
- Nanobateries in tissue regeneration
- Tubo-peritoneal infertility,
- Urinary incontenence.

If in 1990 in 143 centers in Europe have been performed 4234 blood stem cell transplantation in 1994 were 10,066 transplantations performed in 306 similar scientific centers.

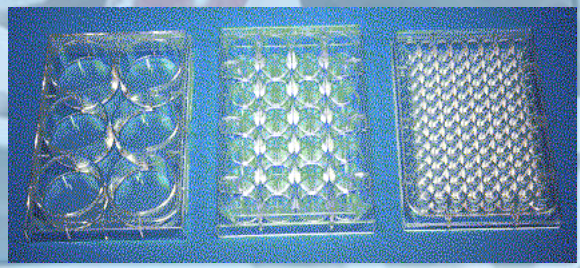
Currently it performs more than 40,000 stem cell transplants each year.

Clonation

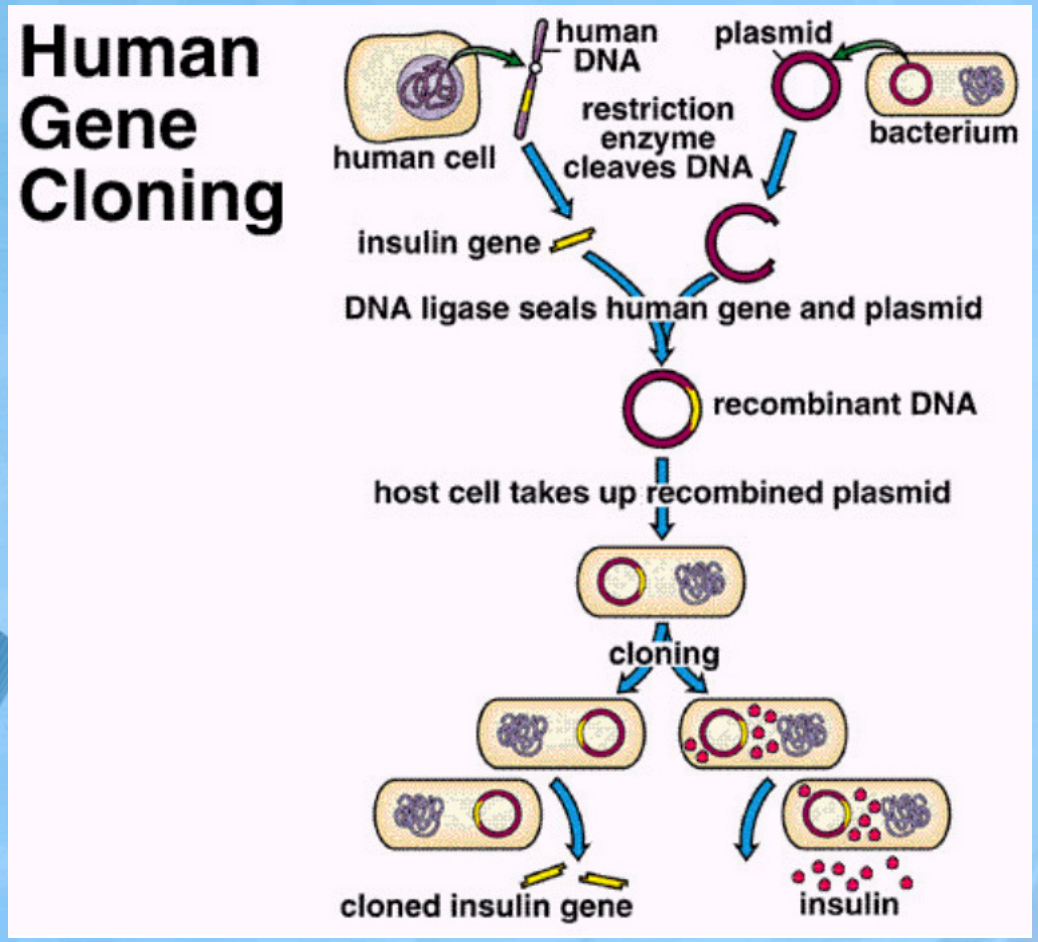
The cells is cultivated in a culture dish and it is divided until forms a colony of identical cells.

1	Natural cloning
2	Molecular cloning
3	Cell cloning
3.1	Cloning unicellular organisms
3.2	Cloning stem cells
4	Organism cloning
4.1	Horticultural
4.2	Parthenogenesis
4.3	Artificial cloning of organisms
4.3.1	First moves
4.3.2	Methods
4.3.3	Dolly the sheep
4.3.4	Species cloned
4.3.5	Human cloning
4.3.6	Ethical issues of cloning
4.3.7	Cloning extinct and endangered species

https://en.wikipedia.org/wiki/Cloning



Human Gene Cloning



https://en.wikipedia.org/wiki/Human_cloning

Fertilization versus clonation

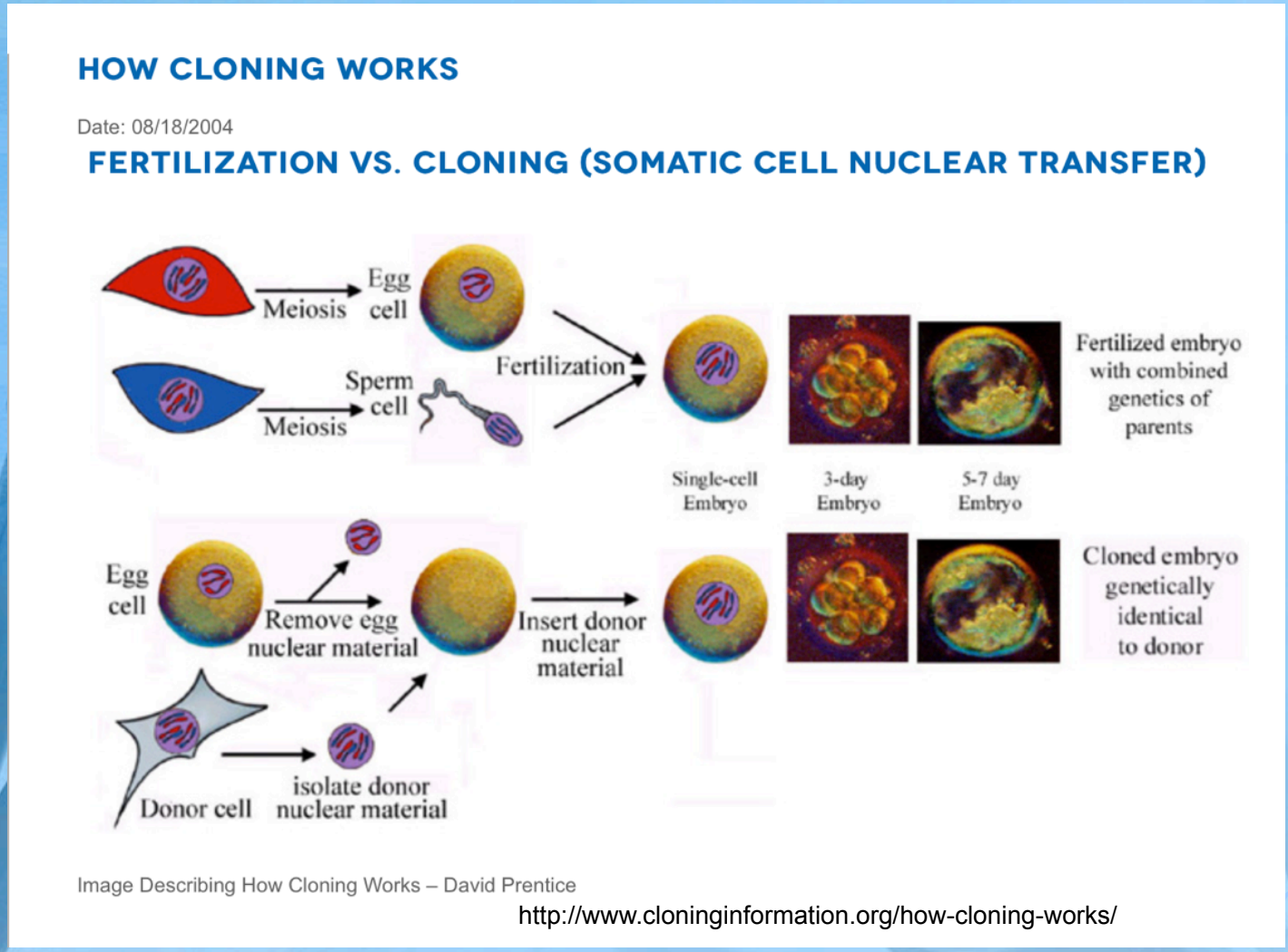


Image Describing How Cloning Works – David Prentice

http://www.cloninginformation.org/how-cloning-works/

- Problems with cloning
- (nuclear transplantation)
- Usually fails (requires many oocytes)
- Born clones have obvious or subtle abnormalities)

- Not a perfect match-some mitochondrial DNA comes from mother or oocyte.

Humpherys D *et al.*; "Epigenetic instability in ES cells and cloned mice"; *Science* 293, 95-97; July 6, 2001
Humpherys D *et al.*; "Abnormal gene expression in cloned mice derived from embryonic stem cell and cumulus cell nuclei"; *Proc. Natl. Acad. Sci. USA* 99, 12889-12894; October 1, 2002

Simerly et al Science 2003;300:297; Science 2003; 300:225

The Commonly Held Belief Was That Heart Cells Did Not Divide, but That Has Been Proven False

"For years there has been a general belief that the number of cells in the heart was established at birth. But how could anyone believe that the heart could contract so many years using the same cells?"

– Dr. Piero Anversa

- **Hearts weakened by chronic or acute loss of blood supply are exceedingly common**
- **Congestive Heart Failure affects 4.8 million people in the U.S.**
  - **400,000 new cases each year**
  - **Heart attack is the major contributor**
- **More than 1 million Americans suffer heart attacks each year**
  - **Out of those who develop Congestive Heart Failure, half die within 5 years as a result of their severely weakened hearts**

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Sources: Wade N. Tracking the Uncertain Science of Growing Heart Cells. *The New York Times*. March 14, 2005.
National Institutes of Health. Stem Cell Information: Can Stem Cells Repair a Damaged Heart? Available at: http://stemcells.nih.gov/info/scireport/chapter9.asp.

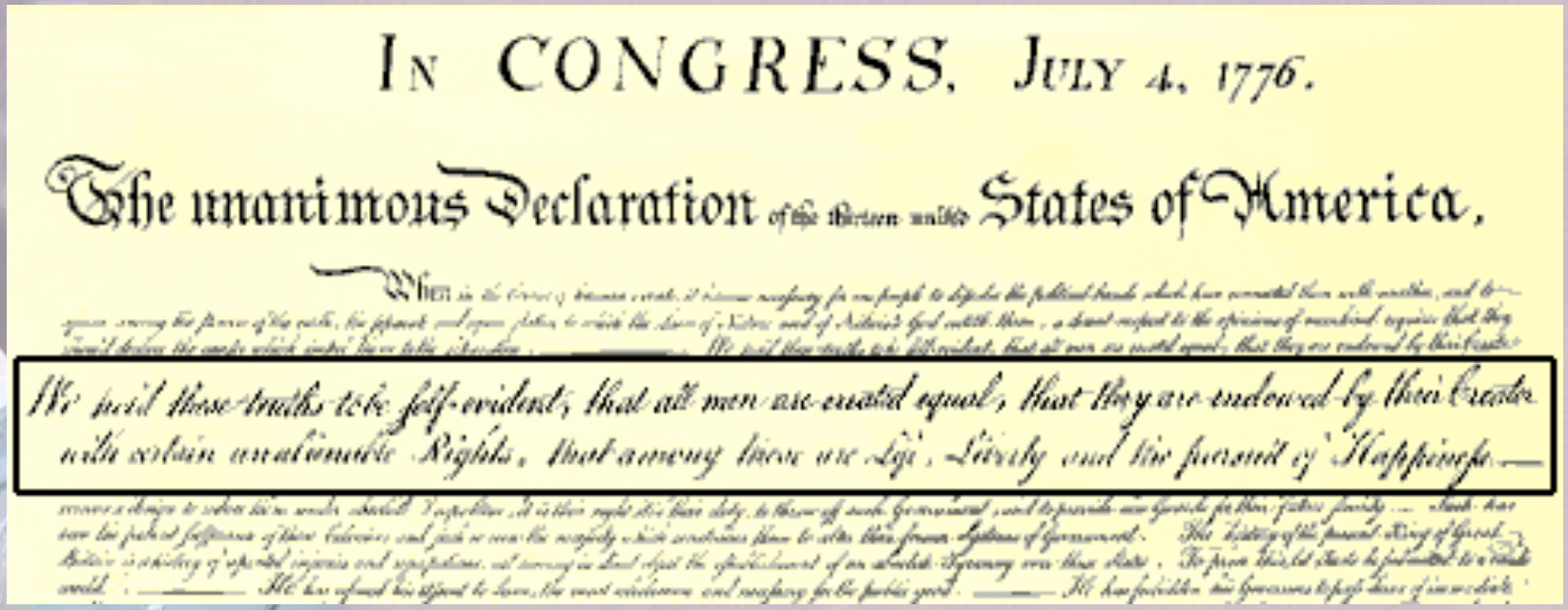
Sources: Touchette N. *Stem Cells Found in the Heart.* Genome News Network. October 17, 2003.
Institute of Science in Society press release. *Patient's Own Stem Cells Mend Heart*. January 13, 2005. Available at: http://www.i-sis.org.uk/POSCMH.php.

The type of stem cells

- Mature
- Foetals
- Embrionyc
- From ombilical cord blood

Right to Life

The Declaration of Independence of the United States guarantees “certain unalienable Rights, that among those are ***Life***, Liberty and the pursuit of Happiness”



IN CONGRESS, JULY 4, 1776.

The unanimous Declaration of the thirteen united States of America,

We hold these truths to be self-evident, that all men are created equal, that they are endowed by their Creator with certain unalienable Rights, that among these are Life, Liberty and the pursuit of Happiness.—

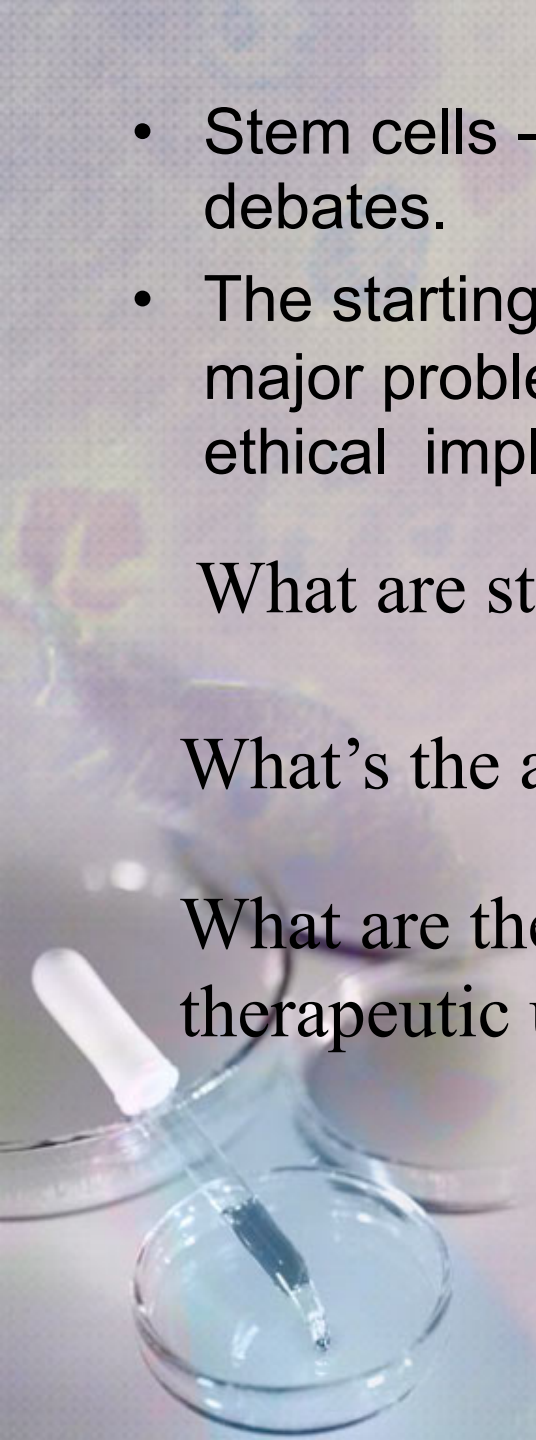
The Ethiques in cellular transplantation

- Stem cells - the target of numerous investigations, debates.
- The starting point of many technologies and an bioethics major problem with scientific, religious, philosophical, ethical implications.

What are stem cells?

What’s the actual level on knowledge's about stem cells?

What are the moral and ethic considerations about therapeutic use of stem cells?



The stem cells, cellular therapy are they a benefit or a ethic problem?

- **“*Everything is possible* for him who believes.”**

Thanks for your attention!!!