Stem Cells
The attractive new medical approach

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Stem Cell – Definition

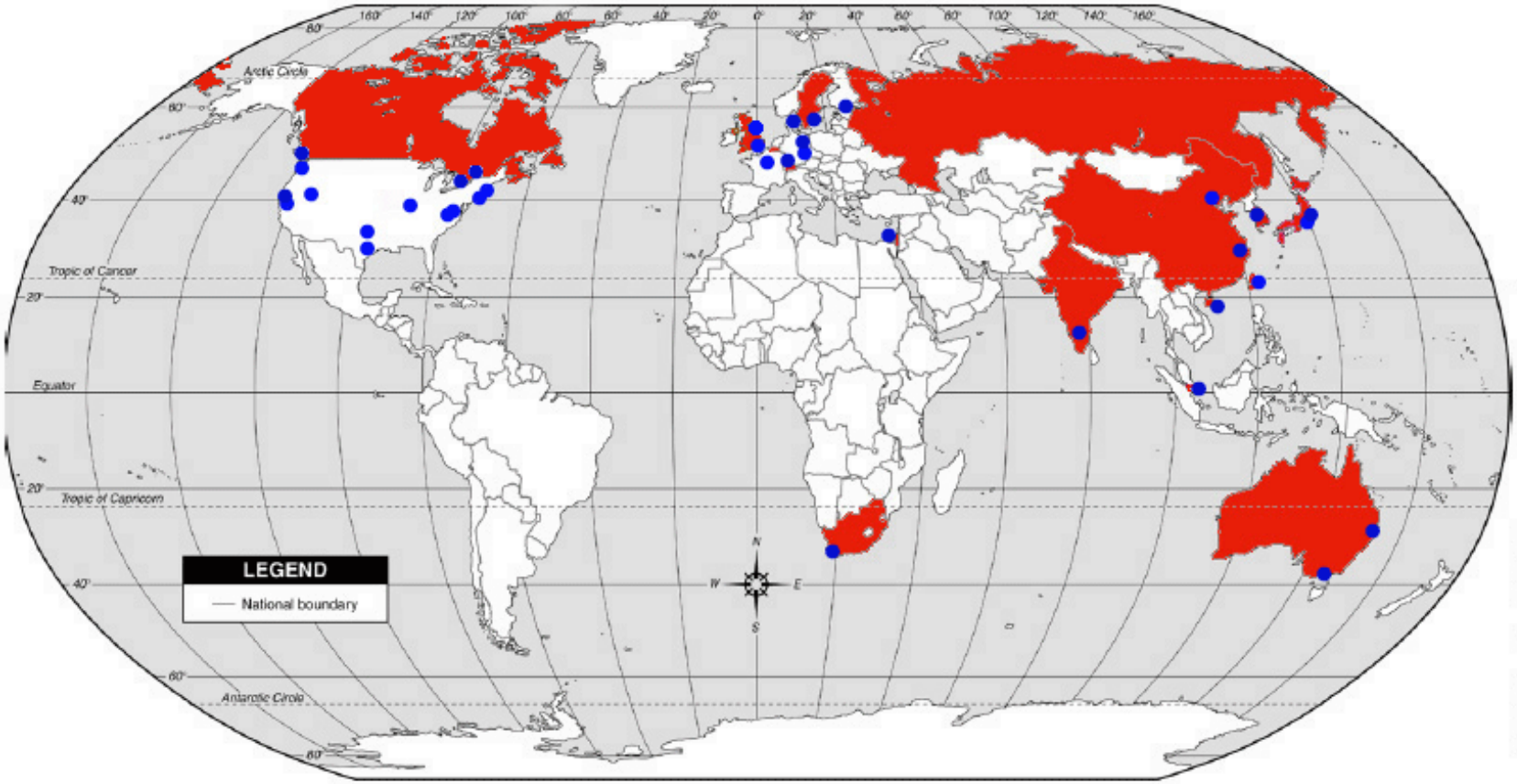
A cell that has the ability to continuously divide and differentiate (develop) into various other kind(s) of cells/tissues

Why is Stem Cell Research So Important to All of Us?

-Stem cells can replace diseased or damaged cells

-Stem cells allow us to study development and genetics

- Stem cells can be used to test different substances (drugs and chemicals)

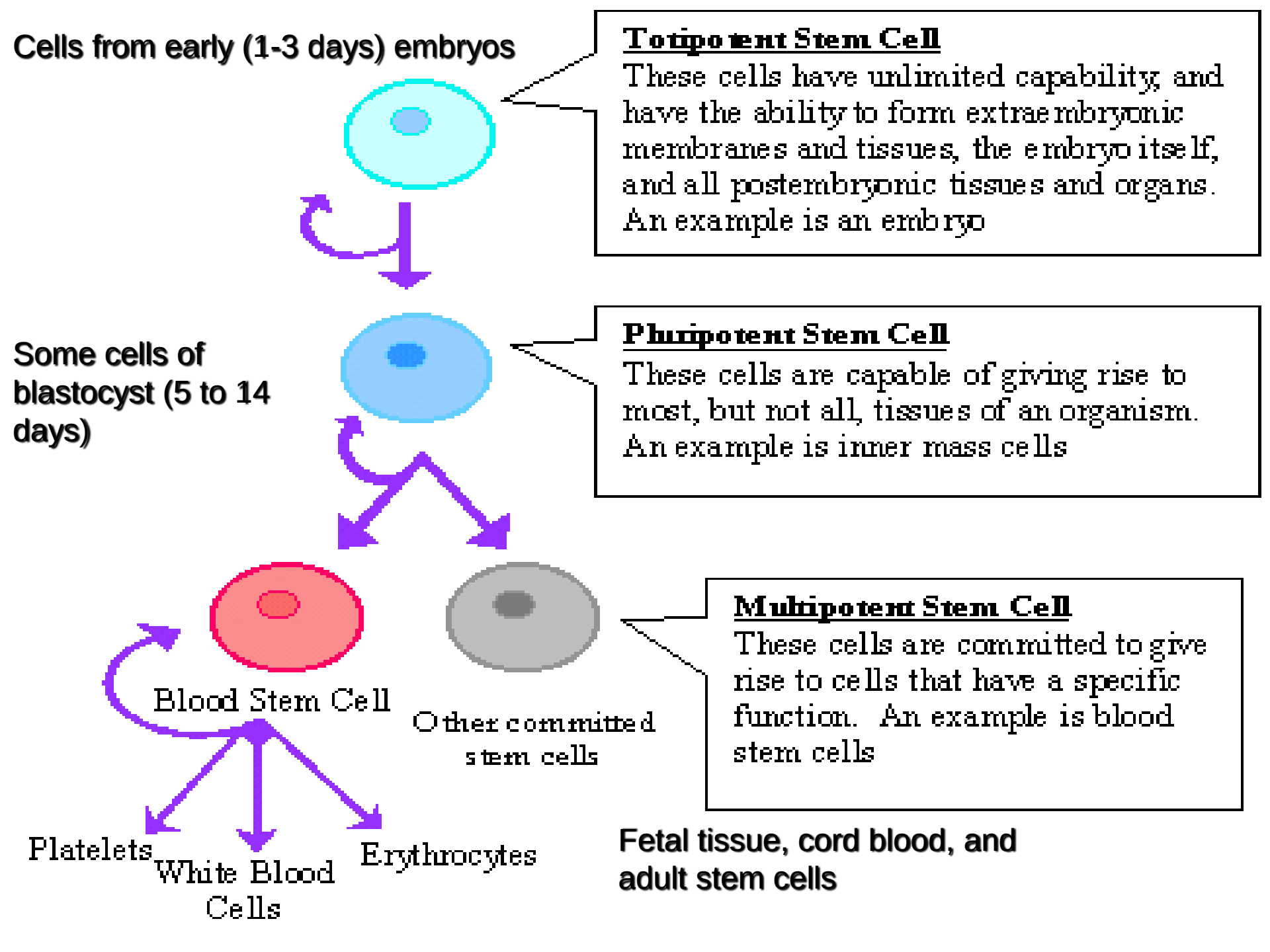


Countries with a permissive or flexible policy on embryonic stem cell research (in red)

- Denotes Genome Sequencing Center

Stem Cell Characteristics

- 'Blank cells' (unspecialized)
- Capable of dividing and renewing themselves for long periods of time (proliferation and renewal)
- Have the potential to give rise to specialized cell types (differentiation)


Cells from early (1-3 days) embryos
Totipotent Stem Cell
These cells have unlimited capability, and have the ability to form extraembryonic membranes and tissues, the embryo itself, and all postembryonic tissues and organs. An example is an embryo
Some cells of blastocyst (5 to 14 days)
Pluripotent Stem Cell
These cells are capable of giving rise to most, but not all, tissues of an organism. An example is inner mass cells
Multipotent Stem Cell
These cells are committed to give rise to cells that have a specific function. An example is blood stem cells
Blood Stem Cell
Other committed stem cells
Platelets
White Blood Cells
Erythrocytes
Fetal tissue, cord blood, and adult stem cells

Kinds of Stem Cells

Embryonic stem cells **come from a five to six-day-old embryo. They have the ability to form virtually any type of cell found in the human body.**

Embryonic germ cells **are derived from the part of a human embryo or foetus that will ultimately produce eggs or sperm (gametes).**

Adult stem cells **are undifferentiated cells found among specialised or differentiated cells in a tissue or organ after birth. Based on current research they appear to have a more restricted ability to produce different cell types and to self-renew.**

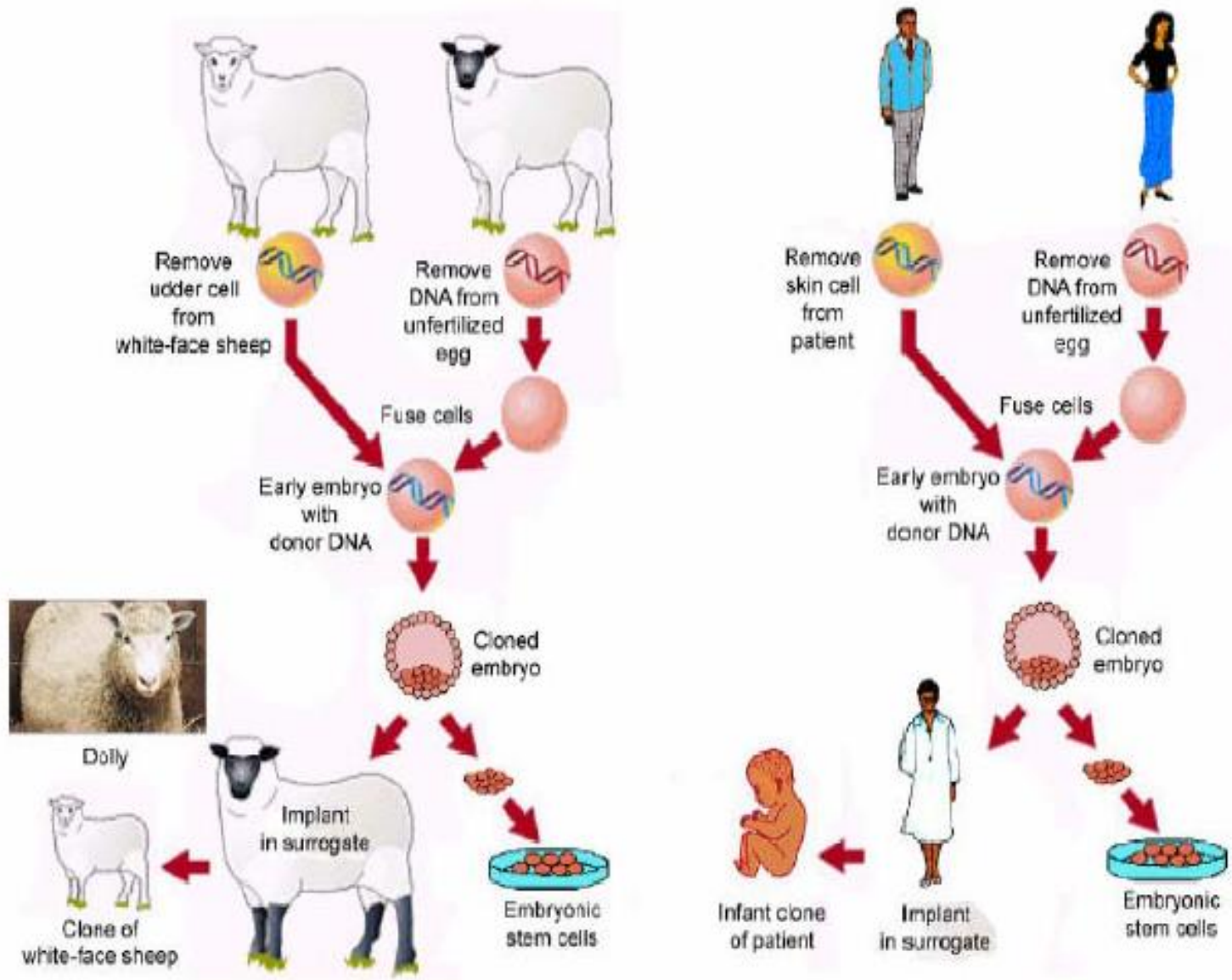
- Isolate individual stem cell populations
- Ensure that cells retain their functionality and potential to differentiate

- Characterize & track stem cell populations
- Ensure that cells are "transplant" ready

- Culture stem cell lines in a stable, multi- or pluri-potent state, free from mutations & to sufficient quantity
- Enable Economical expansion to make cell-therapy a reality

- Control & activate stem cell differentiation to desired lineages
- Functionally active differentiated cells

Sources of Stem Cells

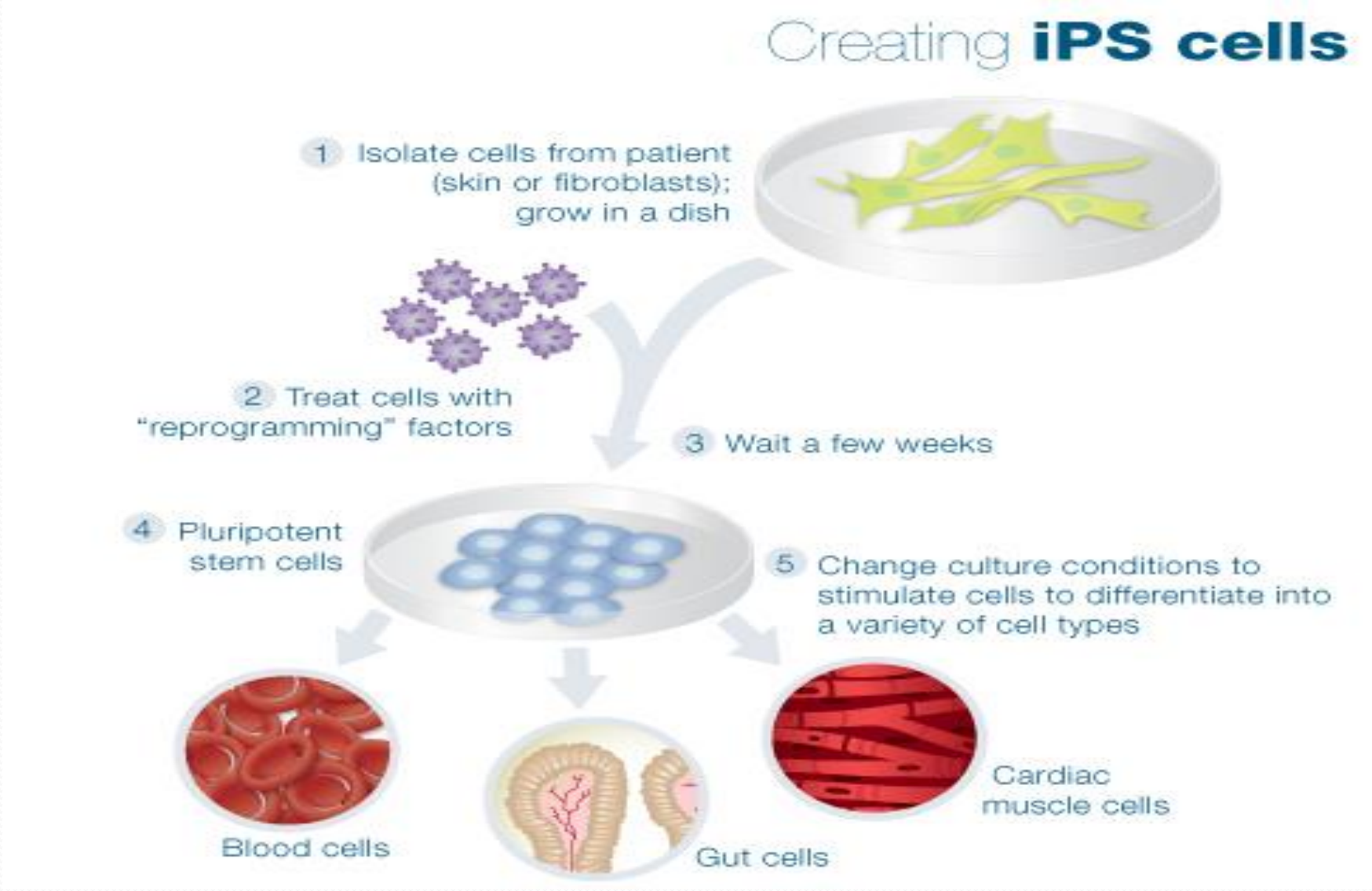

Remove udder cell from white-face sheep
Remove DNA from unfertilized egg
Fuse cells
Early embryo with donor DNA
Cloned embryo
Dolly
Implant in surrogate
Clone of white-face sheep
Embryonic stem cells
Remove skin cell from patient
Remove DNA from unfertilized egg
Fuse cells
Early embryo with donor DNA
Cloned embryo
Infant clone of patient
Implant in surrogate
Embryonic stem cells

Adult Stem Cells

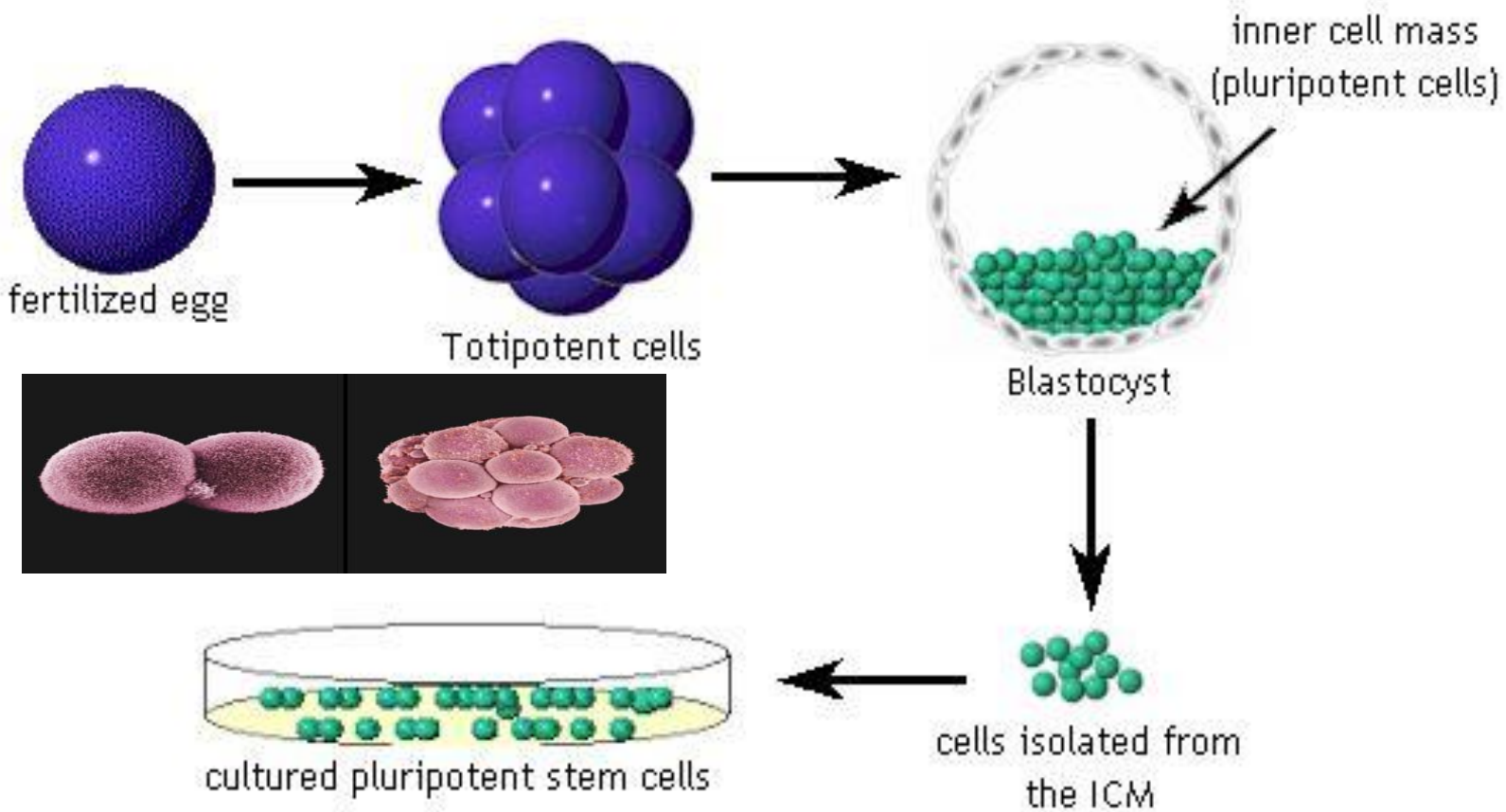
An undifferentiated cells found among specialized or differentiated cells in a tissue or organ after birth

- Skin
- Fat Cells
- Bone marrow
- Brain
- Many other organs & tissues

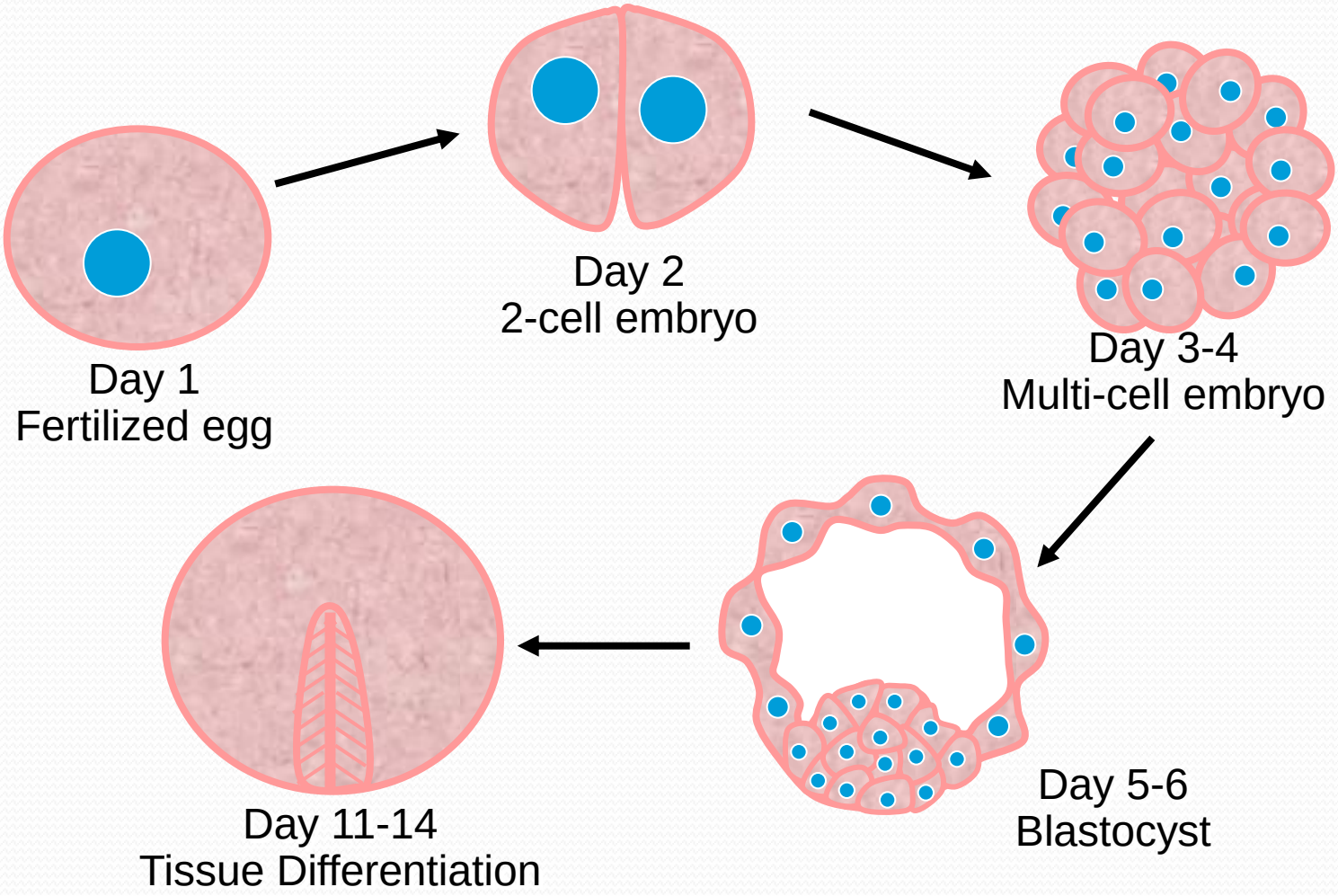
new research – reprogramming cells



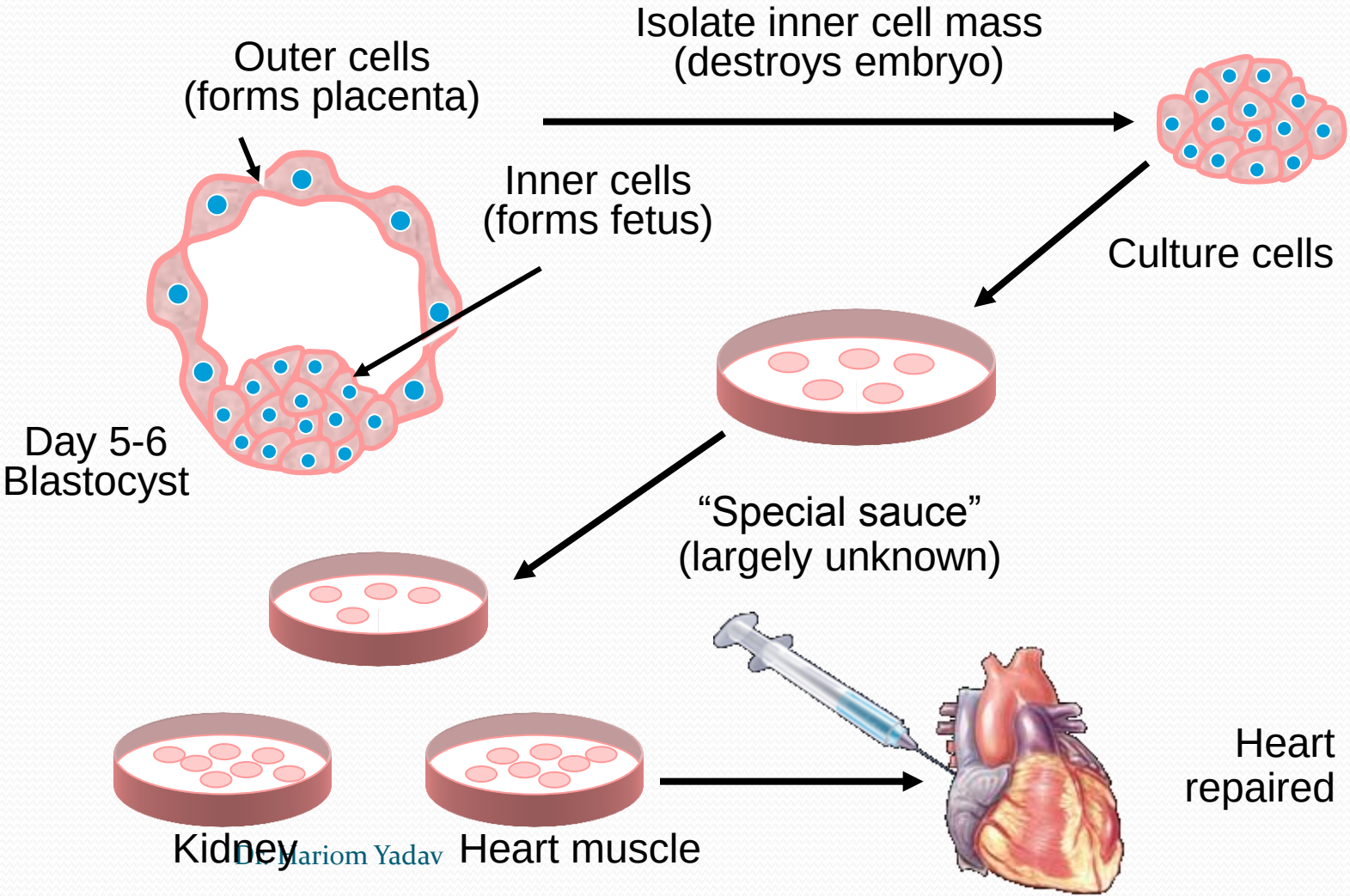
Embryonic Stem Cells

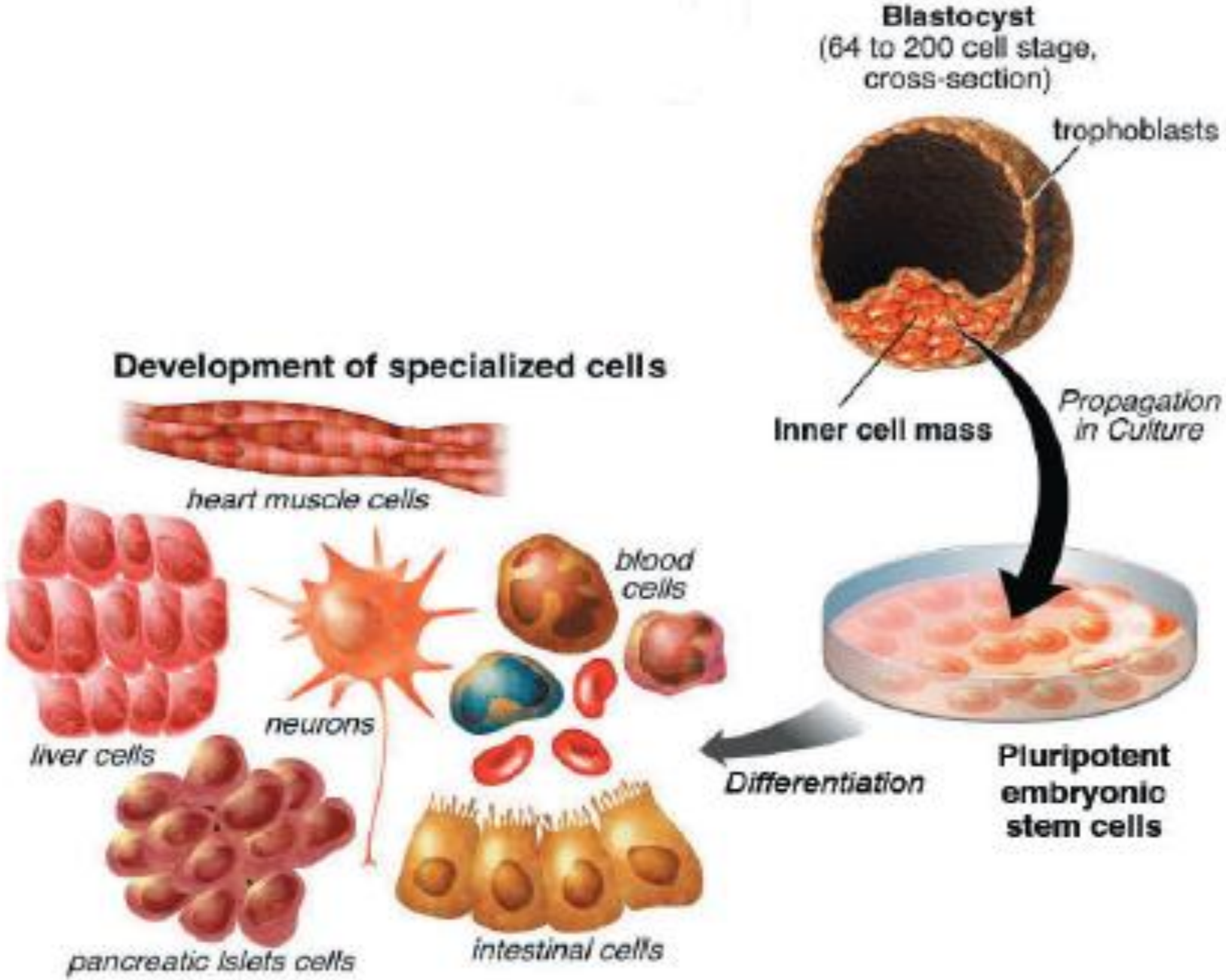


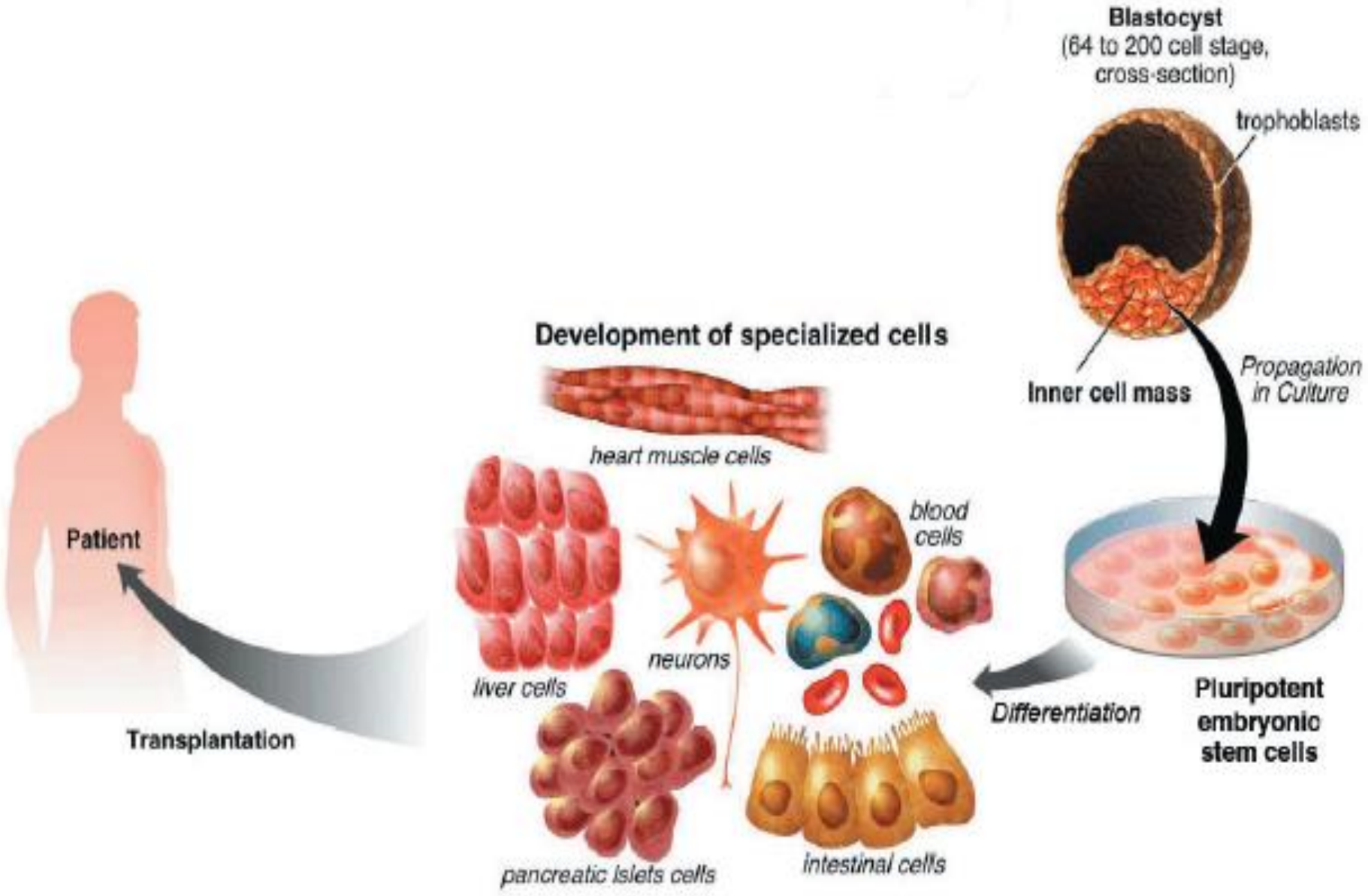
Stages of Embryogenesis



Derivation and Use of Embryonic Stem Cell Lines




Blastocyst
(64 to 200 cell stage,
cross-section)
trophoblasts
Inner cell mass
Propagation
in Culture
Development of specialized cells
heart muscle cells
blood
cells
neurons
liver cells
Differentiation
Pluripotent
embryonic
stem cells
pancreatic islets cells
intestinal cells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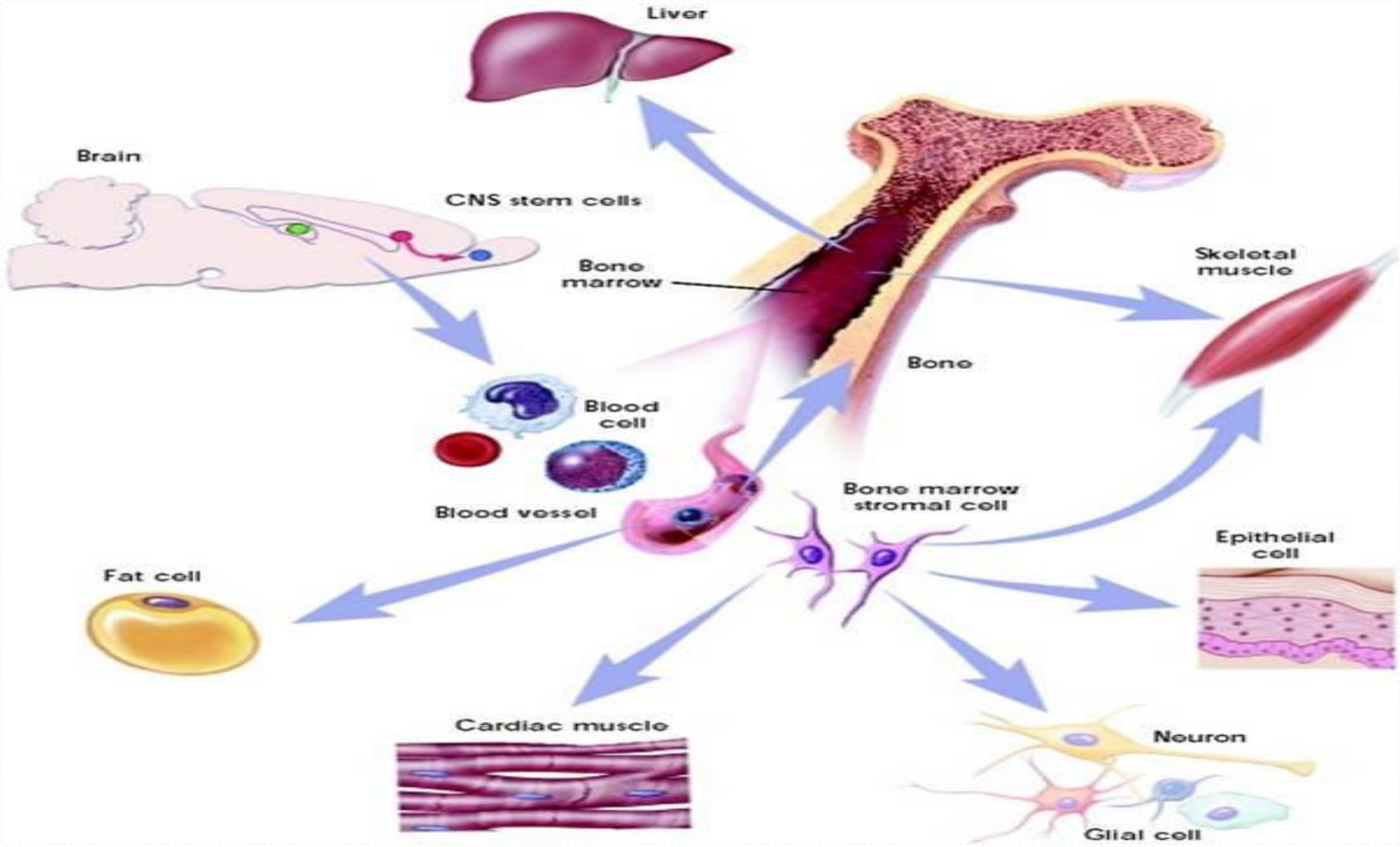
pancreatic islets cells
intestinal cells
Differentiation
Pluripotent embryonic stem cells
Patient
Transplantation

Bone Marrow Stem Cells



Umbilical cord stem cells

- Also Known as Wharton's Jelly
- Adult stem cells of infant origin
- Less invasive than bone marrow
- Greater compatibility
- Less expensive

Umbilical cord stem cells

Three important functions:

- Plasticity: .1
Potential to change into other cell .2 types like nerve cells
.3
- Homing: .4
To travel to the site of tissue .5 damage .6
Engraftment: -
To unite with other tissues

Advantages of UCSC

- Unlimited source of stem cells from biological waste
- Collection of cord stem cells is painless
- Collection of cord stem cells is risk free to mother and baby
- Cord blood stem cells have a greater ability to differentiate into other cell types
- These cells have longer growth potential and have been shown to have a greater rate of engraftment

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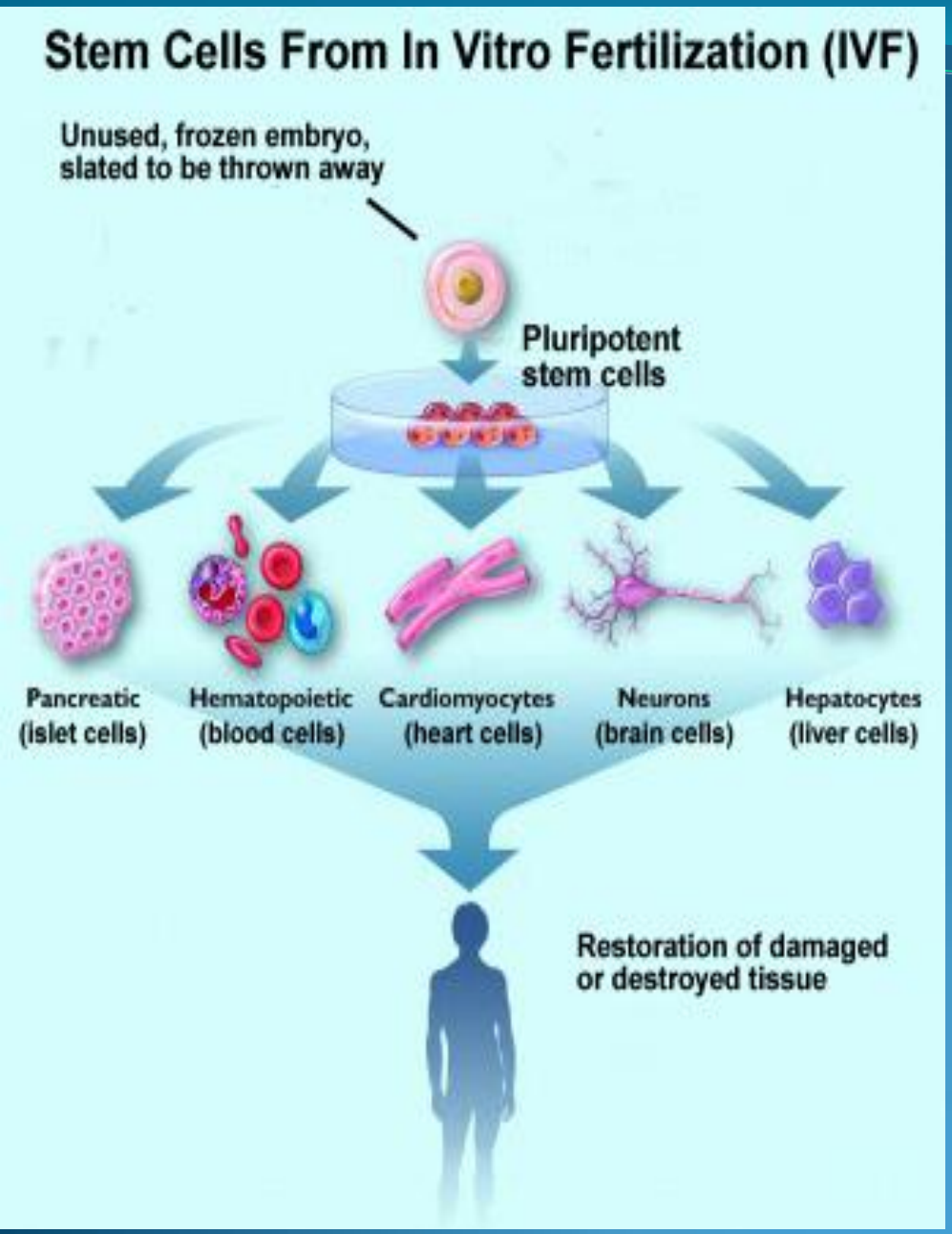
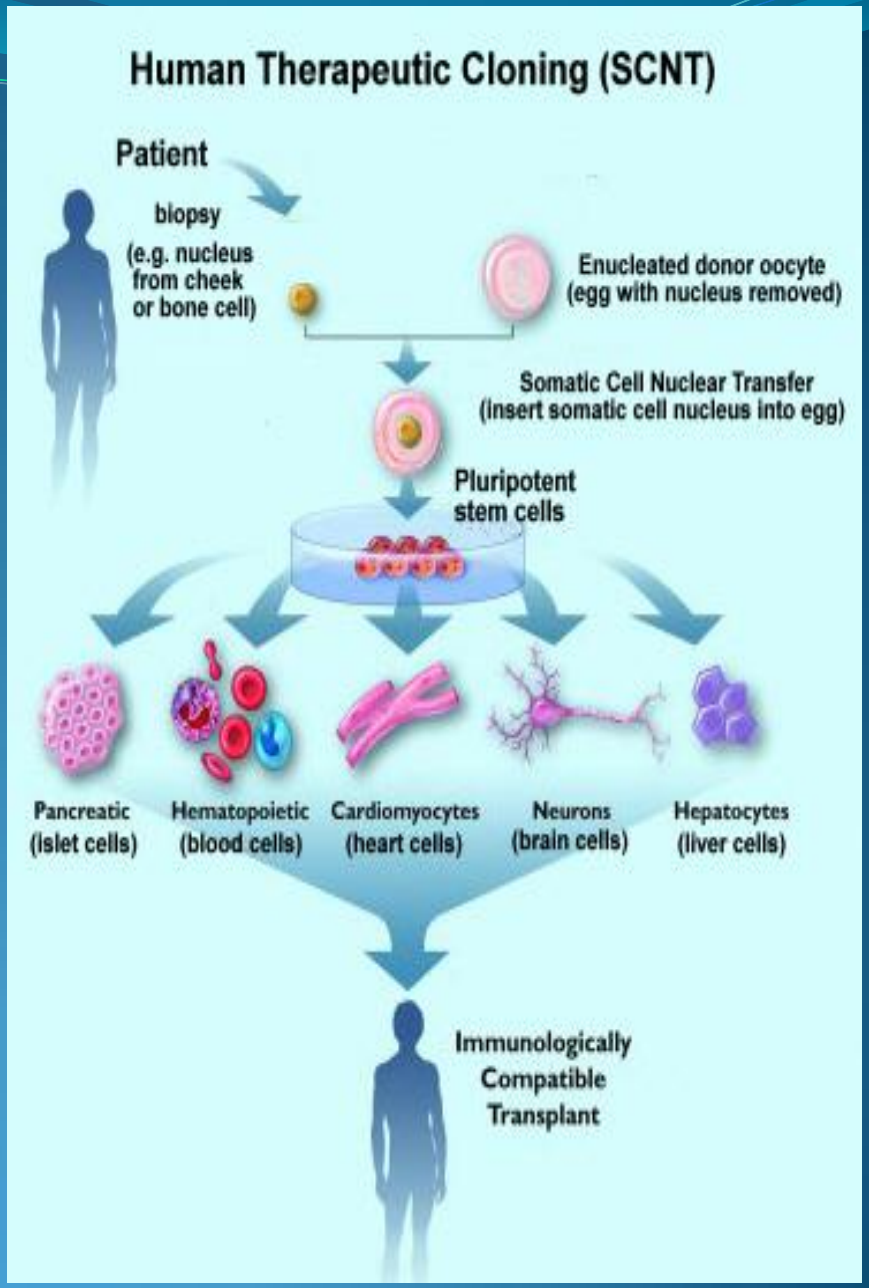
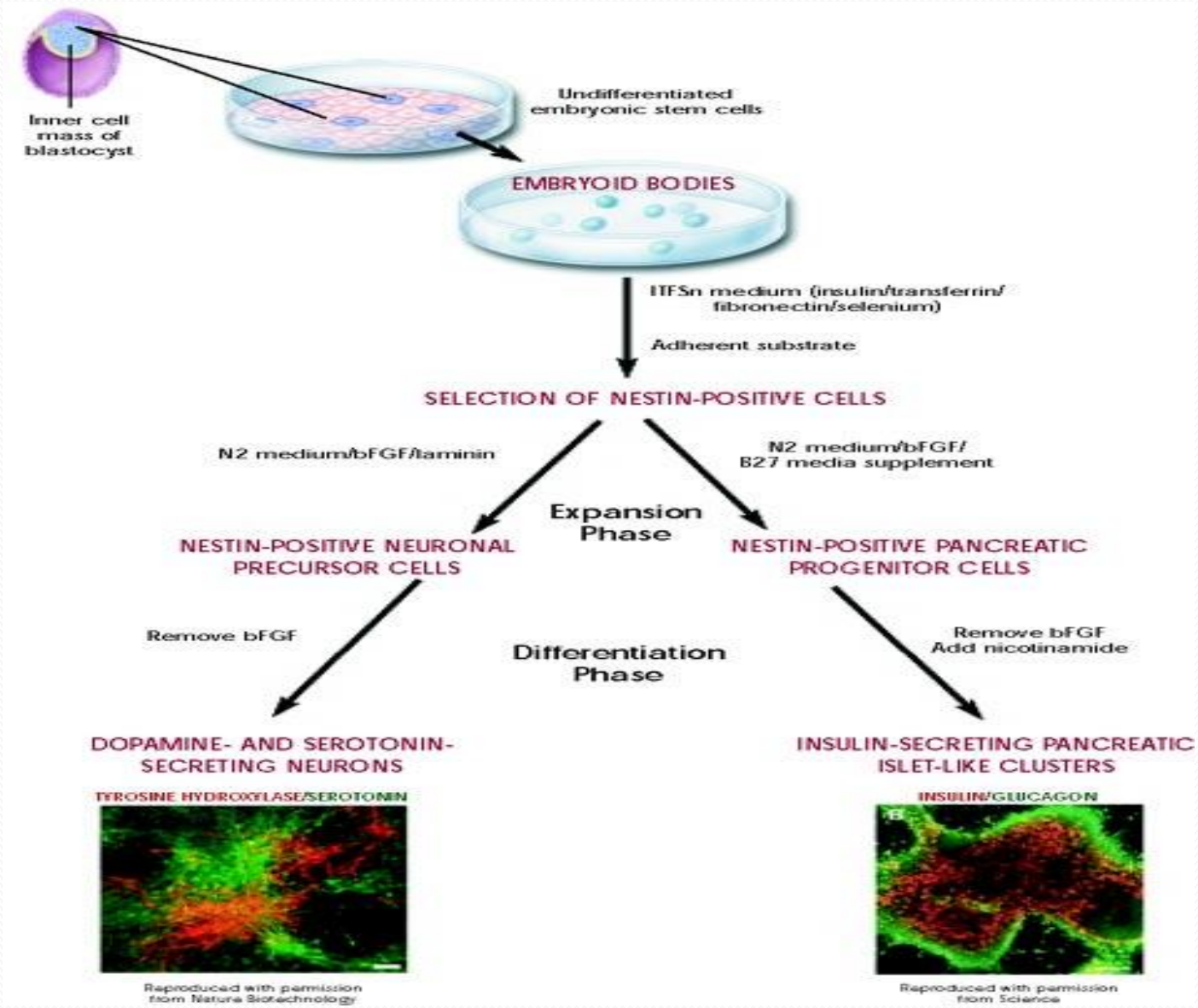
Advantages of UCSC

- Cord blood stem cells are much more tolerant to HLA tissue mismatching than bone marrow therefore leading to lower rate of GVHD
- Cord stem cells are not exposed to the toxins and radiations (we experience in everyday life)
- Cord blood stem cells are being used in the treatment of 40 medical conditions with over 72 potential disease targets
- Research should be oriented towards prolonging their storage and enhancing their expansion

Application of Stem cells


Stem Cells From In Vitro Fertilization (IVF)
Unused, frozen embryo, slated to be thrown away
Pluripotent stem cells
Pancreatic (islet cells)
Hematopoietic (blood cells)
Cardiomyocytes (heart cells)
Neurons (brain cells)
Hepatocytes (liver cells)
Restoration of damaged or destroyed tissue


Human Therapeutic Cloning (SCNT)
Patient
biopsy
(e.g. nucleus from cheek or bone cell)
Enucleated donor oocyte (egg with nucleus removed)
Somatic Cell Nuclear Transfer (insert somatic cell nucleus into egg)
Pluripotent stem cells
Pancreatic (islet cells)
Hematopoietic (blood cells)
Cardiomyocytes (heart cells)
Neurons (brain cells)
Hepatocytes (liver cells)
Immunologically Compatible Transplant


Inner cell mass of blastocyst
Undifferentiated embryonic stem cells
EMBRYOID BODIES
ITFSn medium (insulin/transferrin/ fibronectin/selenium)
Adherent substrate
SELECTION OF NESTIN-POSITIVE CELLS
N2 medium/bFGF/laminin
N2 medium/bFGF/ B27 media supplement
Expansion Phase
NESTIN-POSITIVE NEURONAL PRECURSOR CELLS
NESTIN-POSITIVE PANCREATIC PROGENITOR CELLS
Remove bFGF
Differentiation Phase
Remove bFGF Add nicotinamide
DOPAMINE- AND SEROTONIN-SECRETING NEURONS
TYROSINE HYDROXYLASE/SEROTONIN
Reproduced with permission from Nature Biotechnology
INSULIN-SECRETING PANCREATIC ISLET-LIKE CLUSTERS
INSULIN/GLUCAGON
Reproduced with permission from Science

Tissue Repair

- Regenerate spinal cord, heart tissue or any other major tissue in the body.

Heart Disease

- Adult bone marrow stem cells injected into the hearts arteries are believed to improve cardiac function in victims of heart failure or heart attack.

Leukemia and Cancer

- Studies show leukemia patients treated with stem cells emerge free of disease.
- Injections of stem cells have also reduced pancreatic cancers in some patients.

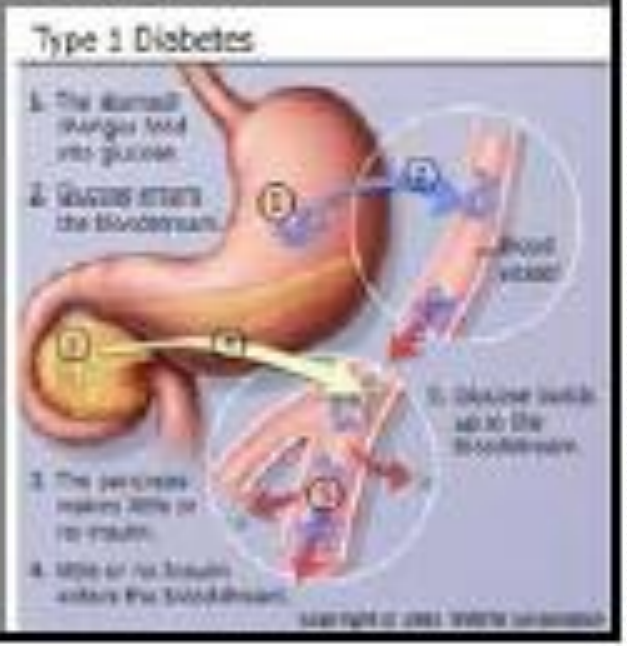
Rheumatoid Arthritis

- Adult stem cells may be helpful in jumpstarting repair of eroded cartilage.

A foot with painful, advanced rheumatoid arthritis

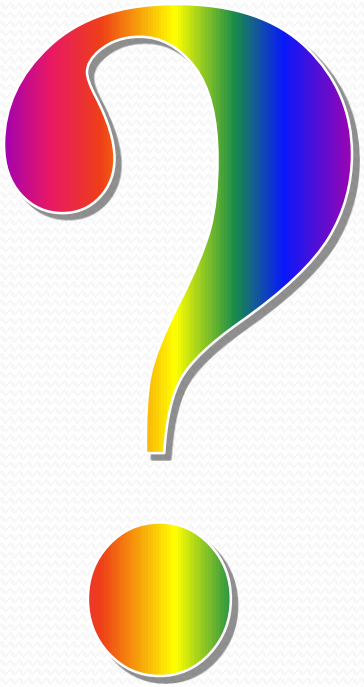
Type I Diabetes

- Pancreatic cells do not produce insulin.
- Basic research focused on understanding how embryonic stem cells might be trained to become pancreatic islets cells needed to secrete insulin.



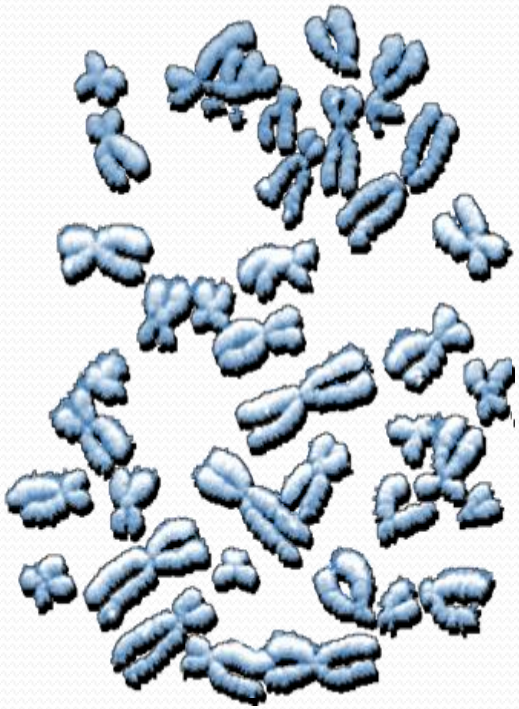
Challenges and Risks

Unknowns in Stem Cell/Cloning Research



- **It is uncertain that human embryonic stem cells *in vitro* can give rise to all the different cell types of the adult body.**
- **It is unknown if stem cells cultured *in vitro* (apart from the embryo) will function as the cells do when they are part of the developing embryo**

Challenges to Stem Cell/Cloning Research



- **--Stem cells need to be differentiated to the appropriate cell type(s) *before* they can be used clinically.**
- **--Recently, abnormalities in chromosome number and structure were found in three human ESC lines.**

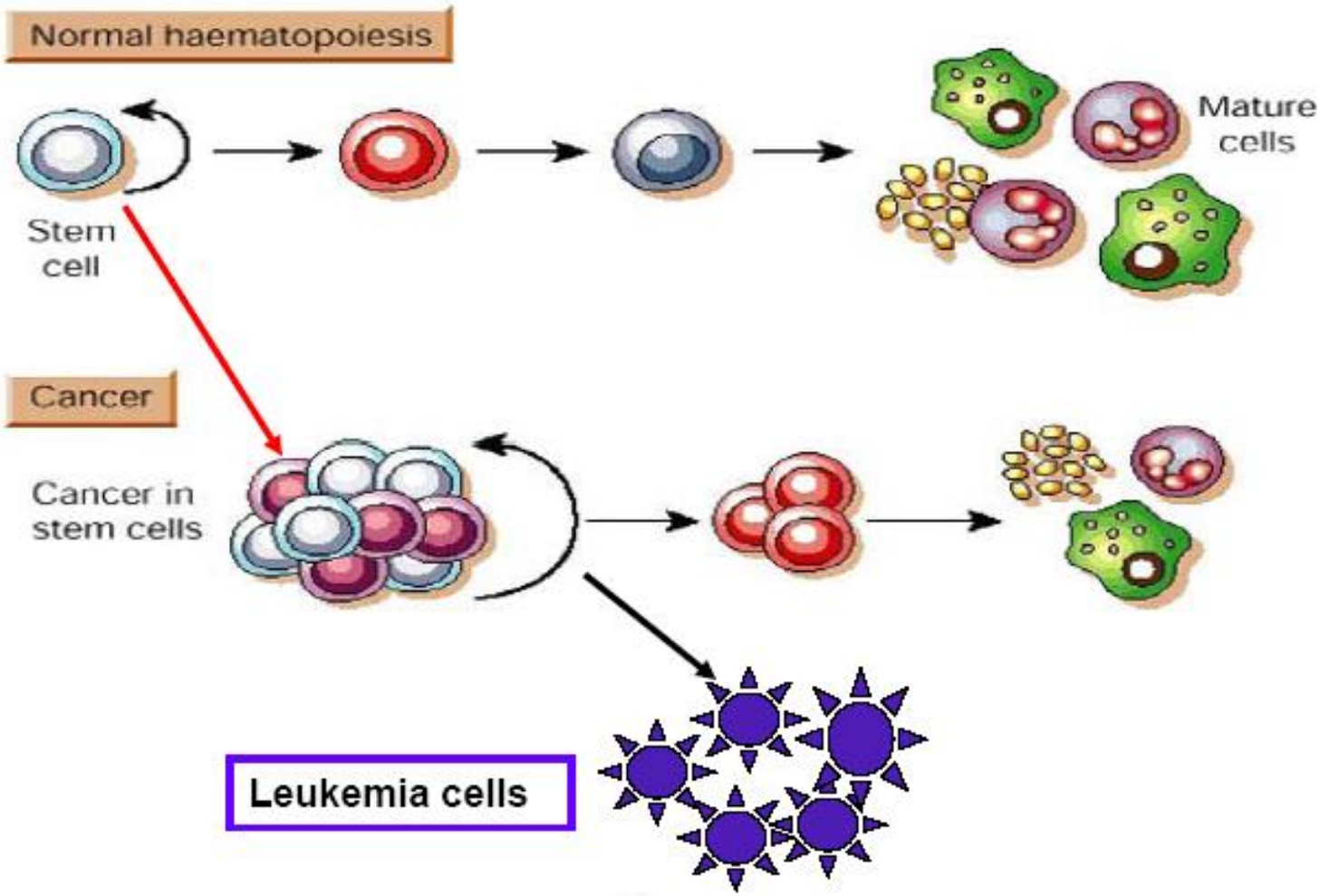
Challenges to Stem Cell/Cloning Research

- **- Stem cell development or proliferation must be controlled once placed into patients.**
- **- Possibility of rejection of stem cell transplants as foreign tissues is very high.**

Challenges to Stem Cell/Cloning Research

- **Contamination by viruses, bacteria, fungi, and Mycoplasma possible.**
- **-The use of mouse "feeder" cells to grow ESC could result in problems.**

Mutations in Stem Cells can Lead to Leukemia



Thank you for listening