

Stem Cells

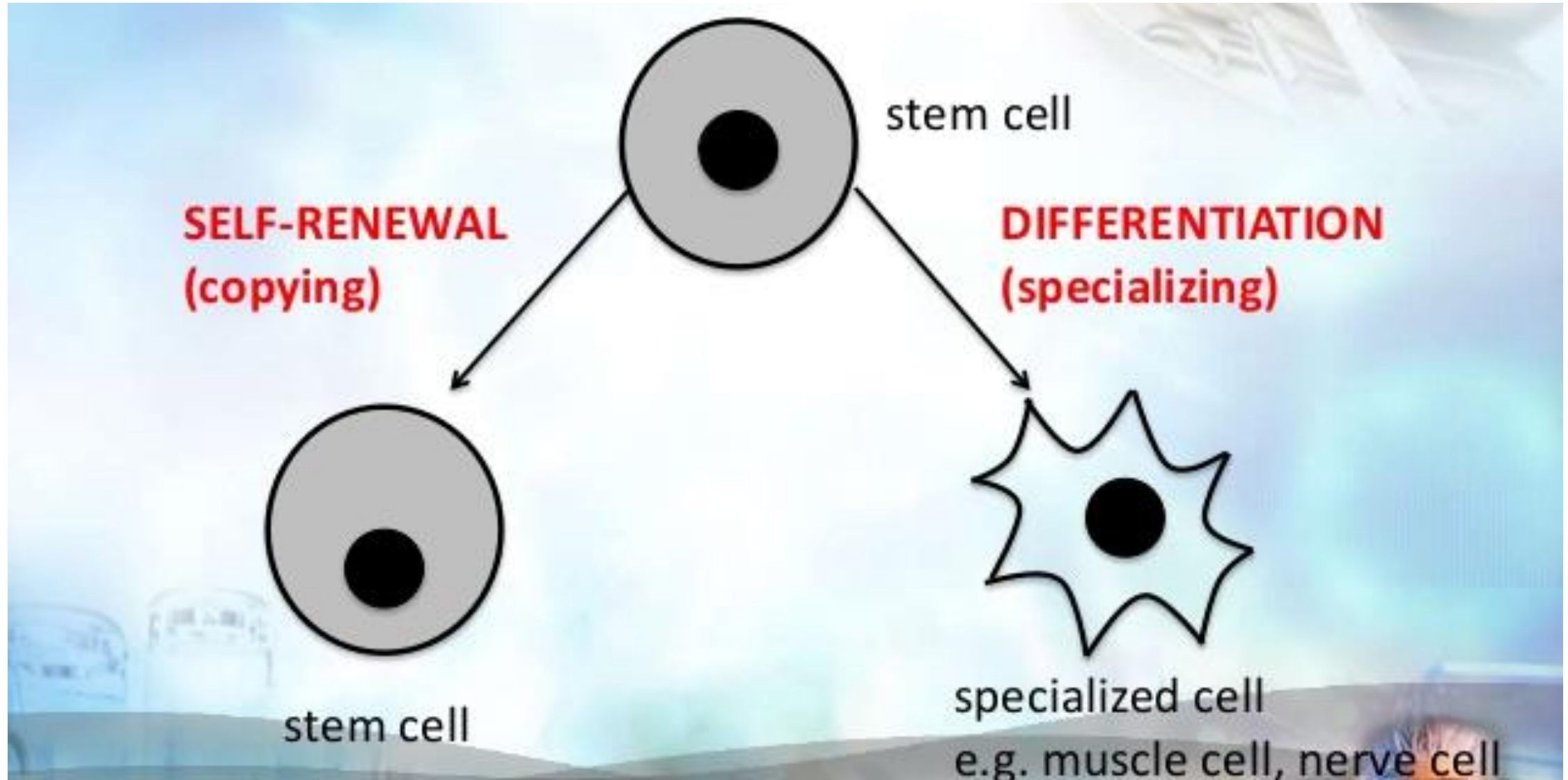
and its potency

Regenerative Medicine

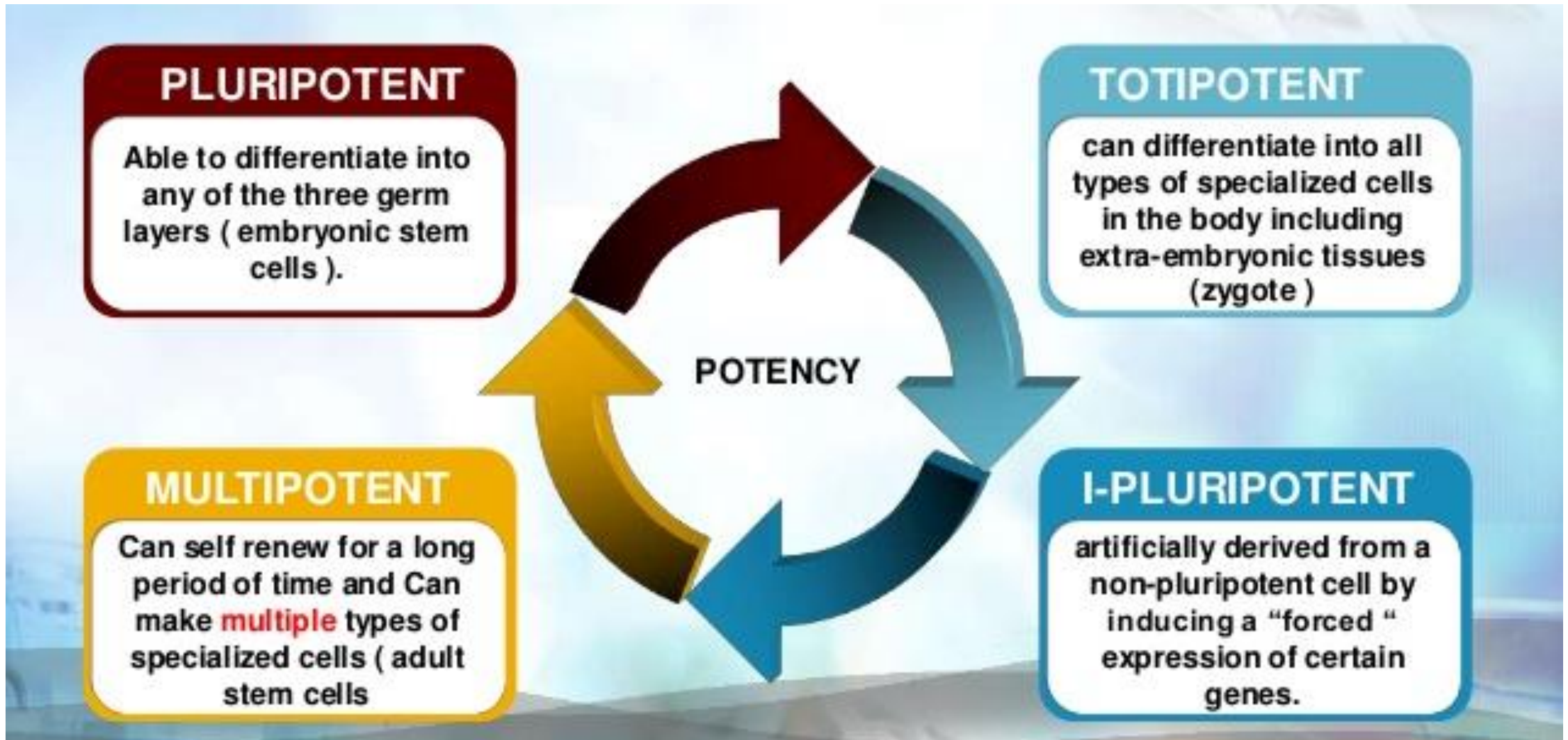
Historical perspectives

- 1908: The term "stem cell" was coined by [Alexander Maksimov](#)
- 1963: [McCulloch](#) and [Till](#) illustrate the presence of self-renewing cells in mouse bone marrow.
- 1968: [Bone marrow transplant](#) between two siblings successfully treats [SCID](#).
- 1978: [Haematopoietic stem cells](#) are discovered in human [cord blood](#).
- 2000: Several reports of [adult stem cell](#) plasticity are published.
- 2007: The Nobel Prize was awarded jointly to Mario R. Capecchi, Sir Martin J. Evans and Oliver Smithies "for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells".
- 2008: Development of human cloned blastocysts following [somatic cell nuclear transfer](#) with adult fibroblasts
- 2012: The Nobel Prize was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent"

What is a Stem Cell?



Stem Cell Jargon

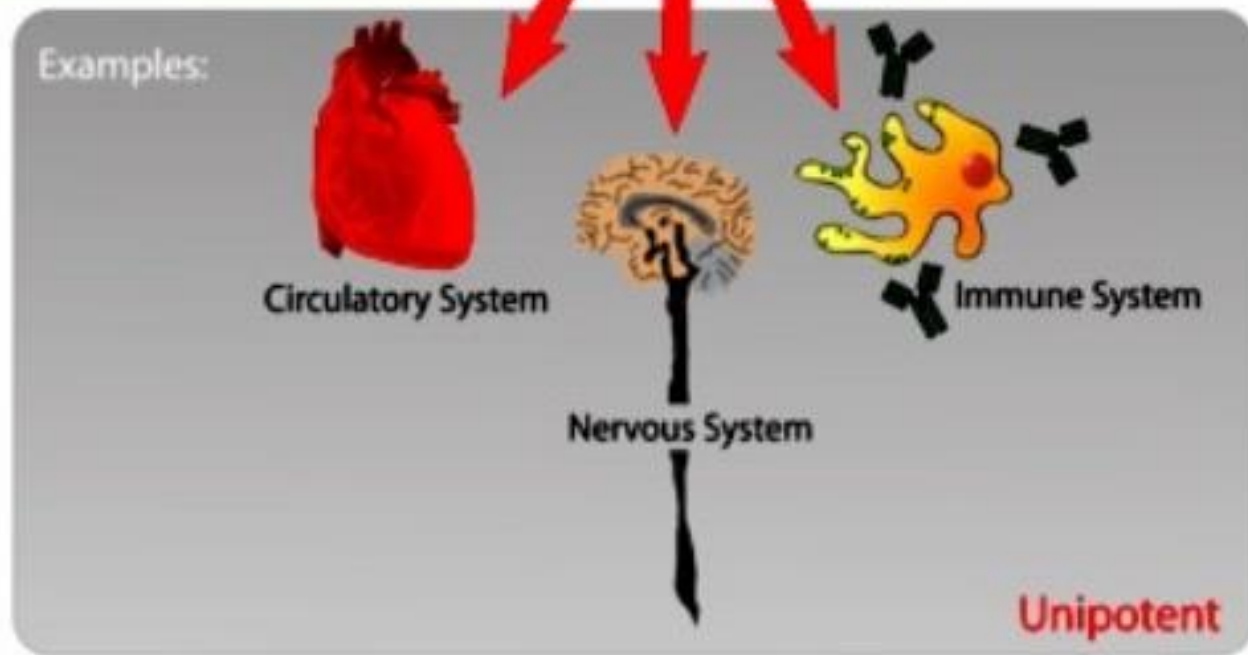
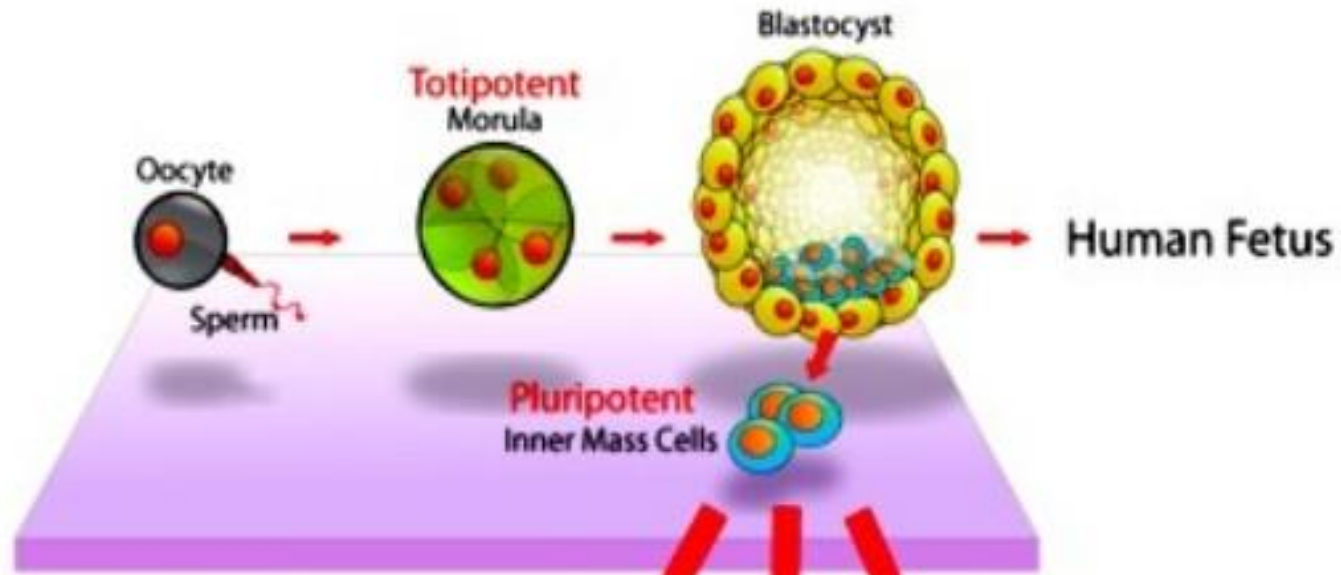


Potency definitions of Stem Cells

- *Totipotent : can differentiate into an entire organism , result from fusion of egg and sperm*
 - *can form any cell of the embryo as well as the placenta.*
- *Pluripotent : can differentiate into any tissue type except placental tissue*

Potency definitions of Stem Cells

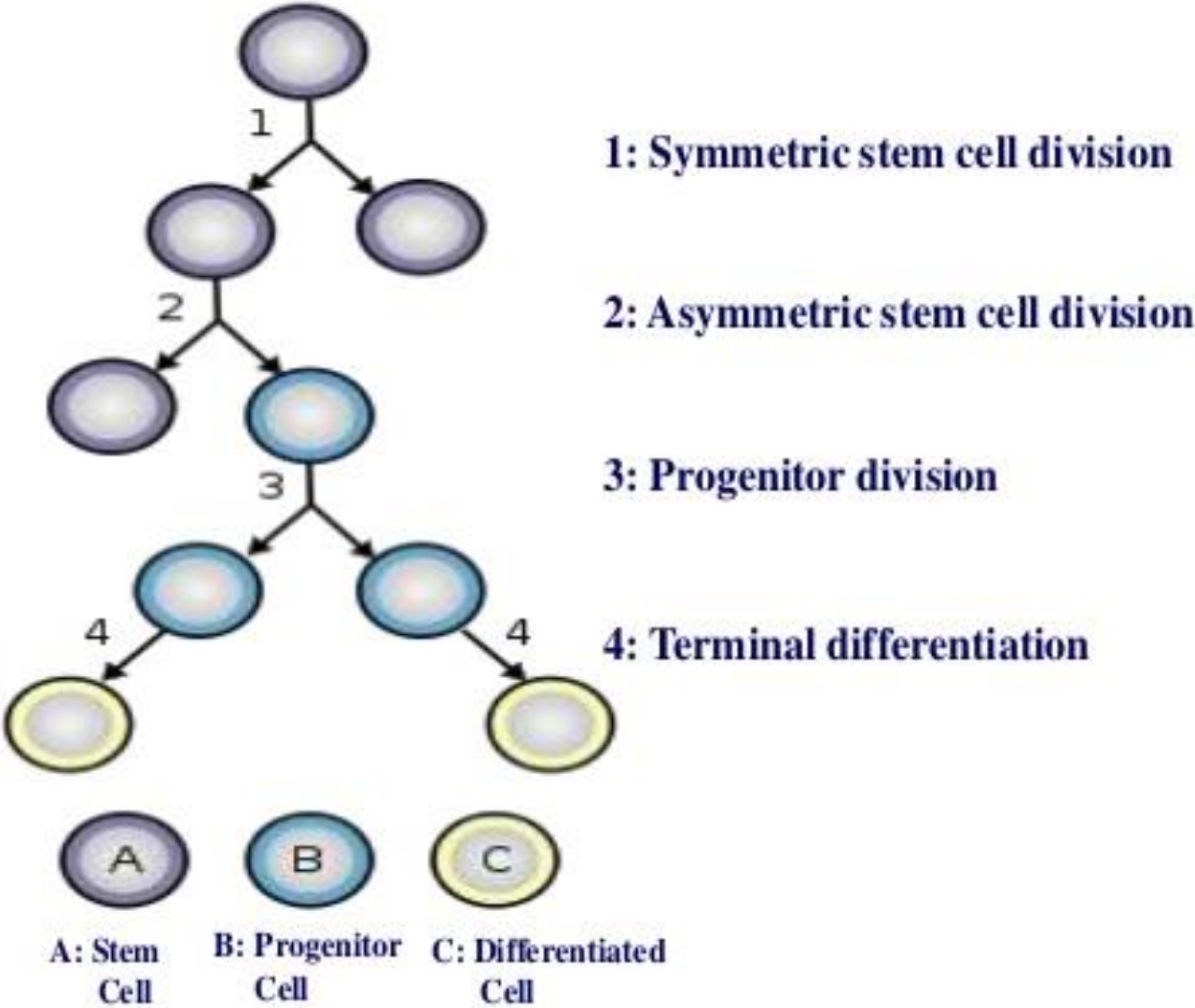
- *Multipotent : can differentiate into multiple specialized cells of a closely related family of cells*
- *Unipotent : these cells only produce one cell type., but have the property of self renewal which distinguishes them from the non stem cells.*



Pluripotent

Unipotent

Stem Cell Division and Differentiation



Types of Stem Cells

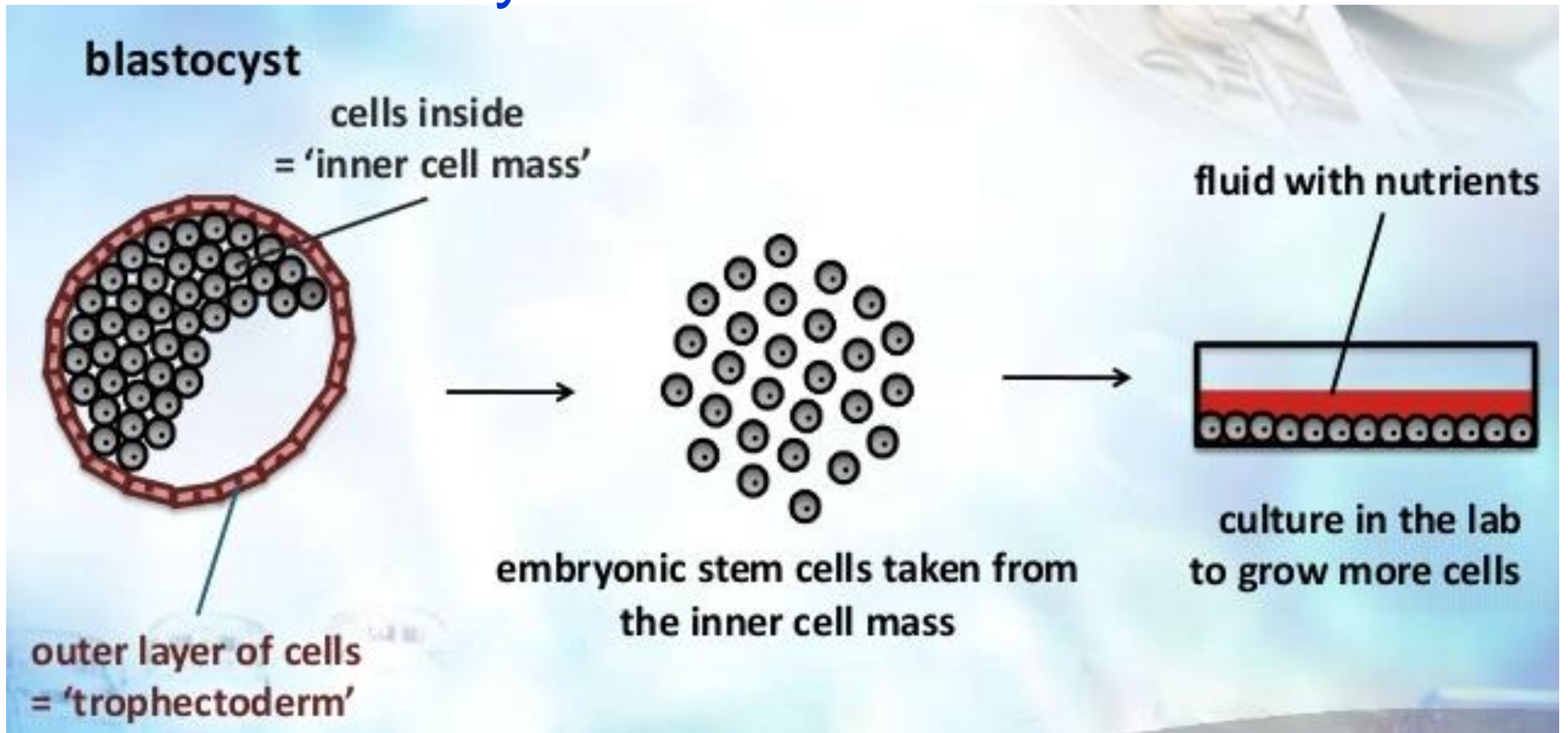
- *Embryonic : derived from the inner cell mass of a blastocyst / human embryo*

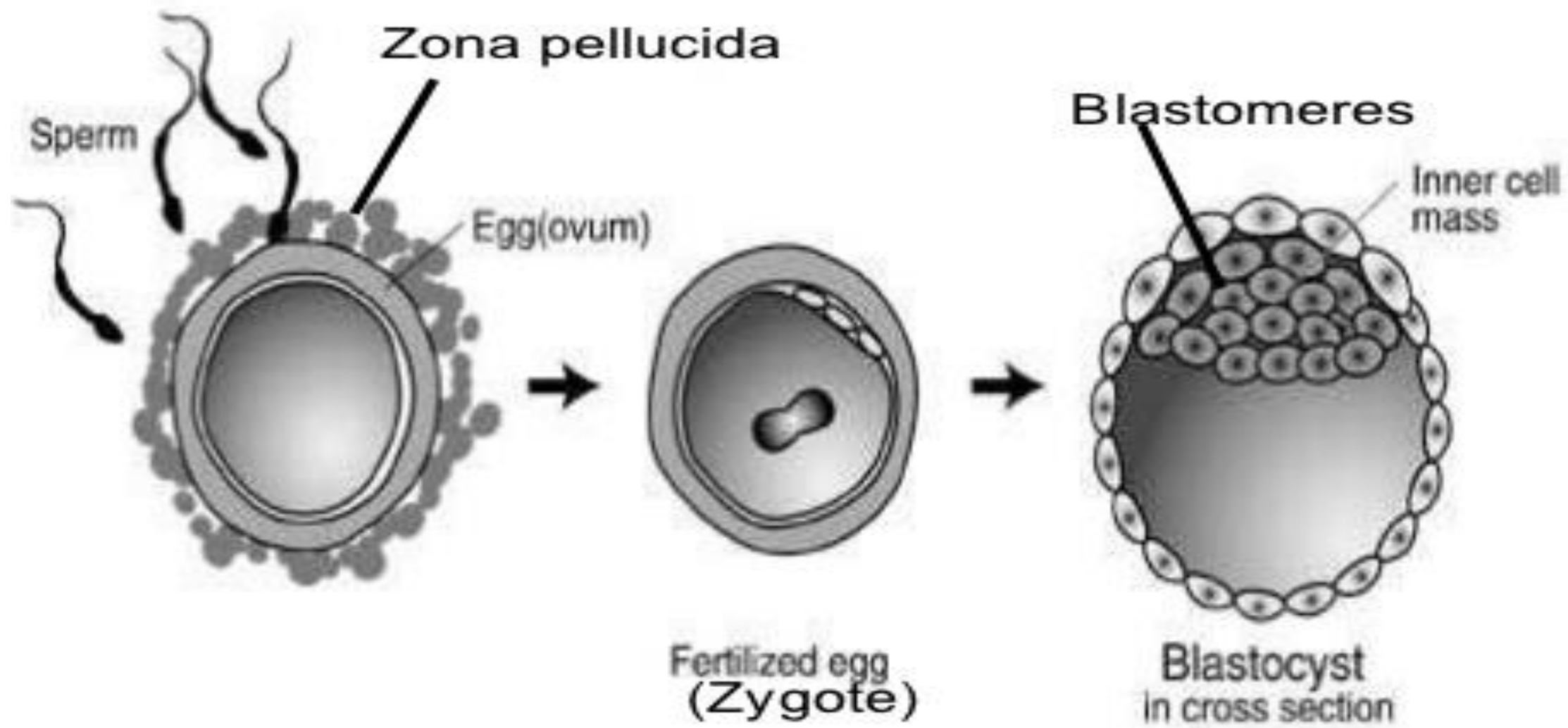
Source :

- 1. Excess fertilized eggs from IVF (in-vitro fertilization) clinics*
- 5. Therapeutic cloning (somatic cell nuclear transfer)*

Embryonic Stem Cells

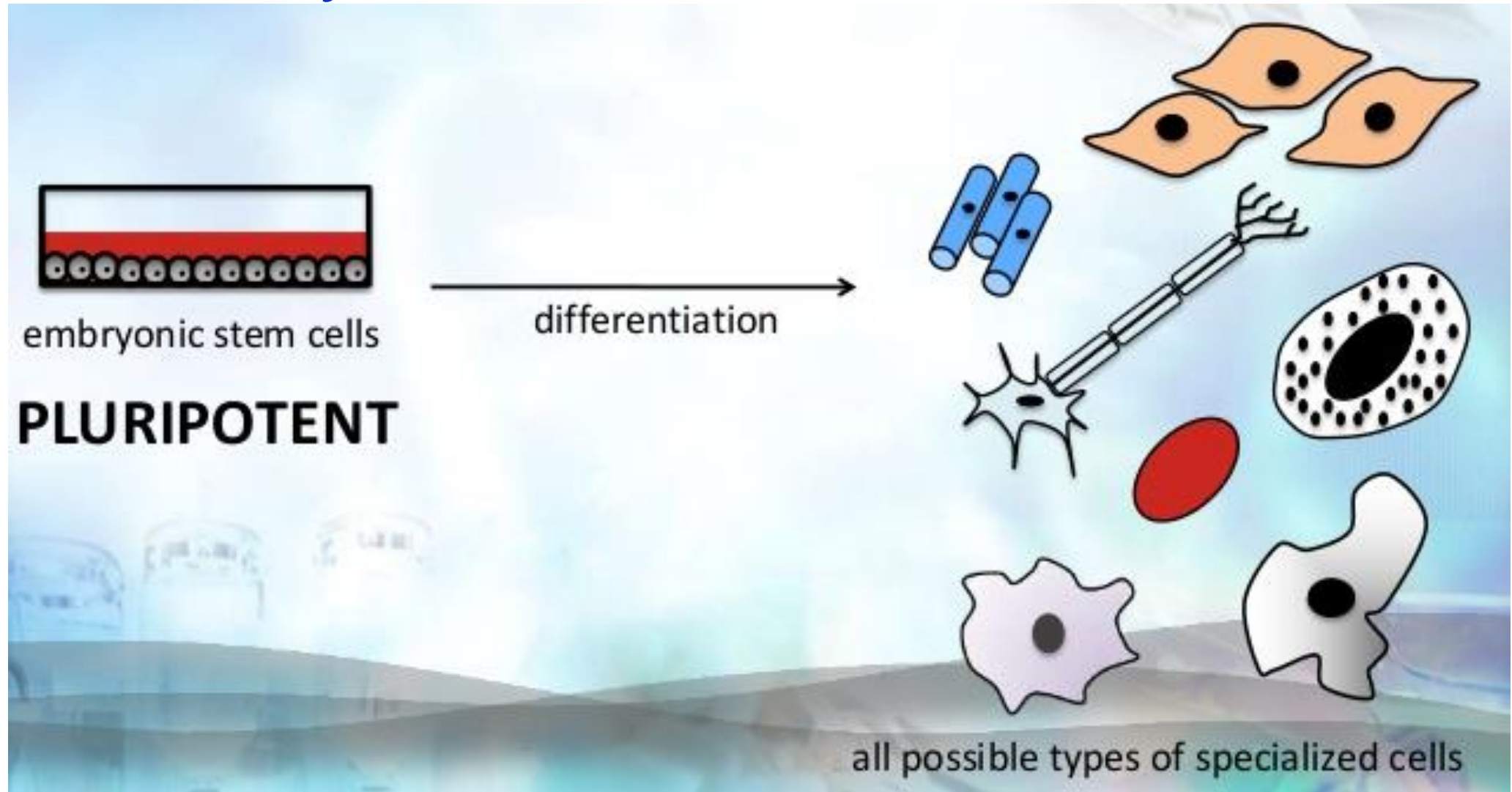
Where are they found???





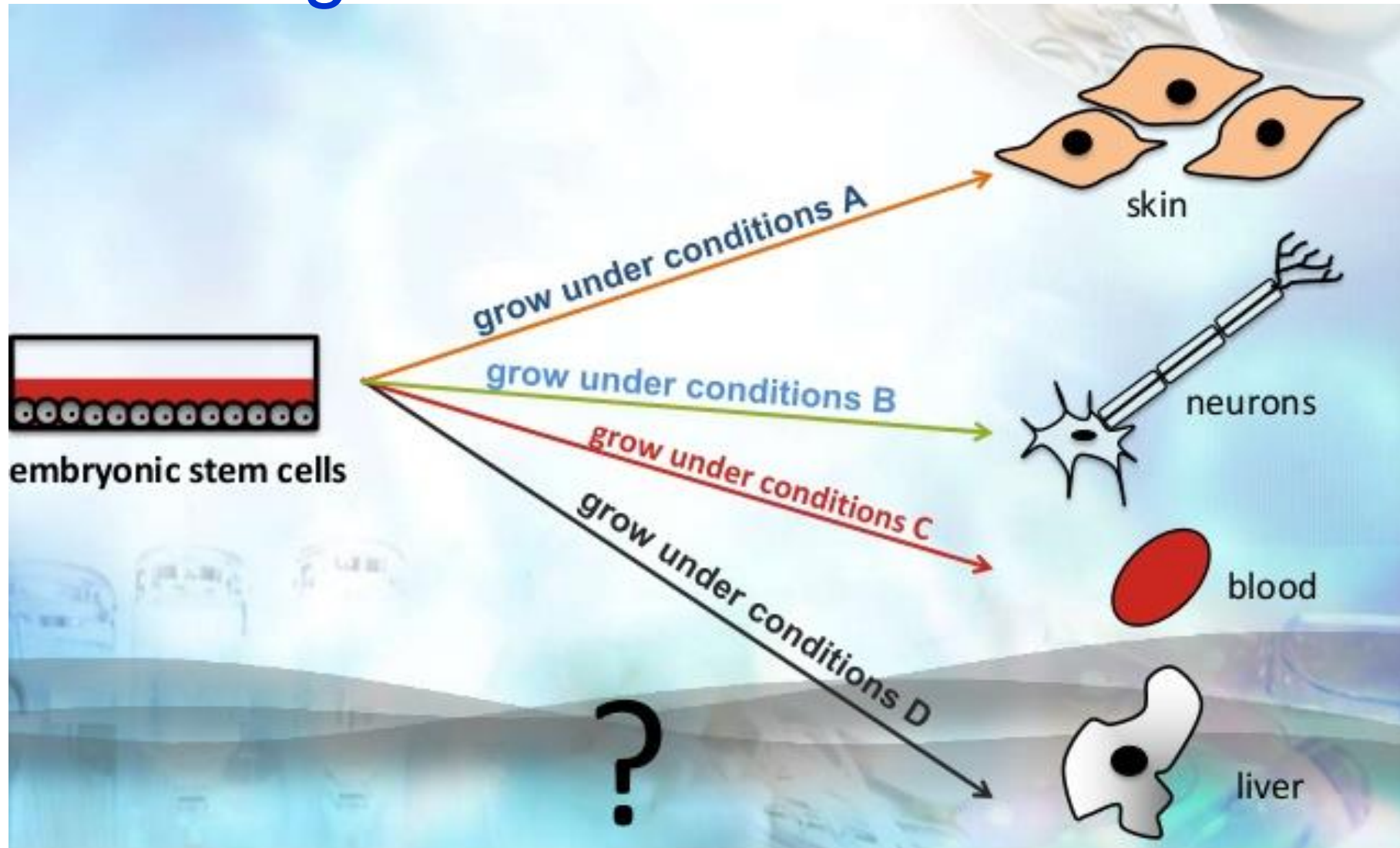
Embryonic Stem (ES) Cells

What they can do?



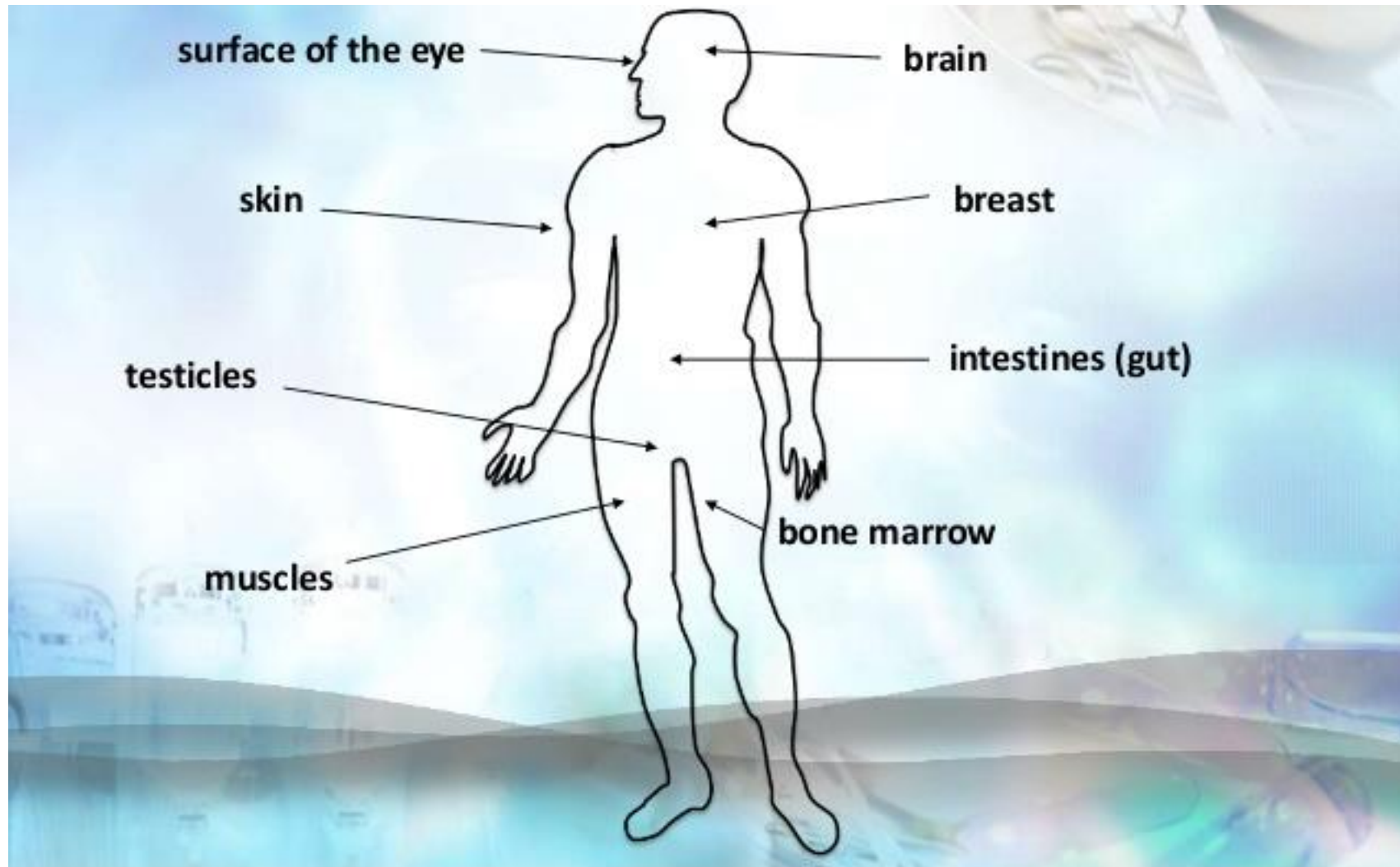
Embryonic Stem Cells (ES)

Challenges....

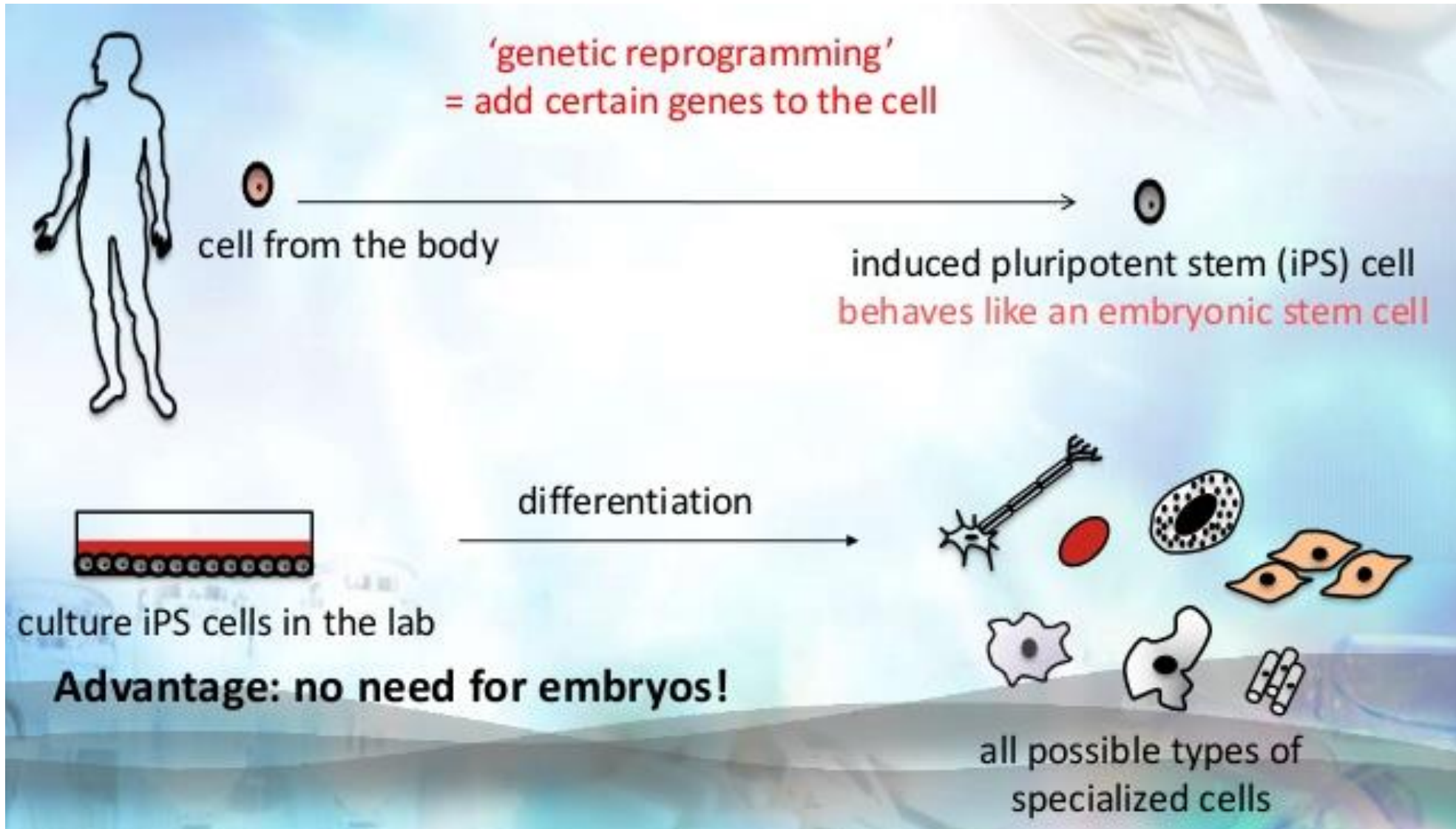


Tissue Stem Cells

Where are they found???

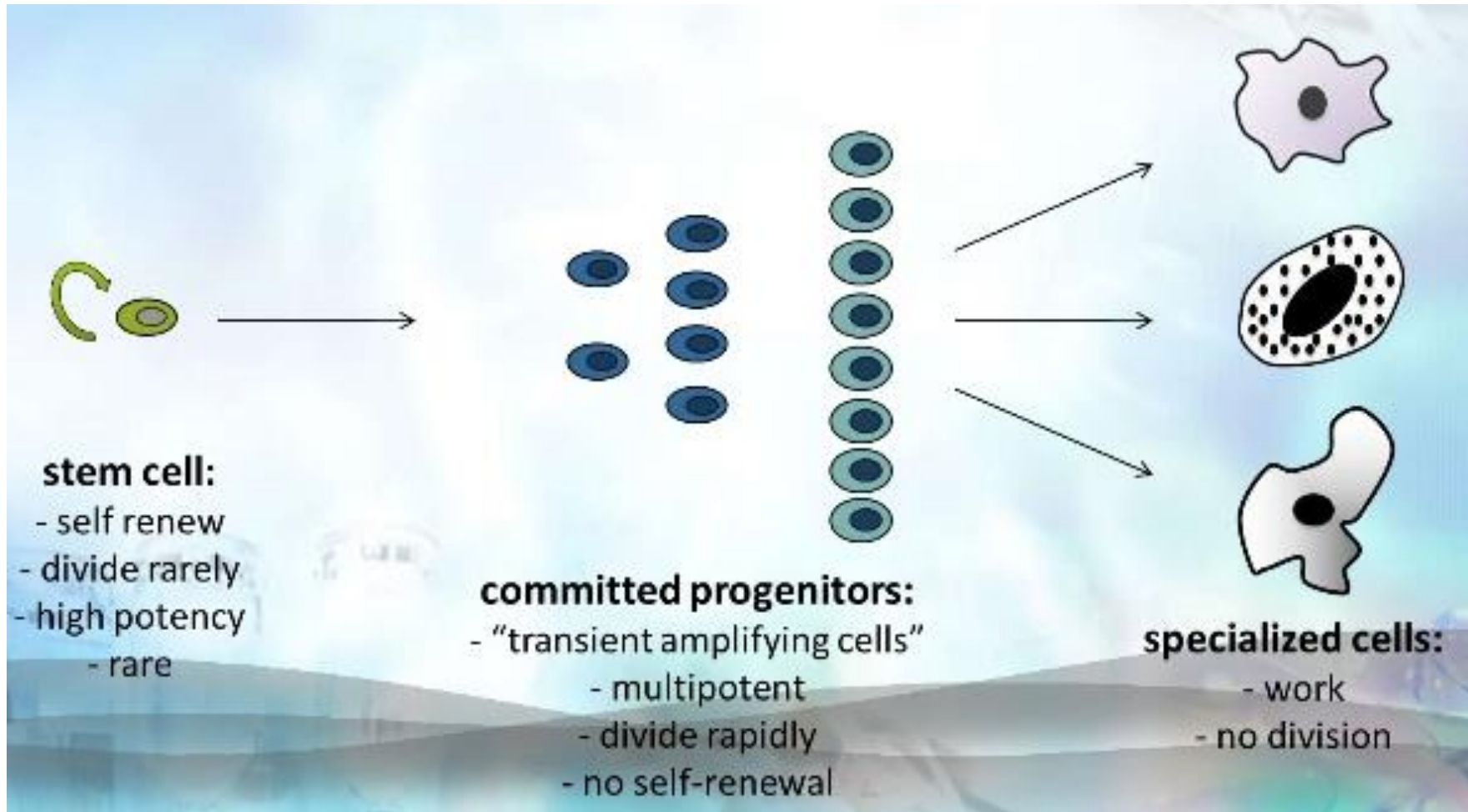


Induced Pluripotent Stem Cells (iPS Cells)



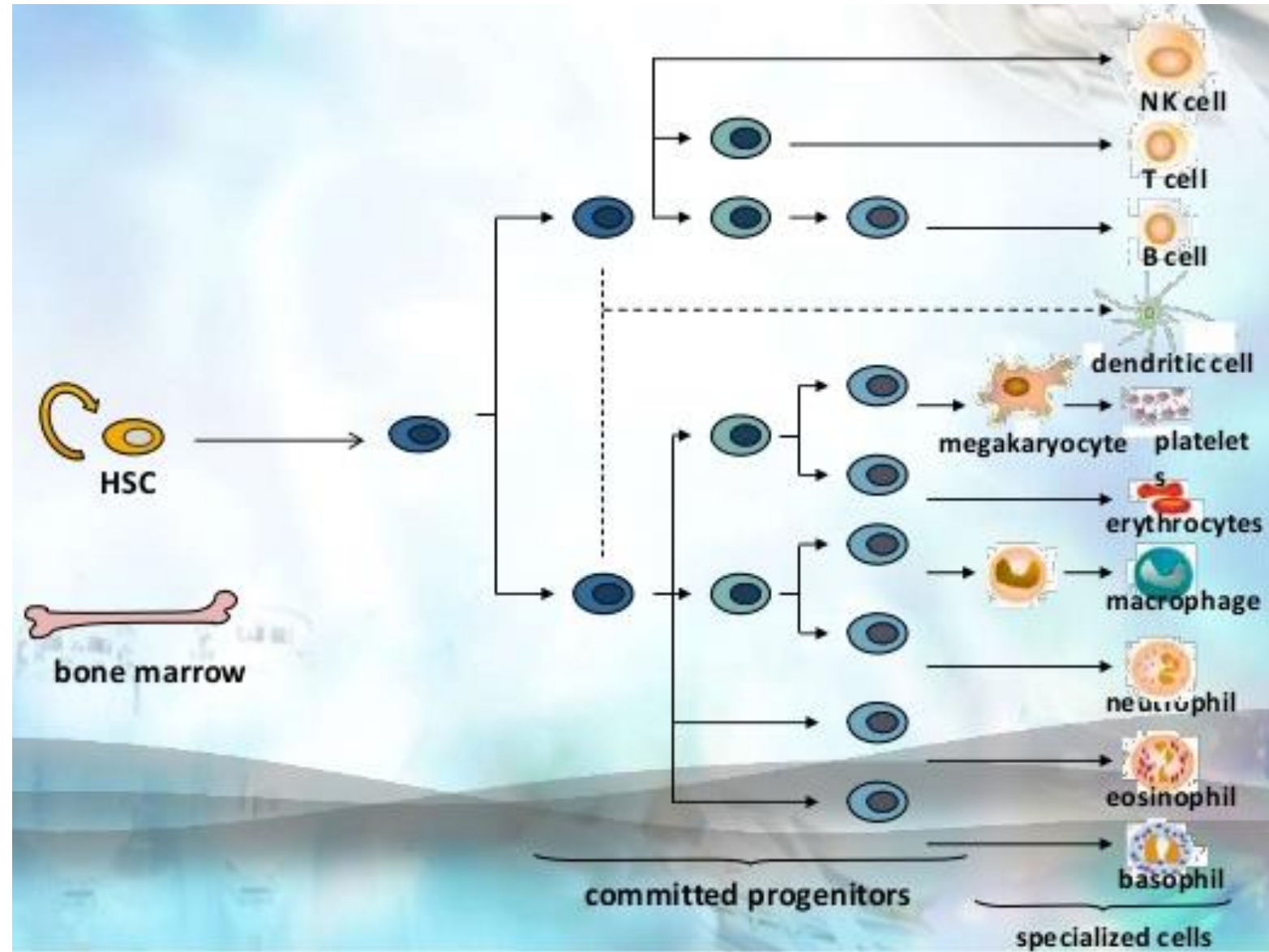
Tissue Stem Cells

Principles of renewing tissues



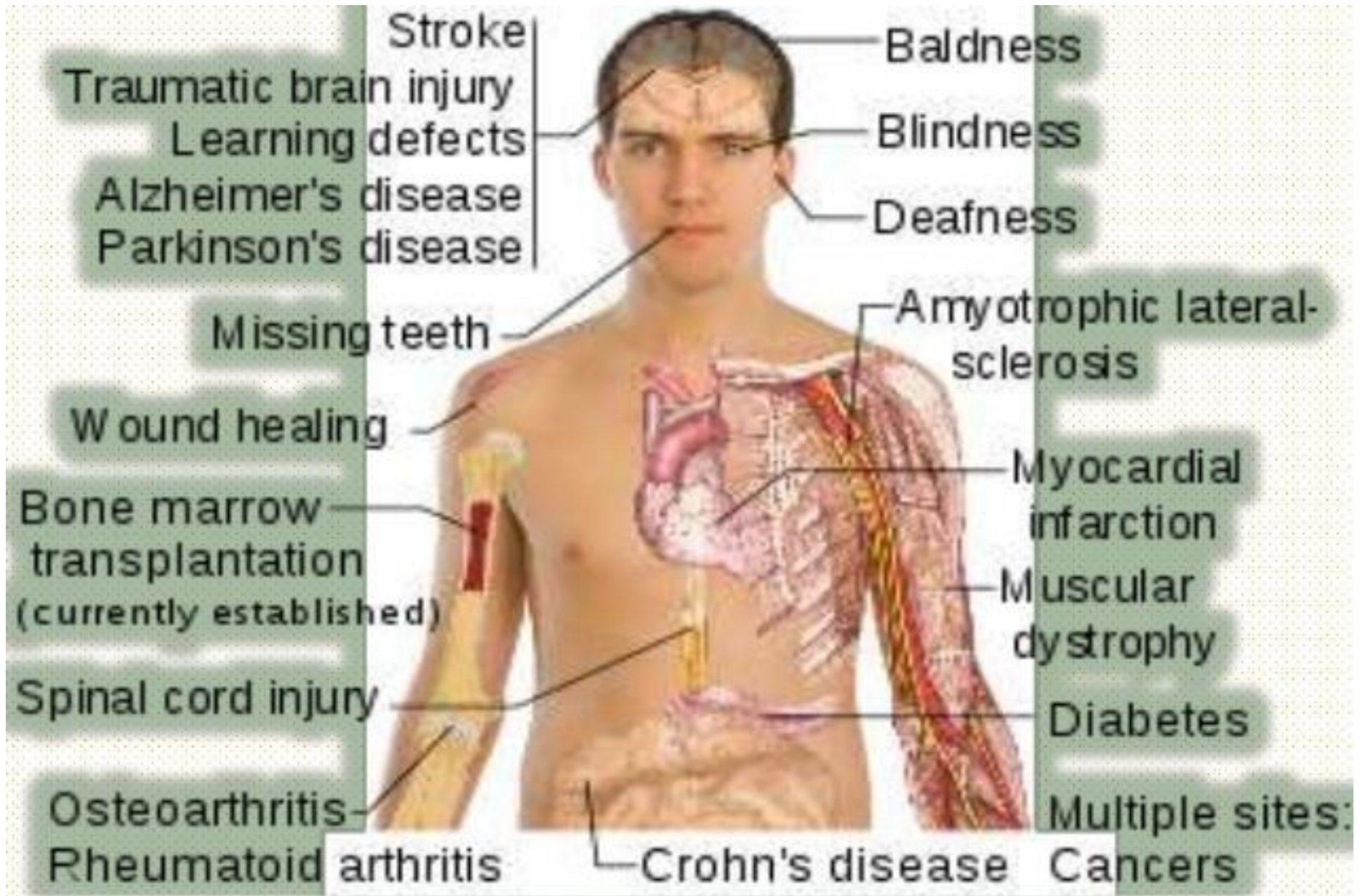
Tissue Stem Cells

Hematopoietic Stem Cells (HSCs)



Stem Cells

Their potential uses



- *Adult : derived from mature organisms that can divide to form more differentiated cells*
 - *but are less versatile and more difficult to identify, isolate, and purify.*

Eg: Stem cells have been found in the blood, bone marrow, liver, kidney, cornea, dental pulp, brain, skin, muscle

- *Fetal : derived from aborted fetal tissue*
- *Umbilical : derived from umbilical cords*
 - *All blood cell types (red blood cells, white blood cells, and platelets)*

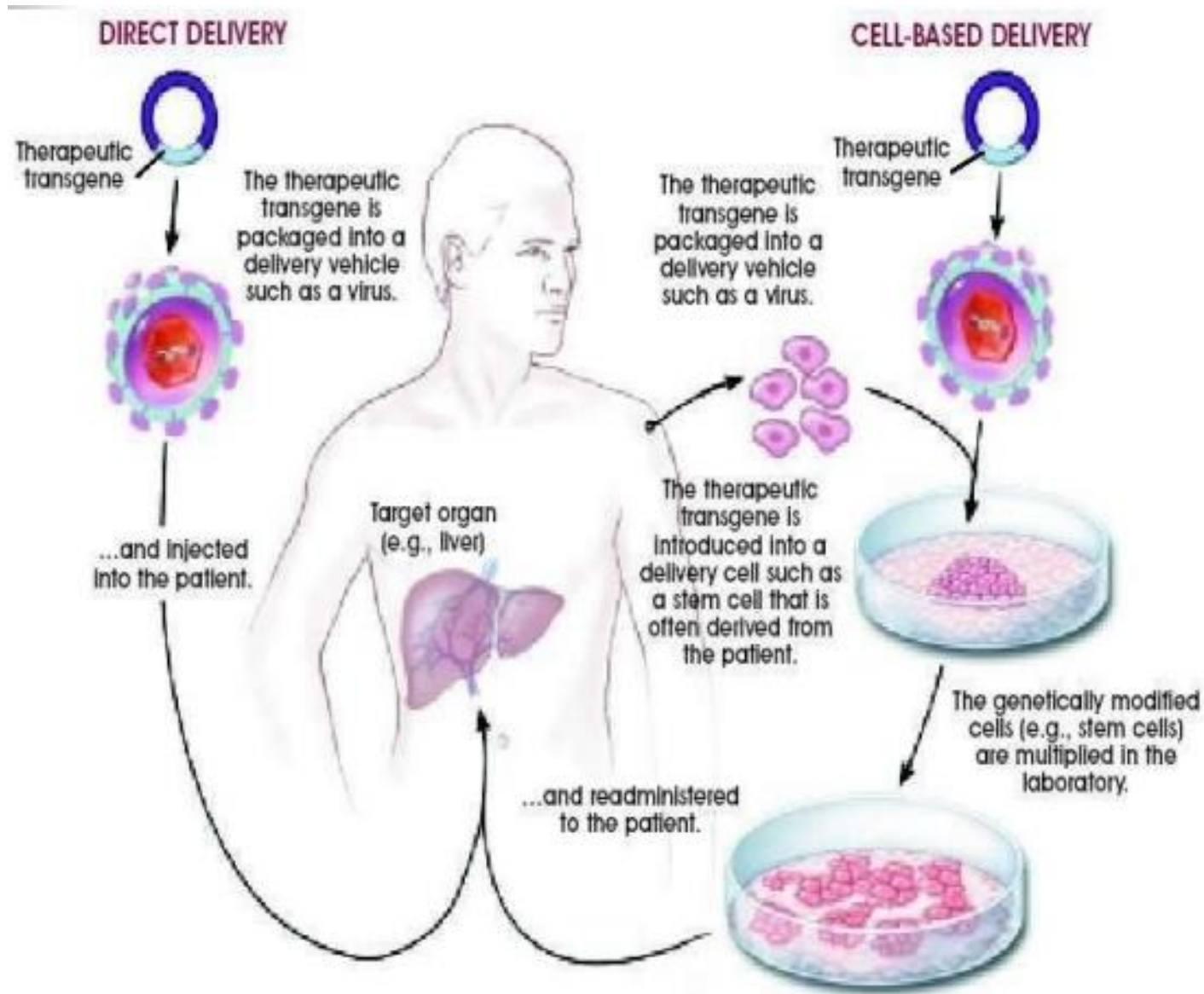
Advantages of Embryonic Stem Cells Over Adult Stem Cells

Embryonic S.C.	Adult S.C.
“Pluripotent” (can become any cell types present in the human body)	“Multipotent” (“can become many but not any”) E.g., blood stem cells can develop into several blood cell types, but cannot develop into brain, kidney, or liver cells
Stable. Can undergo many cell divisions.	Less Stable. Capacity for self-renewal is limited.
Easy to obtain but blastocyst is destroyed.	Difficult to isolate in adult tissue.

How Stem Cell Therapy Works

When stem cells are transplanted into the body and arrive into the injured part, brain being targeted for tissue regeneration, the stem cells are coming in contact with growth chemical's (like EGF's , NGF's and HGF's)in the body. These chemicals program the stem cells to differentitate into the tissue surrounding it.

Use of Stem Cells For Gene Therapy



Advantage

- *The critical shortage of organs available for transplantation may be solved in the future by auto-graft techniques*
- *Security : low toxicity or non toxic*

Challenges in Stem Cell Research

- Identifying stem cells in adult tissues.
- Stem cell integration.
- Immunological rejection.
- Cancer.
- Moral issues surrounding the sources of stem cells.

Possible uses of Tissue derived from **Stem Cells** to treat disease

Cell type	Target disease
Neural (nerve) cells	Stroke, Parkinson's disease, Alzheimer's disease, spinal cord injury, multiple sclerosis
Heart muscle cells	Heart attacks, congestive heart failure
Insulin-producing cells	Diabetes
Cartilage cells	Osteoarthritis
Blood cells	Cancer, immunodeficiencies, inherited blood diseases, leukemia
Liver cells	Hepatitis, cirrhosis
Skin cells	Burns, wound healing
Bone cells	Osteoporosis
Retinal (eye) cells	Macular degeneration
Skeletal muscle cells	Muscular dystrophy

Summary

- *The stem cells inside an embryo will eventually give rise to every cell, organ and tissue in the fetus's body.*
- *Stem cells are unspecialized cells*
- *Stem cells can divide and renew themselves for long periods of time*
- *Stem cells can divide and become specific specialized cell types of the body*
- *Stem cells can replace dying, old or damaged cells.*

Dolly

Sex	Female
Born	5 July 1996 (Roslin Institute)
Died	14 February 2003 (aged 6)
Nation	United Kingdom
Known for	First mammal to be cloned from an adult somatic cell
Offspring	6 lambs
Named after	Dolly Patron



Keith Campbell Dolly



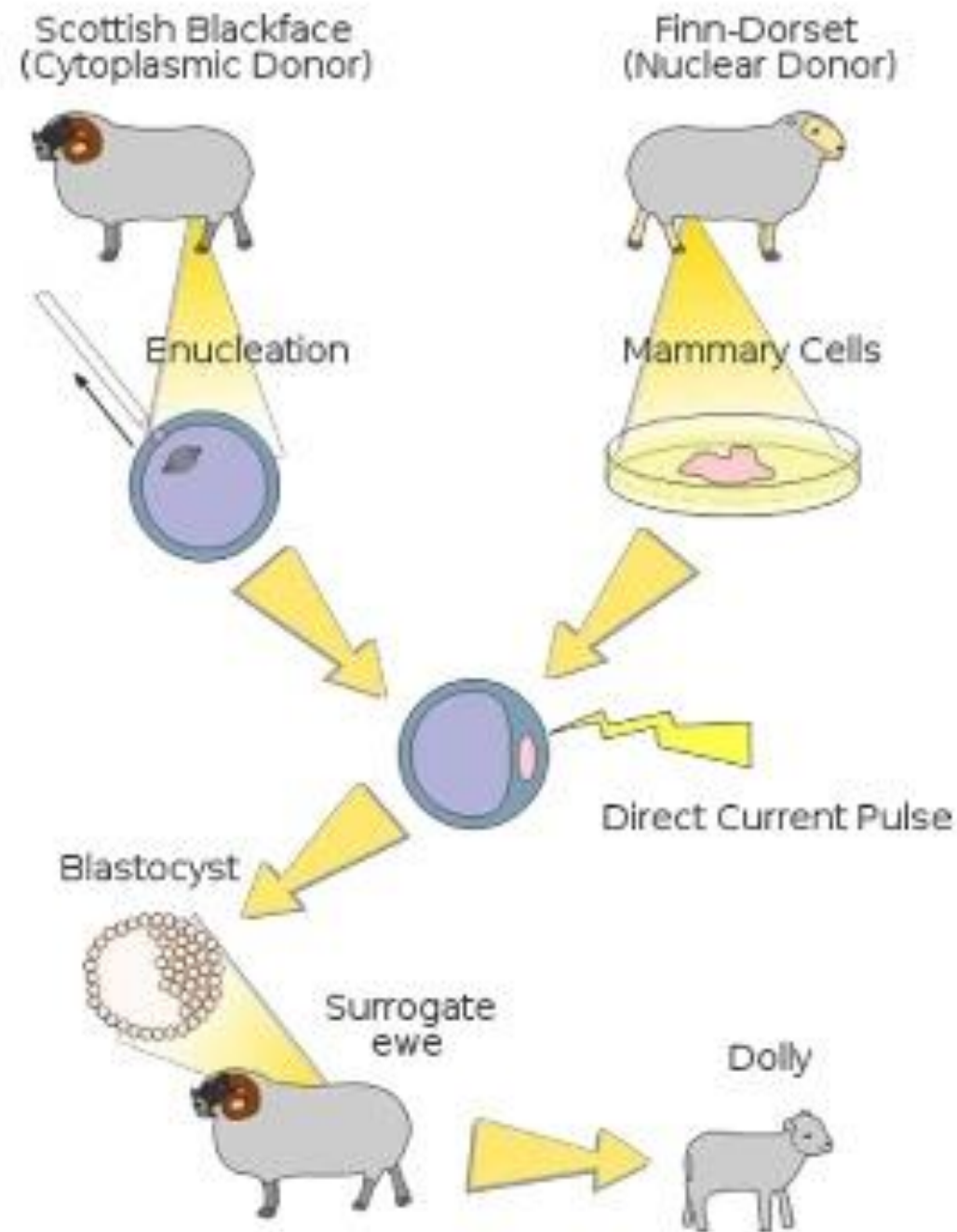
- Dolly the sheep, first mammal to be cloned from an adult somatic cell

Ian Wilmut



- Even though Dolly was not the first animal to be cloned, she gained this attention in the media because she was the first to be cloned from an adult cell

Somatic Cell Nuclear Transfer



- In Dolly, nucleus was transferred came from mammary gland cells from a 6-year-old ewe
- In Polly & molly fibroblast cells were used

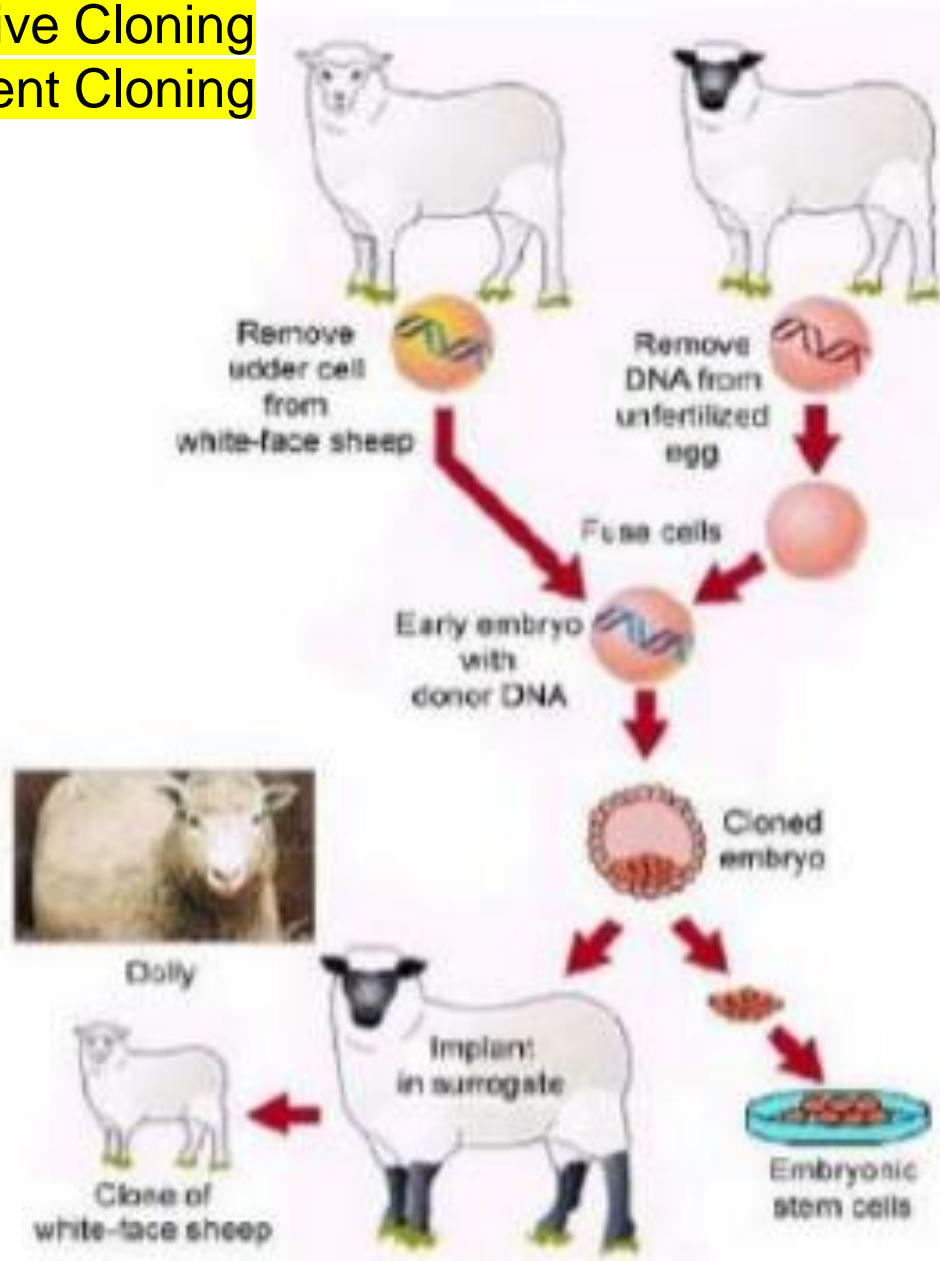


Species Cloned

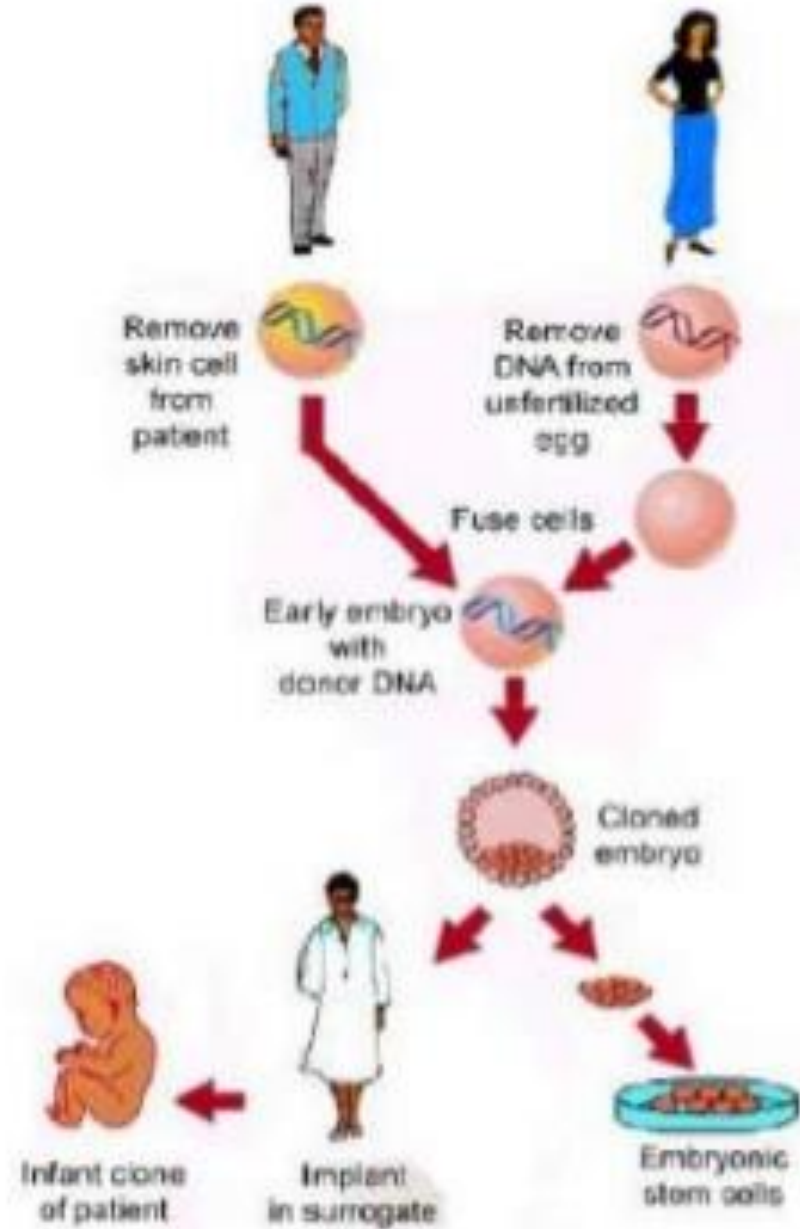
- Tadpole: (1952)
- Carp: (1963)
- Mice: (1986)
- Sheep: first mammal being cloned (1984) from early embryonic cells.
 - ✓ Megan and Morag from differentiated embryonic cells (1995)
 - ✓ Dolly from a somatic cell (1996)
- Rhesus Monkey: (2001)
- Cattle: (2001)
- Rat:
- Mule:
- Horse:
- Dog:
- Wolf:
- Water Buffalo:
- Pyrenean Ibex (2009) was the first "extinct" animal cloned
- Camel: (2009)
- Pashmina goat: (2012) Kashmir, India

Human Cloning is done for:

- Therapeutic cloning
- Reproductive Cloning
- Replacement Cloning

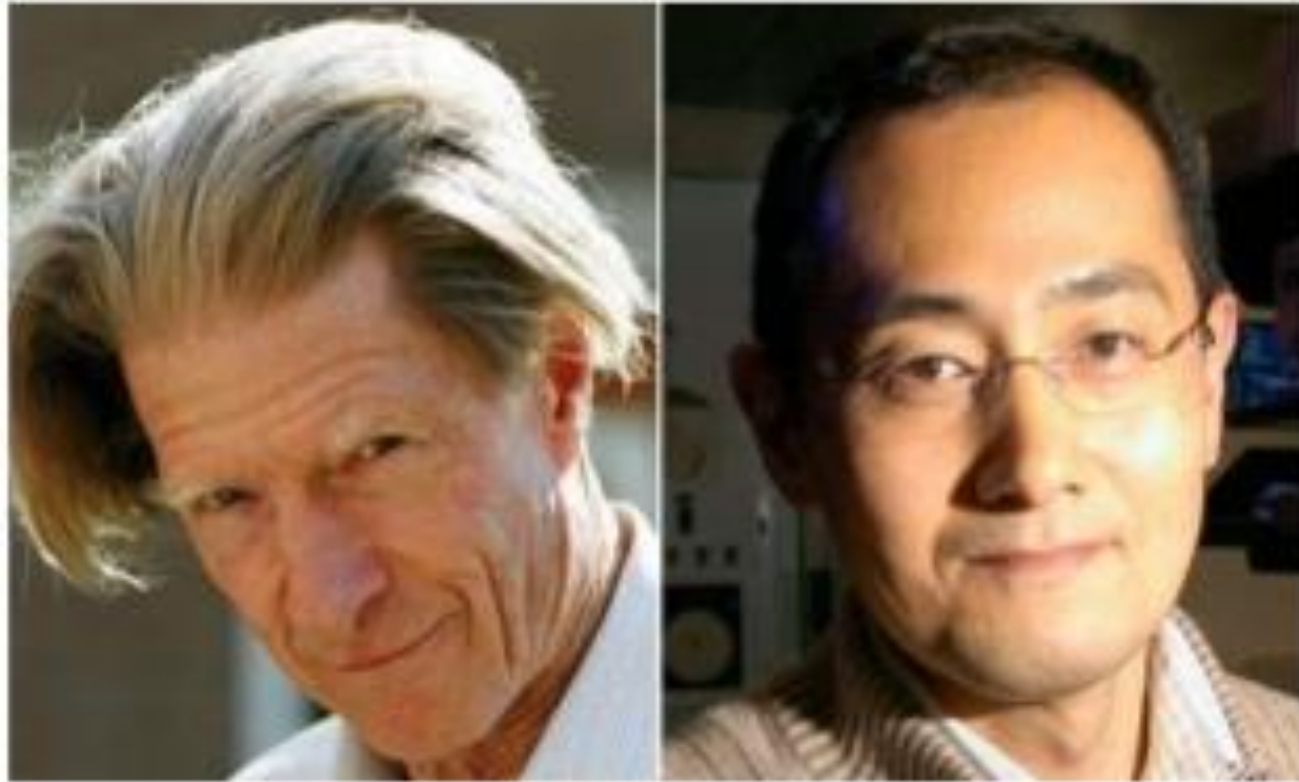


Human Cloning



Induced Pluripotent Stem Cells

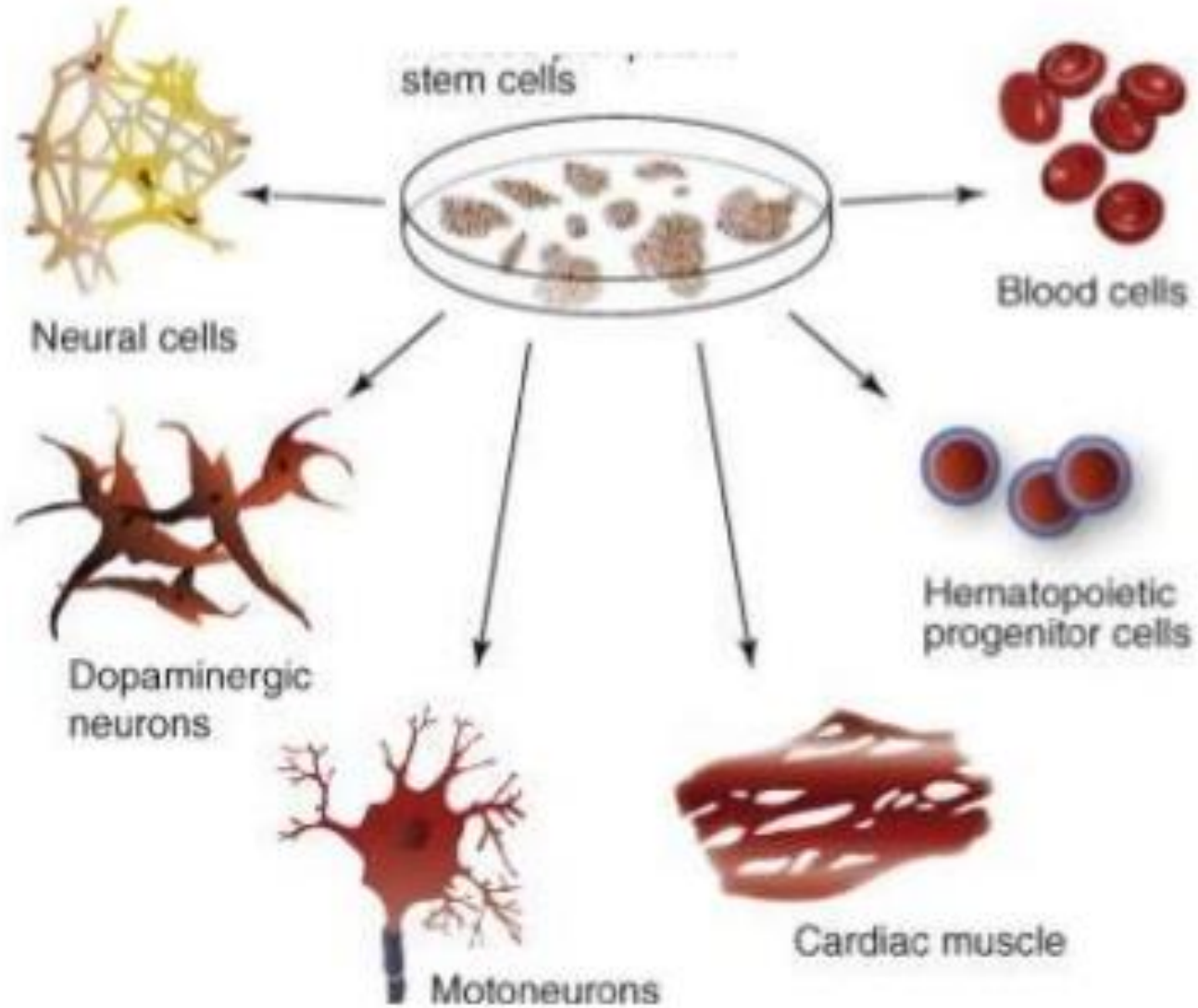
*Nobel prize in physiology or medicine 2012 for the discovery that
"mature cells can be reprogrammed to become pluripotent"*



John B Gurdon

Shinya Yamanaka

Induced Pluripotent Stem Cells



Diseases that are treated by stem cells are:

1) Acute Leukemia

- Acute Lymphoblast Leukemia (ALL)
- Acute Myelogenous Leukemia (AML)
- Acute Biphentotypic Leukemia
- Acute Undifferentiated Leukemia

2) Chronic Leukemia

- Chronic Myelogenous Leukemia (CML)
- Chronic Lymphocytic Leukemia (CLL)
- Juvenile Chronic Myelogenous Leukemia (JCML)
- Juvenile Myelomonocytic Leukemia (JMML)

Syndromes

- Myelodysplastic Syndromes
- Amyloidosis
- Chronic Myelomonocytic Leukemia (CMML)
- Refractory Anemia (RA)
- Refractory Anemia with Excess Blasts (RAEB)
- Refractory Anemia with Excess Blasts in Transformation (RAEB-T)
- Refractory Anemia with Ringed Sideroblasts (RARS)

7) Inherited Immune System Disorders

- Ataxia-Telangiectasia
- Kostmann Syndrome
- Leukocyte Adhesion Deficiency
- DiGeorge Syndrome
- Bare Lymphocyte Syndrome
- Omenn's Syndrome
- Severe Combined Immunodeficiency
- SCID with Adenosine Deaminase Deficiency
- Absence of T & B Cells SCID
- Absence of T Cells, Normal B Cell SCID
- Common Variable Immunodeficiency
- Wiskott-Aldrich Syndrome
- X-Linked Lymphoproliferative Disorder

Other Inherited Disorders

- Lesch-Nyhan Syndrome
- Cartilage-Hair Hypoplasia
- Glanzmann Thrombasthenia
- Osteopetrosis
- Adrenoleukodystrophy
- Ceroid Lipofuscinosis
- Congenital Erythropoietic Porphyria
- Sandhoff Disease

9) Plasma Cell Disorders

- Multiple Myeloma
- Plasma Cell Leukemia
- Waldenstrom's Macroglobulinemia
- Amyloidosis

Abnormalities

1) Inherited Platelet Abnormalities

Congenital Thrombocytopenia

2) Inherited Erythrocyte Abnormalities

- Beta Thalassemia Major
- Sickle Cell Disease
- Blackfan-Diamond Anemia
- Pure Red Cell Aplasia

Other Malignancies

- Ewing Sarcoma
- Neuroblastoma
- Renal Cell Carcinoma
- Retinoblastoma
- Brain tumor
- Ovarian Cancer
- Small Cell Lung Cancer
- Testicular Cancer

Disorders

1) Stem Cell Disorders

- Aplastic Anemia (Severe)
- Fanconi Anemia
- Paroxysmal Nocturnal Hemoglobinuria
- Congenital Cytopenia
- Dyskeratosis Congenita

2) Myeloproliferative Disorders

- Acute Myelofibrosis
- Agnogenic Myeloid Metaplasia
- Polycythemia Vera
- Essential Thrombocythemia

3) Lymphoproliferative Disorders

- Non-Hodgkin's Lymphoma
- Hodgkin's disease
- Prolymphocytic Leukemia

4) Phagocyte Disorders

- Chediak-Higashi Syndrome
- Chronic Granulomatous Disease
- Neutrophil Actin Deficiency
- Reticular Dysgenesis

5) Inherited Metabolic Disorders

- Mucopolysaccharidoses (MPS)
- Hurler's Syndrome (MPS-IH)
- Scheie Syndrome (MPS-IS)
- Hunter's Syndrome (MPS-II)
- Sanfilippo Syndrome (MPS-III)
- Morquio Syndrome (MPS-IV)
- Maroteaux-Lamy Syndrome (MPS-VI)
- Sly Syndrome, Beta-Glucuronidase Deficiency
- Adrenoleukodystrophy
- Mucopolipidosis II (I-cell Disease)
- Krabbe Disease
- Gaucher's Disease
- Niemann-Pick Disease
- Wolman Disease
- Metachromatic Leukodystrophy

6) Histiocytic Disorders

- Familial Erythrophagocytic Lymphohistiocytosis
- Histiocytosis-X
- Hemophagocytosis
- Langerhans' Cell Histiocytosis