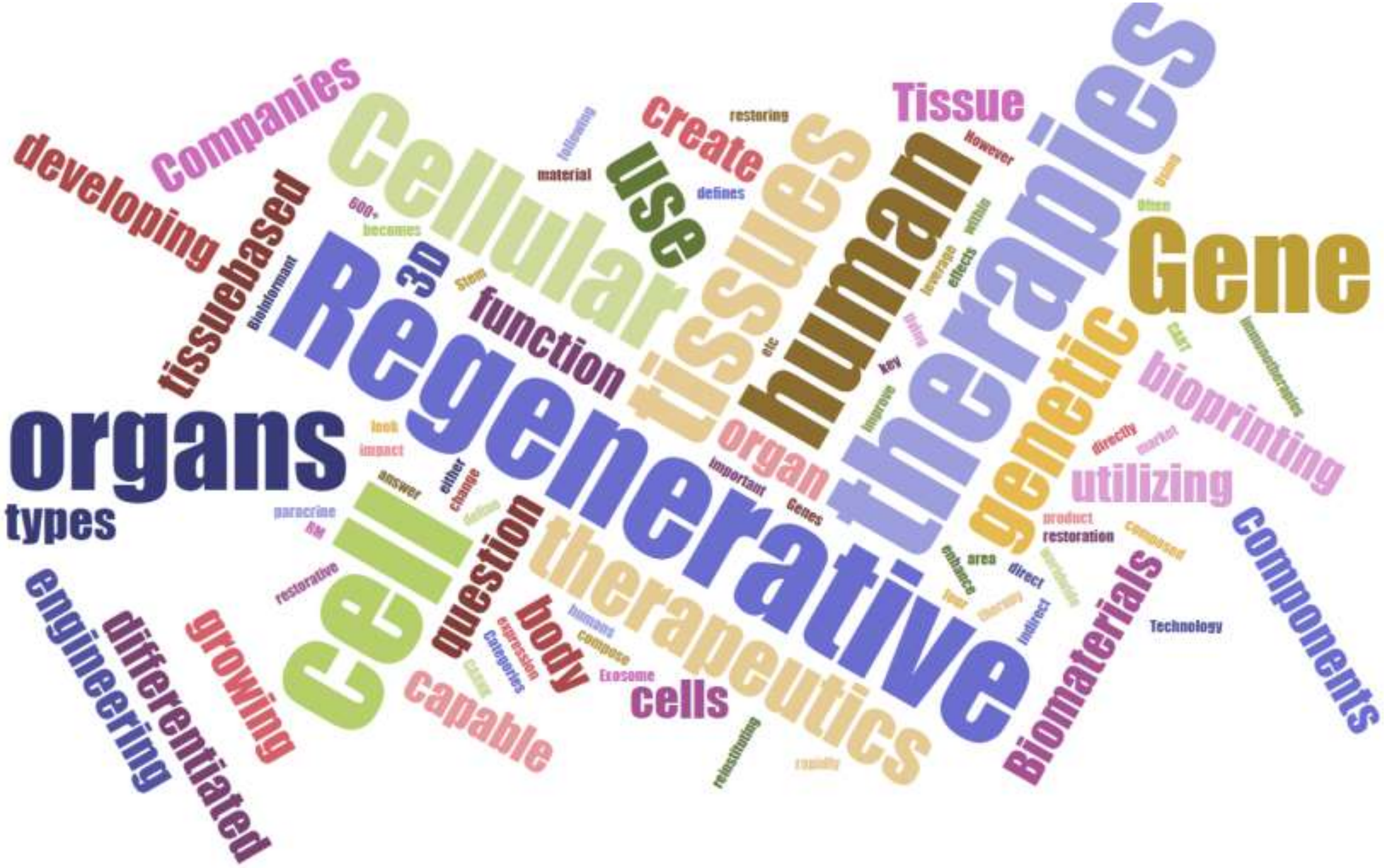
REGENERATIVE MEDICINE USING STEM CELLS



COMPILED BY HOWIE BAUM

REGENERATIVE MEDICINE

It is the most recent and emerging branch of medical science that **develops methods to regrow, repair or replace damaged or diseased cells, organs, or tissues to restore normal function.**

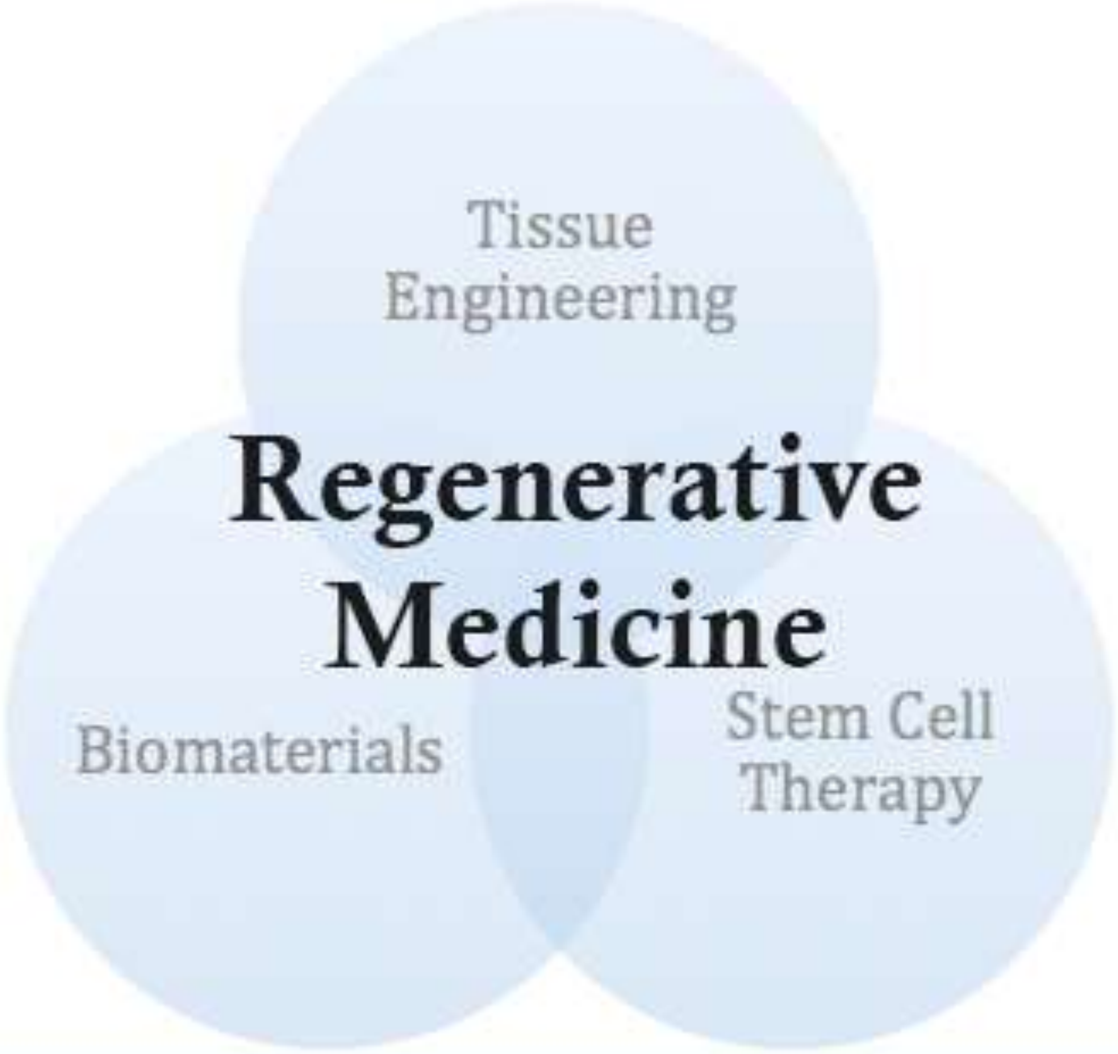
It is also called Stem Cell Therapy

It includes:

1) **The creation and use of therapeutic stem cells to repair a problem area in our body.**

2) **Tissue engineering**

3) **Production of artificial organs.**



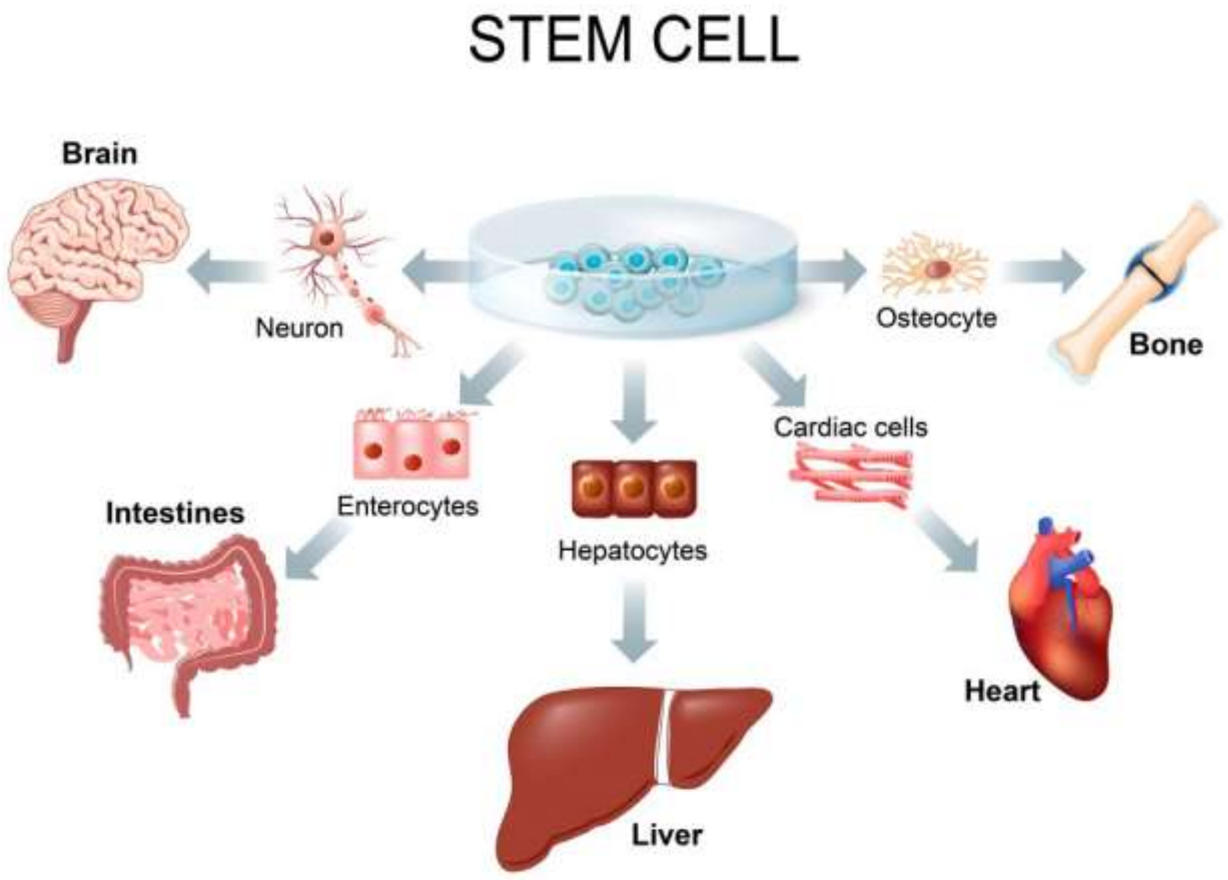
Stem cells have generated incredible interest for repairing failing tissues and organs, which appear to be the only reasonable therapeutic strategy.

They represent a future powerful tool in Regenerative Medicine

It stimulates the body's own repair mechanisms to heal tissues or organs.

It lets scientists grow tissues and organs in the laboratory and safely implant them when the body is unable to heal itself.

https://www.youtube.com/watch?v=qRCxvNXGx9g 2.5 minutes



REGENERATIVE MEDICINE IS BIG BUSINESS

The global regenerative medicine market was worth $35 billion in 2019 and is supposed to grow to over $124 billion by 2025.

There are over 900 medical research companies working on products for it.

Part of the need is because of the increasing number of Baby Boomers who are retiring and getting older who may have medical needs.

Current Global Sector Landscape

Alliance for Regenerative Medicine

906

Regenerative Medicine Companies Worldwide, including Gene and Cell Therapies, and Tissue Engineering Therapeutic Developers

THE COMPLEX REGULATORY ASPECTS OF REGENERATIVE MEDICINE

With more than 200 investigational new drug (IND) applications anticipated by **the US Food and Drug Administration (FDA)** in 2020, Regenerative Medicine should yield many new therapies with enormous benefits to patients, especially those with unmet medical needs.

Companies developing these therapies, need to engage with the FDA early and often throughout the drug development process to identify and overcome potential obstacles for approval.

FDA'S CENTER FOR BIOLOGICS EVALUATION AND RESEARCH (CBER)

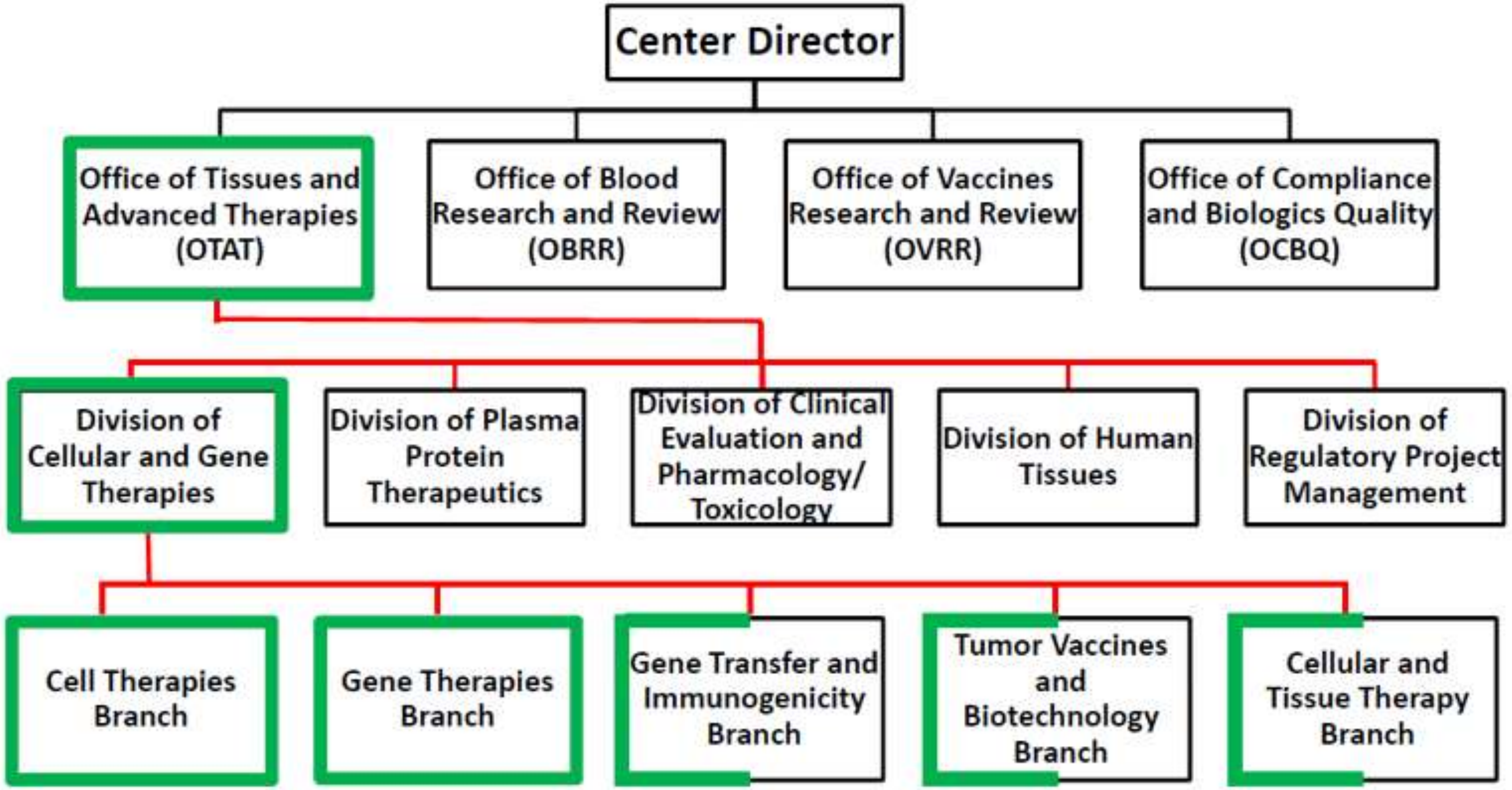


FIGURE CBER organisation for pre- and postmarket regulation

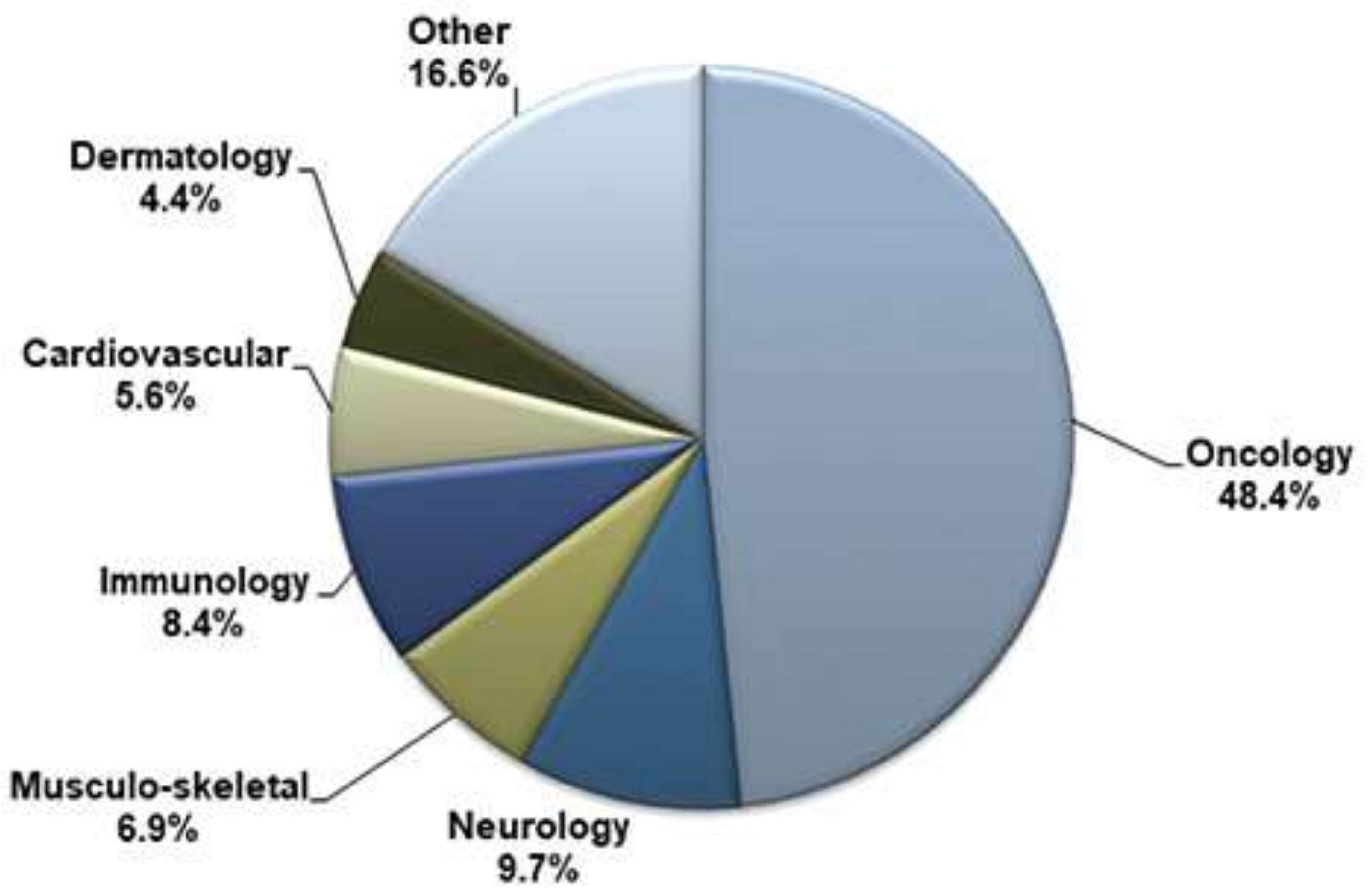
PRODUCT AREAS FOR REGENERATIVE MEDICINE

Globally, there is a shift from chemical drugs to a large-scale adoption of biologic therapies, such as Regenerative medicine.

It is emerging as an alternative solution to treating

- Late-stage cancer
- Juvenile diabetes
- Heart failure
- Other areas, as shown on the diagram.

FIGURE 1



Percentage Breakdown of Pipeline Products, Global

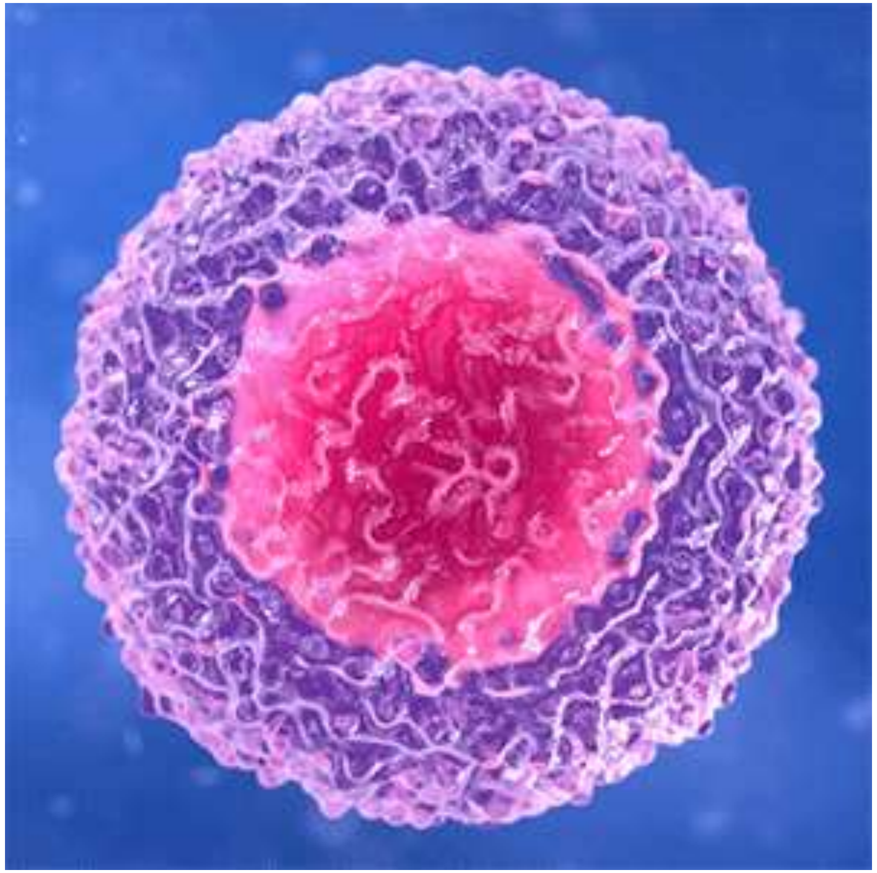
INTRODUCTION TO THE CELL

CELLS are often called the microscopic building blocks of the body.

They are active and dynamic, they continually grow and specialize, function, die, and **replenish themselves, by the millions every second.**

The whole body contains about 37.2 trillion (37,200,000,000,000 cells,

There are 226 different kinds !!



STEM CELLS

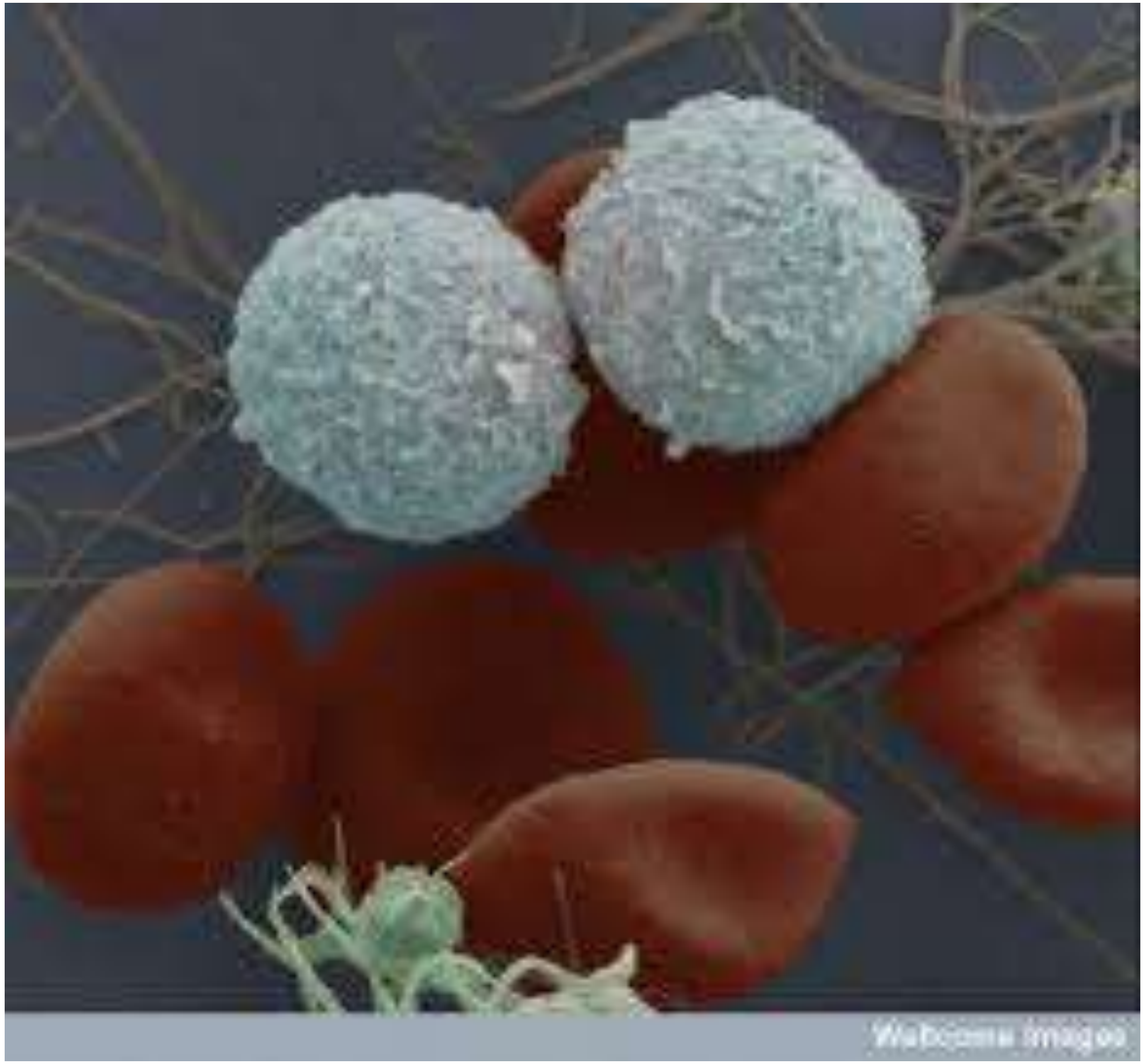
Stem cells are **cells** with the potential to develop into many different types of **cells** in the body.

They serve as a repair system for the body.

There are two main types of **stem cells**: **<u>embryonic</u> stem cells and <u>adult</u> stem cells**

Embryonic stem cells from the very early developing stage – between 4- 5 days after fertilization of an embryo, are still stem cells and are unspecialized into any of the other types of body cells.

They are capable of dividing and renewing themselves for long periods through cell division, to make more Stem cells.



Adult stem cells such as these 2 white ones, are present in bone marrow where they multiply and product millions of the different types of blood cells including red blood cells shown here.

ETHICAL ASPECTS OF USING EMBRYONIC STEM CELLS

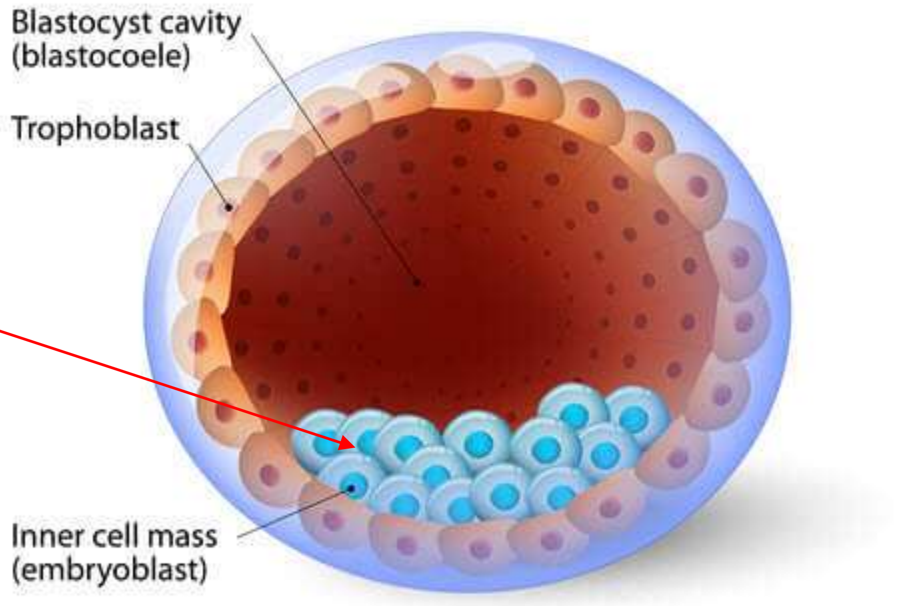
Since the discovery of human **embryonic stem cells**, scientists have had high hopes for their use in treating a wider variety of diseases because they are **"totipotent,"** which means they are capable of differentiating (changing) into any of the 226 cell types in the body.

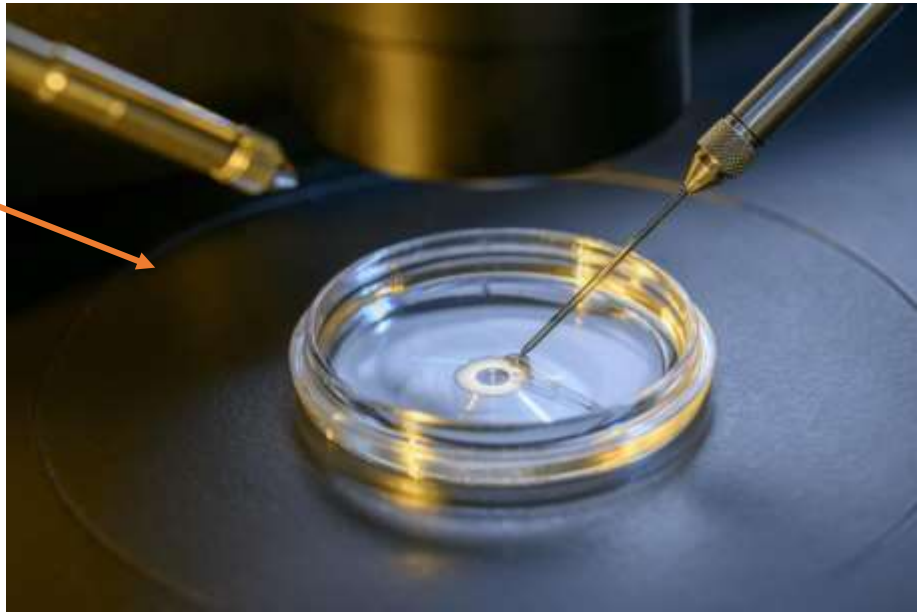
Embryonic stem cell lines originally used, came from only about 16 – 20 stem cells inside 4-5 day-old embryos left over from in-vitro fertilization (IVF) procedures that are done in a lab dish.

It is called a Blastocyst and is smaller than the dot at the top of this i, but the process causes the destruction of the embryo, thus raising ethical concerns.

In 2006, researchers introduced an alternative to harvesting embryonic stem cells, called **induced pluripotent stem (iPS) cells.**

BLASTOCYST

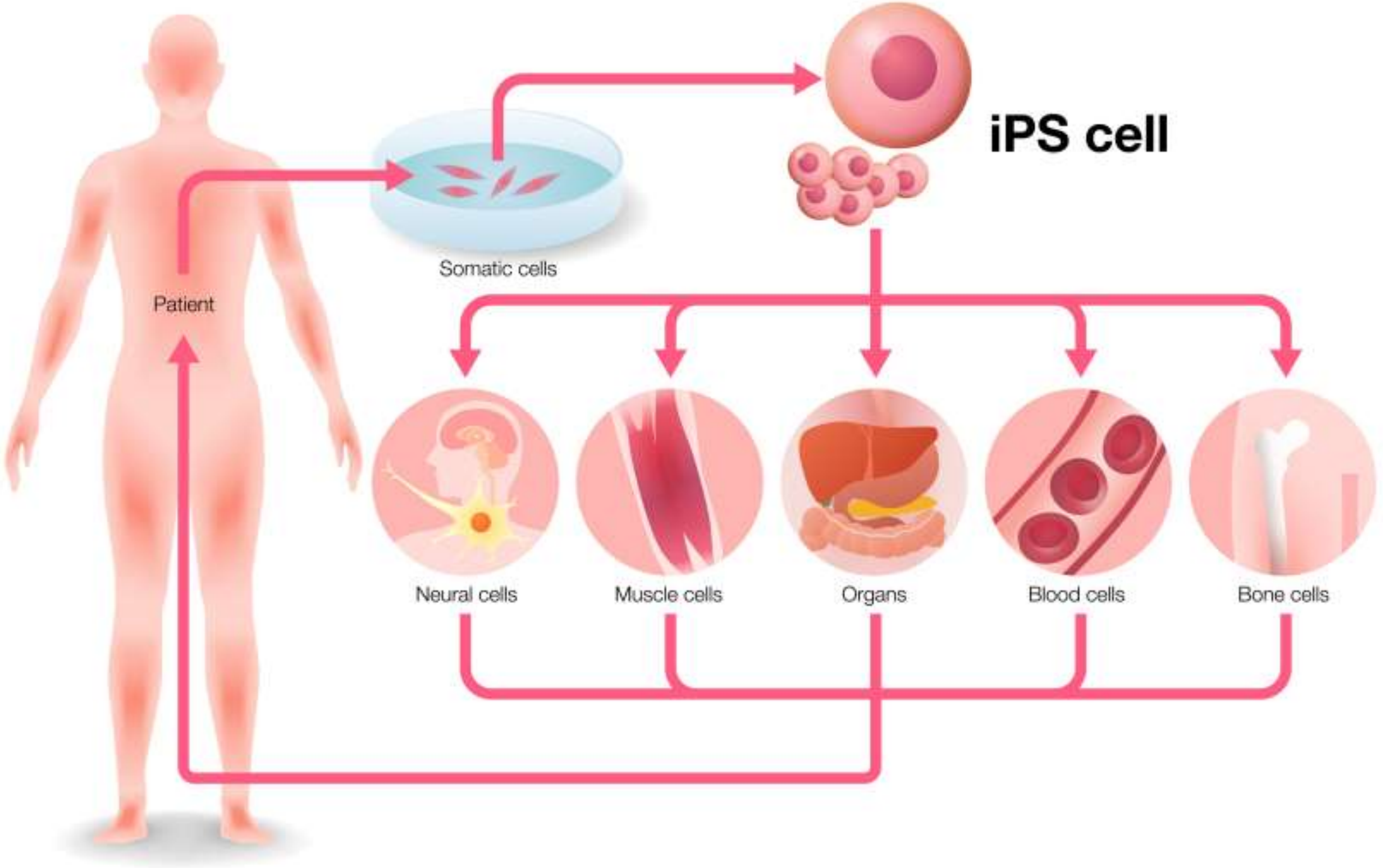




INDUCED PLURIPOTENT STEM CELLS (IPSCS)

Unlike embryonically-derived pluripotent stem cells, **these are adult stem cells, such as skin cells,** that have been genetically reprogrammed back into a pluripotent state, capable of becoming one of many types of cells inside a patient's body.

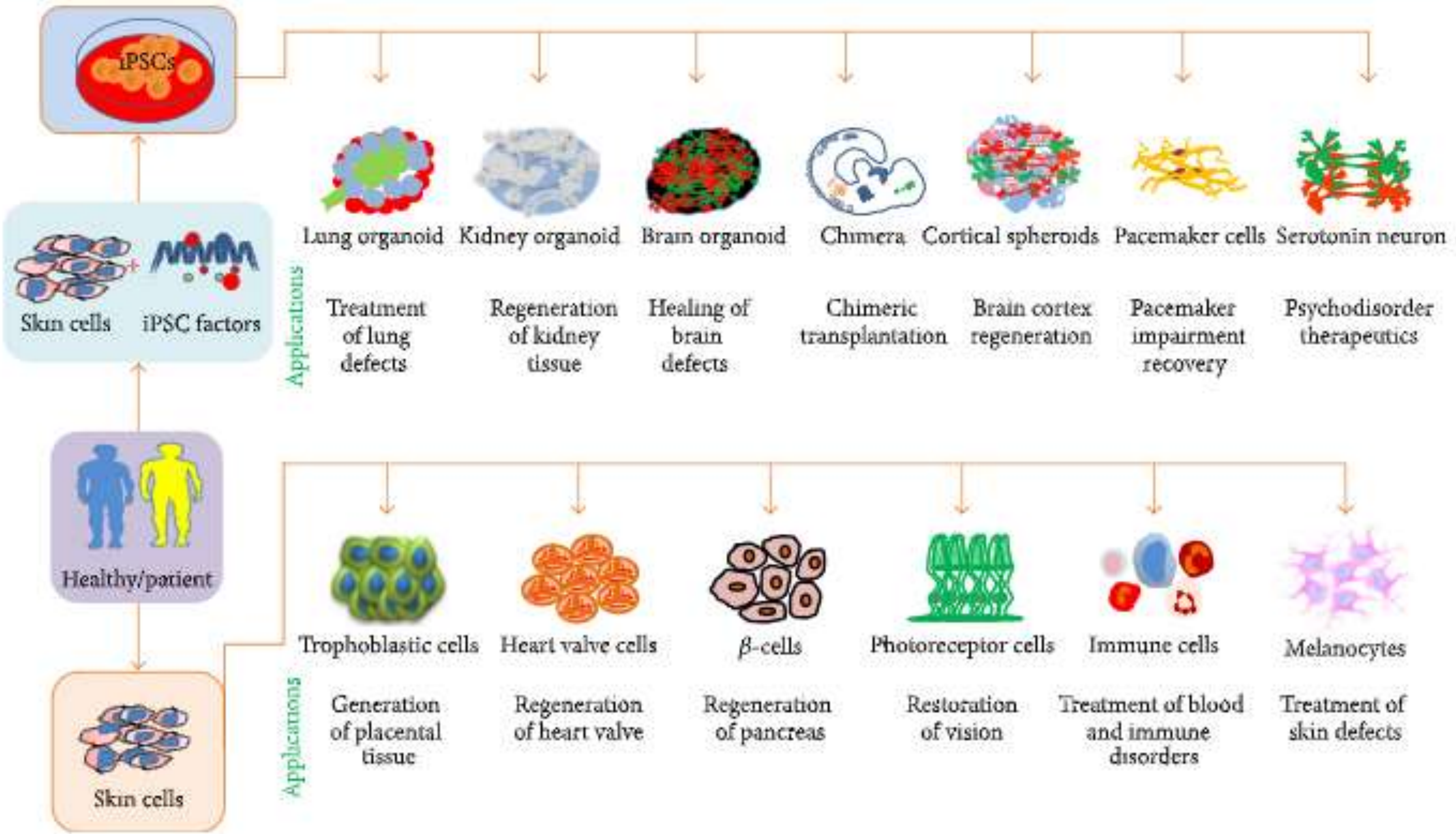
This technology may enable the development of an unlimited type of a specific type of human cells needed for therapeutic purposes.



The Nobel Prize in Physiology or Medicine 2012

In 2012, Dr. Yamanaka was awarded the Nobel Prize in Physiology or Medicine for his discovery that adult somatic cells can be reprogrammed into pluripotent cells. By introducing the genes for four factors, he induced the skin cells of adult mice to become like embryonic stem cells, which he called induced pluripotent stem (iPS) cells. This iPS cell technology represents an entirely new platform for fundamental studies of developmental biology.

iPSCs in regenerative medicine (iPSC - Induced Pluripotent Stem Cells)

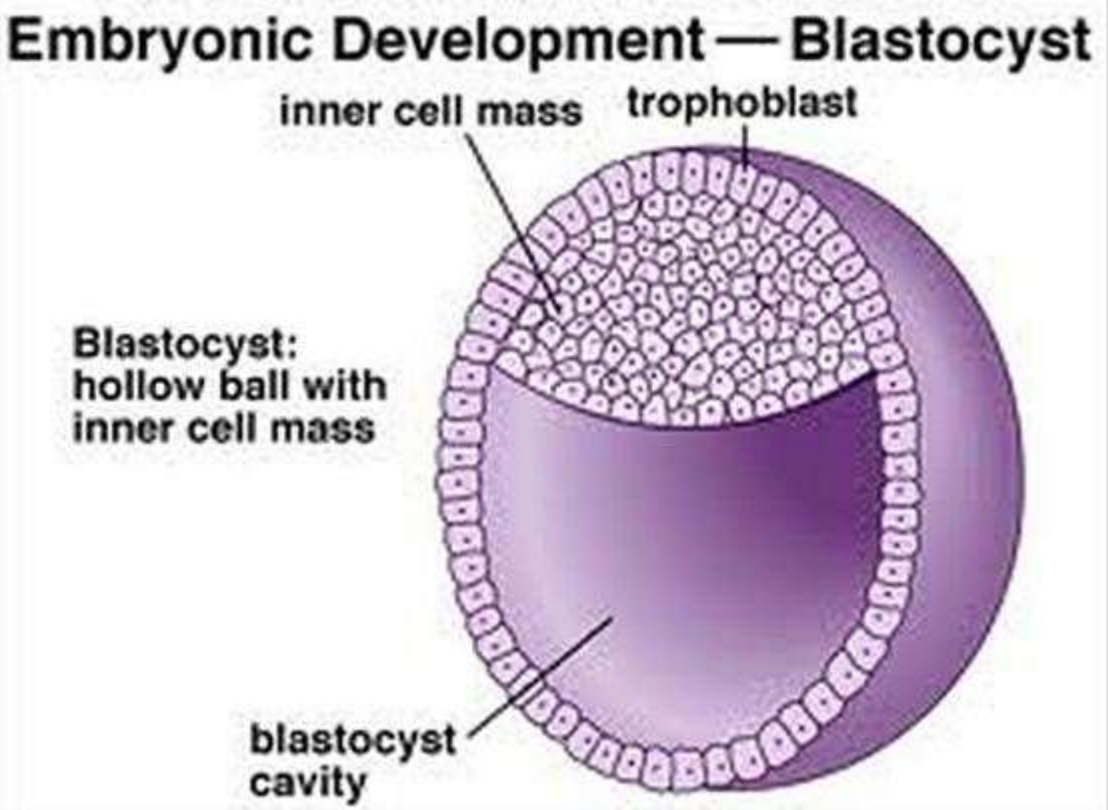


Fertilization of a Human Egg !!

After fertilization happens, the blastocyst is a structure formed in the early development of mammals.

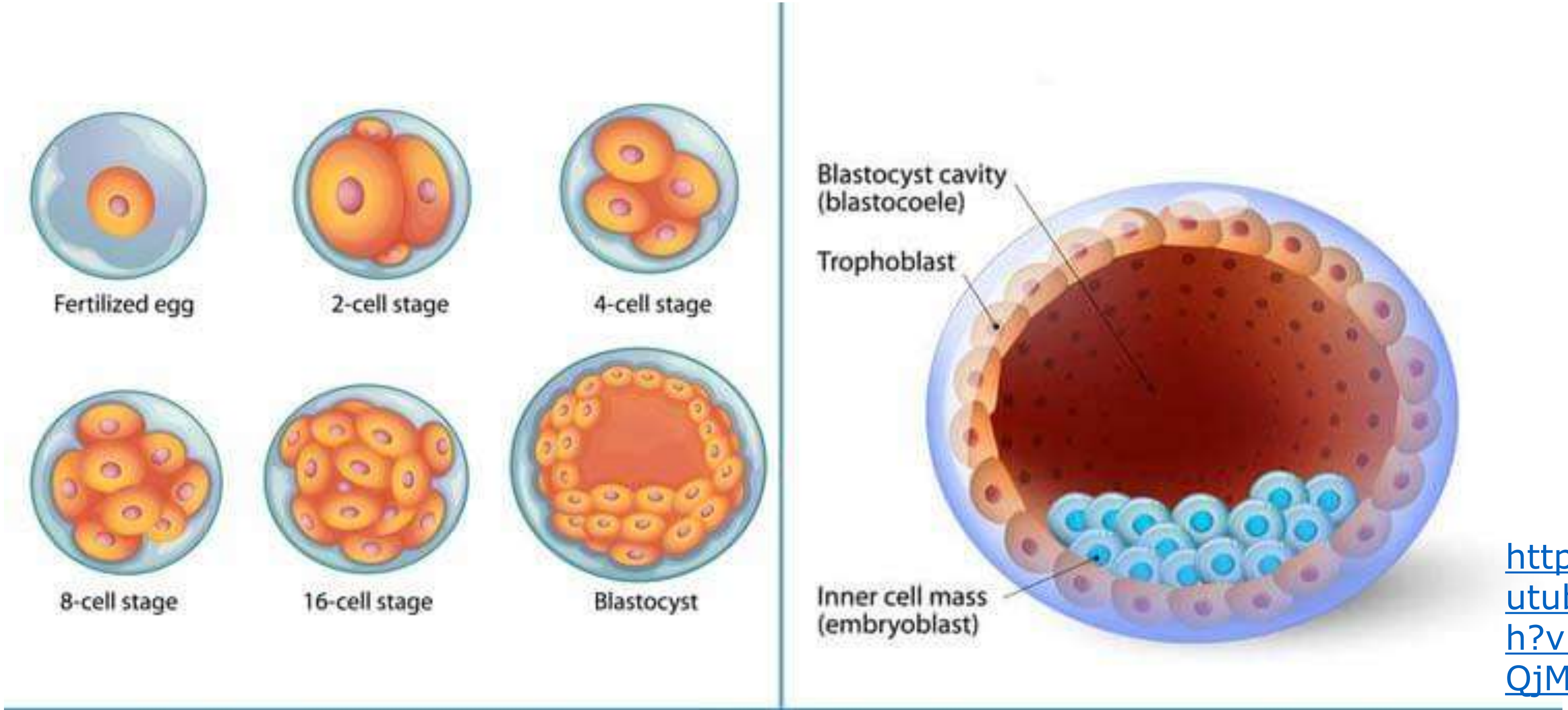
It possesses an inner cell mass (ICM) which subsequently forms the embryo. Up to 4-5 days after fertilization, these are all Totipotent or Embryonic stem cells which were used in the past for stem cell research.

The outer layer of the blastocyst consists of cells collectively called the trophoblast, which becomes the placenta that provides food and removes waste from the growing embryo.



Gastrulation is a phase early in the embryonic development of most animals, during which the single-layered blastula is reorganized into a multilayered structure known as the gastrula.

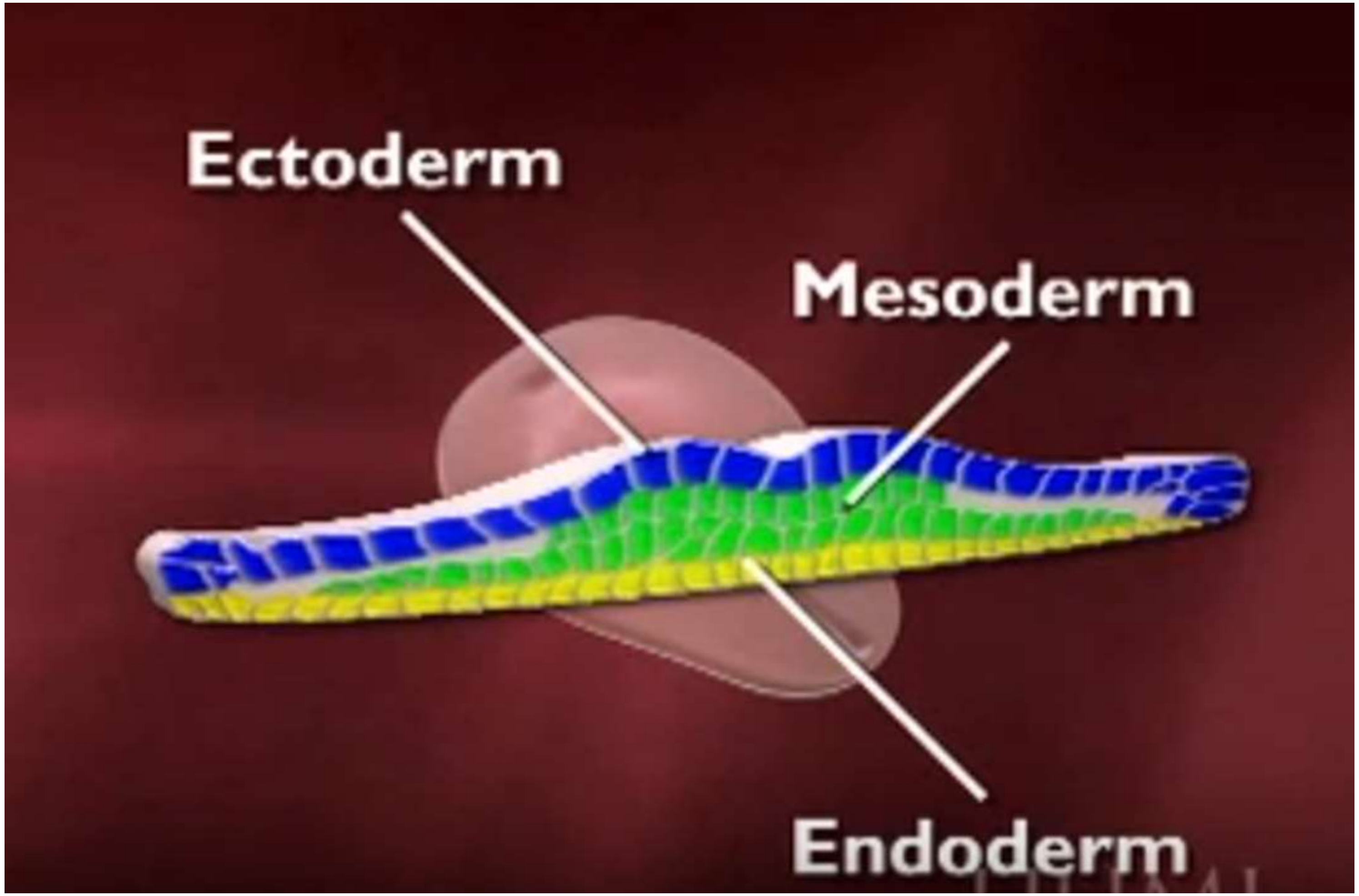
Before gastrulation, the embryo is a continuous epithelial sheet of cells; by the end of gastrulation, the embryo has begun differentiation to establish distinct cell lineages, set up the basic axes of the body (e.g. dorsal-ventral, anterior-posterior), and internalized one or more cell types including the prospective gut.



https://www.youtube.com/watch?v=dgPCDXmcQjM 5 minutes

Organo-genesis is the phase of embryonic development that starts at the end of gastrulation and continues until birth.

Early during development, **<u>stem cells</u>** begin to differentiate into three “germ” layers of specialized cells called the **Ectoderm, Endoderm, and Mesoderm,** also called **embryonic germ cells.**



DIFFERENTATION OF STEM CELLS

Stem cells in the Embryo also have the ability to differentiate (change) into any of the 226 types of specialized cells, as a baby develops.

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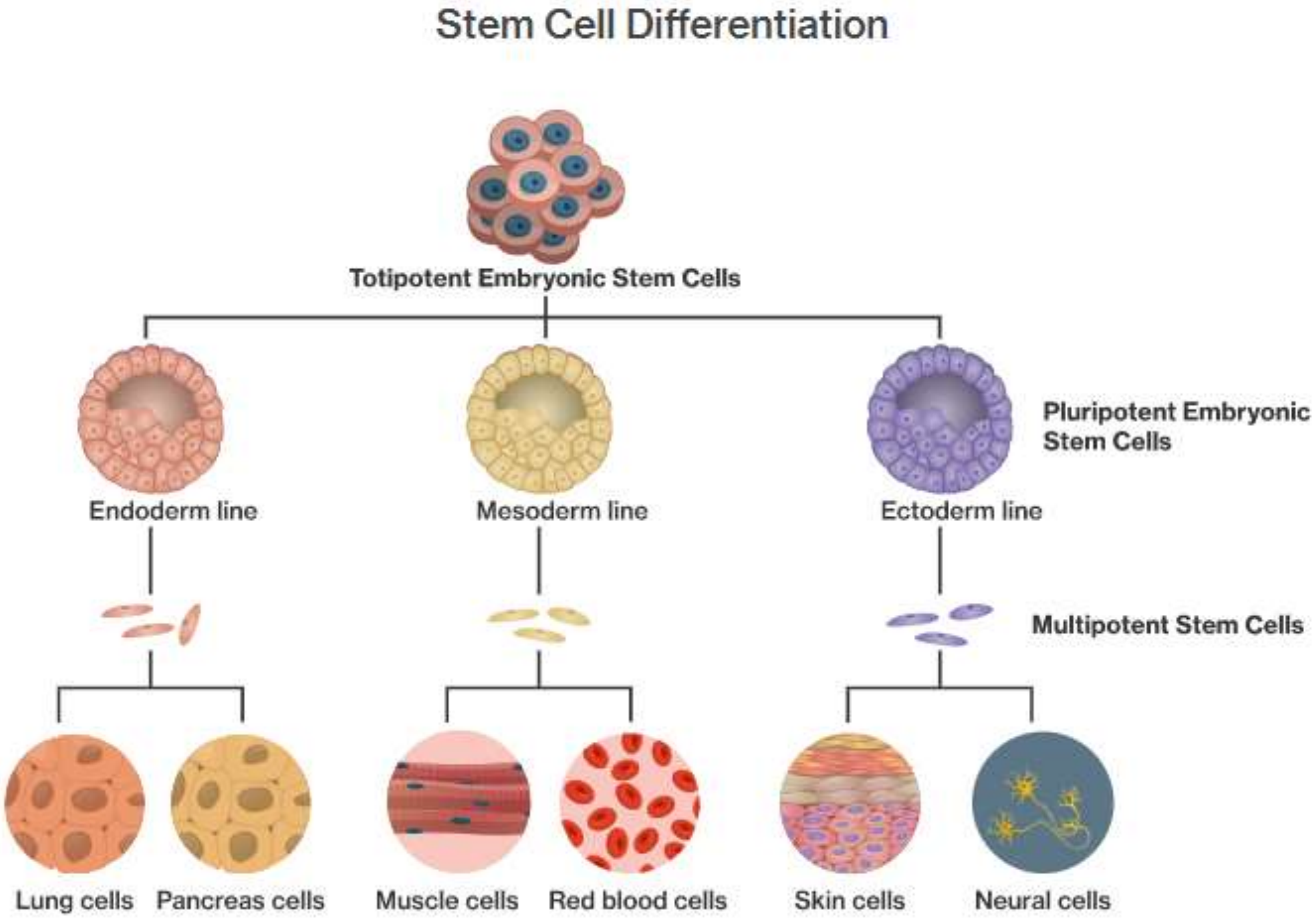
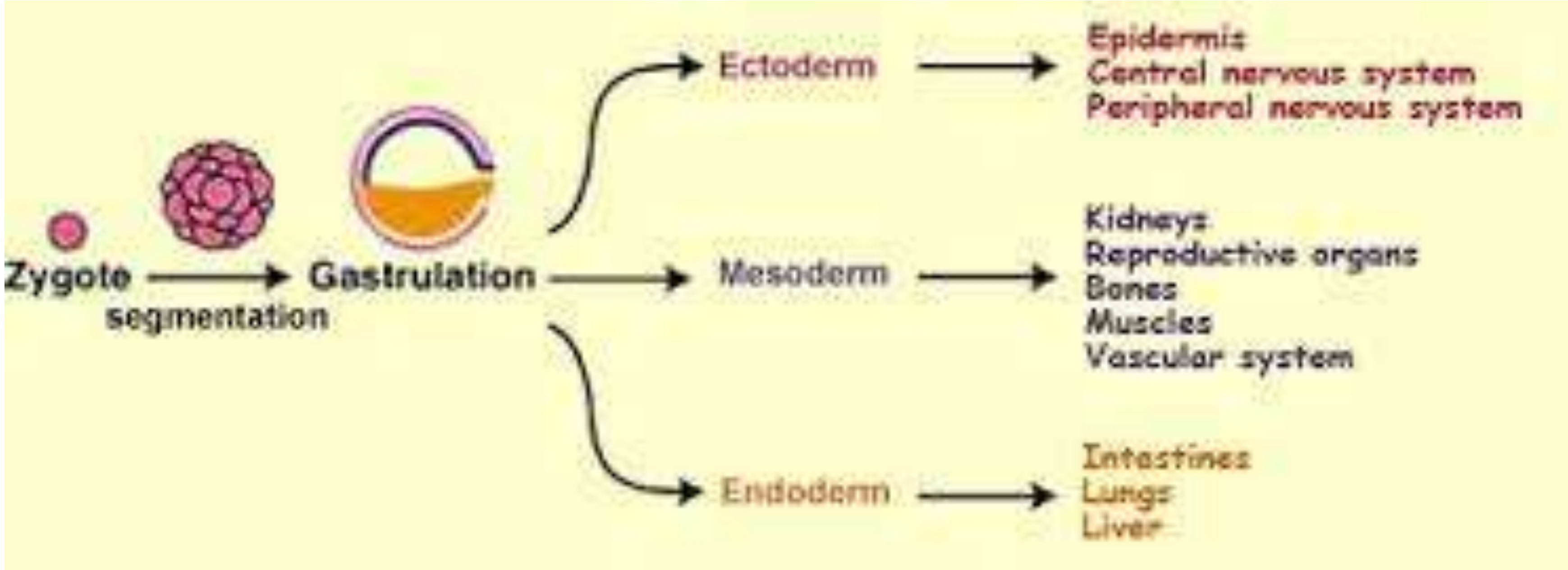


3 TYPES OF CELLS IN THE GASTRULA

Cells of the Ectoderm will form the skin and nails, the epithelial lining of the nose, mouth, and anus, the eyes, the brain and spinal cord, and neurons in the brain.

Cells of the Endoderm will become the inner linings of the digestive tract, the respiratory linings in the lungs, and glandular organs such as the thymus and pancreas.

Mesoderm cells will develop into muscles, tissues within the kidneys, blood cells, and the circulatory & excretory systems.



- Many structures are derived from the three embryonic germ layers during organogenesis

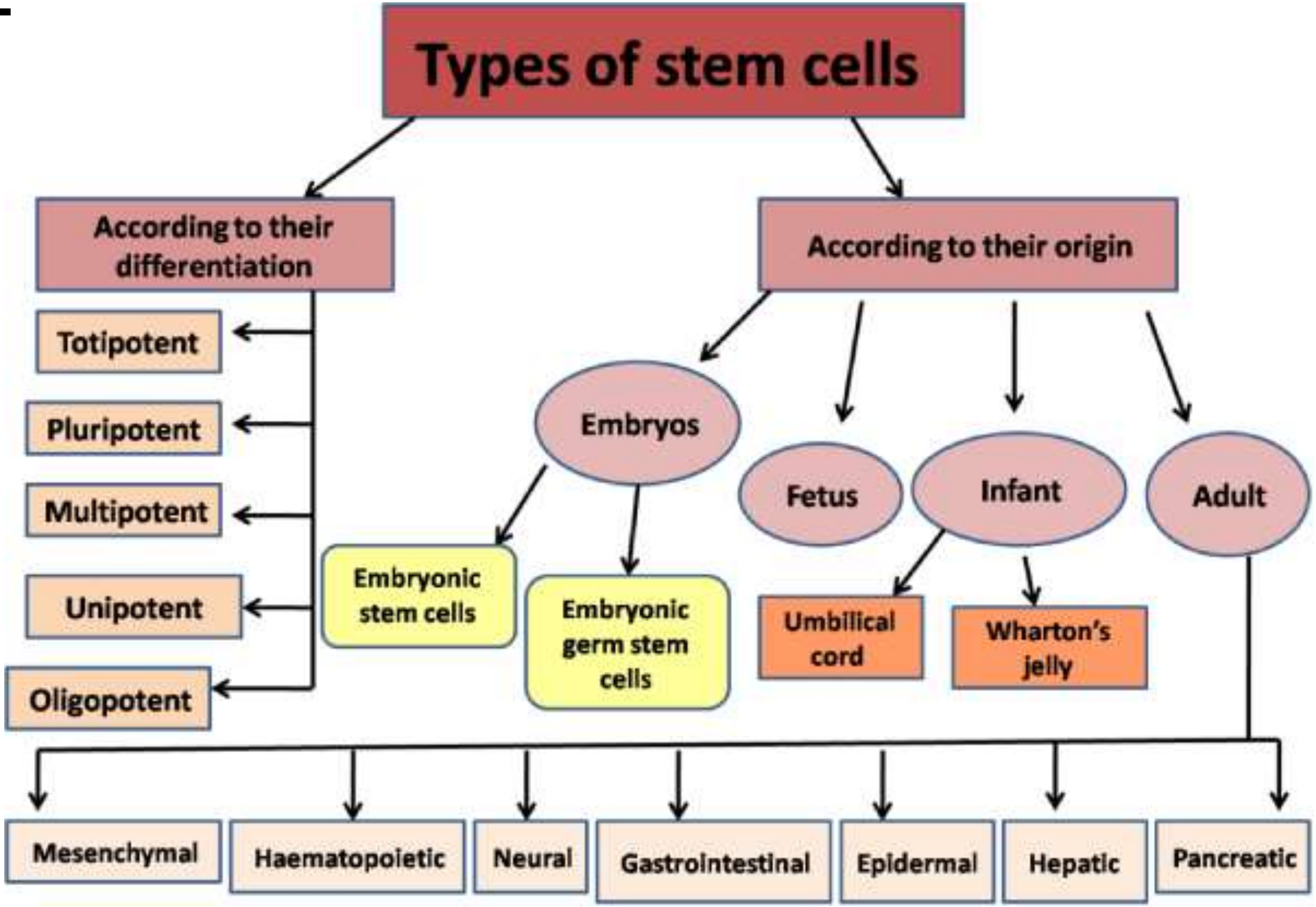
ECTODERM	MESODERM	ENDODERM
• Epidermis of skin and its derivatives (including sweat glands, hair follicles) • Epithelial lining of mouth and rectum • Sensory receptors in epidermis • Cornea and lens of eye • Nervous system • Adrenal medulla • Tooth enamel • Epithelium of pineal and pituitary glands	• Notochord • Skeletal system • Muscular system • Muscular layer of stomach, intestine, etc. • Excretory system • Circulatory and lymphatic systems • Reproductive system (except germ cells) • Dermis of skin • Lining of body cavity • Adrenal cortex	• Epithelial lining of digestive tract • Epithelial lining of respiratory system • Lining of urethra, urinary bladder, and reproductive system • Liver • Pancreas • Thymus • Thyroid and parathyroid glands

THE 2 WAYS TO CLASSIFY & DESCRIBE STEM CELLS:

1) By differentiation potential (what kind of cell can they turn into)

2) By origin (from where they are obtained)

(Wharton’s jelly is a gelatinous substance that provides insulation and protection within the umbilical cord as well as stem cells in the blood there.)



Differentiation Potential

Totipotent can differentiate into all possible cell types. These cells are produced from the fusion of an egg and sperm cell, e.g. zygote formed at egg fertilization.

Pluripotent are the descendants of totipotent cells and can differentiate into nearly all cell types, e. g., embryonic stem cells.

Multipotent can differentiate into those of a closely related family of cells, i.e. bone marrow stem cells.

Unipotent can produce only their own, but have the property of self-renewal, which distinguishes them from non-stem cells, e.g., muscle stem cells.

STEM CELL TYPES

[redacted]

TYPES ACCORDING TO POTENCY

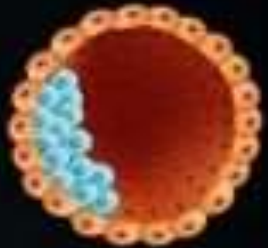
The potency of stem cells refers to the number of differentiations or specializations they can undergo.

① TOTIPOTENT STEM CELLS

- Can differentiate into any kind of cell in the body
- The most versatile kind of stem cell

② PLURIPOTENT STEM CELLS

- Can differentiate into a variety of cell types, but not all types



③ MULTIPOTENT STEM CELLS

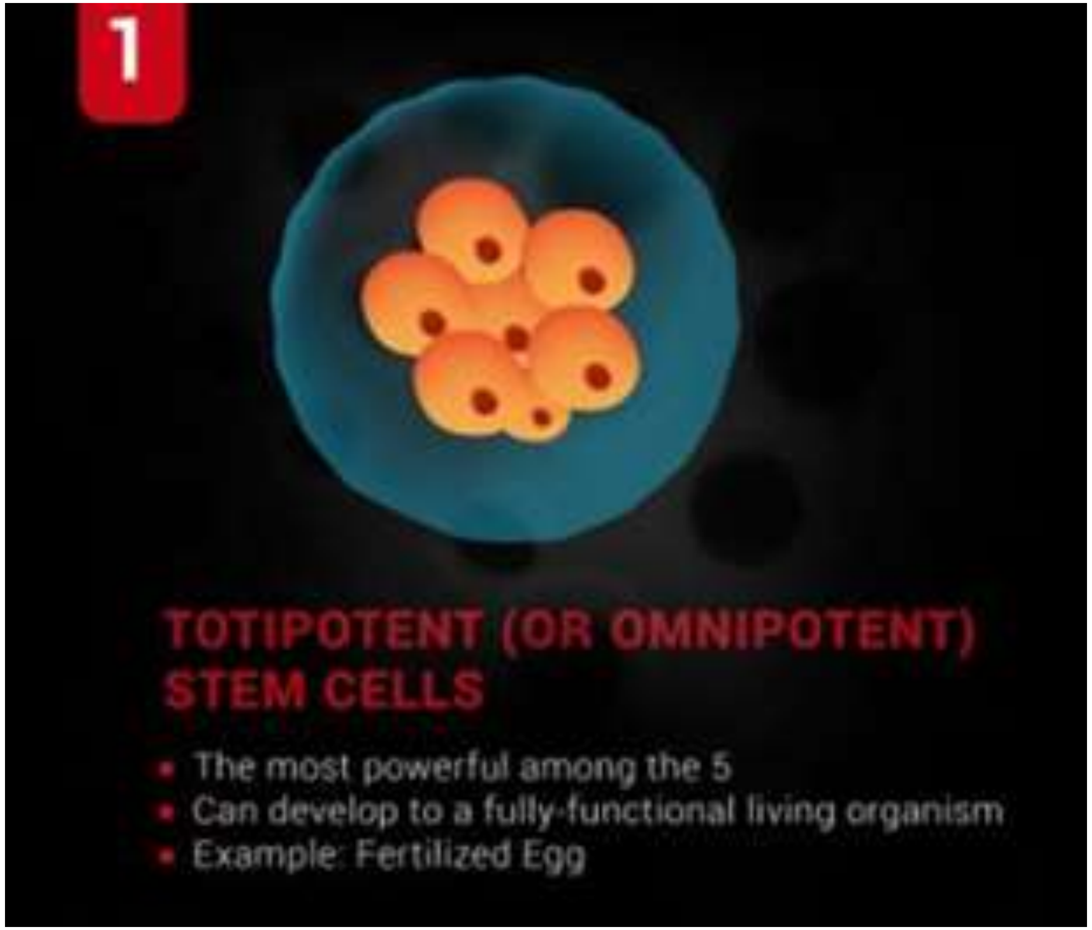
- A level lower than pluripotent stem cells in the potency hierarchy
- Can transform into more than one type of cell
- More limited than totipotent and pluripotent stem cells

④ UNIPOTENT STEM CELLS

- Can differentiate to only one lineage
- Have the lowest potency

THE FOLLOWING ARE DESCRIPTIONS OF THE 5 TYPES OF STEM CELLS BY DIFFERENTIATION POTENTIAL

1) Totipotent (or Omnipotent) stem cells are the most powerful type that exist because they can differentiate into all possible cell types.



They are produced from the fusion of an egg and sperm cell, such as a zygote formed at egg fertilization and are then called **Embryonic stem cells.**

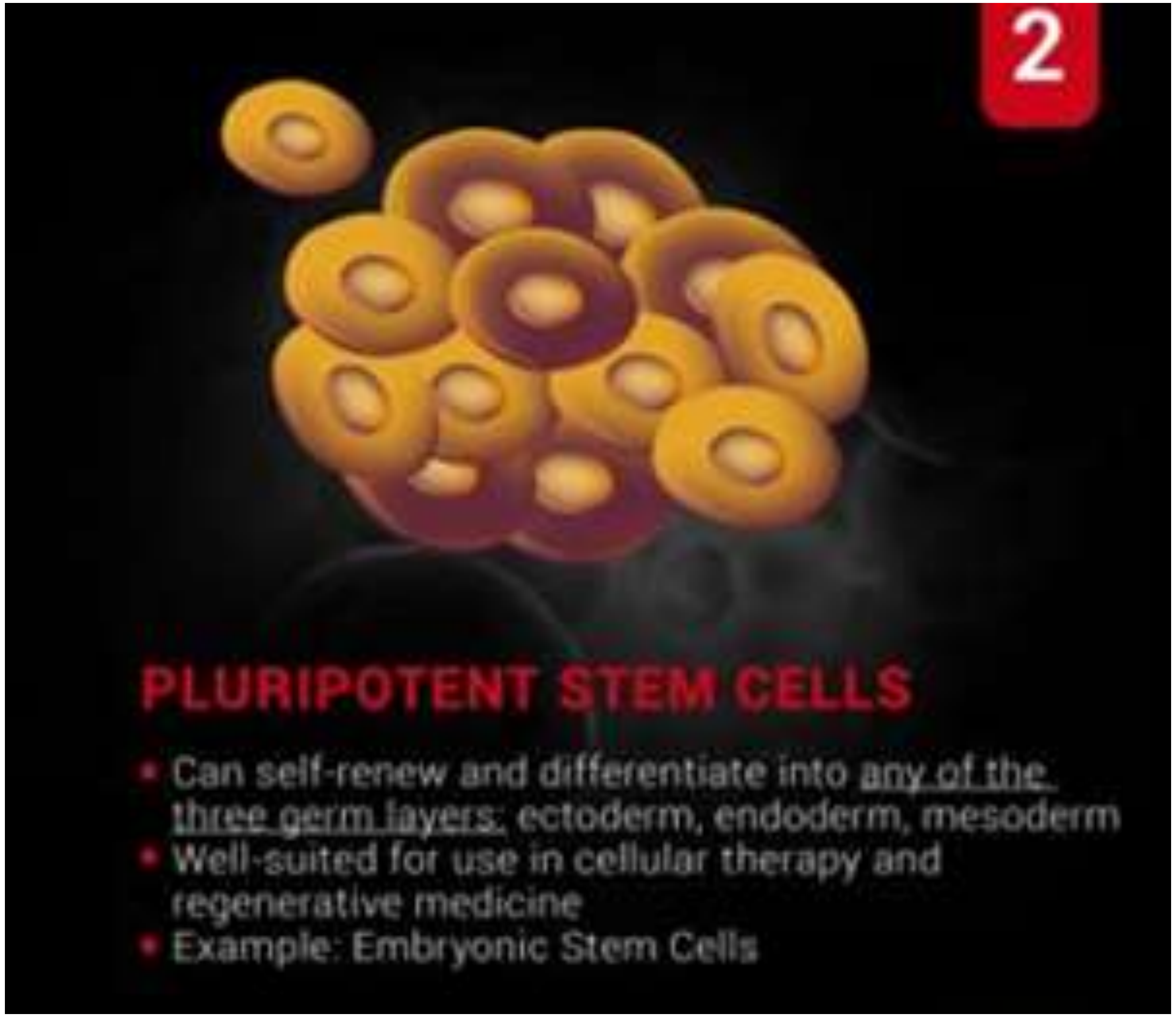
The most important characteristic of a totipotent cell is that it can generate a fully-functional, living organism.

It is around 4 - 5 days after fertilization that these cells begin to specialize into pluripotent cells, which as described next, can also change into other types of cells but cannot produce all of the cells to make an entire organism.

Pluripotent stem cells are the descendants of Totipotent cells and can differentiate into nearly all cell types, such as embryonic stem cells and into any of it's 3 germ layers, which are the ectoderm, endoderm, and mesoderm but **can't produce all of the types of cells to make a person.**

These three germ layers further differentiate to form all tissues and organs within a human being.

Because of their powerful ability to differentiate in a wide diversity of tissues and their non-controversial nature, induced pluripotent stem cells are well-suited for use in cellular therapy and Regenerative Medicine.



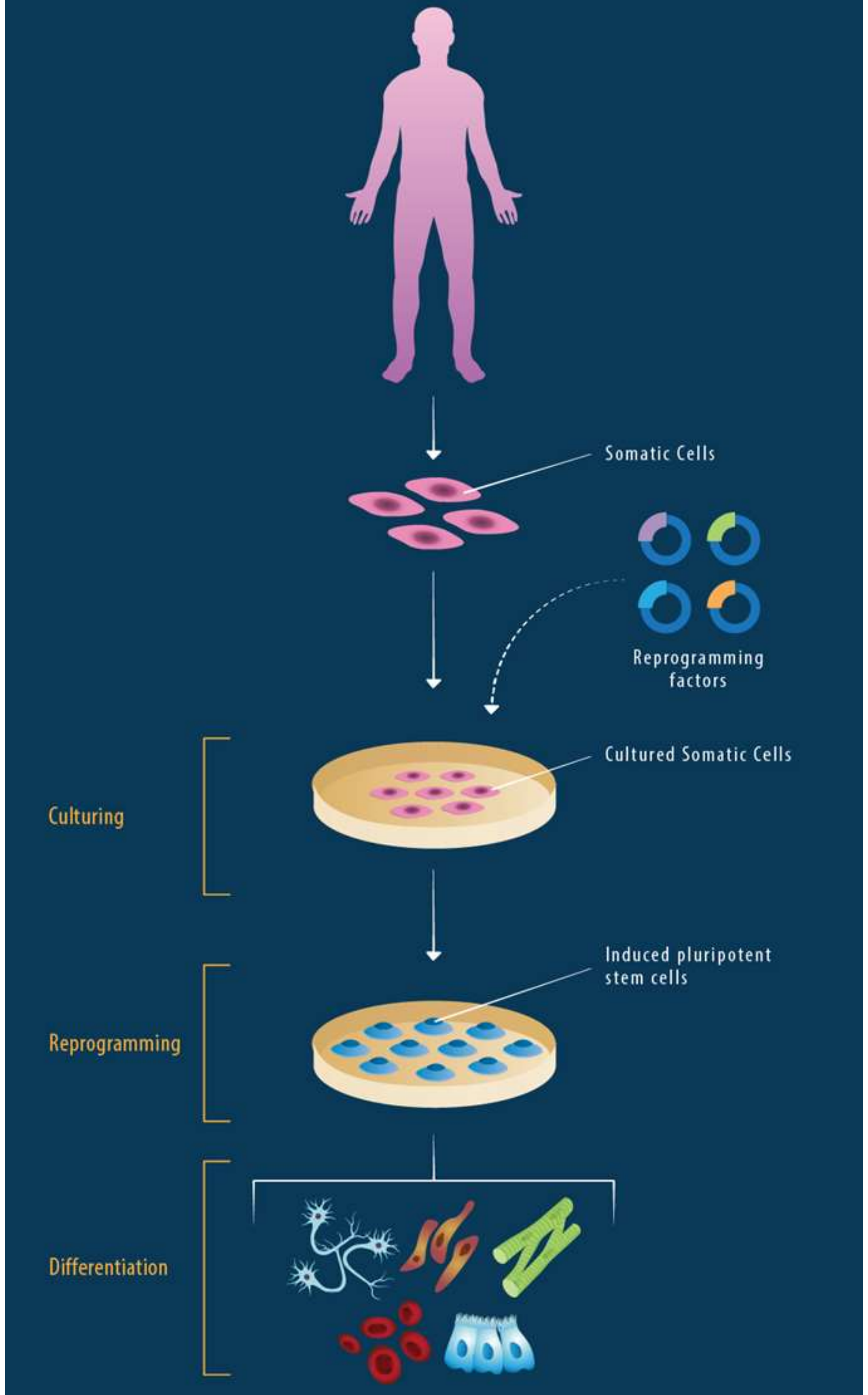
INDUCED PLURIPOTENT STEM (IPS) CELLS

They are cells that have been engineered in the lab by converting tissue-specific cells, such as skin cells, into cells that behave like embryonic stem cells.

IPS cells are critical tools to help scientists learn more about normal development and disease onset and progression, and they are also useful for developing and testing new drugs and therapies.

While IPS cells share many of the same characteristics of embryonic stem cells, including the ability to give rise to all the cell types in the body, they aren’t exactly the same.

Researchers are experimenting with many alternative ways to create IPS cells so that they can ultimately be used as a source of cells or tissues for medical treatments.



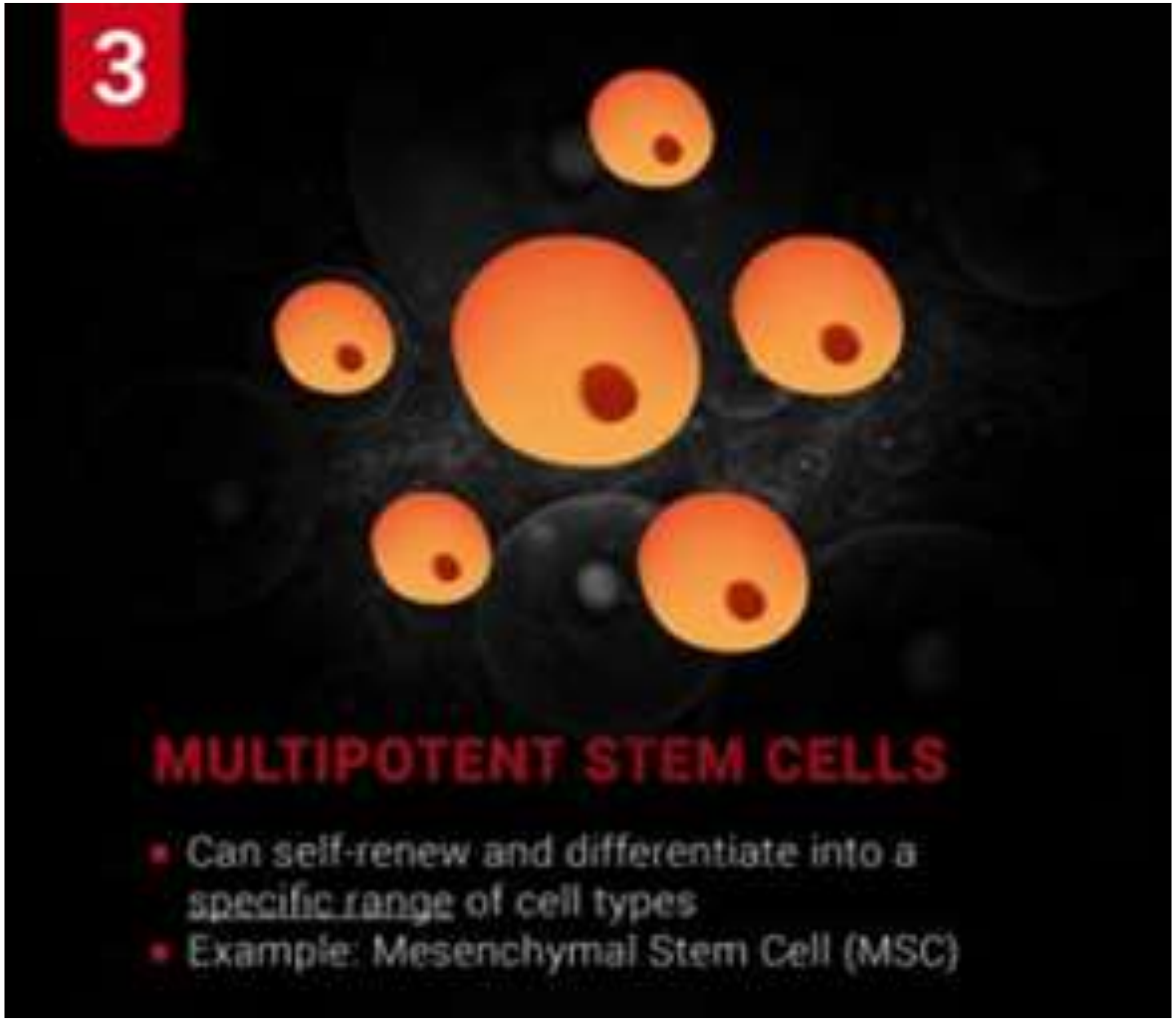
Multipotent stem cells can differentiate into those of a closely related family of cells, such as bone marrow stem cells

They are a middle-range type of stem cell, in that they can self-renew and differentiate into a specific range of cell types.

An excellent example of this cell type is the **mesenchymal stem cell (MSC).**

Mesenchymal stem cells can differentiate into osteoblasts (a type of bone cell), myocytes (muscle cells), adipocytes (fat cells), and chondrocytes (cartilage cells).

These cells types are fairly diverse in their characteristics, which is why mesenchymal stem cells are classified as multipotent stem cells.



Oligopotent Cells

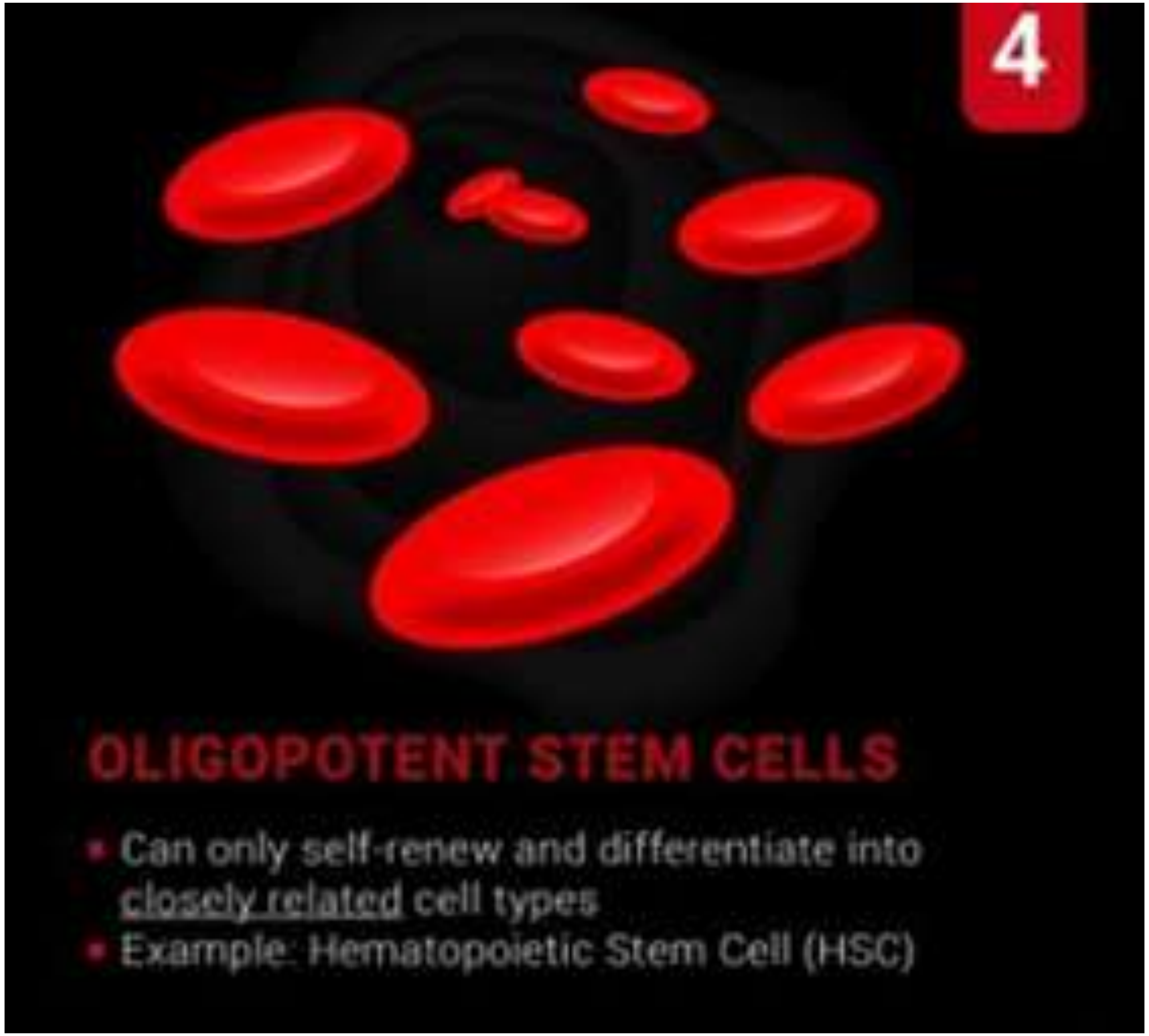
The next type of stem cells, oligopotent cells, are similar to the multipotent stem cells, but they become further restricted in their capacity to differentiate.

They can only do so into closely related cell types.

An excellent example of this cell type is the hematopoietic stem cell (HSC)

They are an immature cell that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets so they are also called blood stem cells.

Hematopoietic stem cells are found in the peripheral blood and the bone marrow.



Unipotent Stem Cells

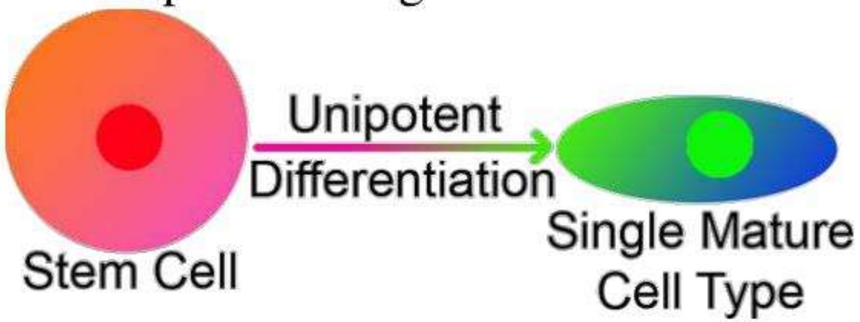
Unipotent stem cells are the least potent and most limited type of stem cell.

They can produce only their own type, but have the property of self renewal, which distinguishes them from non-stem cells, such as muscle stem cells.

An example of this stem cell type are muscle stem cells.

While muscle stem cells can self-renew, they can only do so into other muscle cells.

- **Unipotent Stem Cells**
  - These stem cells have unlimited reproductive capabilities, but can only differentiate into a single type of cell or tissue.
  - Unipotent stem cells are derived from multipotent stem cells and formed in adult tissue.
  - Skin cells are one of the most prolific examples of unipotent stem cells. These cells must readily undergo cell division to replace damaged cells.



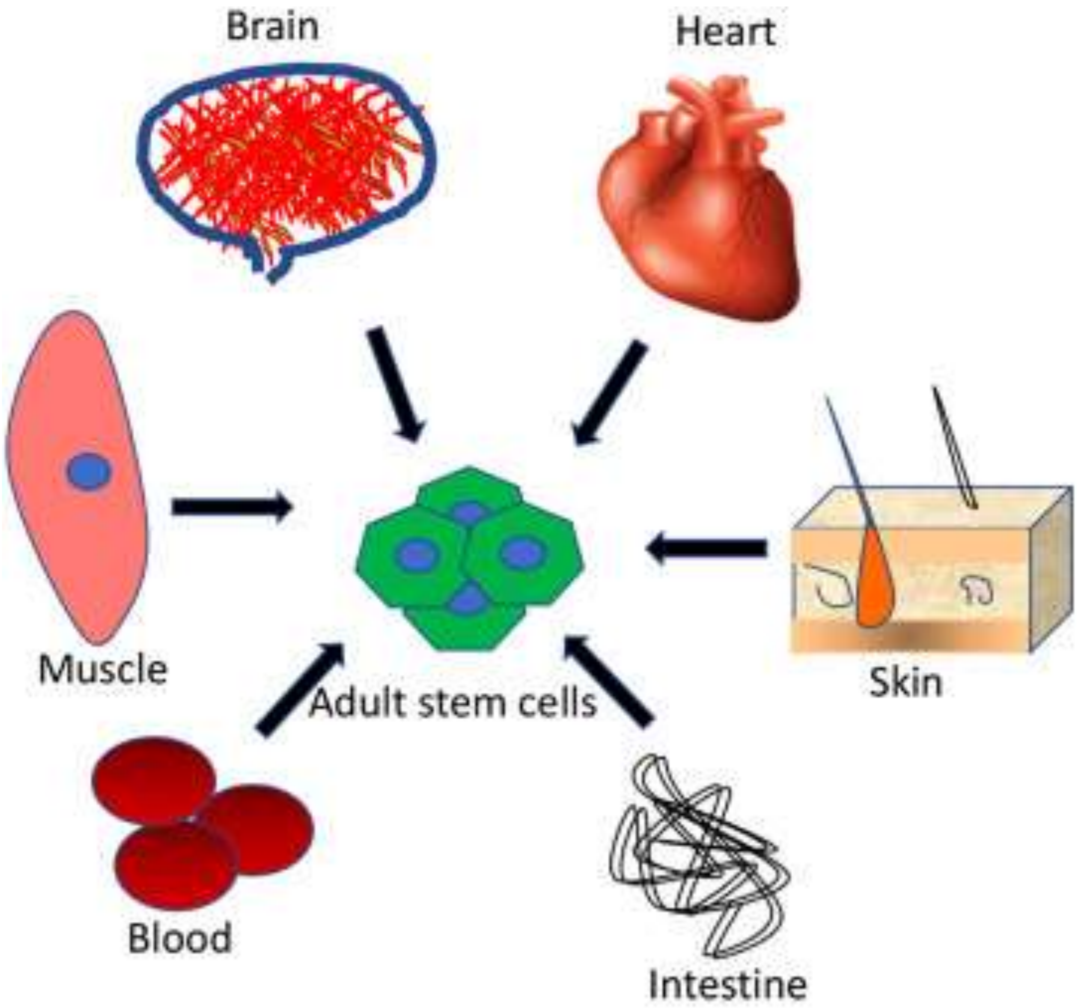
ADULT STEM CELLS (ASCS)

ASCs are undifferentiated cells found living within specific different types of tissues in our bodies, that can renew themselves or generate new cells that can replenish dead or damaged tissue.

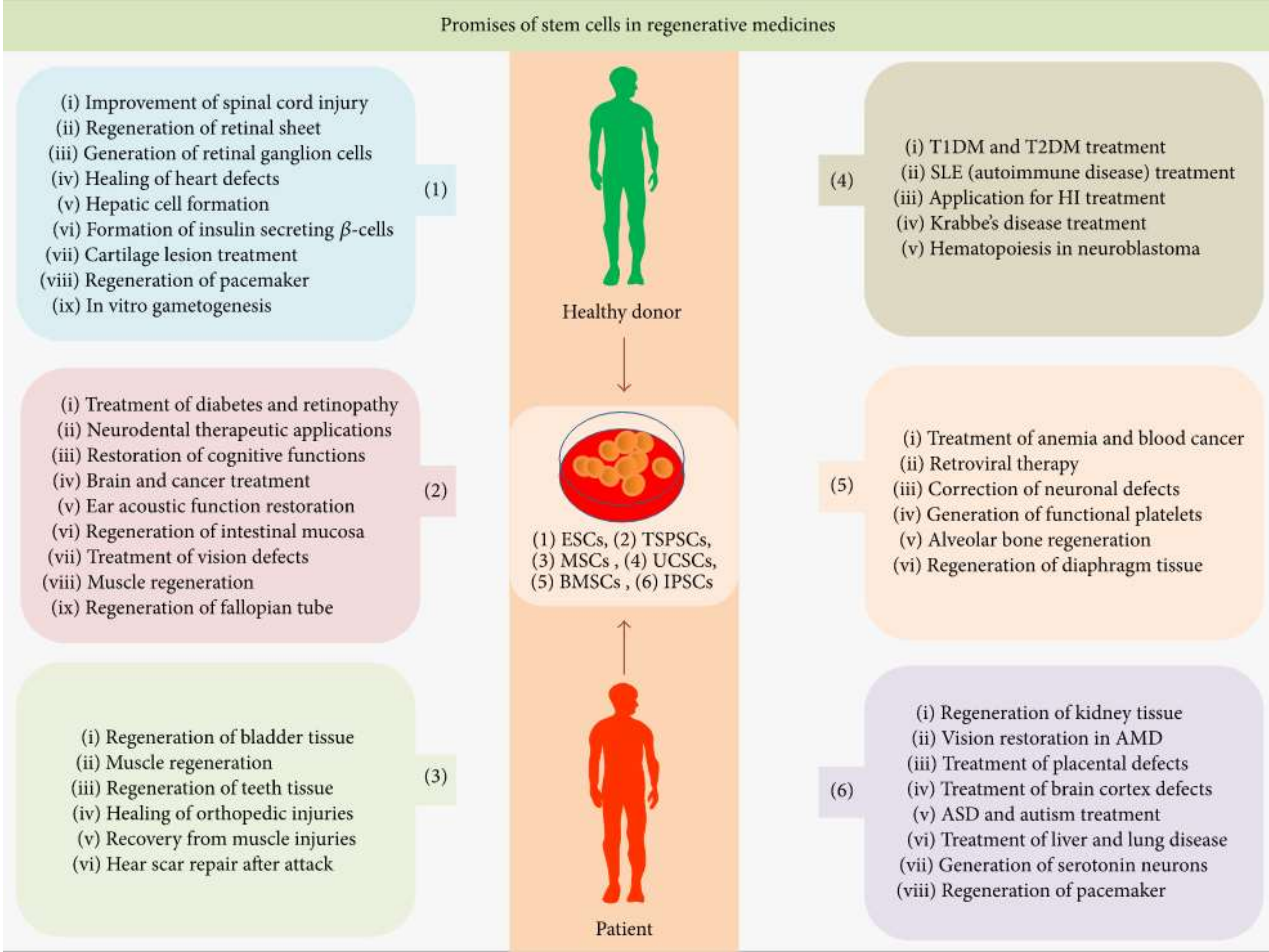
They are **also called somatic stem cells** which refers to non-reproductive cells in the body (eggs or sperm).

They are scarce in tissues so they are difficult to study and extract for research purposes.

ASCs are found in tissues such as the umbilical cord, placenta, bone marrow, muscle, brain, heart, fat tissue, skin, intestines, etc.



PROMISES OF STEM CELLS IN REGENERATIVE MEDICINE



RESEARCH IS BEING DONE IN THE FOLLOWING AREAS:

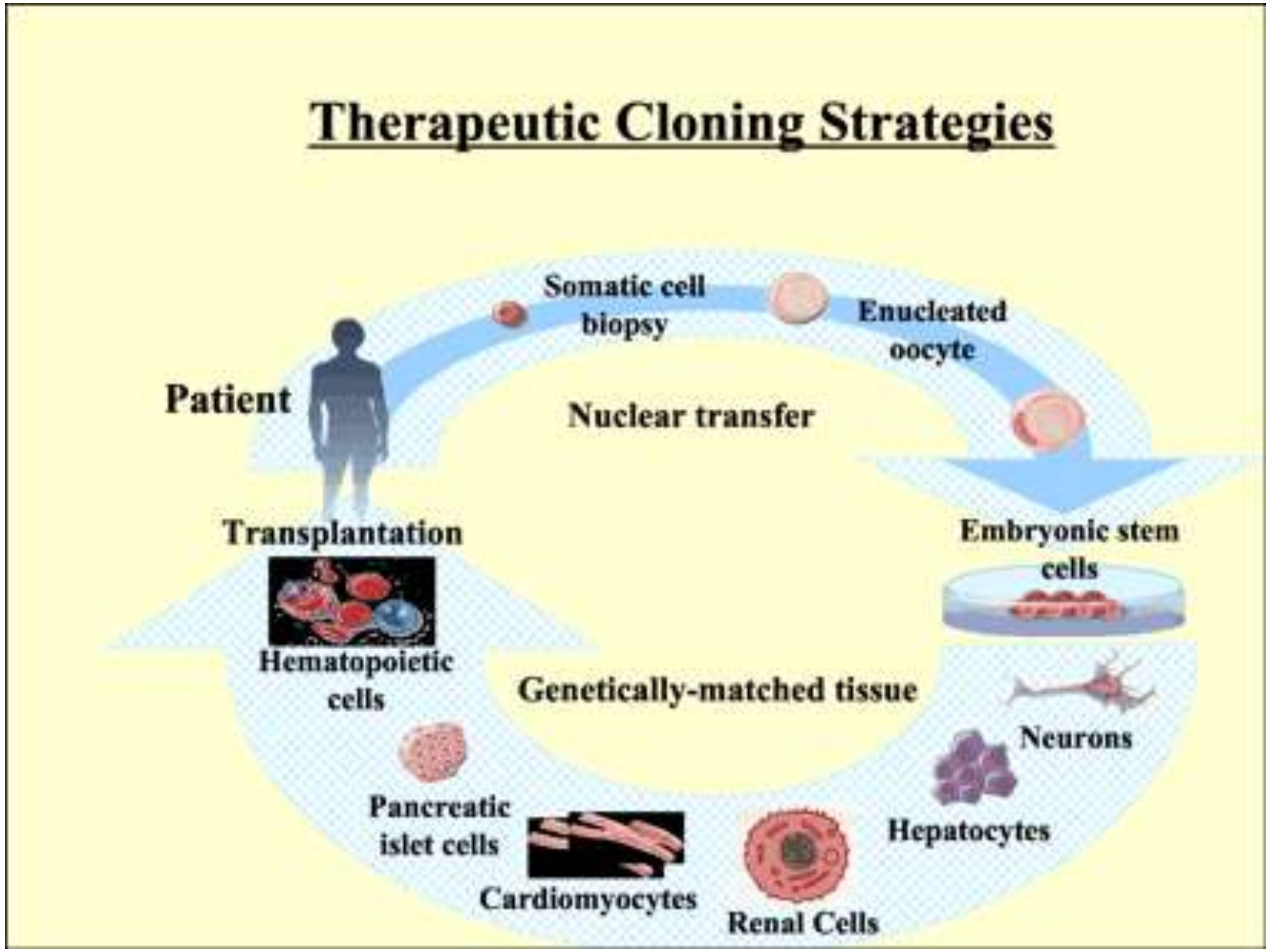
1) **Cell therapies** (the injection of stem cells or progenitor cells)

2) **Regeneration by biologically active molecules** administered alone or as secretions by infused cells.

3) **Tissue engineering** (transplantation of laboratory grown organs and tissues).

4) **Repair or replace portions of or whole tissues** (i.e., bone, cartilage, blood vessels, bladder, skin).

5) It also been applied to efforts to perform specific biochemical functions using cells within an **artificially-created support system** (such as an artificial pancreas or liver).



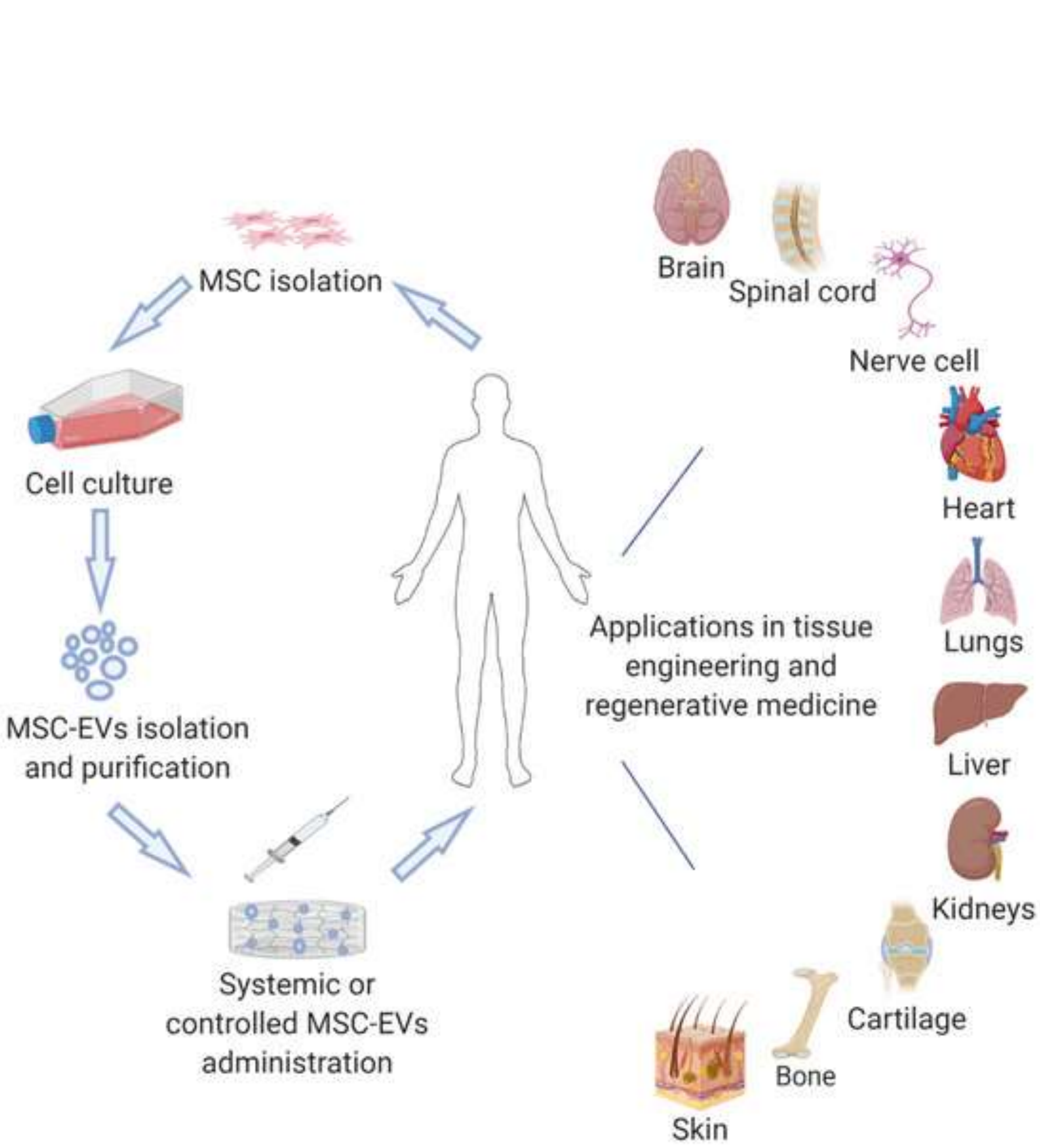
6) **Cardiovascular repair** to observe whether cells selectively migrate to injured cardiac tissue, improve function and blood flow at the site of injury and improve overall heart function

7) **Central nervous system applications** to assess whether cells migrate to the area of brain injury alleviating mobility related symptoms, and **repair damaged brain tissue** (such as that experienced with cerebral palsy).

USE OF STEM CELLS FROM THE UMBILICAL CORD

8) Because a person's own stem cells can be infused back into that individual without being rejected by the body's immune system, cord blood stem cells have become an increasingly important focus of regenerative medicine research.

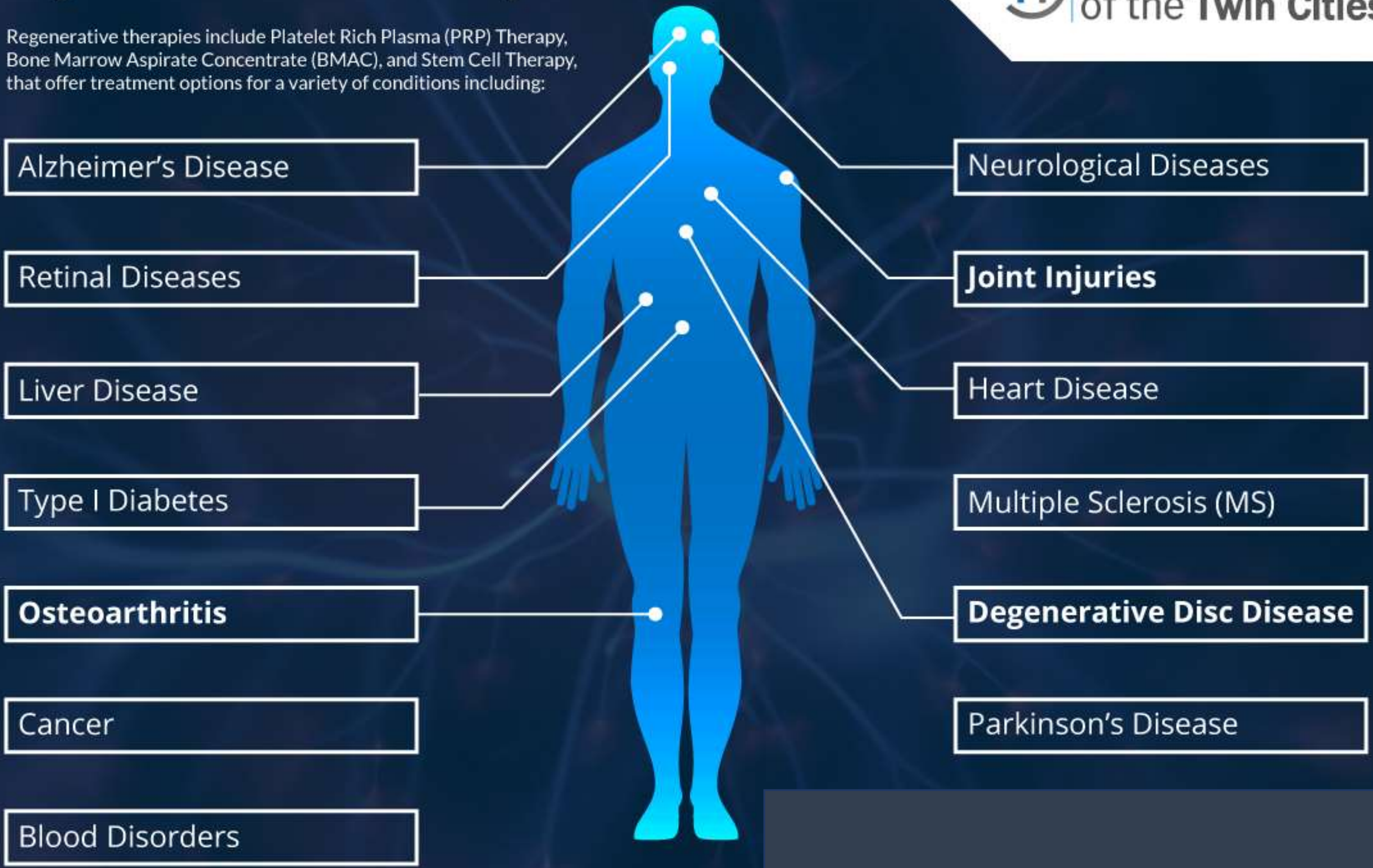
9) Cord blood stem cells are being explored in several applications including Type 1 diabetes to determine if the cells can slow the loss of insulin production in children.

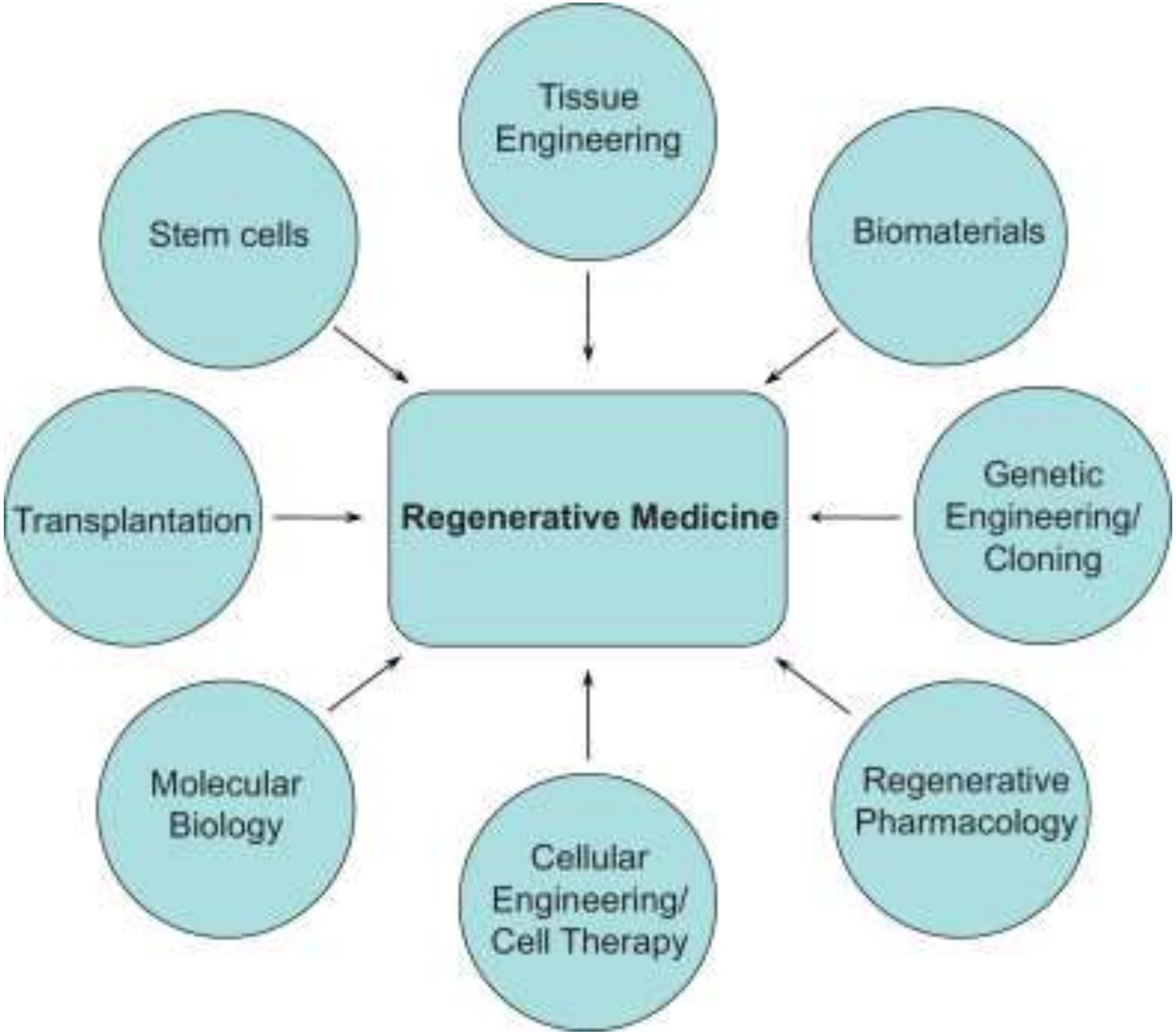


Select Health of the Twin Cities

Regenerative Medicine Therapies

Regenerative therapies include Platelet Rich Plasma (PRP) Therapy, Bone Marrow Aspirate Concentrate (BMAC), and Stem Cell Therapy, that offer treatment options for a variety of conditions including:




Tissue Engineering
Stem cells
Biomaterials
Transplantation
Regenerative Medicine
Genetic Engineering/ Cloning
Molecular Biology
Cellular Engineering/ Cell Therapy
Regenerative Pharmacology

SOURCES OF ADULT STEM CELLS

1) **The bone marrow stroma contain mesenchymal stem cells(MSCs), also called *marrow stromal cells*.**

2) Adipose tissue (fat),which requires extraction by liposuction.

3) Blood is drawn from the donor (similar to a blood donation),passed through a machine that extracts the stem cells and returns the rest of the blood to the donor.

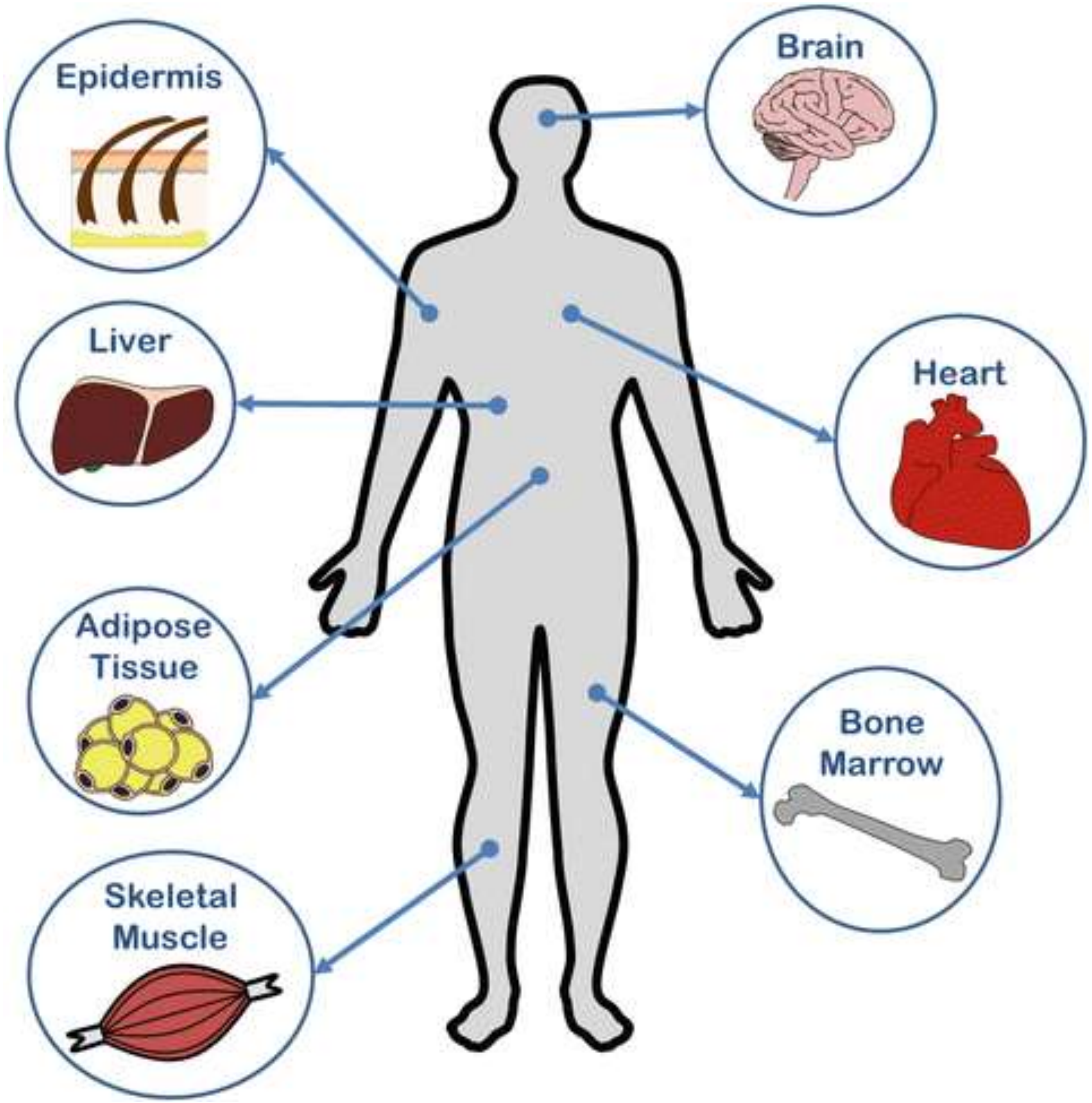
4) In addition, stem cells can also be taken from:

A) umbilical cord blood

B) amniotic fluid

C) adult muscle

D) the dental pulp of deciduous baby teeth.



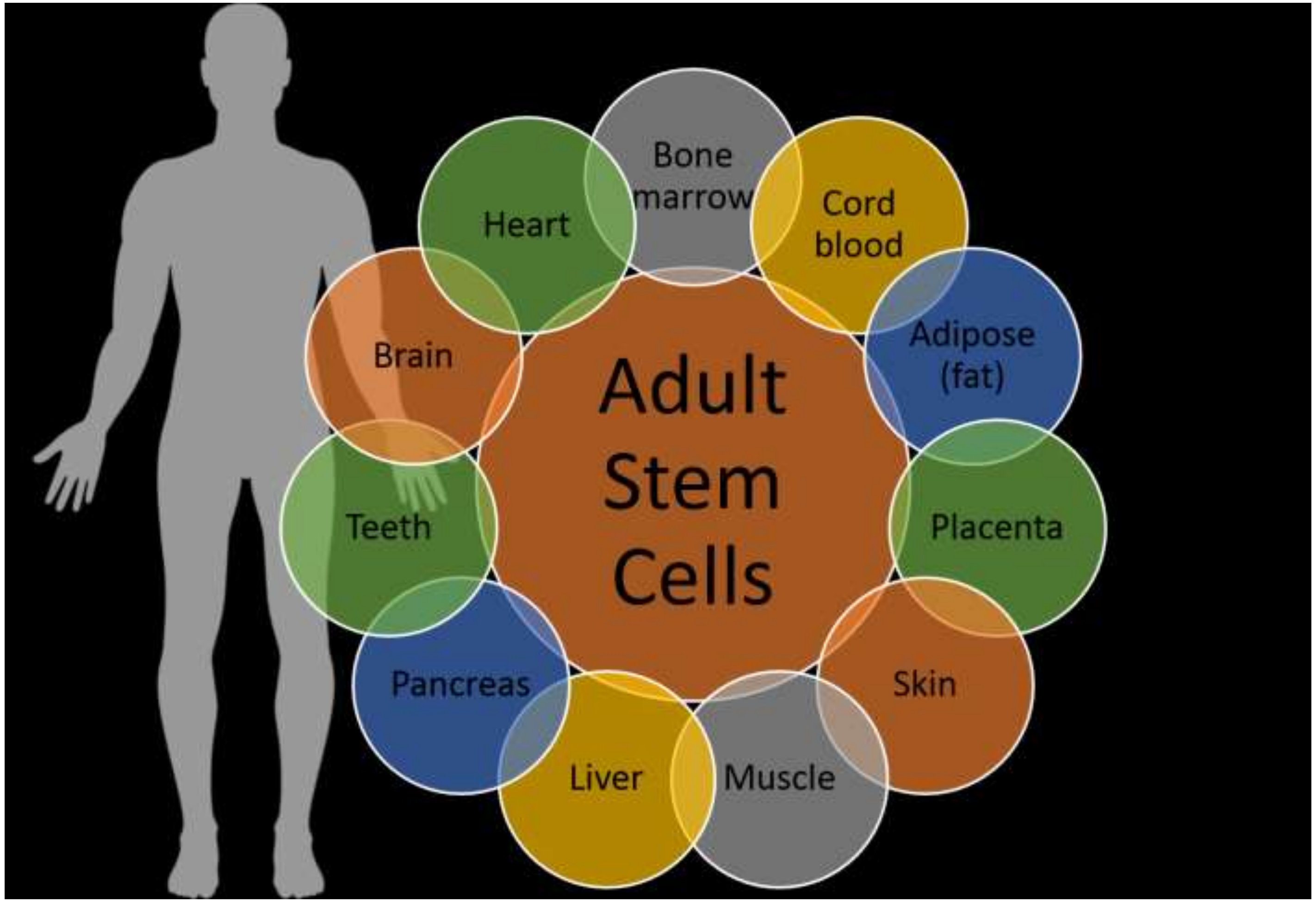
One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin.

Adult bone marrow has three distinct types of stem cells:

Hematopoietic stem cells, which give rise to red blood cells, white blood cells, and platelets

Endothelial stem cells, which give rise to the endothelial cell types that line blood and lymph vessels

Mesenchymal stem cells, which give rise to the different types of muscle cells.



MESENCHYMAL STEM CELLS

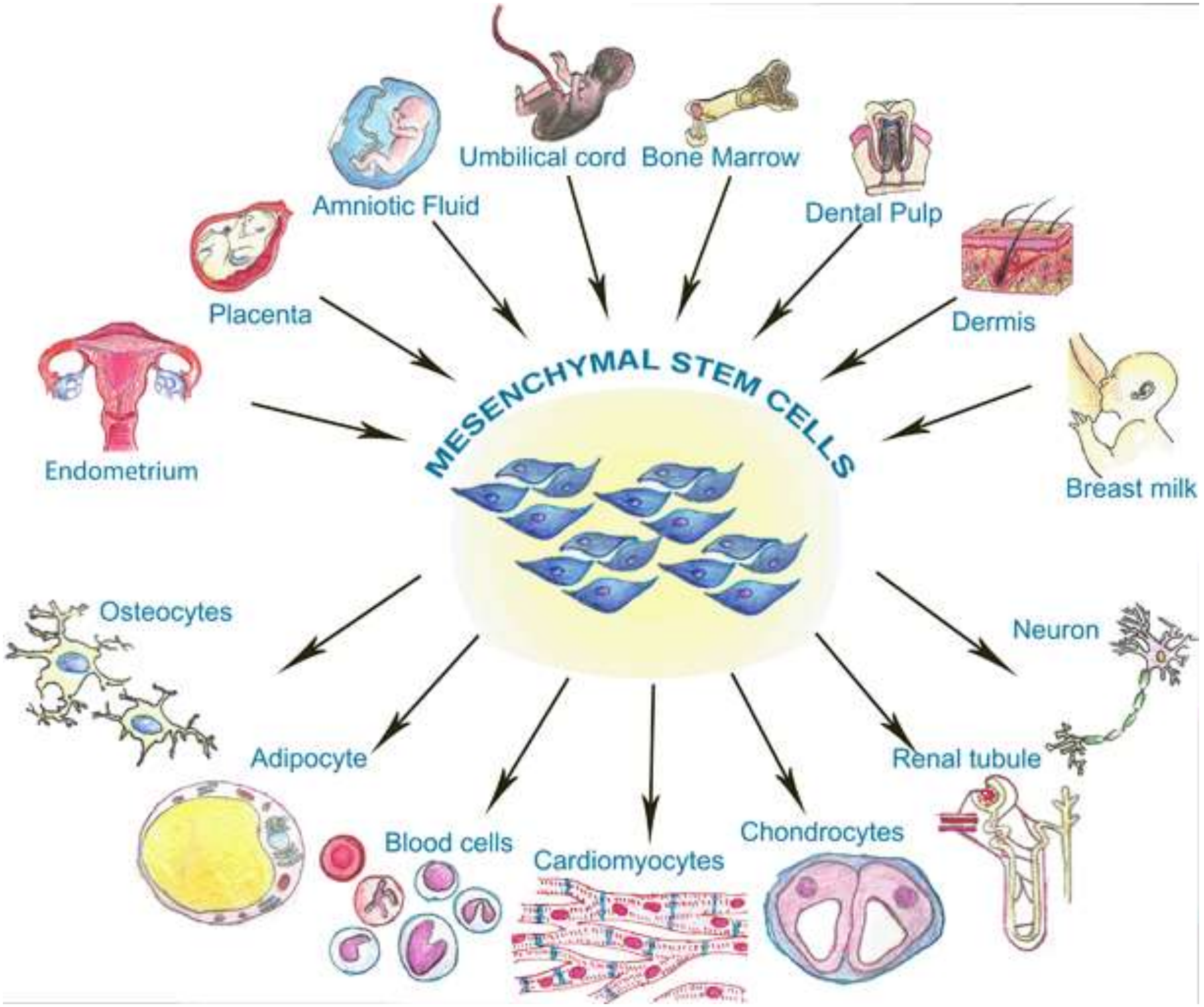
You may hear the term "mesenchymal stem cell" or MSC to refer to cells isolated from stroma, the connective tissue that surrounds other tissues and organs.

Cells by this name are more accurately called "stromal cells" by many scientists.

The first MSCs were discovered in the bone marrow and were shown to be capable of making bone, cartilage and fat cells.

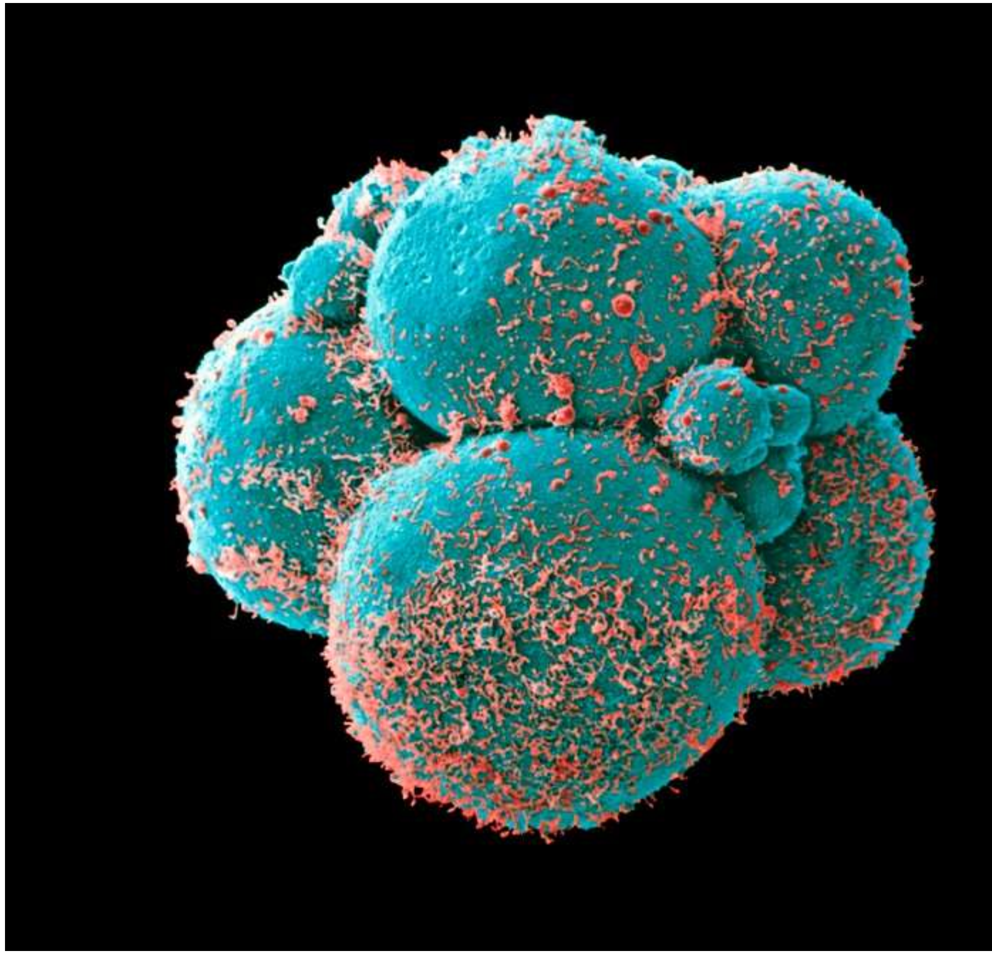
Since then, they have been grown from other tissues, such as fat and cord blood.

Various MSCs are thought to have stem cell, and even immuno-modulatory, properties and are being tested as treatments for a great many disorders, but there is little evidence to date that they are beneficial.



HOW DOES A STEM CELL "KNOW" WHAT KIND OF BODY CELL TO BECOME?

The process is called cell fate decision which means that a stem cell "makes a decision" to differentiate into a more mature cell type.



WHAT CAUSES THIS TO HAPPEN ?

Signals from inside and outside the cell from its environment such as:

1) Certain types of biological chemicals in the cell

2) Extracellular (outside of the cell) proteins, hormones, or other materials

3) Types of neighboring cells

4) The physical environment where the cell is located

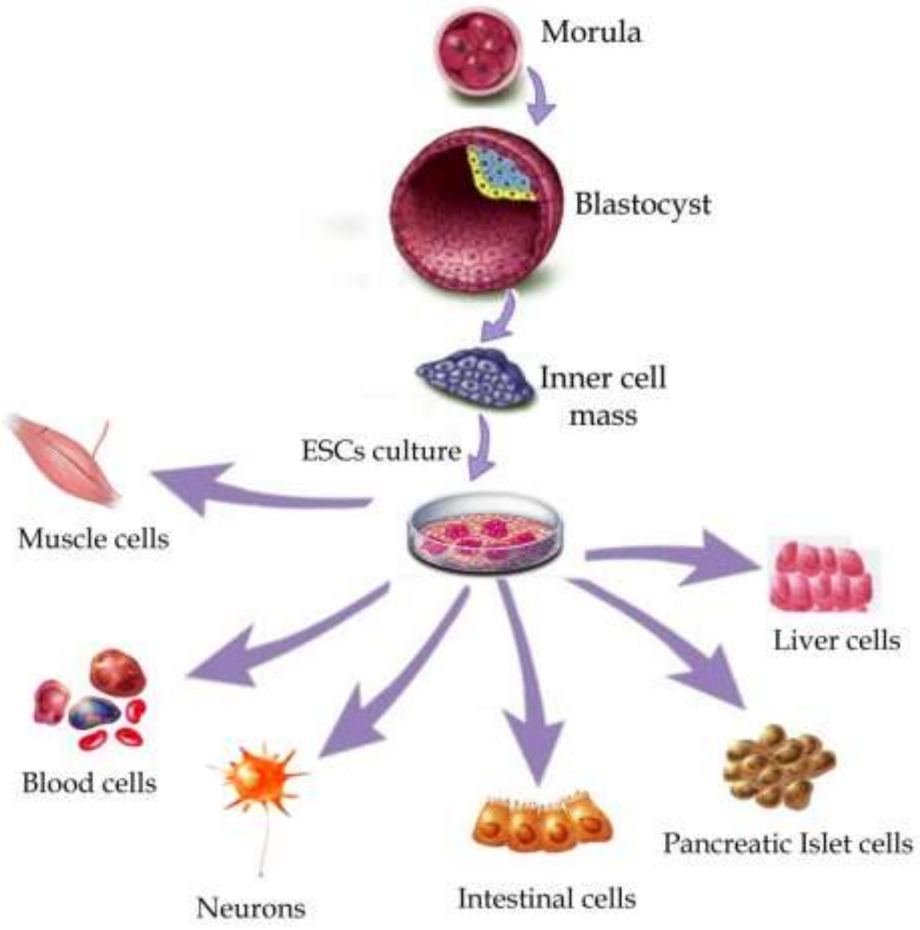
All of these converge on the cell, which activates a signaling cascade that leads to gene expression to make it a more specialized cell.

Similar but different recent findings are shown below:

5) **The stem cell is encoded by how their DNA is arranged inside the cell, and this can be detected by specific protein markers on their outside surface**.
https://phys.org/news/2011-07-stem-cells.html

6) **The amount of slight stiffness around the cell, depending on where it is located is called a traction force and helps to determine what type of cells they turn into.**
https://www.sciencedaily.com/releases/2010/08/100801190257.htm

7) **The stem cell-specific protein OCT4 primes certain genes that, when activated, cause the cell to differentiate, or become more specialized.**
https://www.regmednet.com/new-study-uncovers-role-of-oct4-in-stem-cell-differentiation/



TYPES ACCORDING TO SOURCE

A. Adult Type Specific Stem Cells

Undifferentiated cells found among specialized cells found in tissues and in organs after birth

1 UMBILICAL CORD STEM CELLS

- Found in a newborn's umbilical cord
- Can be cultured to become every type of cell in the blood

2 UMBILICAL BLOOD STEM CELLS

- From residual blood from a newborn's umbilical cord
- Can differentiate into other types of cells, like nerve cells

3 PLACENTAL STEM CELLS

- Can protect against white matter brain injury in preterms
- Harvested from the placenta
- Current application to research on:
  - Type 1 diabetes
  - Alzheimer's
  - Spinal cord injuries

4 AMNIOTIC FLUID STEM CELLS

- Extracted from the amniotic fluid and the amniotic membrane of the placenta
- Can differentiate into these cell and tissue types:
  - Skin
  - Cartilage
  - Cardiac tissue
  - Nerves
  - Muscle
  - Bone

5 GASTRIC EPITHELIAL STEM CELLS

- Closely linked to gastric cancer
- Regarded by scientists as a result of dysregulated differentiation of stem and progenitor cells in the intestines

6 HEART STEM CELLS

- Multipoint stem or progenitor cells
- Found in the hearts of mammals
- Self-renewing
- Generate coronary vessels and heart muscle cells known as cardiomyocytes

7 NEURAL STEM CELLS

- Can differentiate into:
  - Neurons
  - Glia of the nervous system
- Self-renewing

8 HEPATIC STEM CELLS

- The liver's "regenerative capabilities" is attributed to the presence of stem cells
- Studies suggest that liver cells are functional stem cells of the organ

9 EPIDERMAL STEM CELLS

- Multipotent adult stem cells found in our skin
- Are active during skin renewal
- Currently used to grow skin for burn victims

⑩ ADIPOSE STEM CELLS

- Isolated from fat tissues
- They can differentiate into:
  - Bone cells
  - Cartilages

⑪ BONE MARROW STEM CELLS

- Found in the bone marrow
- Can give rise to different blood cell types
- Used for treating blood-related diseases:
  - Leukemia
  - Some types of lymphoma

B. Embryonic Stem Cells

Embryonic stem cells are pluripotent

① EMBRYONIC STEM CELLS

- Usually harvested from embryos that are 5-7 years old
  - Embryos that would otherwise be discarded by fertility clinics
  - Subject to ethical and moral issues

C. Induced Pluripotent Stem Cells

① Genetically reprogrammed to have the pluripotency possessed by embryonic stem cells

- Currently used for:
  - Drug development
  - Modeling of diseases

[redacted]

TYPES ACCORDING TO DIFFERENTIATING CAPABILITIES

① HEMATOPOIETIC STEM CELLS (HSC)

- Can differentiate into all types of blood cells
- Stem cells that are HSCs
  - Found in adult bone marrow
  - Found in umbilical cord blood

② MESENCHYMAL STEM CELLS (MSC)

- Multipotent stem cells capable of differentiating into:
  - Bone cells
  - Cartilage cells
  - Muscle cells
  - Fat cells

CELL POTENCY REFERS TO THE VARYING ABILITY OF STEM CELLS TO DIFFERENTIATE INTO SPECIALIZED CELL TYPES

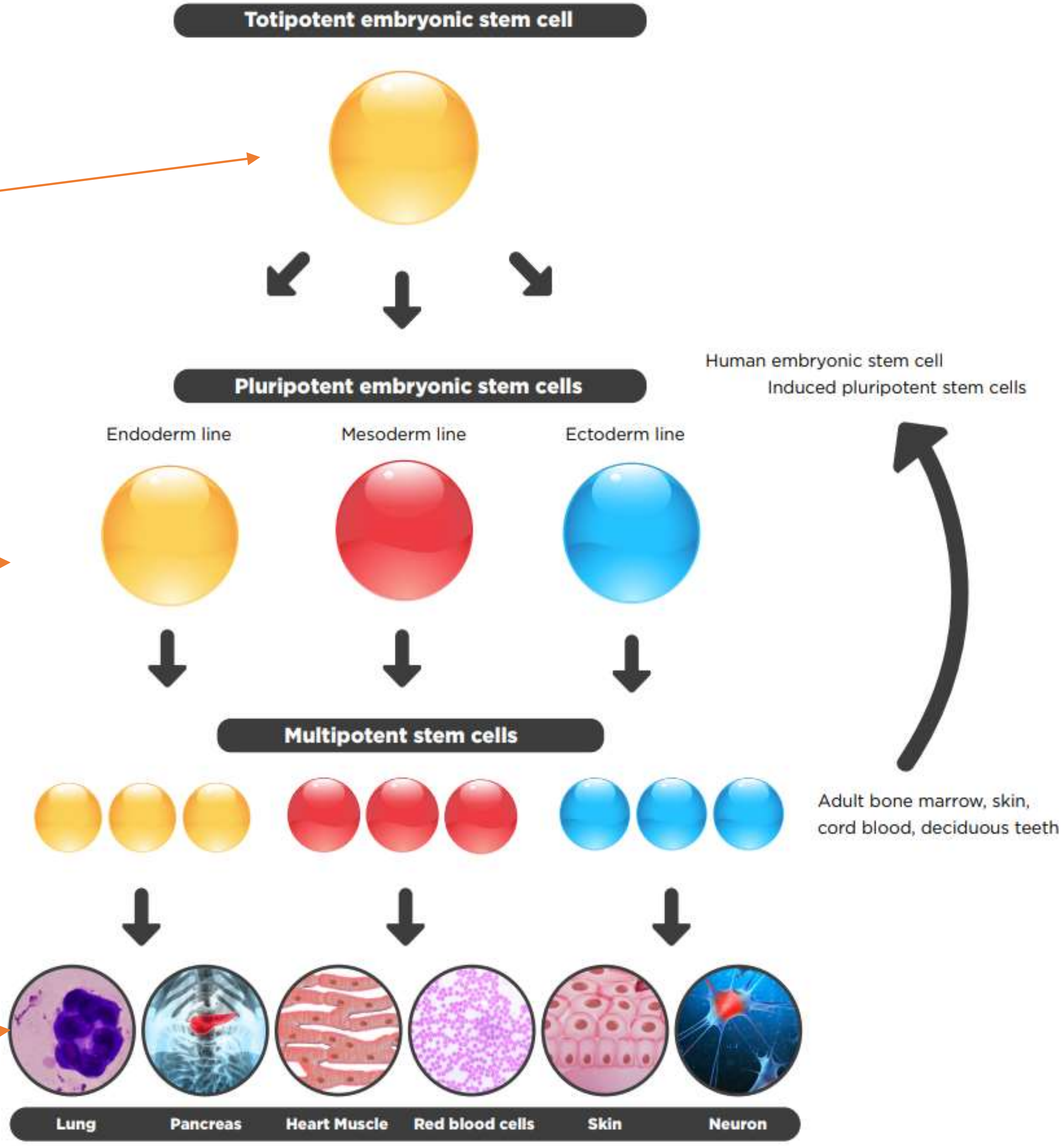
Cells with the greatest potency can generate more cells types than those with lower potency.

Totipotent Stem Cells
They are also called **omnipotent** stem cells and can give rise to any of the 226 cell types found in an embryo as well as extra-embryonic cells (placenta).

Pluripotent Stem Cells (also called Embryonic stem cells)
Pluripotent stem cells can give rise to all cell types of the body (but not the placenta).

Multipotent Stem Cells
Multipotent stem cells can develop into a limited number of cell types in a particular lineage.

Unipotent Stem Cells



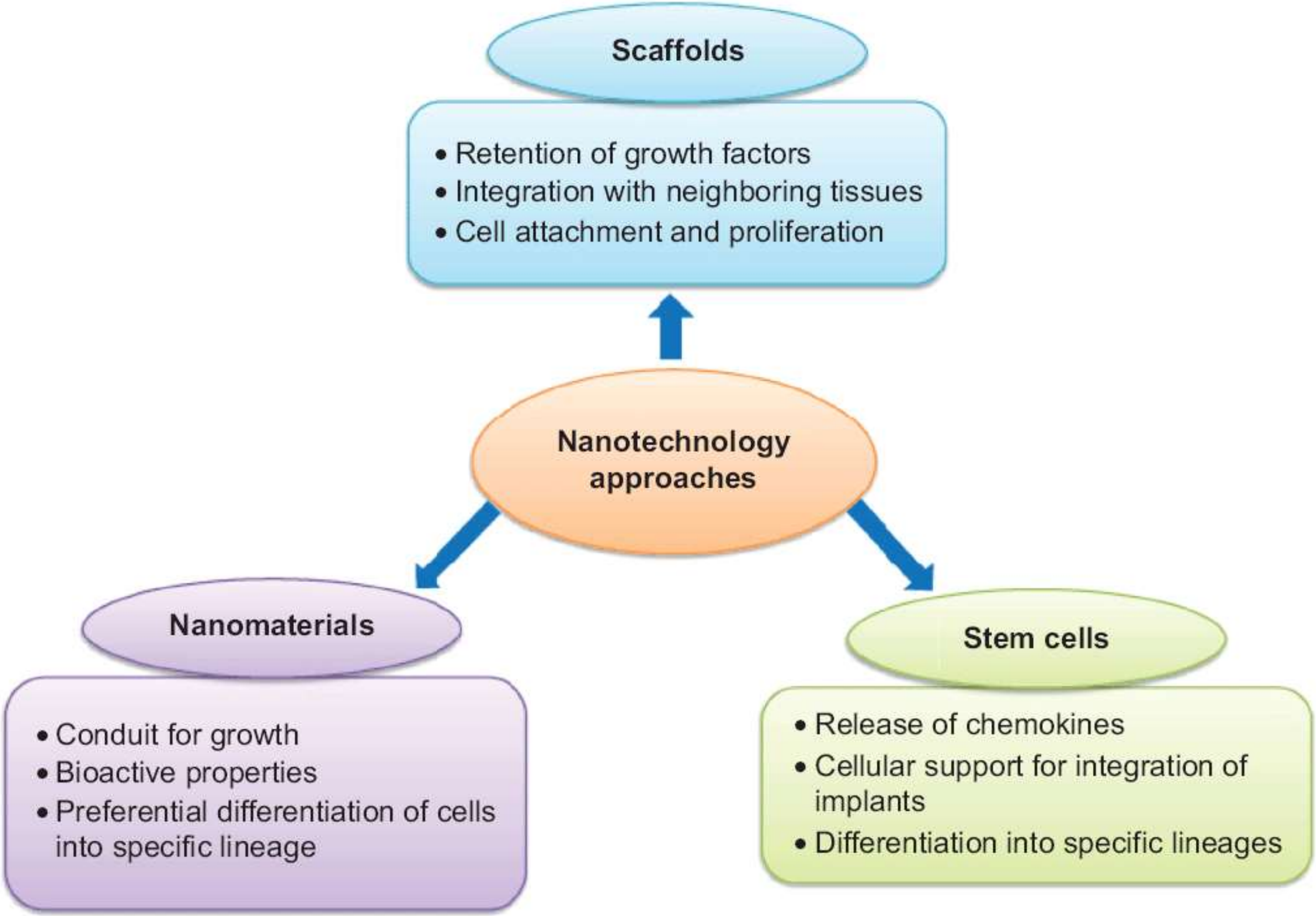


Figure 1 Various nanotechnology approaches in regenerative medicine.

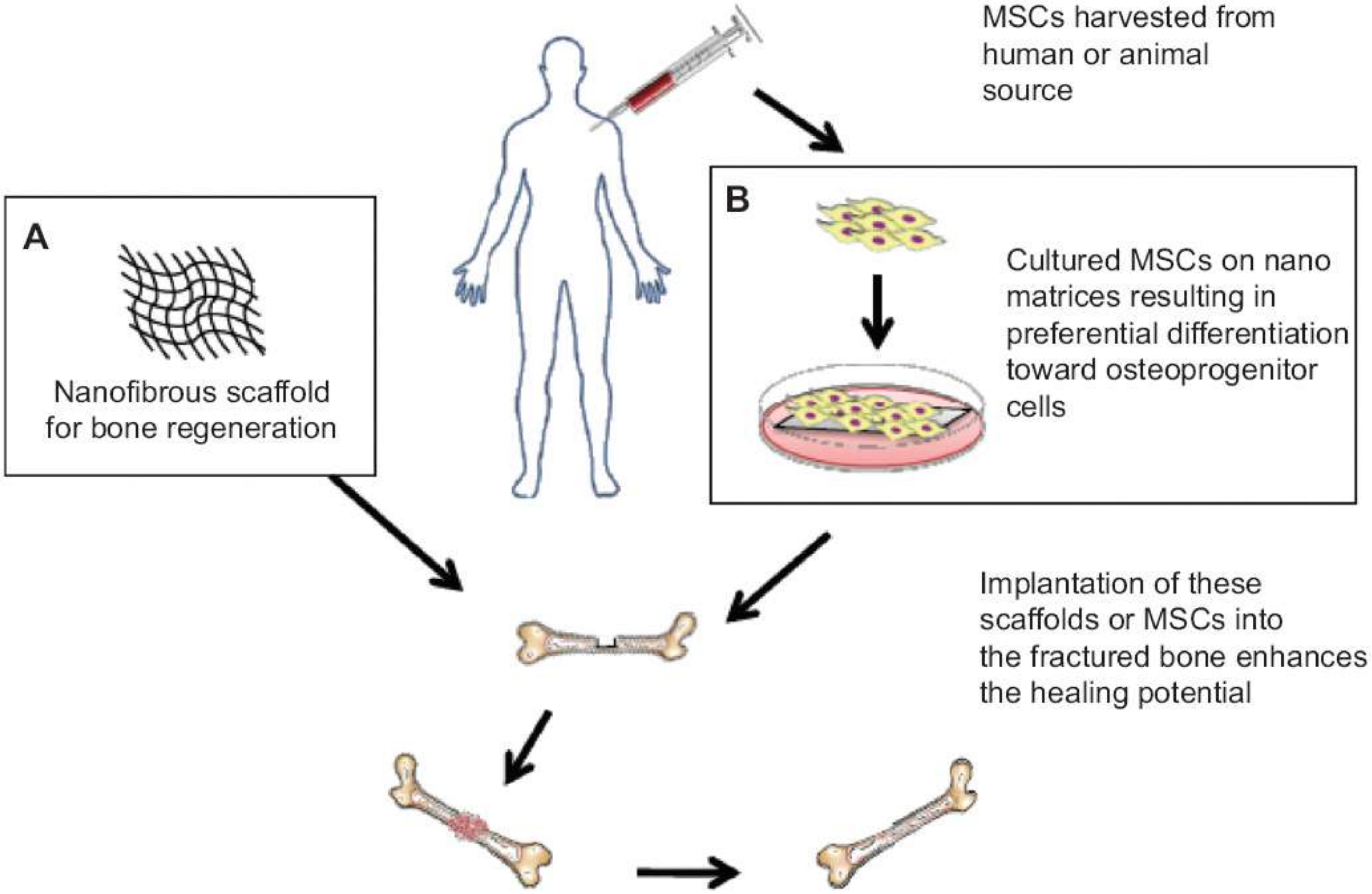
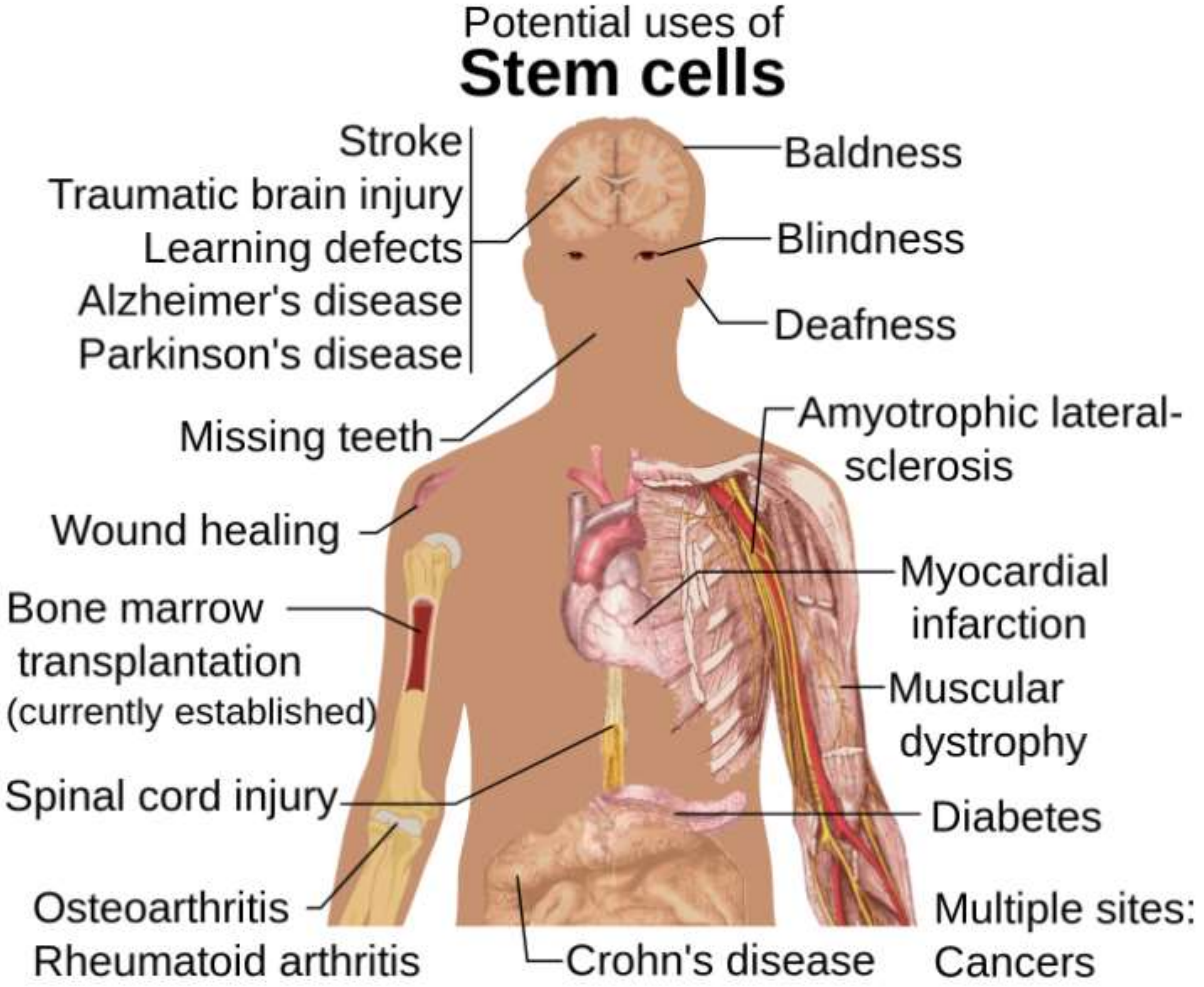
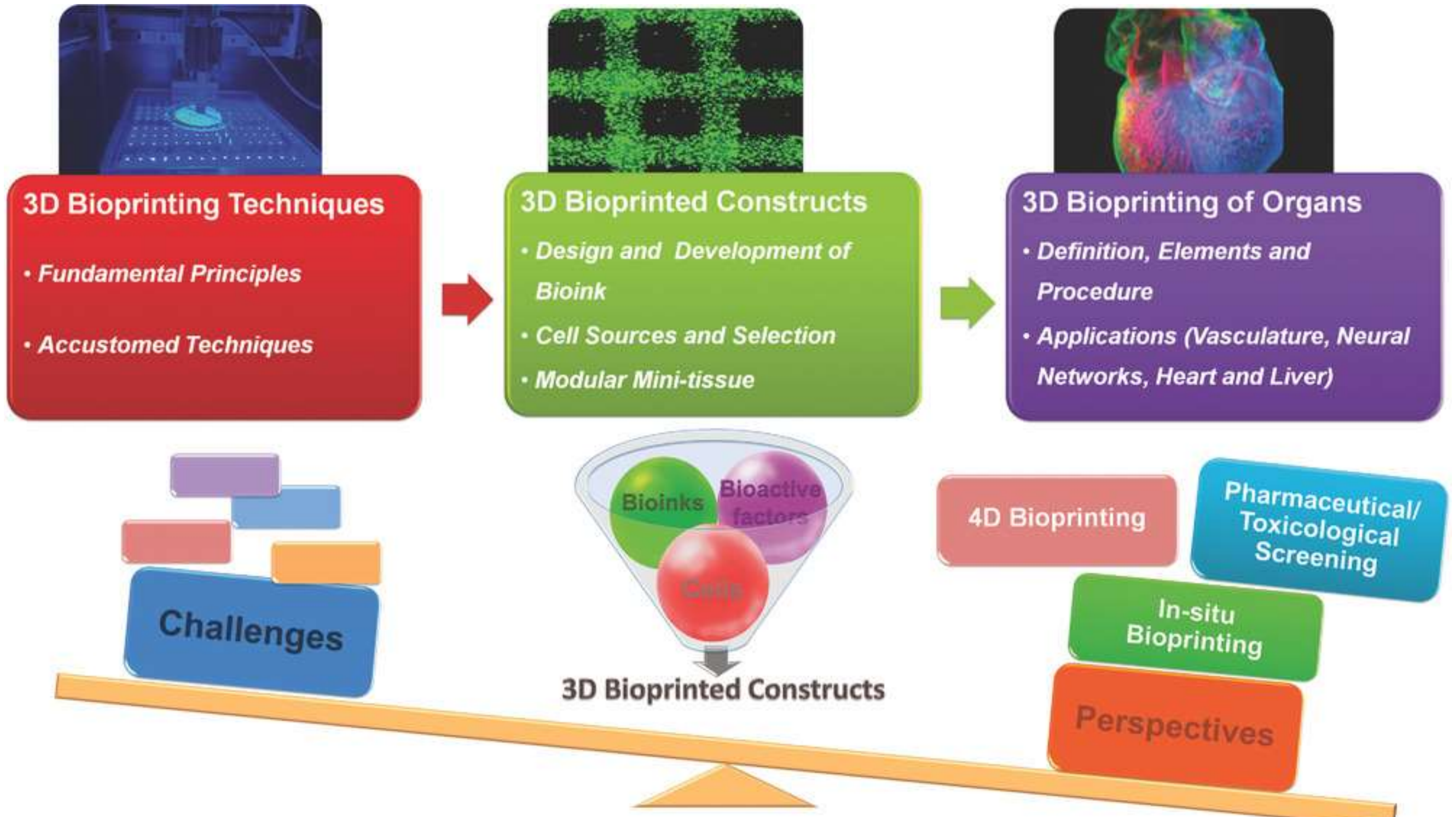


Figure 2 Schematic representation of bone regeneration using nanotechnology.

Notes: Improved bone healing using (**A**) nanofibrous scaffold and (**B**) culturing MSCs on nano matrices.

Abbreviation: MSCs, mesenchymal stem cells.


Potential uses of
Stem cells
Stroke
Traumatic brain injury
Learning defects
Alzheimer's disease
Parkinson's disease
Baldness
Blindness
Deafness
Missing teeth
Amyotrophic lateral-
sclerosis
Wound healing
Myocardial
infarction
Bone marrow
transplantation
(currently established)
Muscular
dystrophy
Spinal cord injury
Diabetes
Osteoarthritis
Rheumatoid arthritis
Crohn's disease
Multiple sites:
Cancers


3D Bioprinting Techniques
• Fundamental Principles
• Accustomed Techniques
3D Bioprinted Constructs
• Design and Development of Bioink
• Cell Sources and Selection
• Modular Mini-tissue
3D Bioprinting of Organs
• Definition, Elements and Procedure
• Applications (Vasculature, Neural Networks, Heart and Liver)
Challenges
Bioinks
Bioactive factors
Cells
3D Bioprinted Constructs
4D Bioprinting
Pharmaceutical/ Toxicological Screening
In-situ Bioprinting
Perspectives

TECHNOLOGIES USED IN REGENERATIVE MEDICINE

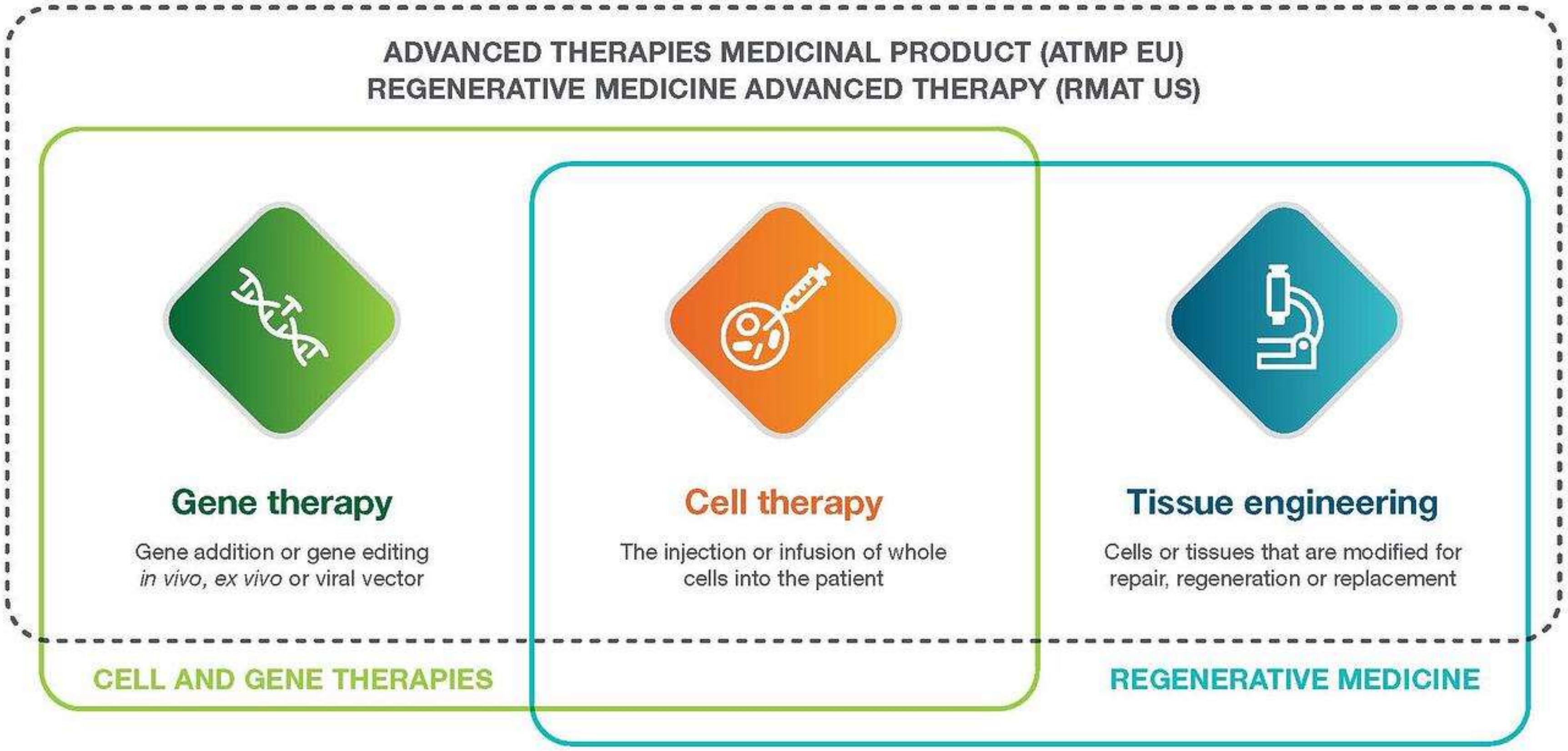
1) Gene therapies

2) Cell therapies

3) Tissue-engineered products

They are used to augment, repair, replace or regenerate organs, tissues, cells, genes, and metabolic processes in the body.

Regenerative medicine aims to alter the current practice of medicine by treating the root causes of disease and disorders.



1) GENE THERAPIES

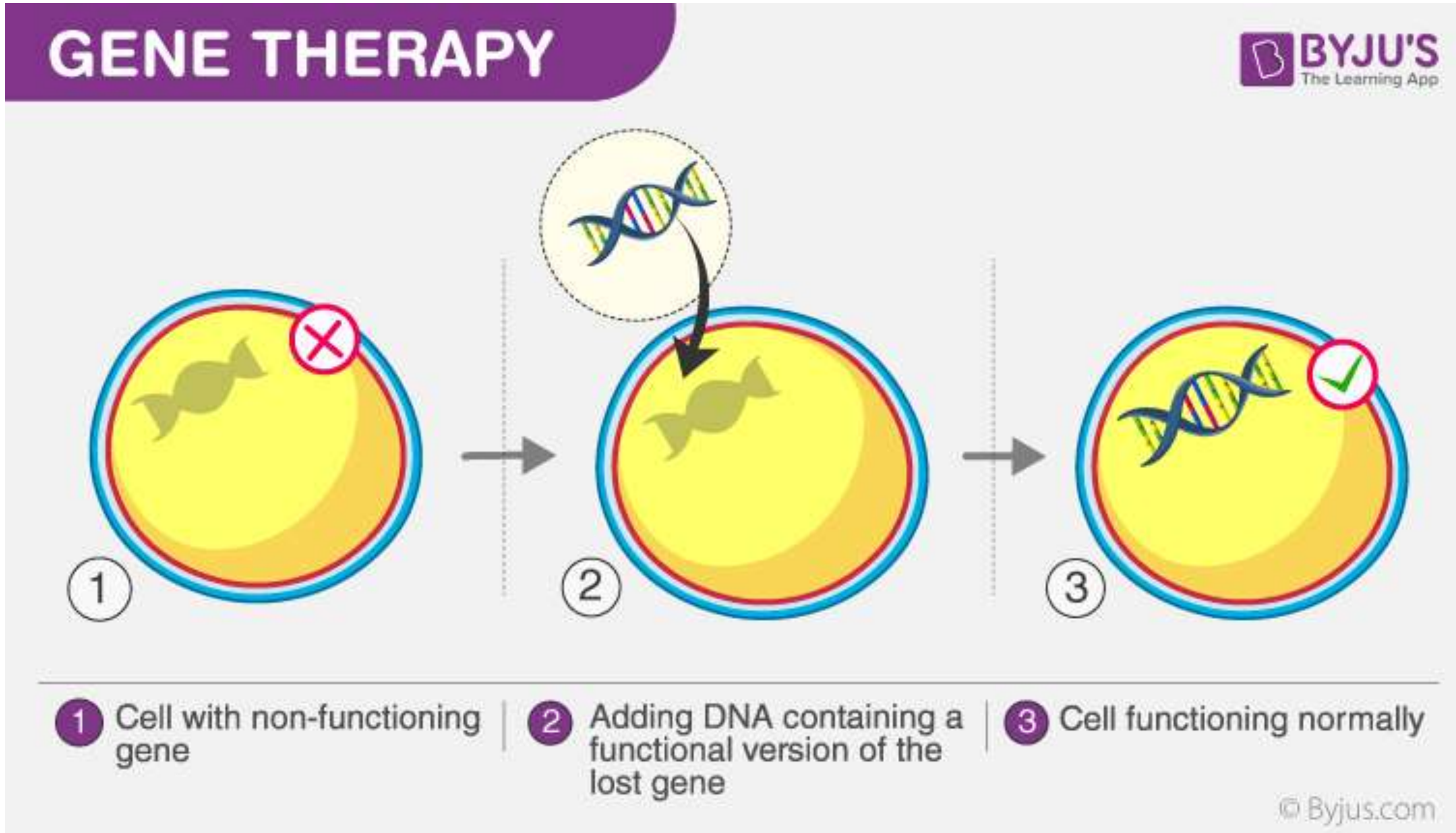
Gene therapy seeks to modify or introduce genes into a patient’s body with the goal of durably treating, preventing or potentially even curing disease, including several types of cancer, viral diseases, and inherited disorders by:

- Replacing a mutated gene that causes disease, with a functional copy

- Introducing a new, correct copy of a gene into the body in order to fight disease.

This is done with deactivated viruses which don’t make patients sick.

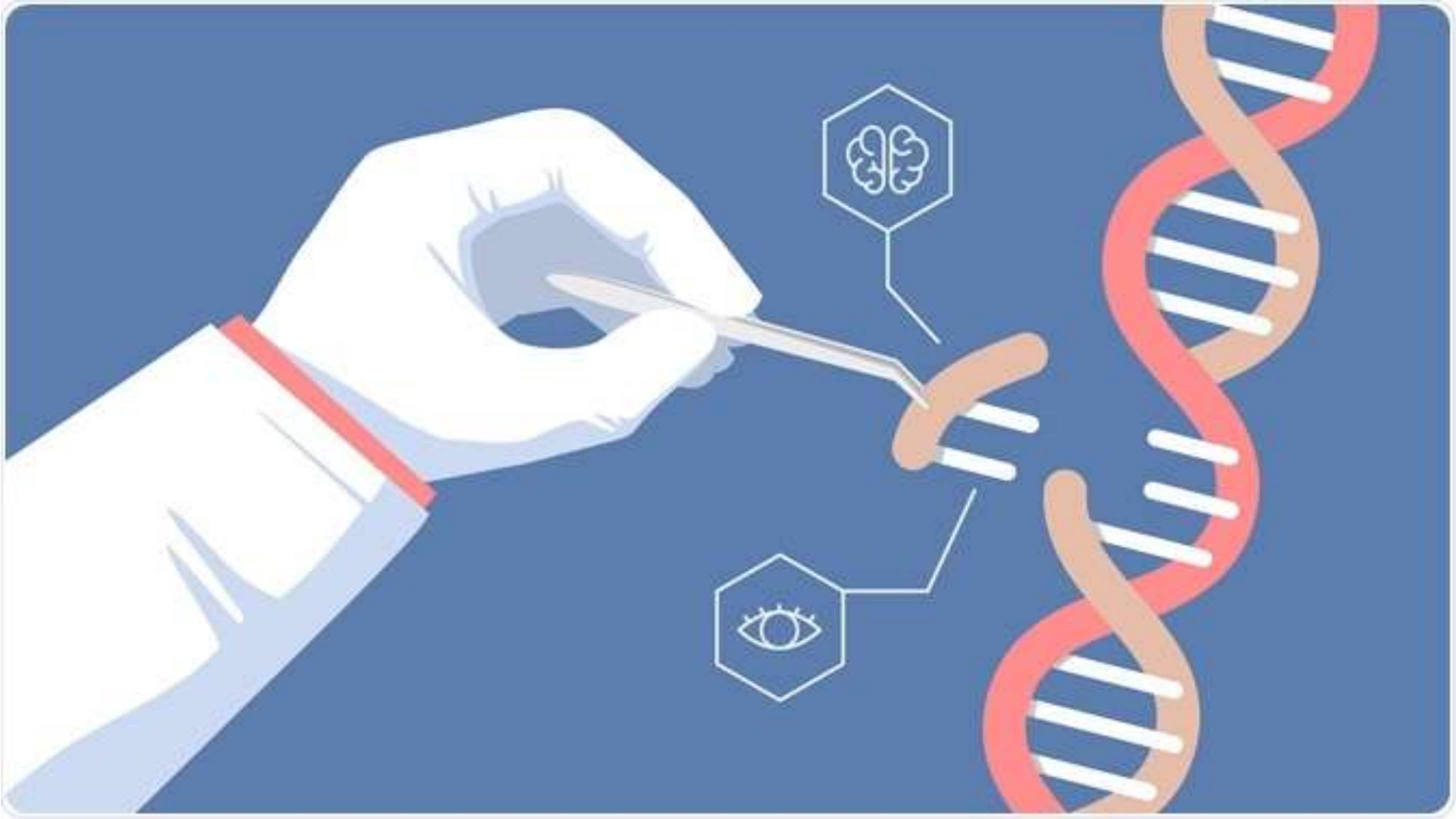
Nanoparticles and Nanospheres have also been used for this.



2) GENOME EDITING

Genome editing is a technique by which DNA is inserted, replaced, removed, or modified at particular locations in the human genome for therapeutic benefit, in order to treat cancer, rare inherited disorders, HIV, or other diseases.

Several approaches rely on the use of "molecular scissors," often an engineered nuclease, to make precise cuts in the patient's DNA at a specific location in the genome.



The new method to do this is called Crispr-CAS9

The breaks are then repaired to create the desired edit and result in a corrected gene.

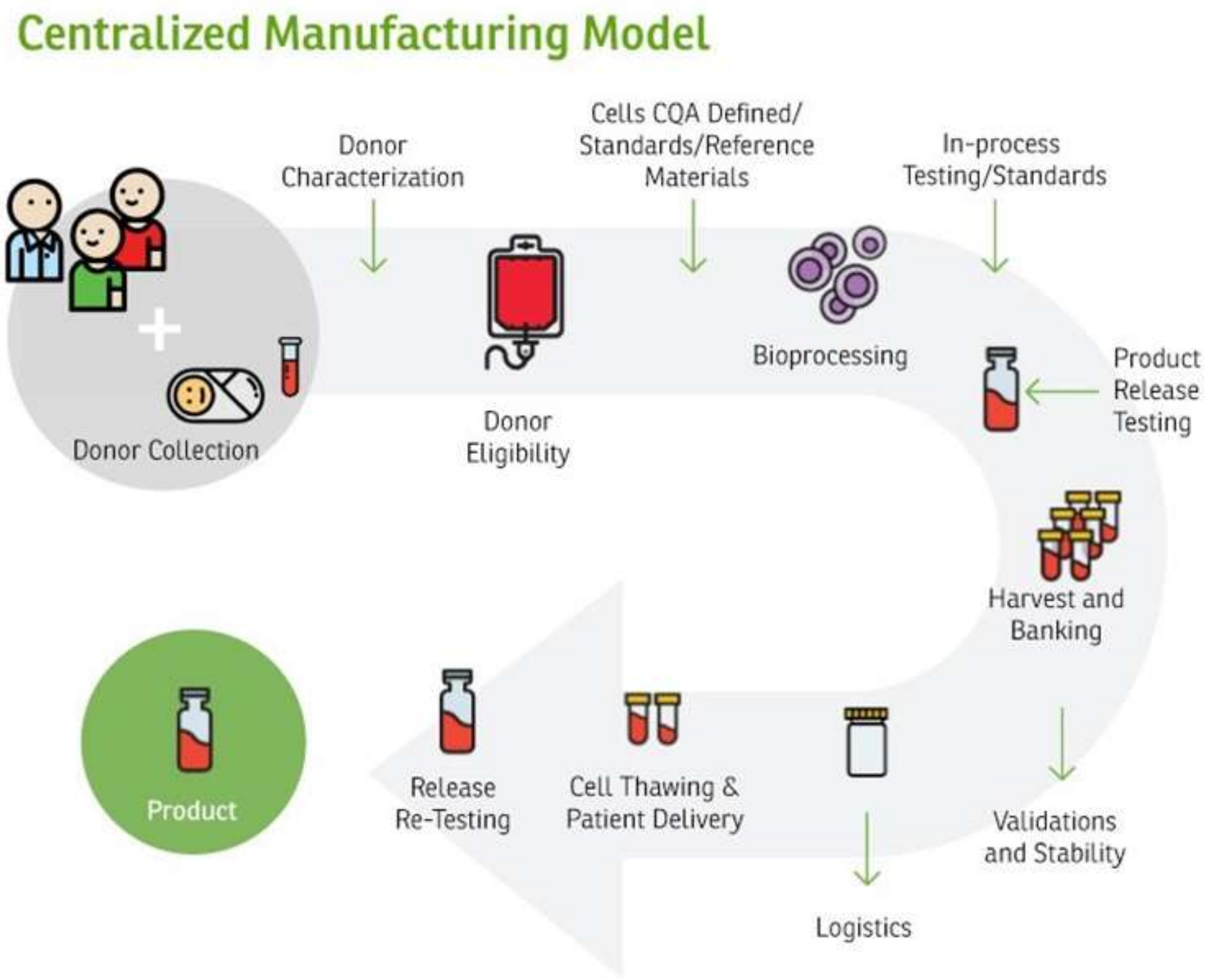
3) CELL THERAPY

It is the administration of viable, often purified cells into a patient's body to grow, replace, or repair damaged tissue for the treatment of a disease.

A variety of different types of cells can be used in cell therapy:

- Blood-forming stem cells
- Skeletal muscle stem cells
- Neural stem cells

Adult stem cells that differentiate into structures as connective tissues, blood, lymphatics, bone, and cartilage, lymphocytes, dendritic cells, and pancreatic cells.



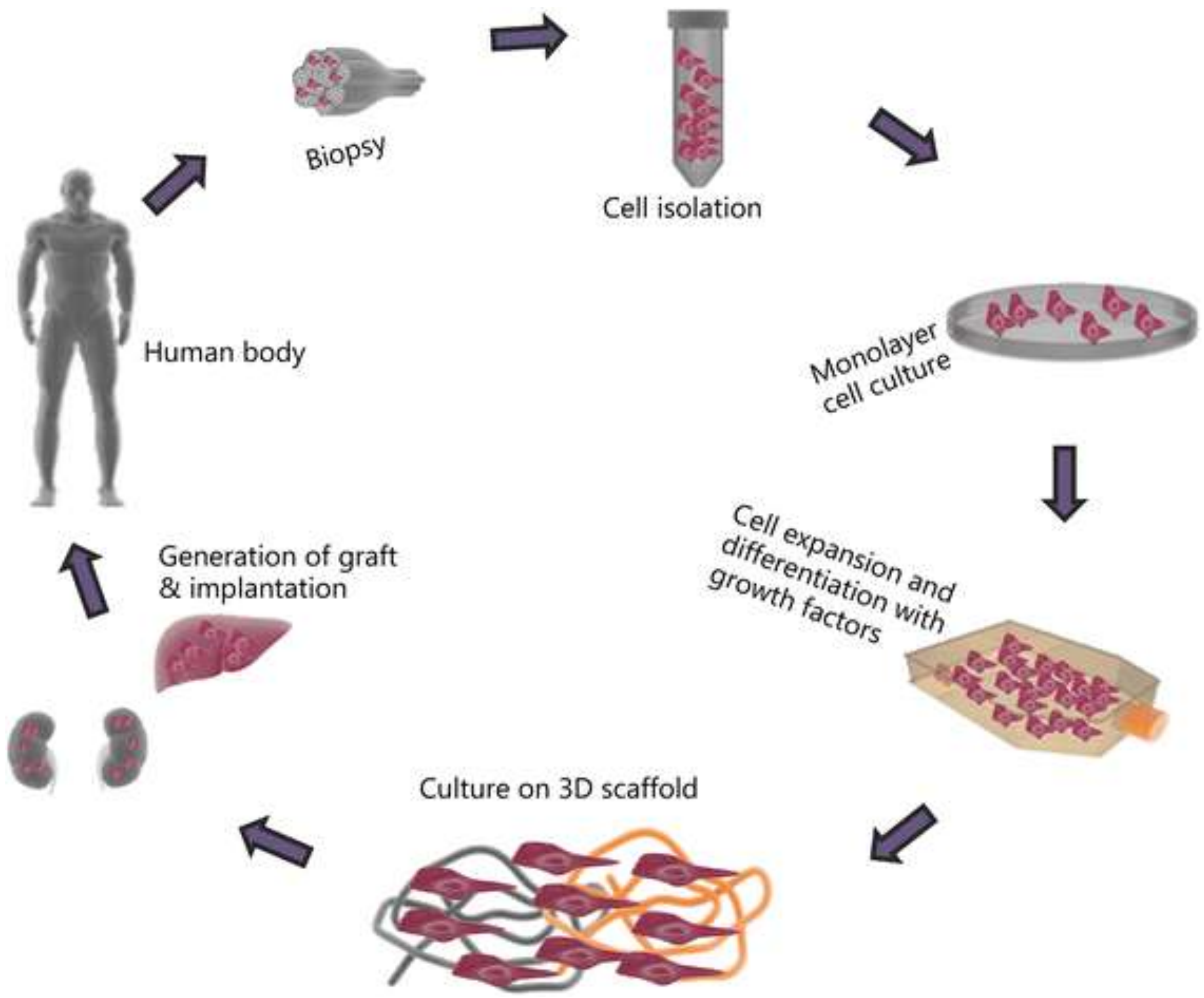
4) TISSUE-ENGINEERED PRODUCTS & BIOMATERIALS

Tissue engineering seeks to restore, maintain, improve, or replace damaged tissues and organs through the combination of scaffolds, cells, and/or biologically active molecules.

It often begins with a scaffold, which may use any of a number of potential materials, from naturally occurring proteins from seaweed or biocompatible synthetic polymers.

One method for this is to use an existing scaffold by removing the cells from a donor organ, a process called decellularization, until only the pre-existing protein-based scaffold or extracellular matrix (ECM) remains.

They then add growth factors to encourage the cells to take root, allowing a tissue or organ to develop and grow in the laboratory before it is put into the patient.



MAKING A 3-D PRINTED BLADDER WITH THE PATIENT'S CELLS

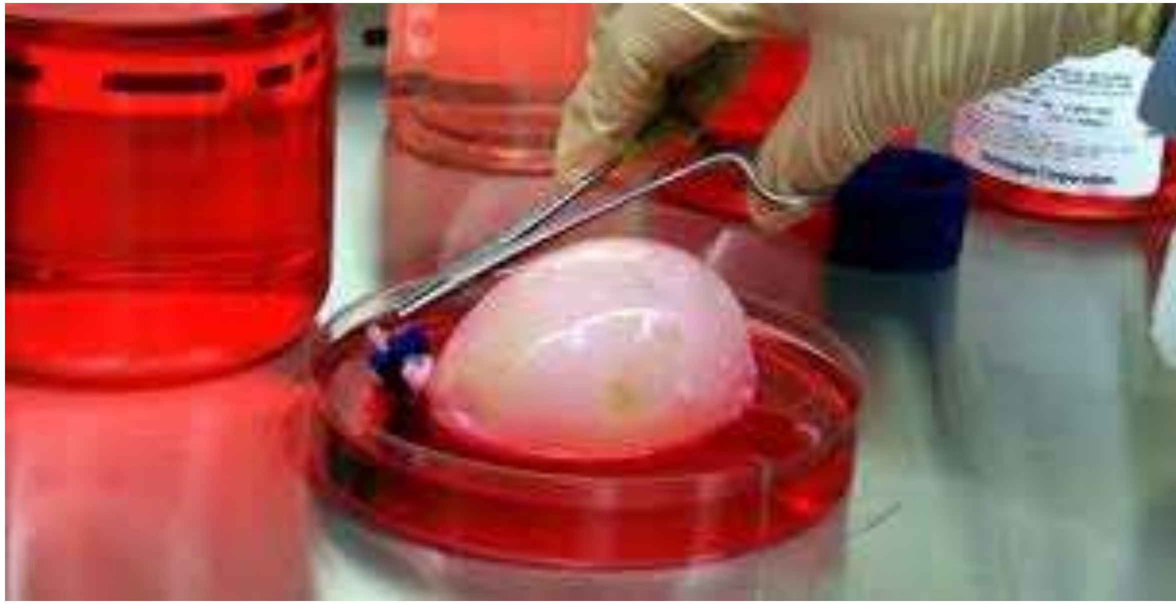
After more than a decade, a 3D bio-printed bladder, created by Dr. Anthony Atala at Boston Children's Hospital, is sustaining the live of a patient.

The 3D bioprinted organ was made to replace patient Luke Massella's defective bladder in 2004. Since then, Massella has not required any further surgery.

The bladder was made using a sample of Massella' bladder tissue, and modified inkjet printer used to build a scaffold/host for the cells.

Incubated in lab condition, the new bladder was grown in 2 months, and then successfully transplanted into the patient.

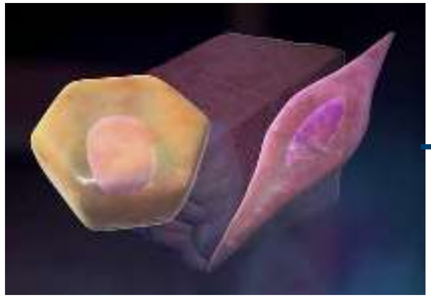
Massella is 1 of 10 people with a bioprinted bladder grown from his own cells.



https://www.youtube.com/watch?v=kpNR7Atvn-A
Go to 4.47 minutes

Neo-bladder – a commercial synthetic bladder

A surgeon takes a small, full-thickness biopsy from the patient's bladder.

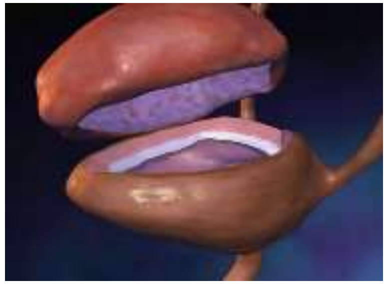


urothelial and smooth muscle cells that are capable of regeneration are isolated.

The isolated cells are cultured separately until there are a sufficient quantity.

The cultured cells are properly seeded onto a biodegradable scaffold shaped like a bladder.

Quality assurance that the cells attach and grow properly throughout the scaffold. After about 8 weeks, the neo-bladder construction is returned to surgeon for implantation



The neo-bladder construct is implanted by the surgeon using standard surgical techniques.

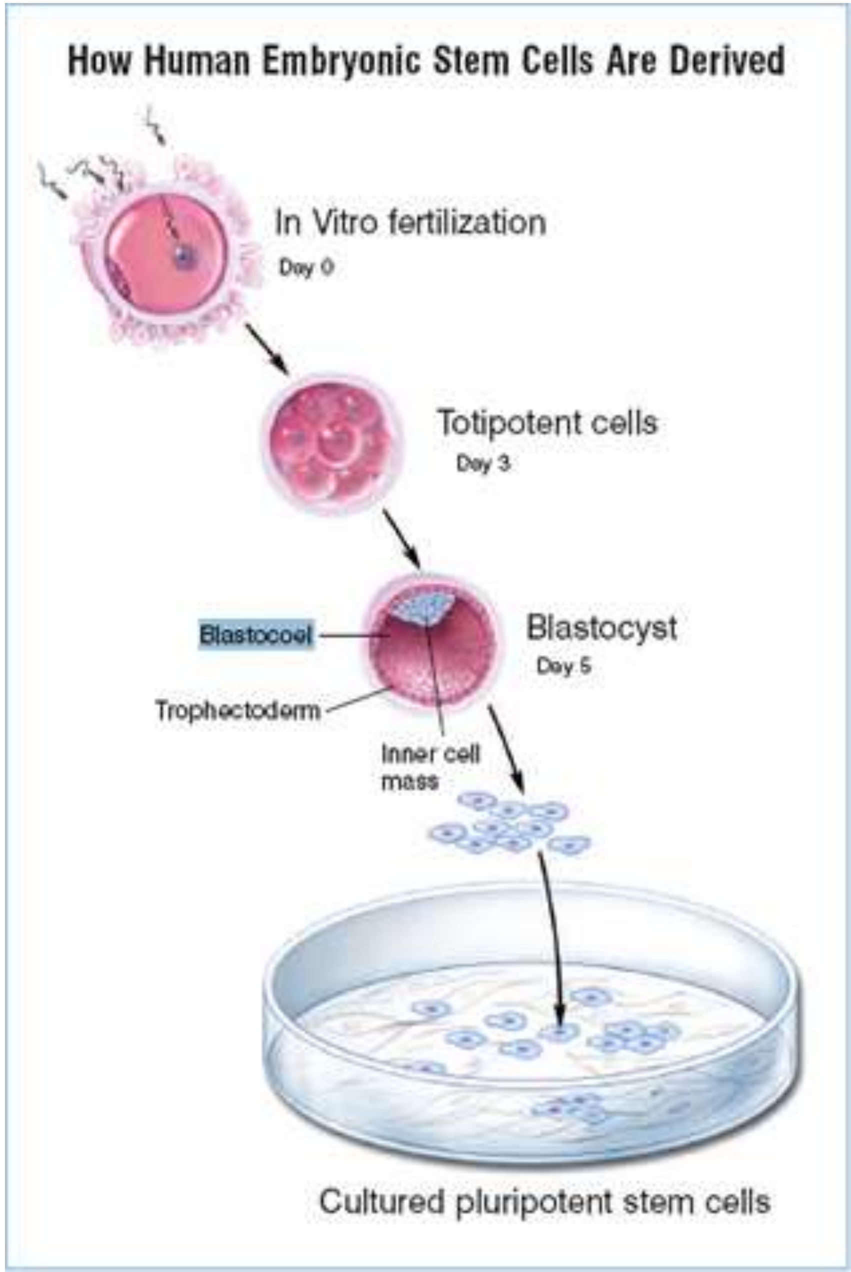
The body uses the neo-bladder construct to regenerate and integrate new tissue, restoring the bladder's functionality.

The biodegradable scaffold dissolves and is eliminated from the body, leaving a functioning bladder made only of the patient's own newly regenerated tissue.

LEGAL REQUIREMENTS FOR USING EMBRYONIC STEM CELLS FOR RESEARCH

The National Institute of Health (NIH) guidelines about the use of are as follows:

1) The Human Embryonic Stem Cells (hESCs) **must be derived from embryos created using an in-vitro fertilization** procedure for reproductive purposes (in a lab dish), **using those that are no longer needed for this purpose.**
2) The donors who sought reproductive treatment have **given written consent f**or the **extra** embryos to be used for research purposes, at the time of donation.
3) **All written consent forms and other documentation must be provided.**
4) Documentation must be provided that all options available to the healthcare facility regarding the embryos in question were explained to the individual who sought reproductive treatment.
5) No payments of any kind can be offered for the donated embryos.
6) Policies and procedures must be in place at the facility where the embryos were donated to ensure that neither donation nor refusal to donate affects quality of care received by the patient.



CRITICS WORRY THAT SOME OF THE TREATMENTS ARE INEFFECTIVE AND DANGEROUS.
HERE'S HOW TO PROTECT YOURSELF.

Currently, stem cell treatments are widely accepted only for only two broad medical indications: to help treat a handful of blood disorders—including leukemia and some forms of anemia—and in some cases to help burn victims.

“Stem cells have taken on this sort of mythic power in people’s minds,” says Sally Temple, Ph.D., a scientist at the Neural Stem Cell Institute in Rensselaer, N.Y. “But there are real limits to what most of these cells can actually do.”

With few consumer protections in place, scientists and federal regulators are increasingly worried about unscrupulous doctors exploiting the capabilities of Stem Cell therapies, for profit.

As evidence of stem cell therapy’s potential grows, so does confusion over what this emerging medicine can and can’t do.

Across the country, clinics are promoting stem cell therapies for a long list of conditions, including joint injuries, sexual dysfunction, COPD, lupus, and diabetes.

These treatments are rarely covered by insurance, and they can cost thousands of dollars. None of them have been proved to work. Some have proved to be dangerous.

THE FDA, THE INTERNATIONAL SOCIETY FOR STEM CELL RESEARCH, AND MEDICAL EXPERTS ADVISE YOU TO BE CAUTIOUS WHEN CONSIDERING STEM CELL THERAPY.

1) BEWARE OF THE HYPE AND HEFTY FEES.

Doctors testing stem cell treatments in carefully controlled clinical trials usually don’t promote their offerings with big, flashy advertisements that promise dramatic improvements or total cures.

They also don’t charge a lot - the treatment itself should be low-cost to participants.

“A large price tag—especially in the range of thousands of dollars—should be a major red flag,” says Marvin M. Lipman, M.D., Consumer Reports’ chief medical adviser.

So should any doctor claiming to treat a wide range of medical conditions, such as autism, arthritis, and erectile dysfunction, with the same therapy.

Different organs and body systems require different expertise—and different medicine—to treat, which is why most doctors specialize.

2) ASK QUESTIONS

Any doctor who offers stem cell therapy should be able to explain where the cells will come from, what will be done to them before they’re injected into your body, and how, exactly, they will resolve your illness or injury.

He or she should also be able to offer you proof of safety and efficacy, even for experimental treatments.

Don’t settle for patient testimonials.

Ask how many people the proposed therapy has been tested on (the more the better) and whether those tests were done in clinical trials or as individual case studies. (Randomized controlled trials, where people given a treatment are compared with a control group that wasn’t, are best.)

It’s also important to find out what the outcomes were. (Ideally, side effects were minimal and significantly more people improved, than did not.)

3) READ THE FINE PRINT

If the treatment is being offered as a clinical trial, make sure the trial has been vetted by the FDA, a process known as securing investigative new drug (IND) approval.

The agency advises that you ask to see the actual approval letter to make sure it has been issued specifically for the treatment you're considering.

Treatments that have cleared this hurdle are much more likely to be safe than those that have not.

You should also make sure that any informed consent document (an explanation of the experimental treatment that study participants are usually asked to sign) provides a clear description of the treatment being offered along with the risks, alternative options, and details about what to expect in the days and weeks after the procedure.

It should not indemnify doctors or their institutions against liability for negligence.

https://www.consumerreports.org/medical-treatments-procedures/trouble-with-stem-cell-therapy/

THE END

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