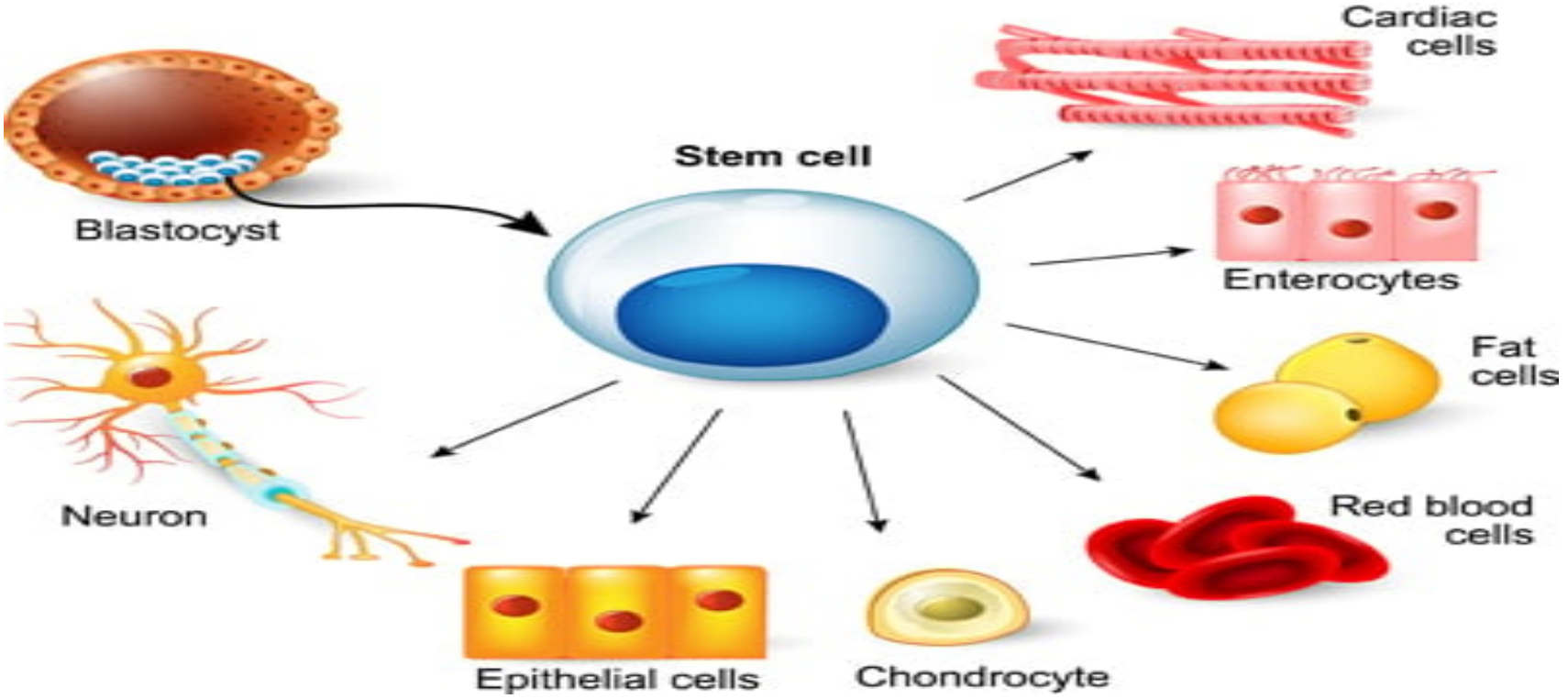
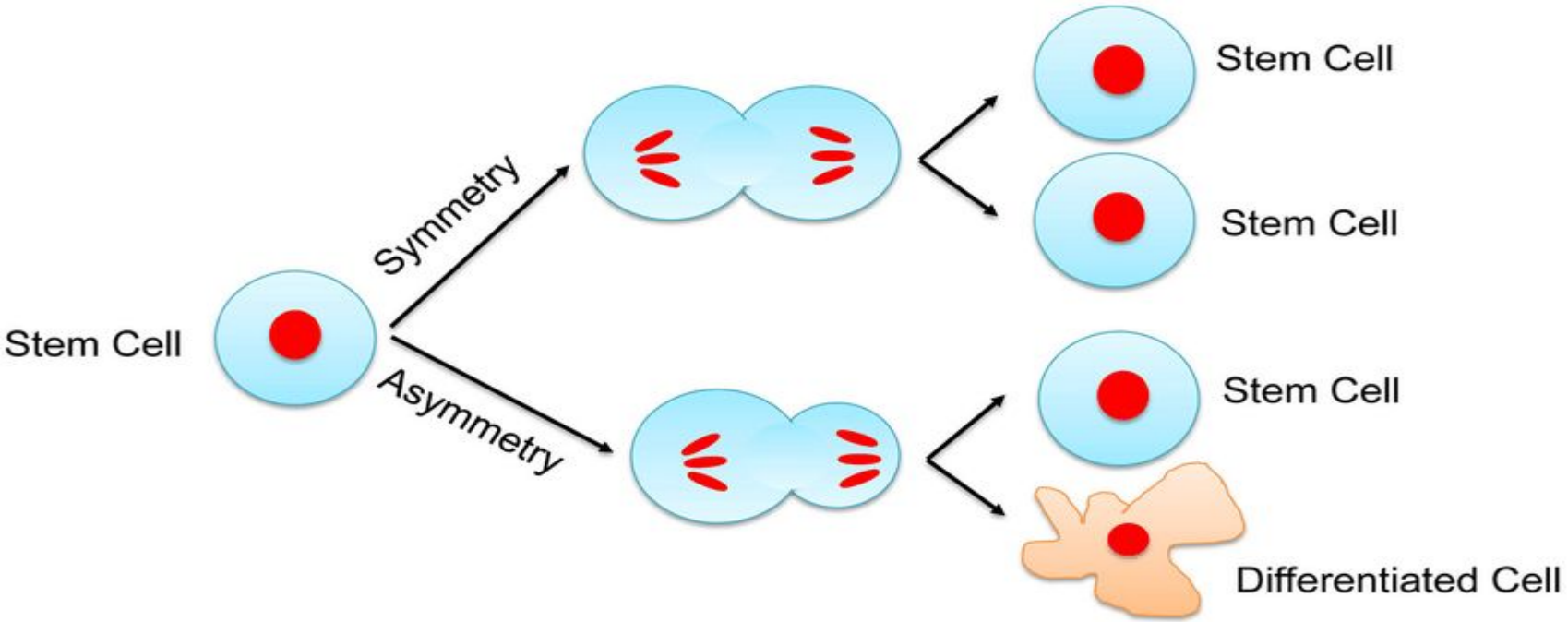
STEM CELLS

INTRODUCTION

Stem cells are a special kind of cell that have the ability to divide indefinitely and have the potential to give rise to specialized cells (any cell of the body).



Unique properties of all stem cells



1. Stem cells are unspecialized

One of the fundamental properties of stem cells is that it does not have any tissue specific structures that allow it to perform specialized function.

2. Proliferation

They are capable of dividing and renewing themselves for indefinite periods

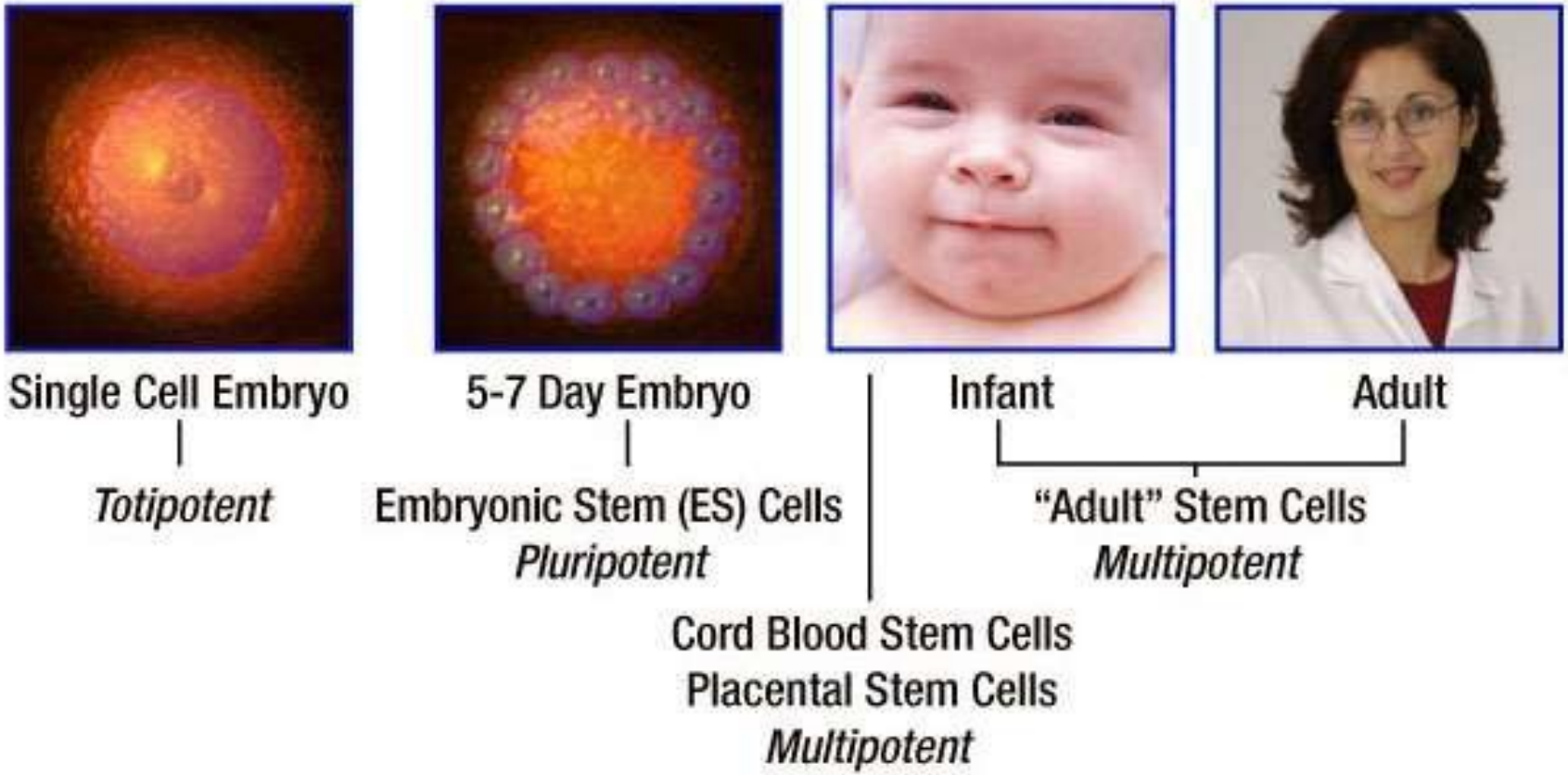
3. Differentiation

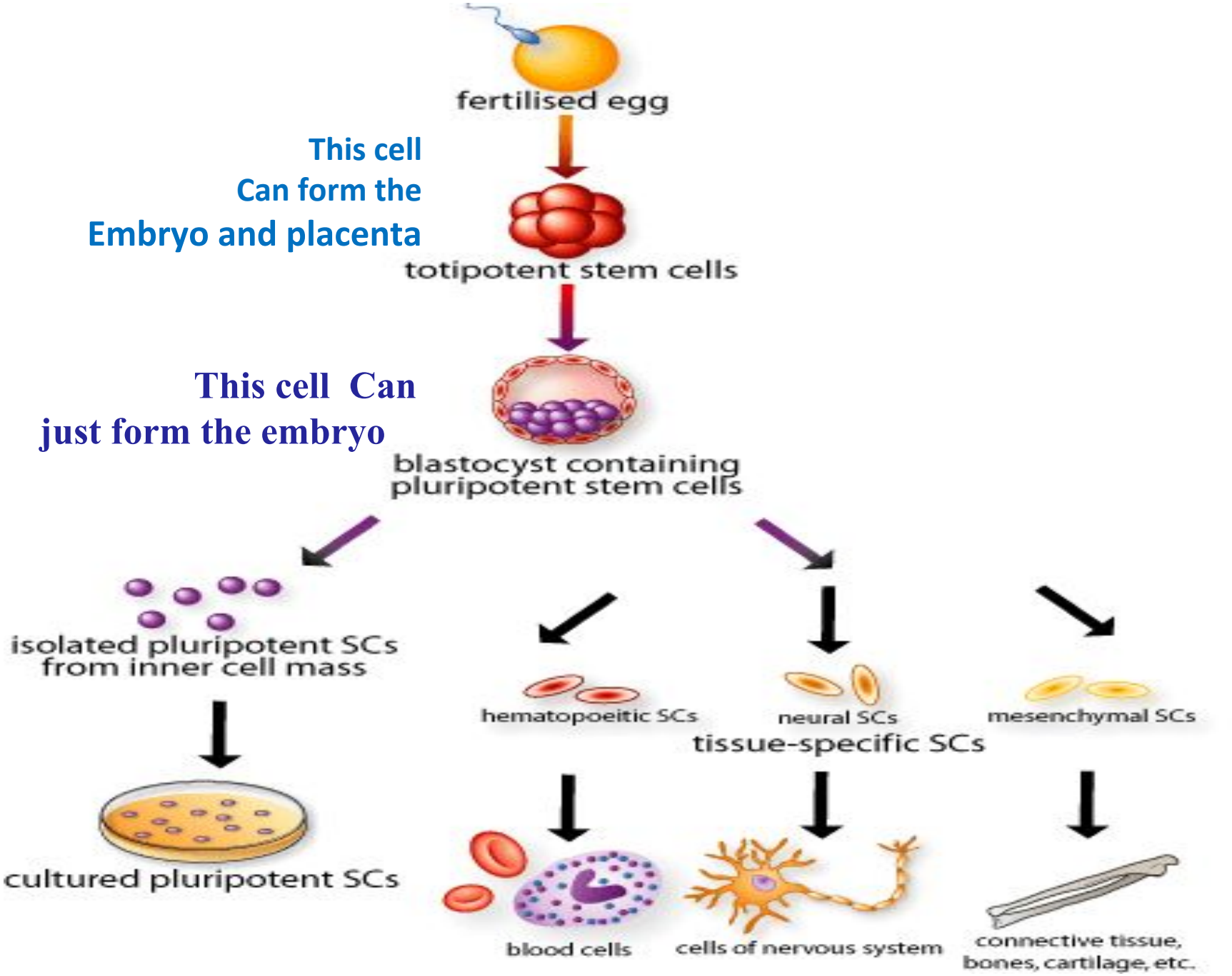
They can give rise to specialized tissue. Under certain **physiological** and **experimental conditions** unspecialized cell can give rise to specialized cells such as including heart muscle cells, blood cells or nerve cells required to repair damaged or depleted adult cell population or tissue.

4. Plasticity

Stem cell from one tissue may be able to give rise to cell types of completely different tissue , a phenomenon known as plasticity. e.g. Blood cells becoming neuron, liver cells producing insulin and haematopoietic

Stem cell Types



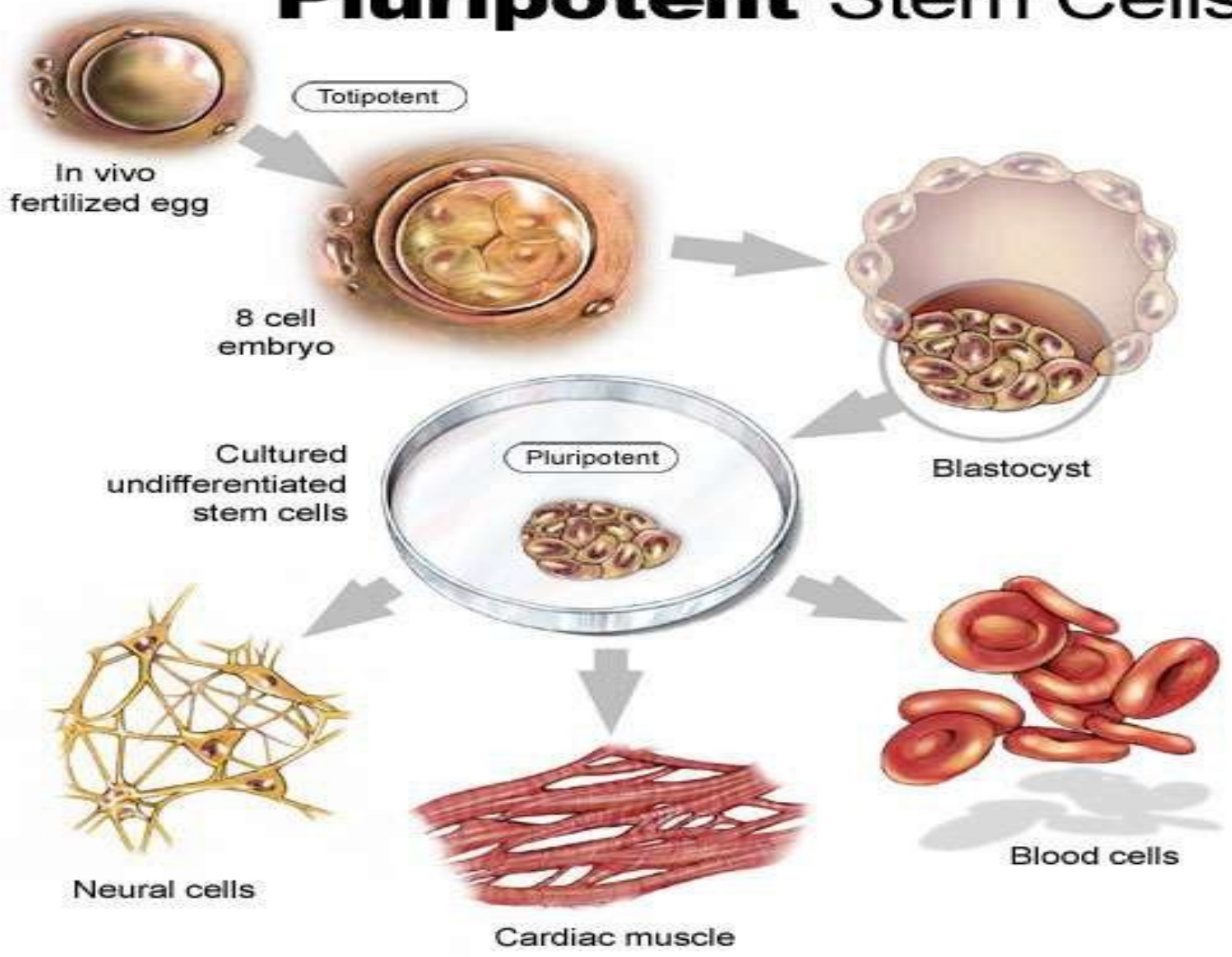

fertilised egg
This cell
Can form the
Embryo and placenta
totipotent stem cells
This cell Can
just form the embryo
blastocyst containing
pluripotent stem cells
isolated pluripotent SCs
from inner cell mass
cultured pluripotent SCs
hematopoeitic SCs
neural SCs
mesenchymal SCs
tissue-specific SCs
blood cells
cells of nervous system
connective tissue,
bones, cartilage, etc.

Pluripotent/embryonic stem cells

Pluripotent stem cells: These are true stem cells, with the potential to make any differentiated cell in the body (but probably not those of the placenta which is derived from the trophoblast).

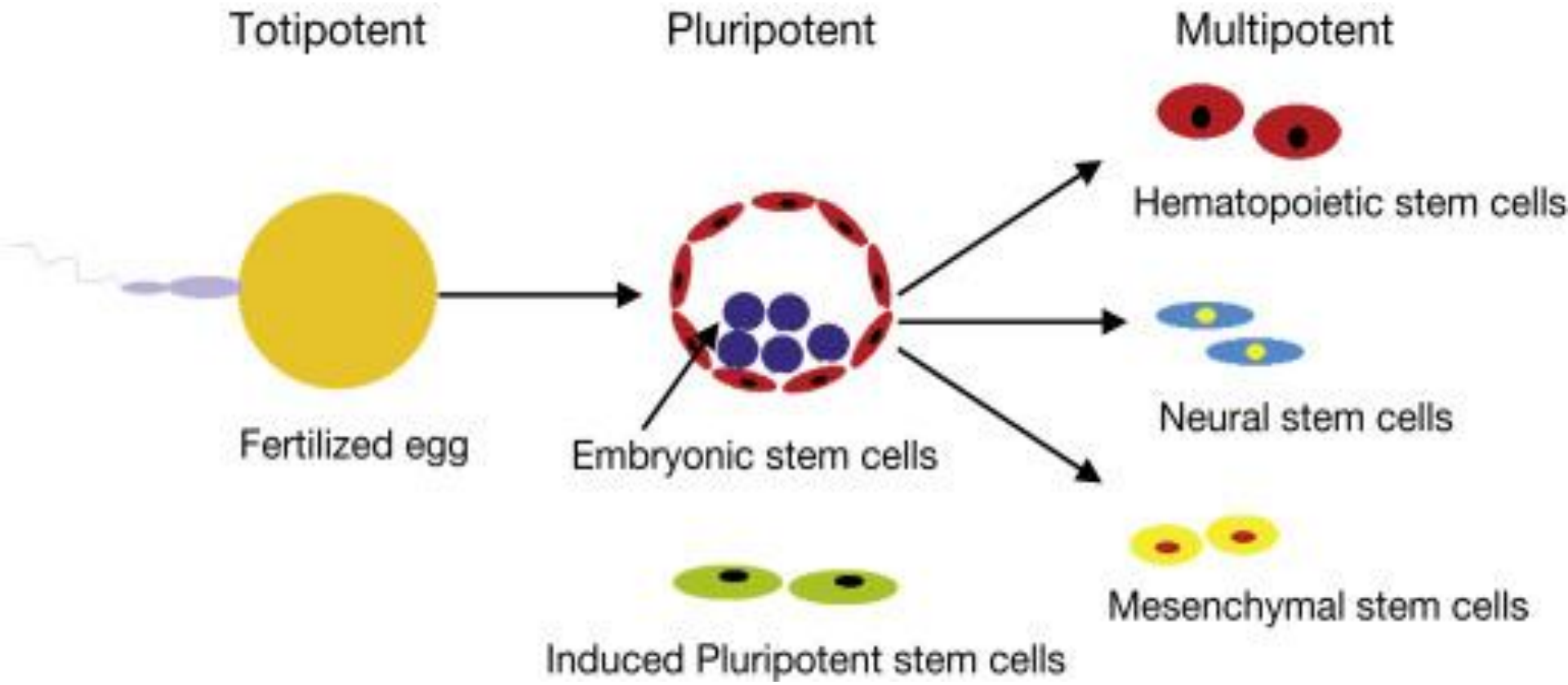
- Human ES cells are derived from 4-5 day old blastocyst
- Blastocyst structures include:
  - Trophoblast: outer layer of cells that surrounds the blastocyst & forms the placenta
  - Blastocoel: ("blastoseel") the hollow cavity inside the blastocyst that will form body cavity
  - Inner cell mass: a group of approx. 30 cells at one end of the blastocoel:

Pluripotent Stem Cells



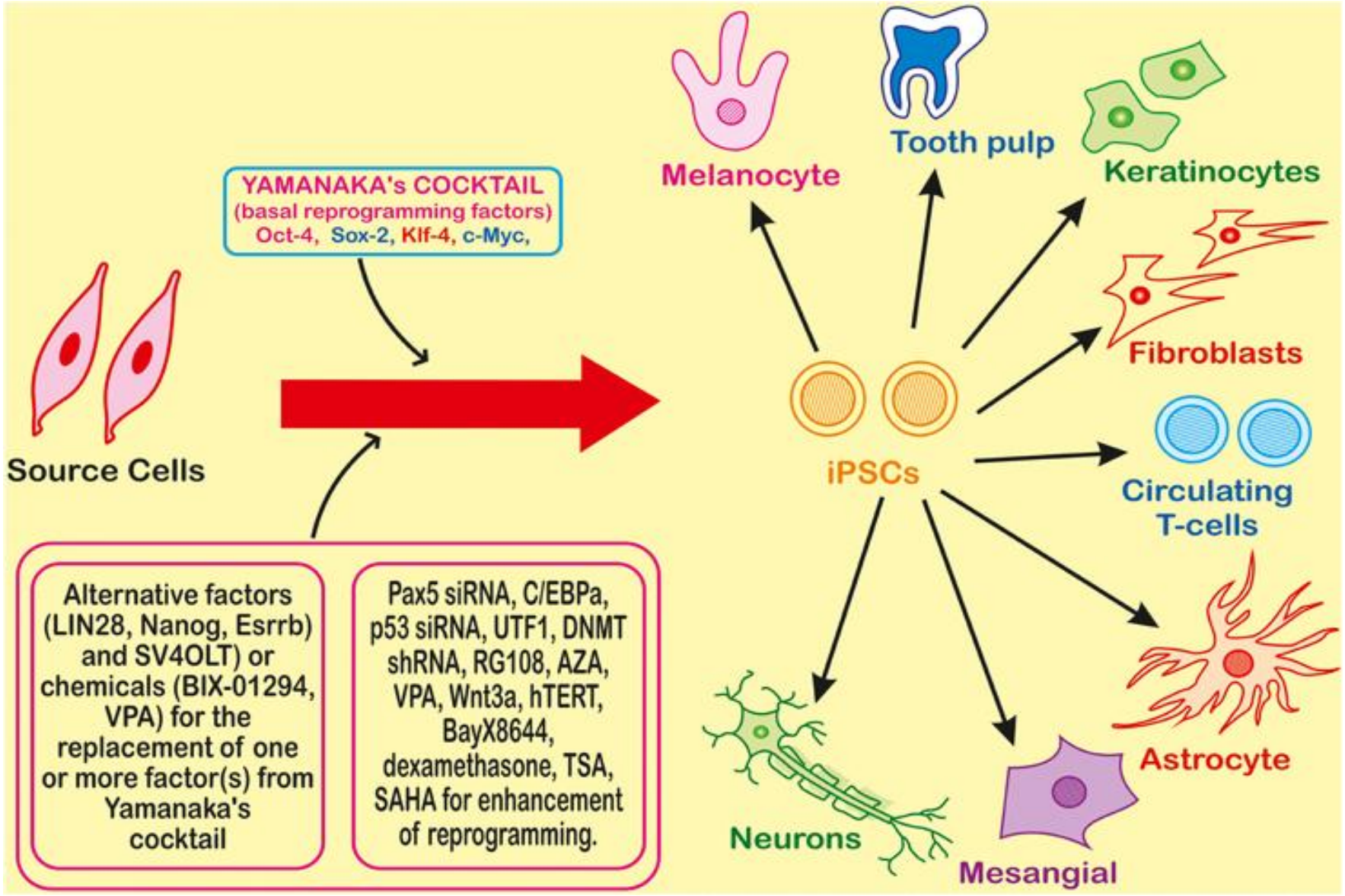
Multipotent /Adult stem cells

- These stem cells can only differentiate into a limited number of types.
  - For example, the bone marrow contains multipotent stem cells that give rise to all the cells of the blood but not to other types of cells.
- Multipotent stem cells are found in adult animals; perhaps most organs in the body (e.g., brain, liver) contain them where they can replace dead or damaged cells.
  - Haematopoietic stem cells – form all type of blood cells
  - Stromal cells – can generate cartilage, fat, and fibrous connective tissue
  - Brain stem cells – astrocytes , oligodendrocytes and neurons


Totipotent
Pluripotent
Multipotent
Hematopoietic stem cells
Neural stem cells
Mesenchymal stem cells
Fertilized egg
Embryonic stem cells
Induced Pluripotent stem cells

INDUCED PLURIPOTENT STEM CELLS

- iPSCs are the cells which are reprogrammed from somatic cells using different transcription factors.
- iPSCs possess unique properties of self renewal and differentiation to many types of cell lineage.
- Could replace the use of embryonic stem cells (ESC), and may overcome the various ethical issues
- Generated by using a combination of 4 reprogramming factors, including Oct4 (Octamer binding transcription factor-4), Sox2 (Sex determining region Y)-box 2, Klf4 (Kruppel Like Factor-4), and c-Myc and were demonstrated both self-renewing and differentiating like ESCs



Introduction of the four transcription factors (Oct-4, Sox-2, Klf-4, and c-Myc) leads to reprogramming of a somatic cell to an Induced Pluripotent Stem Cell (iPSC) which can further differentiate into different types of cel

Potential Applications

- Basic research
  events that occur during human development & understanding molecular basis of cancer
  - Molecular mechanisms for gene control
  - Role of signals in gene expression & differentiation of the stem cell
  - Stem cell theory of cancer

- Biotechnology (drug discovery & development) –

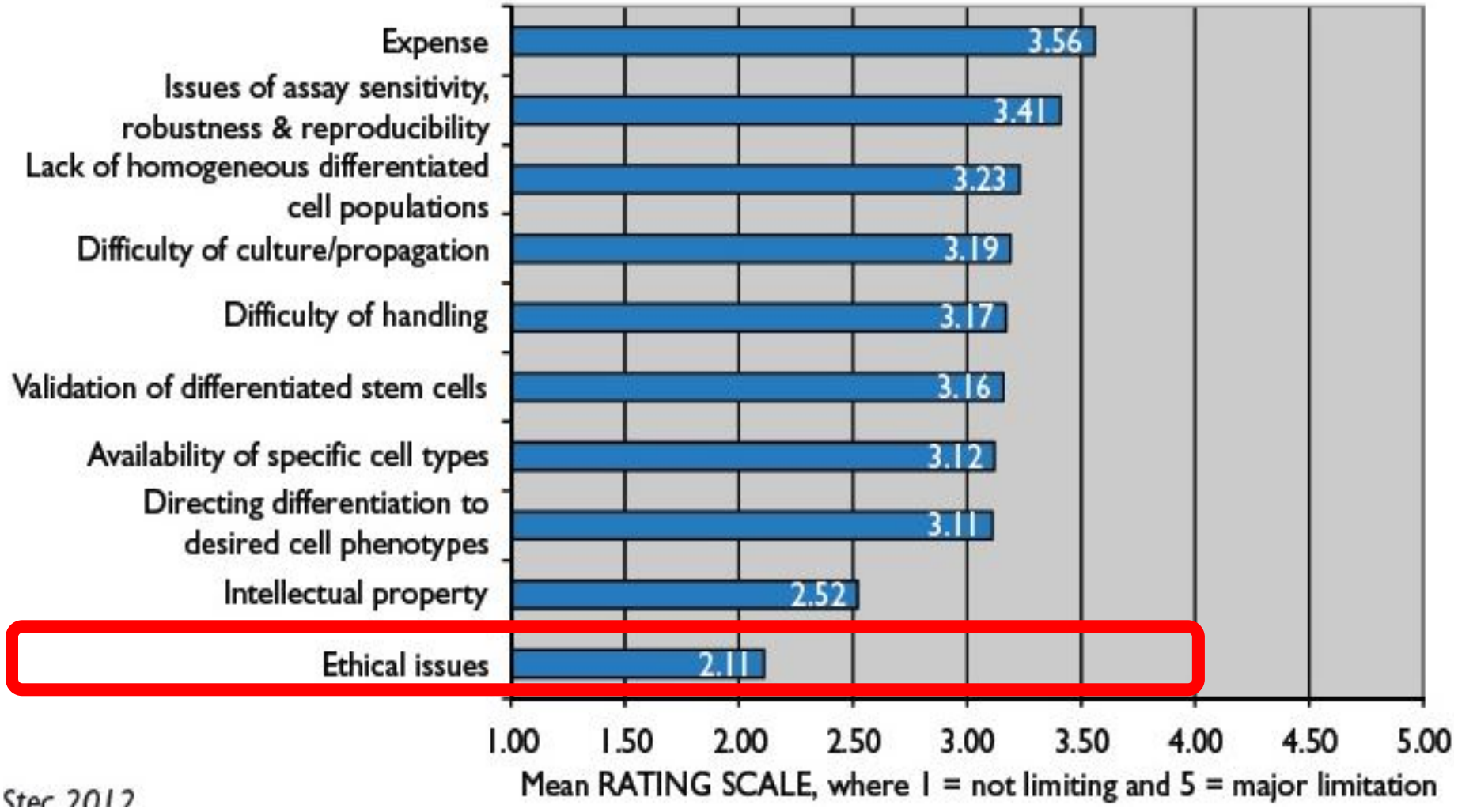
  stem cells can provide specific cell types to test new drugs

  - Safety testing of new drugs on differentiated cell lines.
  - Screening of potential drugs

- Cell based therapies:
  - Regenerative therapy to treat
    - Parkinson's,
    - Alzheimer's,
    - ALS,
    - spinal cord injury,
    - severe burns,
    - heart disease,
    - diabetes,
    - rheumatoid arthritis

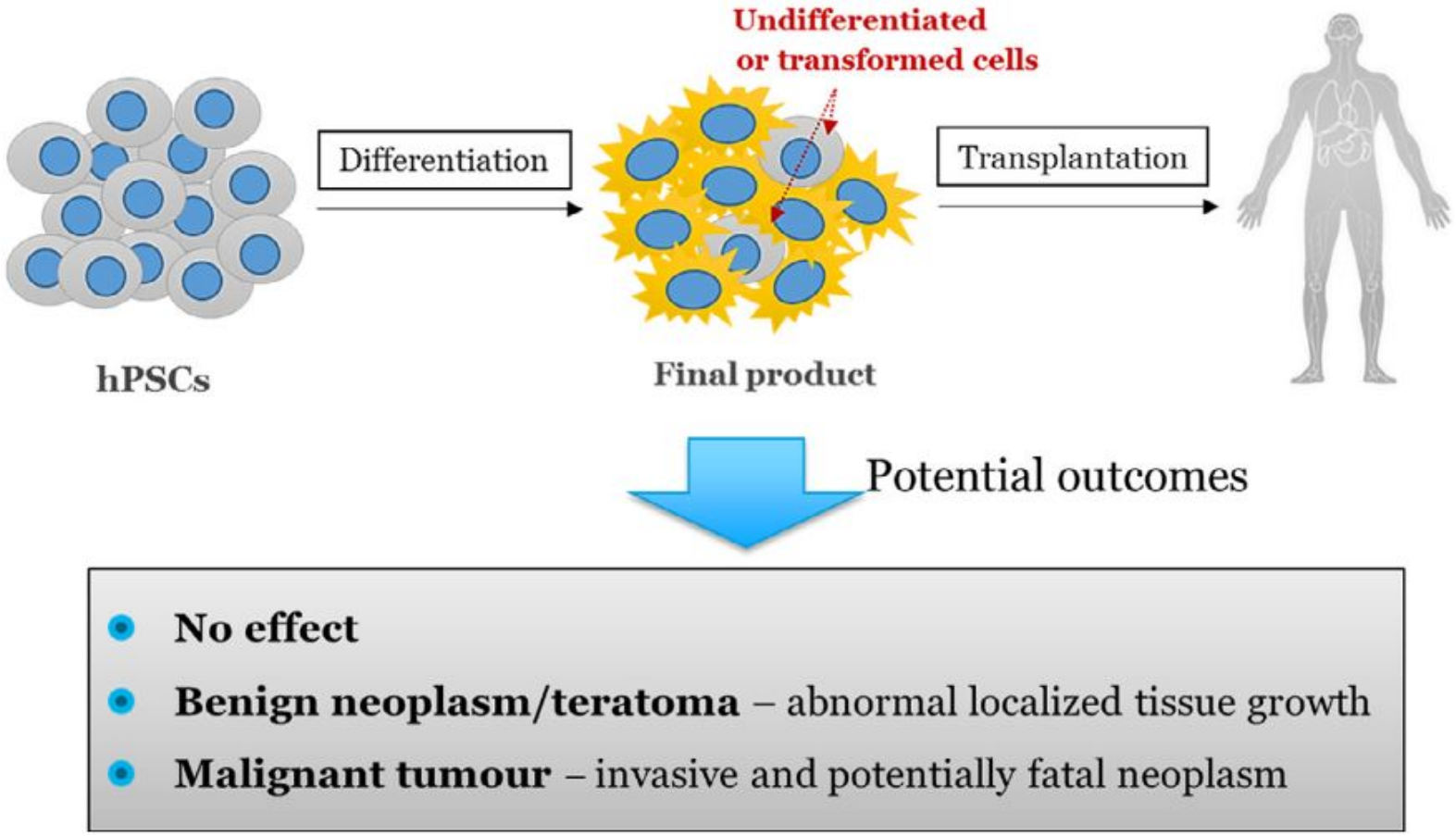
Ethical Issues of Stem Cells

Main Obstacles in Stem Cell Research



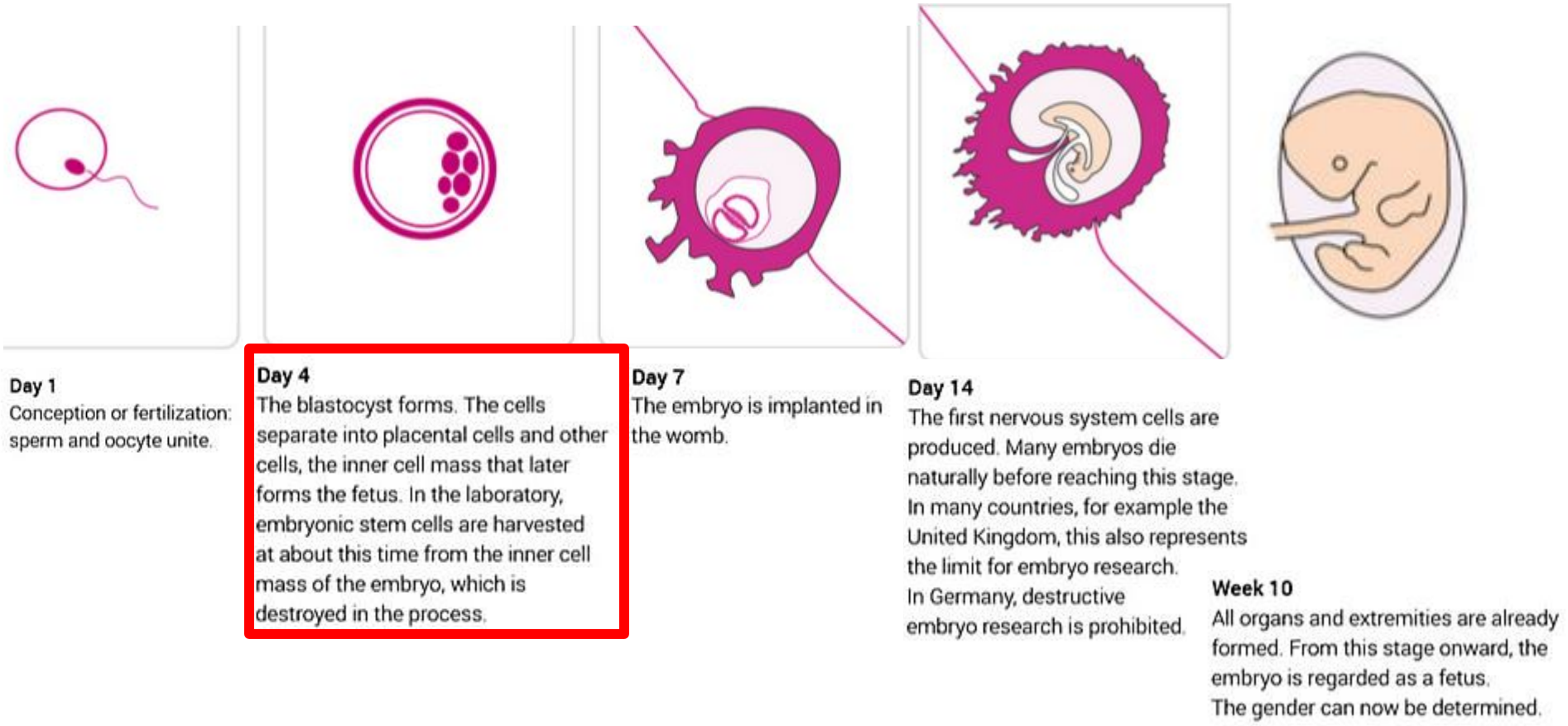
Stec 2012

Ethical Concerns PSCs - Tumorigenicity



- If a few residual, undifferentiated hPSCs persist in the final Cell Therapy Products, these could initiate tumor development in transplanted patients
- *In vivo* tumorigenicity assay, in which cells are implanted at an ectopic site (eg, subcutaneously, under the kidney capsule or testis capsule) in immunodeficient mice and monitored for the formation of tumor masses.

Ethical Concerns of ESCs – Moral Status of the Inner Cell Mass of the Blastocyst and the Fetus



- The ethical debate about making new ESC lines out of spare blastocysts from fertility clinics is primarily due to a disagreement of how blastocysts should be treated. Some people see destroying blastocysts as killing human life.
- At what point does humanness or personhood start in the developing human embryo or foetus?

Ethical Concerns – Accessibility to Stem Cell Therapy and Commercialization

- Who will and will not benefit from ESC-based treatments e.g. ESC-based treatments may not be accessible or affordable for poor people and poor countries.
- Private sectors usually tend to allocate their resources to fields with high potential of financial gain. Private research can raise concerns about commercialization of stem cell research, which may result in unfair distribution of benefits within society.

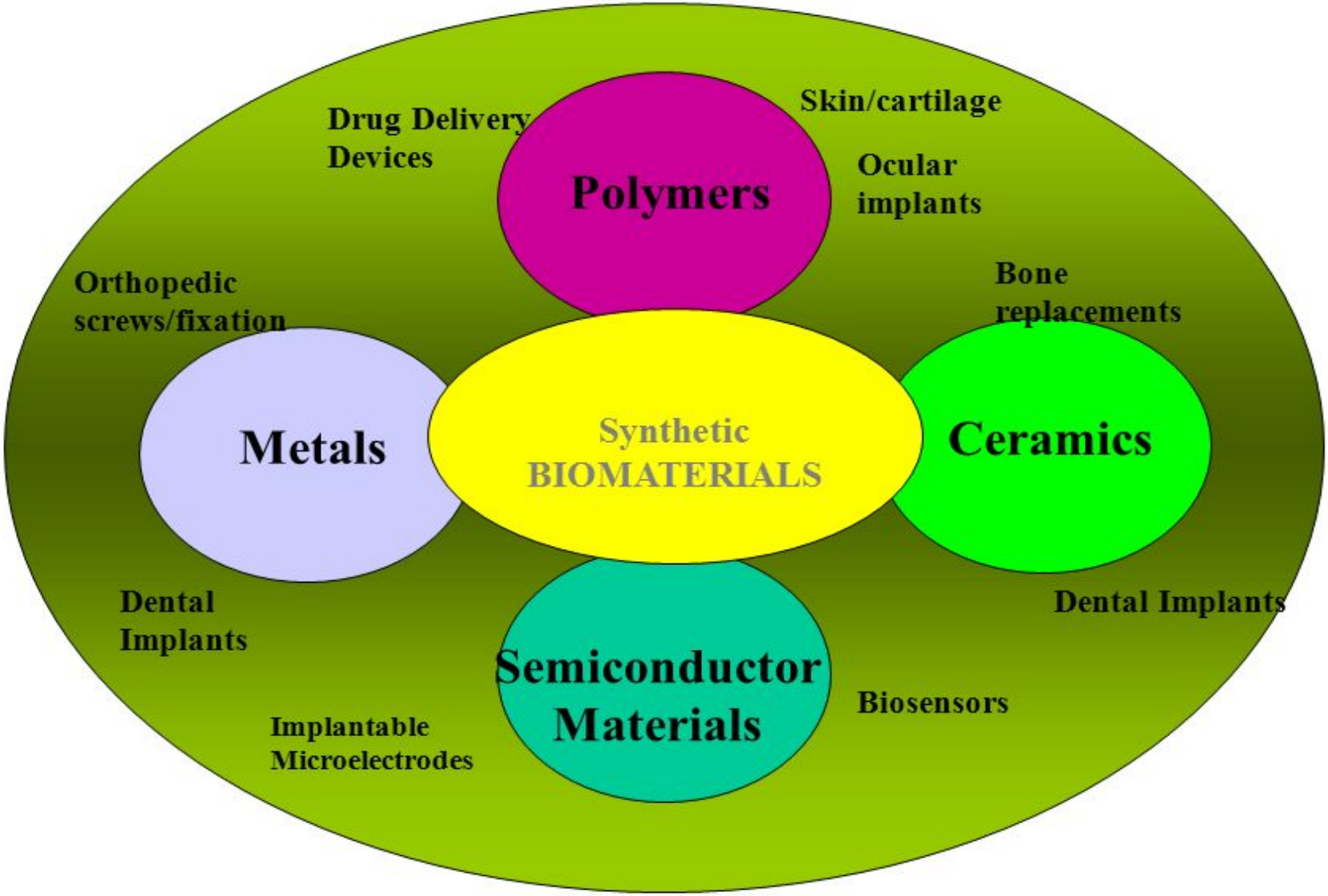
Biomaterials and Tissue Engineering

Biomaterials

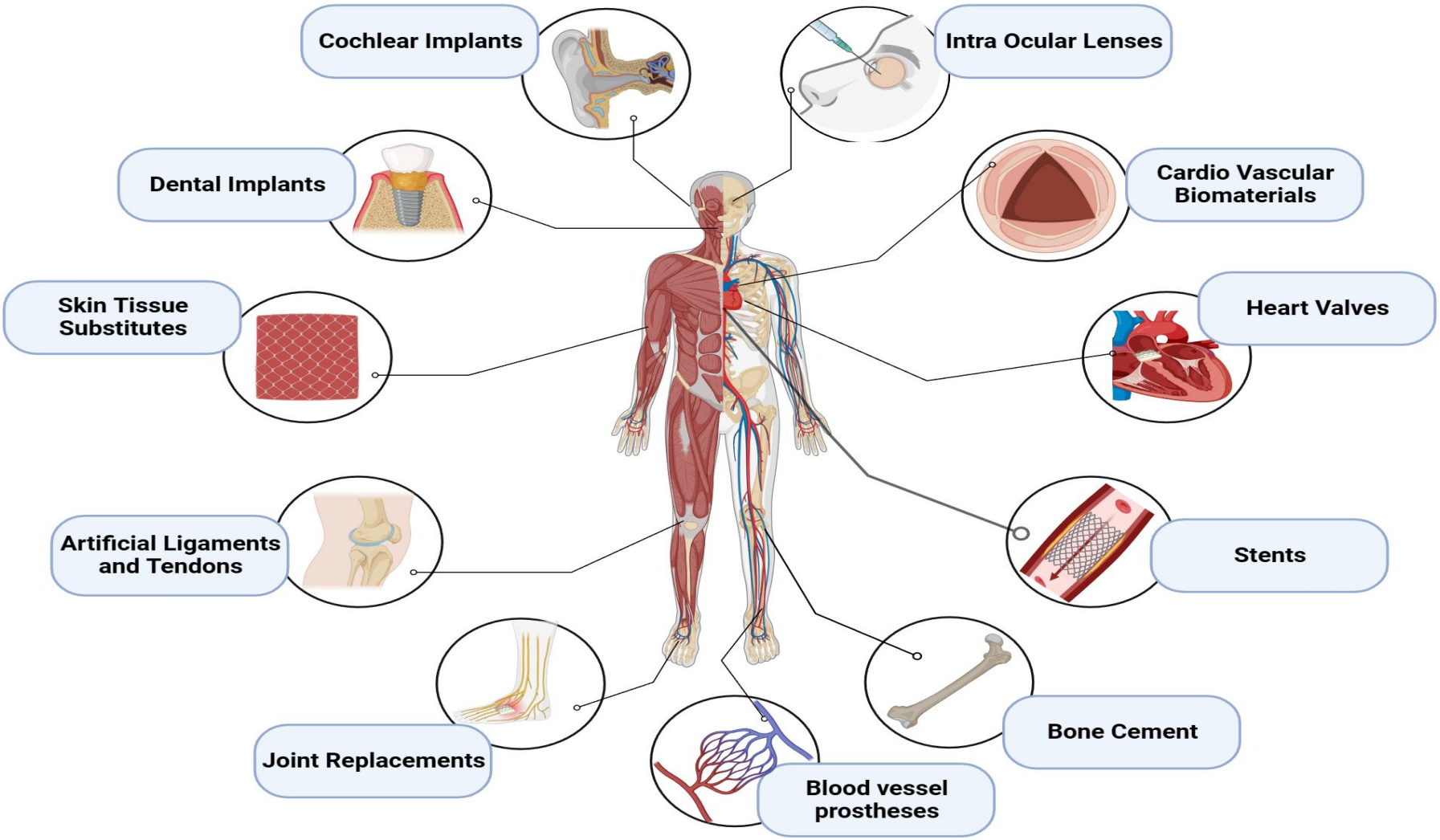
- Any substance (other than drugs) or combination of substances synthetic or natural in origin, which can be used for any period of time, as a whole or as a part of a system which treats, augments, or replaces any tissues, organ, or function of the body

- Biomaterials Properties
  - Biocompatible-Able to perform within appropriate host response without having toxic or injurious effects on biological system
  - Adequate mechanical performance-Has appropriate mechanical performance suitable for its application
  - Repeatable fabrication- Relatively inexpensive, reproducible, easy to fabricate and process for large-scale production

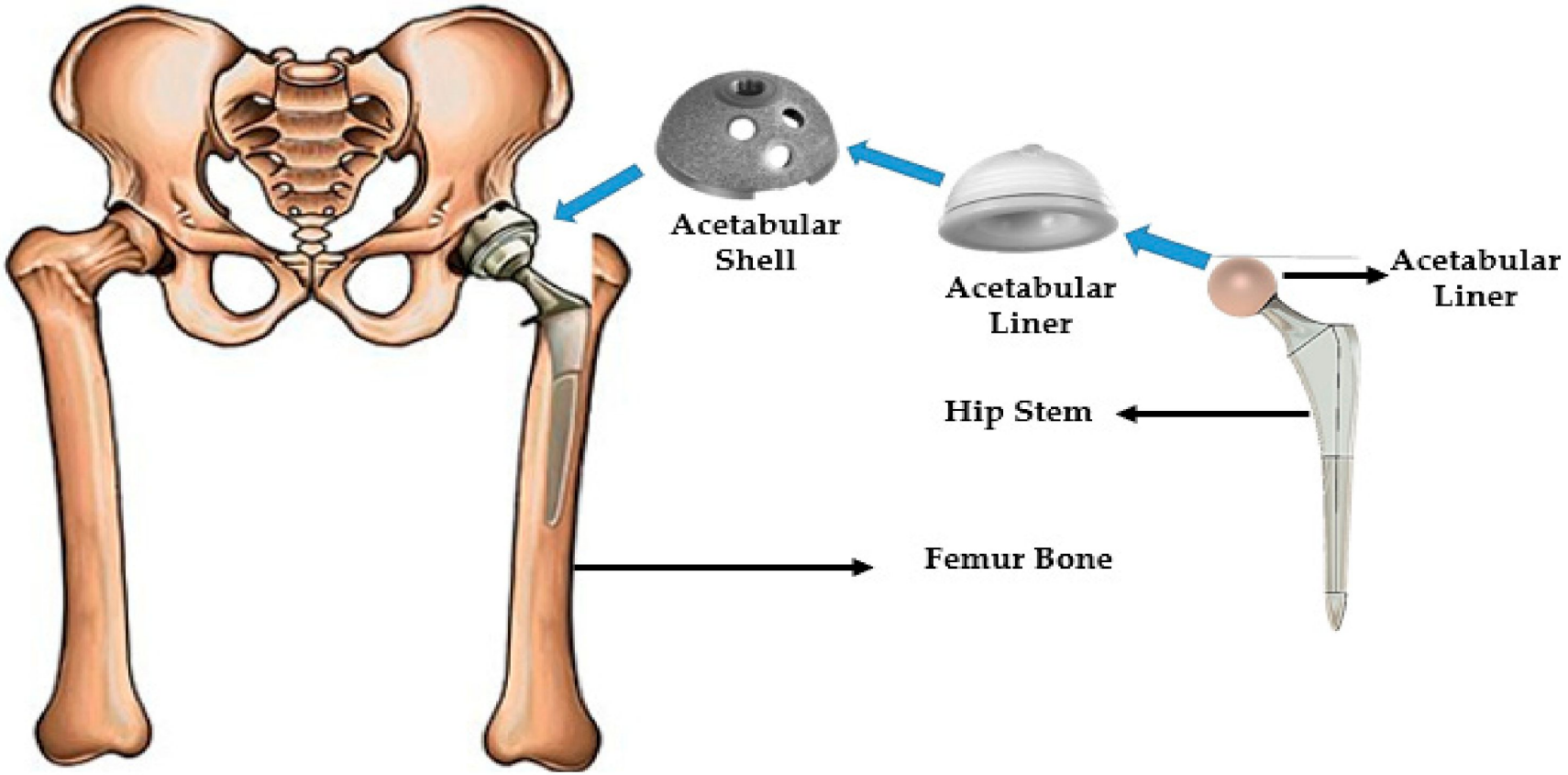
CLASSIFICATION OF BIOMATERIALS



Applications of biomaterials



Hip joint prosthesis



Examples of polymers used as biomaterials

Application	Polymer
Knee, hip, shoulder joints	Ultrahigh molecular weight polyethylene
Finger joints	Silicone
Sutures	Polylactic and polyglycolic acid, nylon
Tracheal tubes	Silicone, acrylic, nylon
Heart pacemaker	polyethylene, polyurethane
Blood vessels	Polyester, polytetrafluoroethylene, PVC
Bone cement	Polymethyl methacrylate

Ceramics uses

- Alumina : Joint replacement, dental implants
- Zirconia: Joint replacement
- Calcium phosphates: Bone repair and augmentation, surface coatings on metals
- Bioactive glasses: Bone replacement
- Porcelain: Dental restorations

Metals uses

- 316L stainless steel: Fracture fixation, stents,
- CP-Ti, Ti-Al-V, Ti-Al-Nb, Ti13Nb-13Zr, Ti-Mo-Zr-Fe : Bone and joint replacement, fracture fixation, dental implants, pacemaker encapsulation
- Co-Cr-Mo, Cr-Ni-Cr-Mo: Bone and joint replacement, dental implants, dental restorations, heart valves
- Ni-Ti: Bone plates, stents, orthodontic wires Gold alloys Dental restorations
- Silver products: Antibacterial agents