

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ



Regenerative Medicine & stem cell therapy for the Elderly

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Regenerative Medicine

The term regenerative medicine has been used to describe a relatively new branch of medicine whose focus is the restoration of normal function in tissues that are damaged or lost due to age, disease, injury, or congenital defects. Regenerative medicine efforts have shown promise in the treatment of both acute injuries and chronic disease across multiple organ systems.

Stem Cell – Definition

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

Stem Cell Characteristics

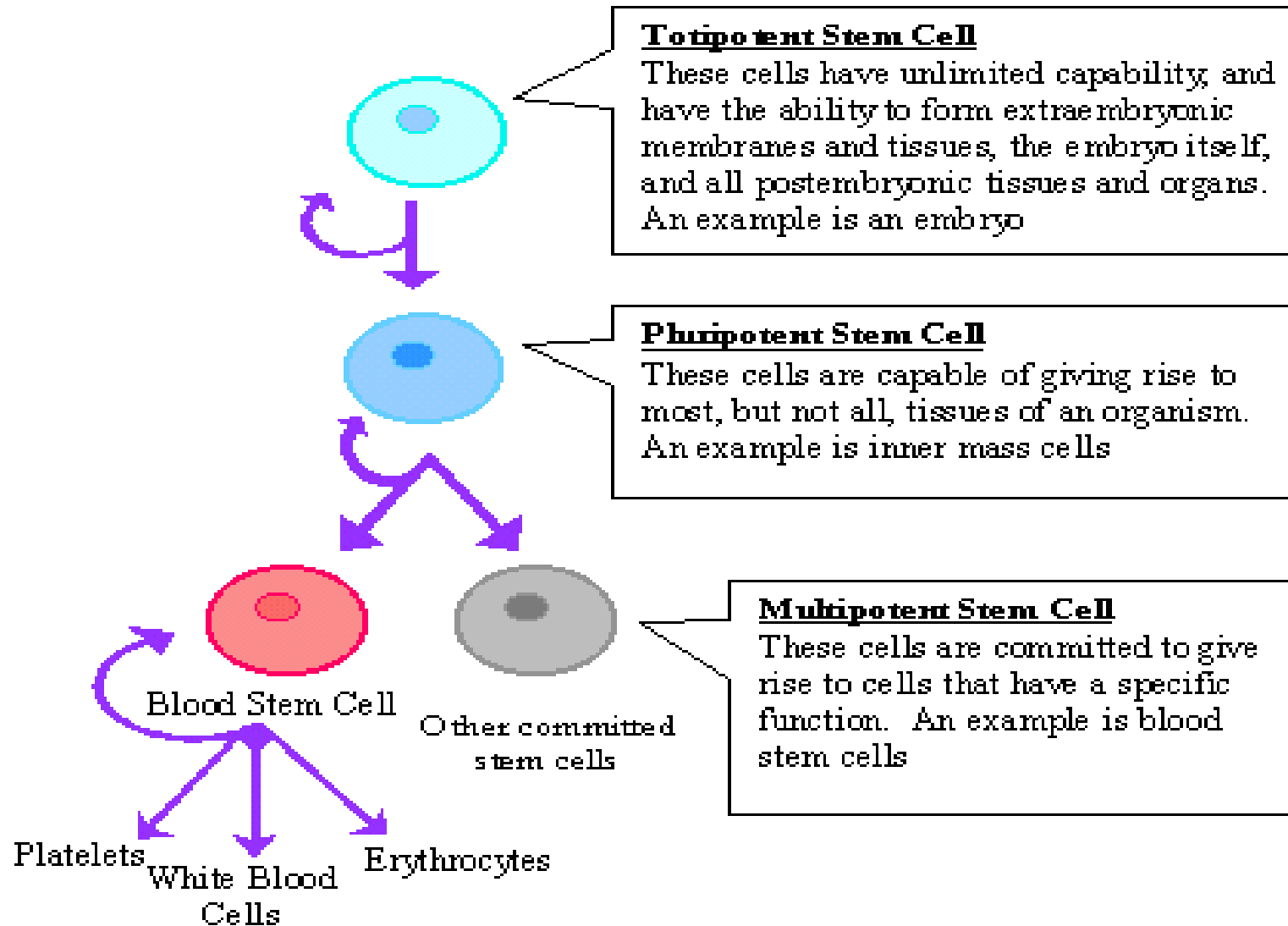
- **‘Blank cells’ (unspecialized)**
- **Capable of dividing and renewing themselves for long periods of time (proliferation and renewal)**
- **Have the potential to give rise to specialized cell types (differentiation)**

- Self renewable: a cell that has the ability to continuously divide
- Pluripotent: ability to develop into several different kinds of cells/tissues
- Repair: ability to return function to damaged cells in the living organism

Kinds of Stem Cells

Stem cell type	Description	Examples
Totipotent	Each cell can develop into a new individual	Cells from early (1-3 days) embryos
Pluripotent	Cells can form any (over 200) cell types	Some cells of blastocyst (5 to 14 days)
Multipotent	Cells differentiated, but can form a number of other tissues	Fetal tissue, cord blood, and adult stem cells

Stem Cell Differentiation



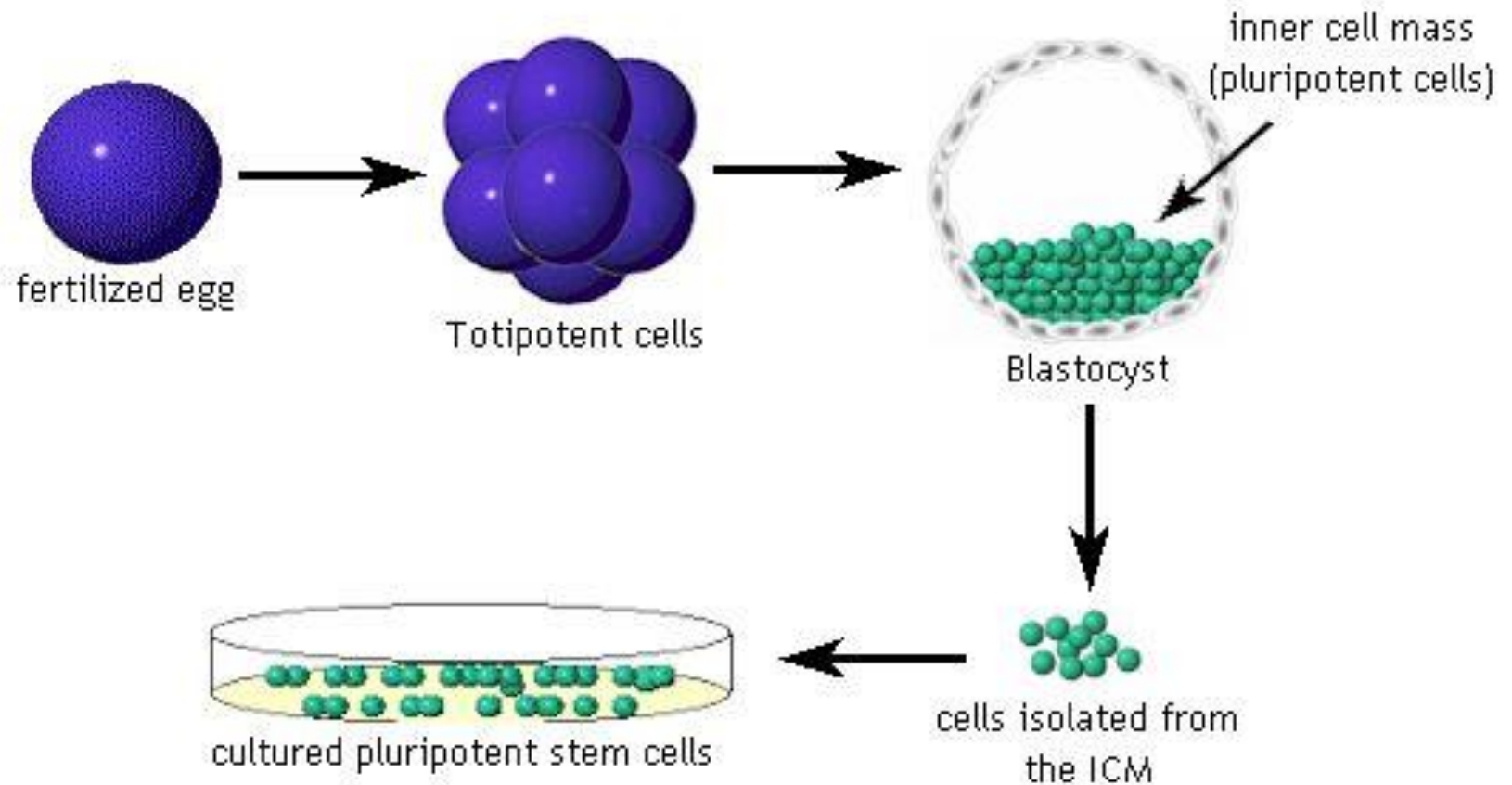
Kinds of Stem Cells

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.

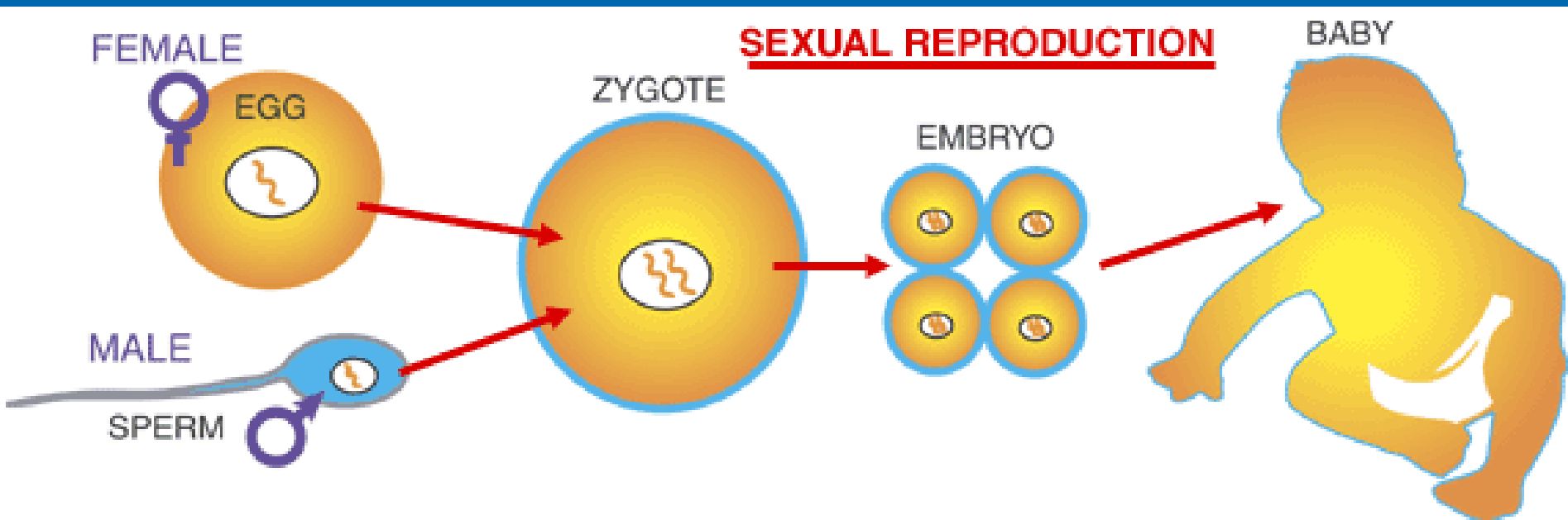
Embryonic germ cells are derived from the part of a human embryo or fetus that will ultimately produce eggs or sperm (gametes).

Adult stem cells are undifferentiated cells found among specialized 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.

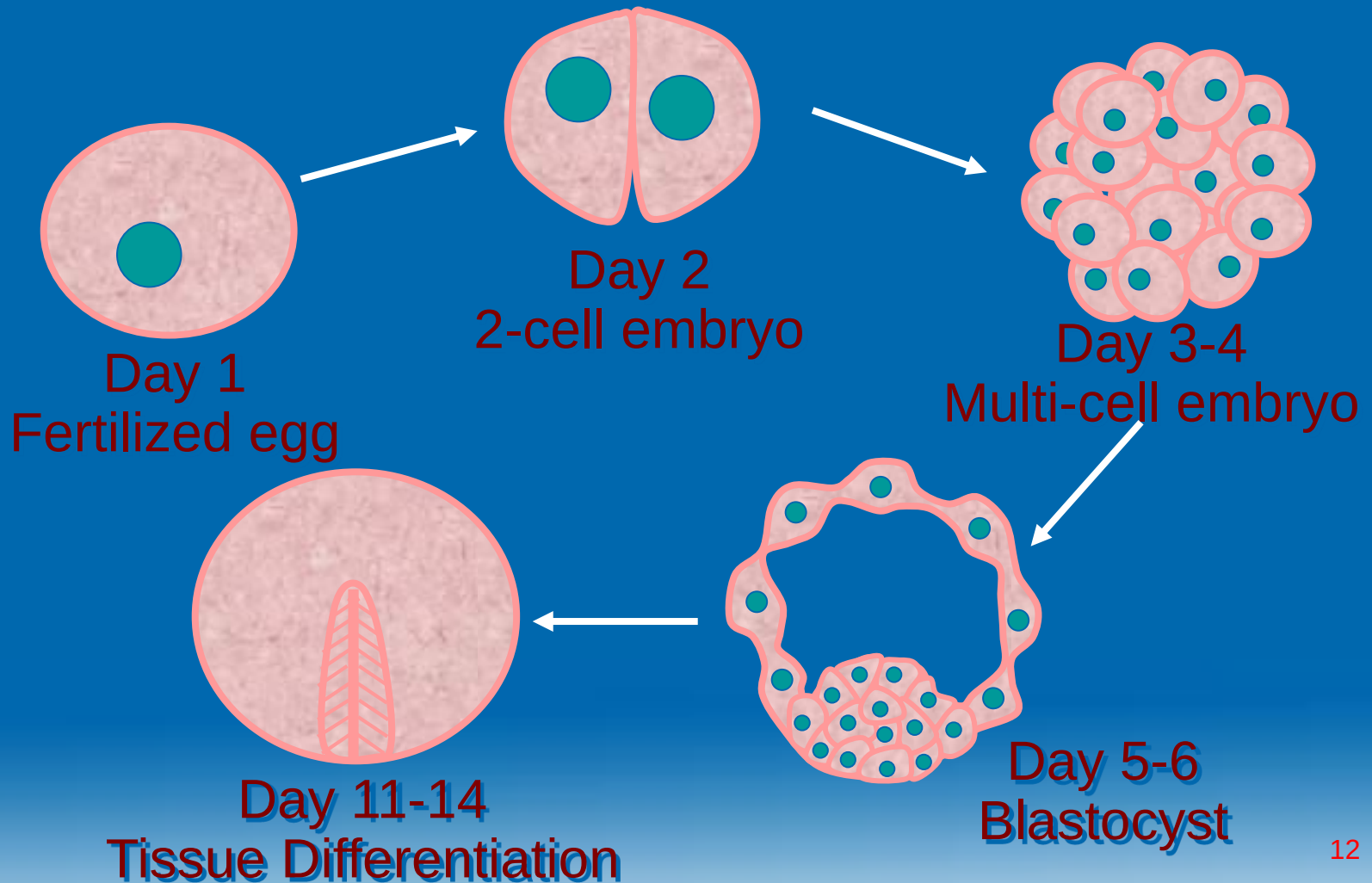
Blastocyst Diagram



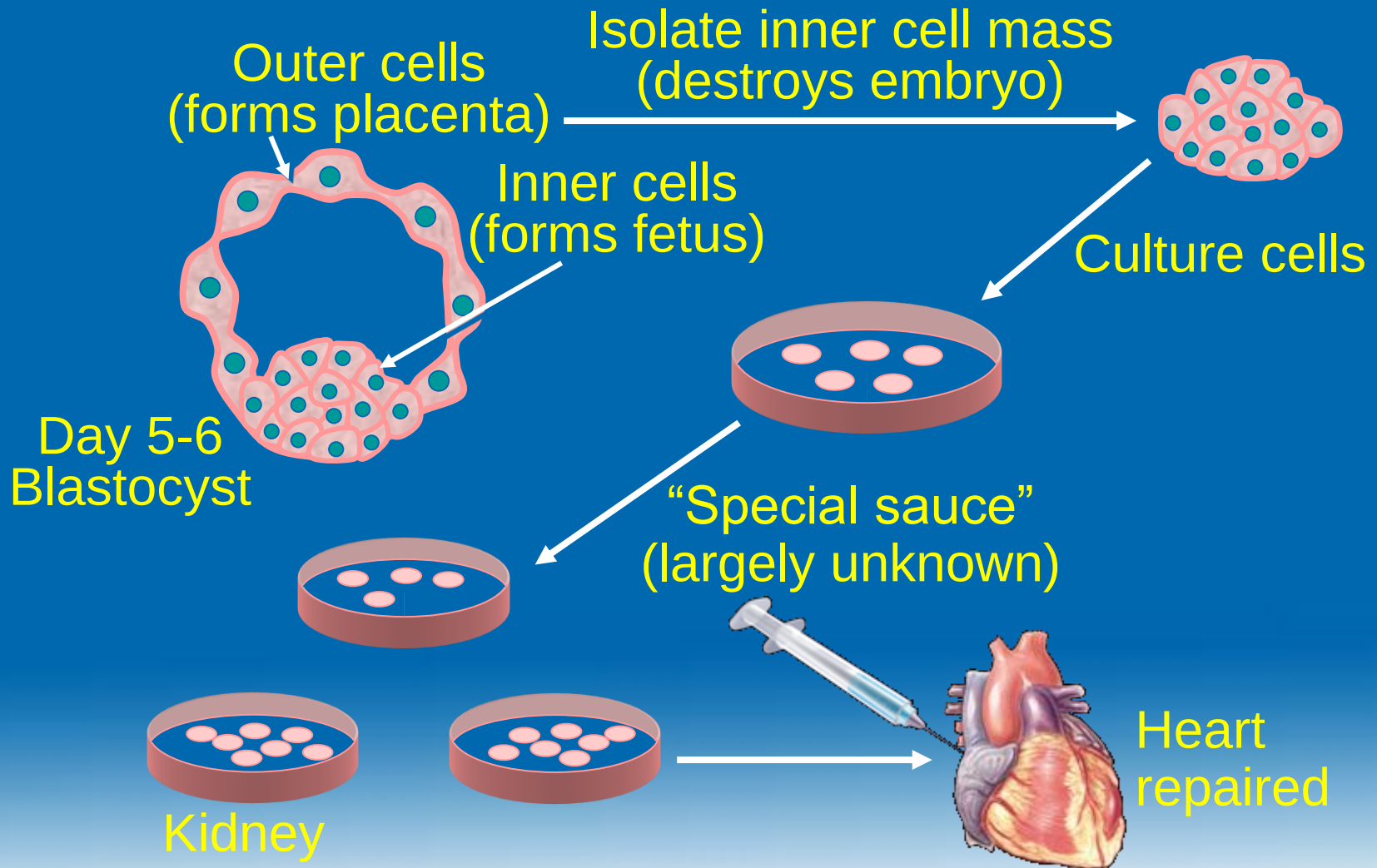
Sexual Reproduction



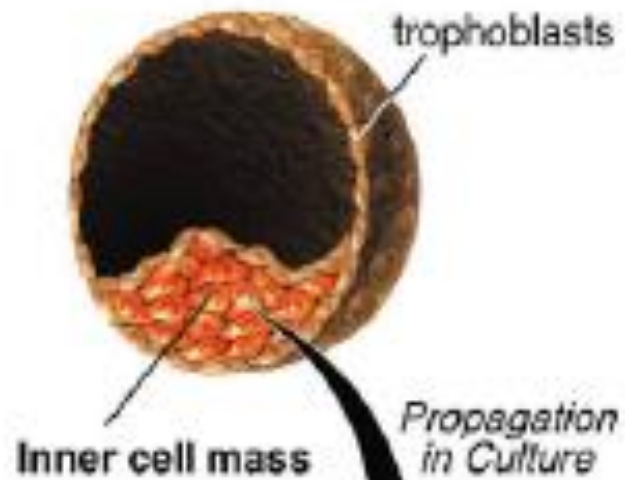
Stages of Embryogenesis



Derivation and use of Embryonic Stem Cell Lines



Blastocyst
(64 to 200 cell stage,
cross-section)



*Propagation
in Culture*



**Pluripotent
embryonic
stem cells**

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

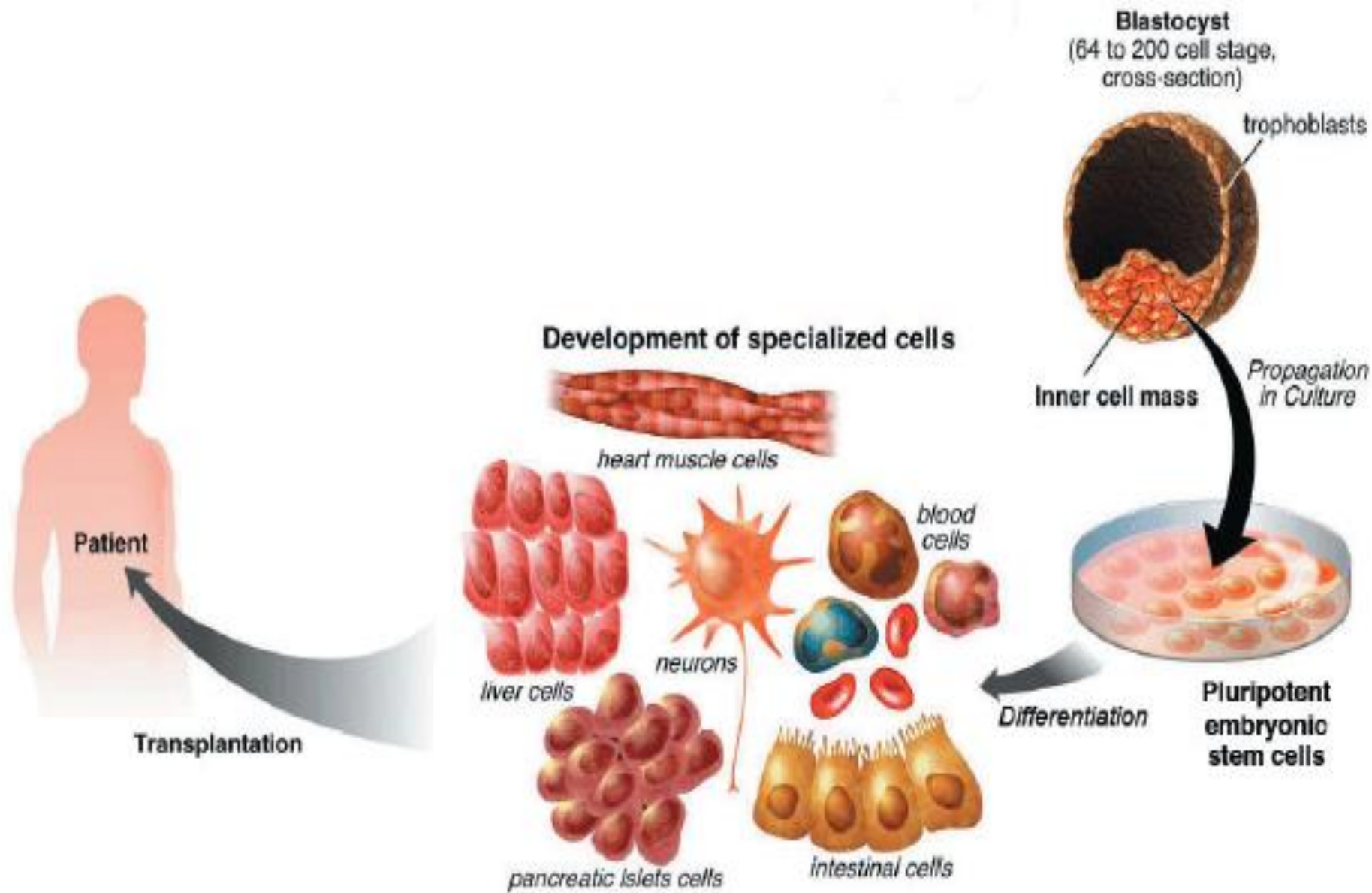
liver cells

pancreatic islets cells

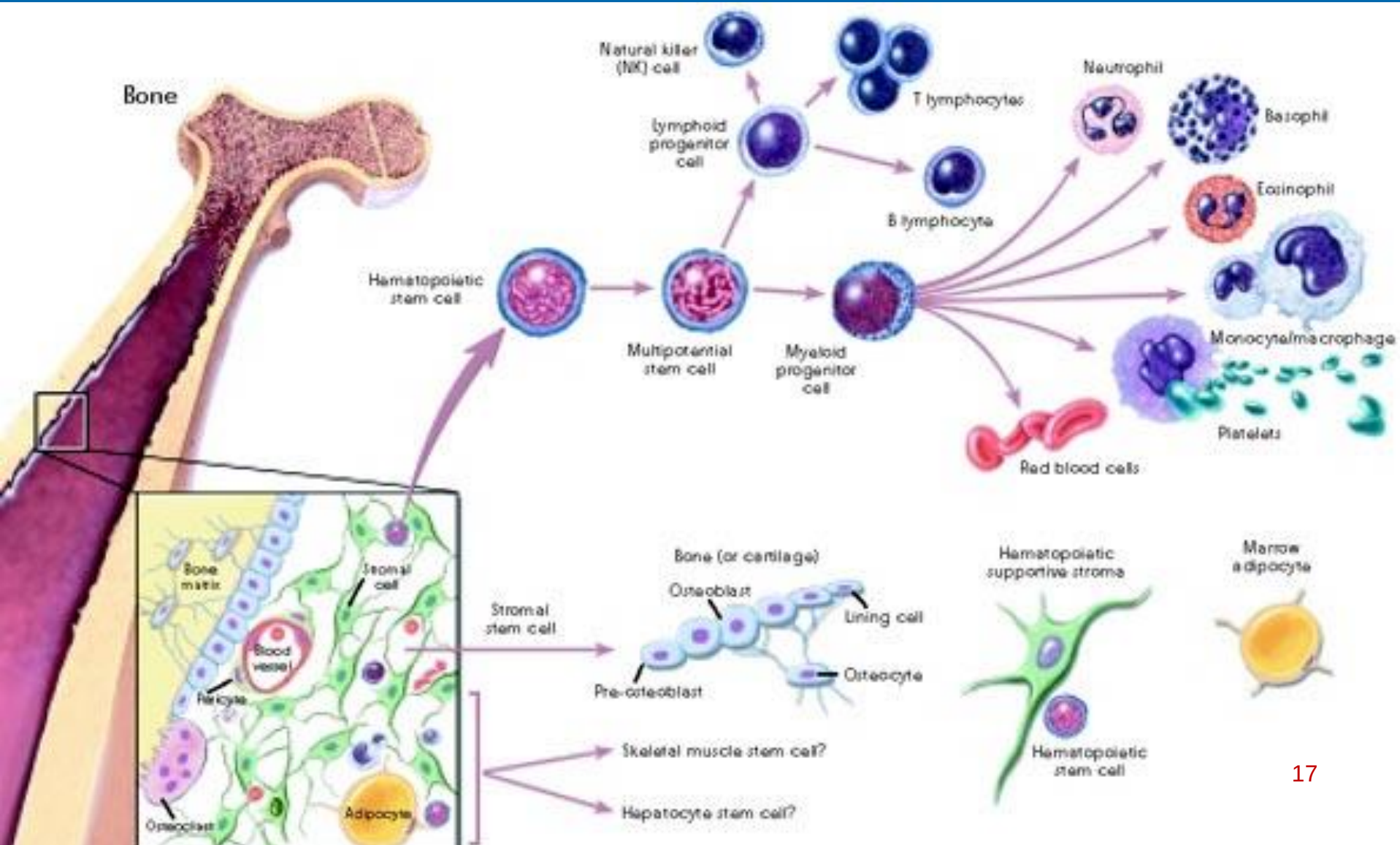
intestinal cells

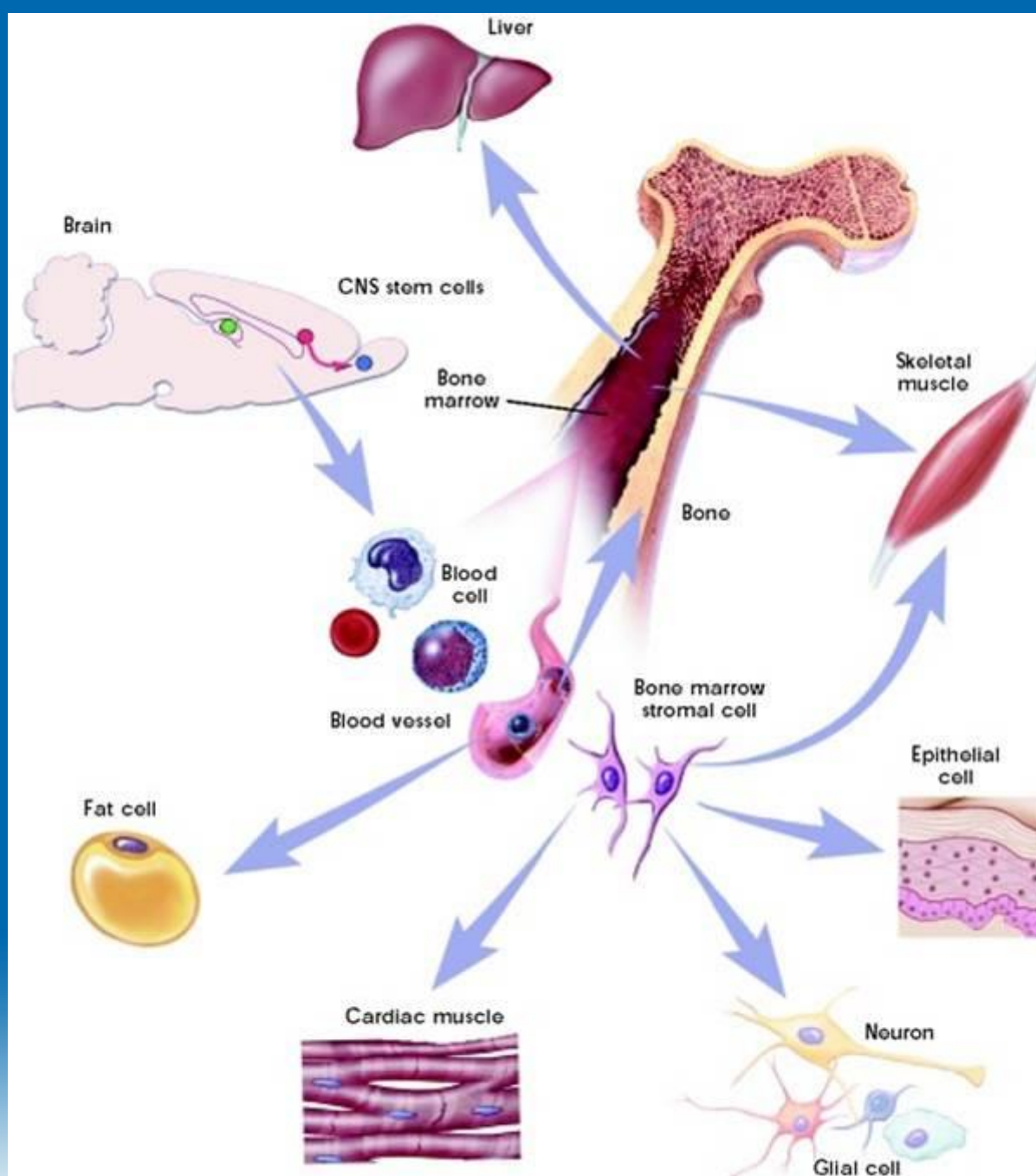
Differentiation

**Pluripotent
embryonic
stem cells**



Adult stem cells







- 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

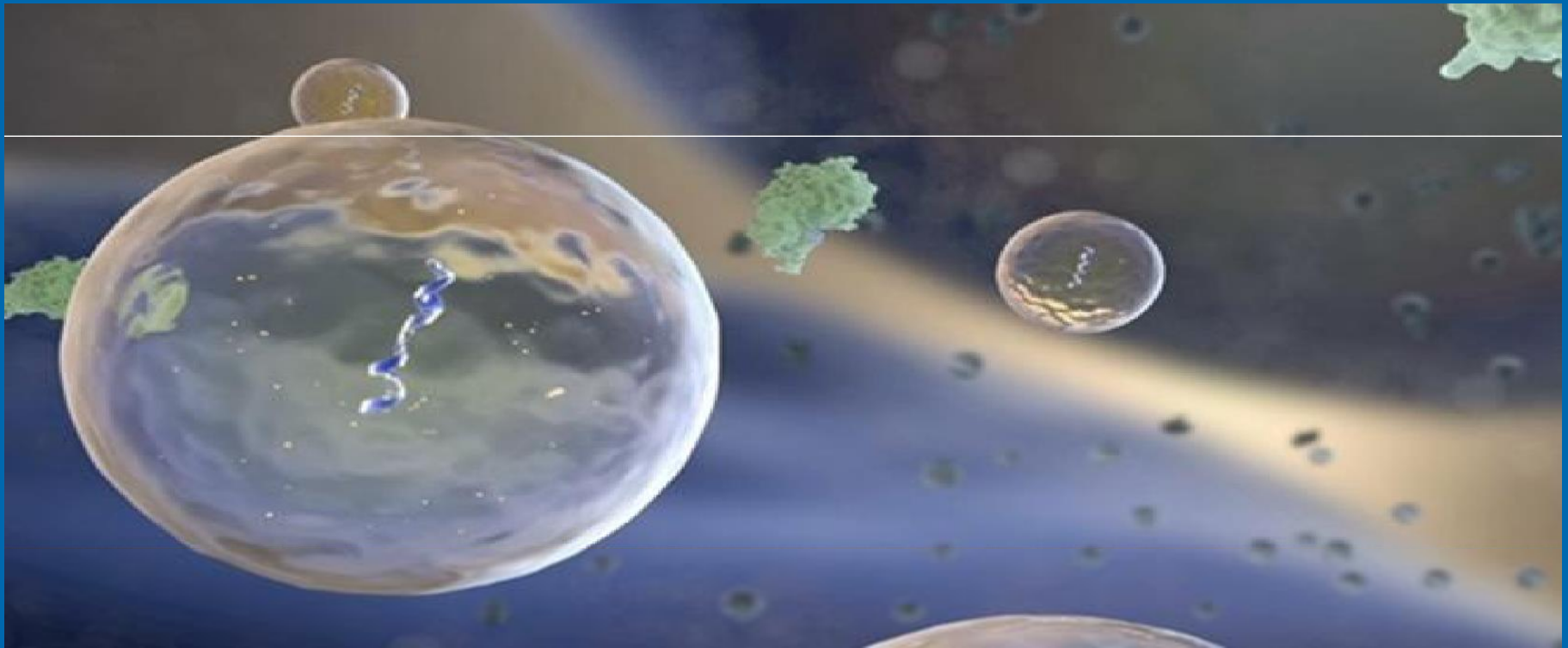
- Culture stem cell lines in a stable, multi- or pluri-potent state, free from mutations & to sufficient quantity

- Enable Economical expansion to make cell-therapy a reality

- Control & activate stem cell differentiation to desired lineages

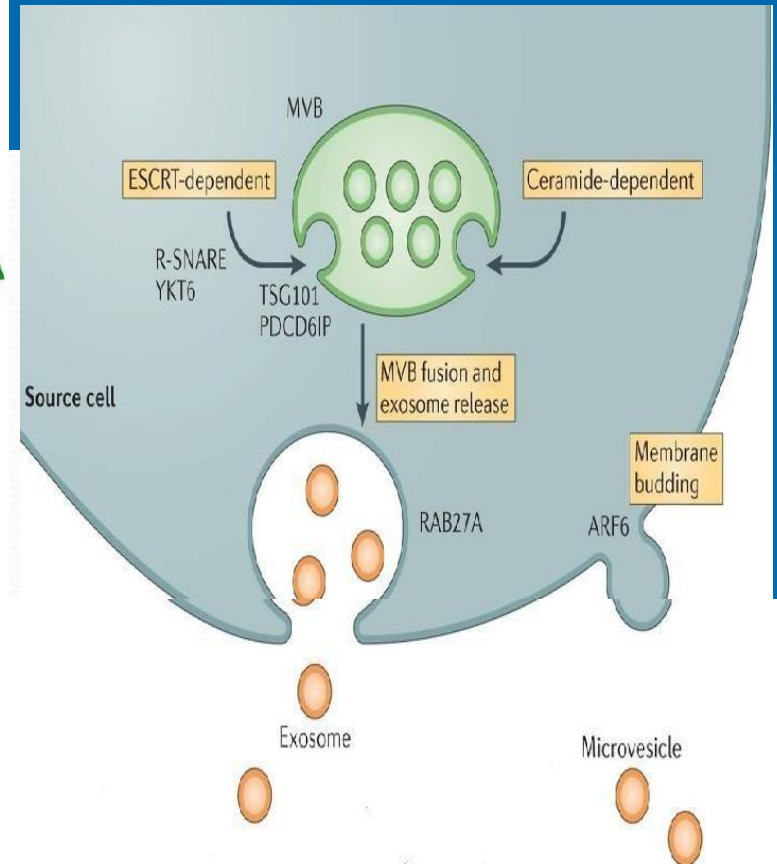
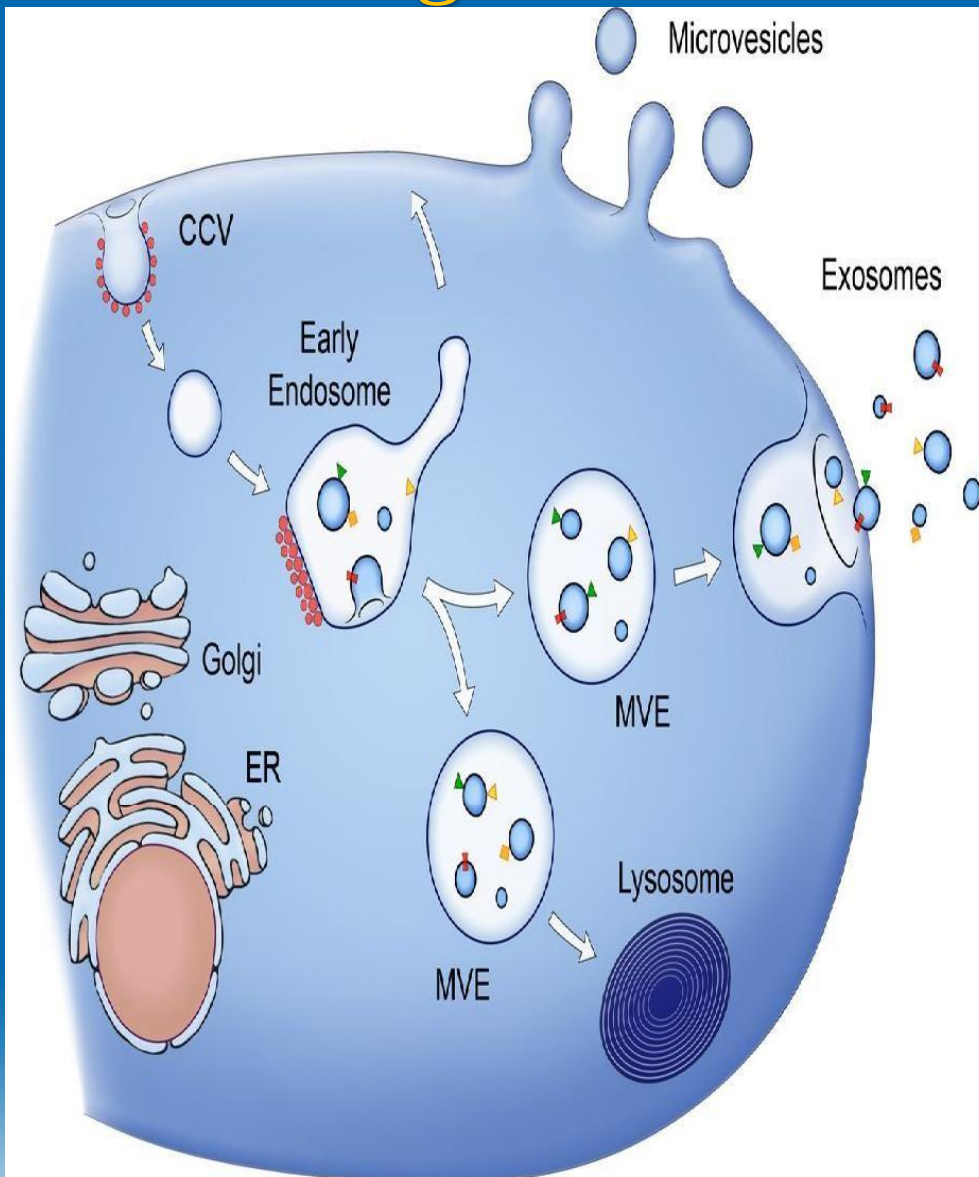
- Functionally active differentiated cells

Exosome Origins: Why the Cell Source Matter



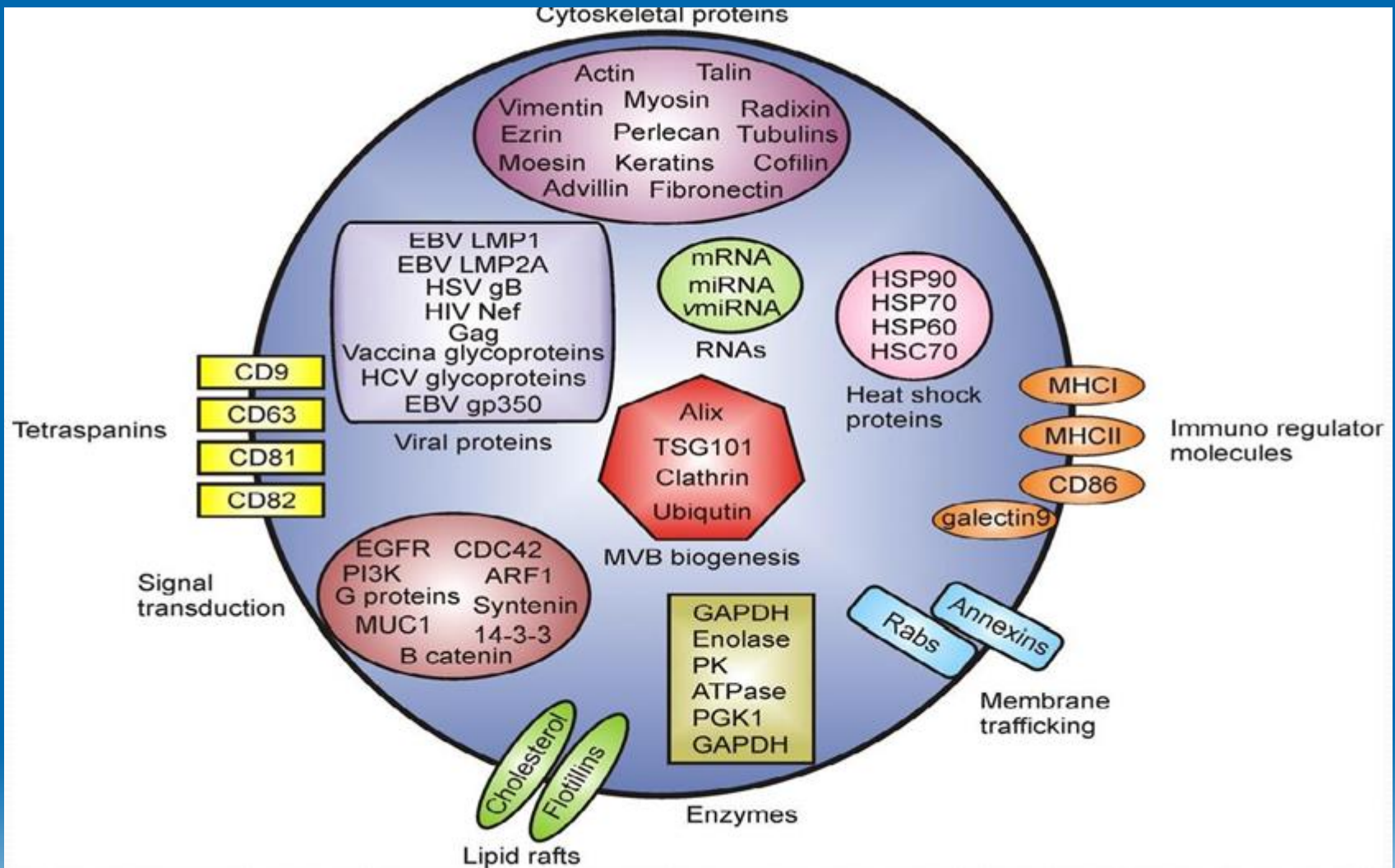
Kamran Mansouri
Associate Professor of Molecular Medicine

Biogenesis and Release of EMV



Nature Reviews | Drug Discovery

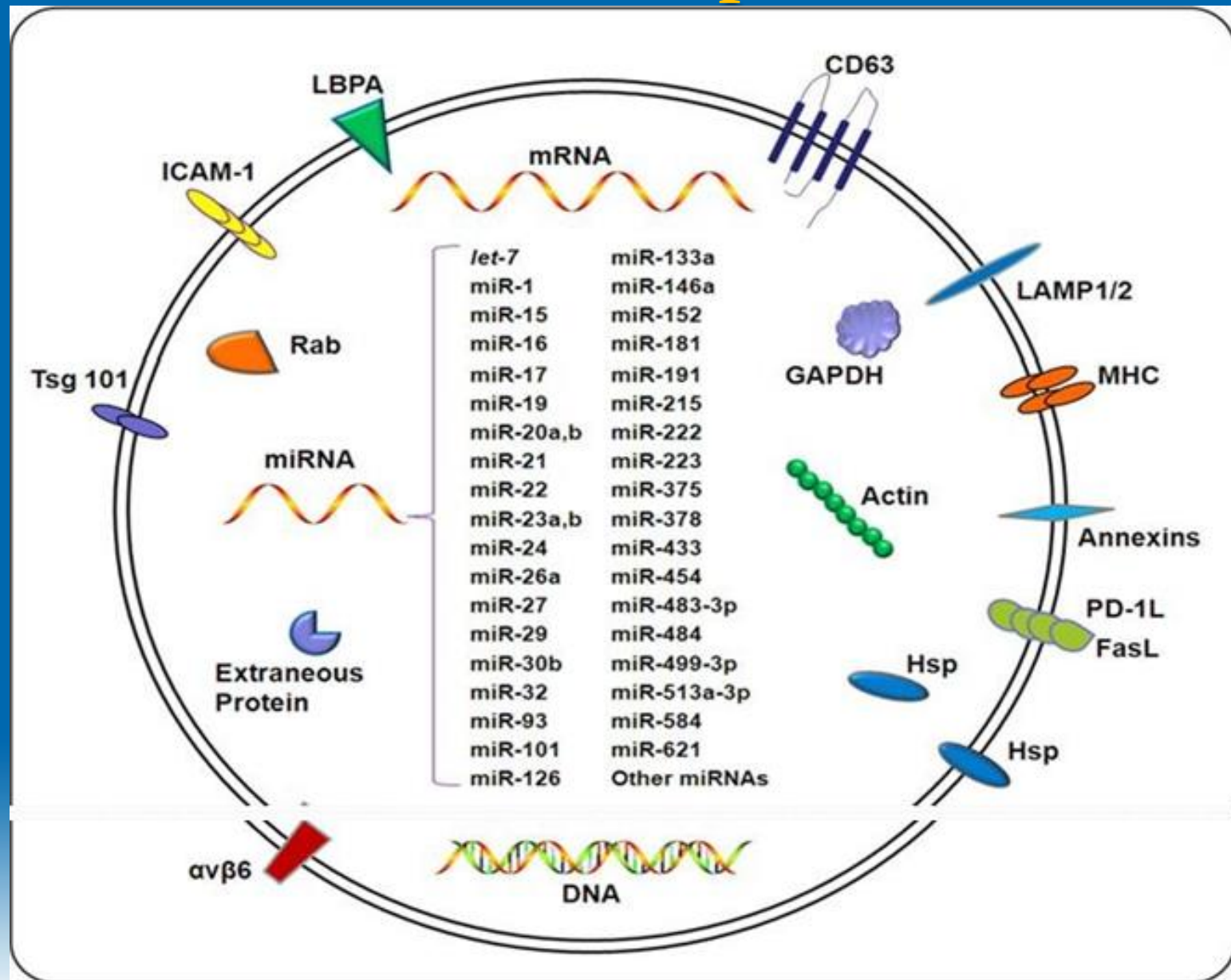
Exosome composition



A complete database of exosomal proteins can be found at ExoCarta (exocarta.ludwig.edu.au/) (Mathivanan et al., .(2012)

Virol. 2011;85:12844-12854

Exosome composition

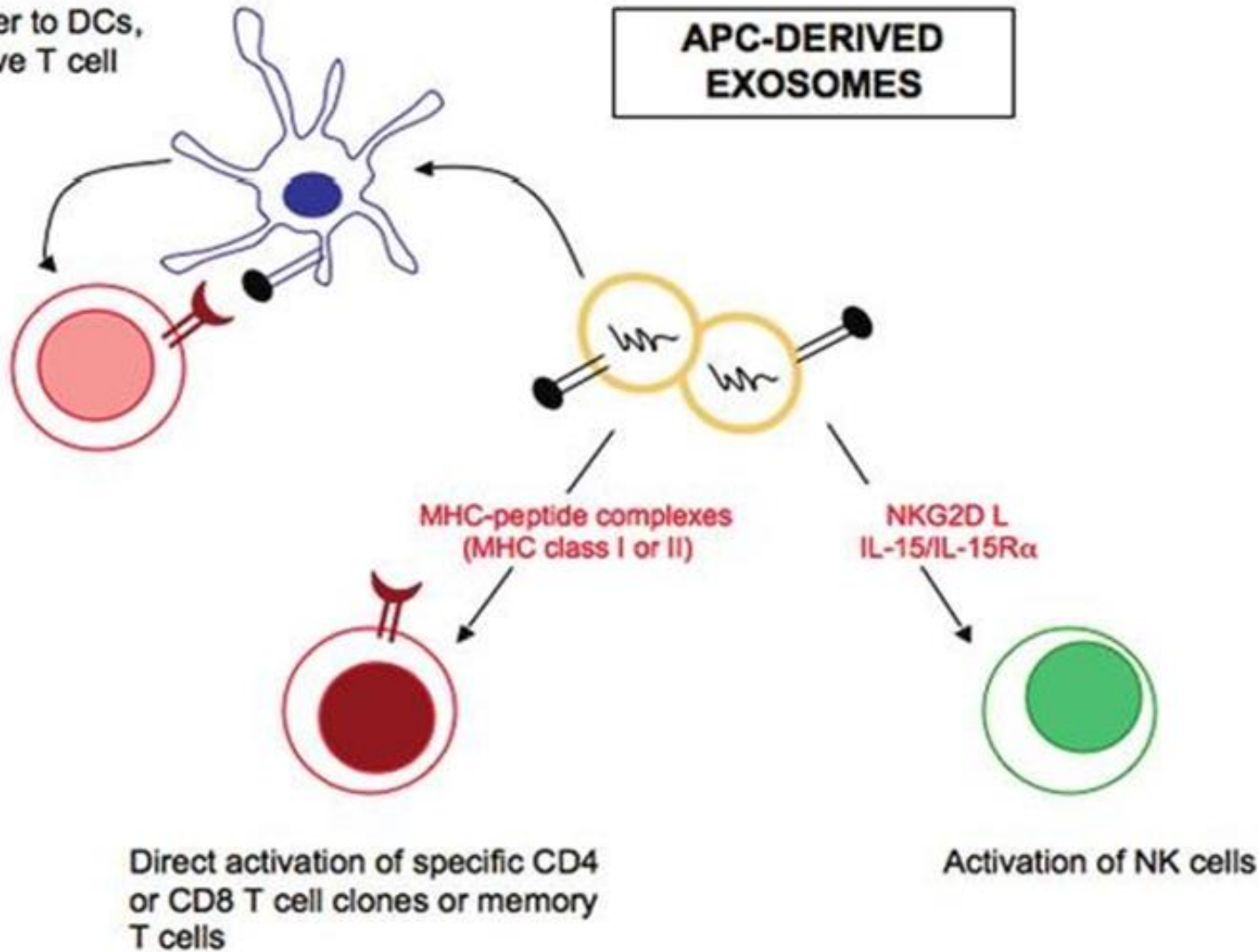


Exosomes as intercellular communicators

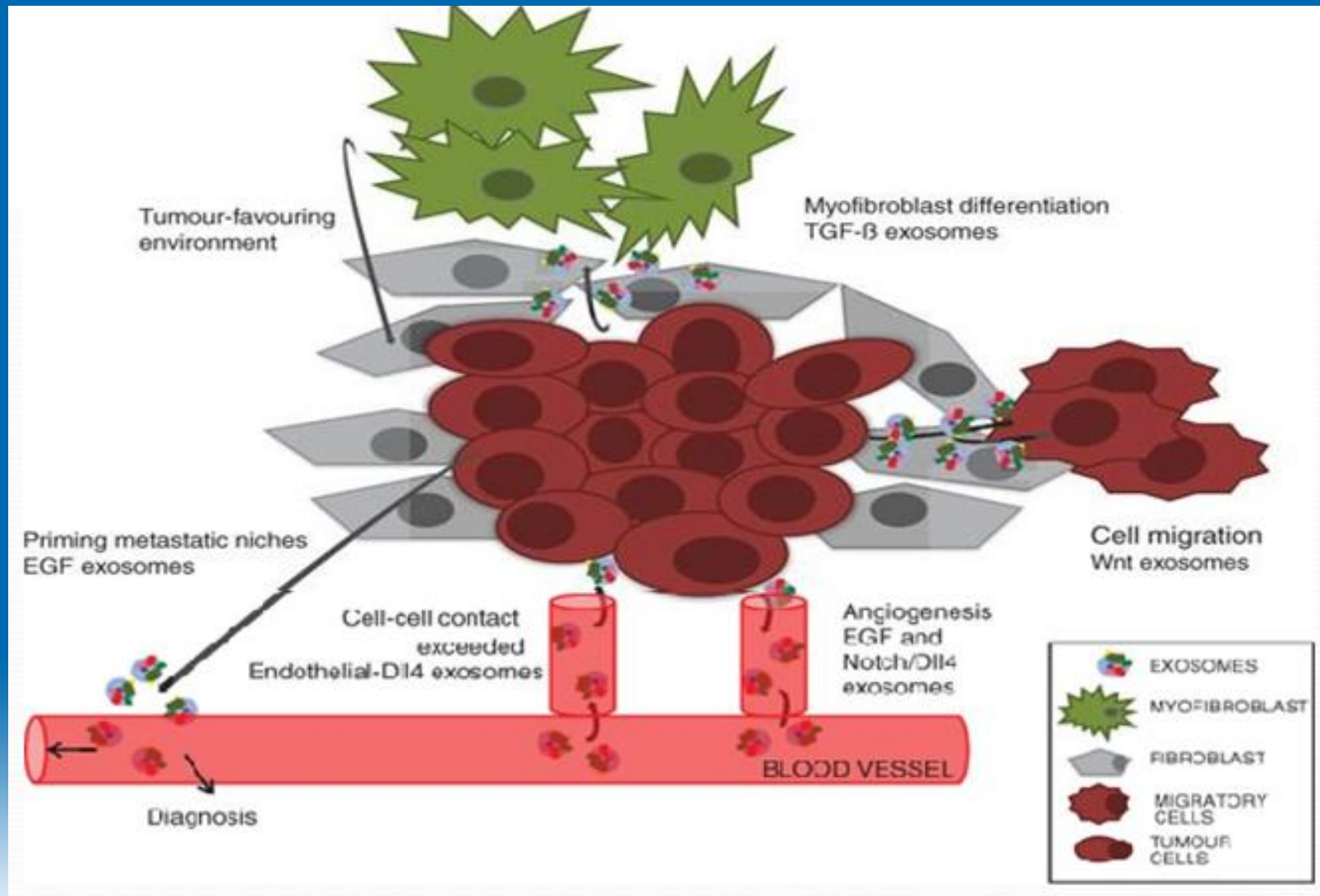
Proposed antigen presenting functions of exosomes

Antigen transfer to DCs,
leading to naïve T cell
activation

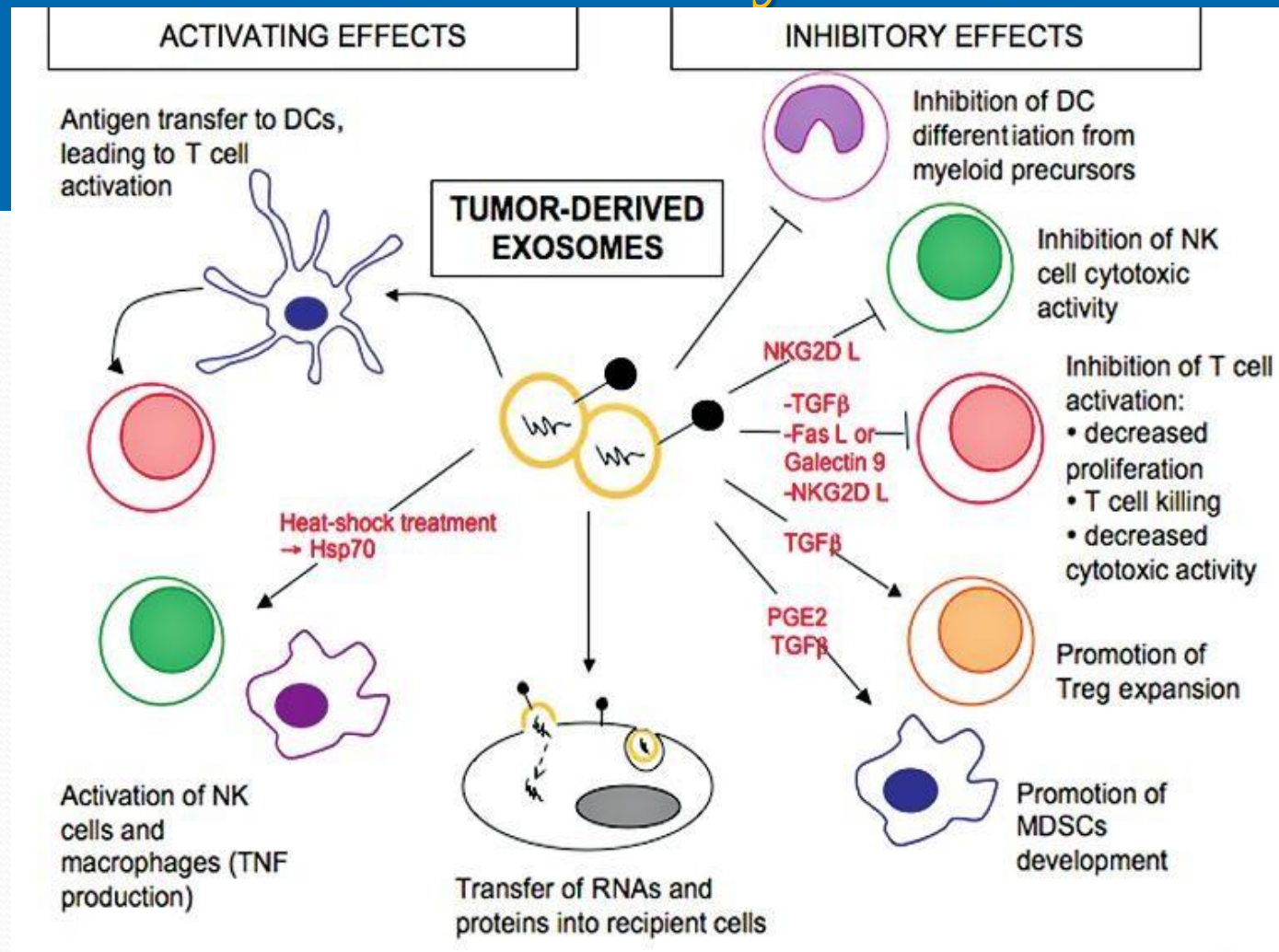
**APC-DERIVED
EXOSOMES**



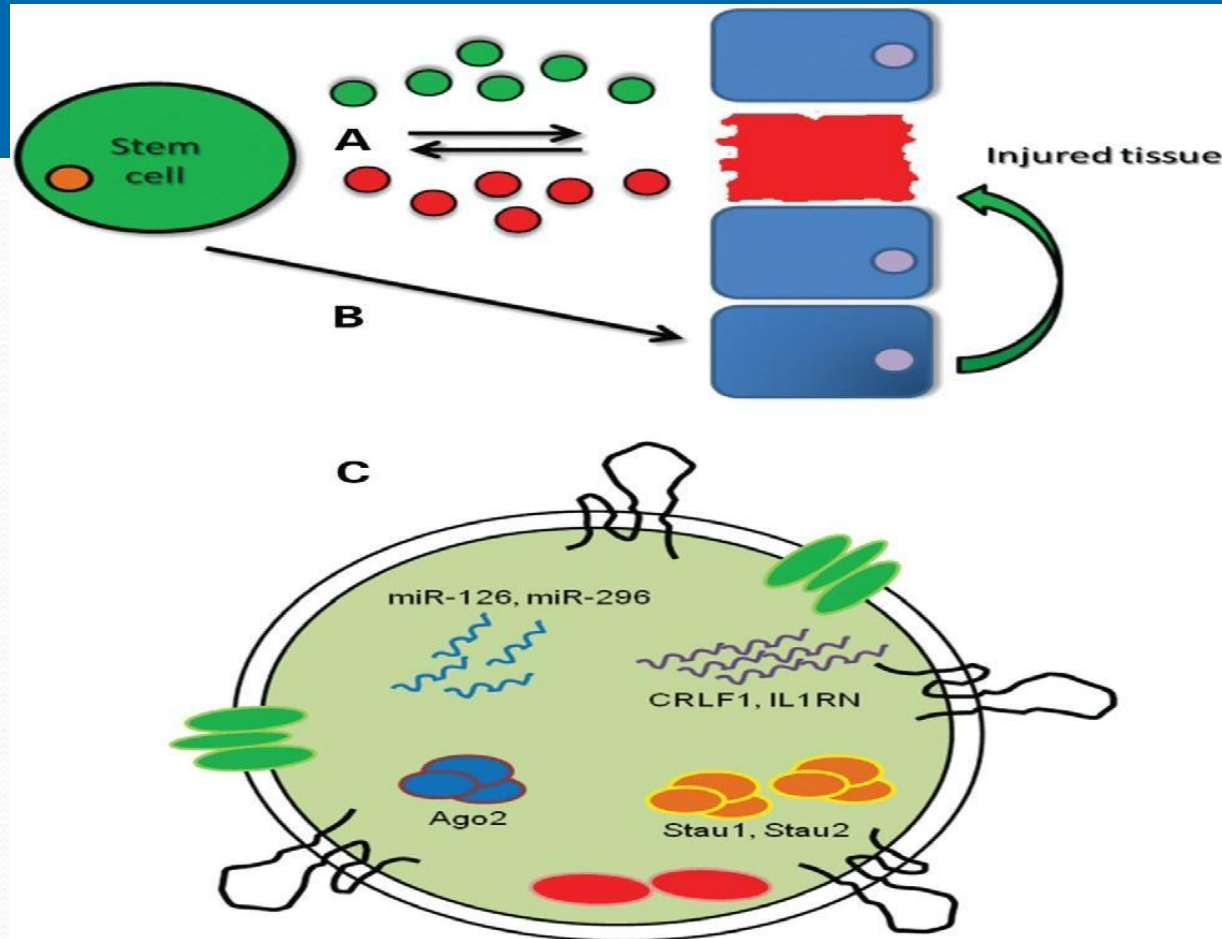
Cell communication through cell-fate signals carrying exosomes in tumor microenvironment



Proposed immunological functions of exosomes secreted by tumors



The mechanisms of stem cell exosome/microvesicle-mediated regeneration of injured tissues



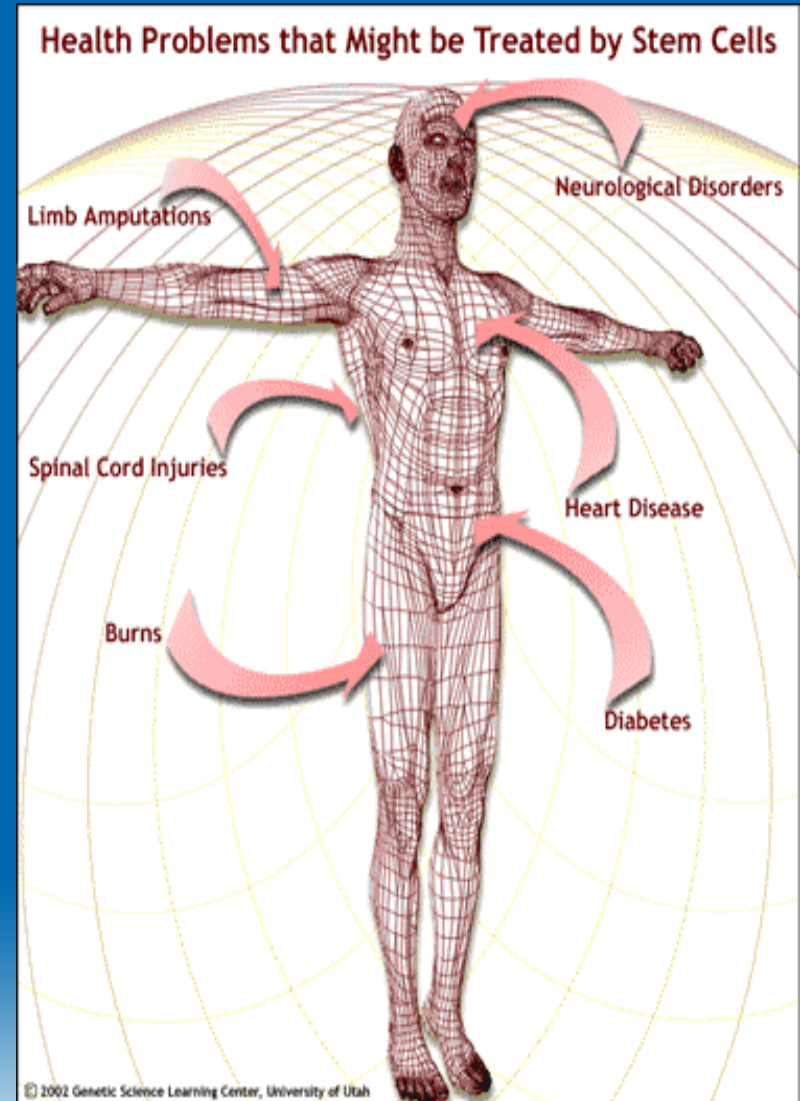
Applications

➤ Disease

- Diabetes, Spinal cord injury, Parkinson's disease, heart disease

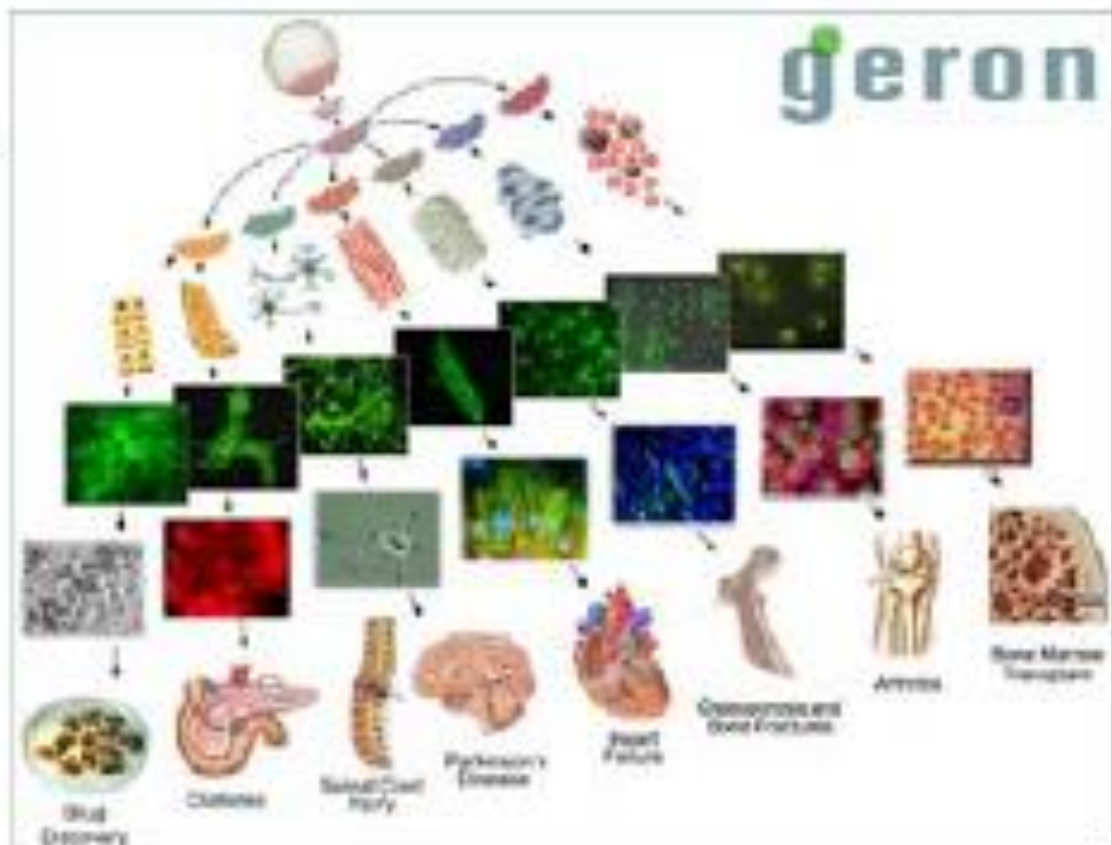
➤ Genetic based Disease

- Cystic fibrosis, Huntington's



How they could treat certain types of diseases?

- Tissue repair
- Heart Disease
- Cancer
- Arthritis
- Parkinson's disease
- Diabetes



Tissue Repair

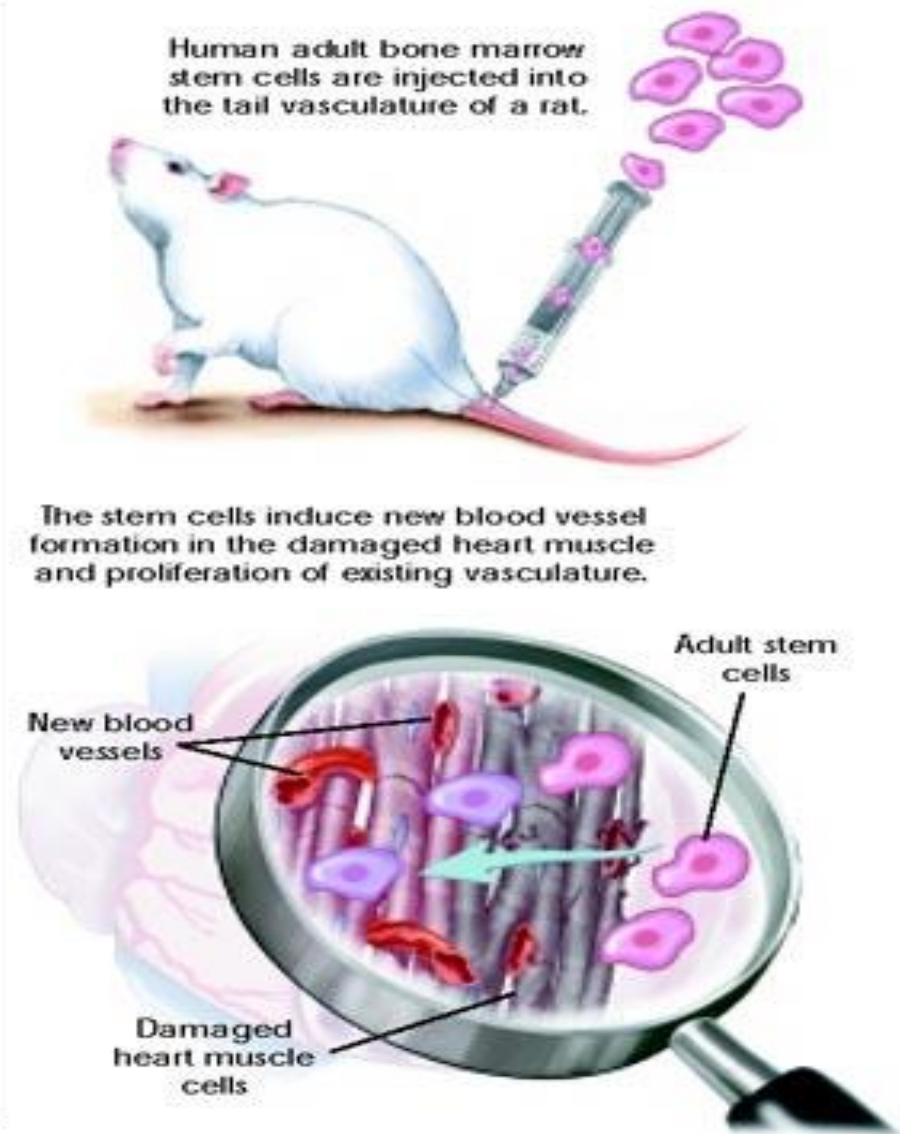
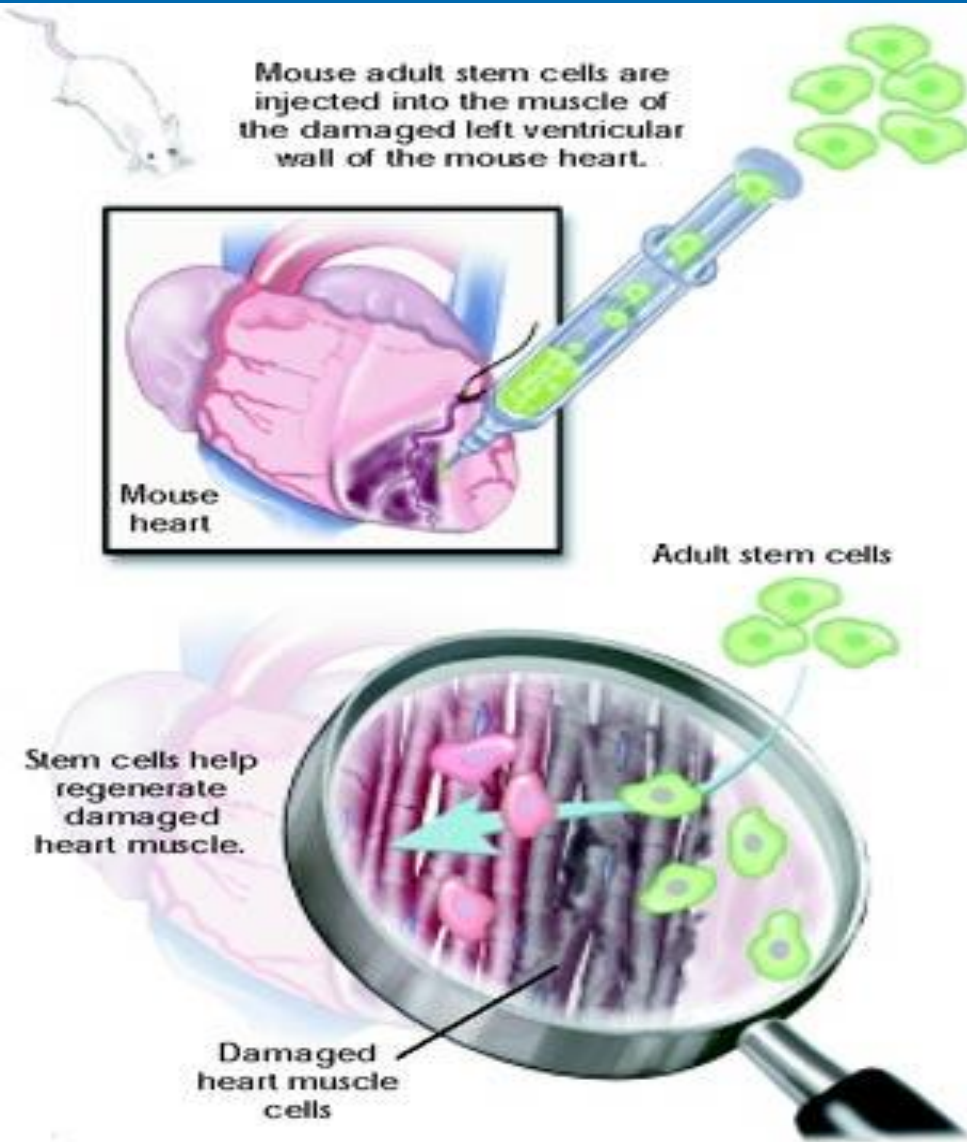
- Regenerate spinal cord, heart tissue or any other major tissue in the body.



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.

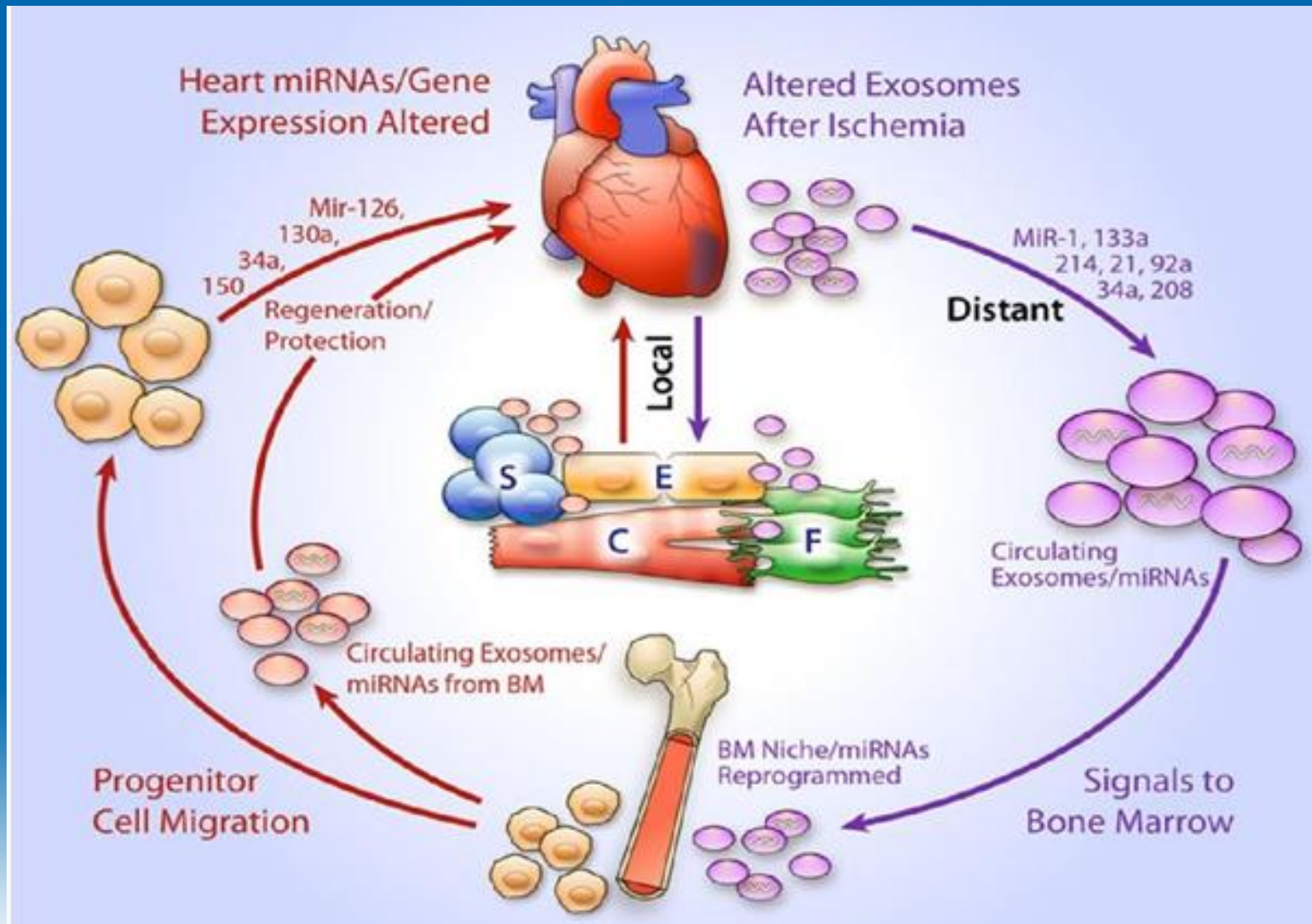


Type I Diabetes

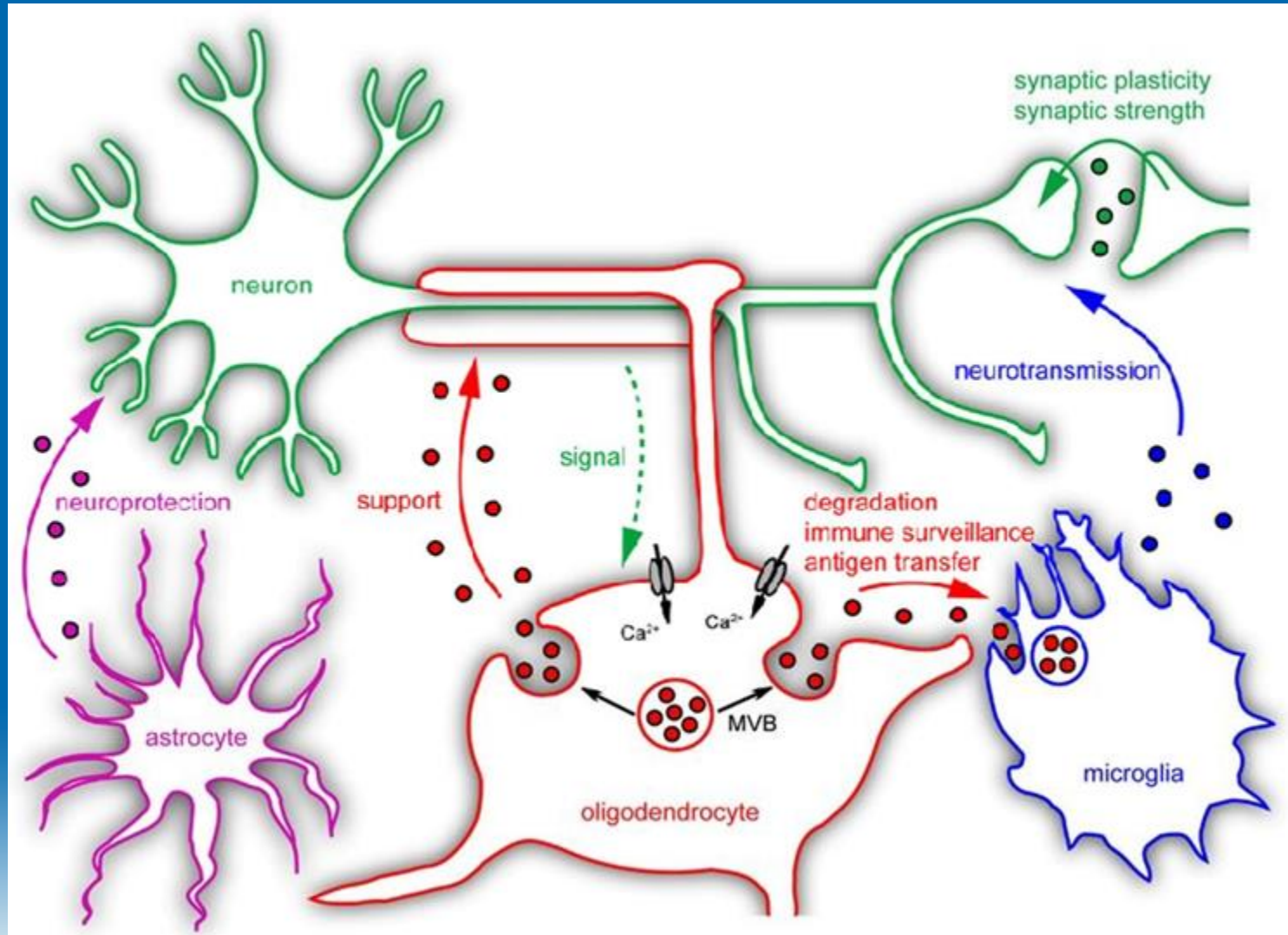
- Pancreatic cells do not produce insulin.
- Basic research focused on understanding how embryonic stem cells might be trained to become pancreatic islets cells needed to secrete insulin.

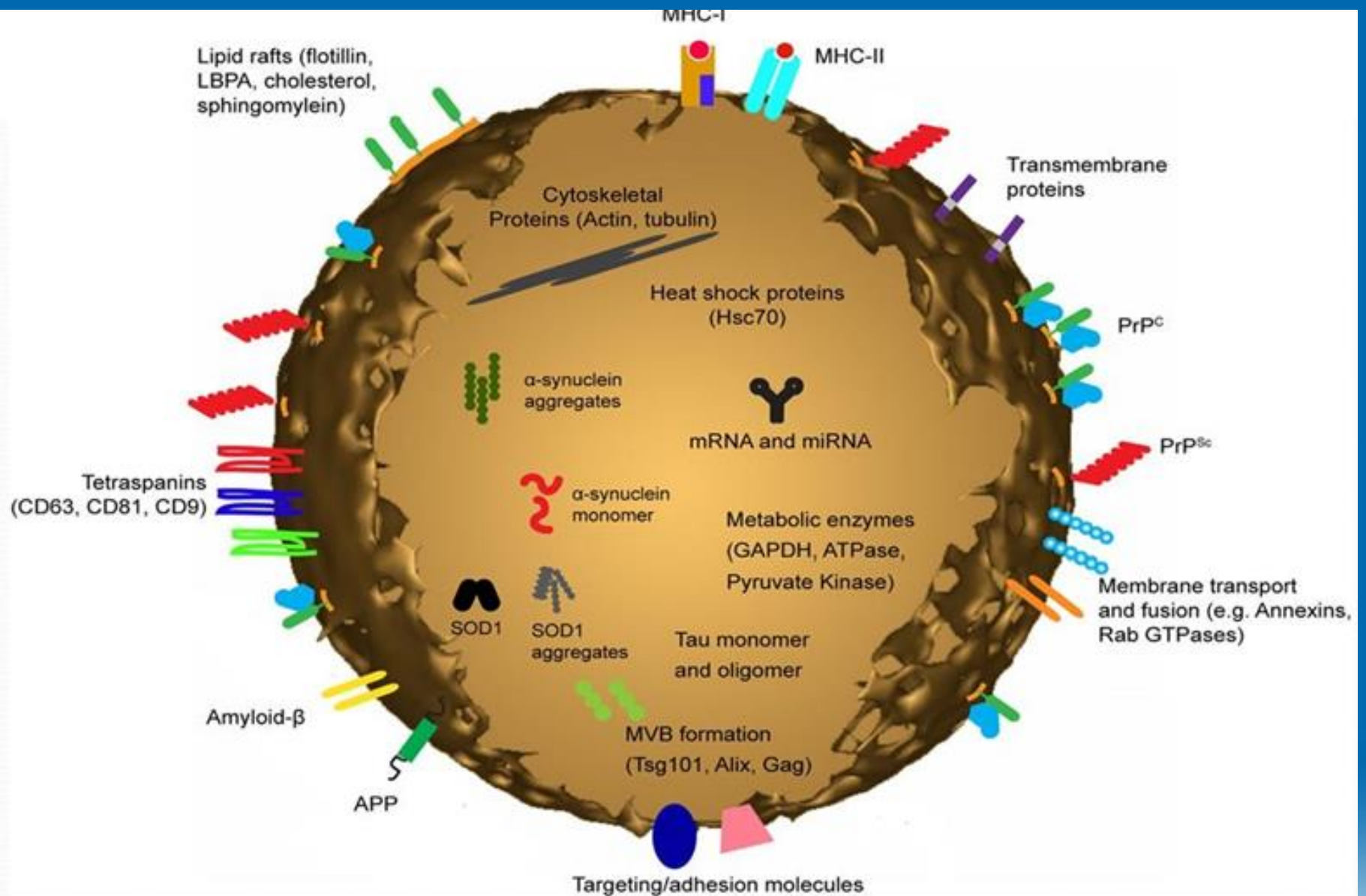


A suggested hypothesis on the role of exosomes released from a damaged heart as a potential intercellular communicator



Postulated roles of exosomes/microvesicles in neural cell communication







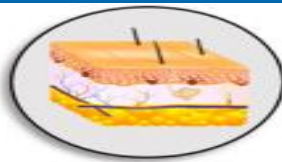
Bone marrow



Adipose tissue



**Umbilical cord
Umbilical cord blood
Placenta**



Dermis



**Synovial
membrane**



**Dental pulp
Periodontal
ligament**



Isolated MSC



Immunomodulation

**PGE₂ IDO iNOS
HGF TGF- β 1 LIF**

Engraftment

**SDF-1/CXCL12
CXCR4 MCP-1**

Angiogenesis

**VEGF IGF-1
MCP-1 bFGF IL-6**

Wound healing

**EGF KGF IL-1 β
Angiopoietin-2**

Anti-apoptosis

**VEGF TGF- β IGF-1
HGF bFGF GM-CSF**

Chemoattraction

**CCL2 CCL5 CX3CL1
CXCL2 CXCL12**

Exosomes, Microvesicles

Cytokines, Growth Factors

FGF IL-1 iNOS IGF-1
IL-6 TPO VEGF
SDF-1 SCF IL-8 IL-11
PDGF GM-CSF IDO M-CSF
IL-7 TGF- β G-CSF
IL-1RA LIF
IL-10 PGE2 IL-12
HGF KGF TSG-6 MCP-1
LL-37

miR-145
mtDNA
mRNA
miR-23b
miR-146b
Growth Factors
Cytokines
miR-21

Mitochondria
miR-22
miR-125b
miR-133b

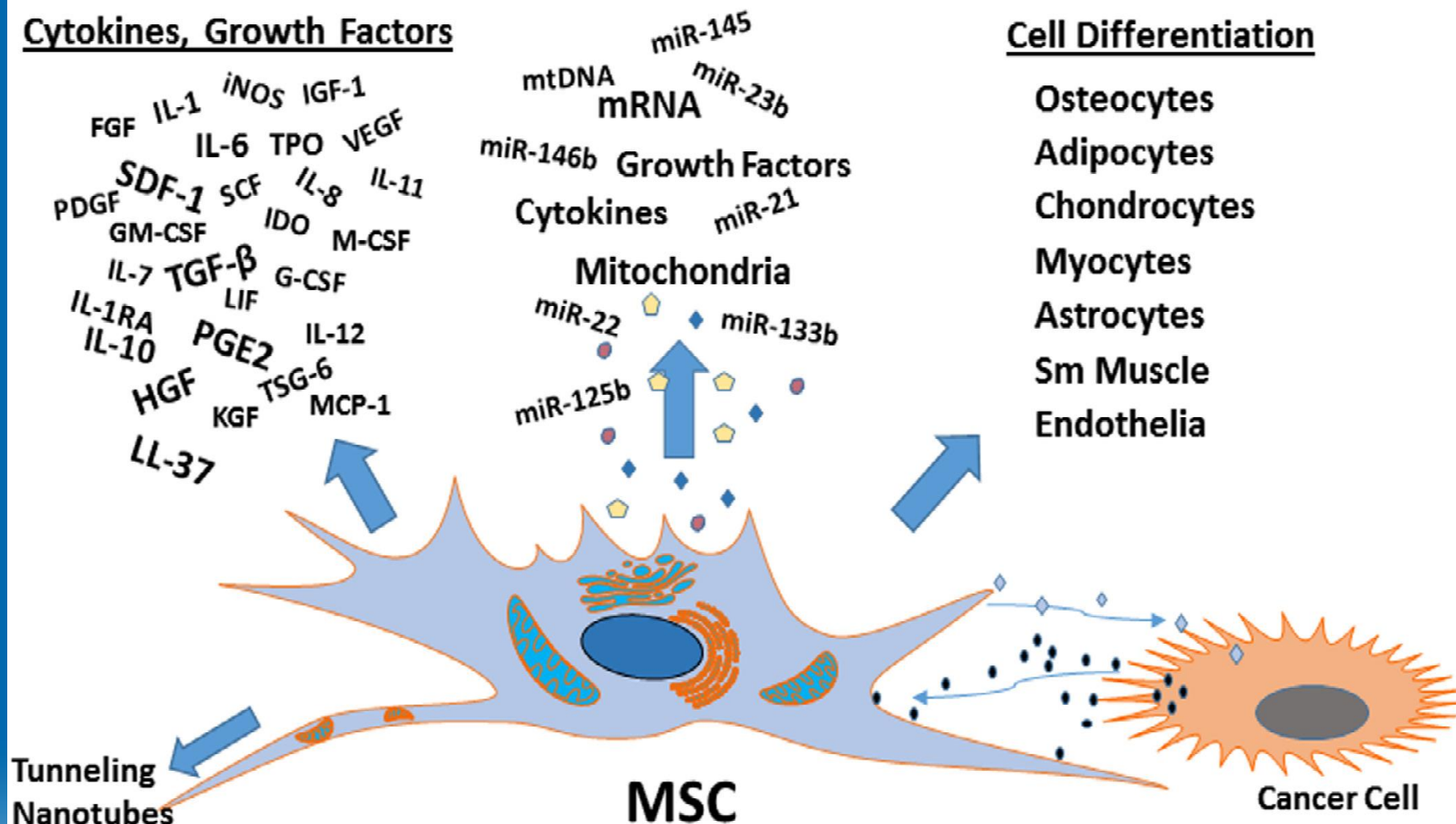
Cell Differentiation

Osteocytes
Adipocytes
Chondrocytes
Myocytes
Astrocytes
Sm Muscle
Endothelia

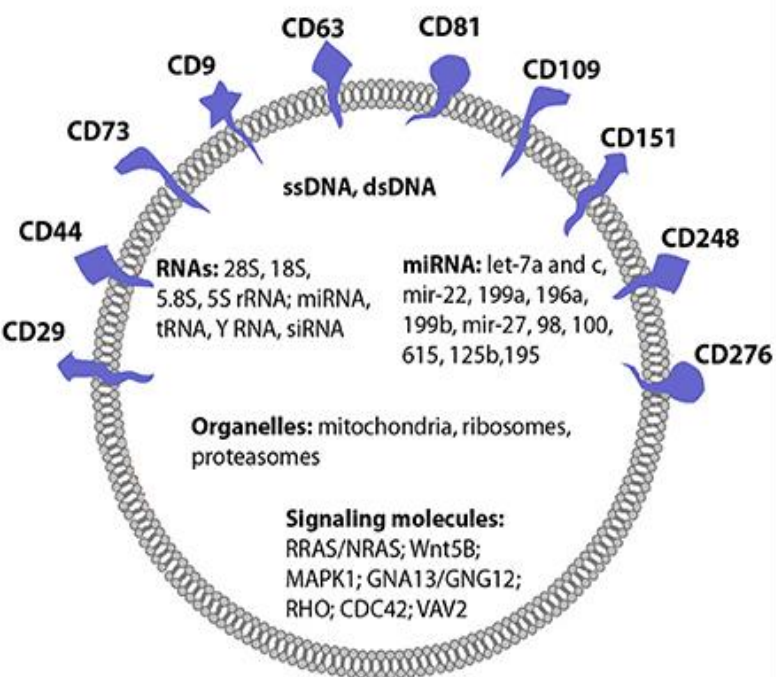
Tunneling
Nanotubes

MSC

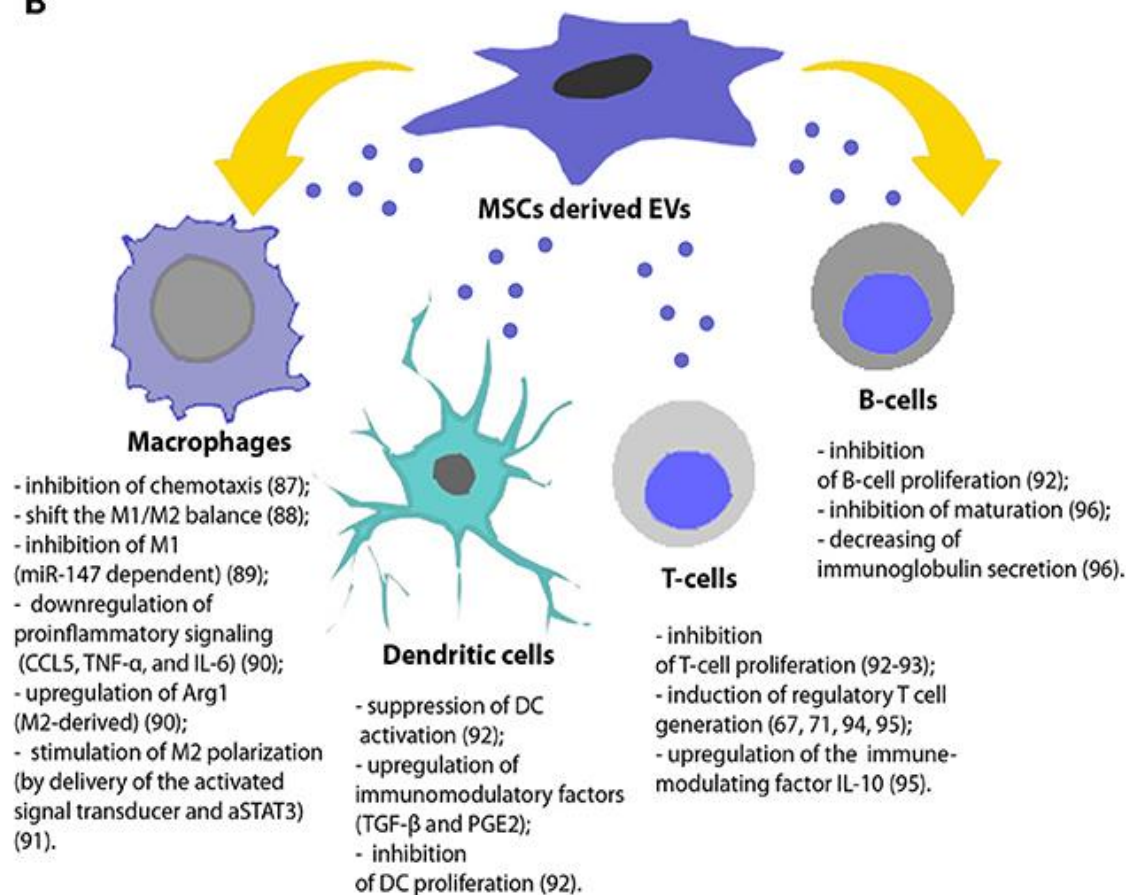
Cancer Cell

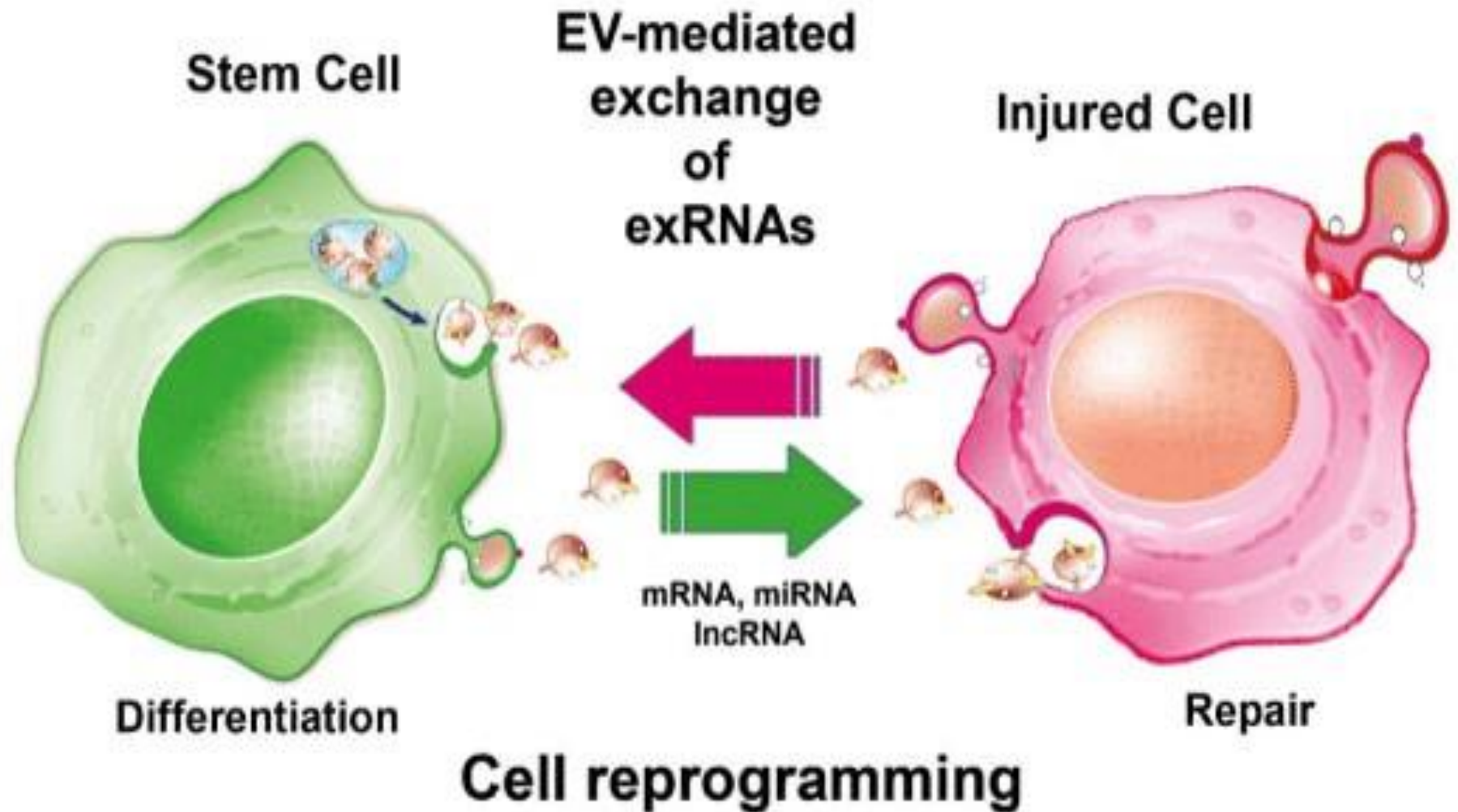


A



B





با تشکر از حسن توجه شما

در مسیحی (؟) حسن توجه شما

