RAMA UNIVERSITY

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Faculty of Engineering & Technology

Medical Biotechnology MBT-413

Submitted by-
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Department of Biotechnology

DEFINITION

Stem cells are the generic cells which are a class of undifferentiated cells that are able to differentiated into specialized cell

SOURCES

THE MAJOR SOURCES OF STEMCELLS ARE

- Embryos
- Adult tissues/organs
- Umbilical cords
- Cadavers (survival of neural progenitor cells from human post-mortem tissues up to 20hr after death)

TYPES

BASED ON THE TYPE OF ORIGIN AND POTENCY

- EMBRYONIC STEM CELLS
- ADULT STEM CELLS

PROPERTIES

- **Self-renewal**

  The ability to go through numerous cycles cell division by maintaining undifferentiated state

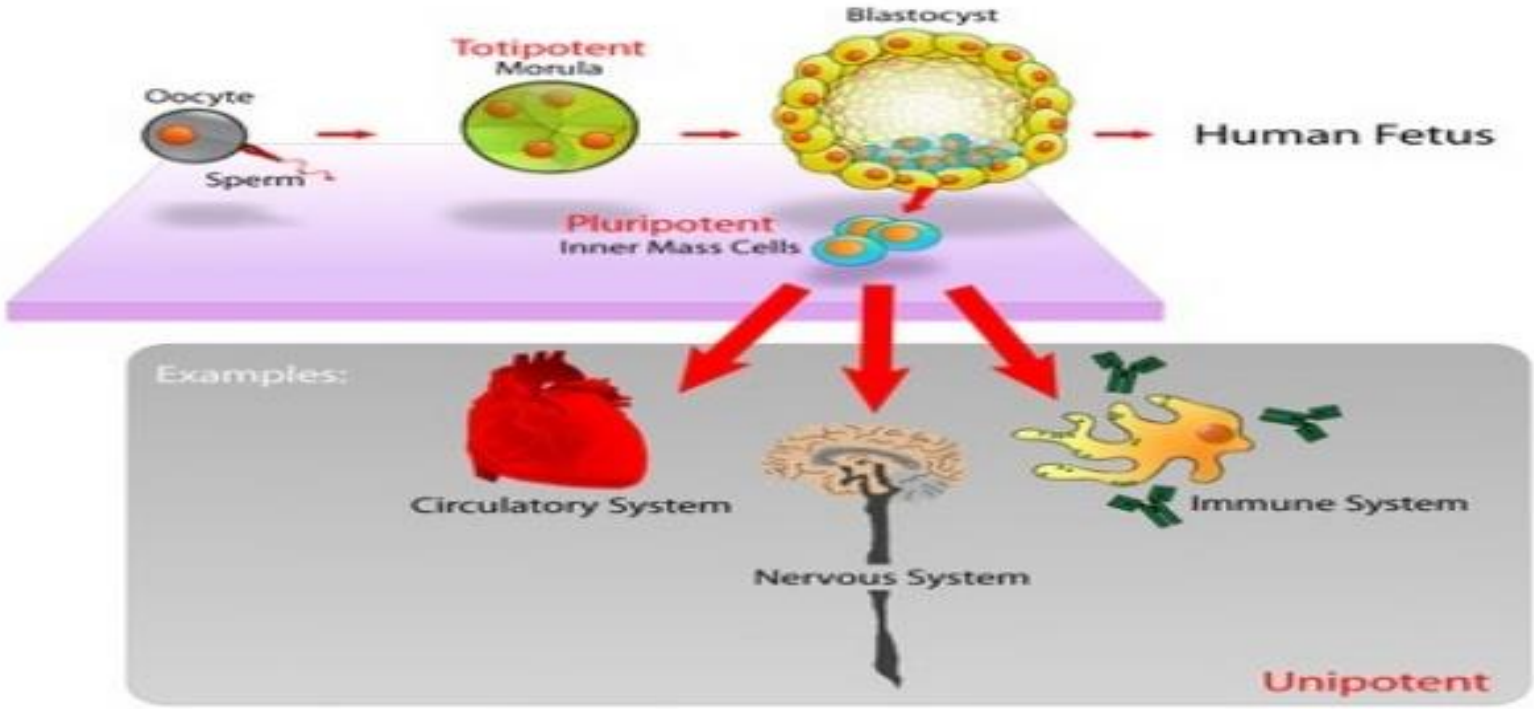
- **Potency**

  The capacity to differentiate into specialized cell types

Self-renewal

Two mechanisms are involved

- Obligatory asymmetric replication
- Stochastic differentiation



POTENCY

Potential classification includes

- **Totipotent:**
  Ex: zygote
- **Pluripotent:**
  Ex: embryonic stem cells
- **Multipotent:**
  Ex: hematopoietic stem cells(RBC&WBC)
- **Oligopotent:**
  Ex: lymphoid/myeloid stem cells
- **Unipotent:**
  Ex: muscle stem cells

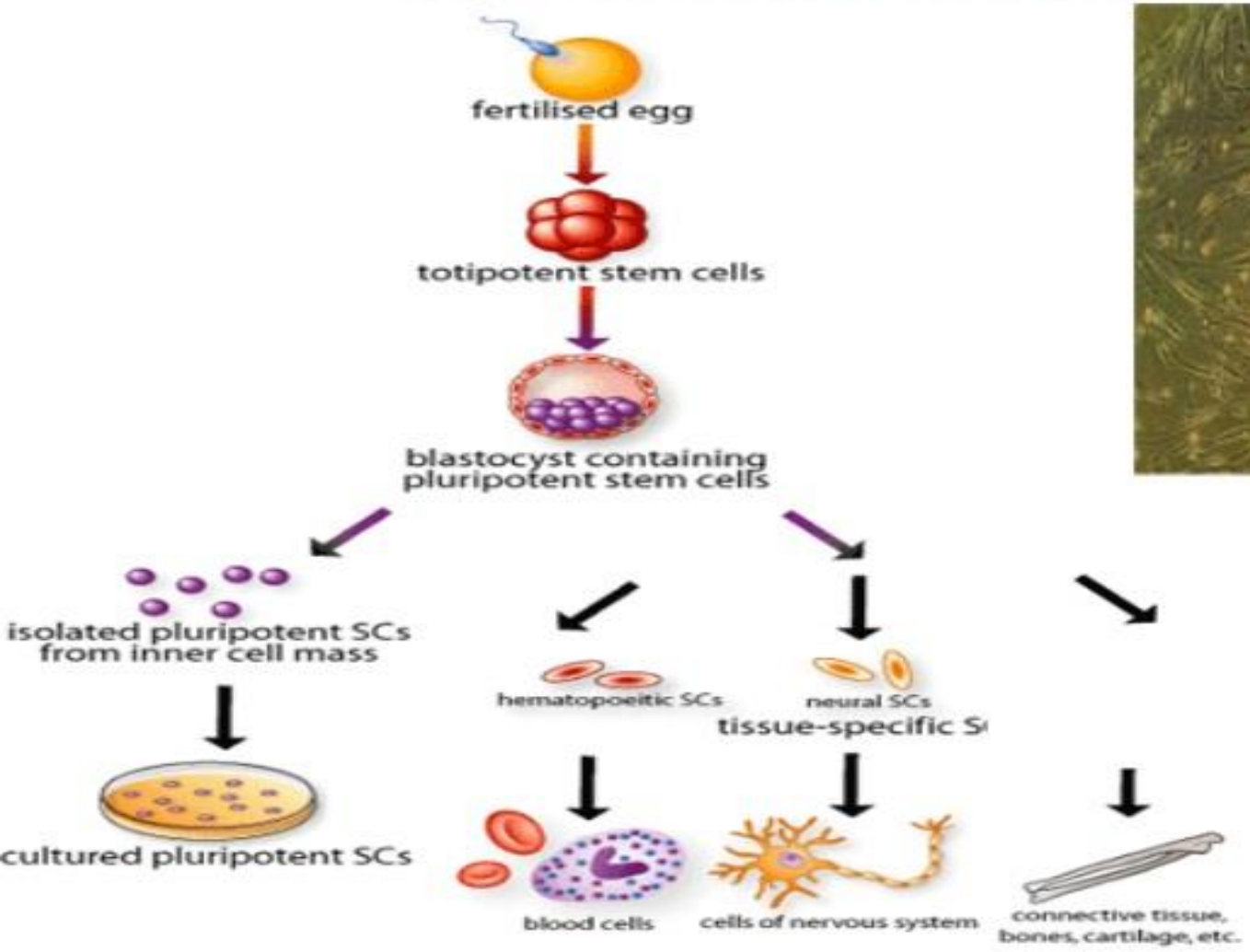
IDENTIFICATION

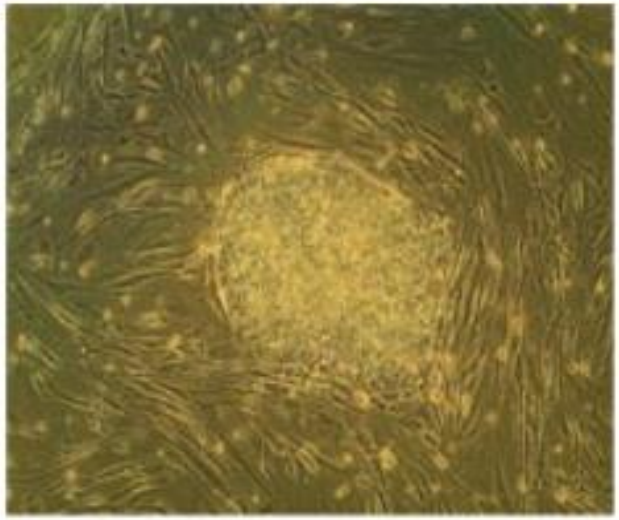
- **Examining chromosomes under microscope**
- **Presence of surface markers**

1.Transcription factors like proteins oct-4,nanog,sox-2

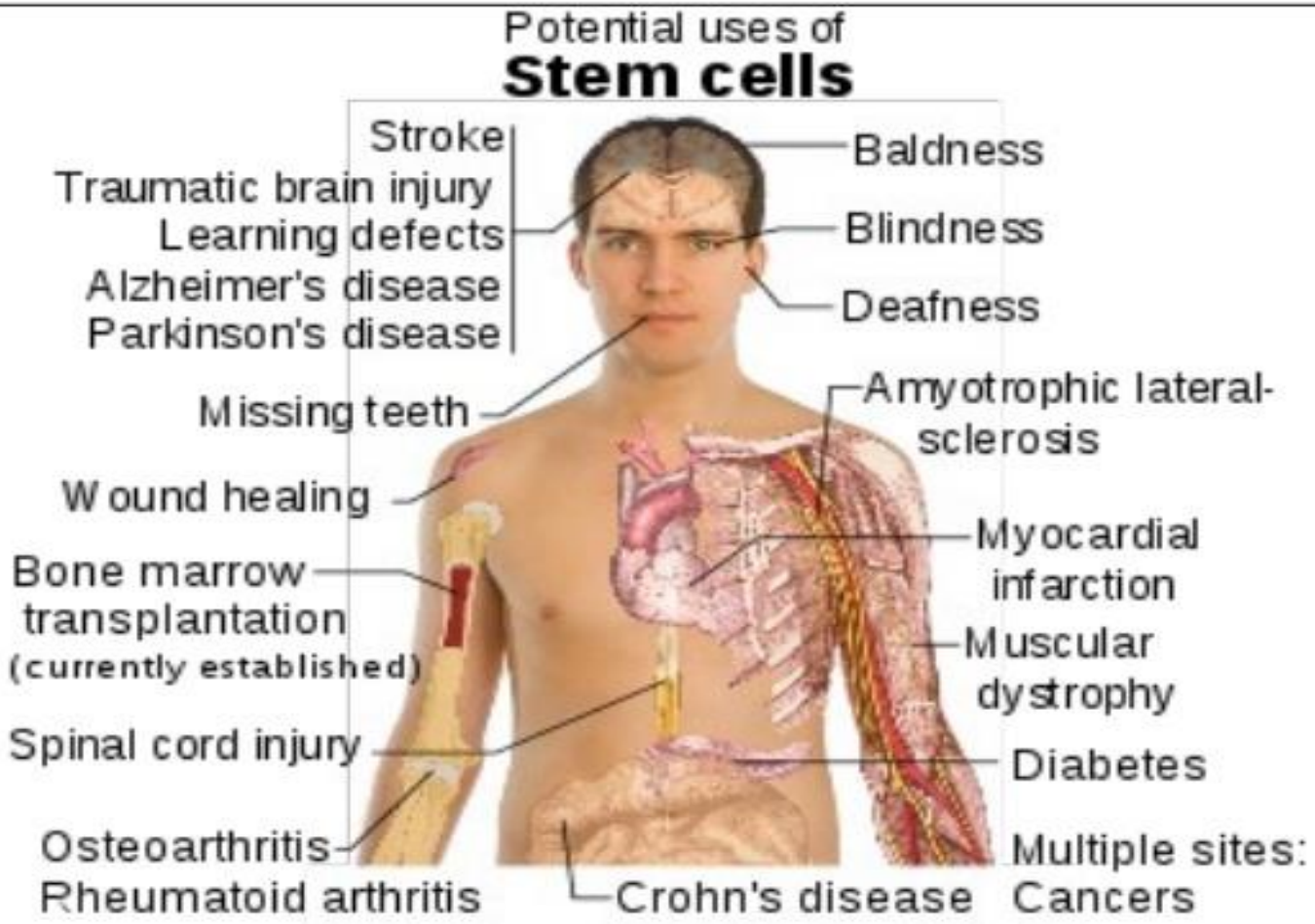
2.Cellsurface antigens-glycolipids,keratan sulfate antigen

STEM CULTURES





TREATMENTS

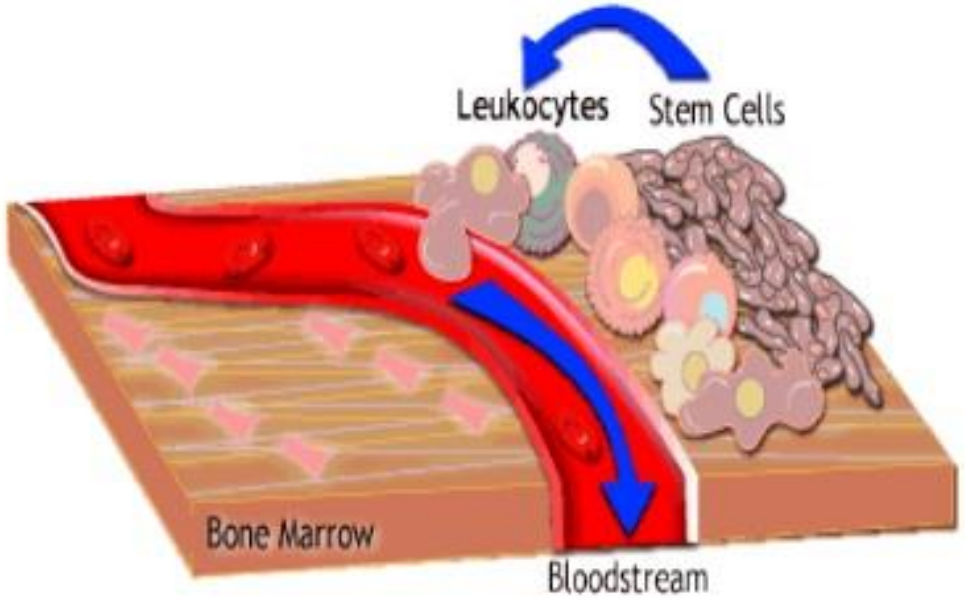

Potential uses of
Stem cells
Stroke
Traumatic brain injury
Learning defects
Alzheimer's disease
Parkinson's disease
Missing teeth
Wound healing
Bone marrow transplantation
(currently established)
Spinal cord injury
Osteoarthritis
Rheumatoid arthritis
Baldness
Blindness
Deafness
Amyotrophic lateral-sclerosis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

THERAPIES

- **ADULT STEMCELL TRANSPLANT**
  BONE MARROW STEM CELLS
- **ADULT STEMCELL TRANSPLANT**
  PERIPHERAL BLOOD STEM CELLS
- **UMBILICAL CORD BLOOD STEM CELL TRANSPLANT**

STEM CELL TRANSPLANTS

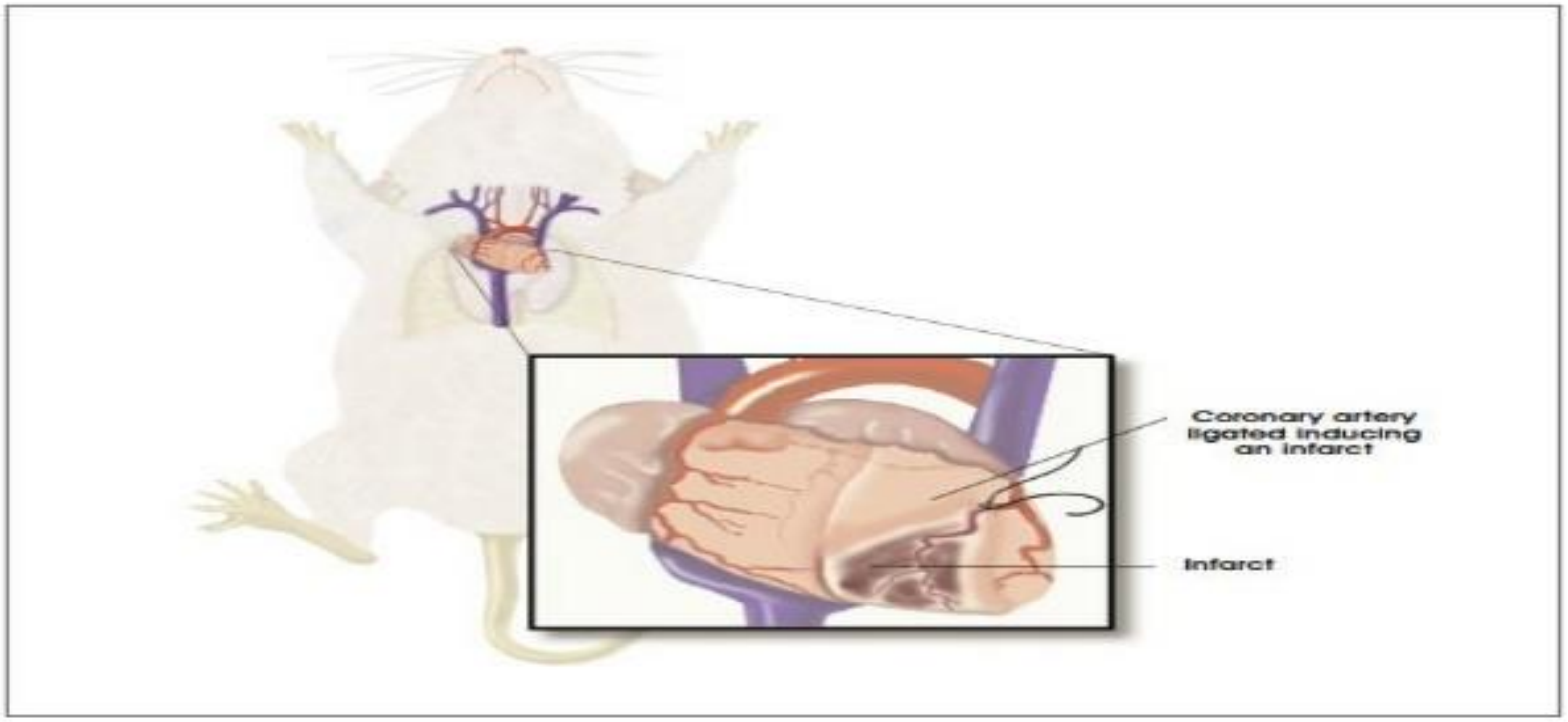
BONE MARROW STEM CELLS



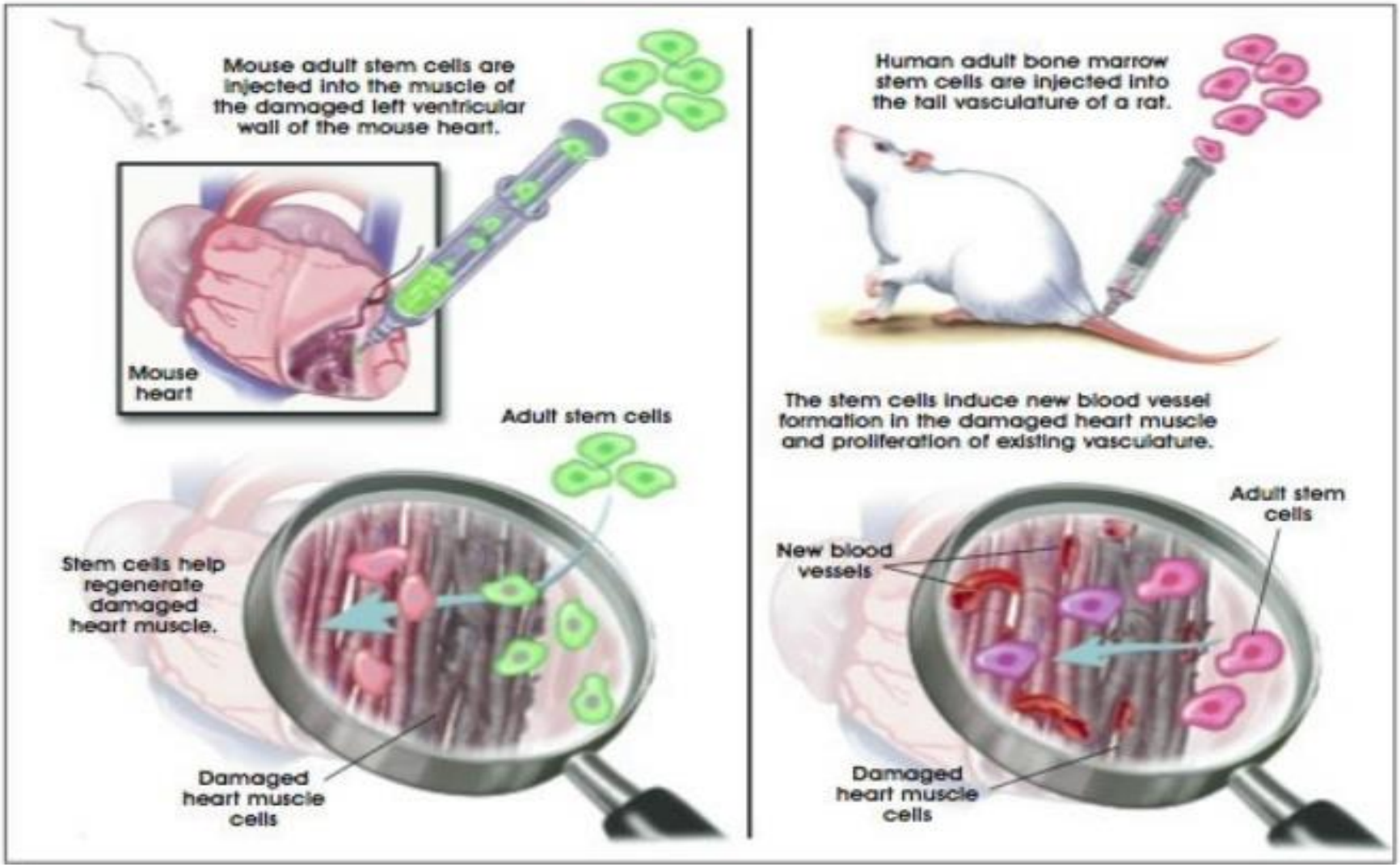
Umbilical Cord Blood Stem Cell Transplant

CAN THESE STEM CELLS CURE HEART DISEASES?

- **Rodent Model of Myocardial Infarction**



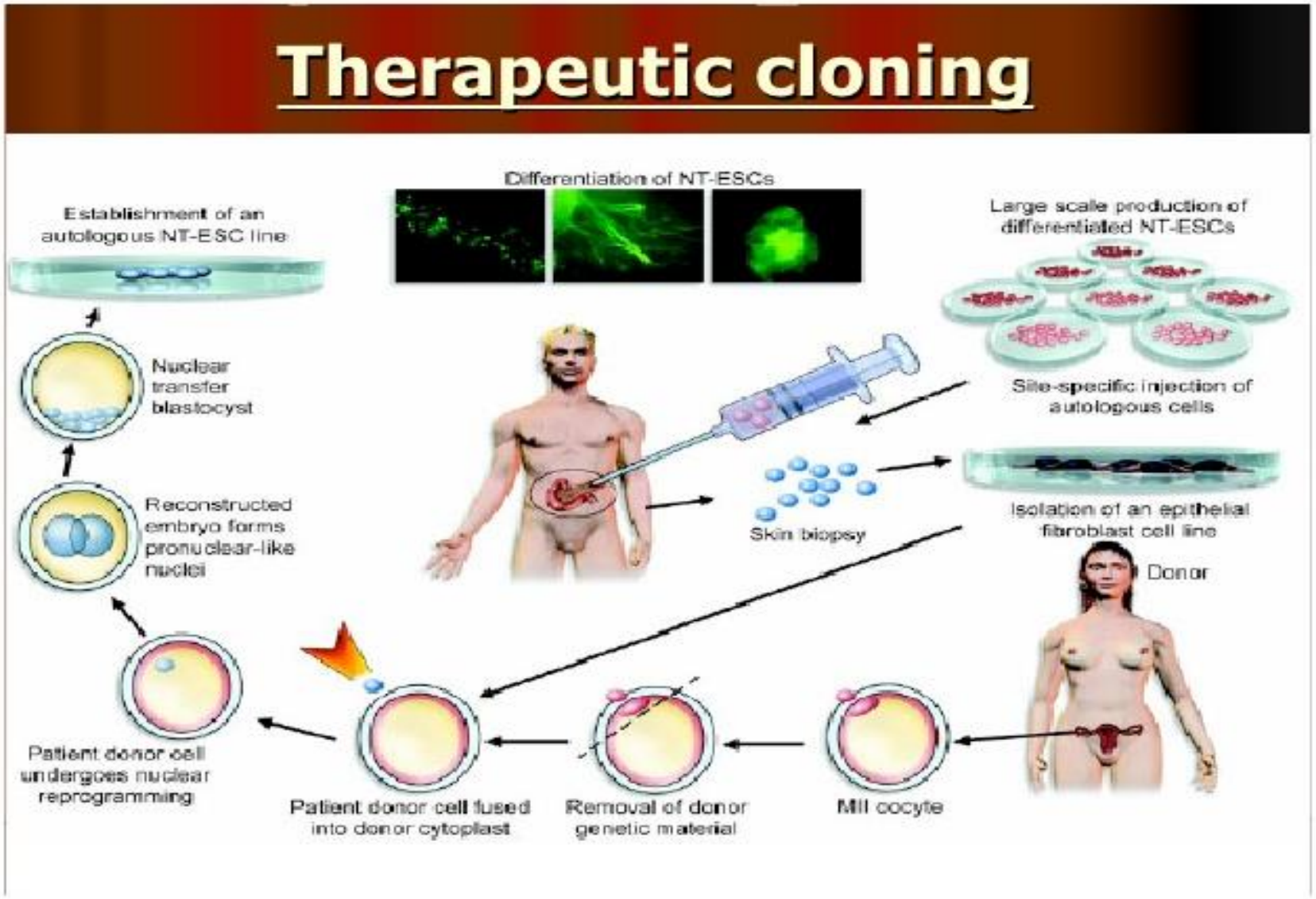
Heart Muscle Repair with Adult Stem Cells



CONCLUSION

Now days these stem cells are effectively used in the treatment of heart diseases & addressing the nations leading causes of death.

Therapeutic applications of stem cells in neurodegenerative diseases,



Non-Controversial Stem Cells

- Umbilical Cord Blood Stem Cells
- Bone Marrow Stem Cells
- Adult Peripheral Blood Stem Cells

-Therapeutic-

Stem Cell Banking

- **Cord Blood banking** is now becoming popular for autologous as well as for allogeneic donor
- **Adult Peripheral Blood** collection and cryopreservation can also be used for future diseases
- **Stem cells can be collected** from UCB, Adipocytes and Peripheral Blood by Apheresis
- **Stem cells can be Cryopreserved** for use in Cancers, CAD, Stroke, Diabetes, Burns, Spinal Cord injury, Osteoarthritis, Regenerative medicine, etc.

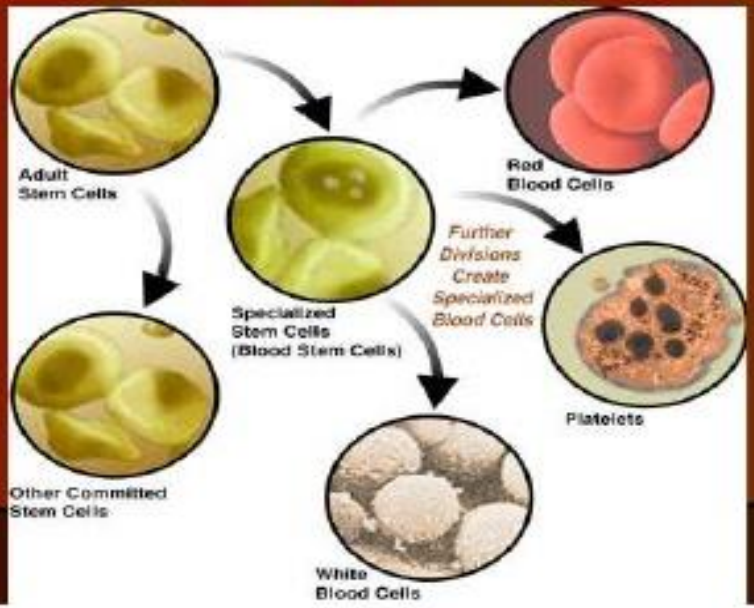
Diseases Treatable with Stem Cells — Today

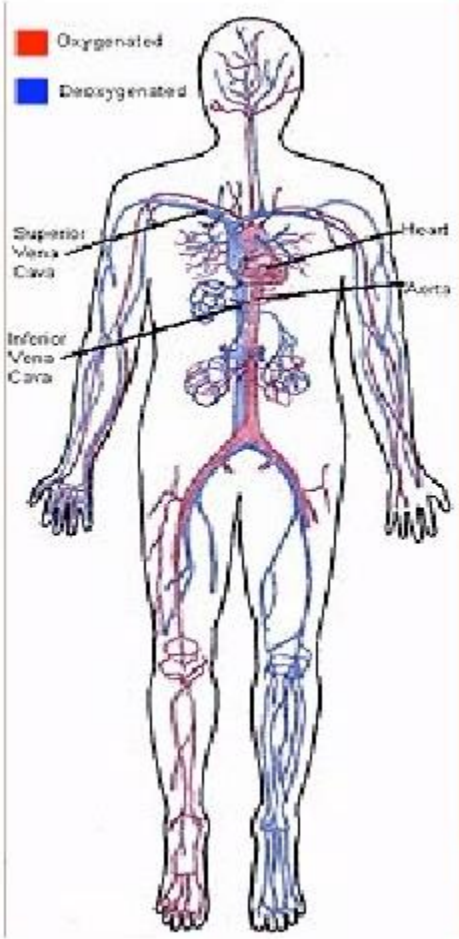
- Leukemias
- Lymphoma
- Multiple Myeloma
- Coronary Heart Disease
- Radiation Sickness
- Multiple Sclerosis
- Lupus Erythematosis
- Other Autoimmune Diseases
- Tissue Repair & Burns
- Orthopedics
- Etc.

Target Diseases for Stem Cell Therapy

Blood Diseases

- Bone marrow transplants (BMT) are a well known clinical application of hematopoietic stem cell (HSC) therapy
- HSCs can regenerate all of the different cell types in blood
- BMT is used for the treatment of blood cancers like leukemia and lymphoma, as well as breast cancer and any other disease requiring immune system regeneration





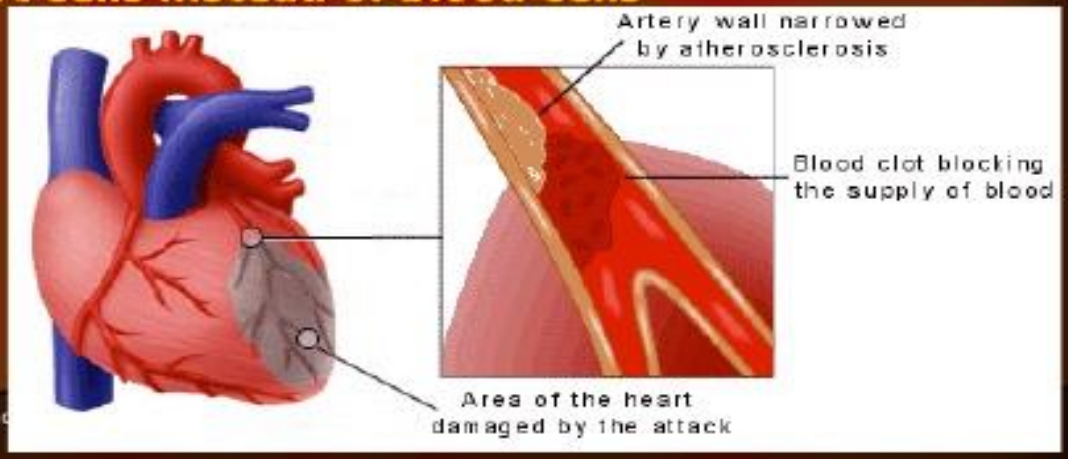
- **The cardiovascular** circulatory system's main role is to transport nutrients and oxygen to the 50-100 trillion cells that makes up our body and remove the waste material from the body.
- The most prevalent disease that affects the CVS is:

1. Atherosclerosis
2. Hypertension
3. Acute myocardial infarction
4. Stroke

Target Diseases for Stem Cell Therapy

Heart Disease

- ES cells can be induced to form cardiac muscle cells that actually beat in culture
- When transplanted into damaged hearts, these cells can form gap junctions and contract in unison with surrounding cells
- HSCs can also be grafted into damaged heart muscle and, in this new environment, are reprogrammed to produce heart cells instead of blood cells



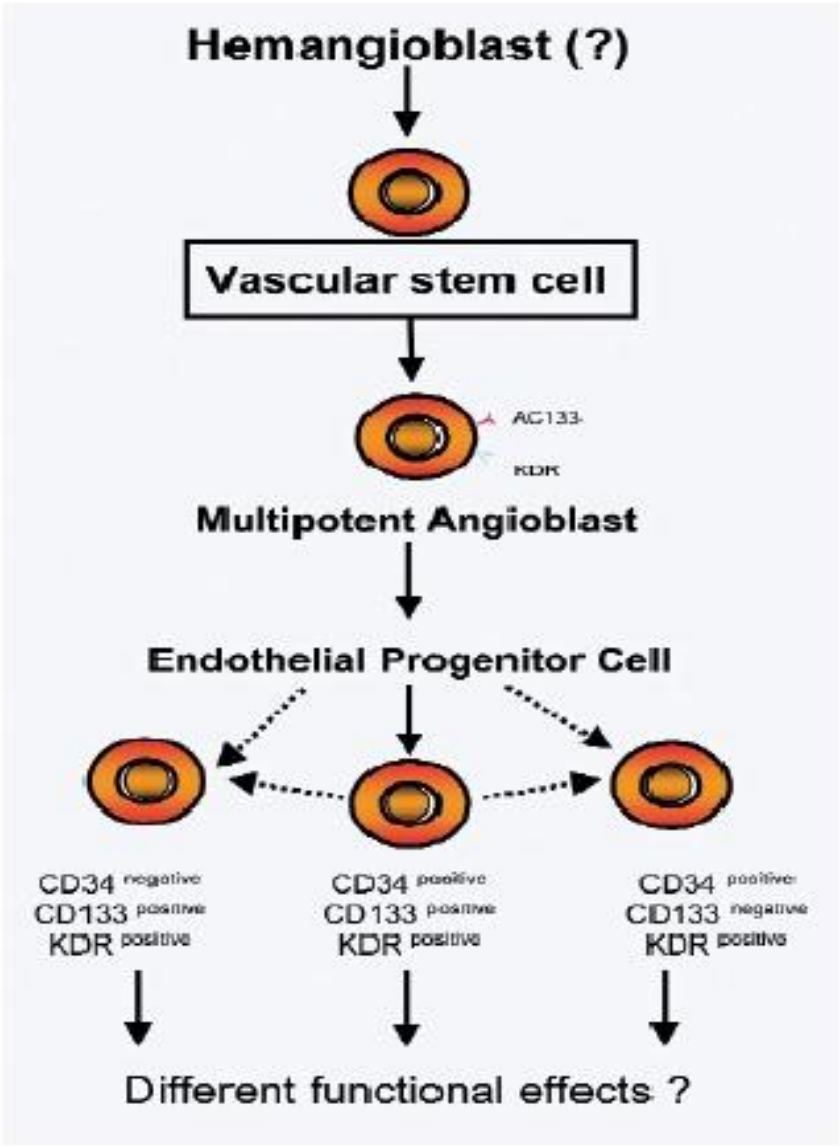
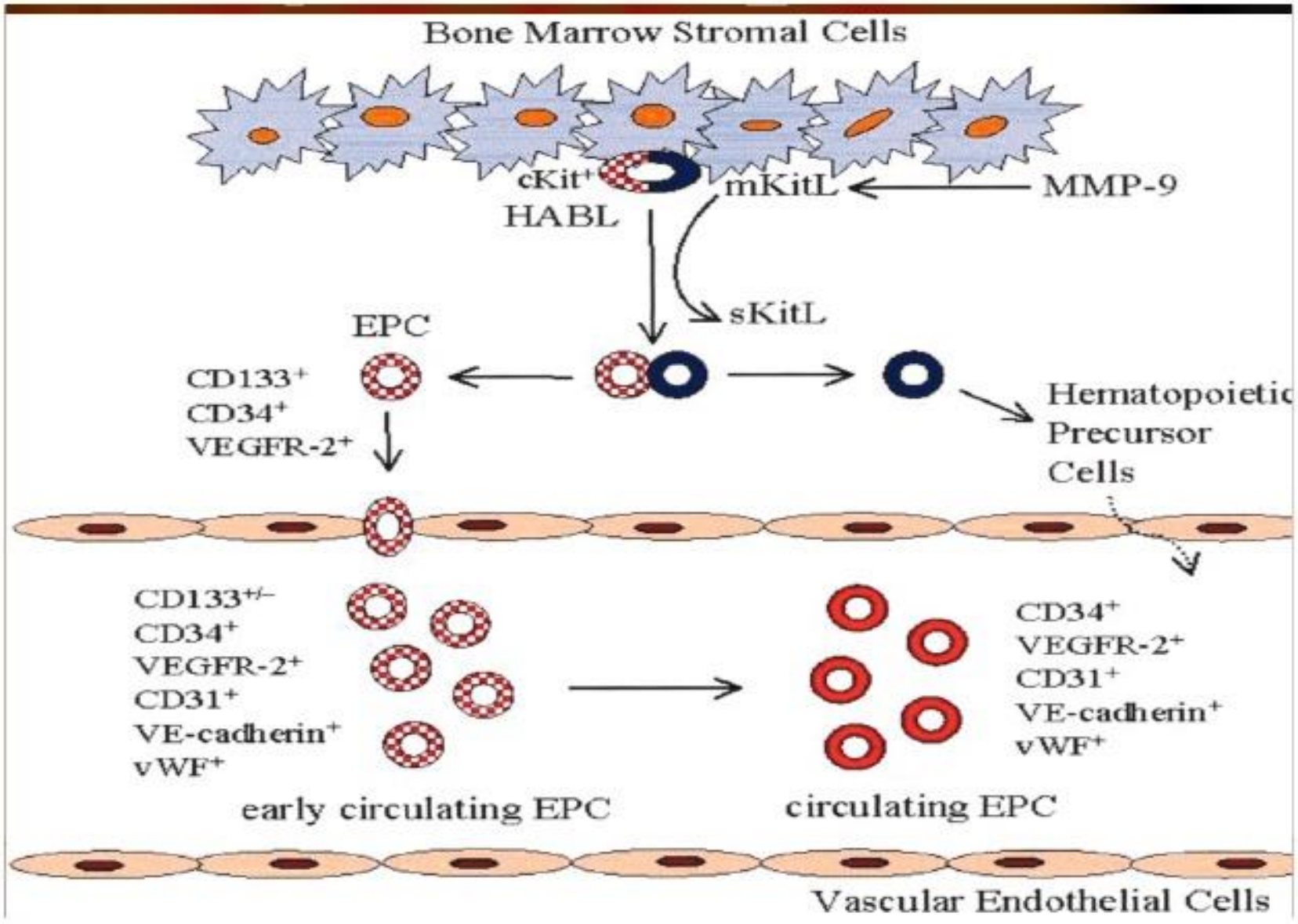
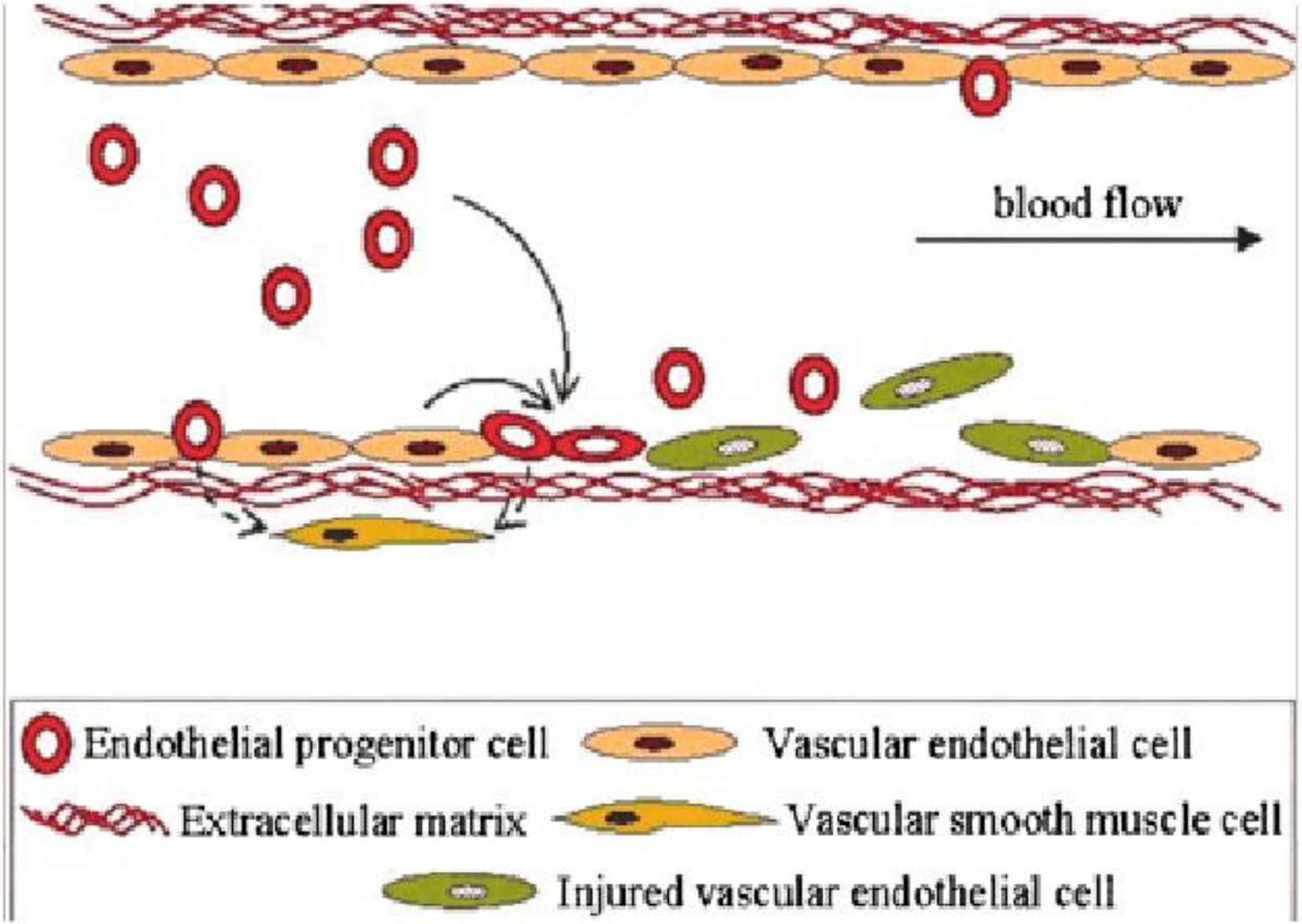


Fig. 1 Endothelial progenitor cells are putatively derived from the hemangioblast, circulate in peripheral blood and have the potential to differentiate into mature endothelial cells. The surface markers CD34, KDR (VEGFR2), CD133 define circulating endothelial progenitor cells. Recently, it has been demonstrated that different subpopulation display different functional activities concerning angiogenesis and endothelial cell repair. The CD34 negative, CD133 and VEGFR2 positive EPC subpopulation is a precursor of the CD34/CD133 positive EPC population and preferably homes to sites of ischemia.


Bone Marrow Stromal Cells
cKit+
HABL
mKitL
MMP-9
sKitL
EPC
CD133+
CD34+
VEGFR-2+
Hematopoietic
Precursor
Cells
CD133+/–
CD34+
VEGFR-2+
CD31+
VE-cadherin+
vWF+
early circulating EPC
CD34+
VEGFR-2+
CD31+
VE-cadherin+
vWF+
circulating EPC
Vascular Endothelial Cells


blood flow
Endothelial progenitor cell
Vascular endothelial cell
Extracellular matrix
Vascular smooth muscle cell
Injured vascular endothelial cell

Pediatric Research 59:26R-32R (2006)

DOI: 10.1203/01.pdr.0000203553.46471.18

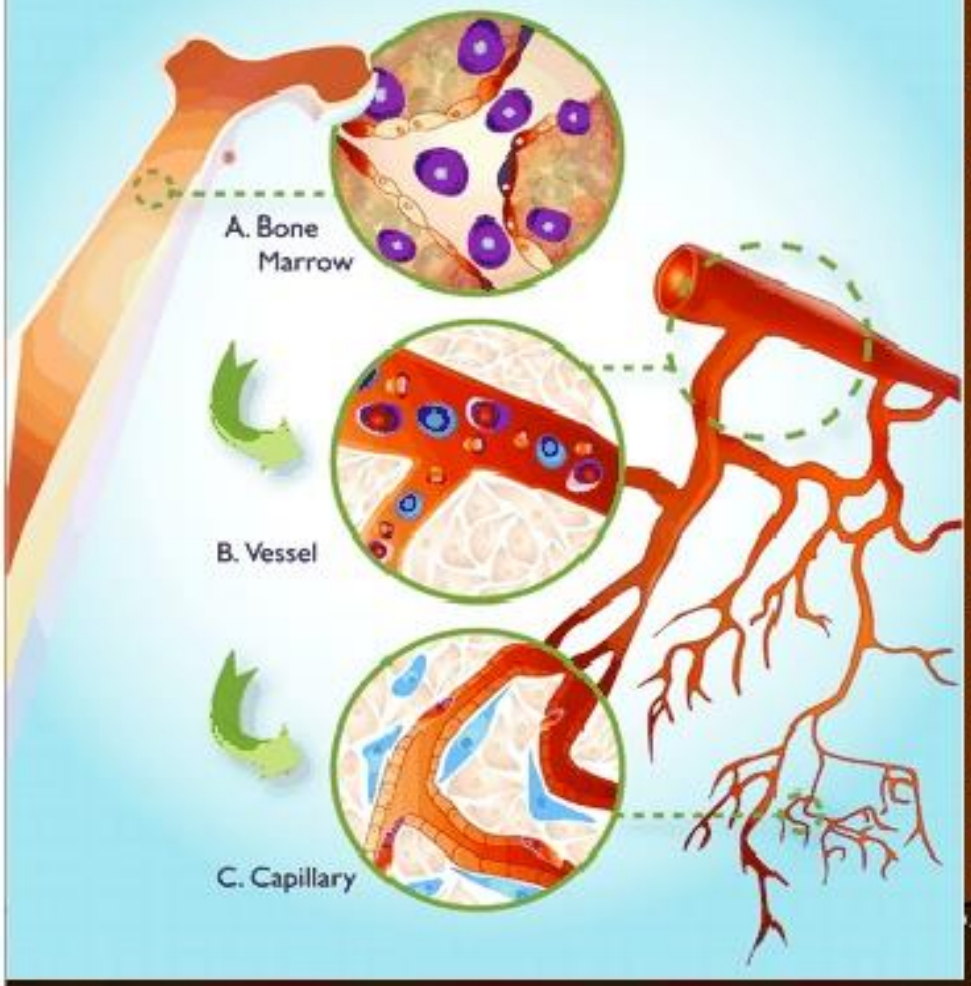
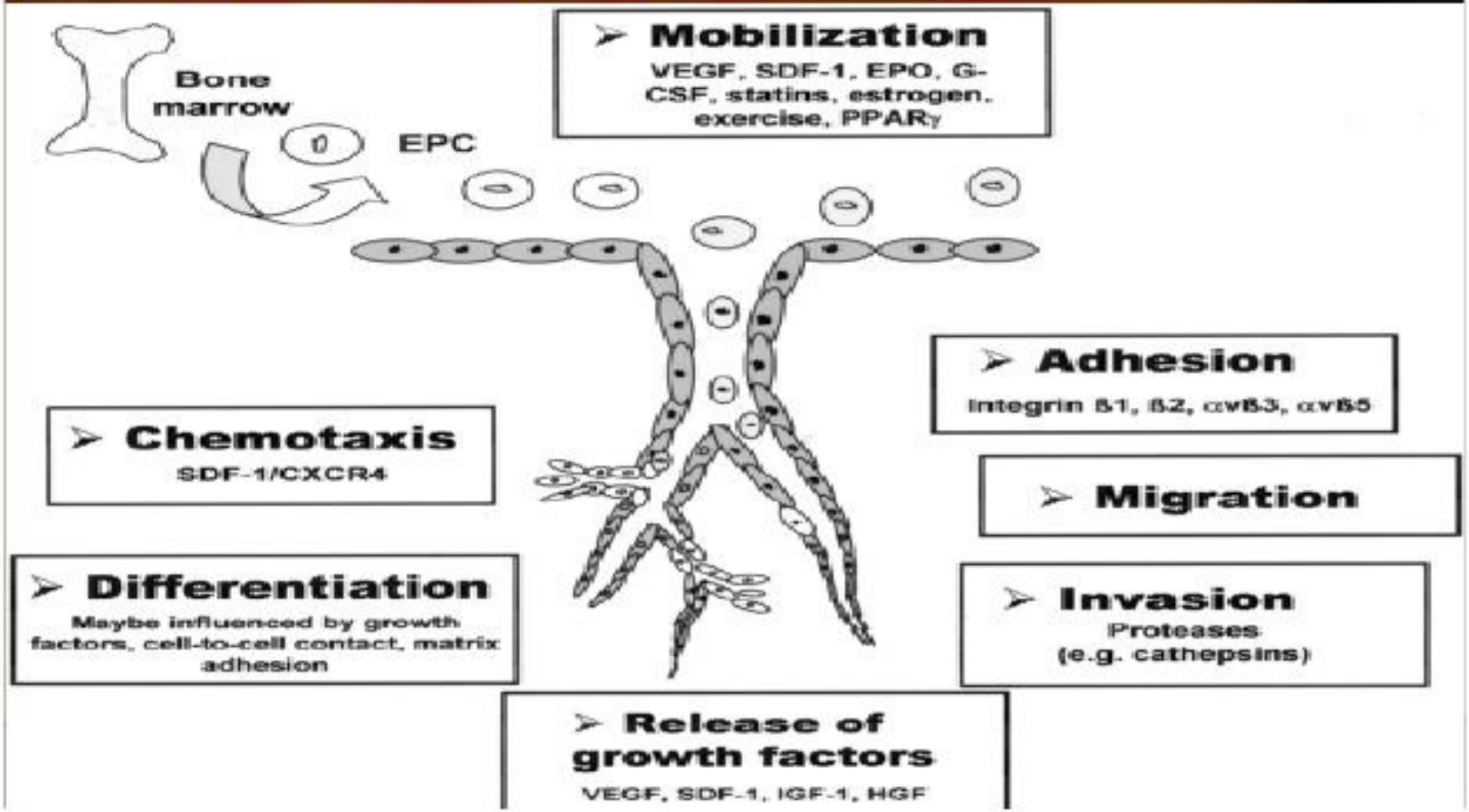
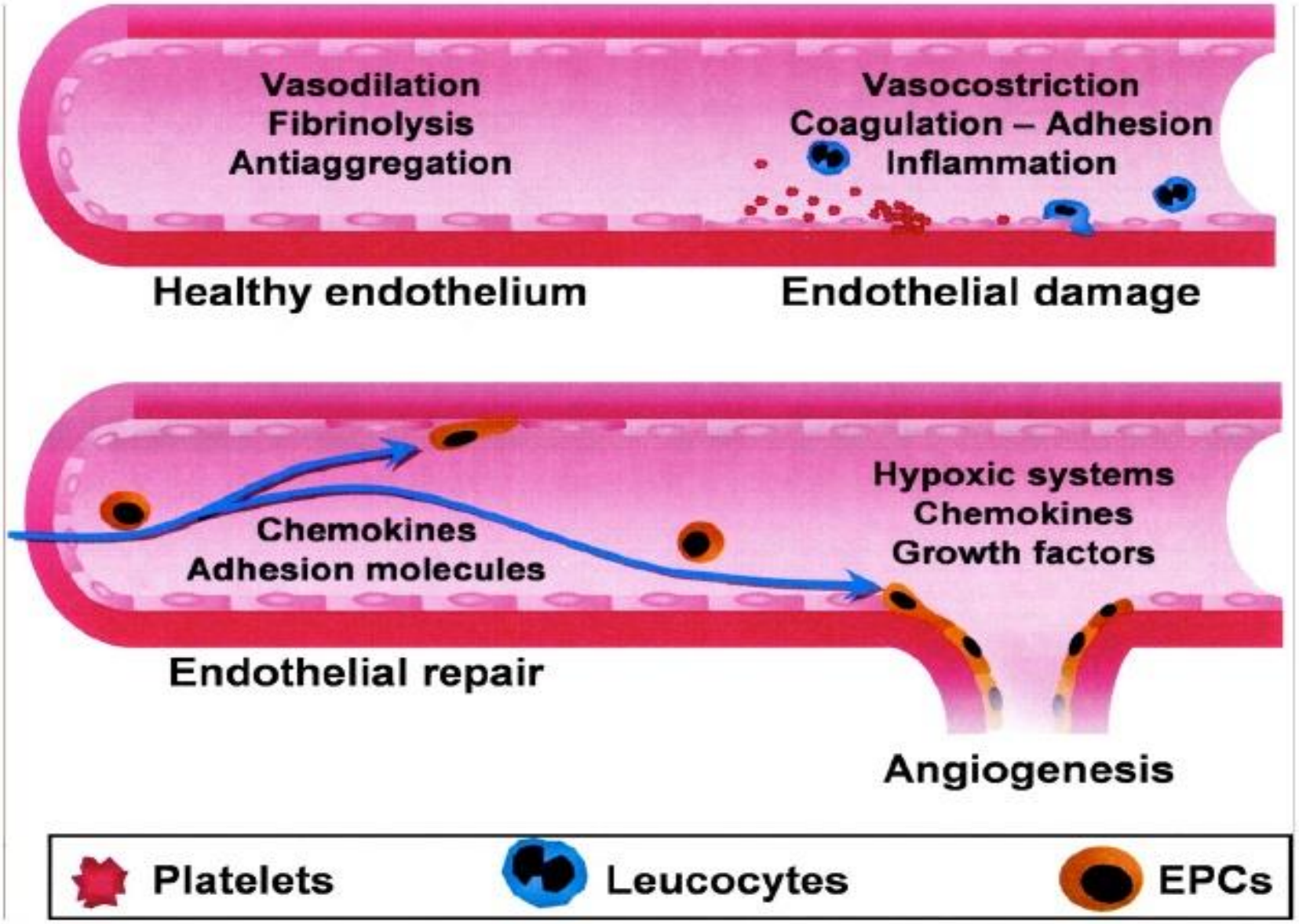
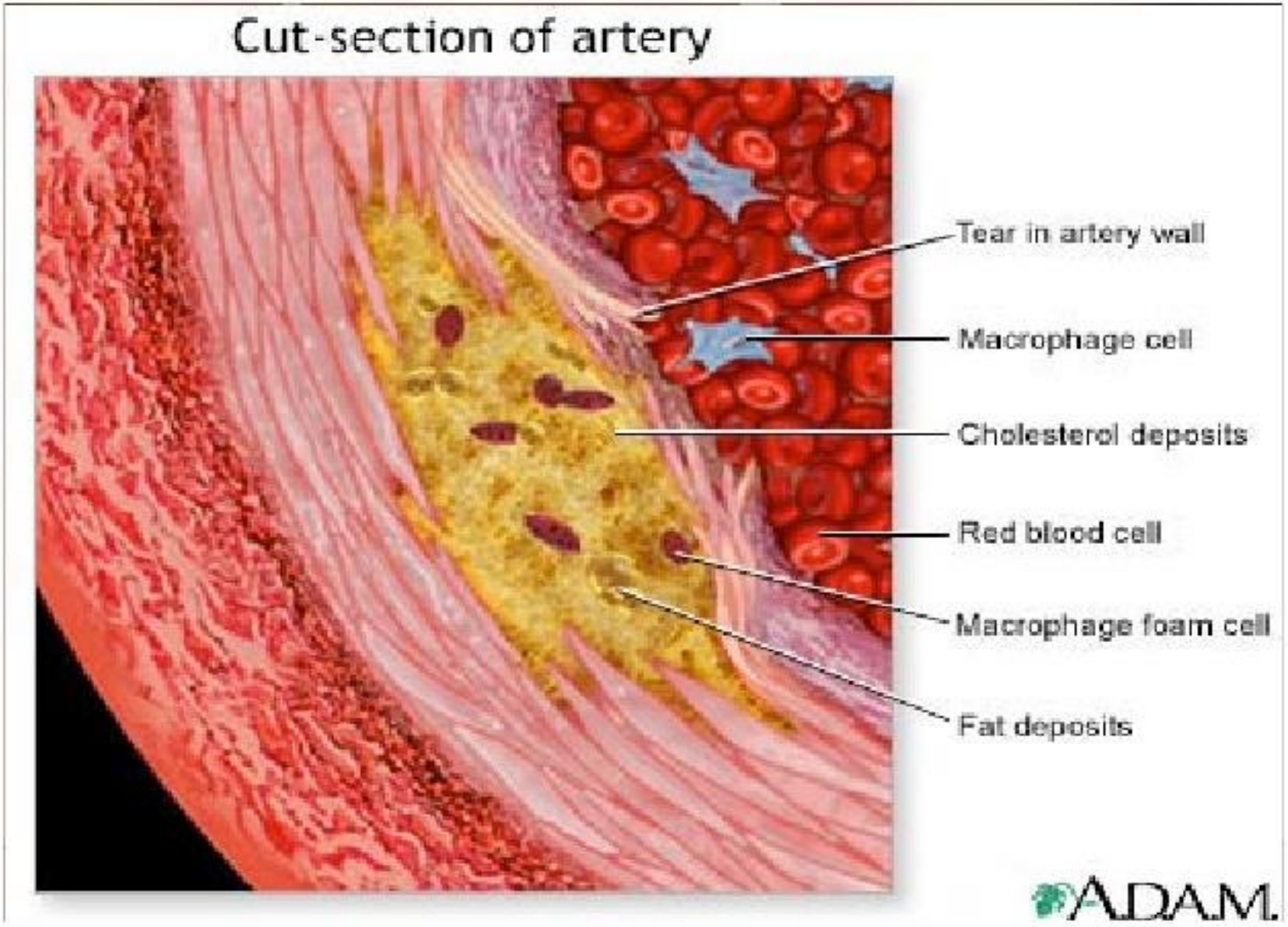


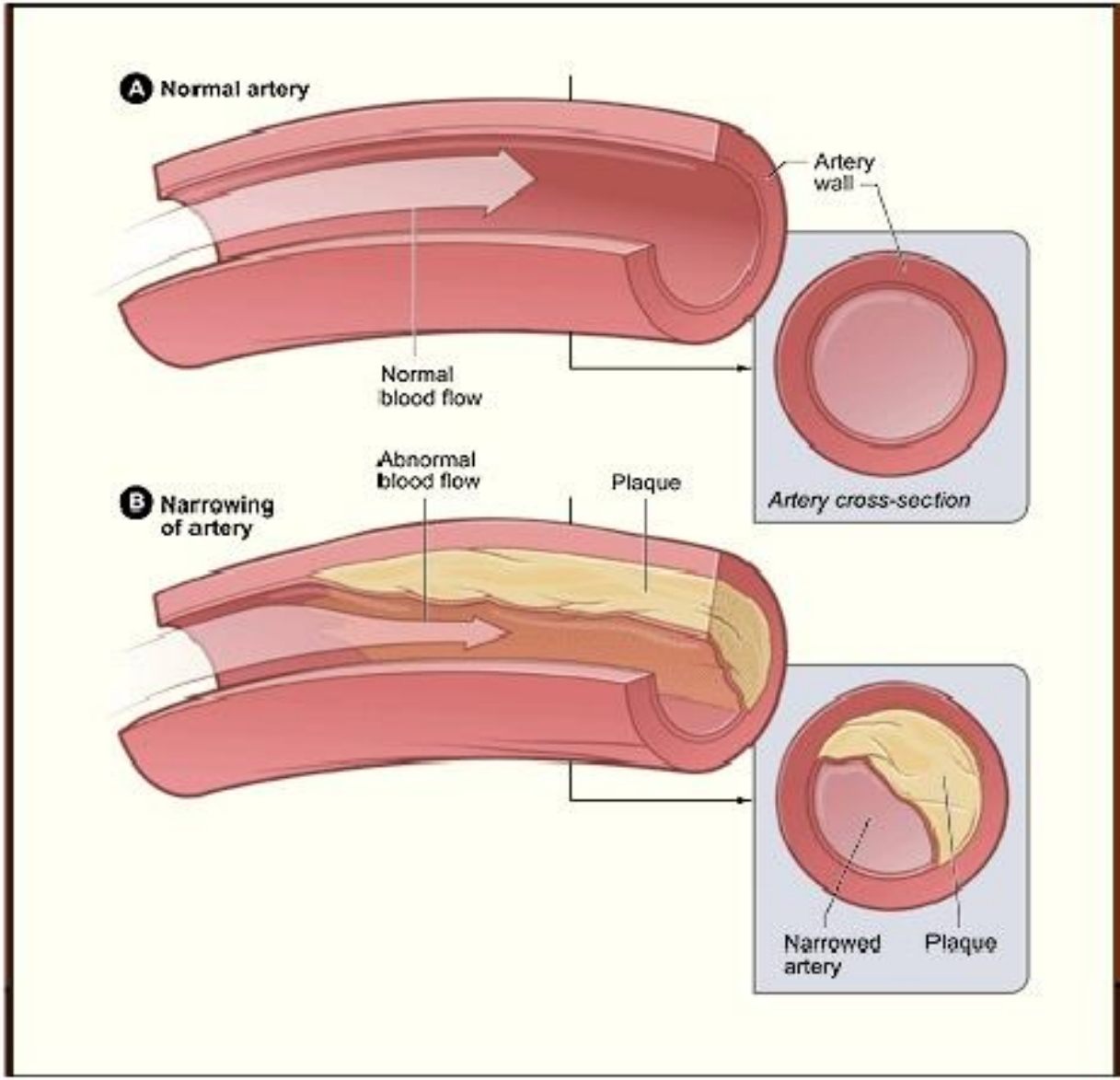
Figure 1. EPCs are bone marrow-derived cells that contribute to postnatal angiogenesis. EPCs (seen in purple at *A*) can be mobilized from the bone marrow stroma by various growth factors and exit through sinusoidal vessels. Once in the bloodstream (*B*), EPCs begin to differentiate (indicated by the color change). Subsequently, these cells home to sites of angiogenesis in capillary beds (*C*) and attach to the endothelium. Unknown mechanisms drive endothelial precursors (red) to incorporate into the endothelial wall or pro-angiogenic monocytes (blue) to locate behind the endothelial wall and support the stability and viability of the local endothelium by paracrine mechanisms

Figure 3. Mechanism of EPC homing and differentiation. Recruitment and incorporation of EPCs into ischemic tissue requires a coordinated multistep process including mobilization, chemoattraction, adhesion, transmigration, migration, tissue invasion, and in situ differentiation. Factors that are proposed to regulate the distinct steps are indicated

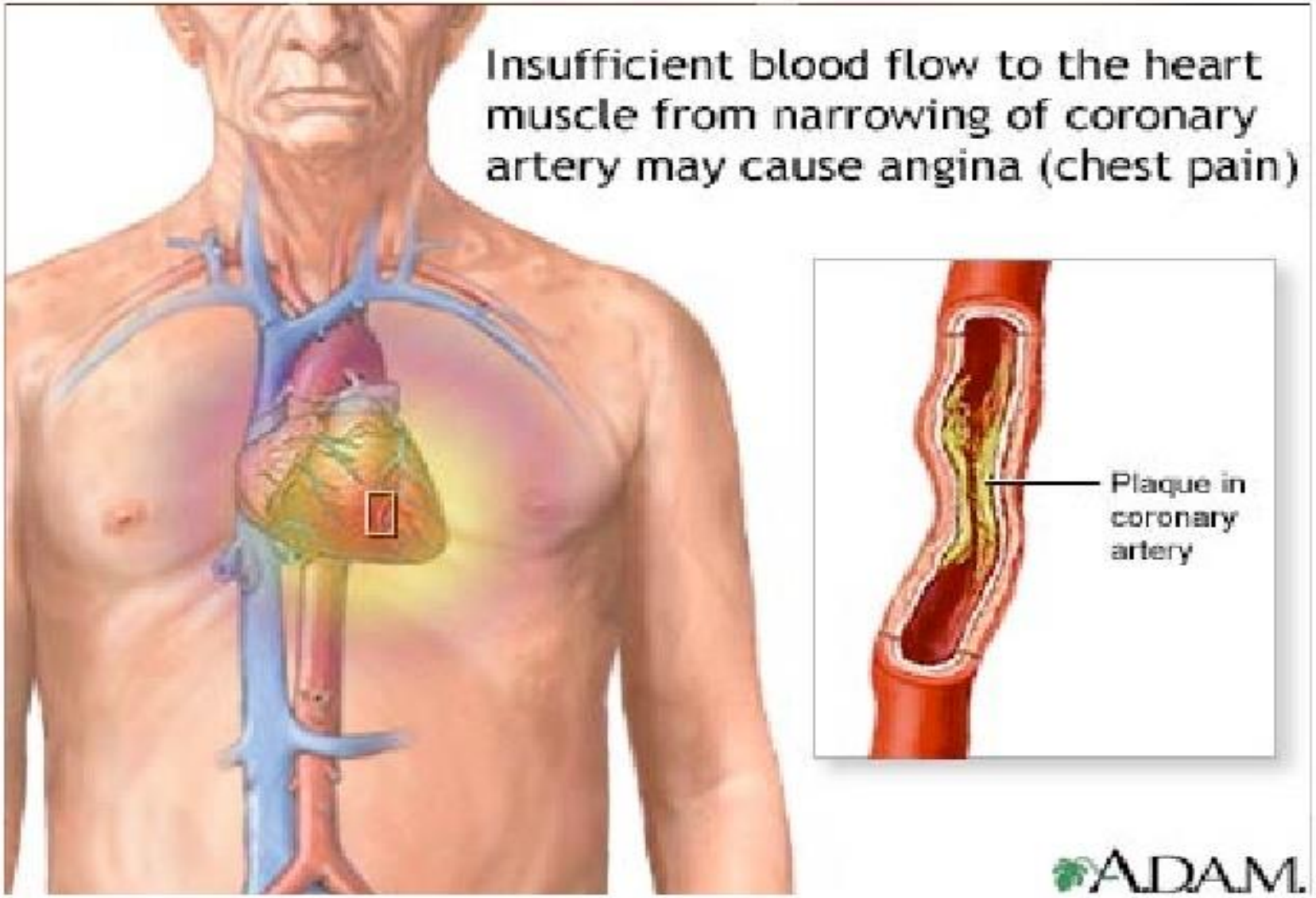



Vasodilation
Fibrinolysis
Antiaggregation
Vasocostriction
Coagulation – Adhesion
Inflammation
Healthy endothelium
Endothelial damage
Chemokines
Adhesion molecules
Hypoxic systems
Chemokines
Growth factors
Endothelial repair
Angiogenesis
Platelets
Leucocytes
EPCs

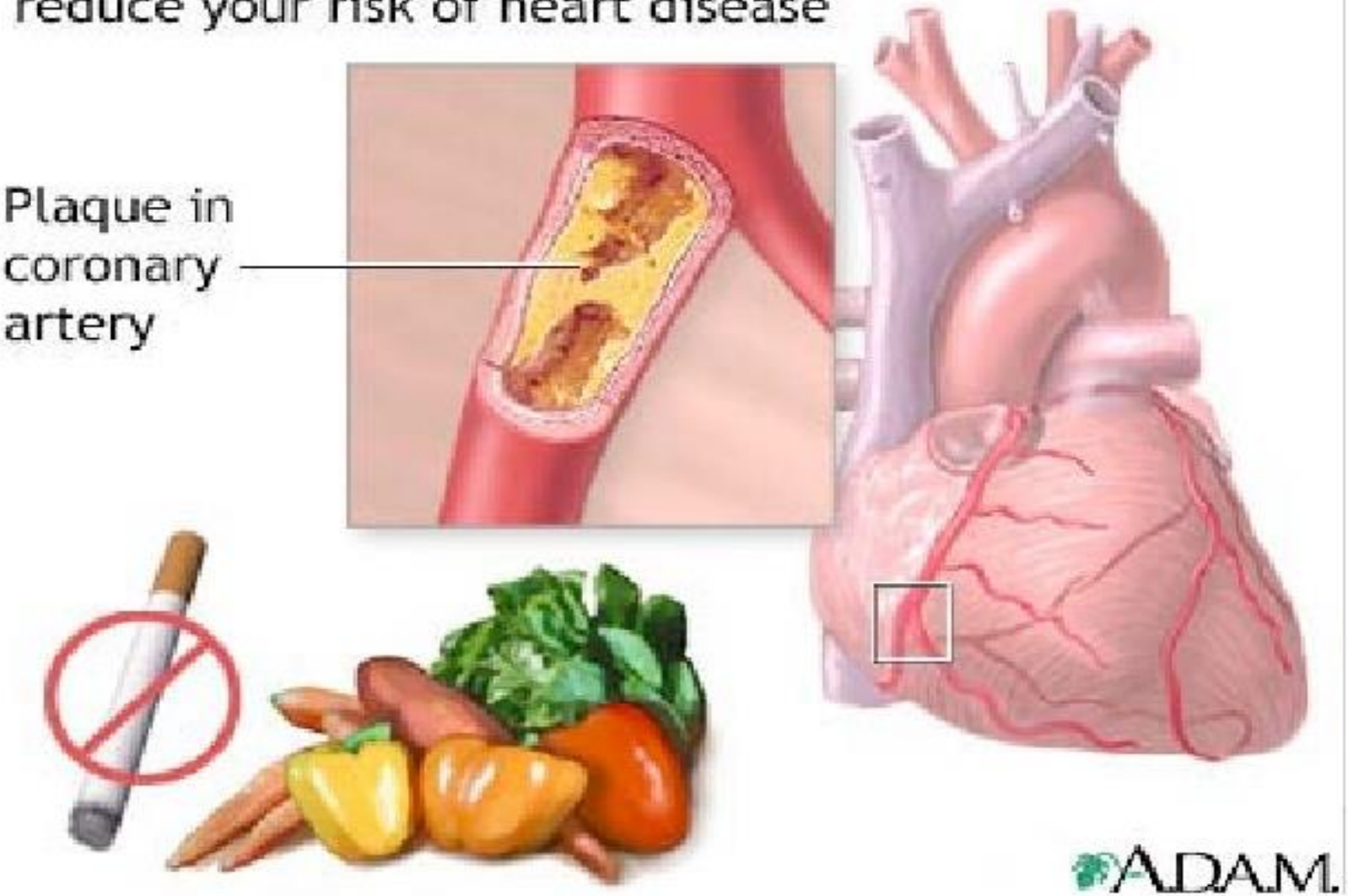

Cut-section of artery
Tear in artery wall
Macrophage cell
Cholesterol deposits
Red blood cell
Macrophage foam cell
Fat deposits
A.D.A.M.



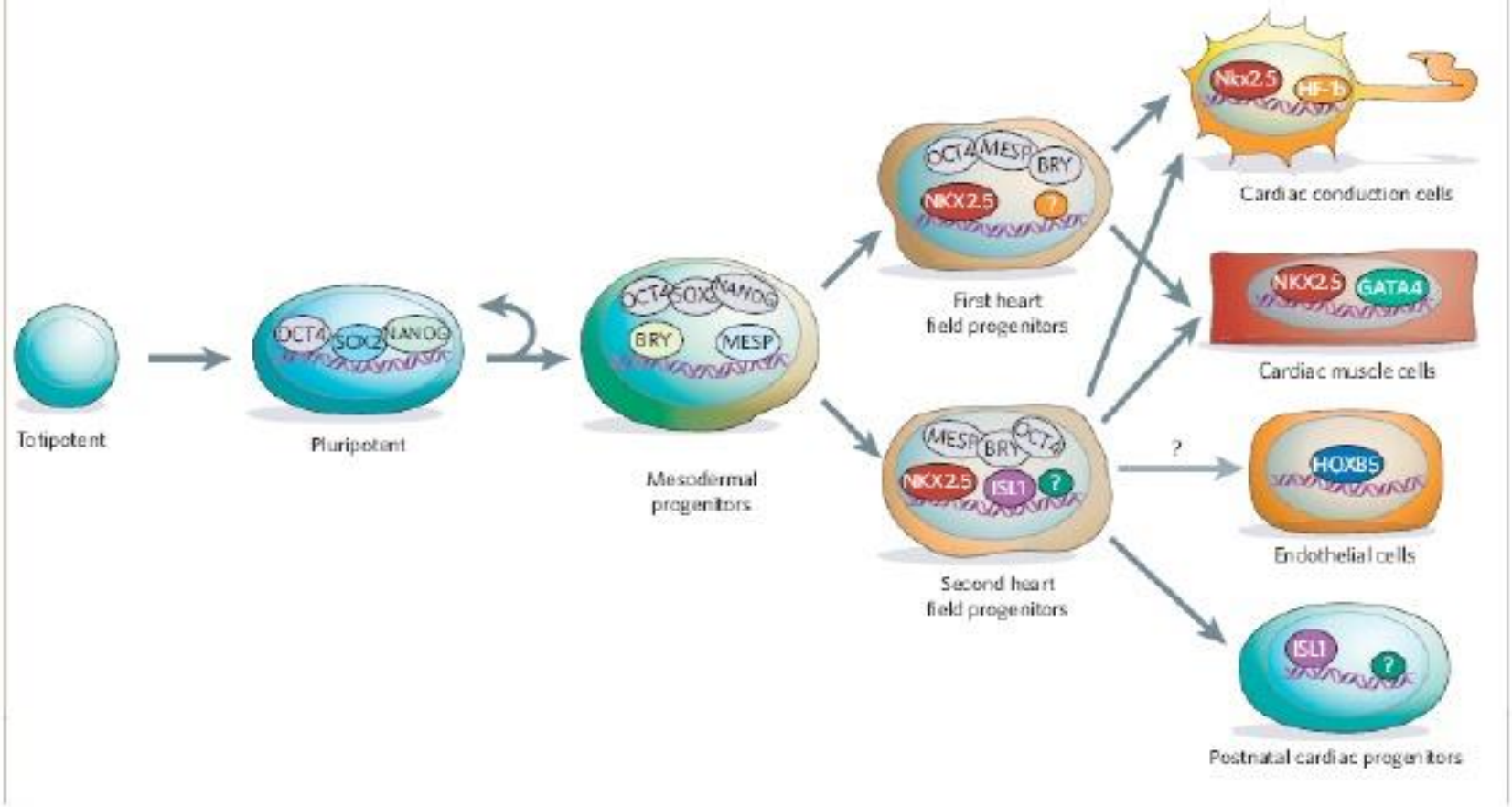
- **To Prevent Athero-sclerosis**
  - Control cholesterol level
  - Control Hypertension
  - Exercise
  - Diet
  - No smoking


Insufficient blood flow to the heart muscle from narrowing of coronary artery may cause angina (chest pain)
Plaque in coronary artery
A.D.A.M.

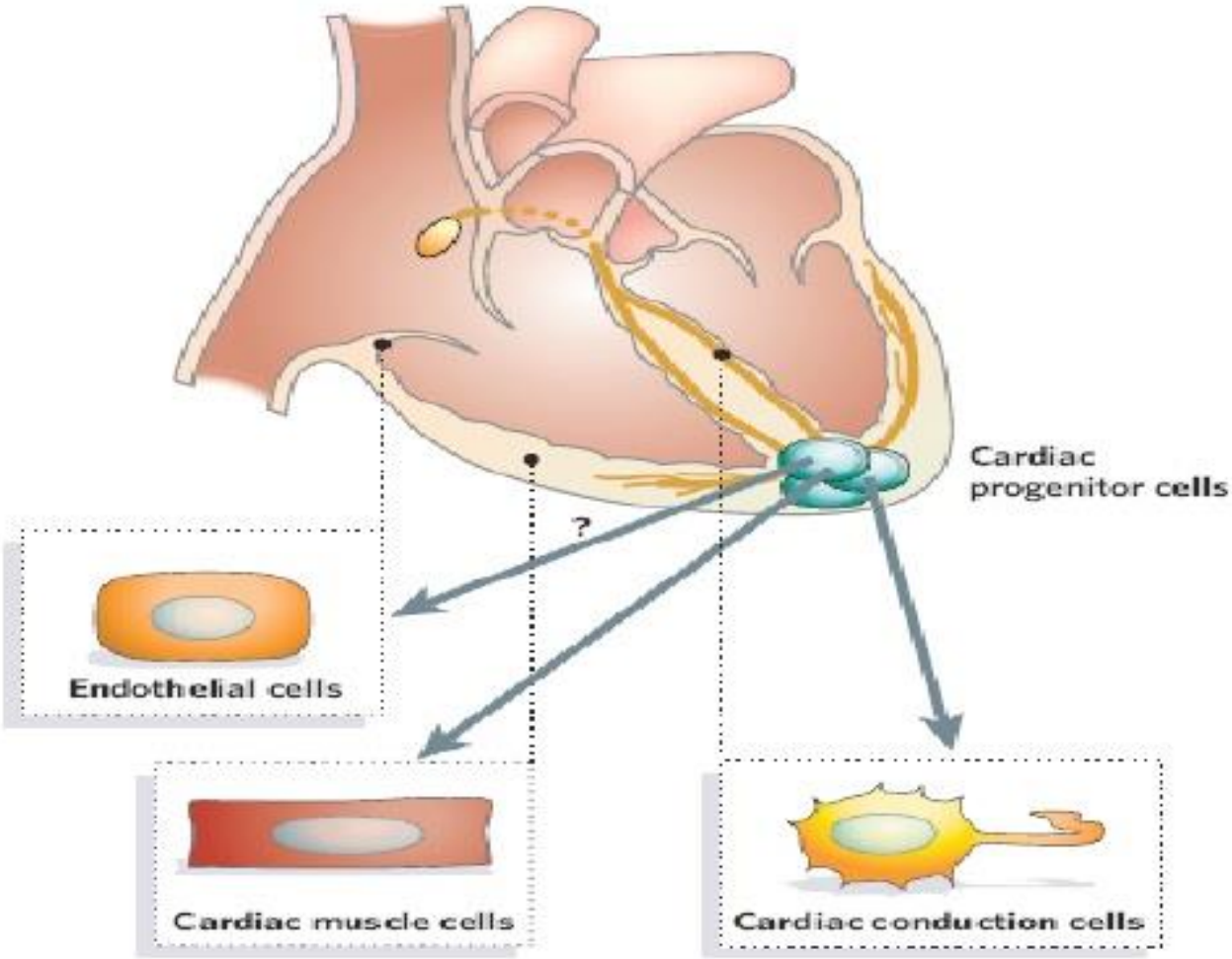
Quitting smoking, a healthy diet and exercise may reduce your risk of heart disease

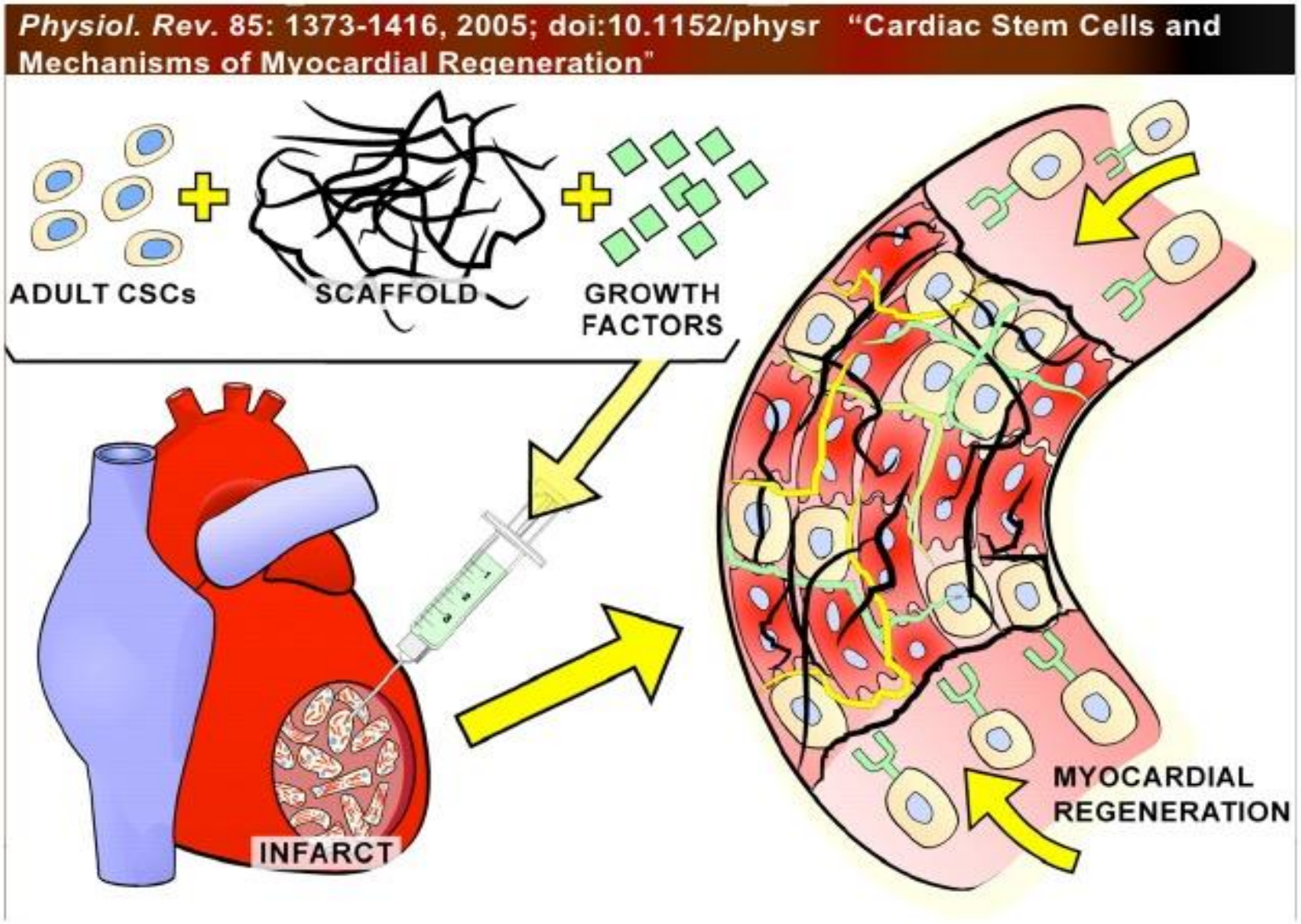


Differentiation of embryonic cells into the cardiac lineage

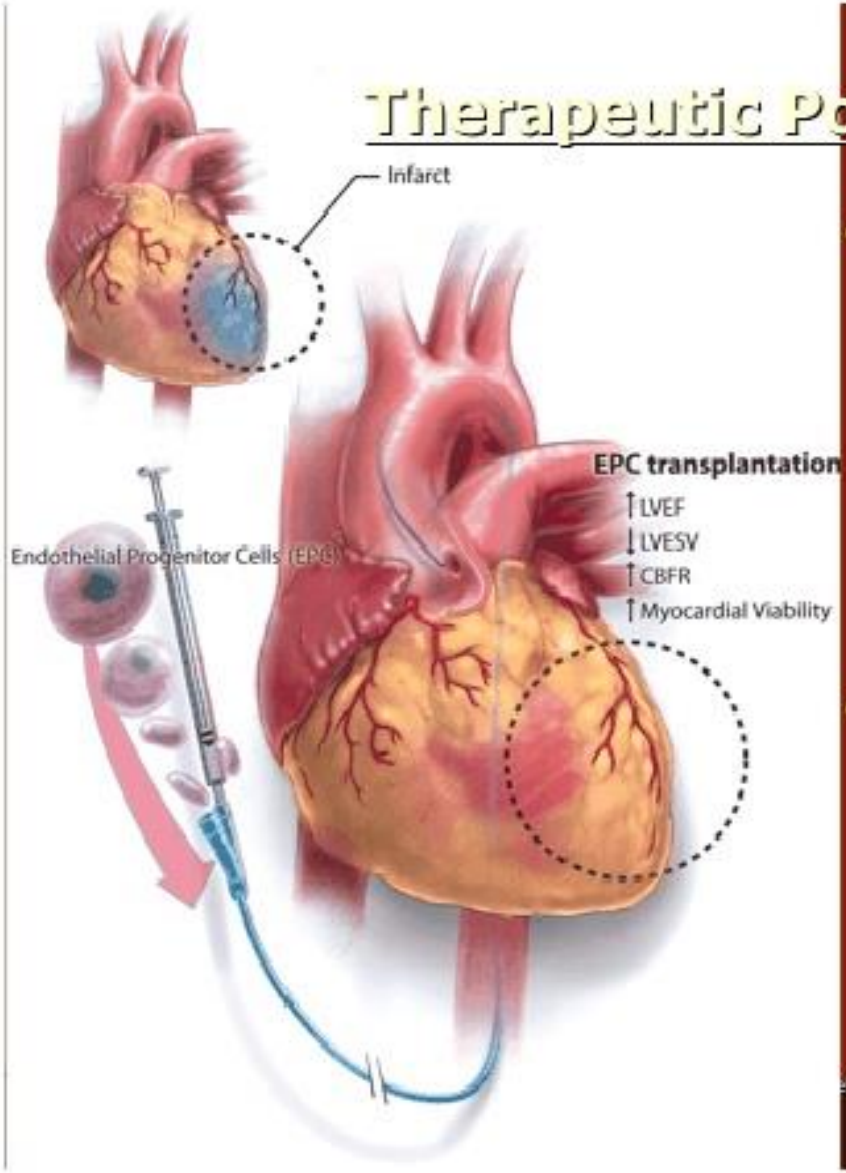


NATURE|Vol 441|29 June 2006




Physiol. Rev. 85: 1373-1416, 2005; doi:10.1152/physr "Cardiac Stem Cells and Mechanisms of Myocardial Regeneration"
ADULT CSCs
SCAFFOLD
GROWTH FACTORS
INFARCT
MYOCARDIAL REGENERATION

Therapeutic Potential of EPC in AMI

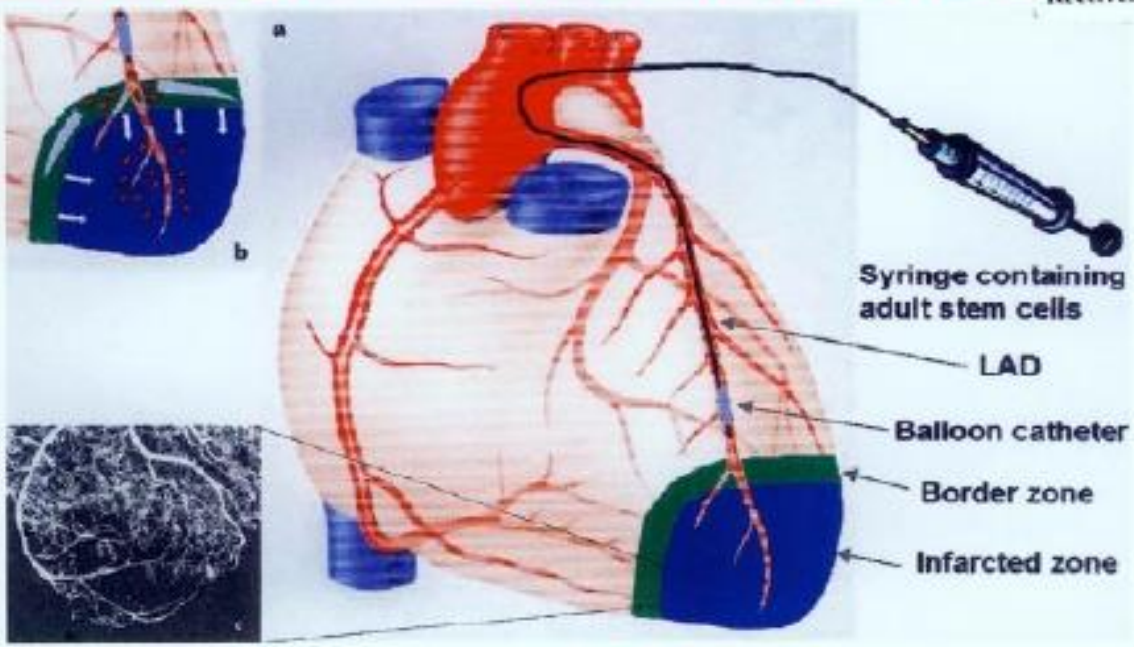


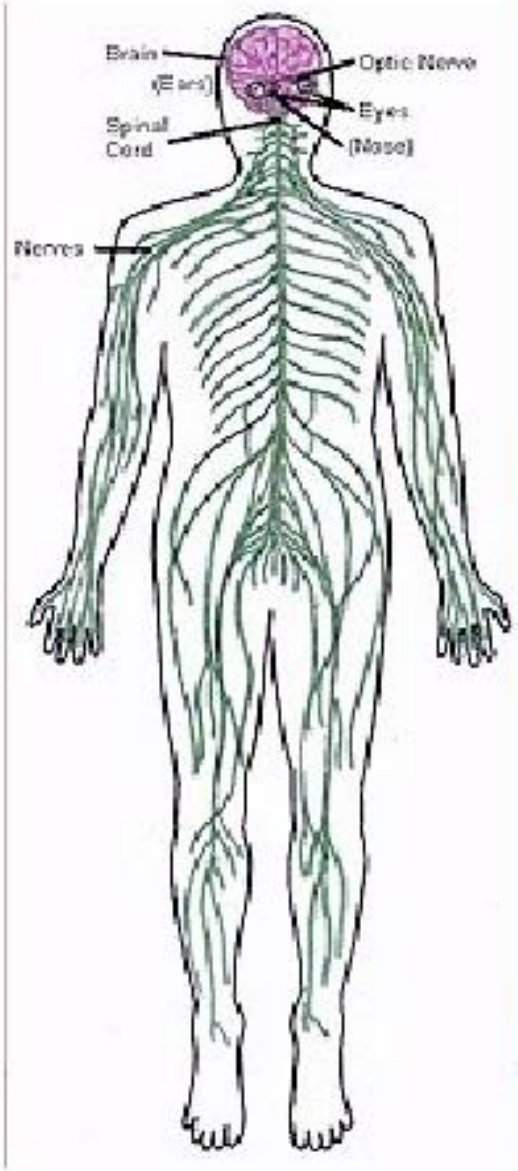
- Figure 2. Therapeutic potential of EPCs. Intracoronary infusion of EPCs in patients with AMI may have the potential to restore myocardial function to the damaged area.
- EPC transplantation increases left ventricular ejection fraction (LVEF), coronary blood flow reserve, and myocardial viability and decreases left ventricular end-systolic volume (LVESV).66

Fighting Heart Disease and Stroke

Circulation

JOURNAL OF THE AMERICAN HEART ASS





- **Major Role CNS:**
  The main role of the nervous system is to relay electrical signals through the body. The nervous system directs behaviour and movement and, along with the endocrine system, controls physiological processes such as digestion, circulation, etc.
- **The most prevalent diseases that affect the CNS is Stroke, Parkinson's disease, Alzheimer's disease, ALS and Autism**

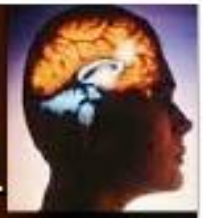
dr.Boenjamin Setiawan,Ph.D.

Proposed Mechanism for Stem Cells in Neurodegenerative Diseases

- Implanted stem cells migrated & integrated extensively throughout the brain
- Some of the transplanted cells replaced damaged nerve cells and transmitted nerve impulses→ integrate electrically and functionally into a diseased brain
- stem cells employ multiple mechanisms → not just cell replacement - which collaborate to benefit disease

Lee et al, Nature 2007

Brain Cell Transplantation

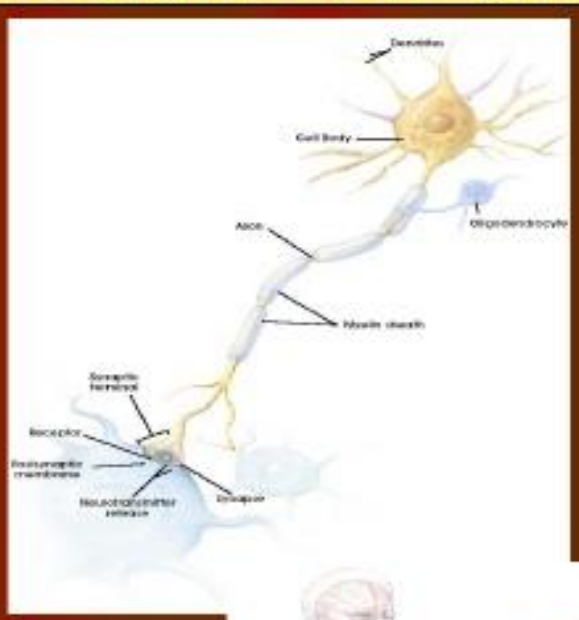


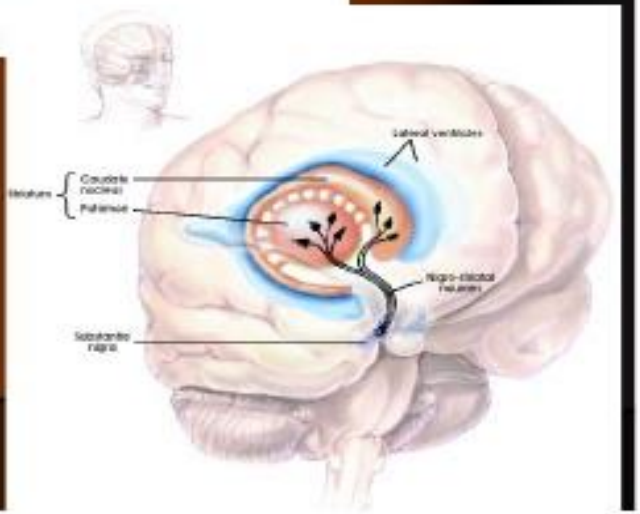
- The identification and localisation of neural stem cells, both embryonic and adult, has been a major focus of current research.
- Potential targets of neural stem cell transplants
- **1. include stroke, 2. spinal cord injury, and**
- **3. neurodegenerative diseases such as Parkinson's Disease, 4. Alzheimer**
- Stem cells can provide dopamine - a chemical lacking in victims of Parkinson's Disease
- Over 250 patients have already been transplanted with human fetal tissue

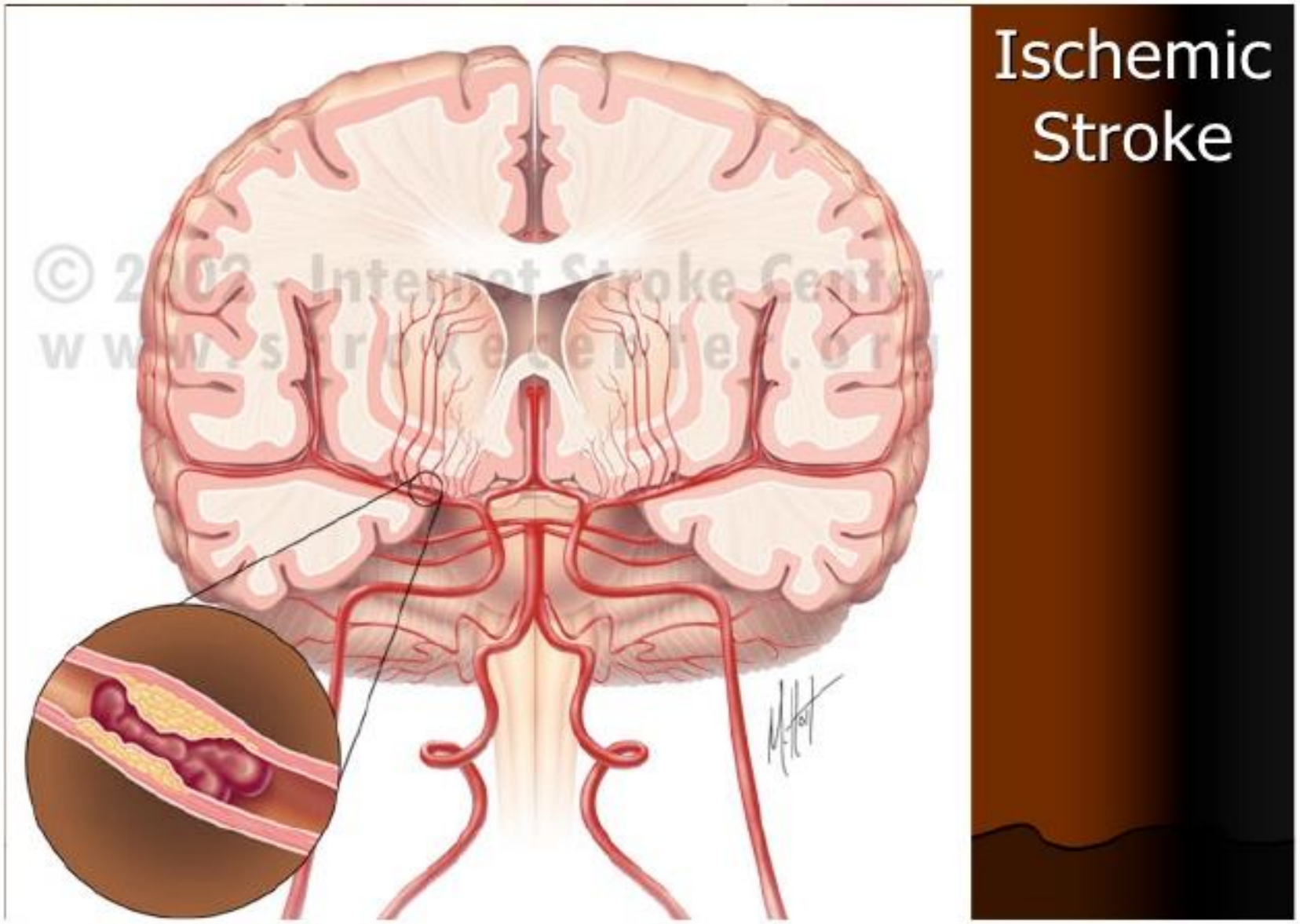
Target Diseases for Stem Cell Therapy

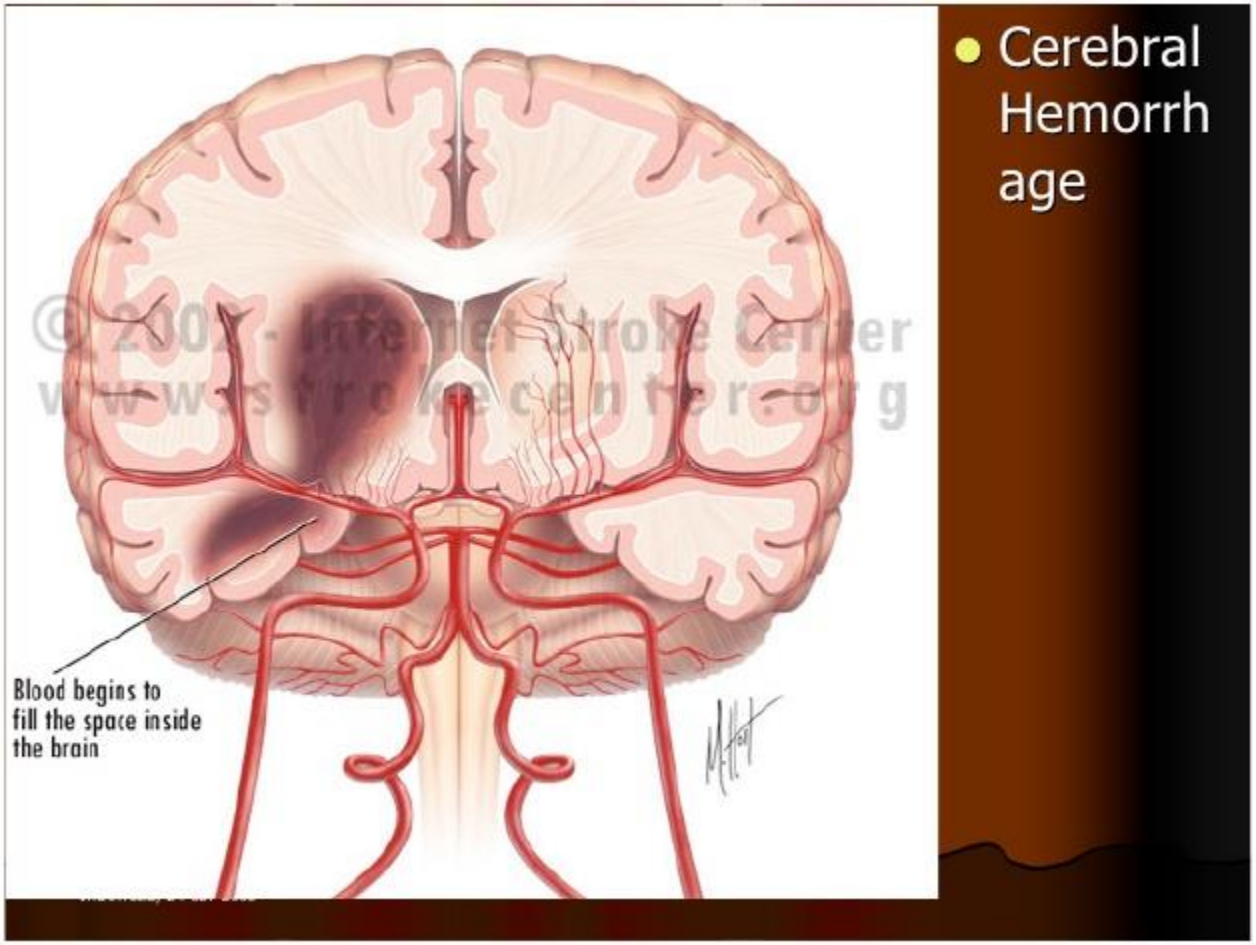
Brain and Spinal Cord Injury

- Neural stem cells can be isolated from adult brains or generated from ES cells in culture
- HSCs can also be transplanted into the brain where they are reprogrammed to generate neurons and glial cells
- Potential applications include Parkinson's disease, ALS, Huntington's disease, stroke, Alzheimer's disease, paralysis
- Animal and early human trials are underway






Ischemic
Stroke



- Cerebral Hemorrhage

Spinal Cord Injuries

Hwang Mi-Soon: South Korea

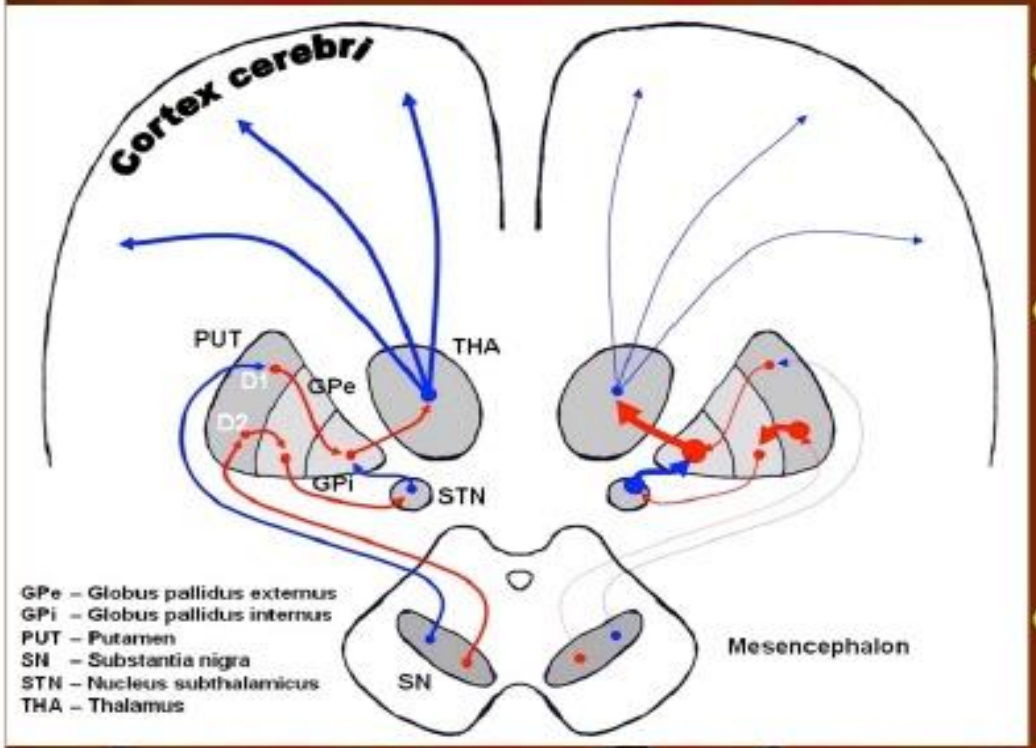
Paralyzed 19 years

Multipotent adult stem cells injected into her spinal cord

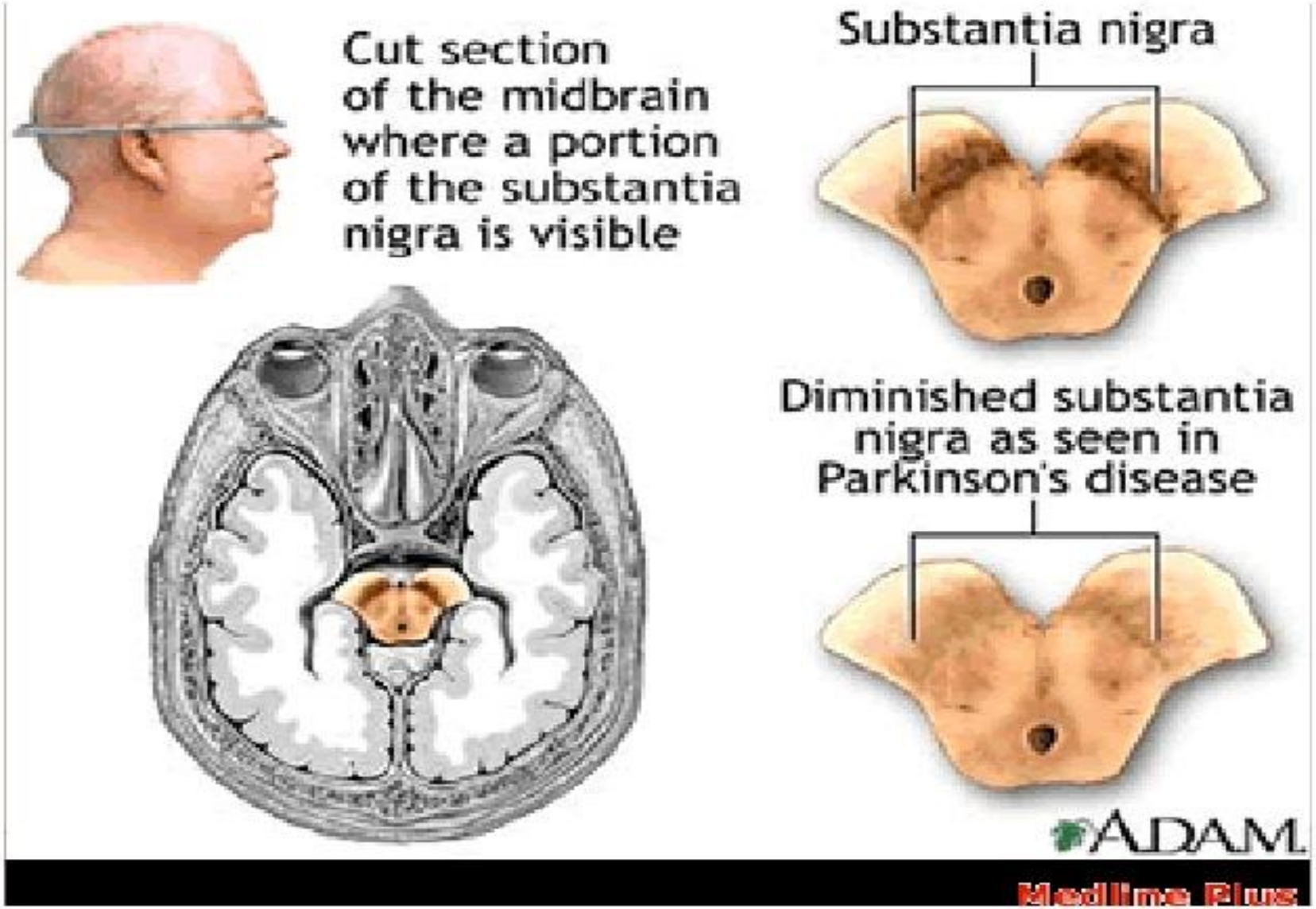
Currently: debilitating pain

Published in 2005 (*Cytotherapy*)

Parkinson's Disease : Degeneration of brain cells



- Cells in the *substantia nigra*
- Loss of the chemical *dopamine*
- No clear reason why


Cut section of the midbrain where a portion of the substantia nigra is visible
Substantia nigra
Diminished substantia nigra as seen in Parkinson's disease
A.D.A.M.
Medline Plus

„ The war against Parkinson is winnable –
And you can take part in the victory“

Michael J. Fox