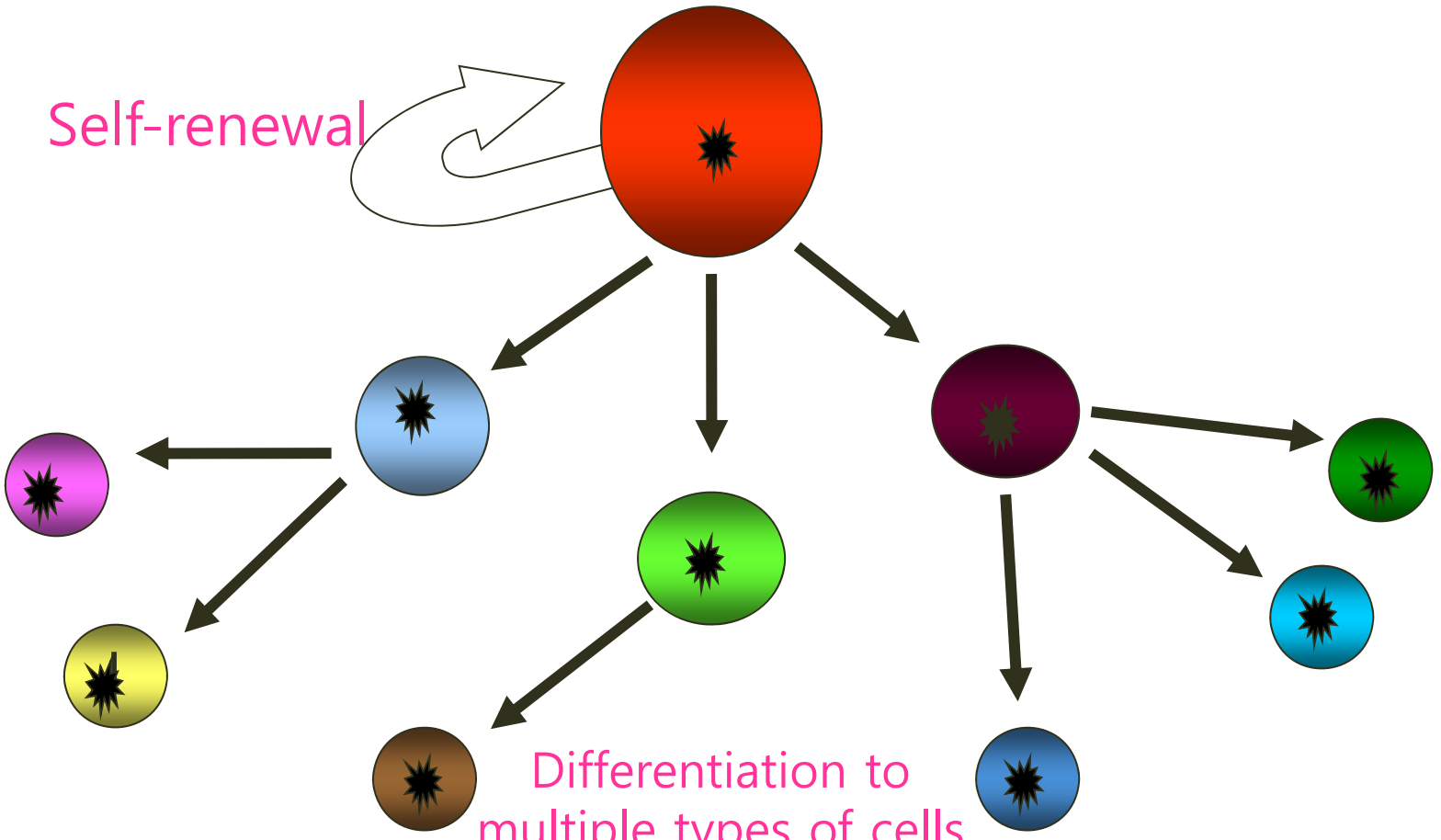
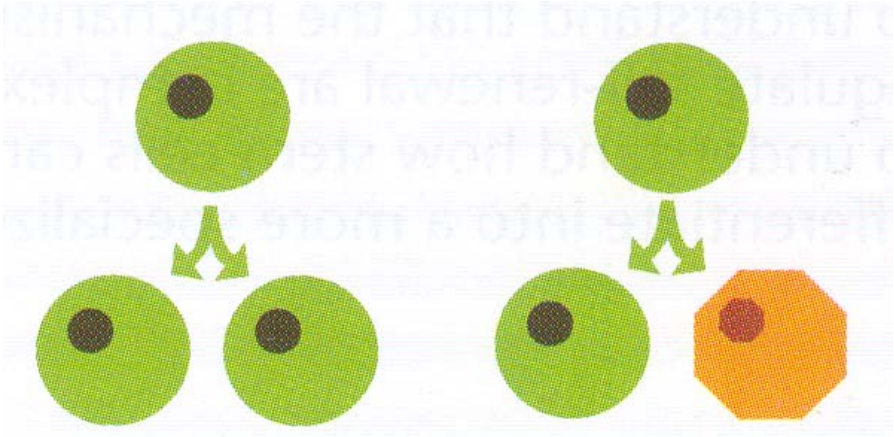
# Stem Cell

# What is stem cell?



# Stem cell self-renewal

During a stem cell division, one or both daughter cells maintain the stem cell phenotype. This process is called a self-renewal.

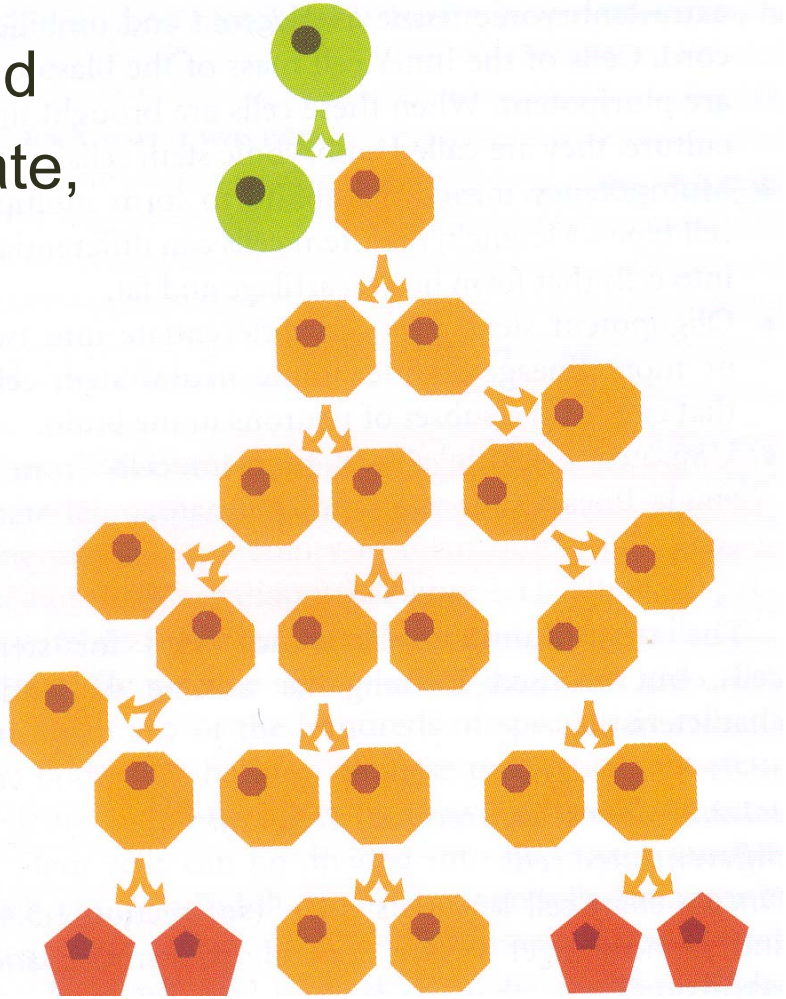


Symmetric vs Asymmetric cell division

# Stem cell, precursor, & differentiated cells

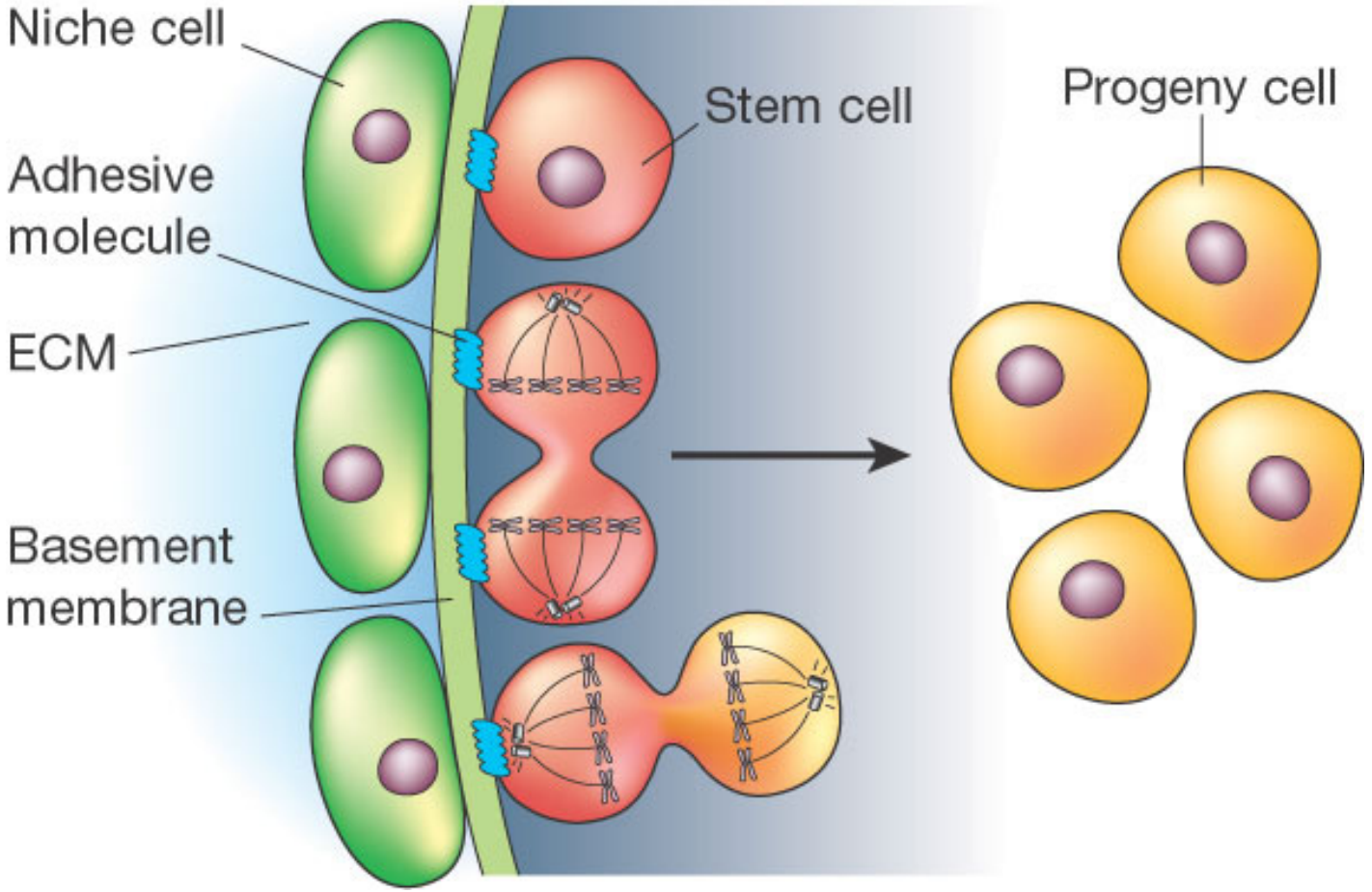
- Once a stem cell leaves its niche and is no longer in the undifferentiated state, they would start to differentiate into specific lineages.

- Stem cell division results in many differentiated cells via transit amplifying cells.



# Stem cell niche

**Stem cell niche** is '*the microenvironment in which stem cells are found*', which interacts with stem cells to regulate stem cell fate




Nature 414, 98-104 (2001)

# Potential of stem cells

Stem cells

↓

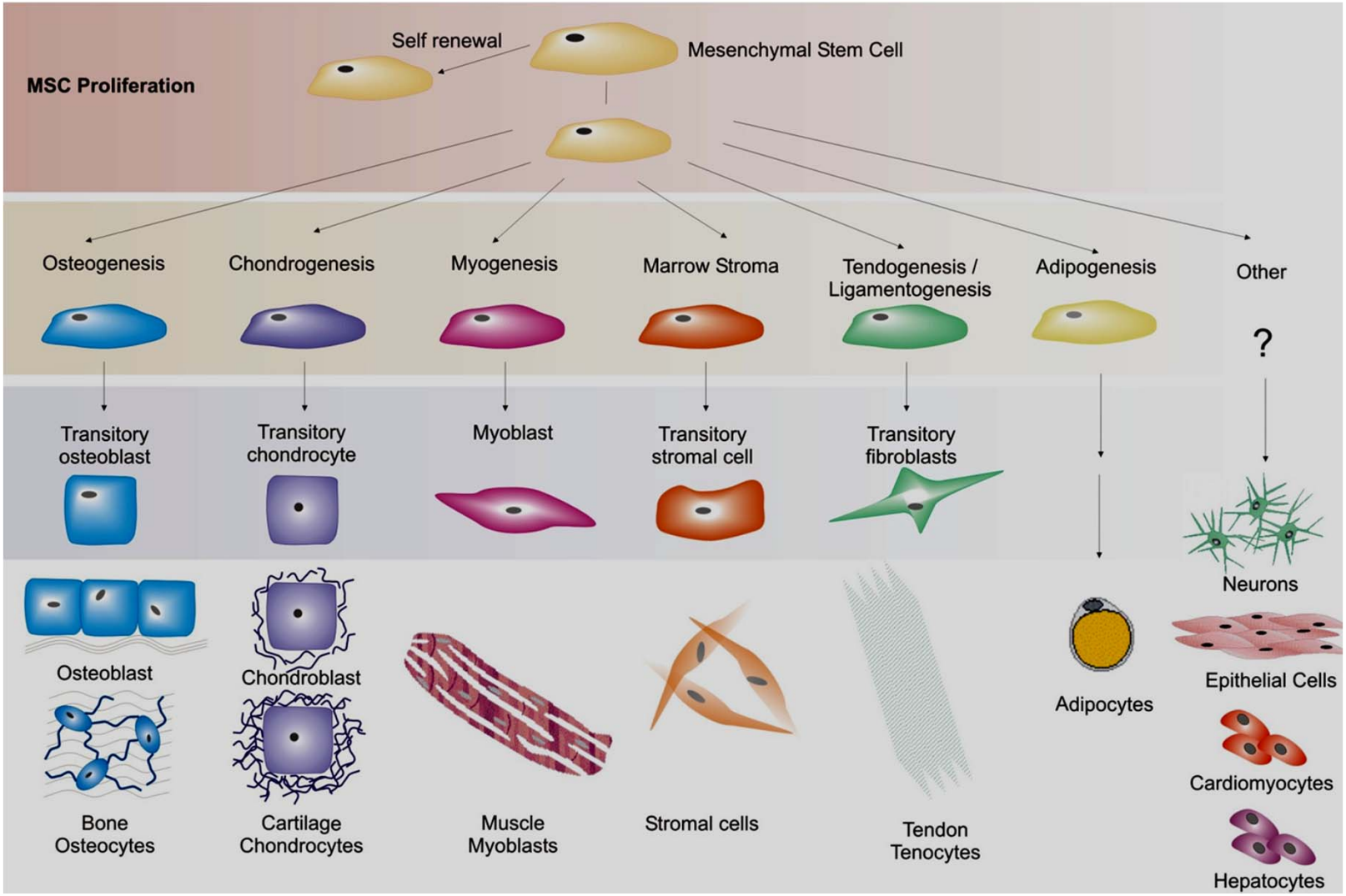
Progenitor cells

↓

Mature cells

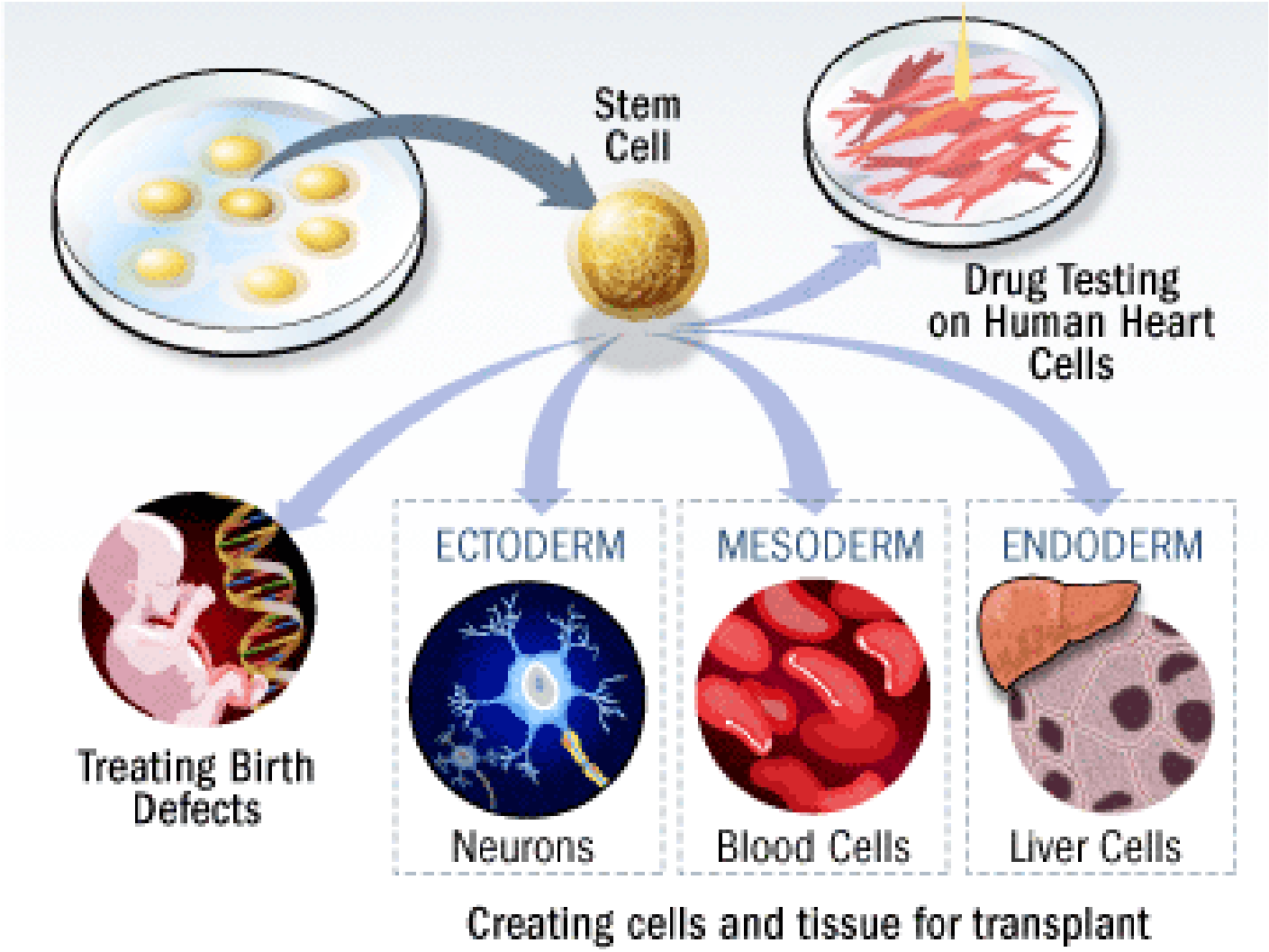
↓

Terminally differentiated cells



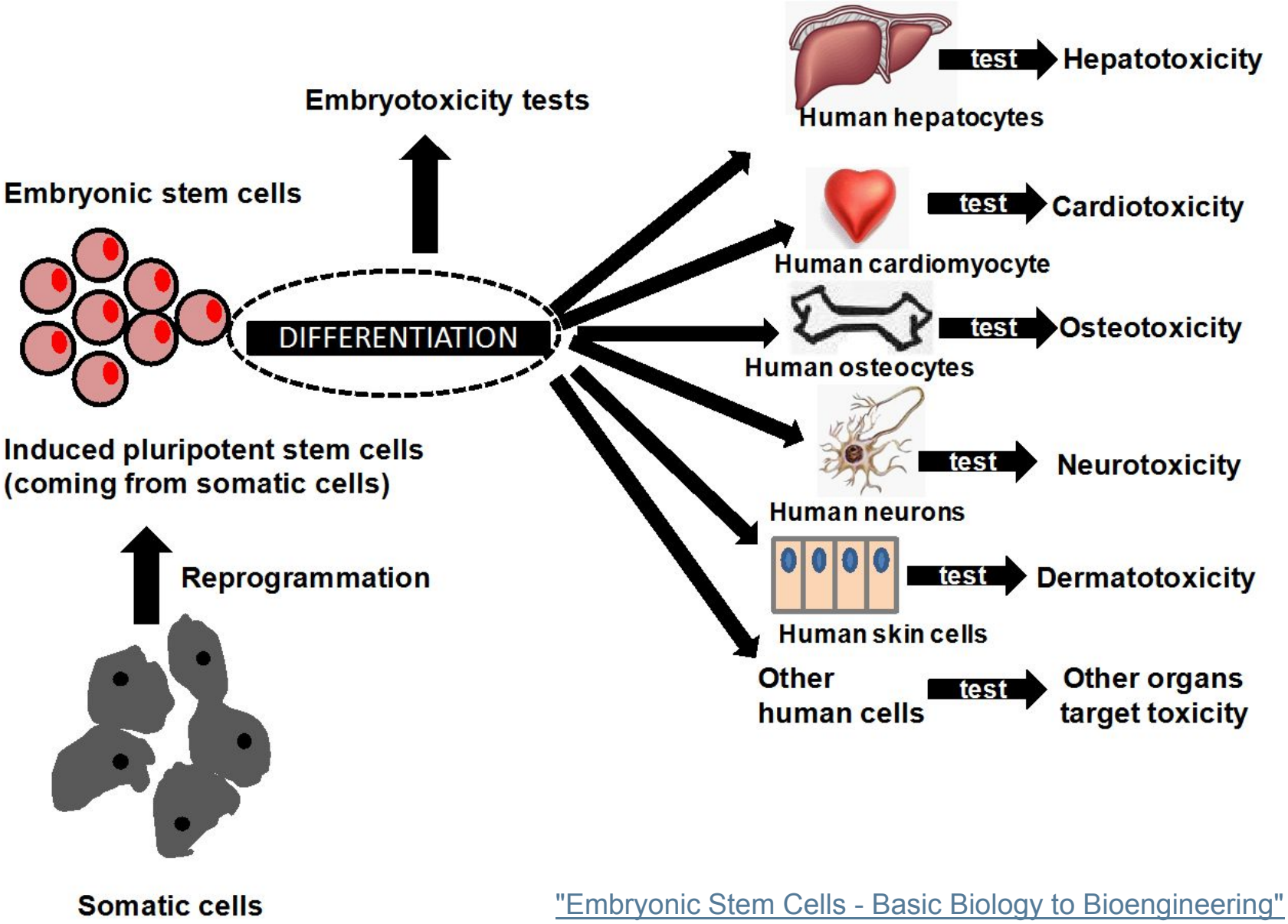

www.york.ac.uk/res/btr/MSC%20diff.jpg

# Stem cell applications



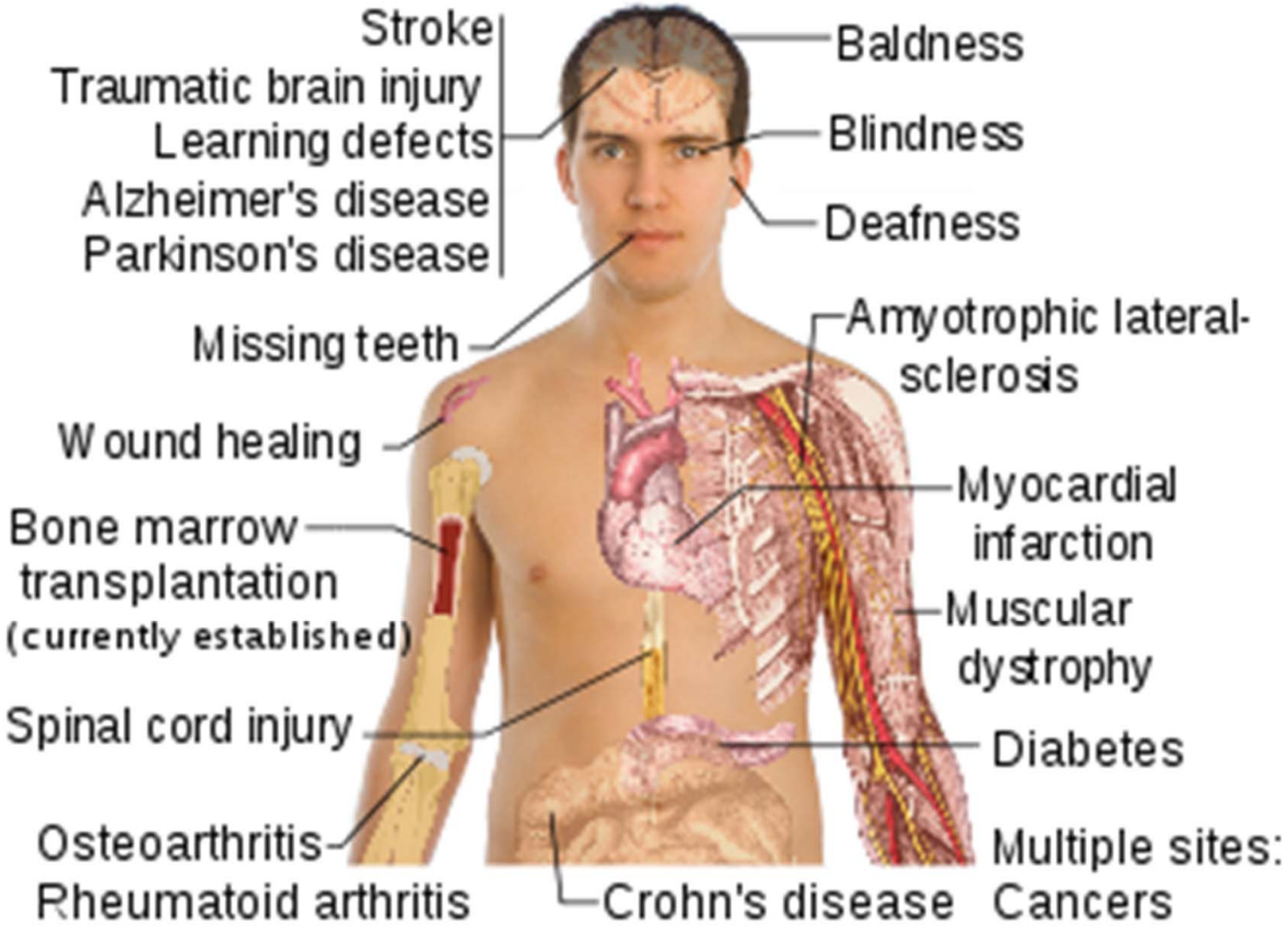

http://science.howstuffworks.com/life/cellular-microscopic/stem-cell5.htm

# Stem Cells in Toxicological Studies



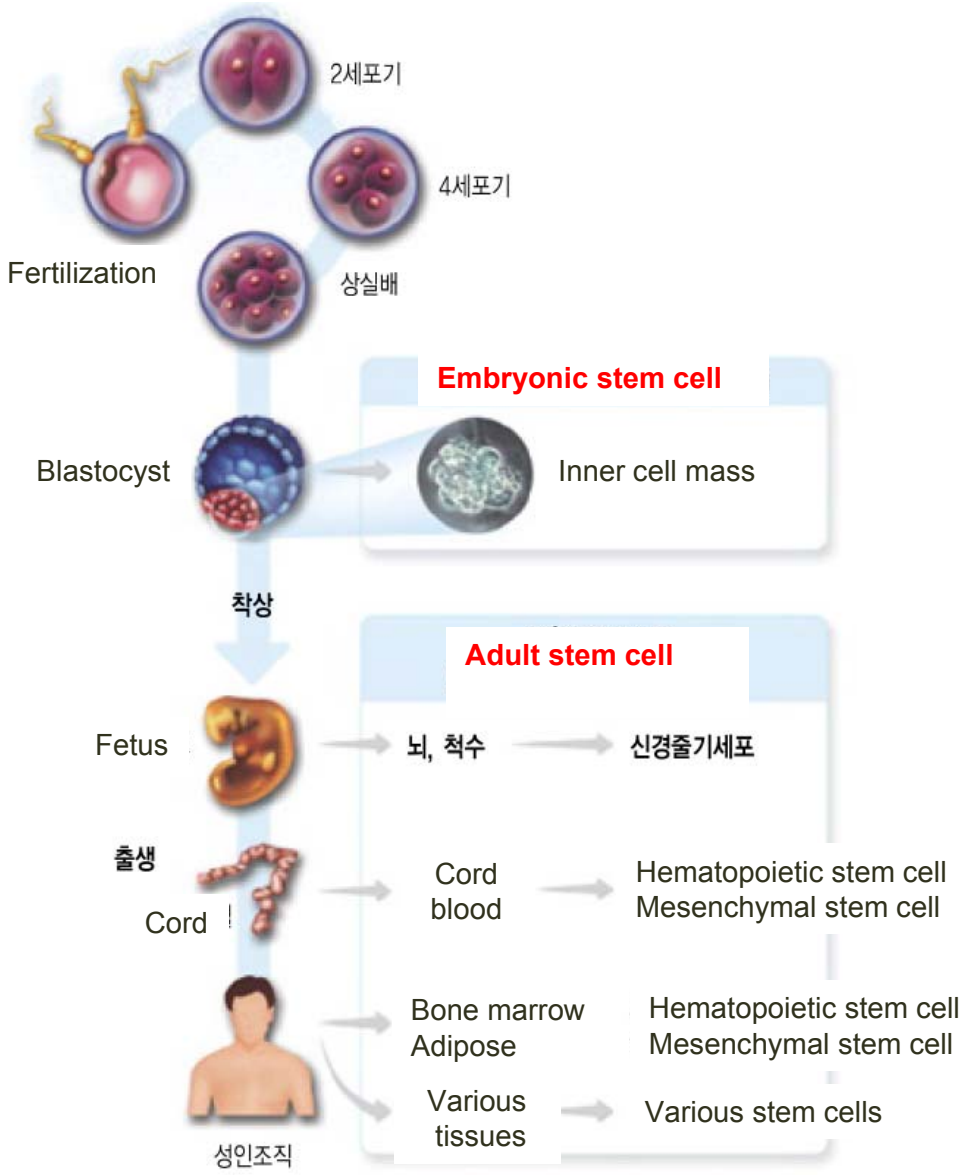

"Embryonic Stem Cells - Basic Biology to Bioengineering"

# Diseases that can be treated with stem cell therapy




carecurechina.com

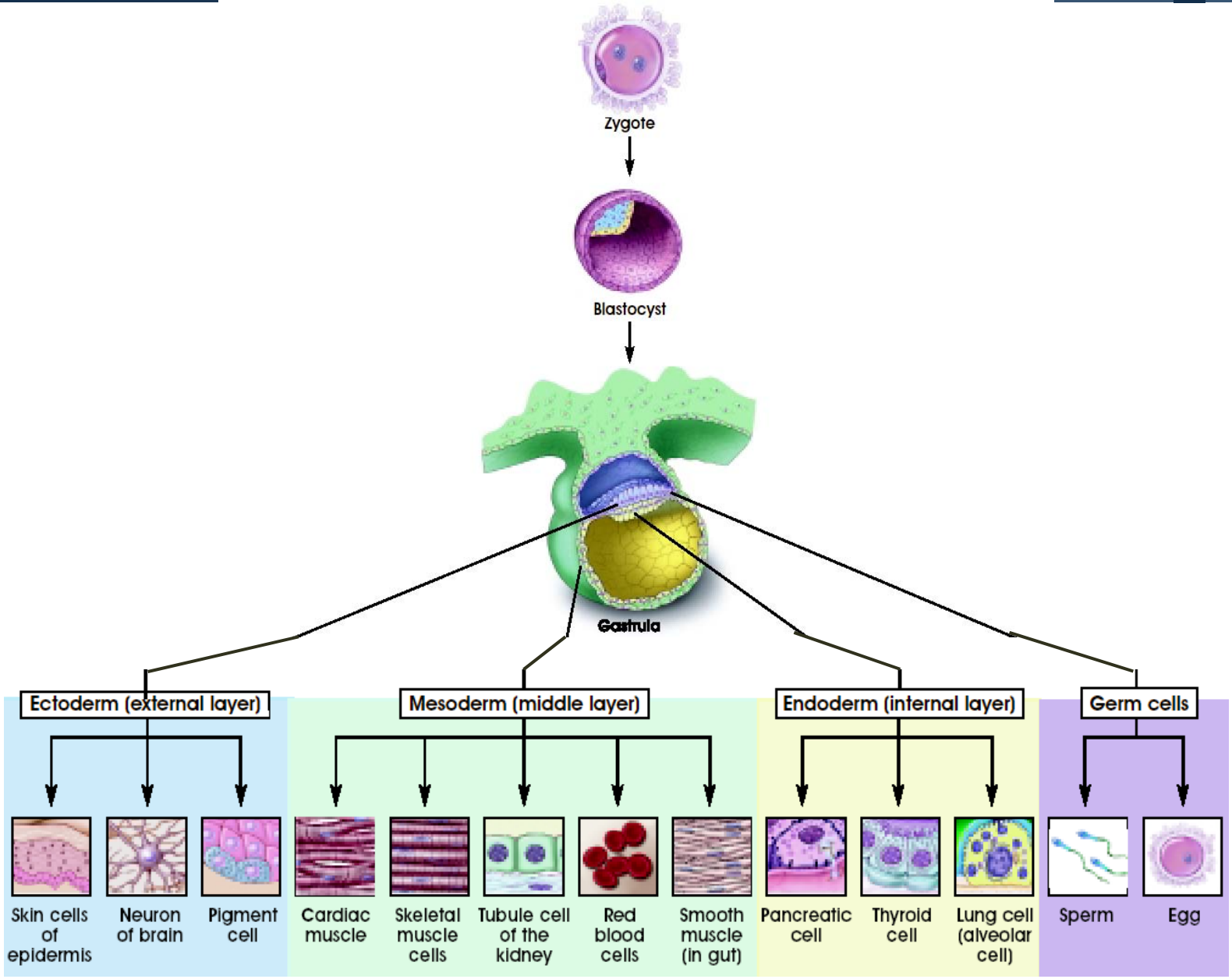
# Stem cell source



# Stem Cell Potencies

- **TOTIPOTENT**
  - Recreates the entire organism
- **PLURIPOTENT**
  - Gives rise to tissues of all three germ layers
- **MULTIPOTENT**
  - Generates multiple, different tissues

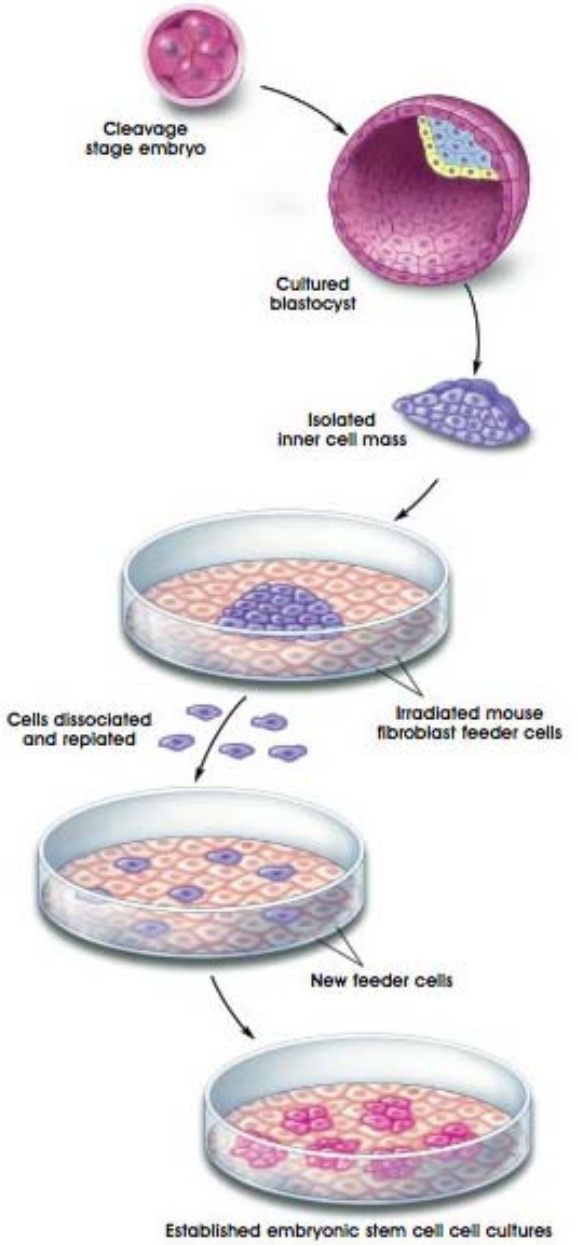
# Stem Cell Potencies



# Organogenesis during embryonic development

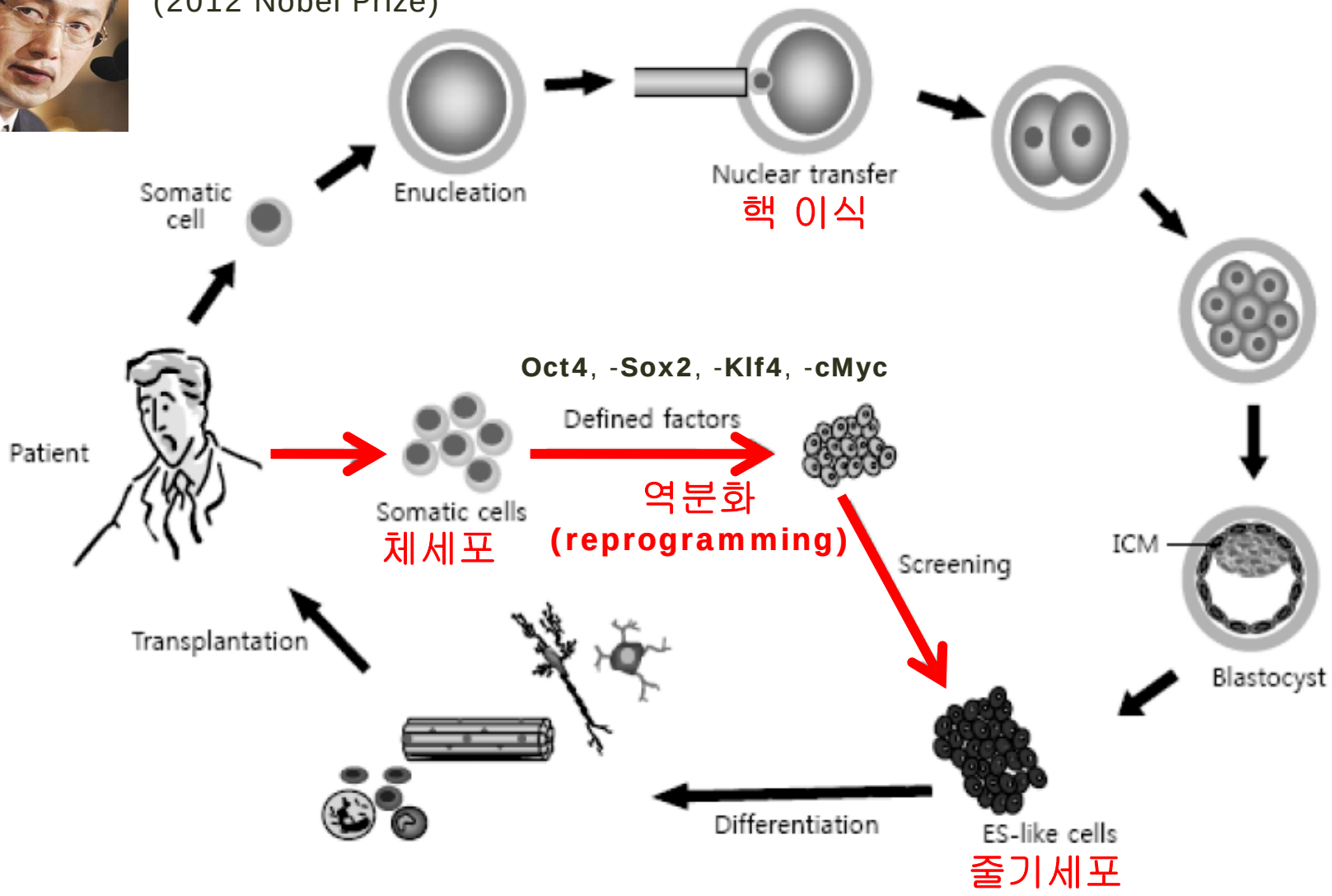
| Germ layer | Differentiated organ/tissue |
|---|---|
| Endoderm | Thymus<br>Thyroid, parathyroid glands<br>Epithelial lining of larynx, trachea, lung, respiratory tract<br>Epithelial lining of urinary bladder, vagina, urethra<br>Liver, pancreas, lining of gastrointestinal tract |
| Mesoderm | Cardiac, skeletal and smooth muscle<br>Heart and blood vessels<br>Bone marrow (blood)<br>Lymphatic tissue<br>Connective tissues, e.g. bone, cartilage, fibroblast, lipocyte<br>Adrenal cortex |
| Ectoderm | Urogenital system<br>Skin<br>Neural tissue<br>Adrenal medulla<br>Pituitary gland<br>Eyes, ears, connective tissue of head/face |

# Embryonic Stem Cell Culture



# Induced pluripotent stem cell (iPS cell; induced pluripotent stem cell) : patient specific, no immune rejection

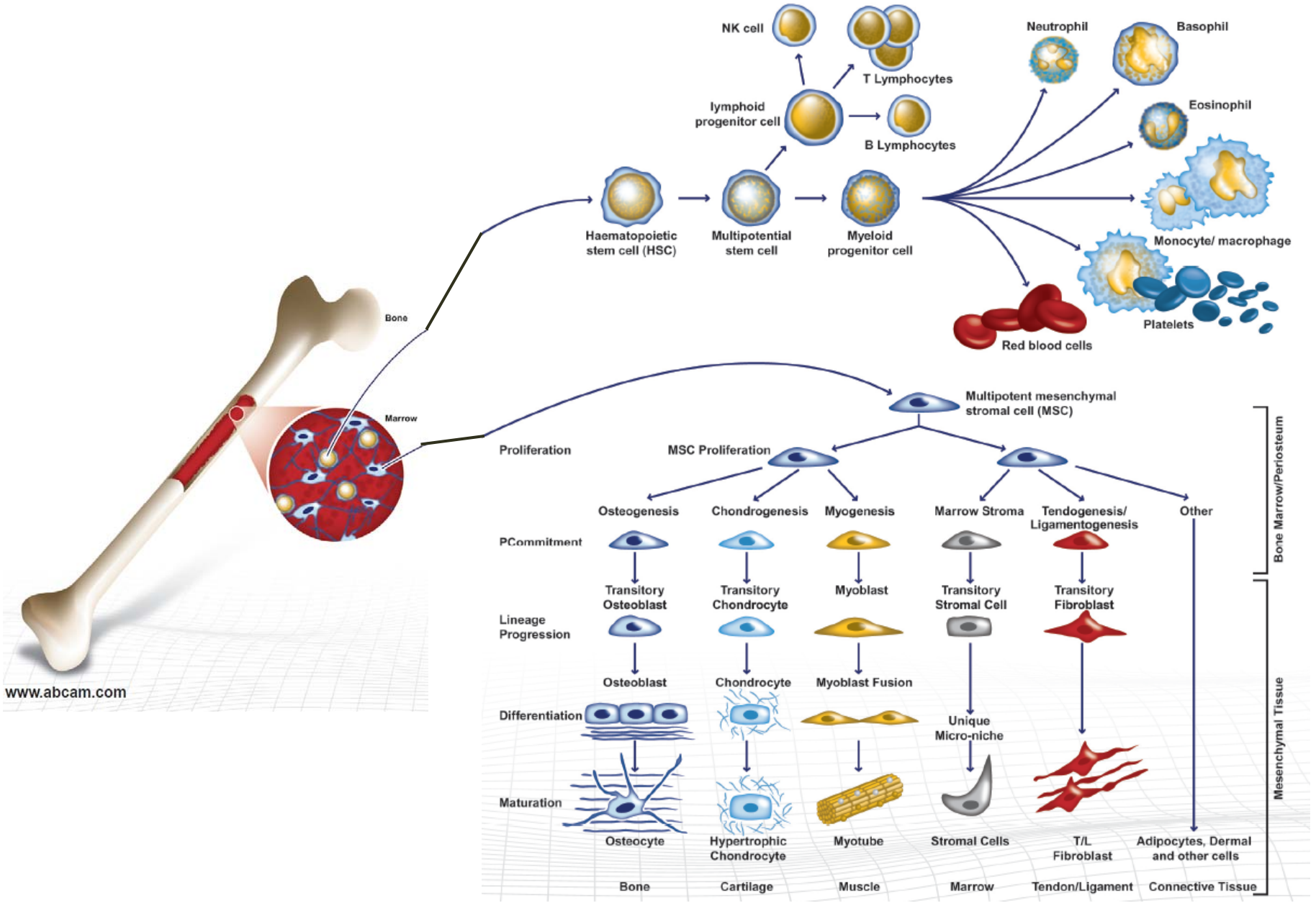
Prof. Yamanaka
(2012 Nobel Prize)

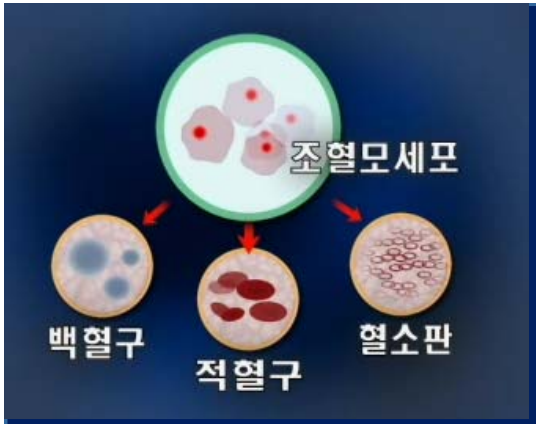


# Adult Tissues where stem cells reside

- **Bone Marrow**
- **Fat**
- **Umblical cord blood**
- **Skin**
- **Peripheral Blood**
- **Nerve**
- **Pancreas**
- **Liver**
- **G-I tract**
- **Corenea, Retina**

# Hematopoietic and mesenchymal stem cell differentiation






# Hematopoiesis

Hematopoietic Stem Cell

Lymphoid Progenitor

CFU-GEMM

CFU-Meg

CFU-M

CFU-G

CFU-E

CFU-Eo

CFU-Bas

Pre B Cell

Pre T Cell

Megakaryocyte

Platelets

Monocyte

Macrophage

Neutrophil

Reticulocyte

Erythrocytes

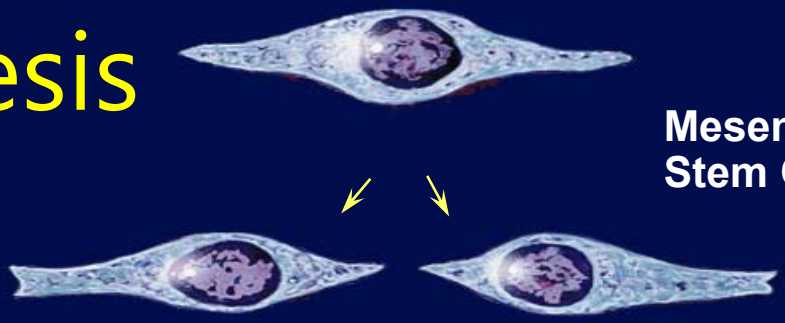
Eosinophil

Basophil

B cell

T cell

# Mesengenesis



# Examples of Stem Cell–Fed Maturational Lineages

## *Bone Marrow and Blood Cell Formation*

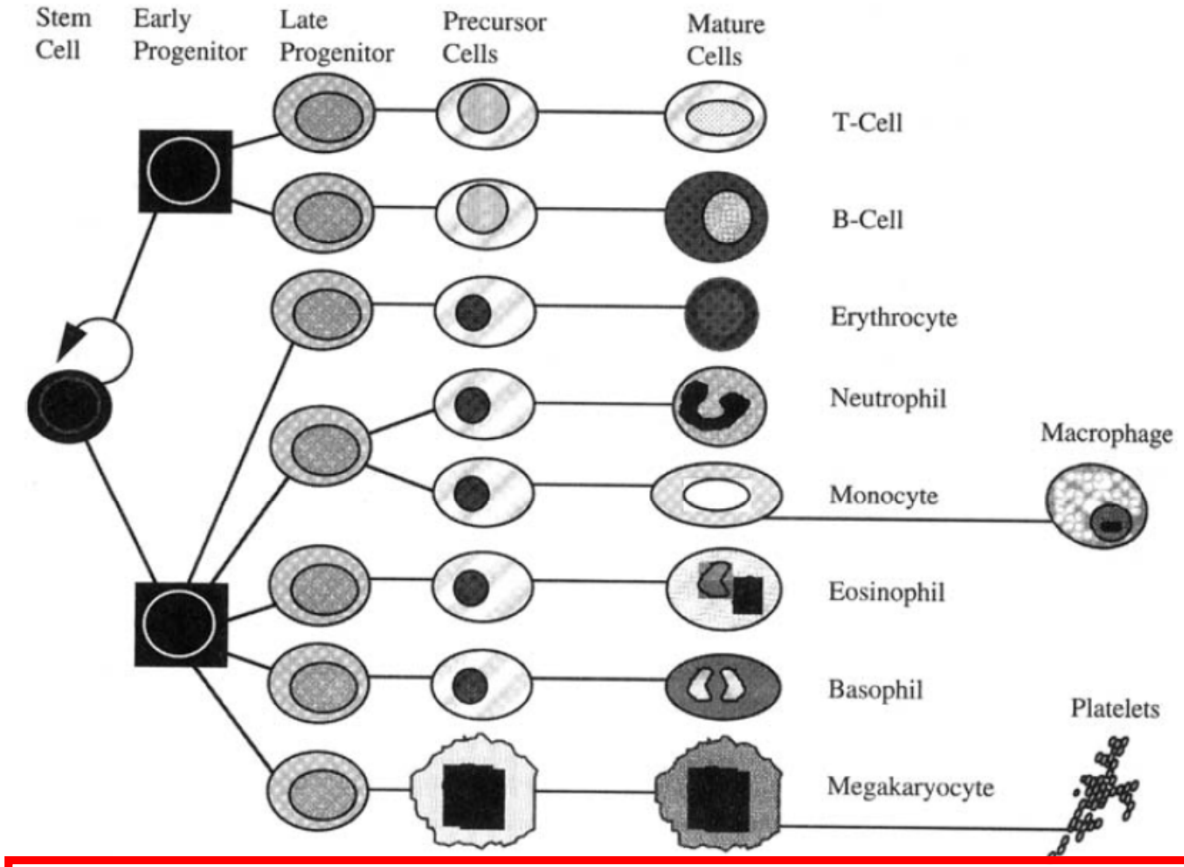



**Figure 7.3** Hematopoietic cell production. The production fluxes through the lineages can be estimated based on the known steady-state concentration of cells in circulation, the total volume of blood, and the half-lives of the cells. Note that the 400 billion cells produced per day arise from a small number of stem cells (from Koller and Palsson, 1993).

- **Cells reached certain maturational stages**

  ↓

  **enter the circulation from bone marrow**

  ↓

  **perform their mature cell functions**

  ↓

  **die and replaced.**

# Examples of Stem Cell–Fed Maturational Lineages

## *The Villi in the Small Intestine*

- **Villi(villus) : the lining of the small intestine**
- **The intestinal epithelial cell**
  - turns over every 5 days, the body's second most prolific tissue
- **the cells are mature, they migrate to the outer edge of the crypt.**
  - they move over a period of about 5 days, from the base of villus to the top, where they die and slough off.

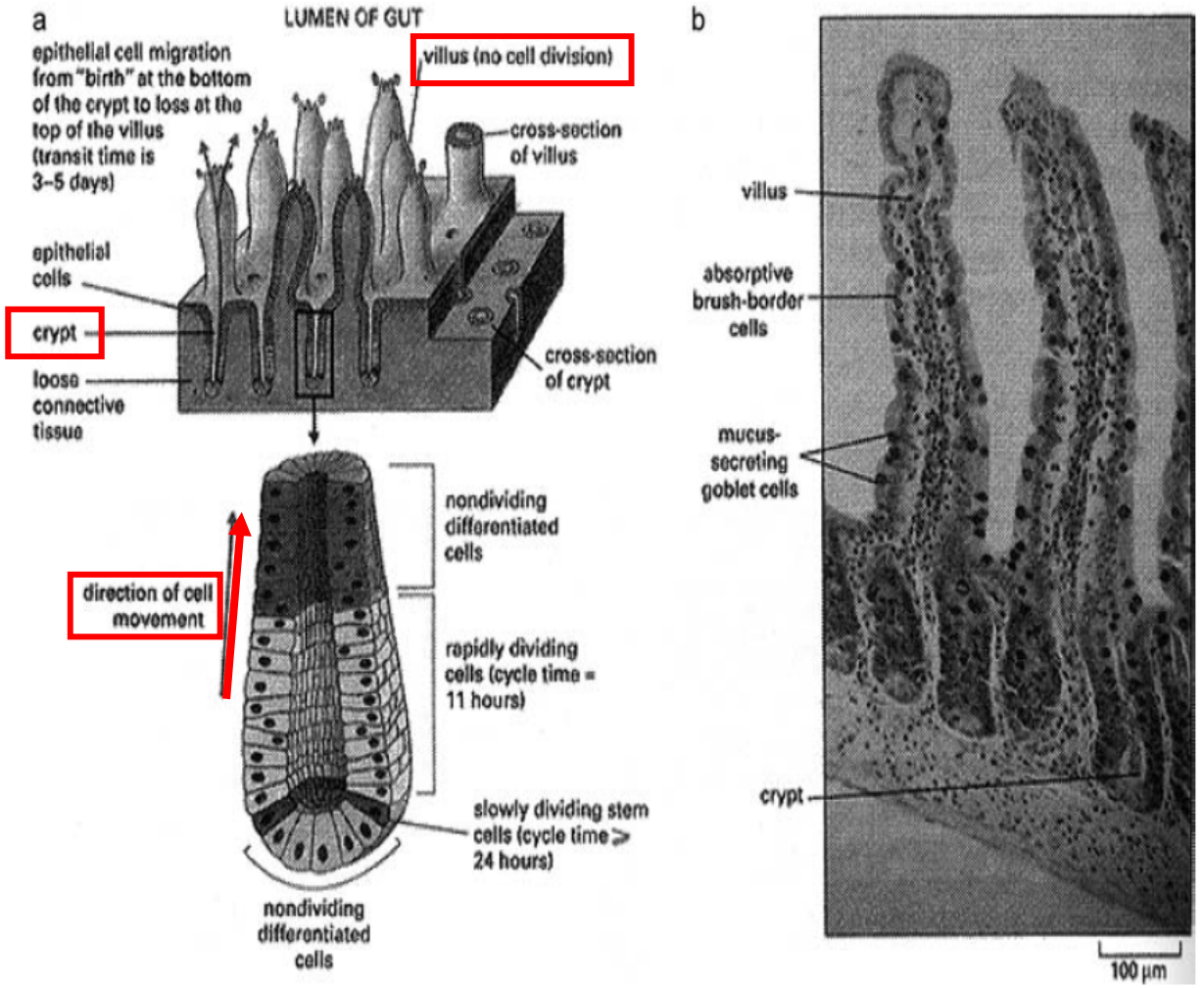



**Figure 7.10** Villi in the small intestine. (a) A schematic showing the villi and the crypt indicating the mitotic state of the cells in various loactions. (b) Rows of villi of epithelial intestinal cells (the diameter of a villi is about 80 μm) (from Alberts et al., 1994).

# Examples of Stem Cell–Fed Maturational Lineages
## *Skin*

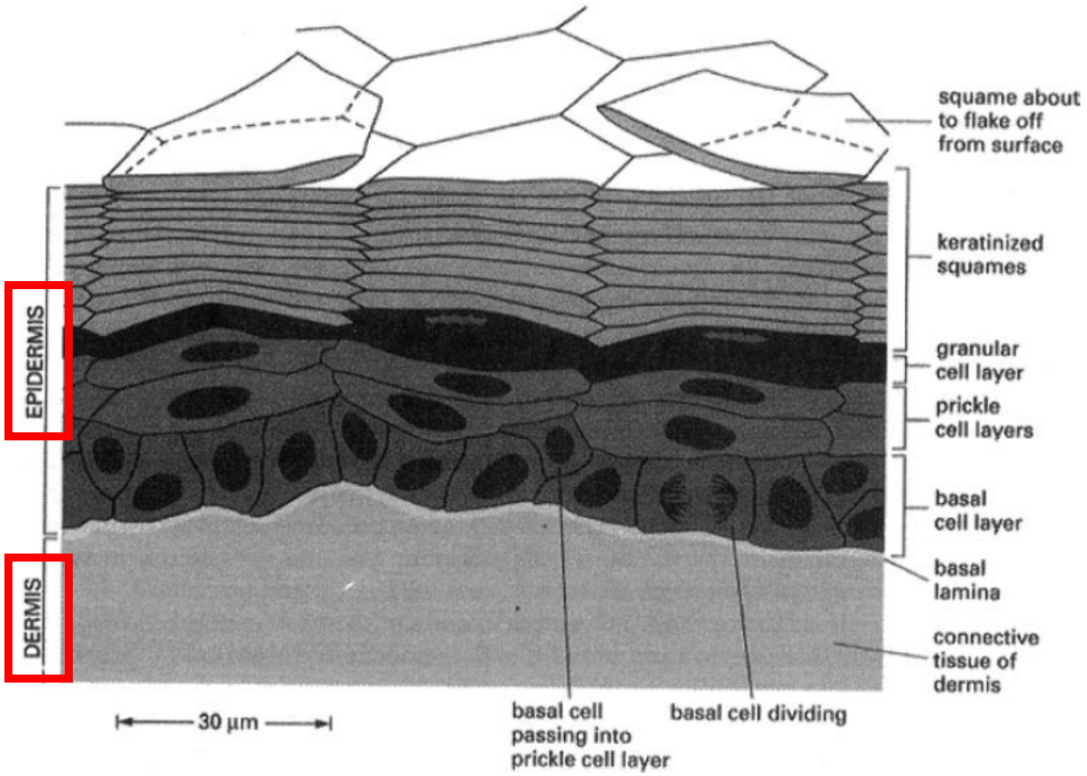
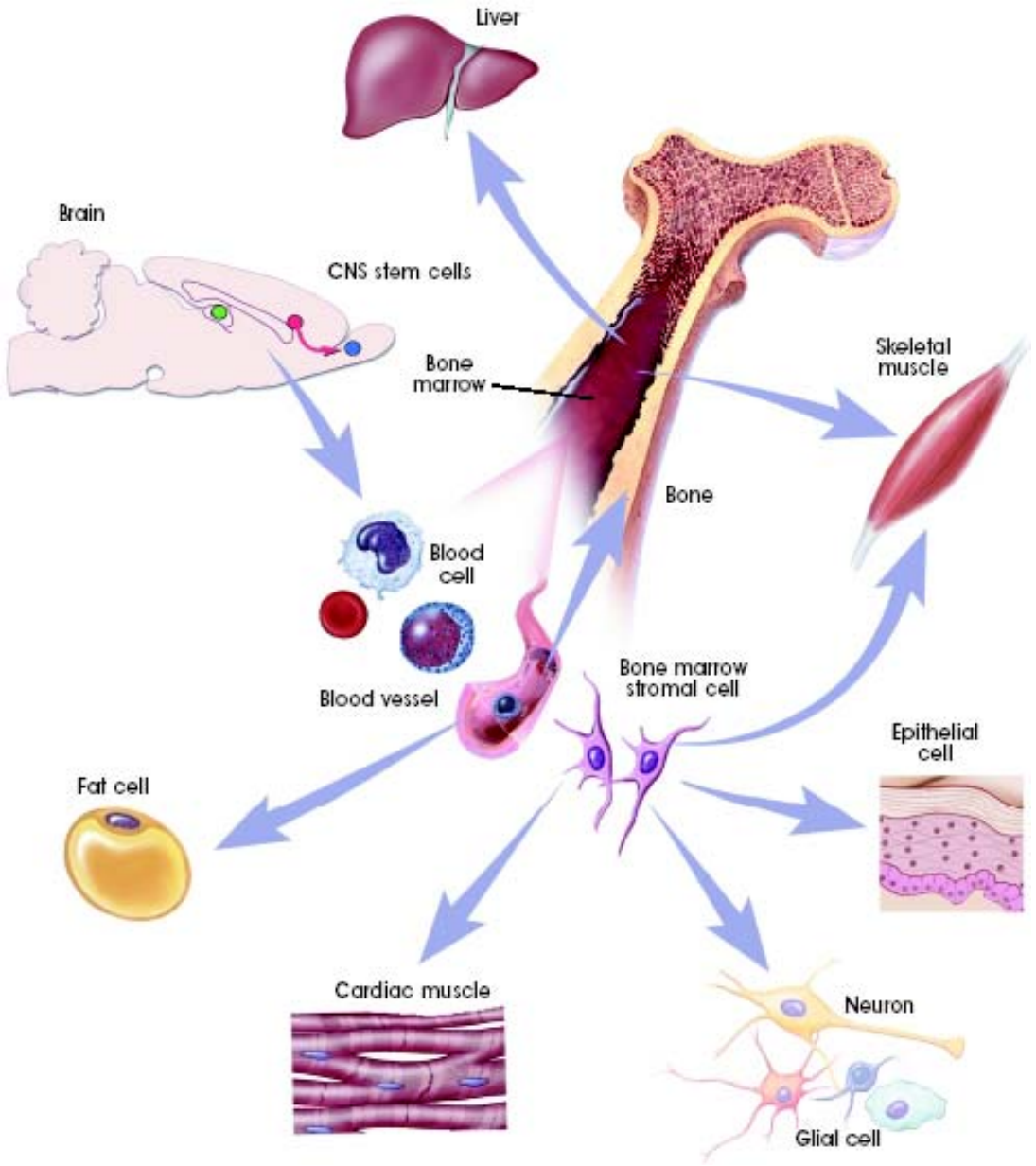


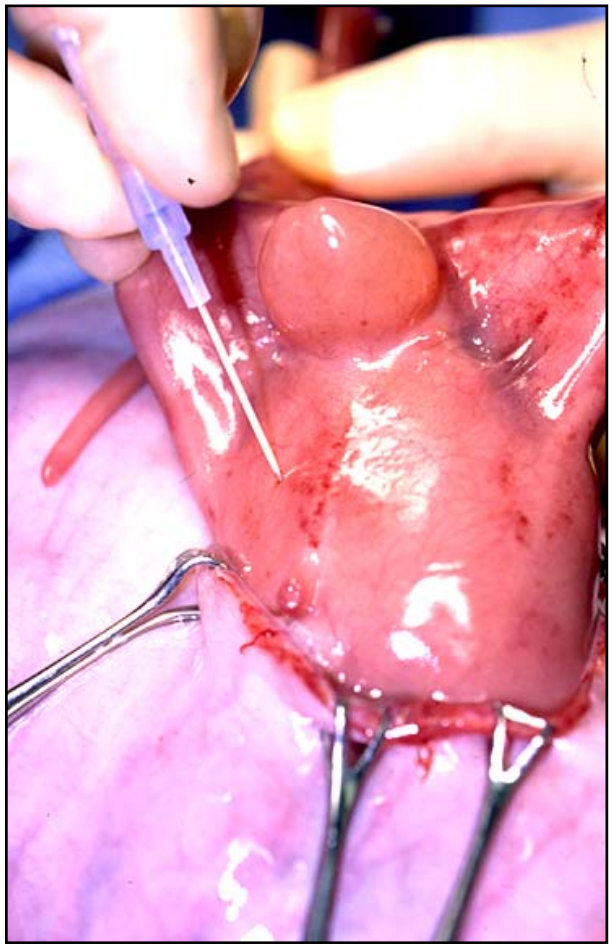

**Figure 7.4** The cellular arrangement and differentiation in skin. The cross section of skin and the cellular arrangement in the epidermis and the differentiation stages that the cells undergo (from Alberts et al., 1994).

- stem cell in the deep pockets within the epidermis/dermis undulations and also in bulges near hair follicles.
- committed progenitors migrate into the shallow pockets and from there into cells that line the entire basal lamina.
- the epidermal cells adherent to the basal lamina are cycling
- cells that lose their attachment to the basal lamina move upward and differentiate into succeeding stages of cells.
- Ultimately, they turn into granular cells, keratinized squames, eventually flake off.

# Plasticity of adult stem cells



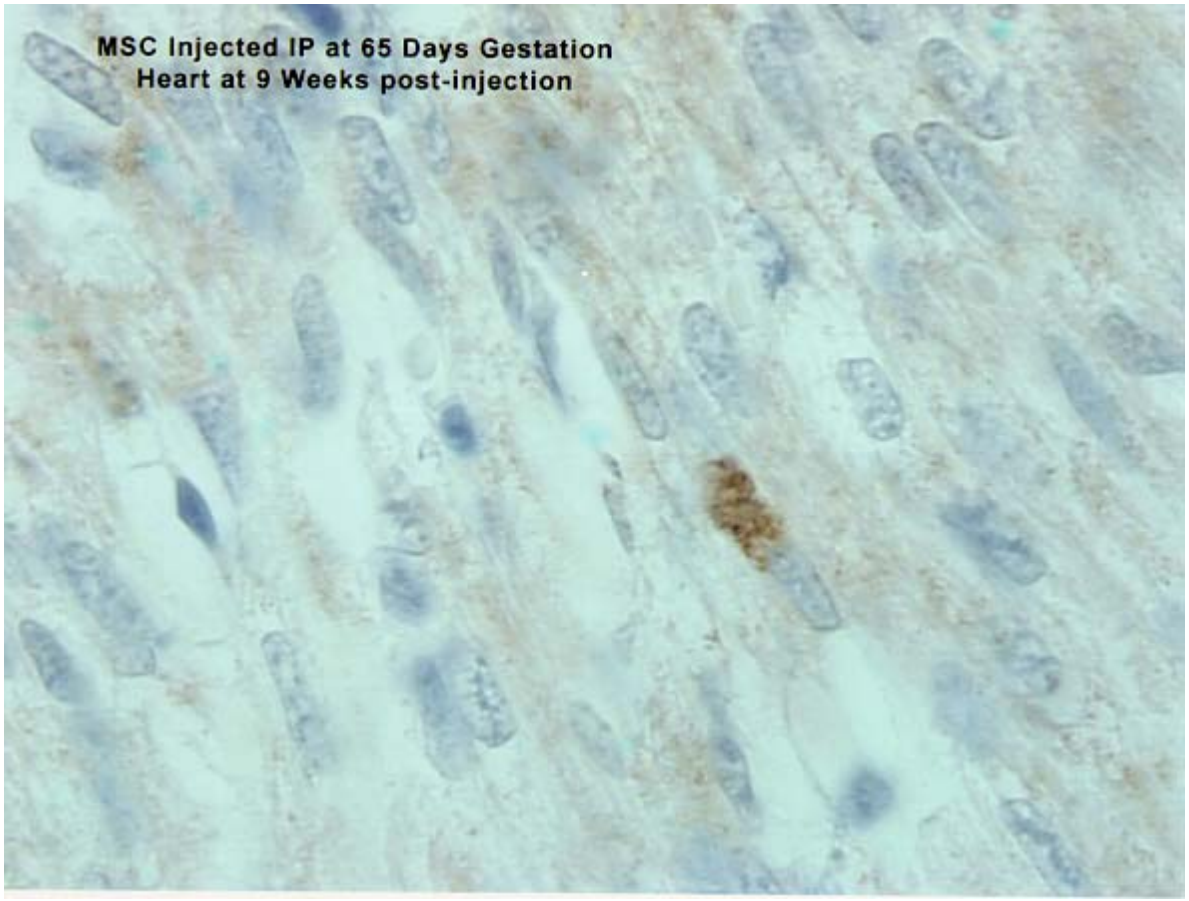
# Human MSC Chimerism in Fetal Sheep (*in utero*)



- Human MSCs injected  i.p.
- 65 or 85 Day gestation fetal sheep
- Harvest at 9 weeks;
- Human β-2 microglobulin immunohistochemistry

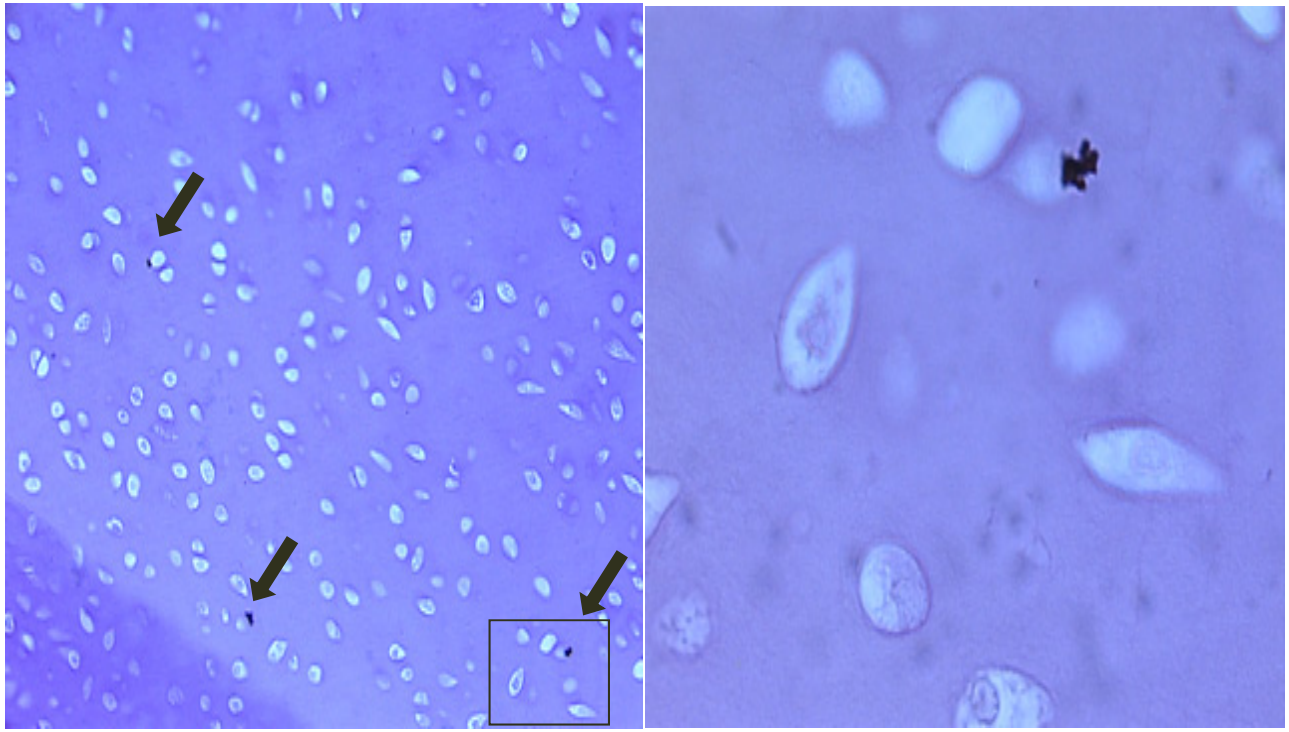
# Human MSC Chimerism in Fetal Sheep (heart)

Q: What does this experiment tell?



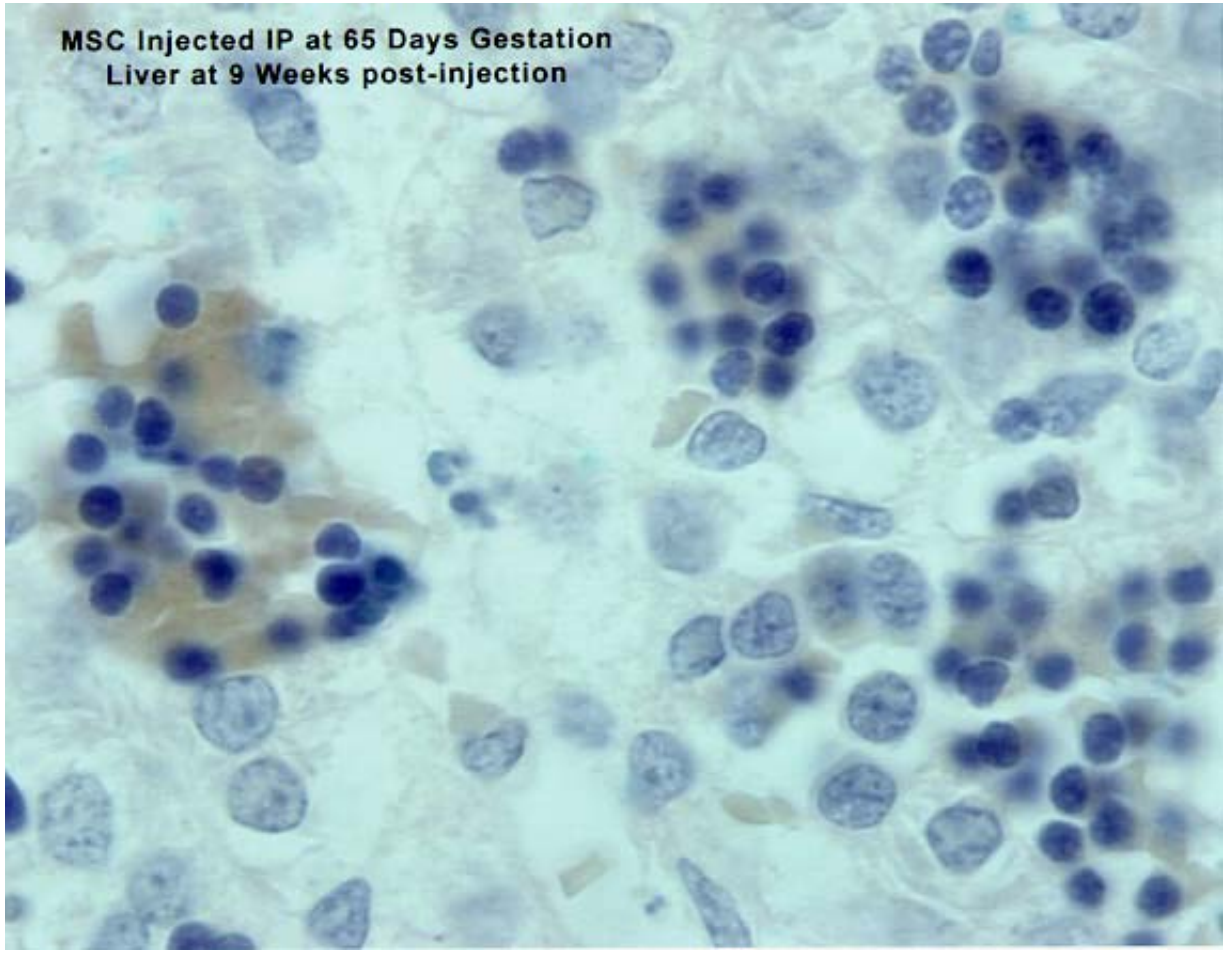

**9 wks**
**(immuno-permissive animals)**

# hMSC Engraftment *in utero* (*human antigen immunostaining*)



**hMSCs form chondrocytes following *in utero* injection**

# Human MSC Chimerism in Fetal Sheep (liver)



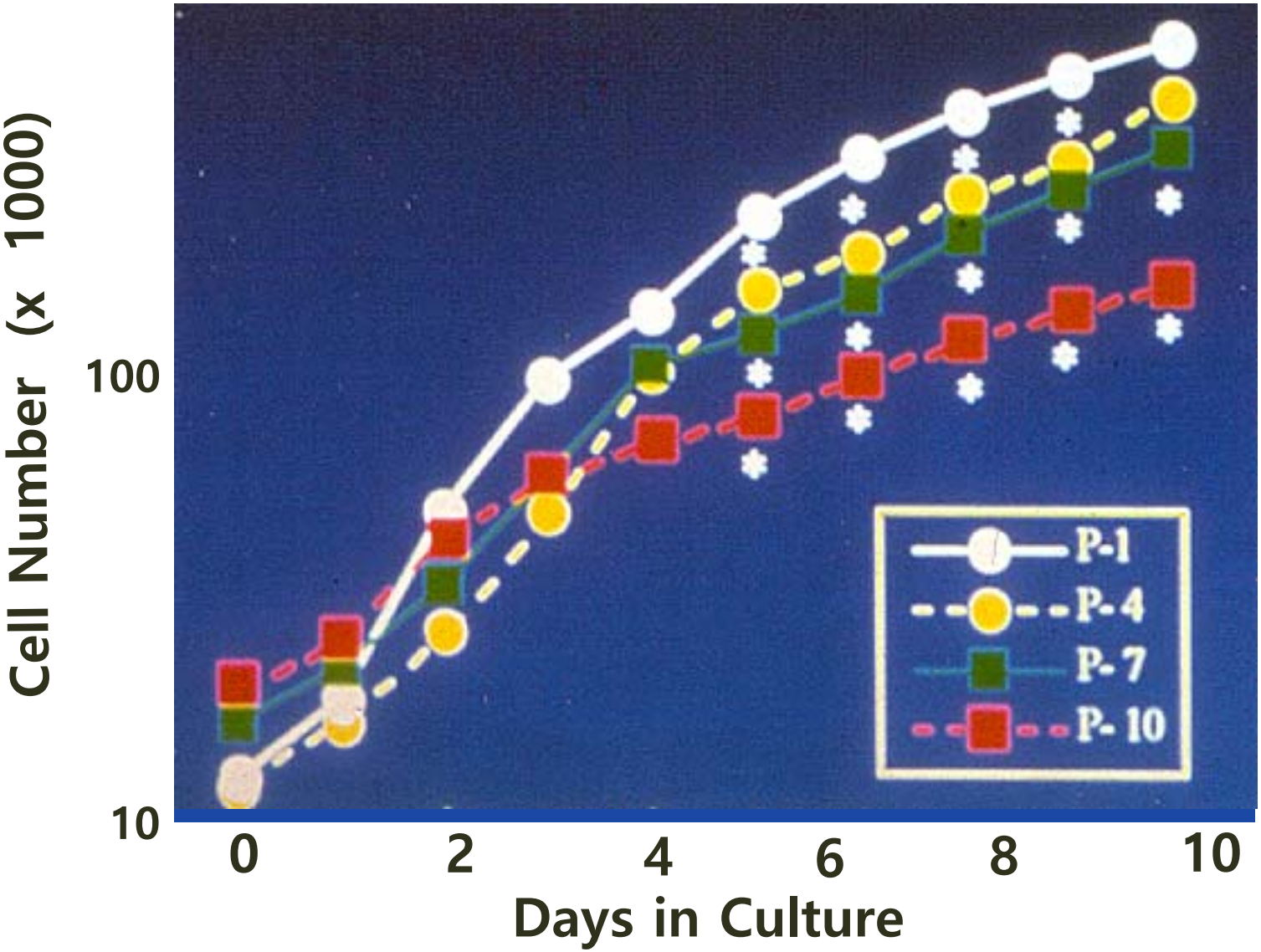

**Engraftment at 9 wks**

**(immuno-permissive animals)**

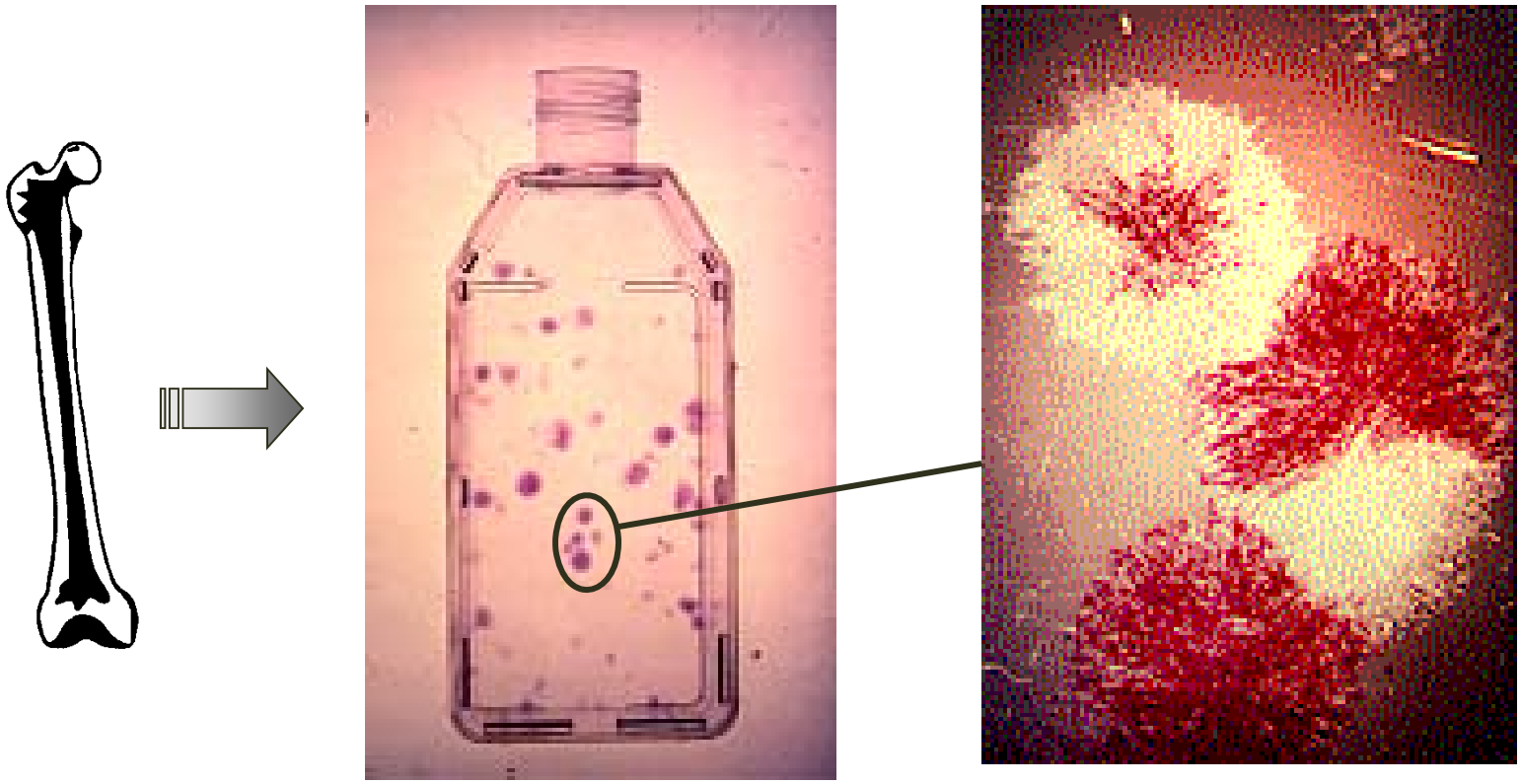
# Summary of *in utero* Engraftment

- Human MSCs repopulate mesenchymal tissues *in vivo* during mammalian fetal development.
- Human MSCs are not rejected in a fetal, xeno-geneic engraftment models.

# Cell Expansion Kinetics of hMSCs

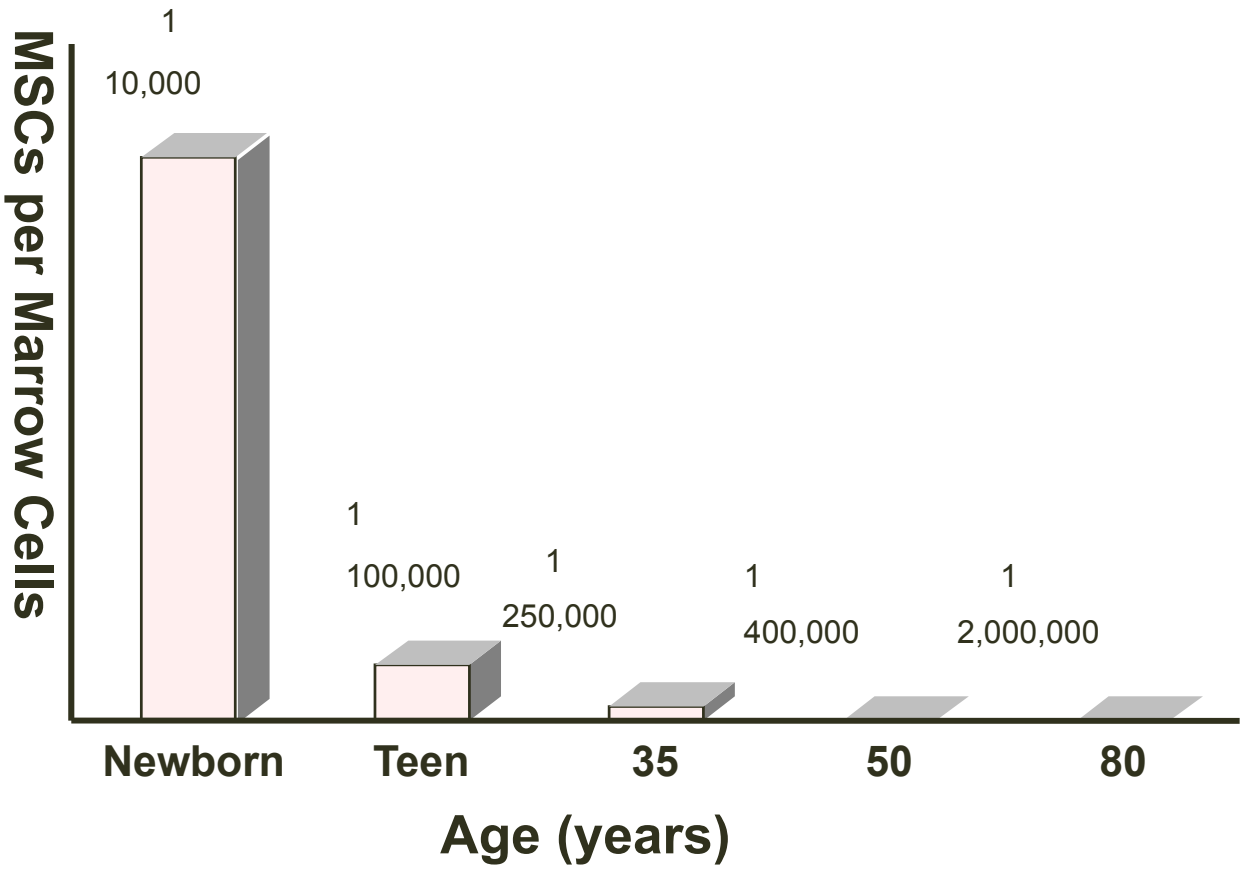


# CFU (colony forming unit) assay

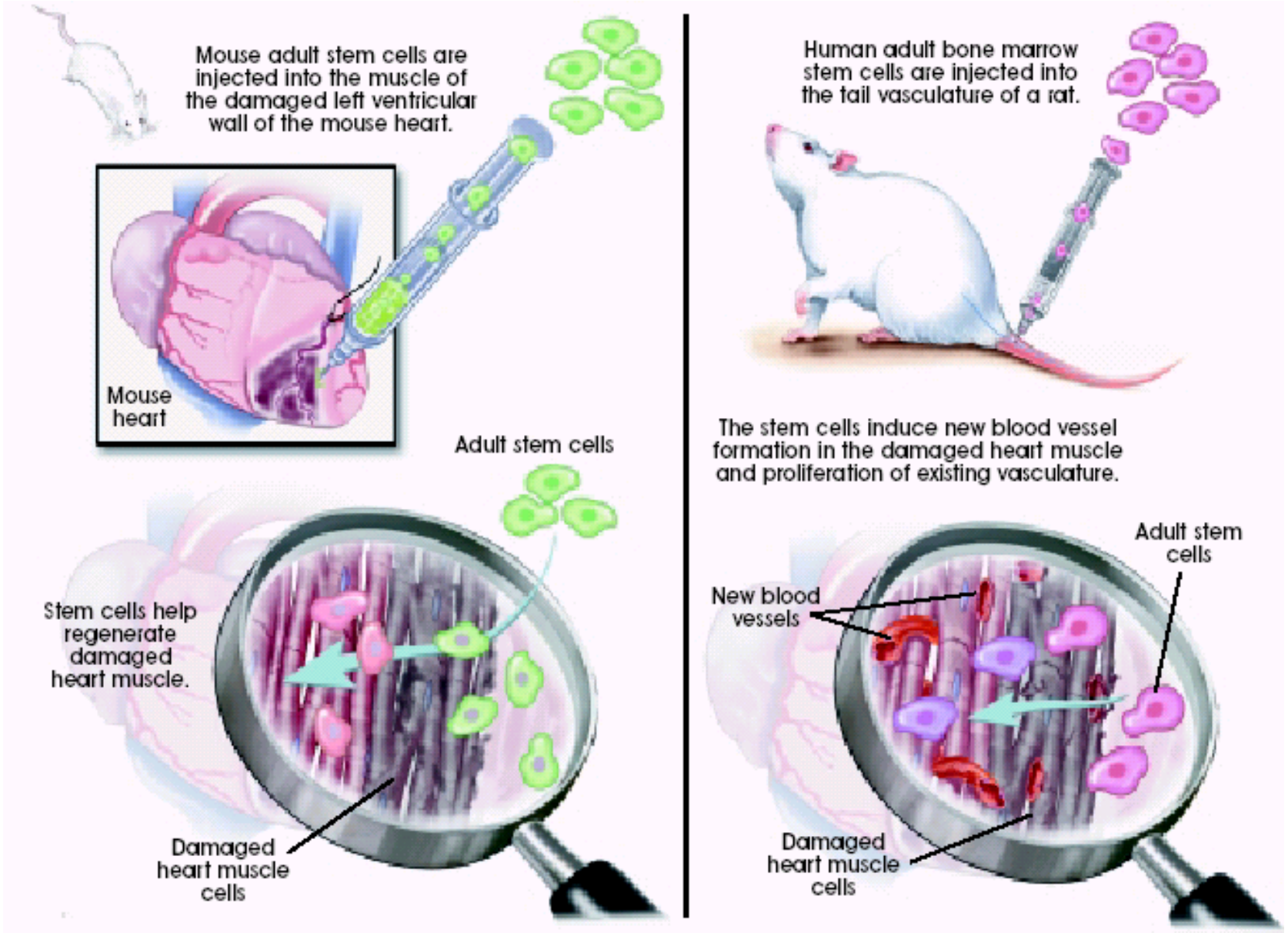


- Marrow CFU number or colony-forming efficiency
- Proliferative and osteogenic capacity of CFU

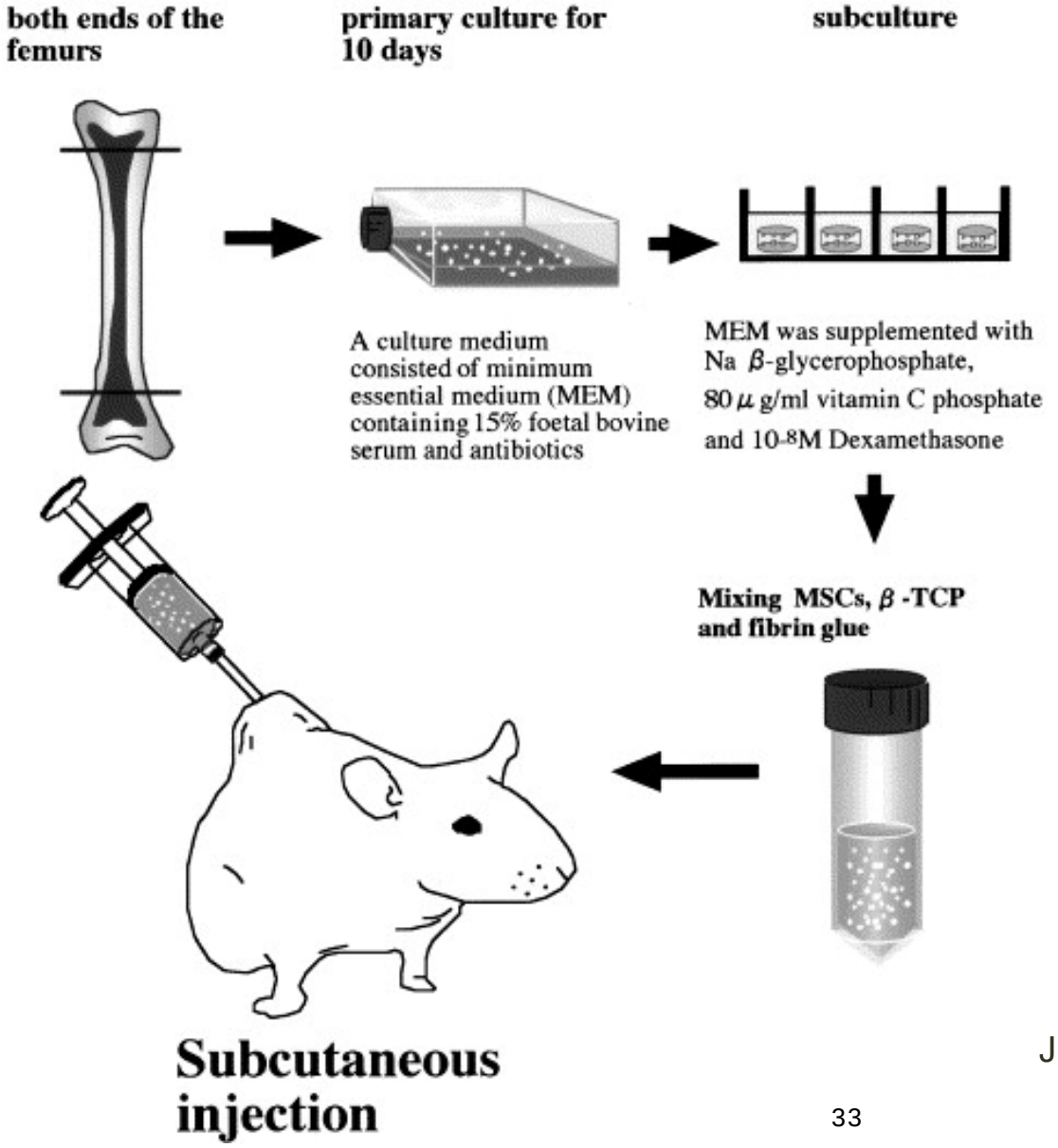
# Age-Related Decline in the Number of Human Mesenchymal Stem Cells in Bone Marrow

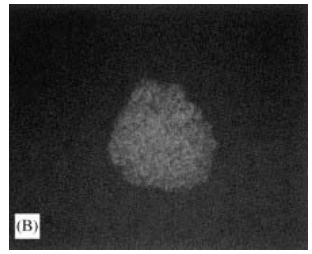


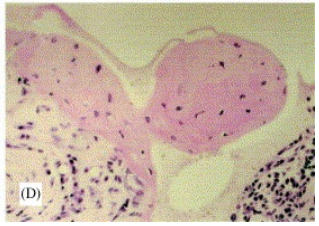
# Stem cell transplantation for myocardial infarction treatment



# Bone regeneration by implantation of mesenchymal stem cells and scaffold

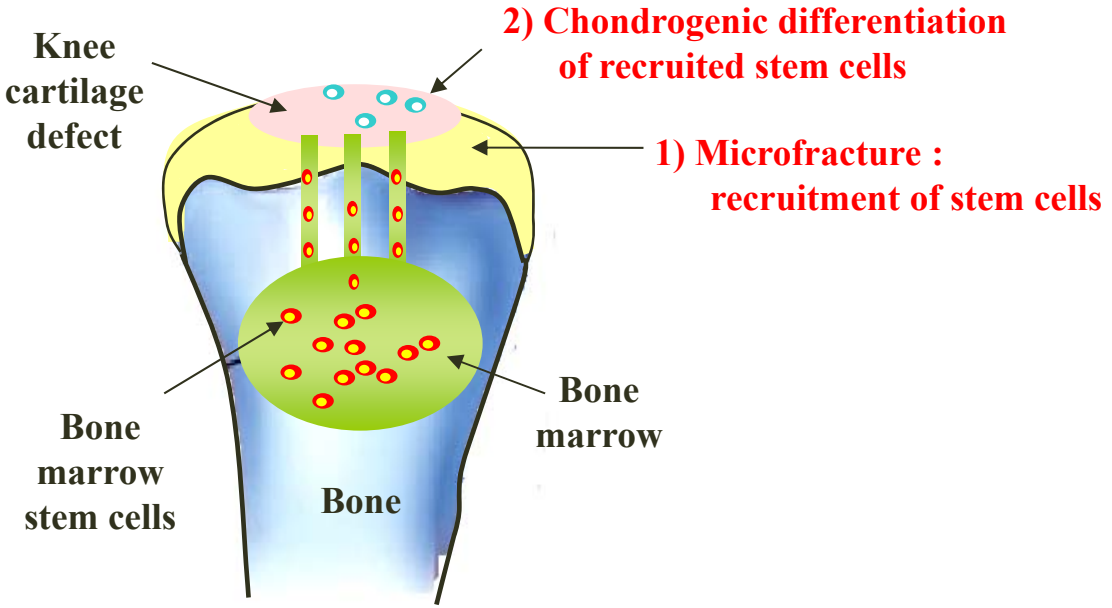


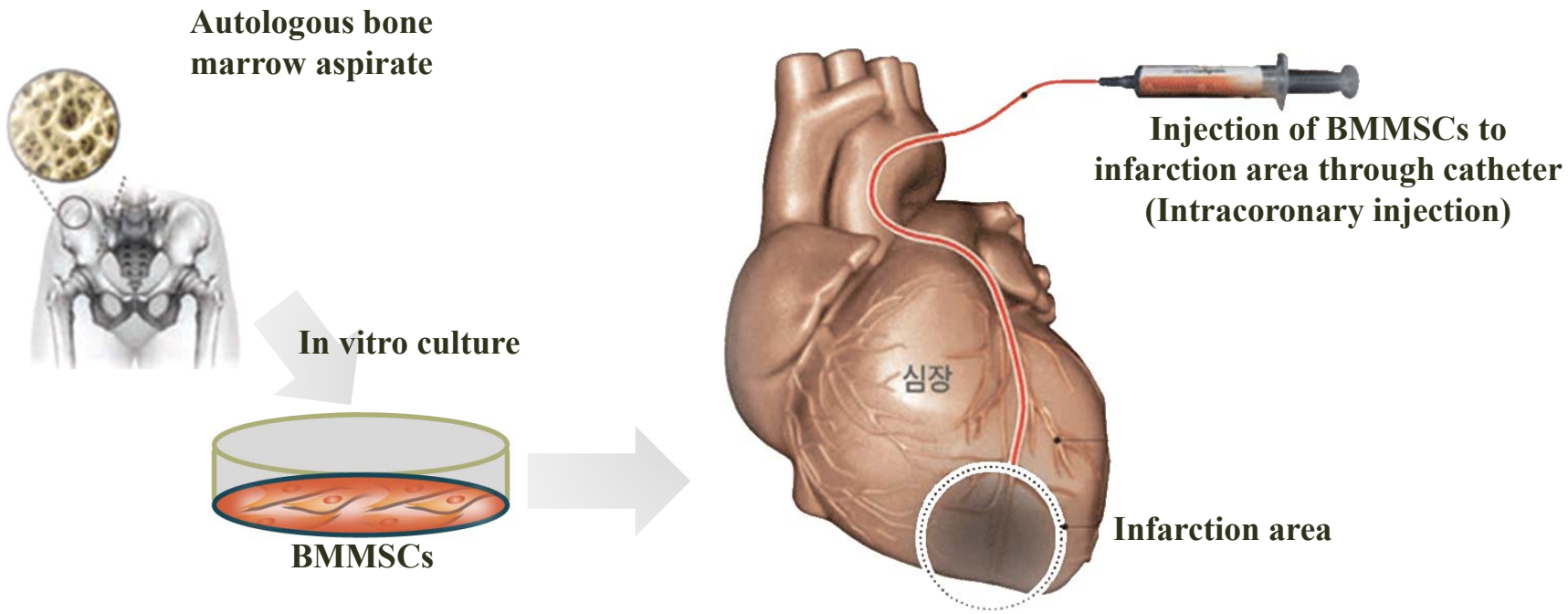

J Cranio-Maxillofac Surg 2003, 31; 27-33

# Cartilage repair using endogenous stem cells




1 year later

# Bone marrow stem cells in market for myocardial infarction




FCB-Pharmicell, Inc (Korea)