

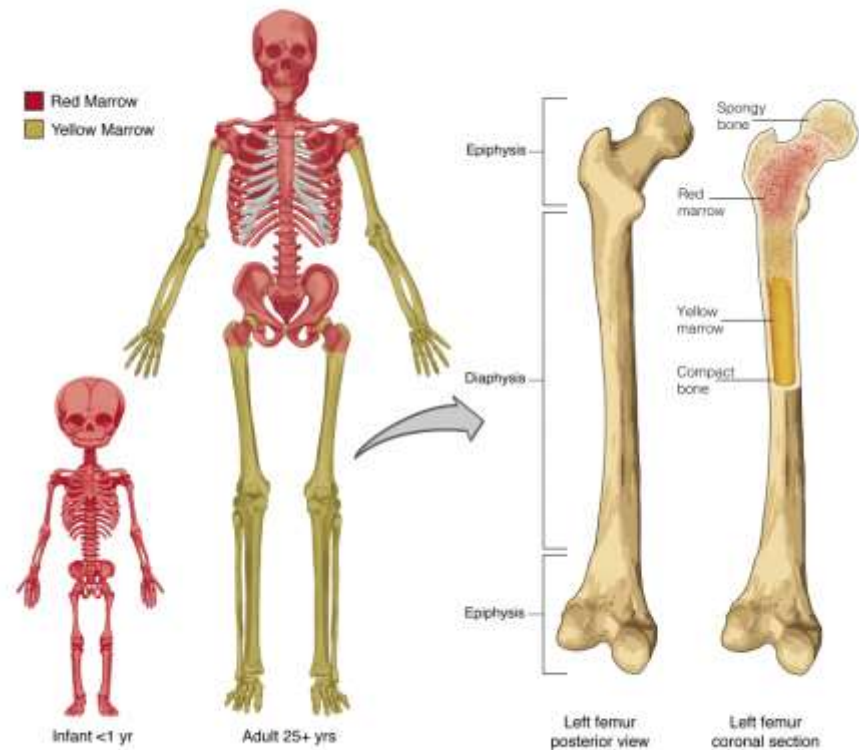
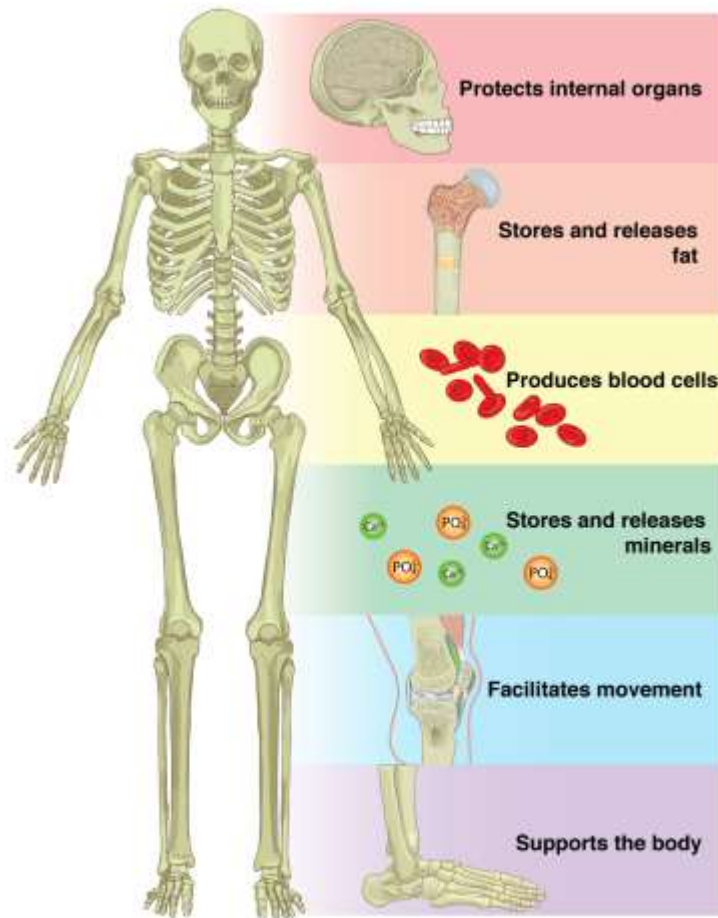


# 骨髓间充质干细胞 (Bone marrow mesenchymal stem cells)

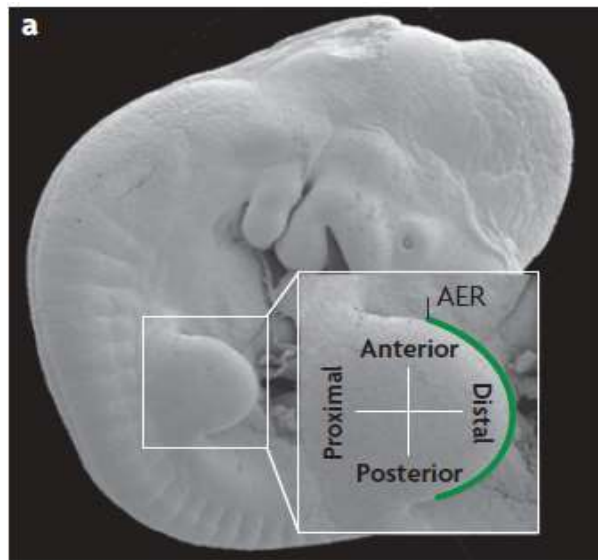
岳锐 教授

同济大学生命科学与技术学院  
同济大学附属东方医院

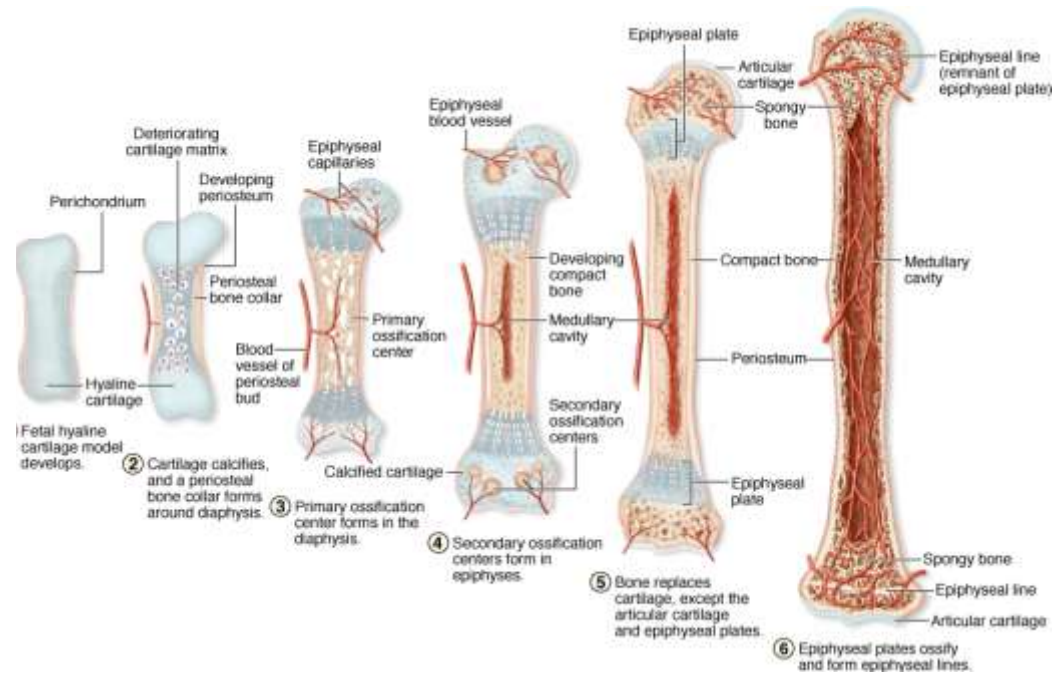
# Skeleton is more than an articulated set of bones



# Long bone development

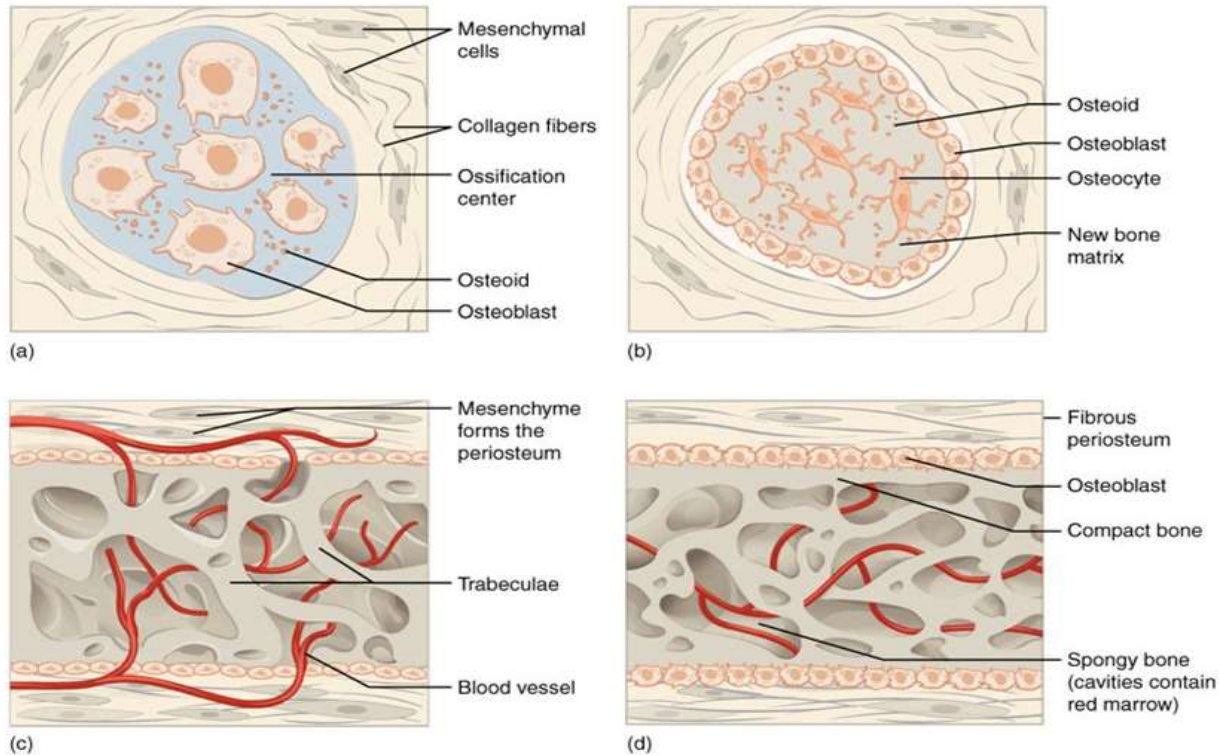


Limb bud development



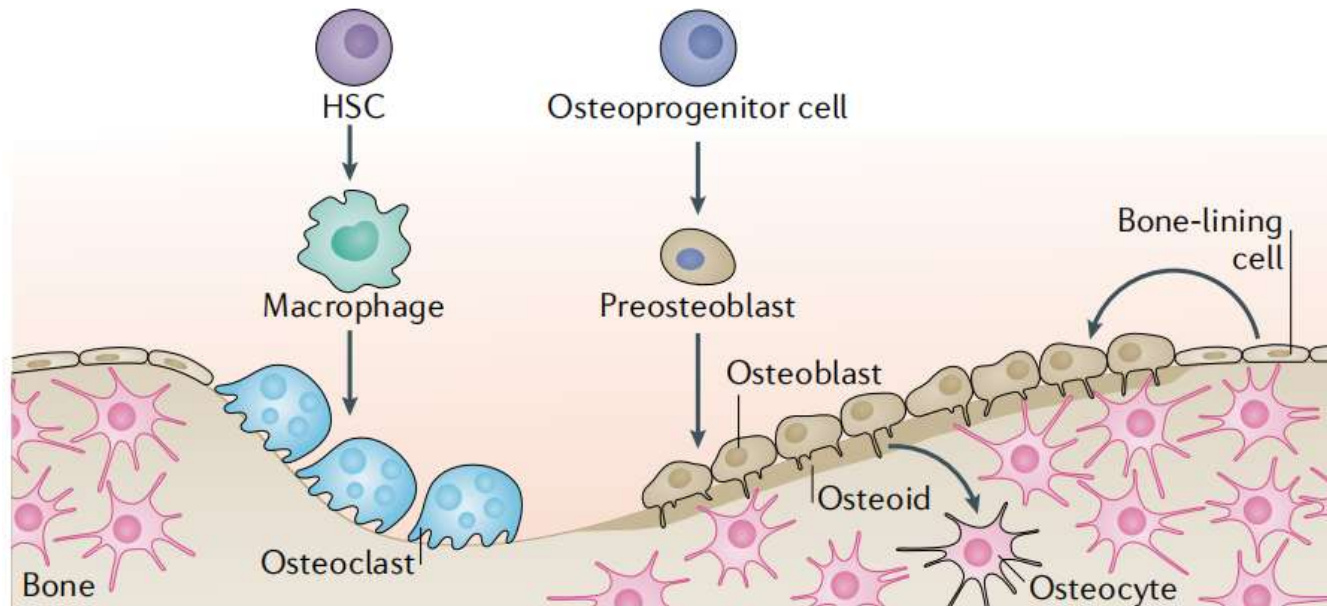
Endochondral ossification

# Calvarial development



## Intramembranous ossification

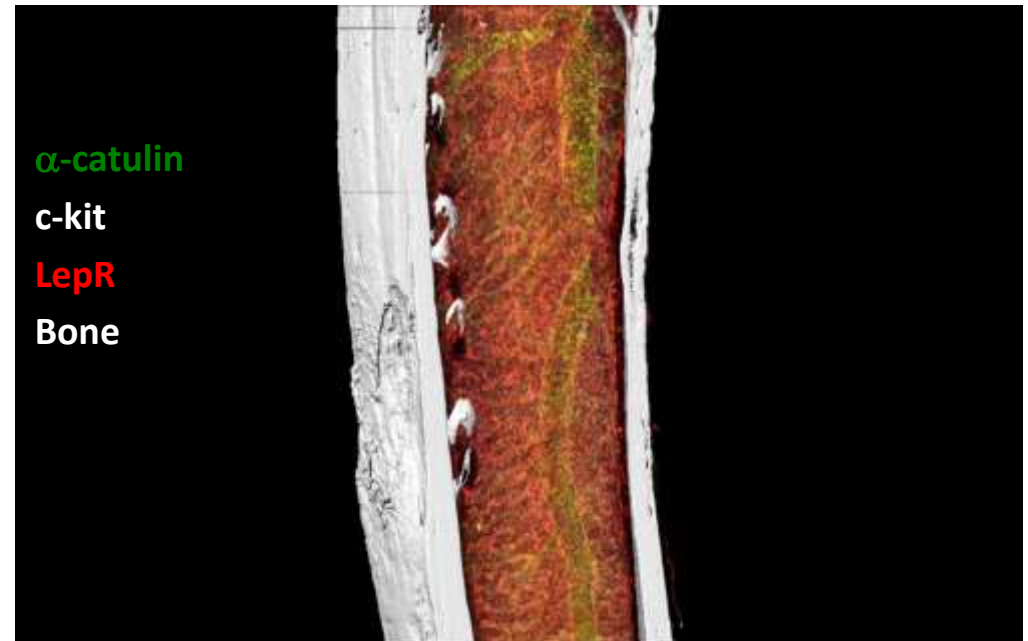
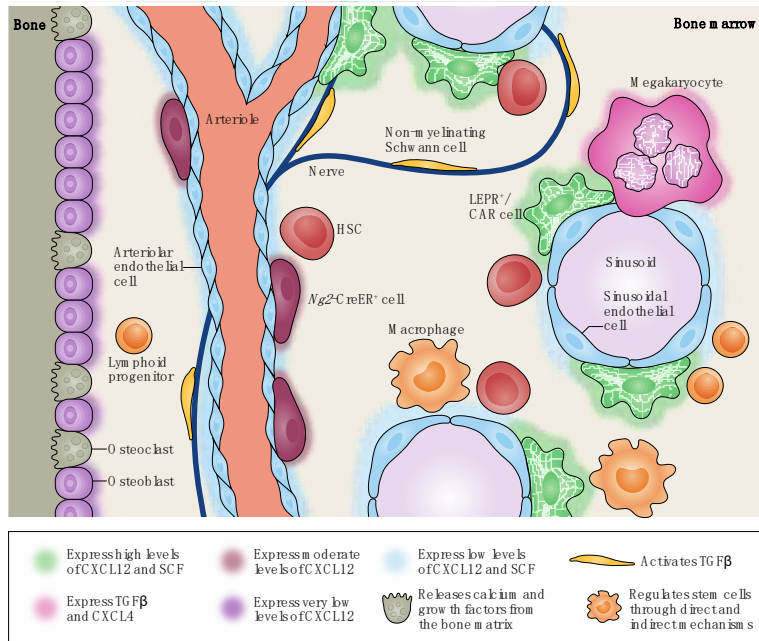
# Bone remodeling



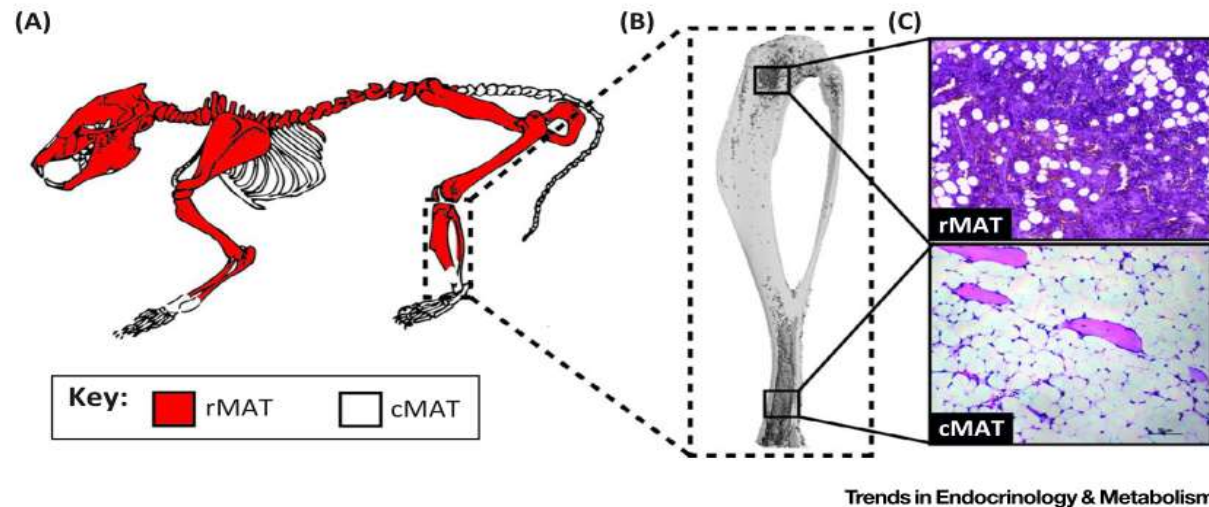
Salhotra et al., *Nat Rev Mol Cell Biol*, 2020



# Bone marrow microenvironment



# Bone marrow adipocytes



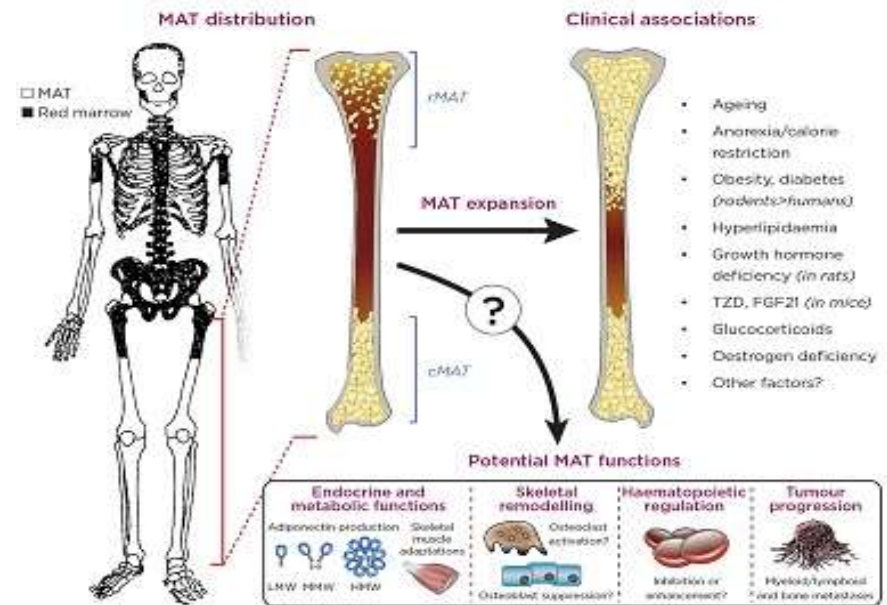
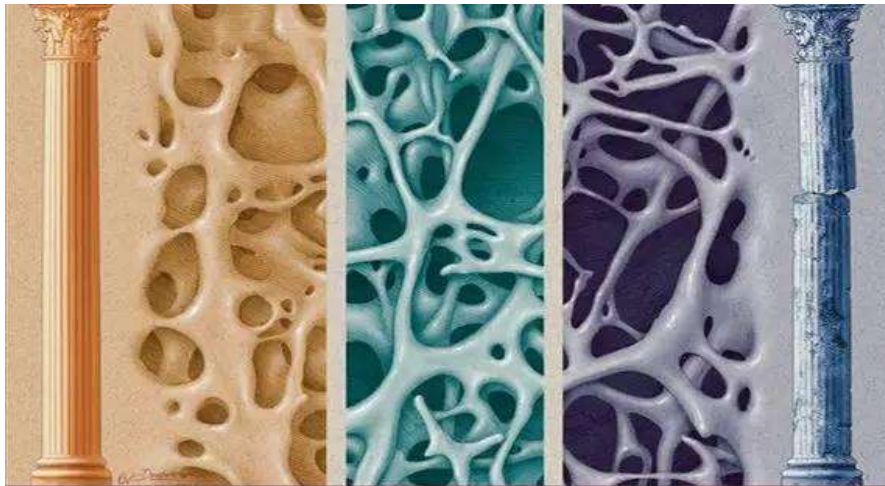
**regulated Marrow Adipose Tissue (rMAT):**  
Inducible

**constitutive Marrow Adipose Tissue (cMAT):**  
Appears early in postnatal life

Scheller et al. *Trends in Endocrinology & Metabolism* Tem, 2016

# Bone aging: Osteoporosis and fatty marrow

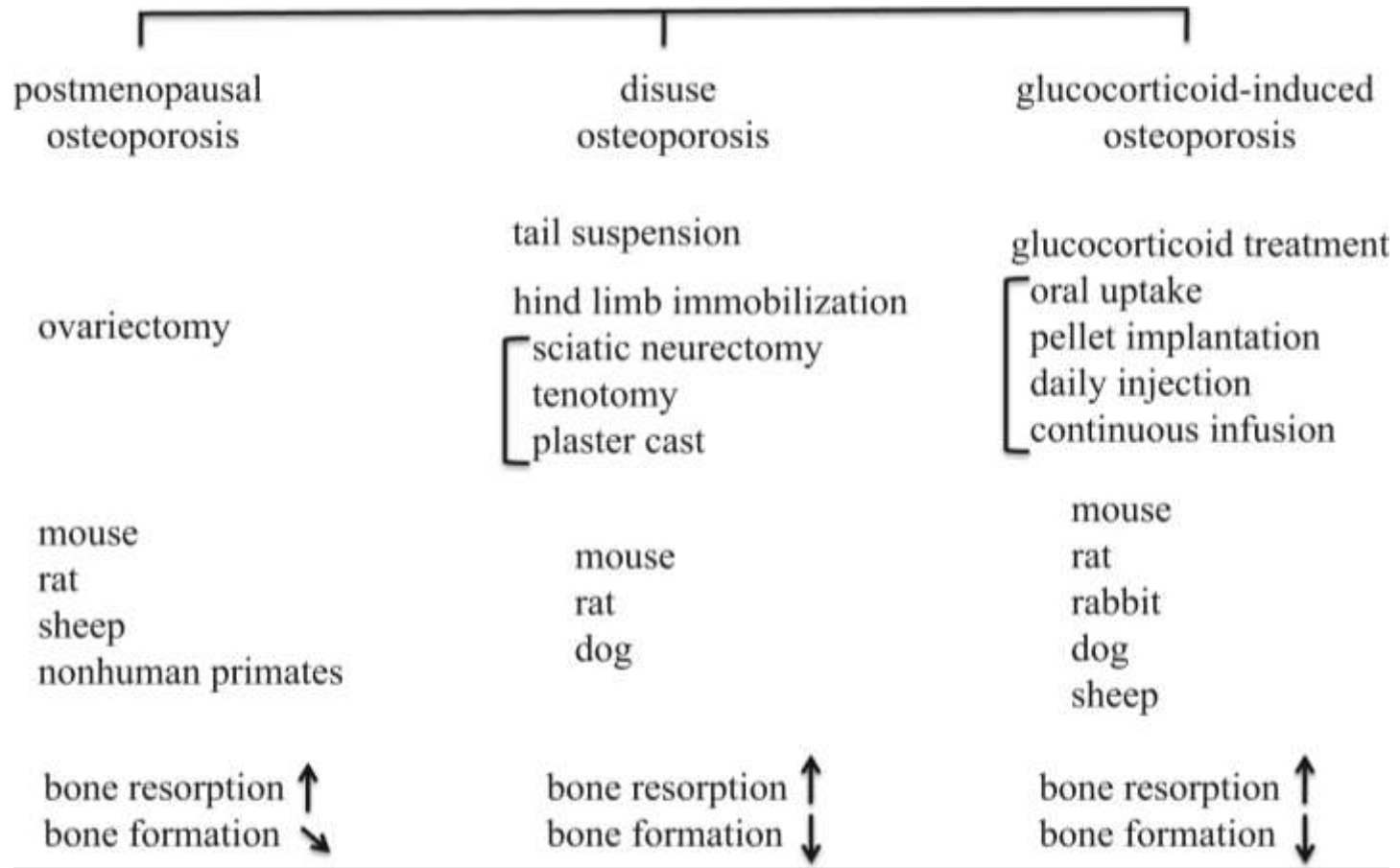
## Osteogenic activity



Kricun ME, Skeletal radiology, 1985

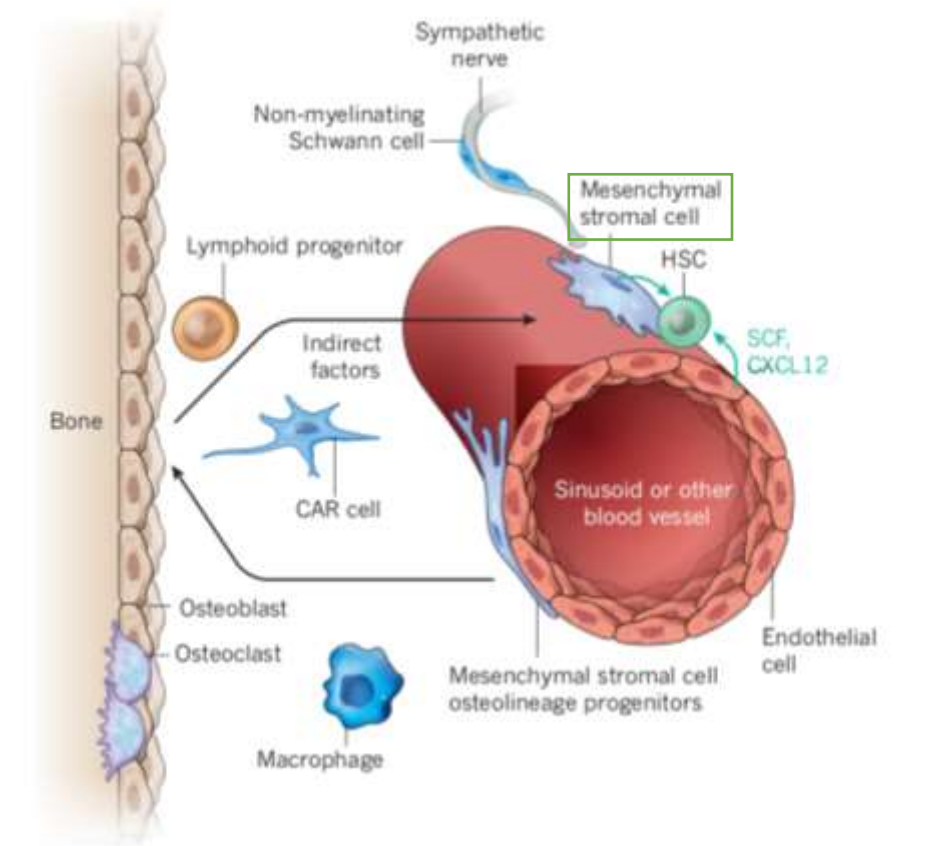


# Animal models for osteoporosis



# 1. What is mesenchymal stem cells?

## ■ Definition of BMSC



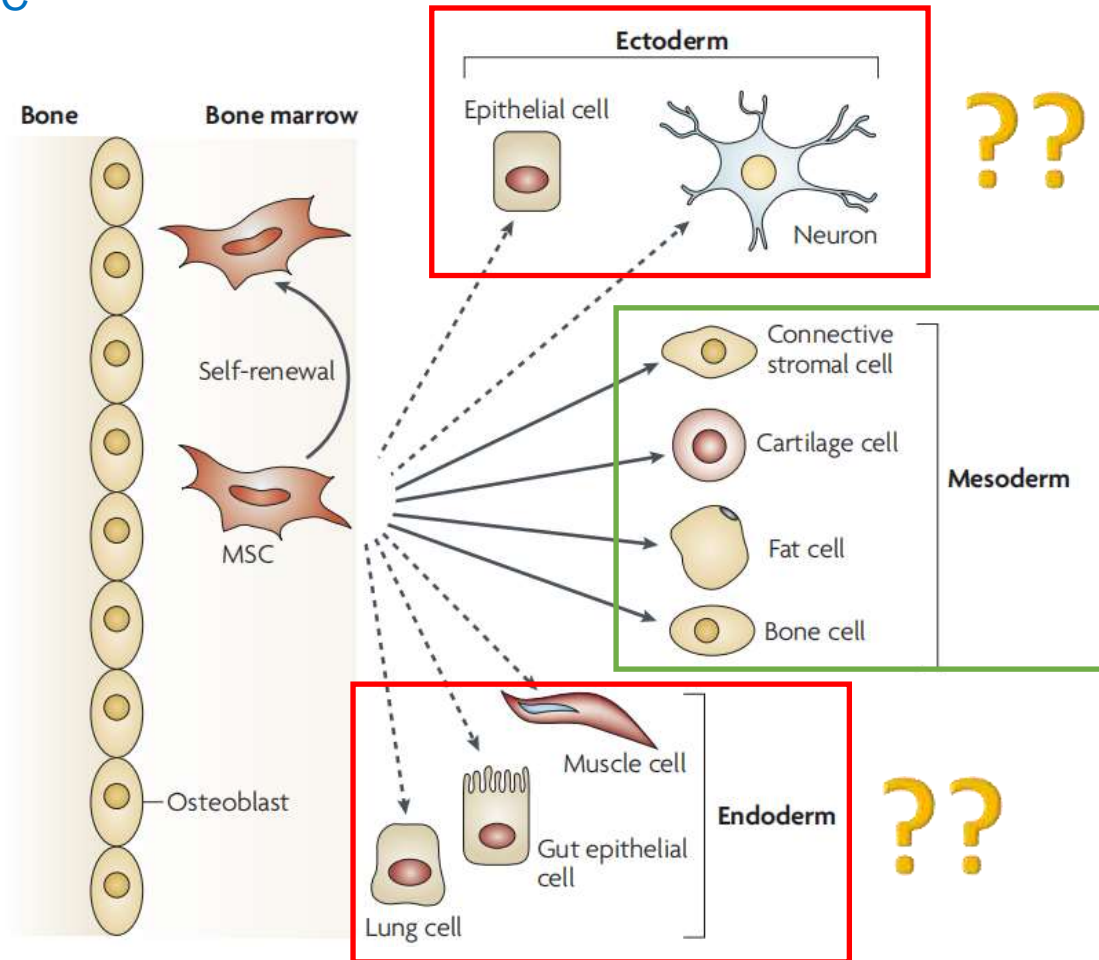
Stem cells {

- Self-renewal
- Multilineage differentiation

- BMSC: Bone marrow stromal cells
- HSC: Hematopoietic stem cells

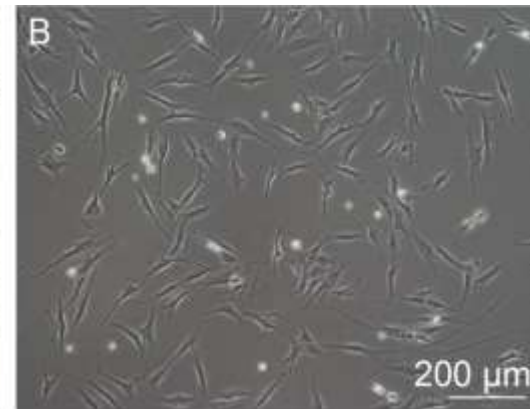
# 1. What is mesenchymal stem cells?

## ■ Definition of BMSC

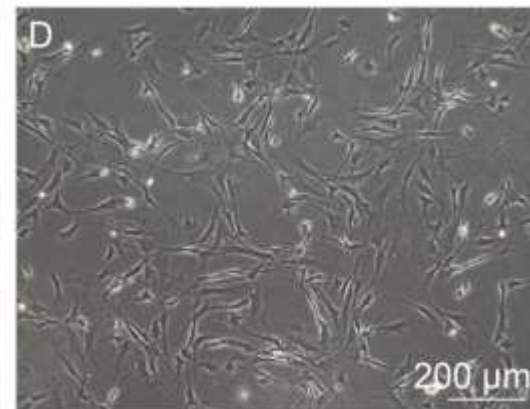
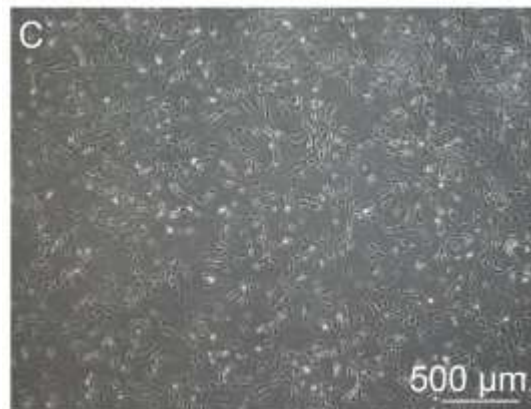


# Morphologies of mouse and human BMSCs

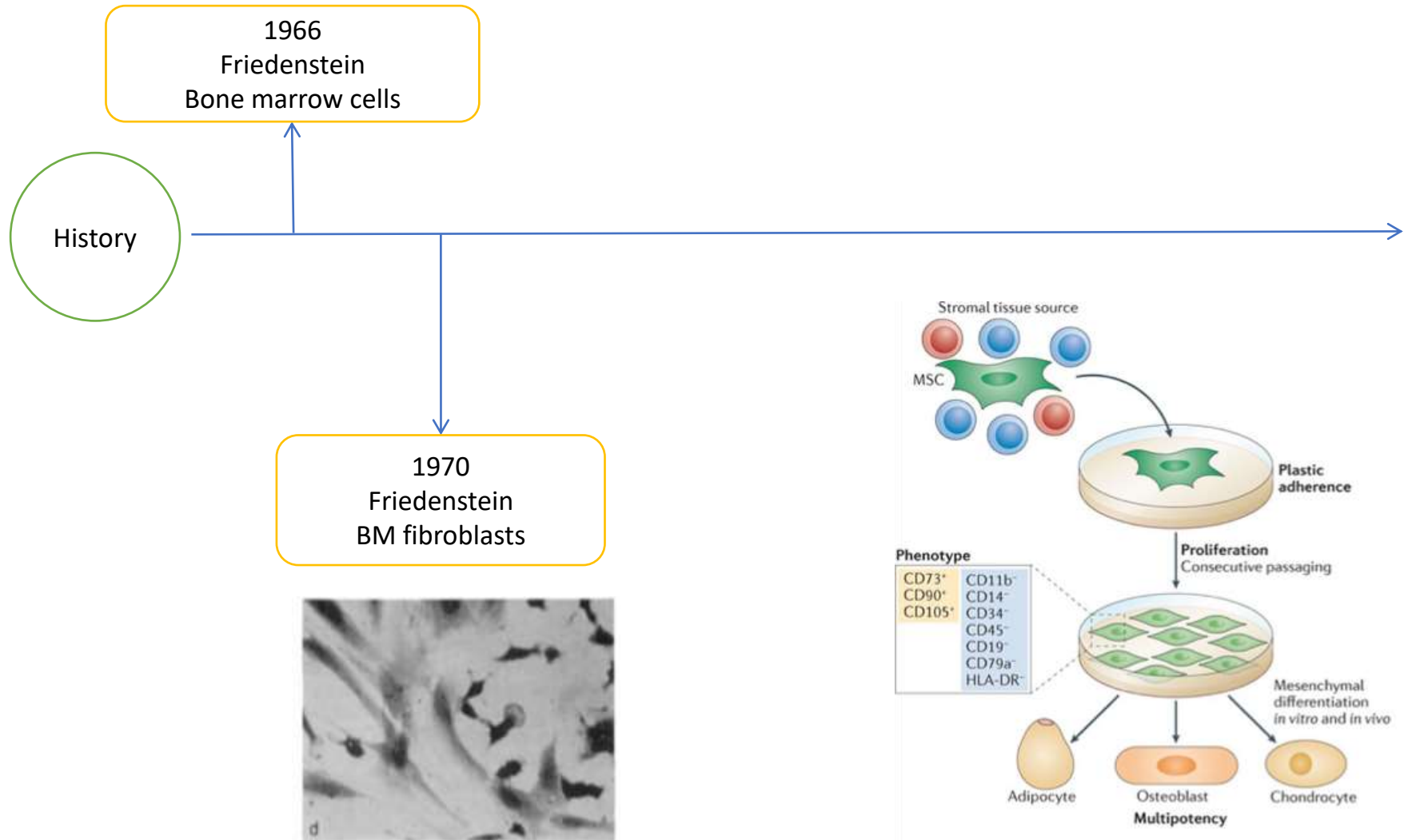
Human



Mouse



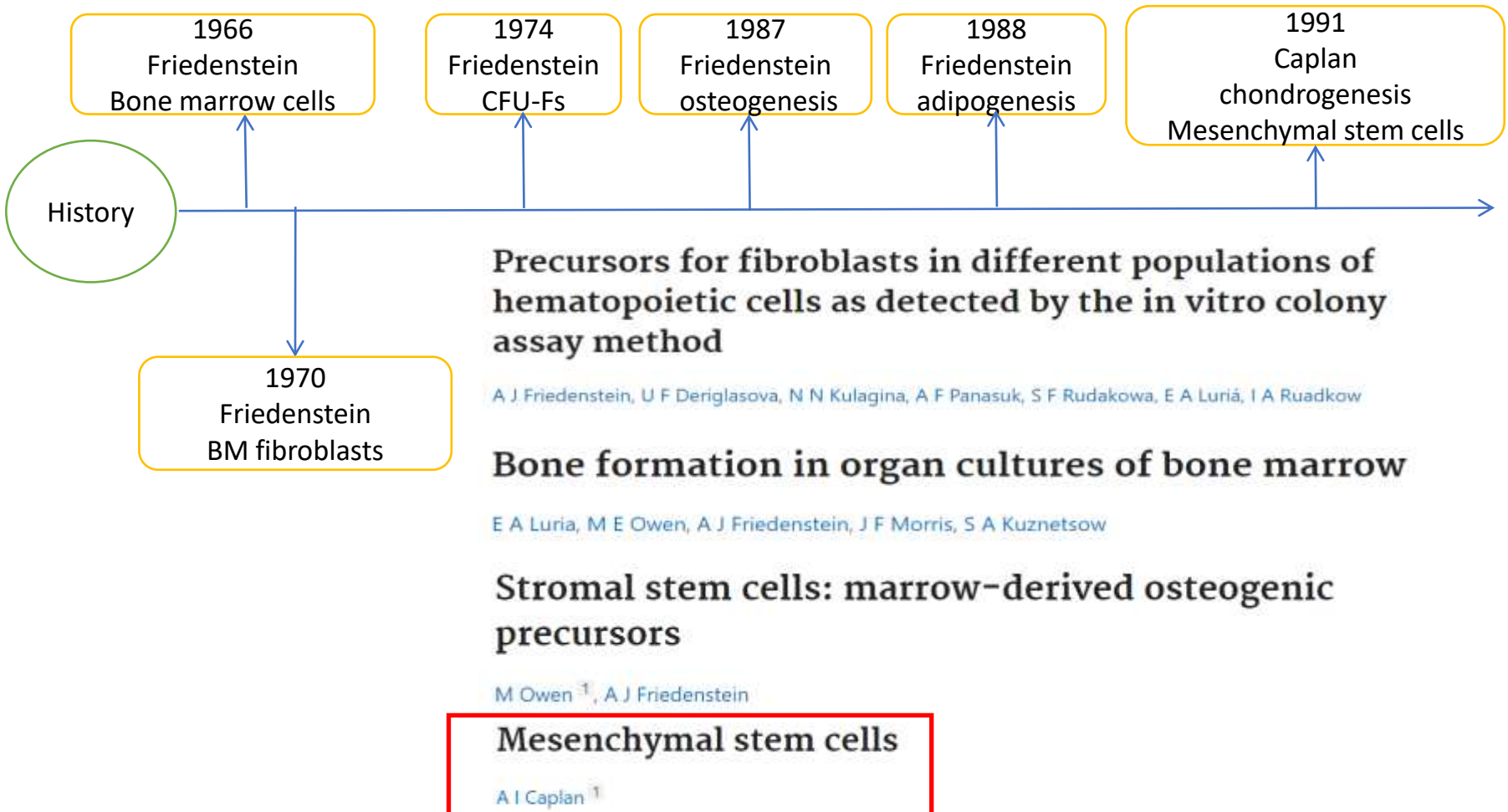
## 2. History of BMSC



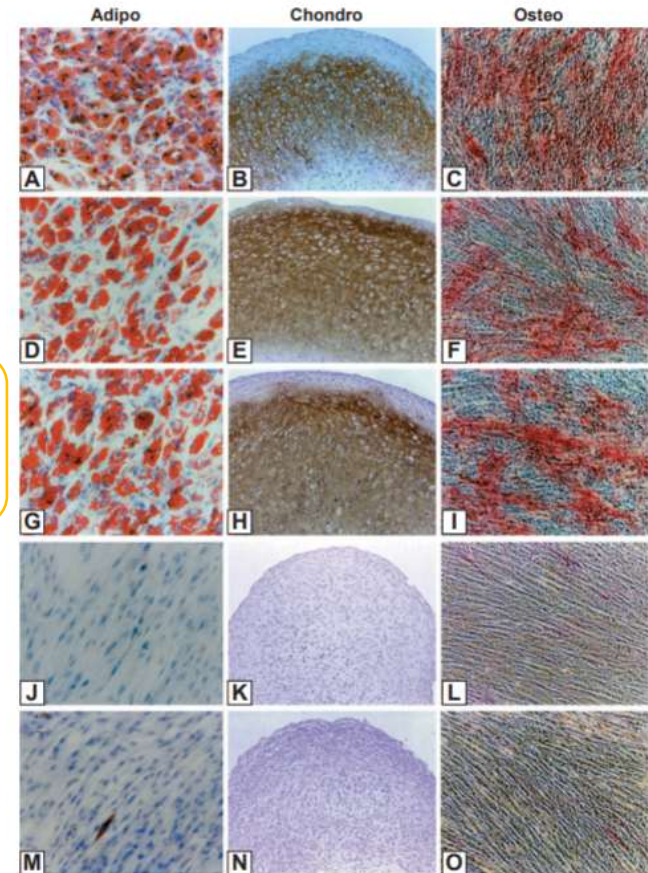
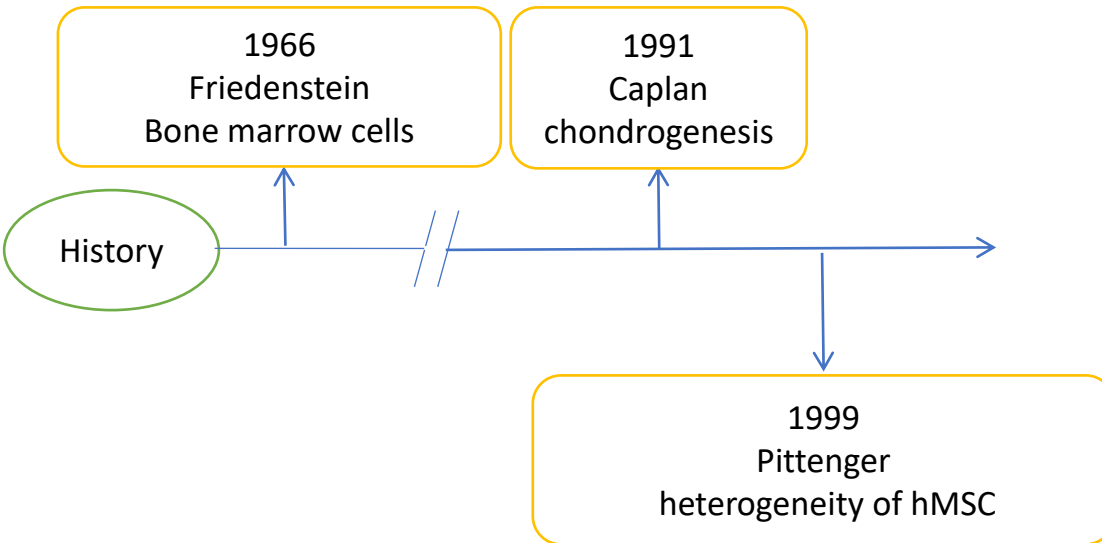
Friedenstein AJ, Chailakhjan RK, Lalykina KS. *Cell Tissue Kinet.* 1970



## 2. History of BMSC

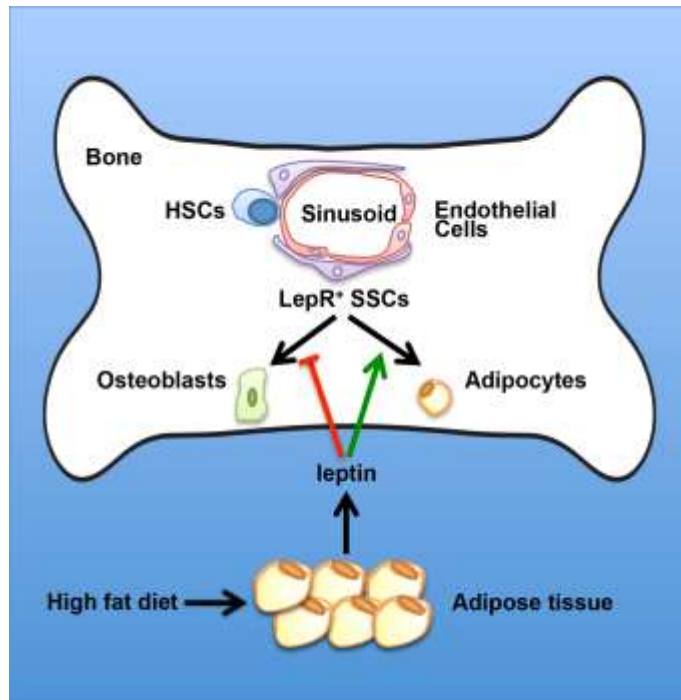
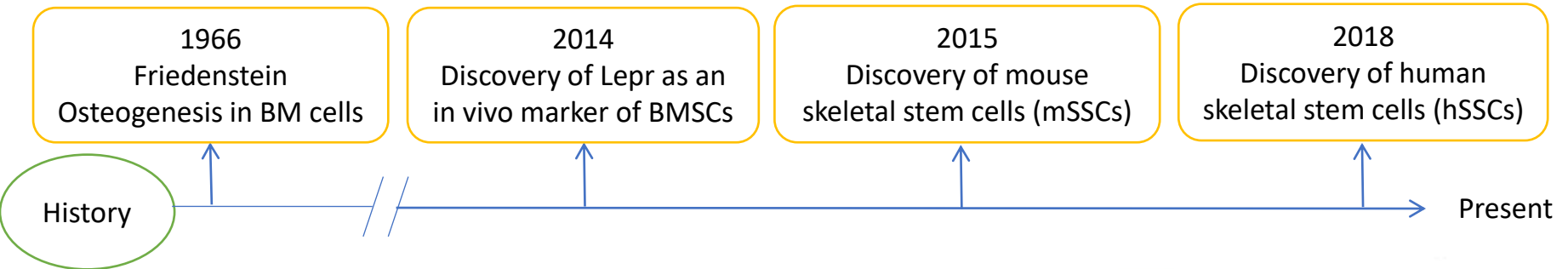


## 2. History of BMSC

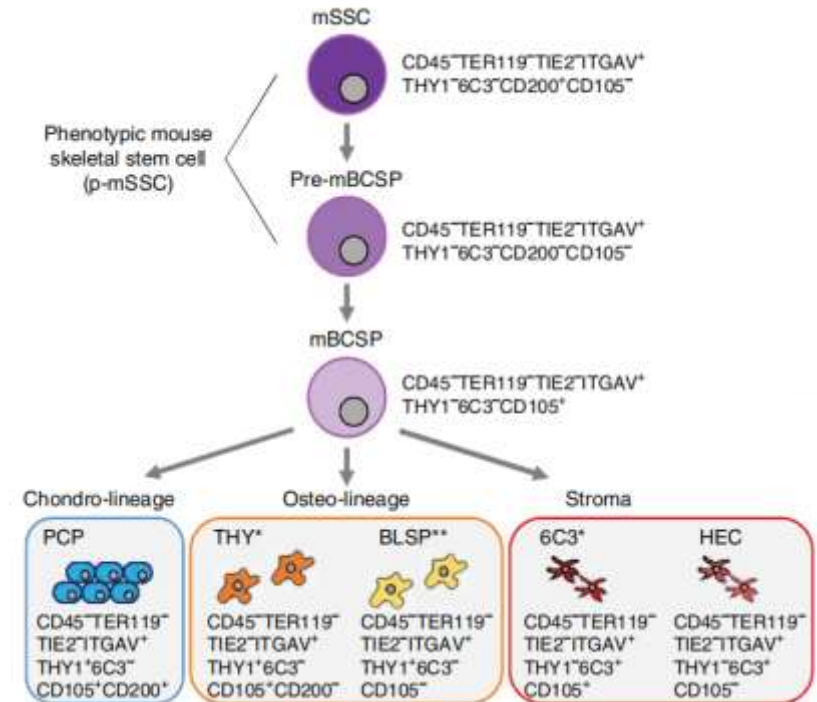


Pittenger MF, Mackay AM, Beck SC, et al. *Science*. 1999

## 2. History of BMSC

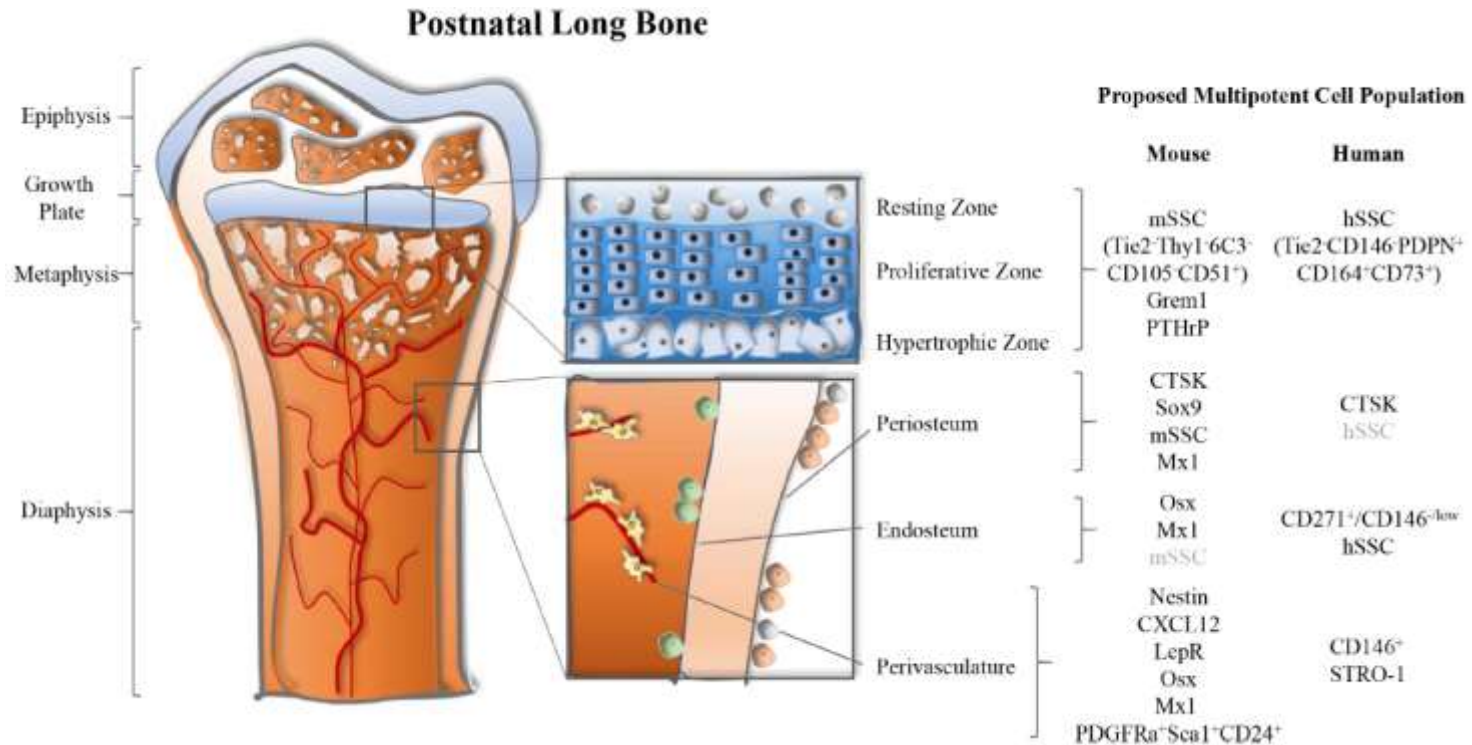


Yue et al. *Cell*, 2016



Chan et al. *Cell*, 2015, 2018

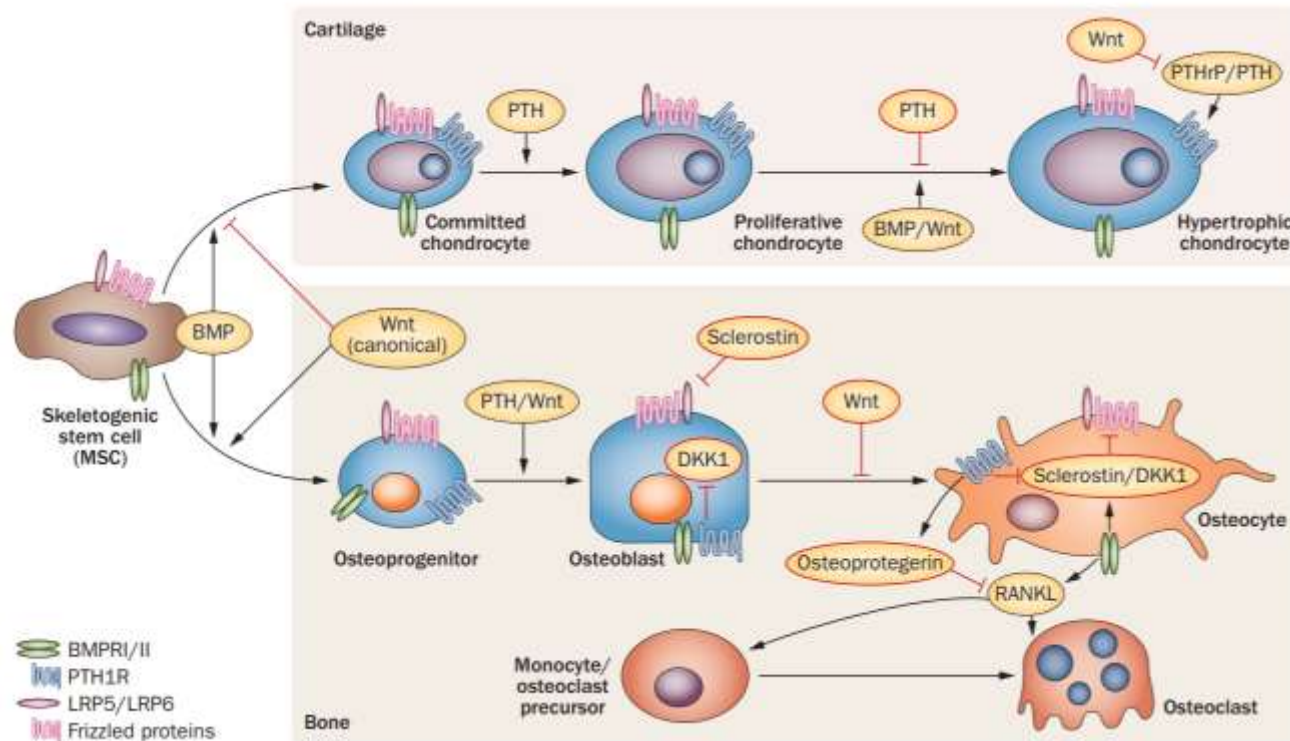
## Summary of distinct sources of SSCs



Ambrosi *et al.*, Frontiers in Cell and Dev. Bio., 2019

### 3. Function of BMSC

#### ■ Maintain bone homeostasis and fracture repair

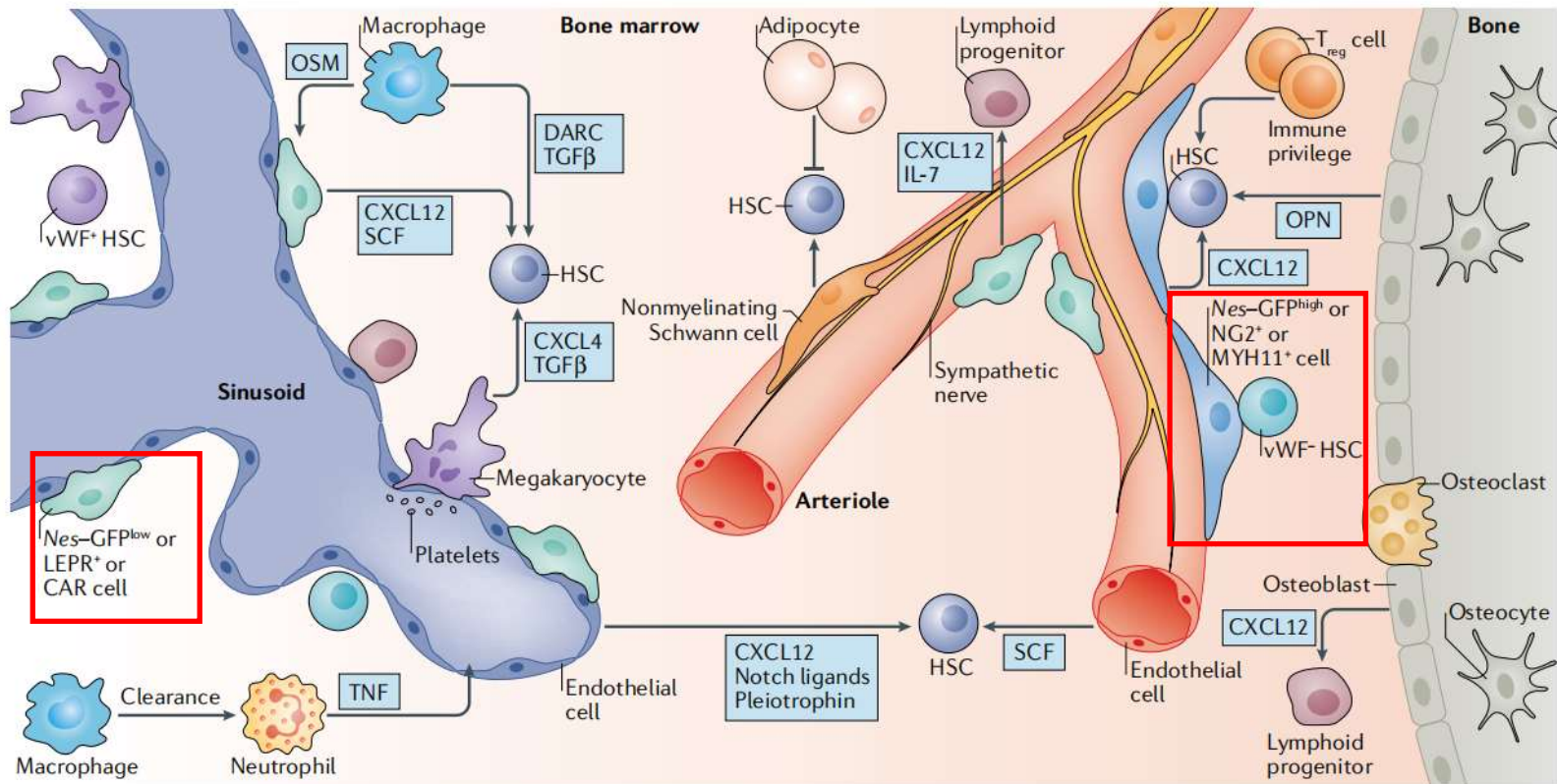


Einhorn, T., Gerstenfeld, L. *Nat Rev Rheumatol.* 2015



### 3. Function of BMSC

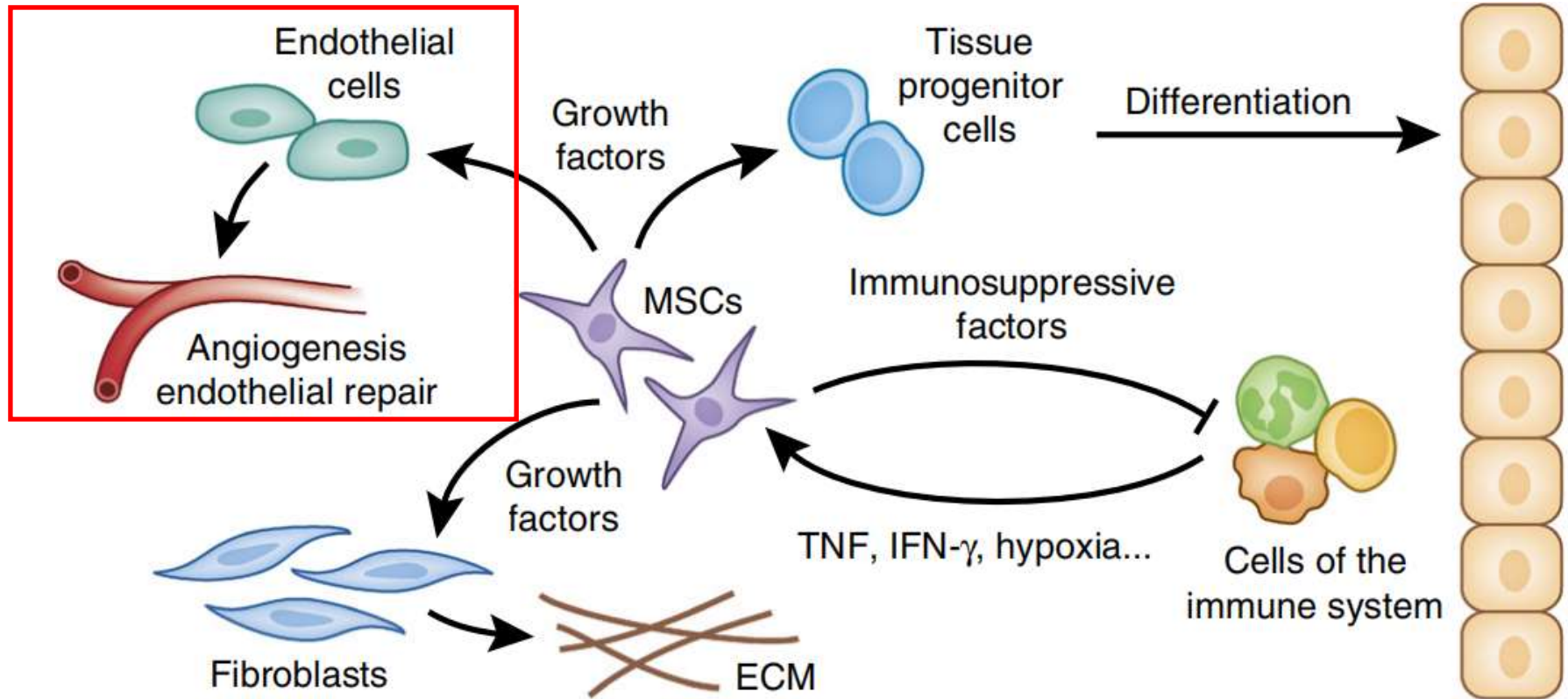
#### ■ Formation of HSC niche in the bone marrow



Pinho S, Frenette PS. *Nat Rev Mol Cell Biol.* 2019

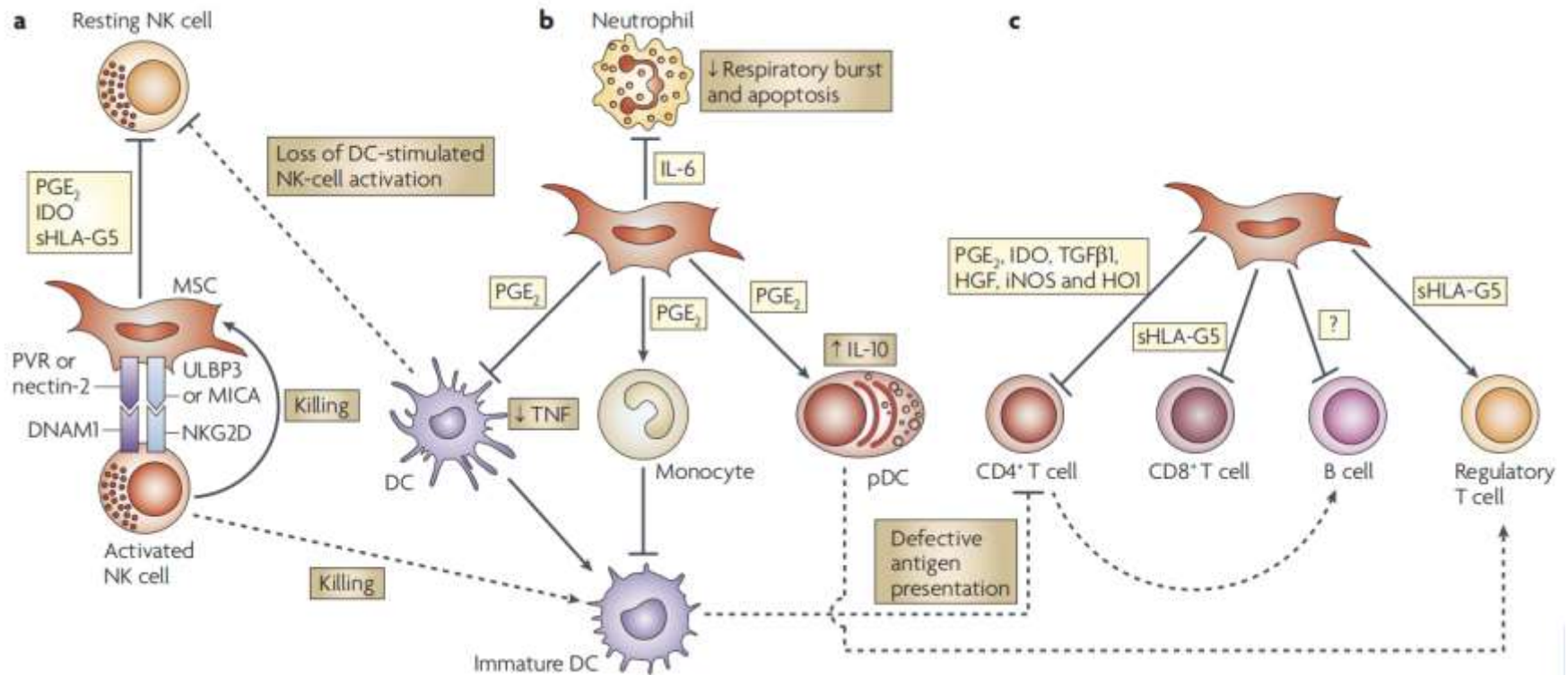
### 3. Function of BMSC

#### ■ Angiogenesis



### 3. Function of BMSC

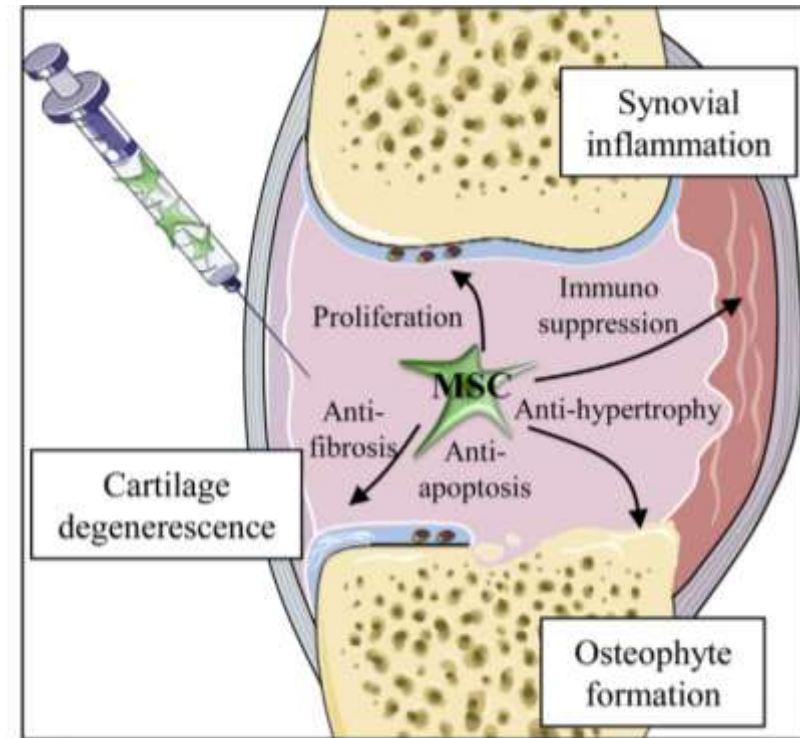
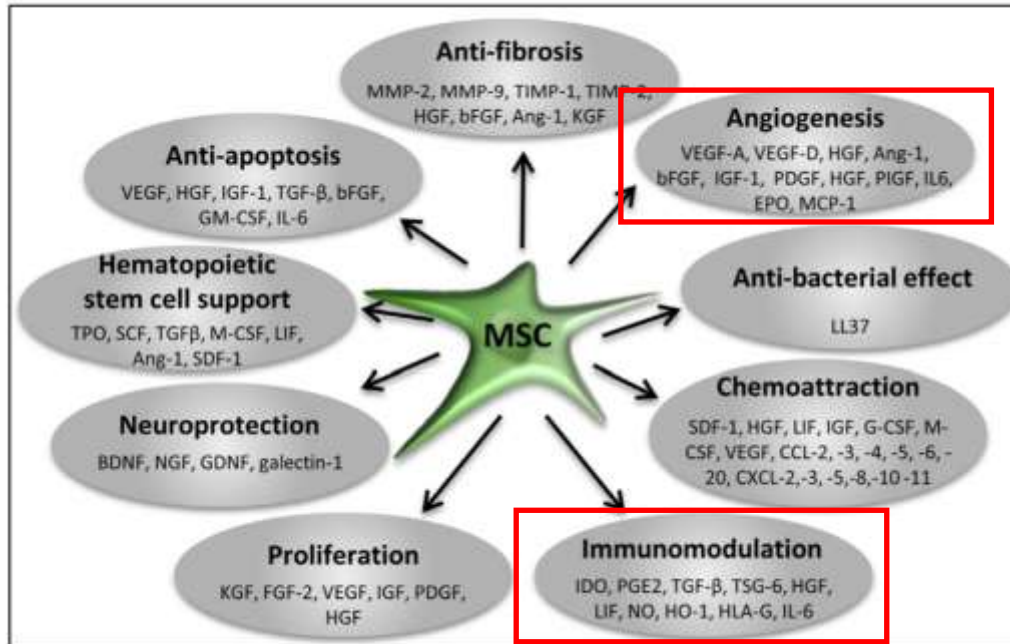
#### ■ The effects of MSCs on immune cells



Uccelli A, Moretta L, Pistoia V. *Nat Rev Immunol.* 2008

## 4. Clinical application of BMSC

### ■ Mechanisms





## 4. Clinical applications of BMSC

Disease	Target organ	Mechanism of MSC
Myocardial infarction	Heart	Generation of new myocytes and vascular structures
Skin-graft rejection	Skin	Inhibition of T cells
Stroke	CNS	Release of trophic factors and induction of neurogenesis
Melanoma	Skin	Inhibition of tumour-specific T cells by CD8 <sup>+</sup> T cells
Acute renal failure	Kidney	Inhibition of pro-inflammatory cytokine production and induction of anti-apoptotic and trophic factors
EAE	CNS	Inhibition of myelin-specific T cells and induction of peripheral tolerance
Diabetes	Pancreas & renal glomeruli	Induction of local progenitor cells and inhibition of macrophage infiltration
Rheumatoid arthritis	Joint	Inhibition of T cells and of production of pro-inflammatory cytokines; induction of regulatory T cells
Retinal degeneration	Eye	Decreased retinal degeneration through anti-apoptotic and trophic molecules
Acute lung injury	Lung	Inhibition of production of pro-inflammatory cytokines
Acute renal failure	Kidney	Tubular-cell regeneration through IGF1 secretion
Hepatic failure	Liver	Inhibition of leukocyte invasion through the release of cytokines and chemokines