

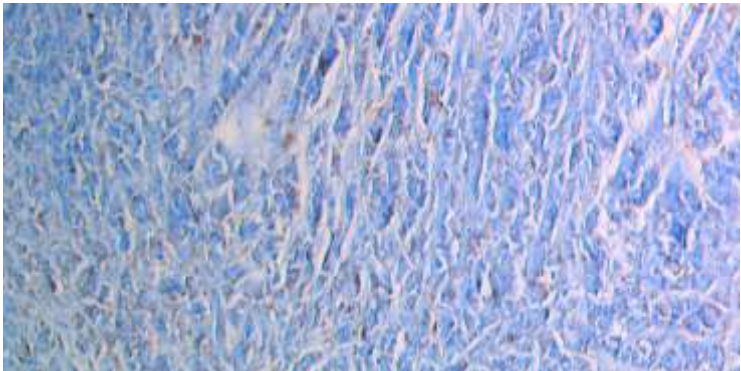
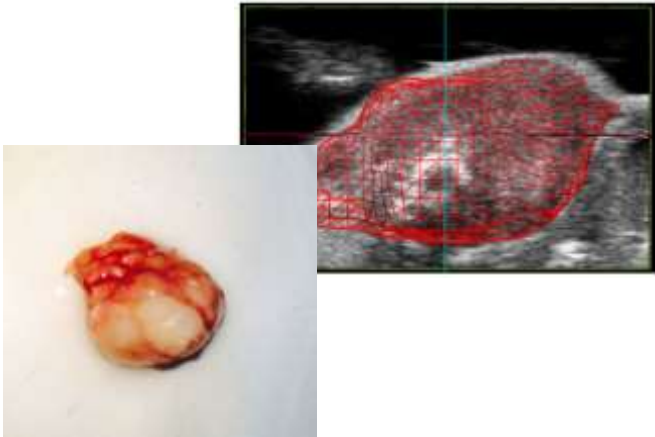
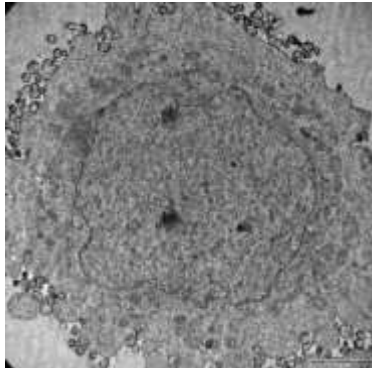
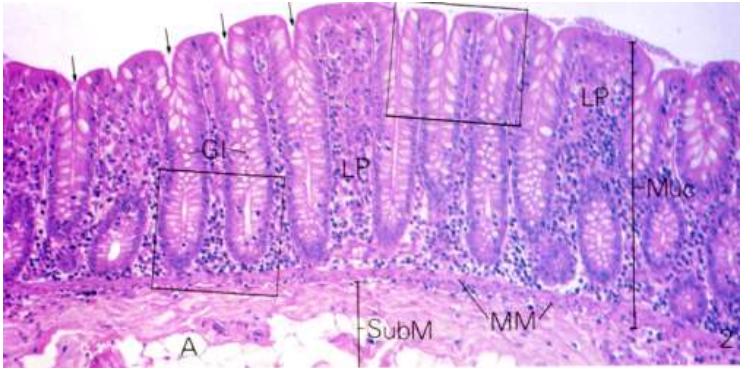
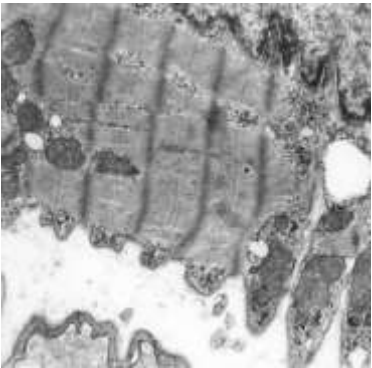
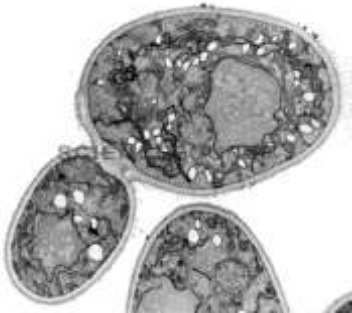
# Tissue concept and classification

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and Embryology,  
Faculty of Medicine MU

[pvanhara@med.muni.cz](mailto:pvanhara@med.muni.cz)

# How the variability of a multicellular body develops?

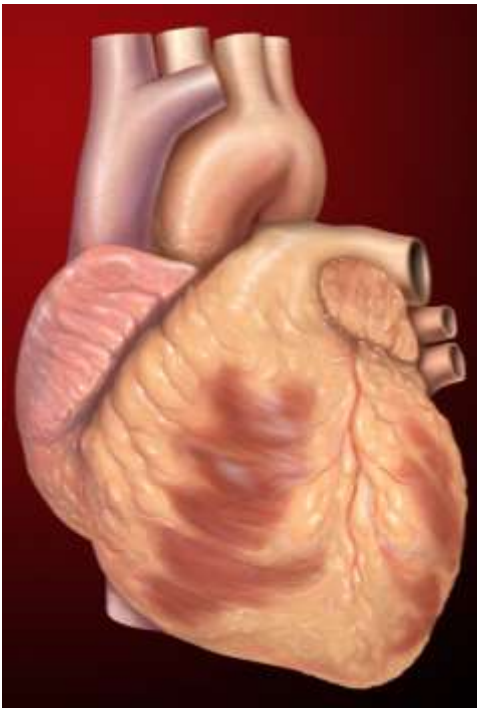
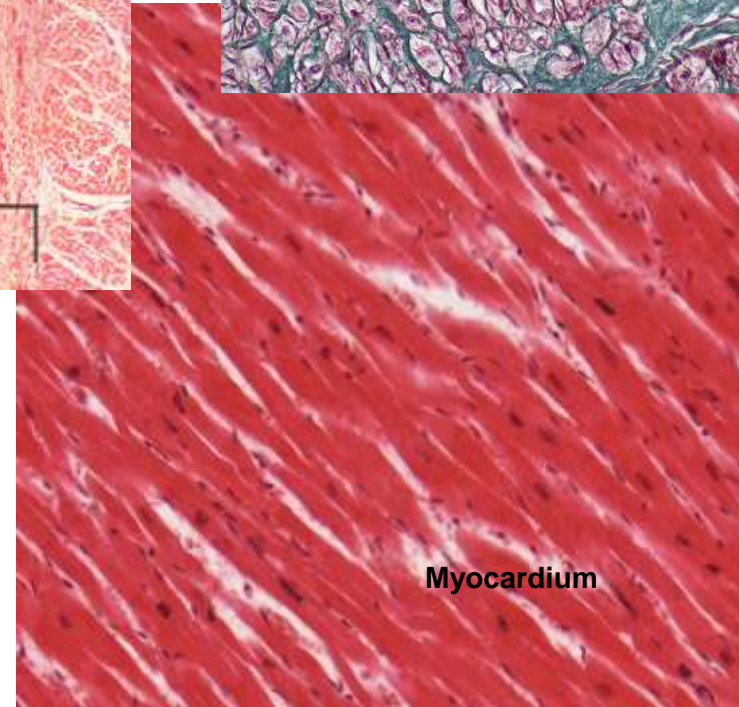
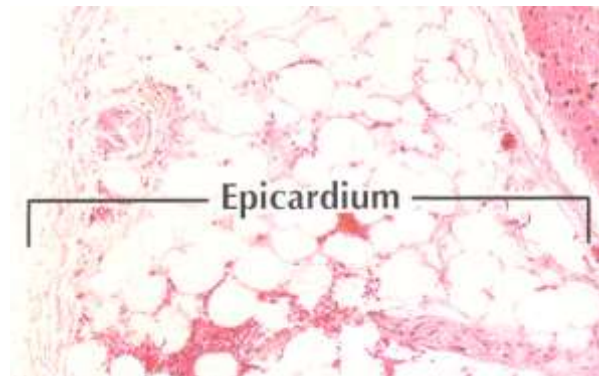
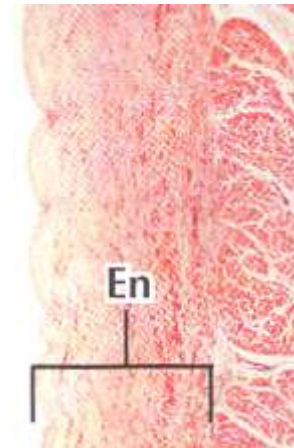
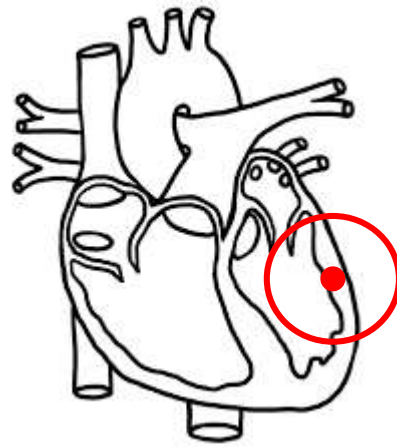
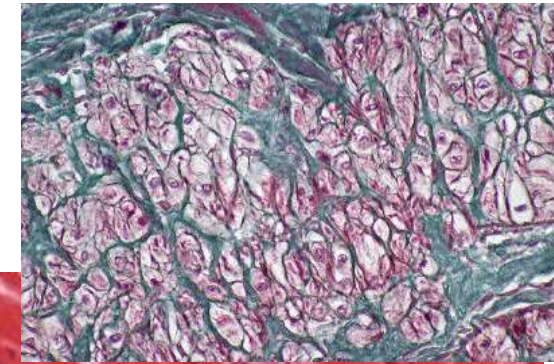
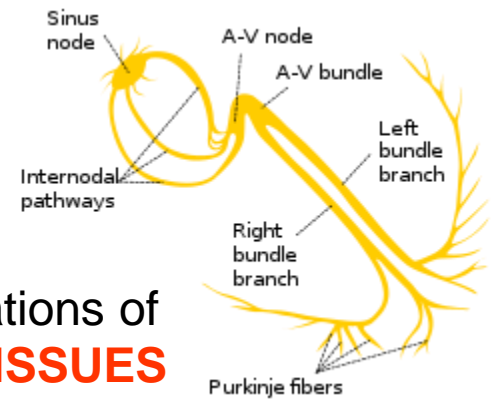


# ■ Tissues and organs

-  $6 \times 10^{13}$  **CELLS** of **200** different types

- cells form **functional, three-dimensional, organized** aggregations of morphologically similar cells and their products or derivatives - **TISSUES**

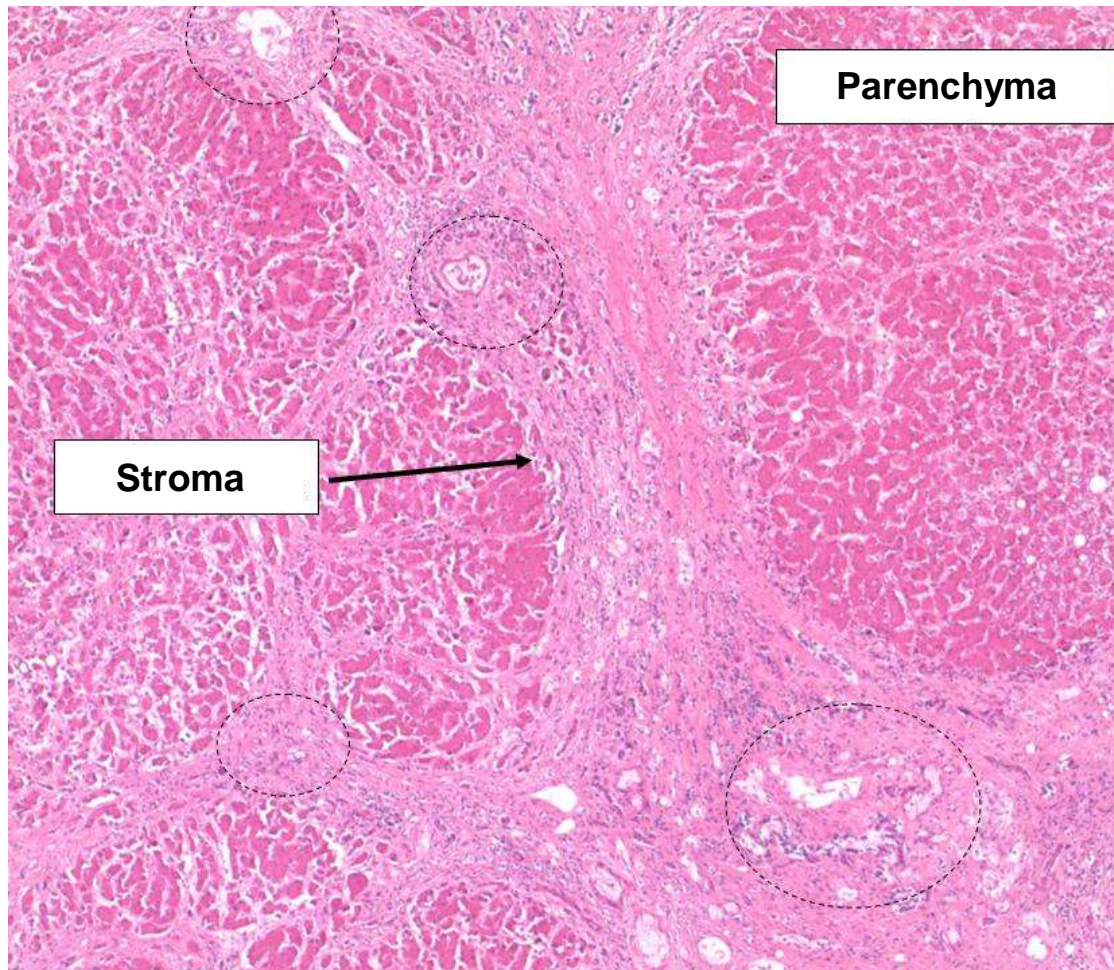
- tissues constitutes **ORGANS** and organ systems



# ■ Tissues and organs

**Parenchyma:** functional component of a tissue  
(liver, lung, pancreatic, kidney parenchyma)

**Stroma:** surrounding, supportive tissue



## LIVER

### **Parenchyma:**

- Hepatocytes
- Sinusoids and adjacent structures

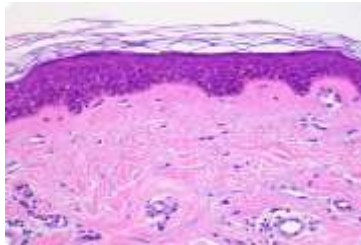
### **Stroma:**

- Connective tissue and adjacent structures
- Vessels
- Nerves
- Bile ducts

# ■ Contemporary tissue classification

Based on **morphology** and **function**:

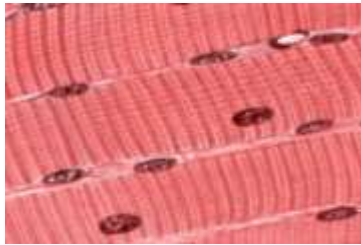
## Epithelium



Continual, avascular layers of cells with different function, oriented to open space, with specific junctions and minimum of ECM and intercellular space.

Derivates of all three germ layers

## Muscle

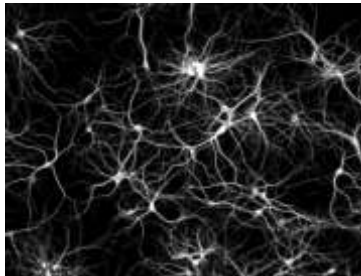


Myofibrils → contraction

Mesoderm – skeletal muscle, myocard, mesenchyme  
– smooth muscles

Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

## Nerve

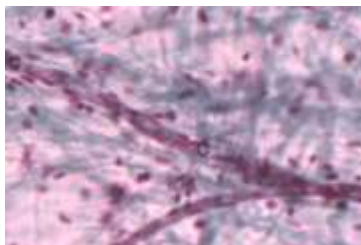


Neurons and neuroglia

Reception and transmission of electric signals

Ectoderm, rarely mesoderm (microglia)

## Connective



Dominant extracellular matrix

Connective tissue, cartilage, bone...

Mesenchyme

# ■ Basic principles of histogenesis

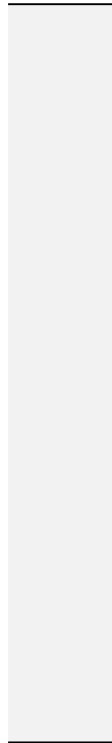
Proliferation

Diferentiation

Migration

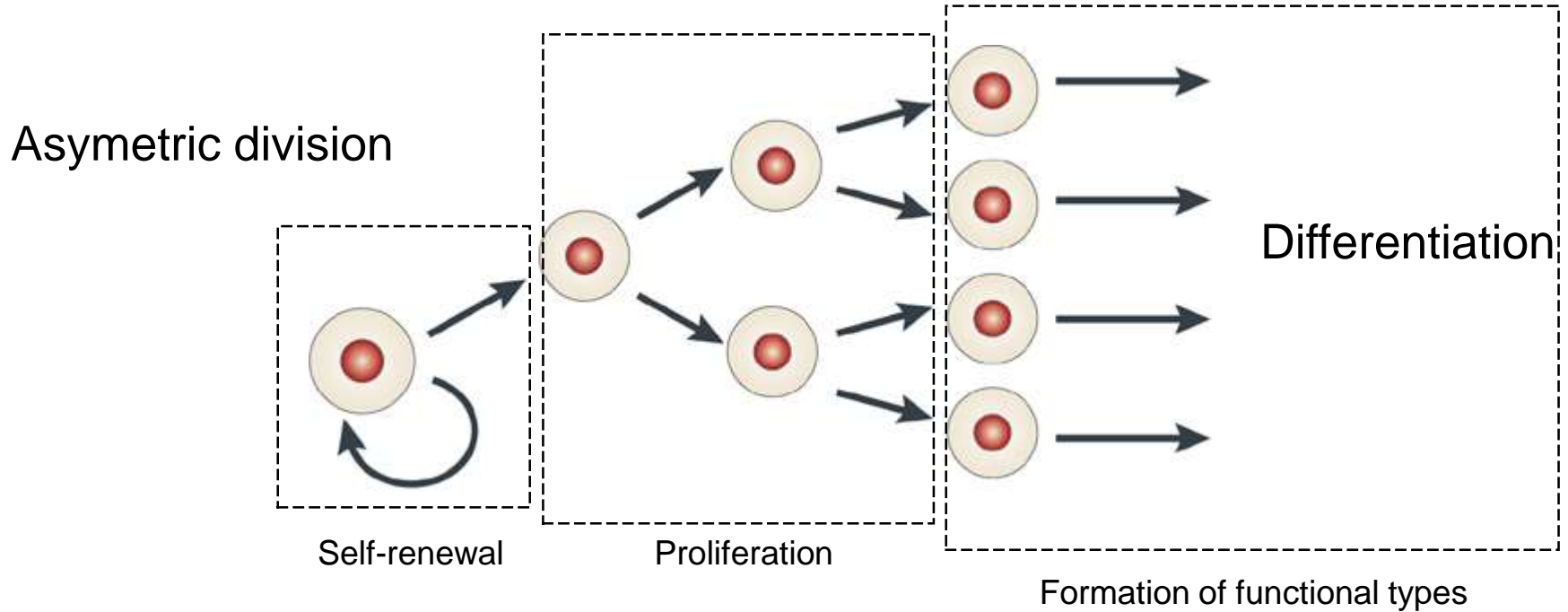
Apoptosis

Tissue patterns



- Functional cells of tissues differentiate from stem cells

Stem cells are capable of **differentiation** and **self-renewal**



# Stem cells

## Totipotent

- Constitute all cells of the body incl. extraembryonic tissues
- Zygote and early stages



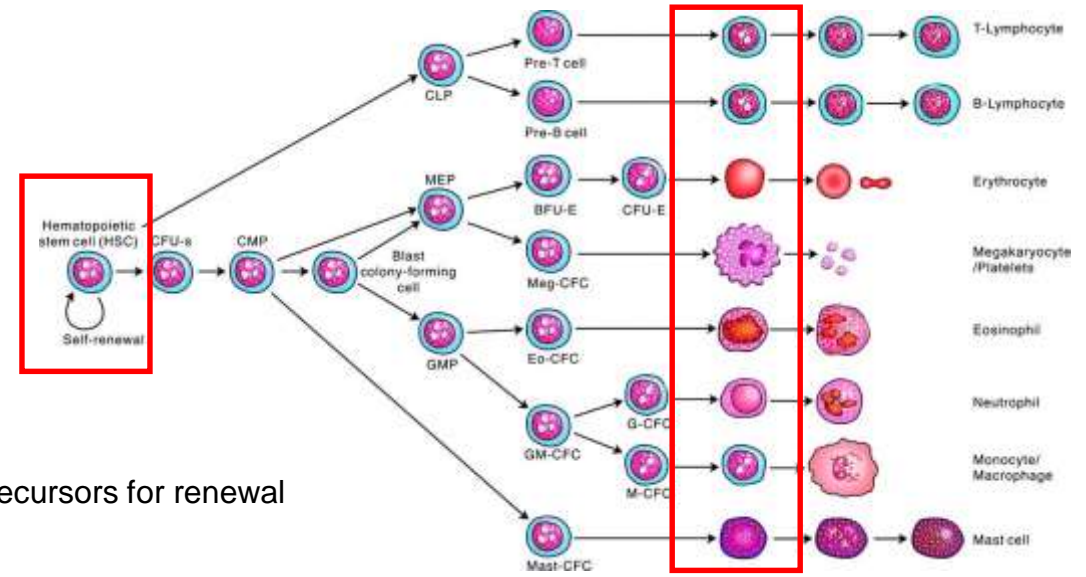
## Pluripotent

- All cells in the body except for trophoblast
- Blastocyst – Inner cell mass - ICM (embryoblast)
- Embryonic stem cells



## Multipotent

- Give rise to various cell types of a particular tissue
- Mesenchymal SC, hematopoietic SC



## Oligo- a unipotent

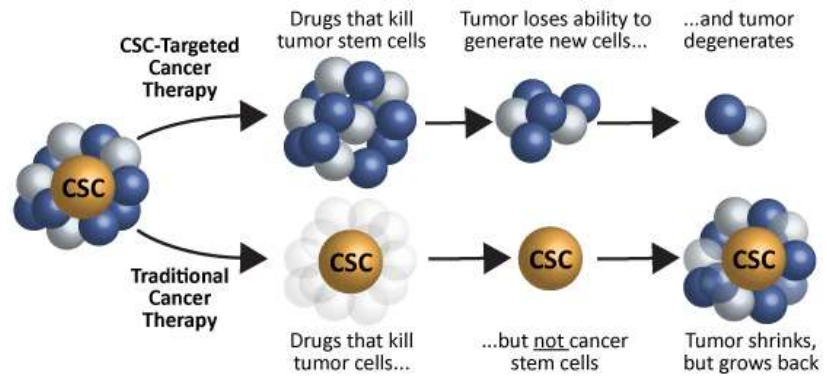
- One or several cell types – hematopoietic, tissue precursors for renewal of intestinal epithelia, etc.



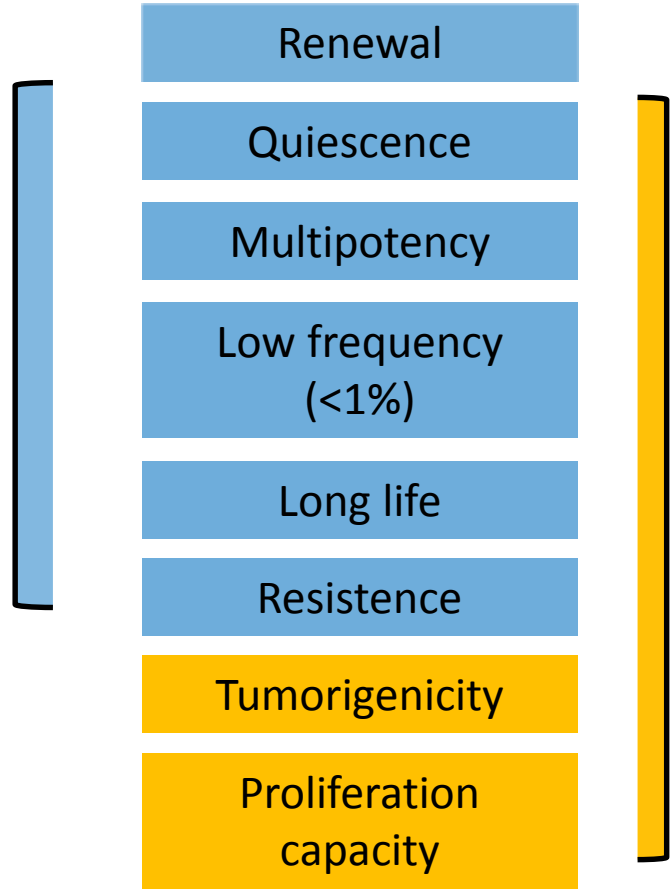
# Stem cells as a foe

## Cancer stem cells

- solid tumor is always heterogeneous
- small population of cells with stem cell character can repopulate tumor tissue after cytotoxic therapy



Tissue stem cells



Cancer stem cells

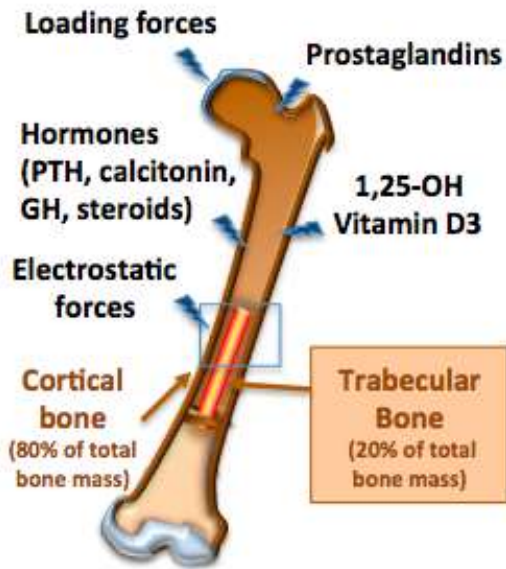
- Microenvironment regulates tissue function and reflects its tissue composition

Huge number of **biological** and **physically-chemical** parameters

**Stem cell niche**

- Embryonic development
- Intercellular interaction
- Space organization (dimensionality)
- Gradient of morphogenes
- Epigenetic profile
- Gene expression dynamics
- Partial pressure of gases
- ECM composition
- Mechanical stimulation
- Perfusion and interstitial flows
- Local immunity response
- Metabolites

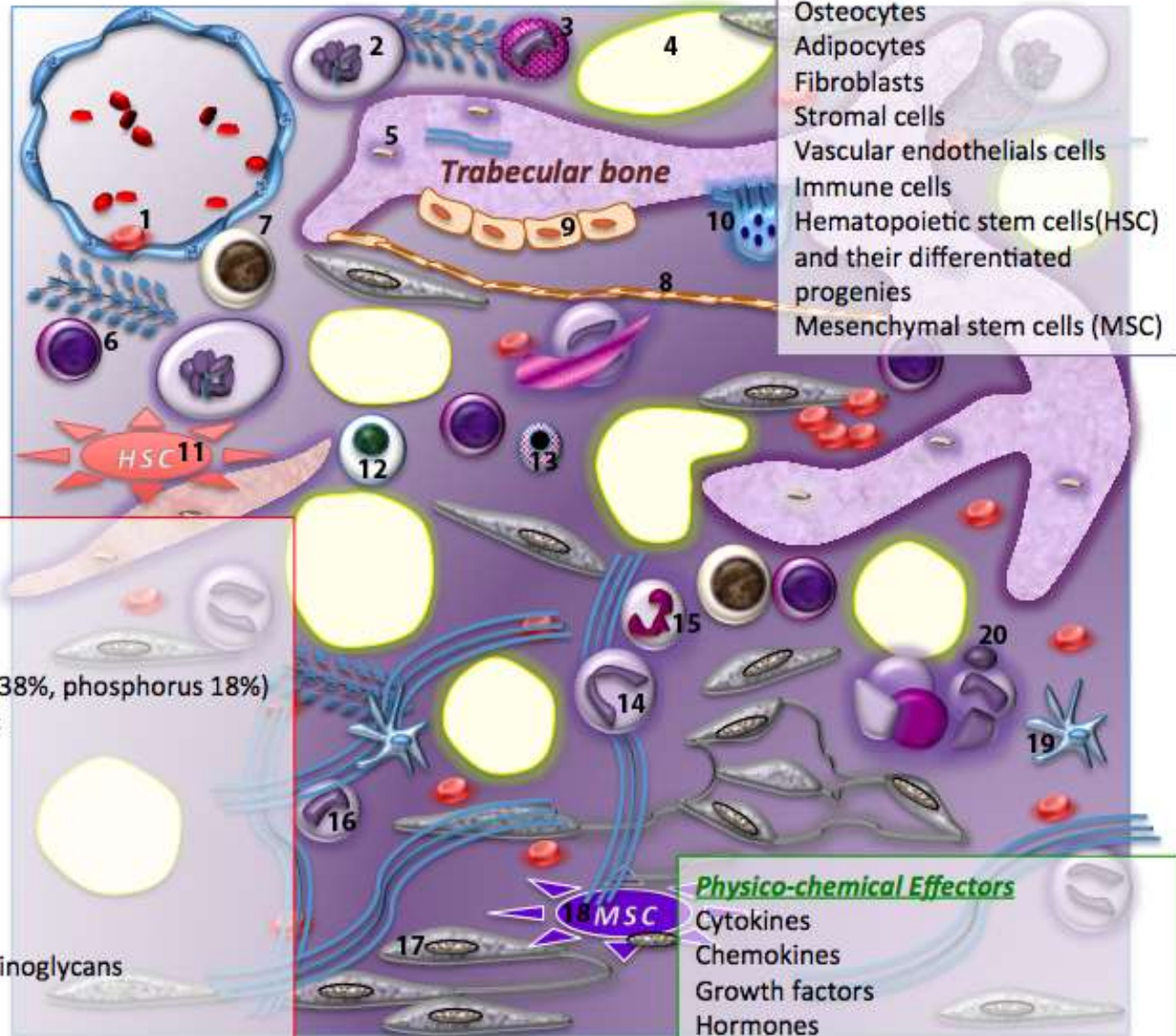
## Bone



## Stem cell niche?

### Bone & Bone Marrow cells

Osteoblasts  
Osteoclasts  
Osteocytes  
Adipocytes  
Fibroblasts  
Stromal cells  
Vascular endothelial cells  
Immune cells  
Hematopoietic stem cells (HSC) and their differentiated progenies  
Mesenchymal stem cells (MSC)



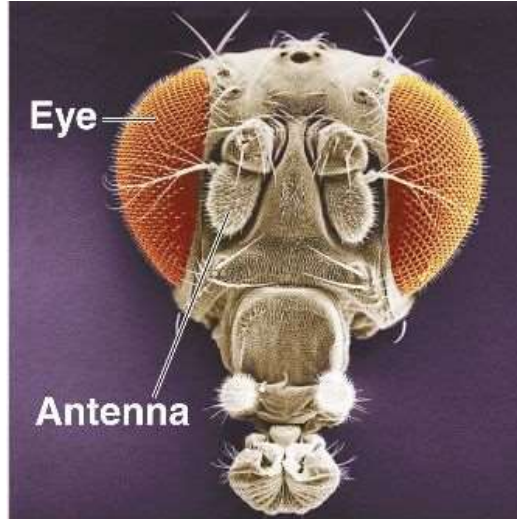
### ECM components

Fibronectin  
Laminin  
Collagens  
Apatite crystals (calcium 38%, phosphorus 18%)  
Bone promoting proteins  
Bone sialoproteins  
Osteonectin  
Osteoprotegerin  
Osteocalcin  
Integrins  
Alcaline Phosphatase  
Proteoglycans, Glycosaminoglycans  
Osteopontin  
MMPs & TIMPs  
Receptors  
Adhesion molecules

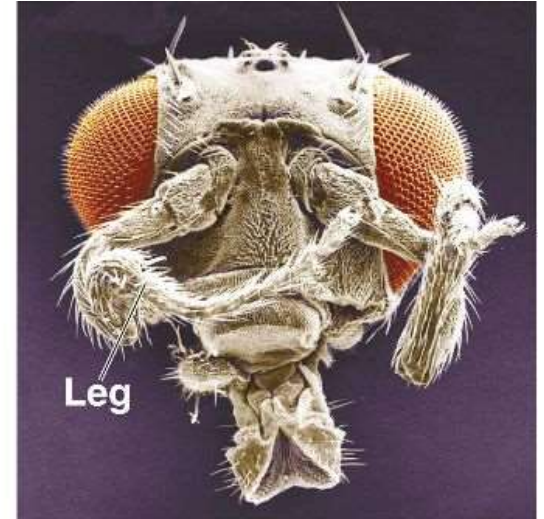
### Physico-chemical Effectors

Cytokines  
Chemokines  
Growth factors  
Hormones  
Physico-mechanical forces  
Biochemical regulators (pH, oxygen concentration, nutrients...)

# Molecular principles of histogenesis



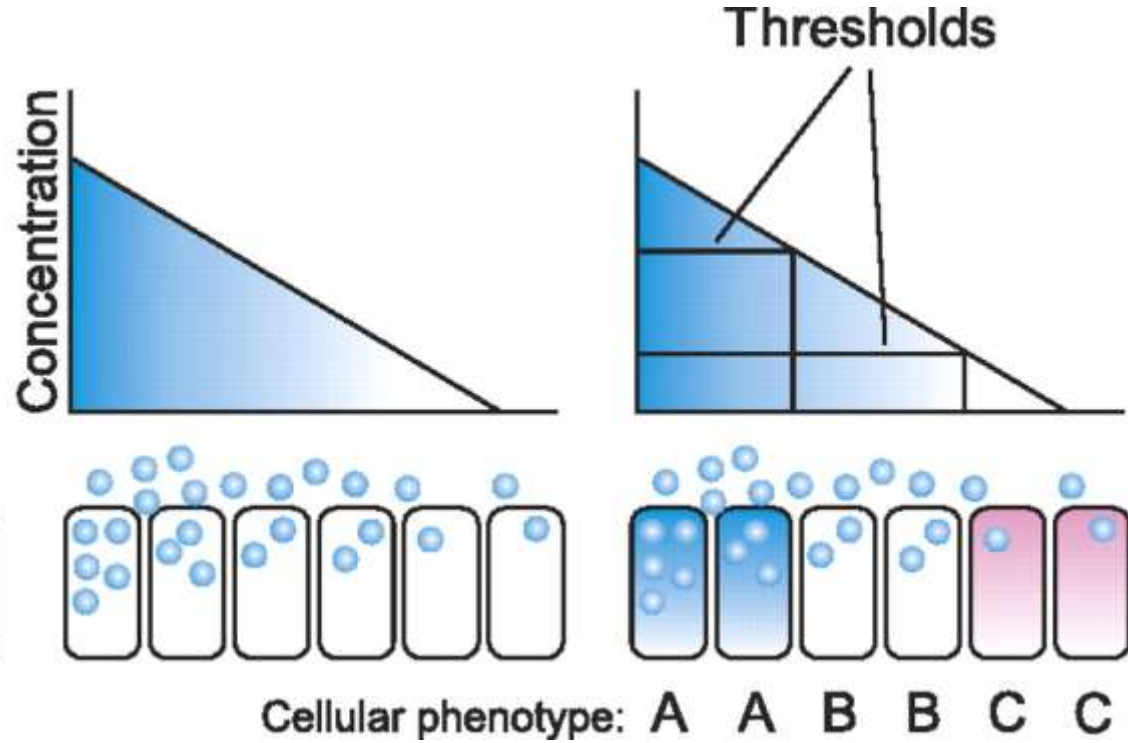
Wild type



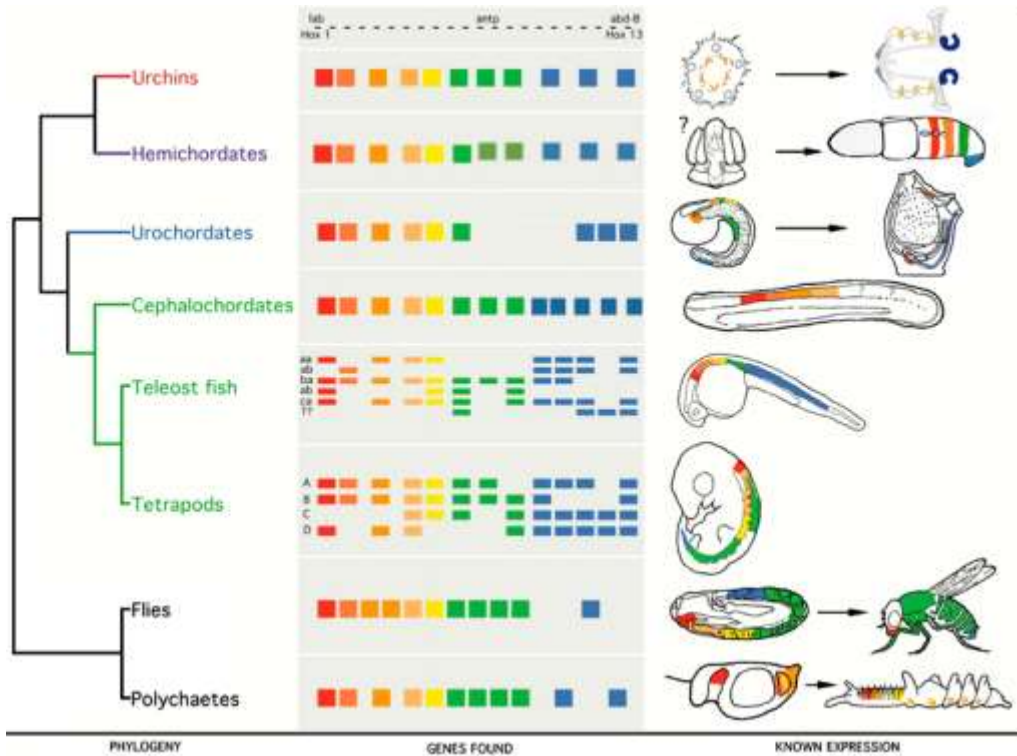
Mutant



# ■ French flag model



# Hox complex



## Hox genes

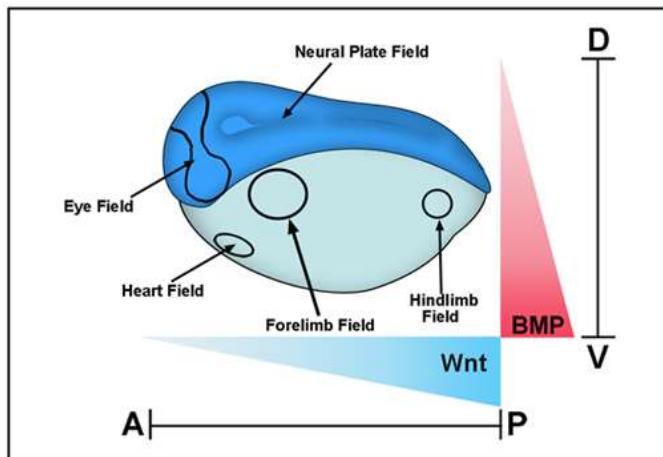
Highly conserved family of transcription regulators that determine body polarity, orientation and axis

Tissue differentiation along antero-posterior axis

Human (39 genes)

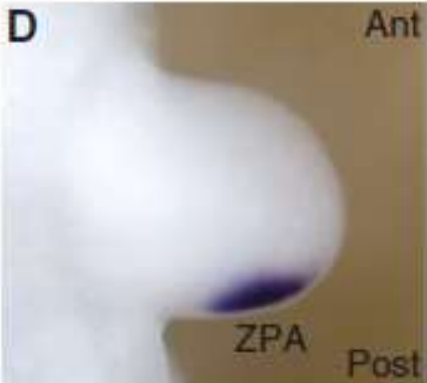
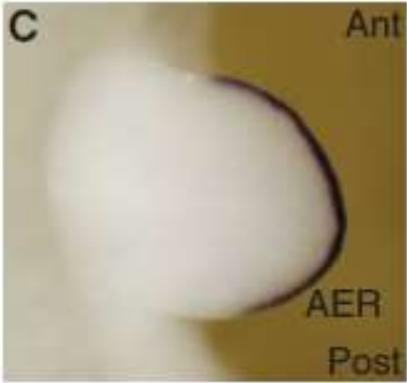
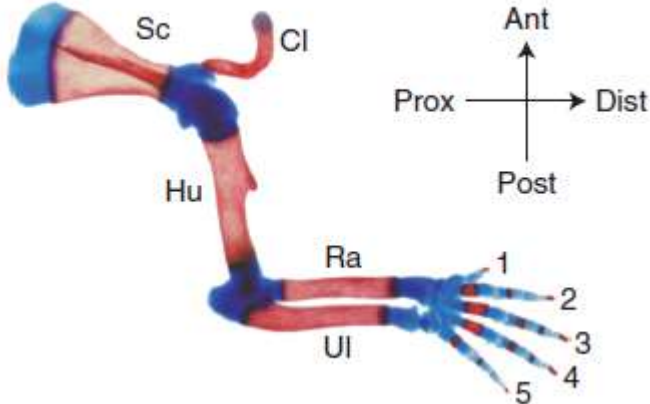
Cluster	Chromosome	# Hox genes
HoxA	7	11
HoxB	17	10
HoxC	12	9
HoxD	2	9

doi:10.1038/sj.hdy.6800872

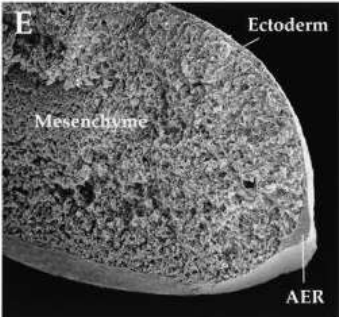
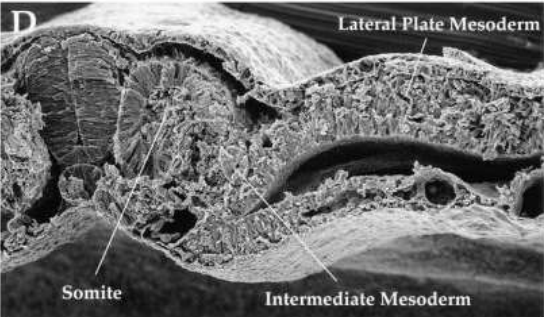


# Microenvironment controls embryonic organogenesis

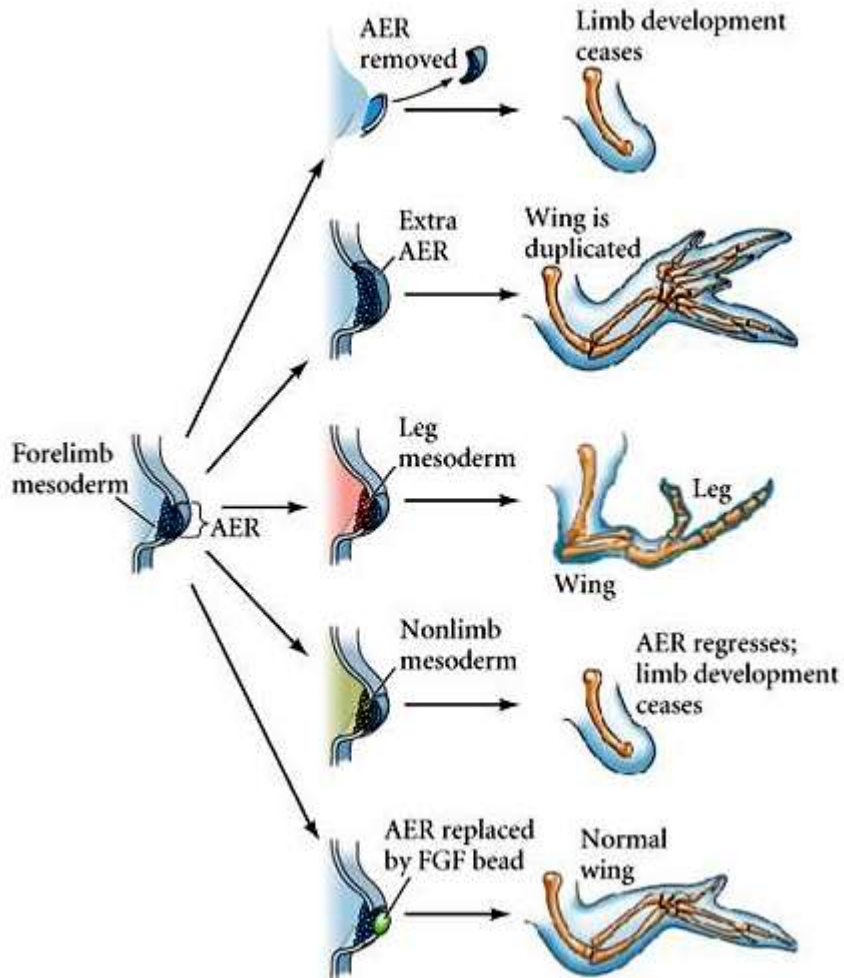
## Apical ectodermal ridge (AER)



## Zone of polarizing activity (ZPA)

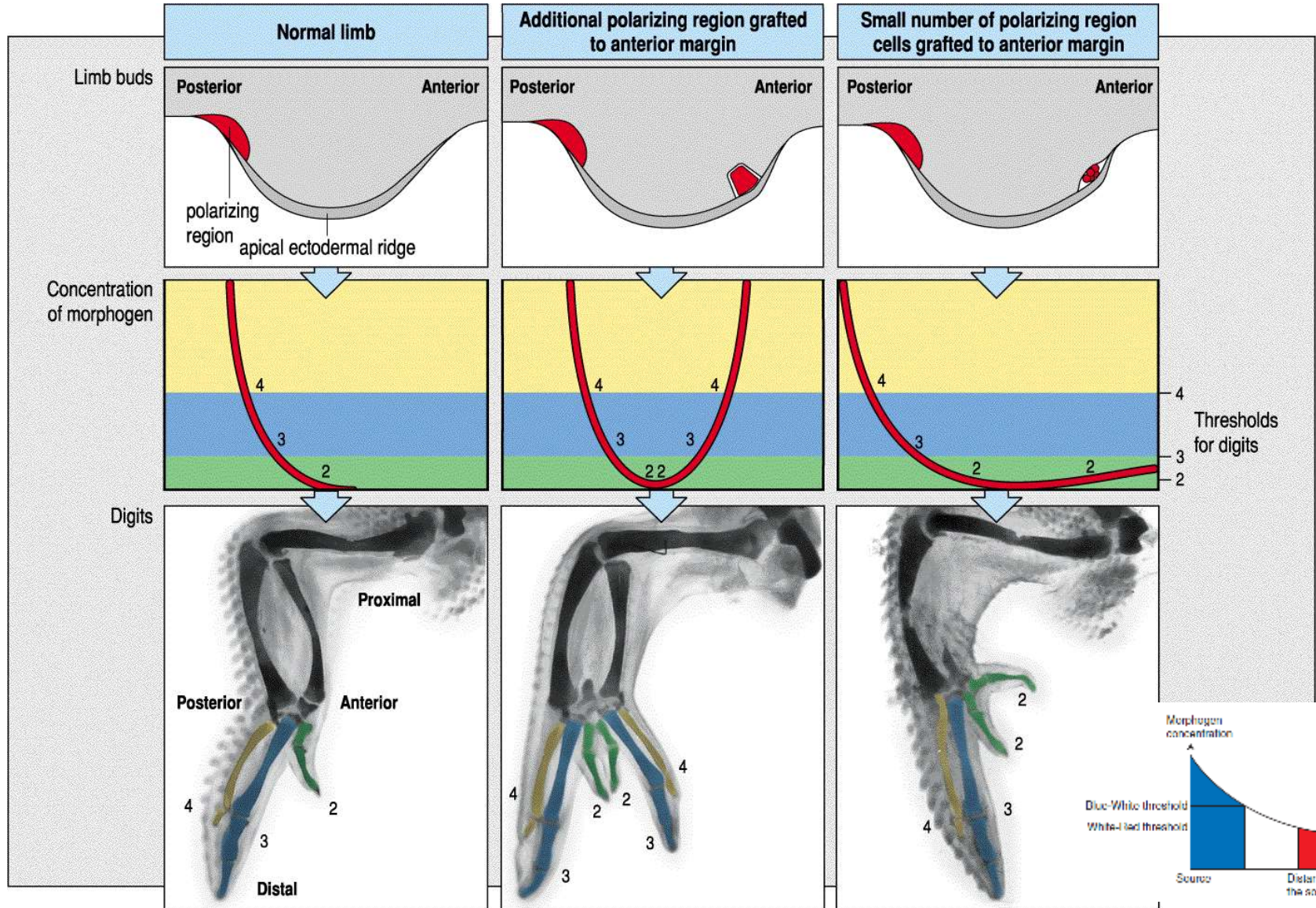


# Manipulation with AER changes the instructions for limb development



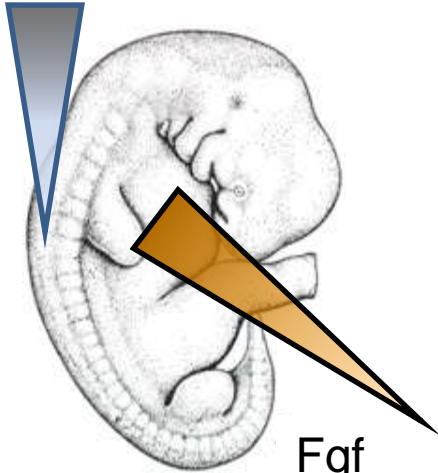


# Gradients of morphogenes from AER and ZPA defines limb formation

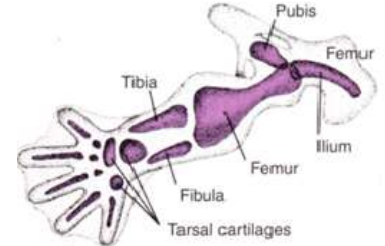
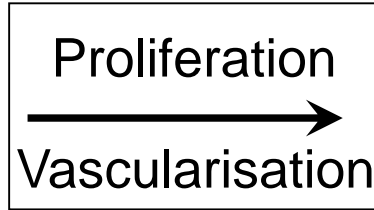
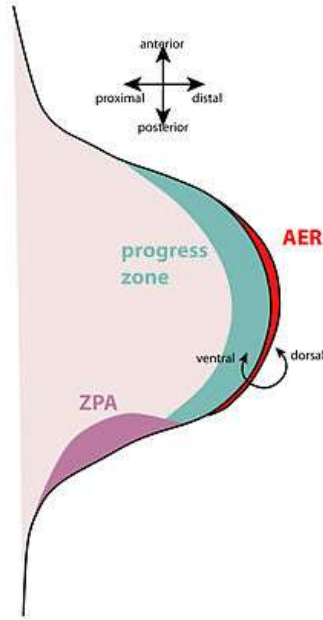


# Thalidomid

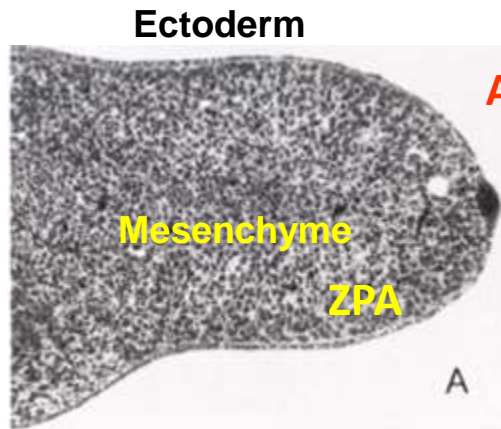
HOX



Fgf  
Shh  
...



T  
**Thalidomid**

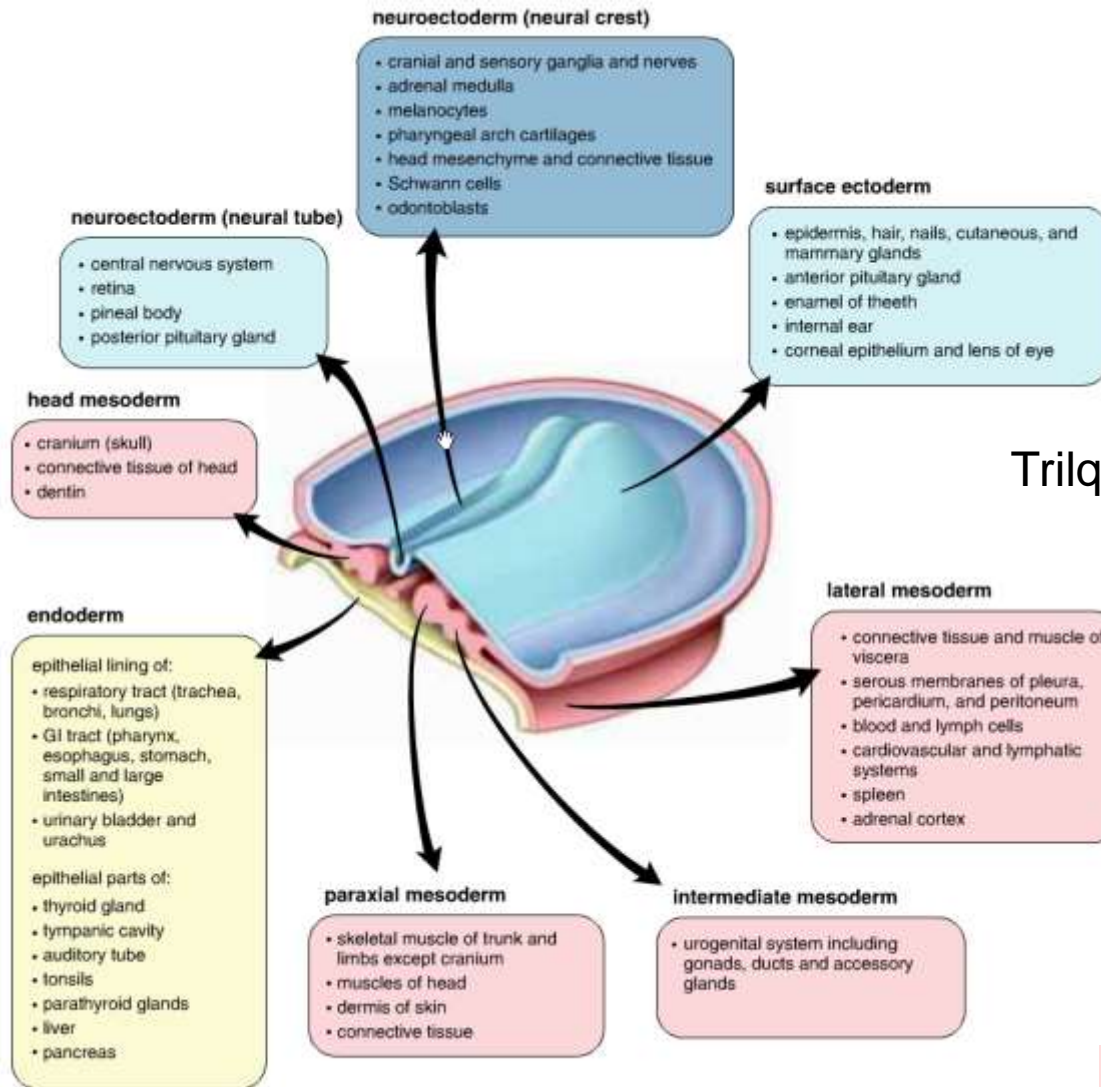


AER



# Histogenesis and organogenesis

## Ectoderm



## Entoderm

## Mesoderm

# Embryonic development

## Ectoderm

### Surface ectoderm

- Epidermis, hair nails, cutaneous and mammary glands
- Corneal epithelium and lens of eye
- Enamel of teeth
- Internal ear
- Anterior pituitary gland
- Epithelium of oral cavity and part of anal canal

### Neuroectoderm

- **Neural tube** and derivatives
  - CNS
  - Retina
  - Posterior pituitary gland
  - Pineal body
- **Neural crest** and derivatives:
  - Cranial and sensory ganglia and nerves
  - Schwann cells
  - adrenal medulla
  - Enteroendocrine cells
  - Melanocytes
  - Head mesenchyme and connective tissue
  - Odontoblasts

## Mesoderm

### head

- Connective tissue of head
- Cranium, dentin

### Paraxial

- Skeletal muscle of trunk and limbs except cranium
- Dermis of skin
- Muscles of head

### Intermediate

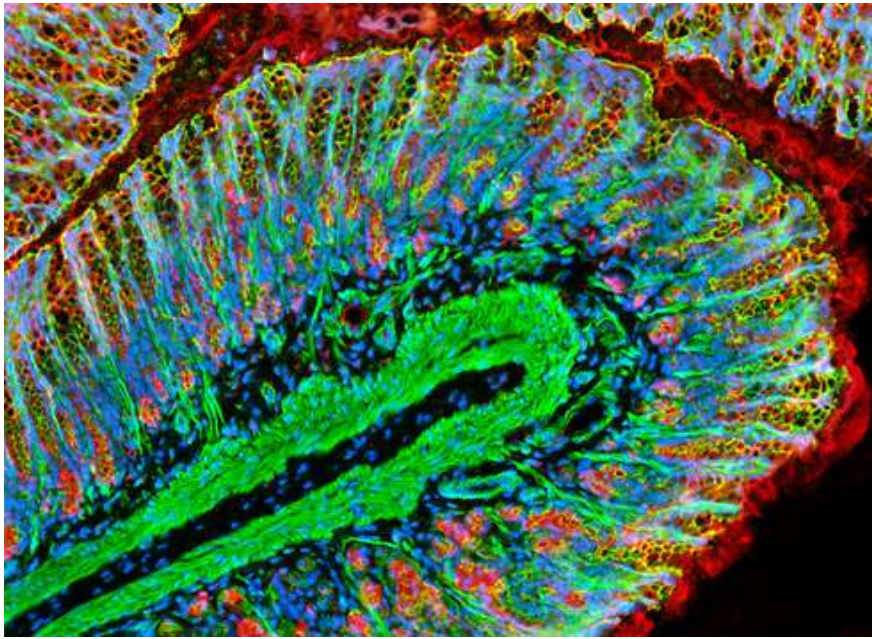
- Urogenital system + ducts, glands and gonads

### Lateral

- Visceral muscle and connective tissue
- Serous membranes of pleura, peritoneum and pericardium
- Blood cells, leukocytes
- Cardiovascular and lymphatic system
- Spleen
- Adrenal cortex

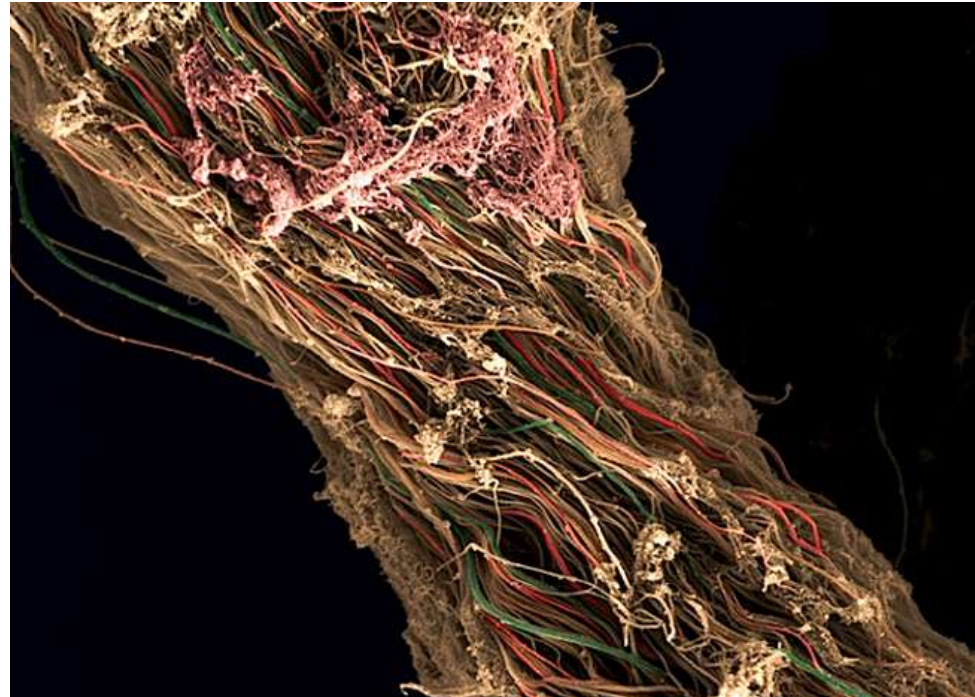
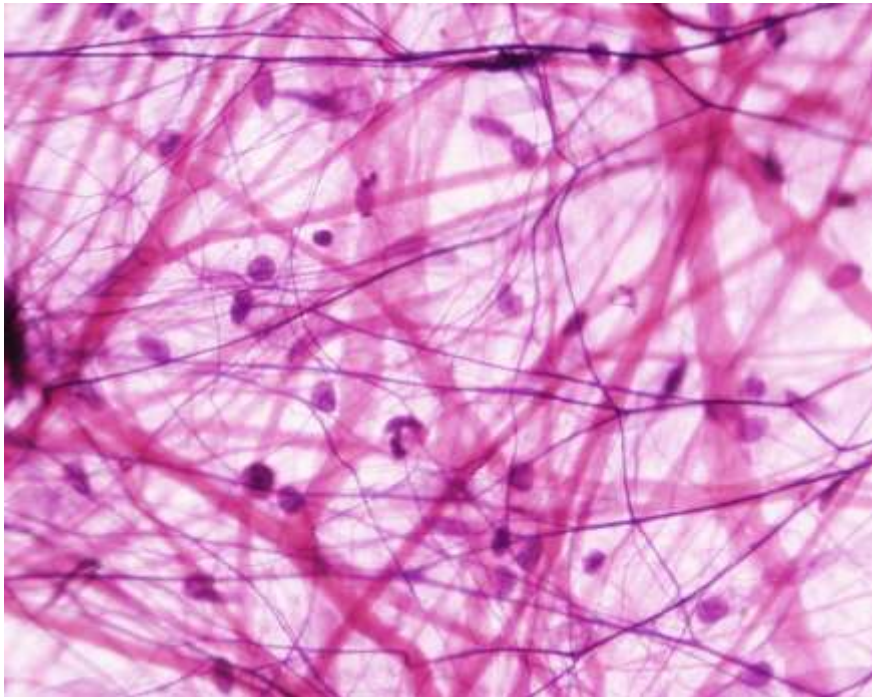
## Endoderm

- GIT epithelium except oral cavity and part of anal canal
- Extramural glands of GIT
- Epithelium of bladder
- Epithelium of respiratory system
- Thyroid gland, parathyroid glands, thymus
- Tonsils
- Epithelium of cavum tympani and Eustachian tube



## 6. Connective tissue

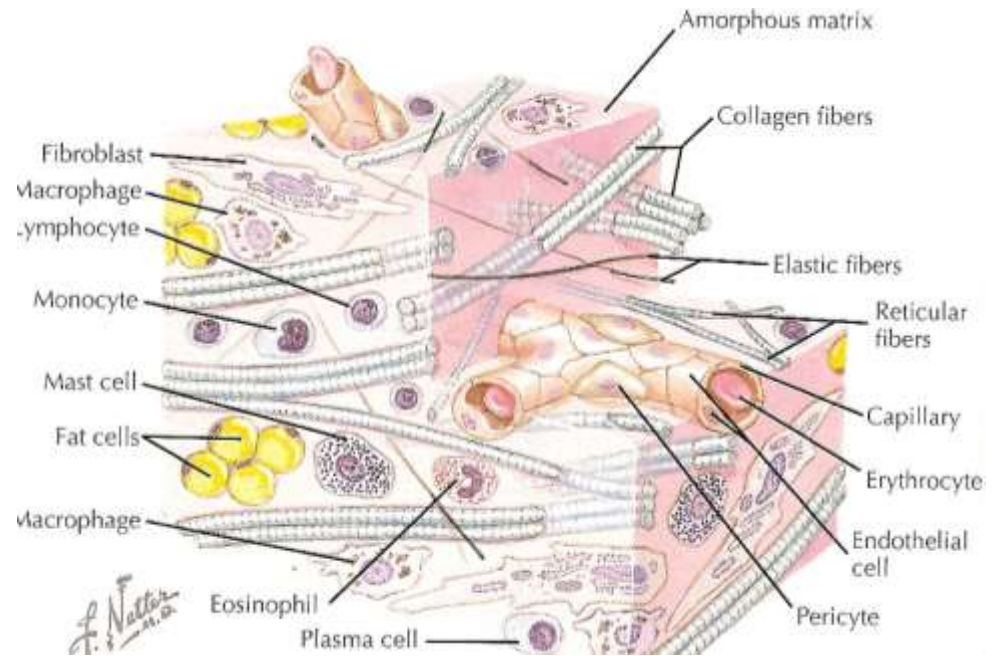
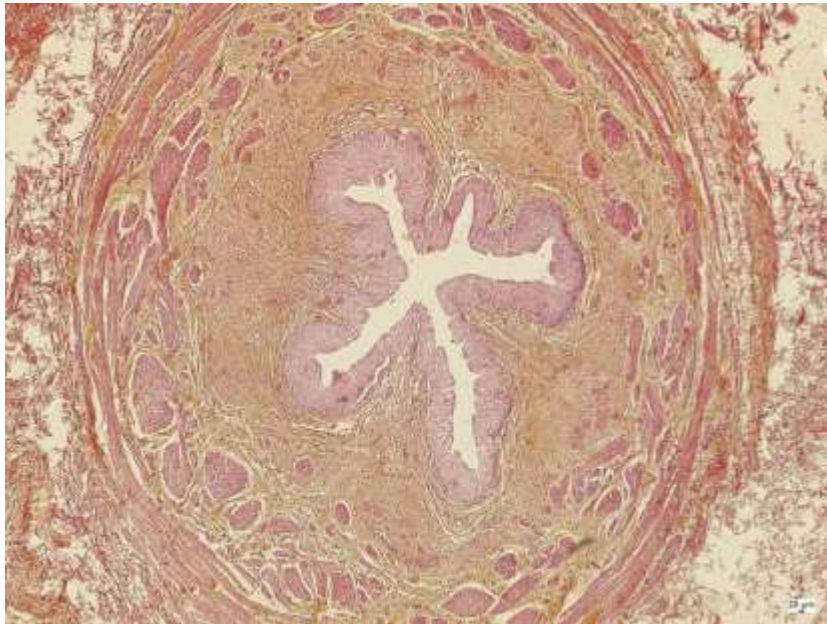
*Not only a tissue glue...*



# ■ Connective tissue

## Mechanical and biological properties

→ surrounds other tissues, compartmentalization, support, physico-chemical environment, immunological support, storage



# ■ General composition of connective tissue (CT)

## Cells and extracellular matrix

- **Cells**

**Connective tissue** – permanent and transient cell populations (fibroblasts/myofibroblasts, immune cells, adipocytes, adult stem cells)

**Cartilage** – chondroblasts/chondrocytes

**Bone** – osteoblasts/osteocytes/osteoclasts

- **Matrix** – fibrous and amorphous

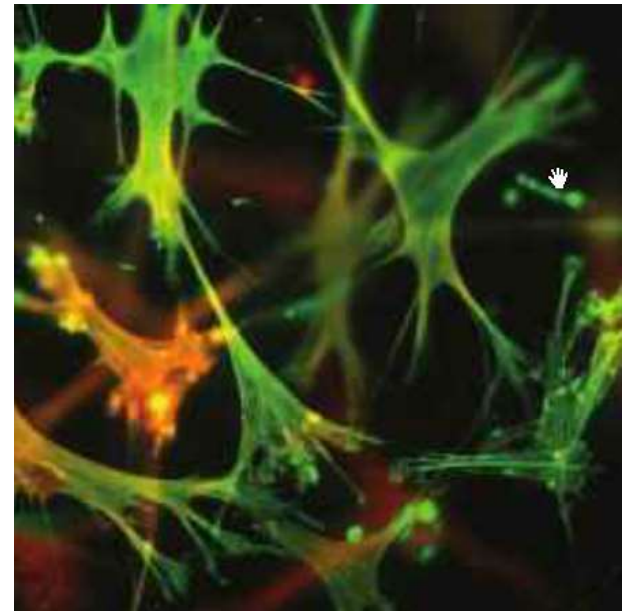
### **Fibrous component**

- collagen
- reticular
- elastic

### **Amorphous component** (amorphous ground substance)

- Complex matrix consisting of glycosaminoglycans, glycoproteins and proteoglycans,

depending on tissue type (connective × ligament × cartilage × bone)



# ■ Classification of CT

## Embryonic CT

- Mesenchyme
- Jelly-like CT (Wharton jelly, dental pulp, stroma of iris)

## Adult CT

- Areolar (loose, interstitial) CT
- Dense collagen irregular CT

- Dense collagen regular CT
- Fat (adipose tissue)
- Cartilage
- Bone

- Blood and hematopoietic tissue
- Lymphatic tissue

} CT

} Specialized CT

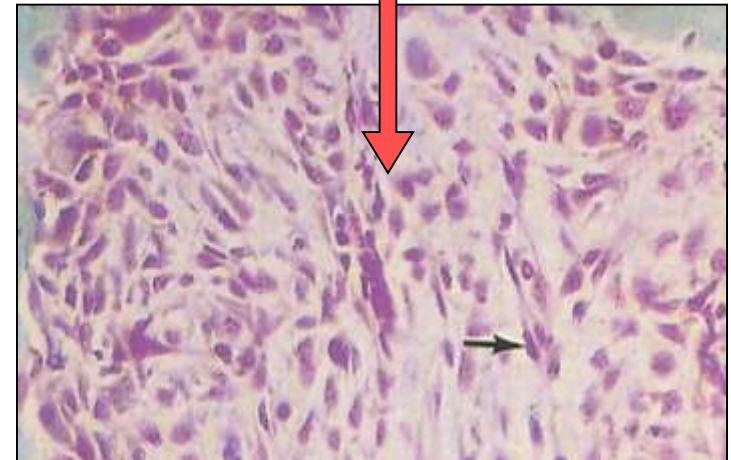
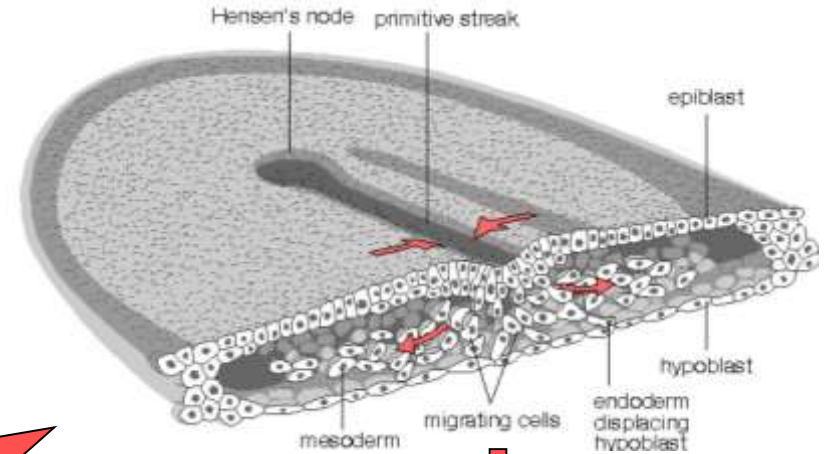
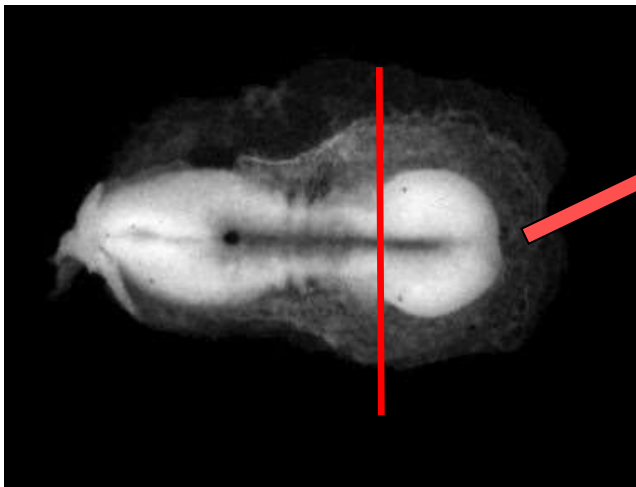
} Trophic CT (body liquids)



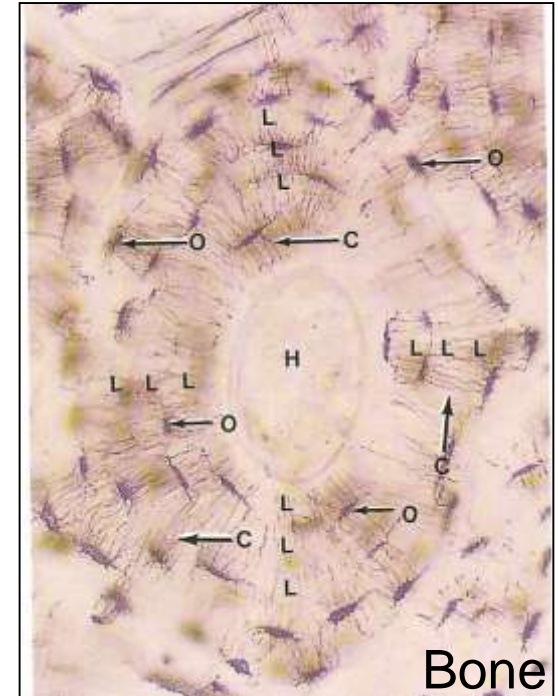
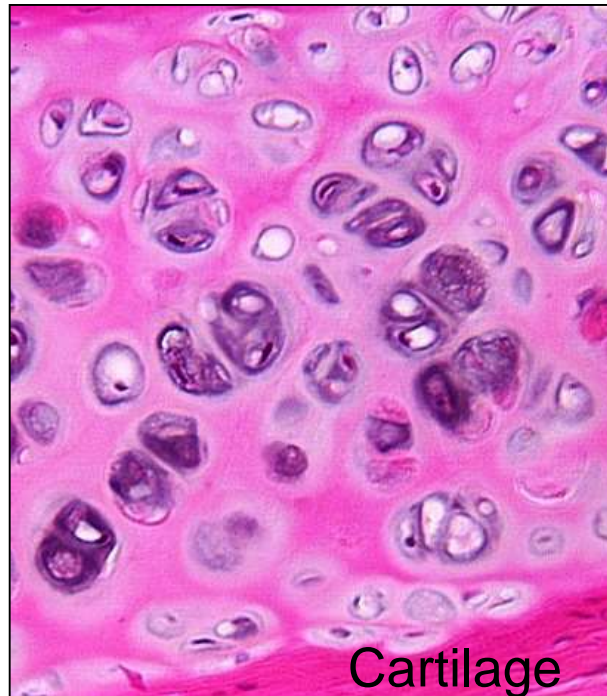
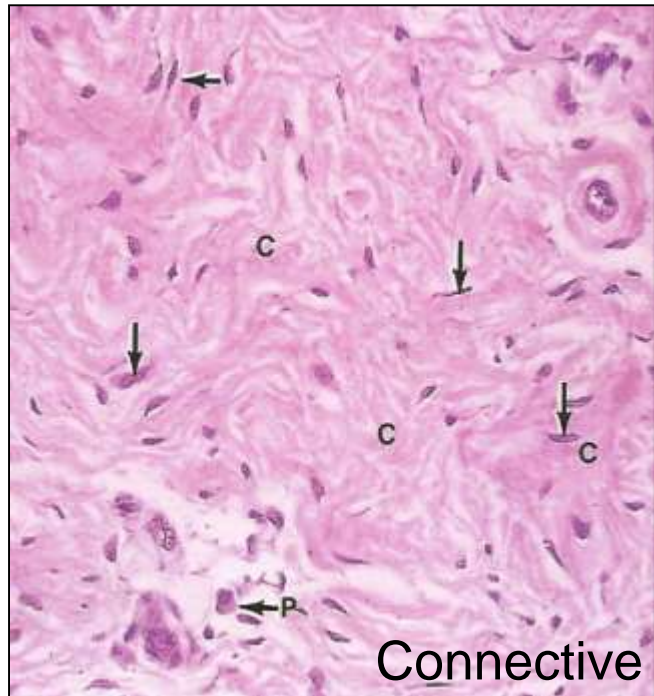
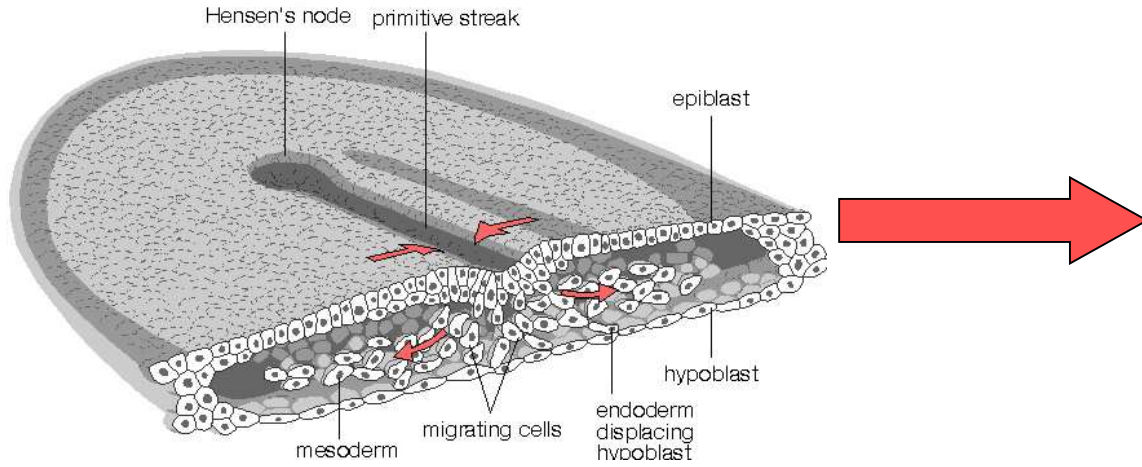
# ■ Embryonic origin of CT

- Mesenchyme = loose tissue between germ layers
- Complex network of star- or spindle-shaped cells
- Jelly-like amorphous ground substance

Week 3 of embryonic development



# Basic derivatives of CT



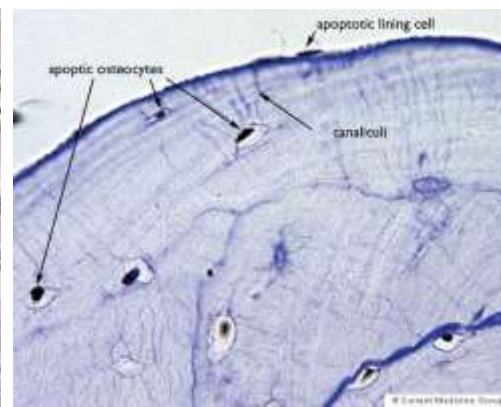
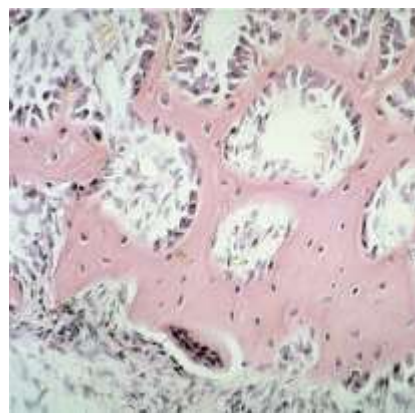
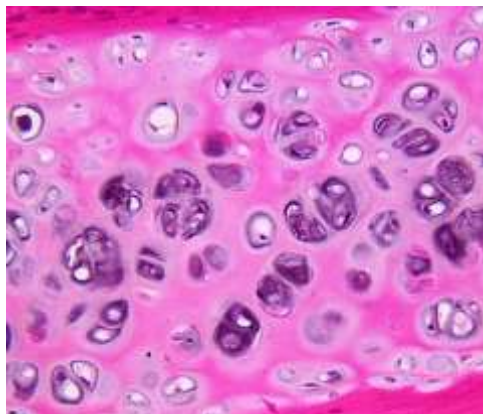
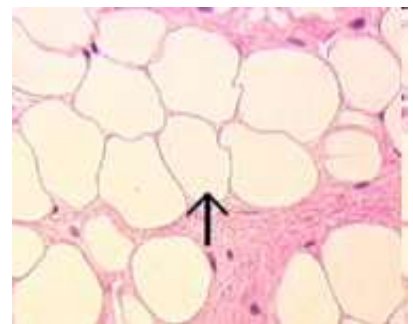
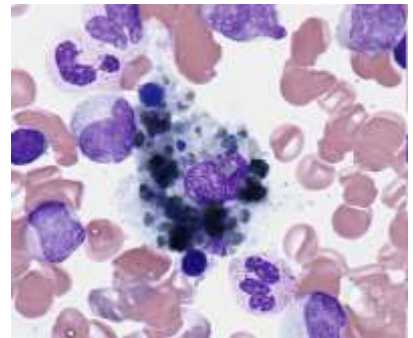
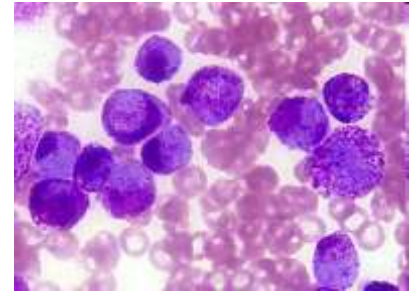
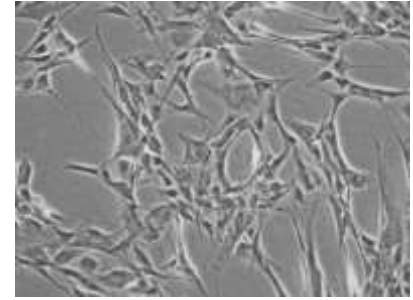
# ■ Cells of connective tissue

## Cells

- Fibroblasts/fibrocytes/myofibroblasts
- Heparinocytes
- Macrophages of CT = histiocytes
- Plasma cells
- Lymphocytes
- Adipocytes
- Adult stem cells

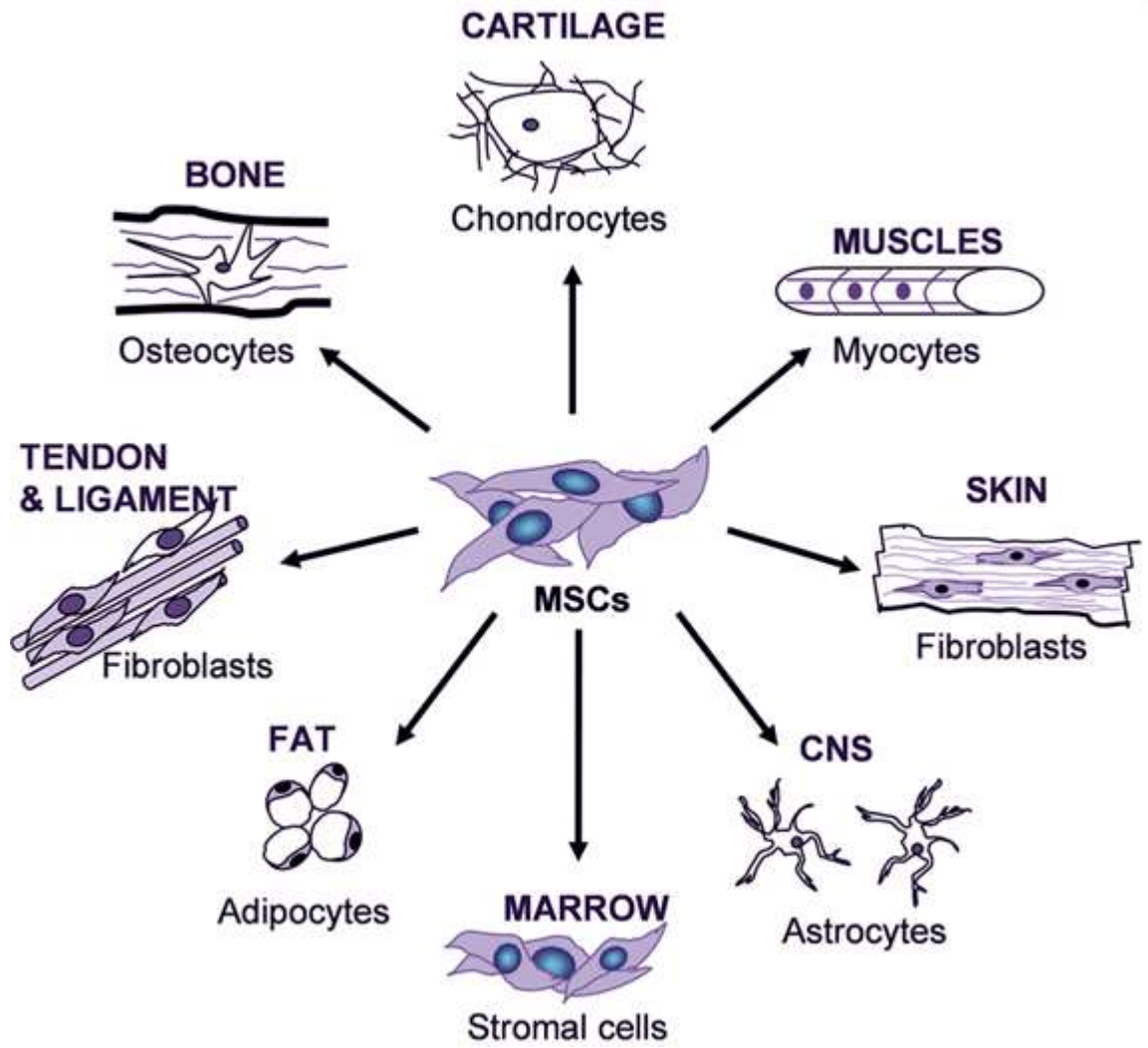
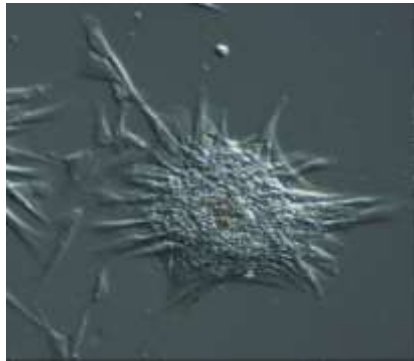
## Extracellular matrix

- Fibrous compound
- Amorphous ground substance



# Cells of connective tissue

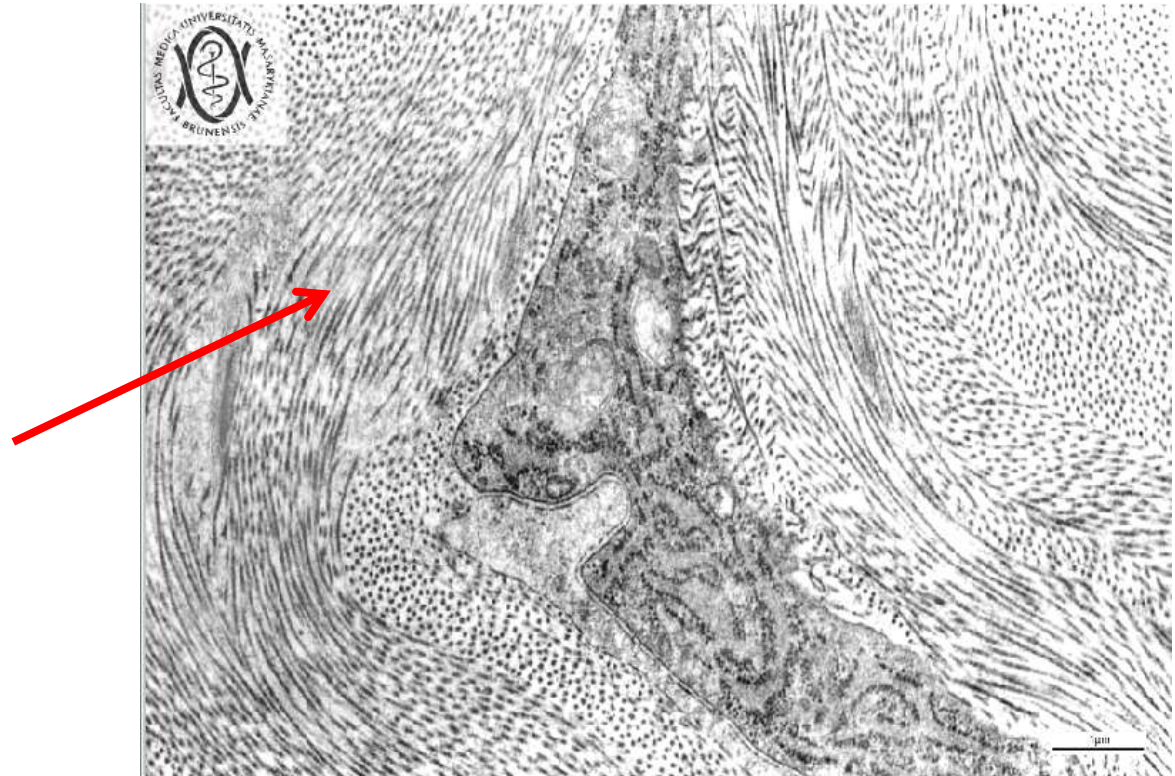
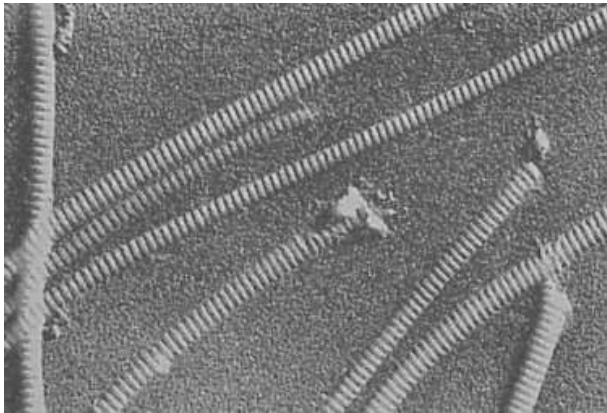
Mesenchymal (adult) stem cells



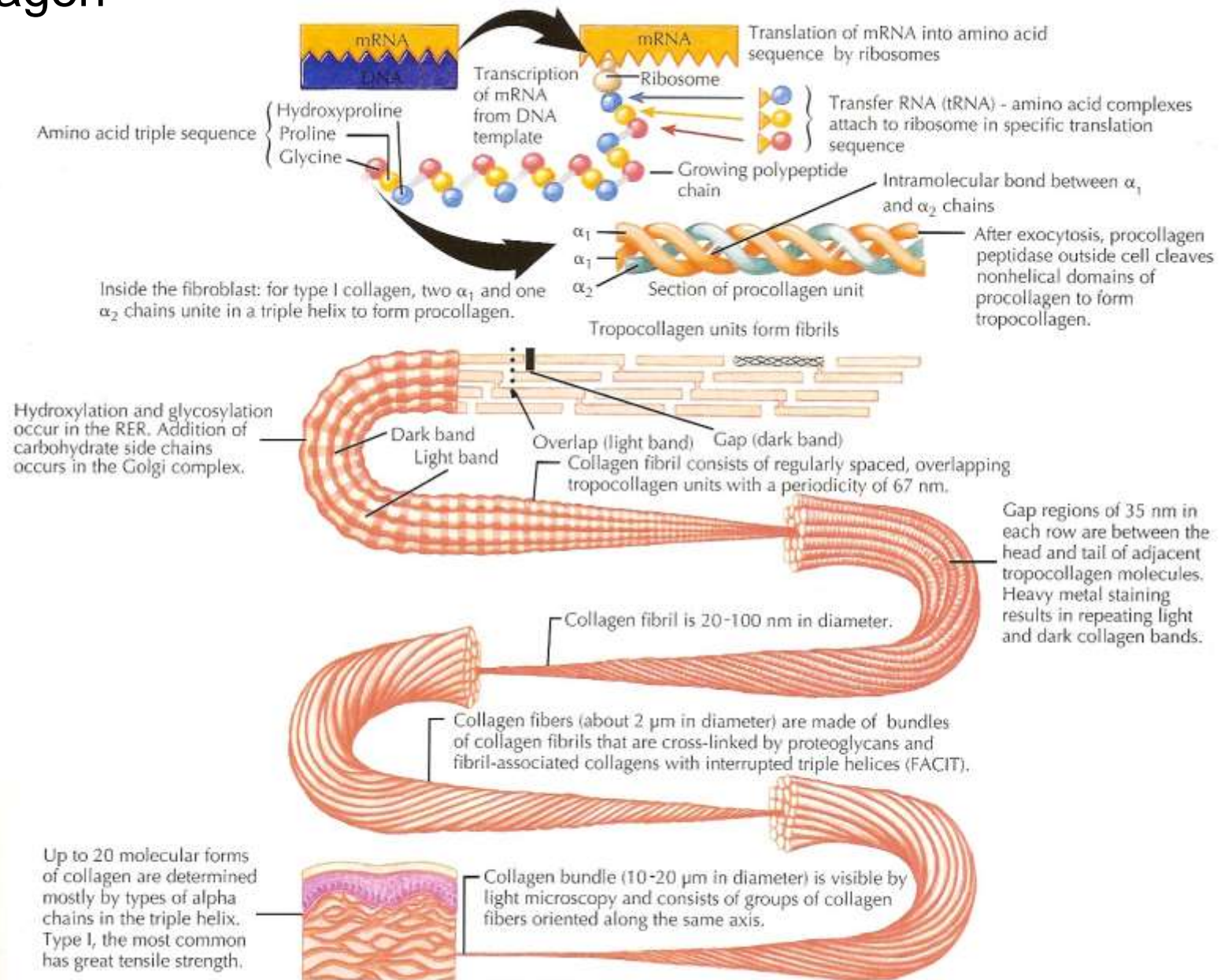
# ■ Extracellular matrix – fibrous component

## Collagen fibers

- family of fibrous proteins encoded by >35 genes (2013)
- polymer – subunit = tropocollagen; triple helix
- different structural and mechanical properties (strength, elasticity, pliability...)
- most abundant protein in human body ( 30% dry weight)



# Collagen



# ■ Collagen

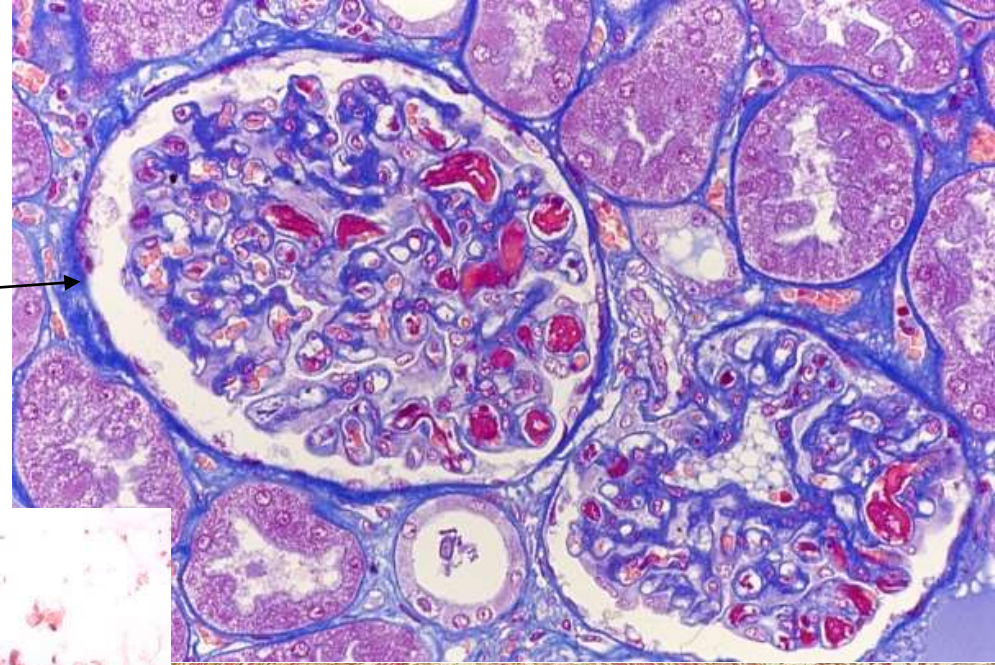
Type	Localization	Structure	Main function
I	Bone, tendons, meniscus, dentin, dermis, capsules of organs, loose CT 90% of type I	Fibrils (75nm) – fibers (1-20µm)	Resilience in pull
II	Hyaline and elastic cartilage	Fibrils (20nm)	Resilience in pressure
III	Skin, veins, smooth muscles, uterus, liver, spleen, kidney, lung	Like I, high content of proteoglycans and glycoproteins, reticular network	Shape formation
IV	Basal lamina of epithelium and endothelium, basal membranes	No fibrils or fibers	Mechanical support
V	Lamina of muscle cells and adipocytes, fetal membranes	Like IV	
VI	Interstitial tissue, chondrocytes – adhesion		Connecting dermis and epidermis
VII	Basal membrane of epithelium		
VIII	Some endothelia (Cornea)		
X	Growth plate, mineralized cartilage		Growth of bones, mineralization

■ Collagen in LM

HE

HES

AZAN





**Julian Voss-Andreae**  
**"Unraveling**  
**Collagen",**

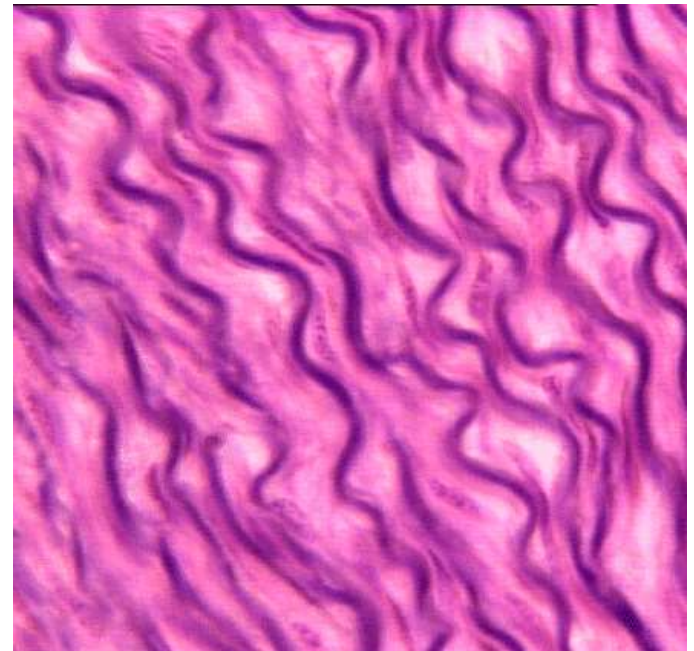
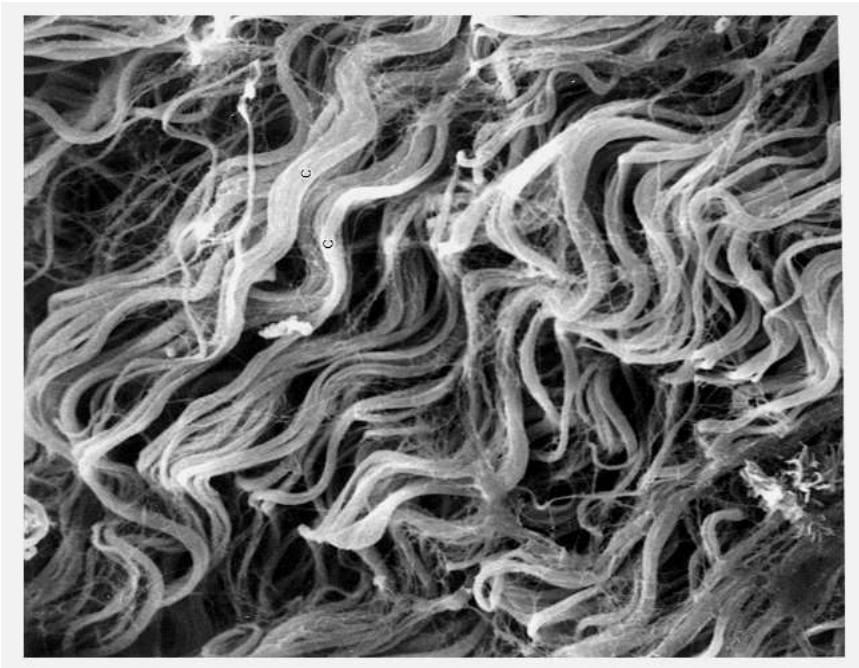
**2005**

Orange Memorial Park  
Sculpture Garden, City of  
South San Francisco, CA



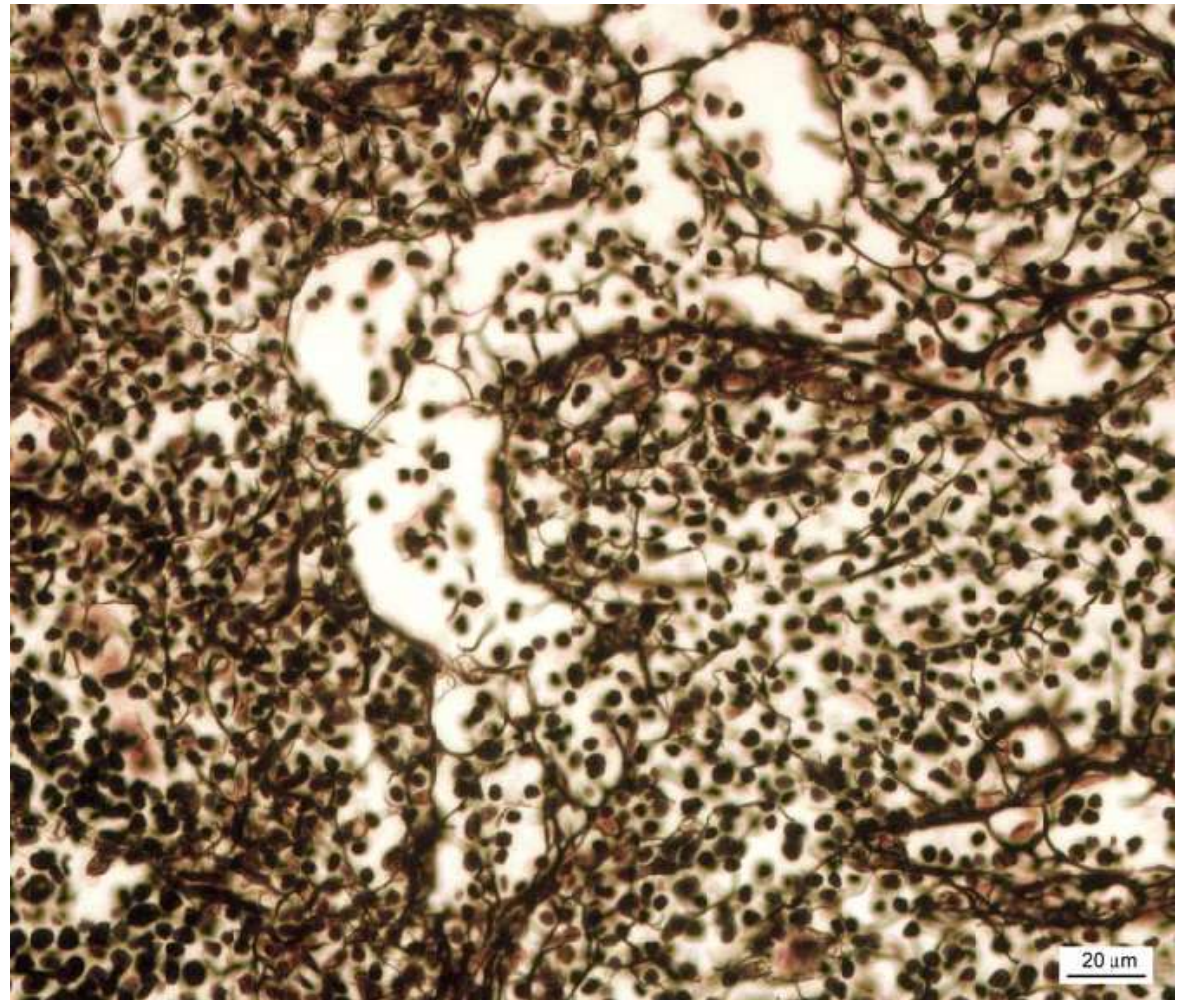
## ■ Elastic fibers

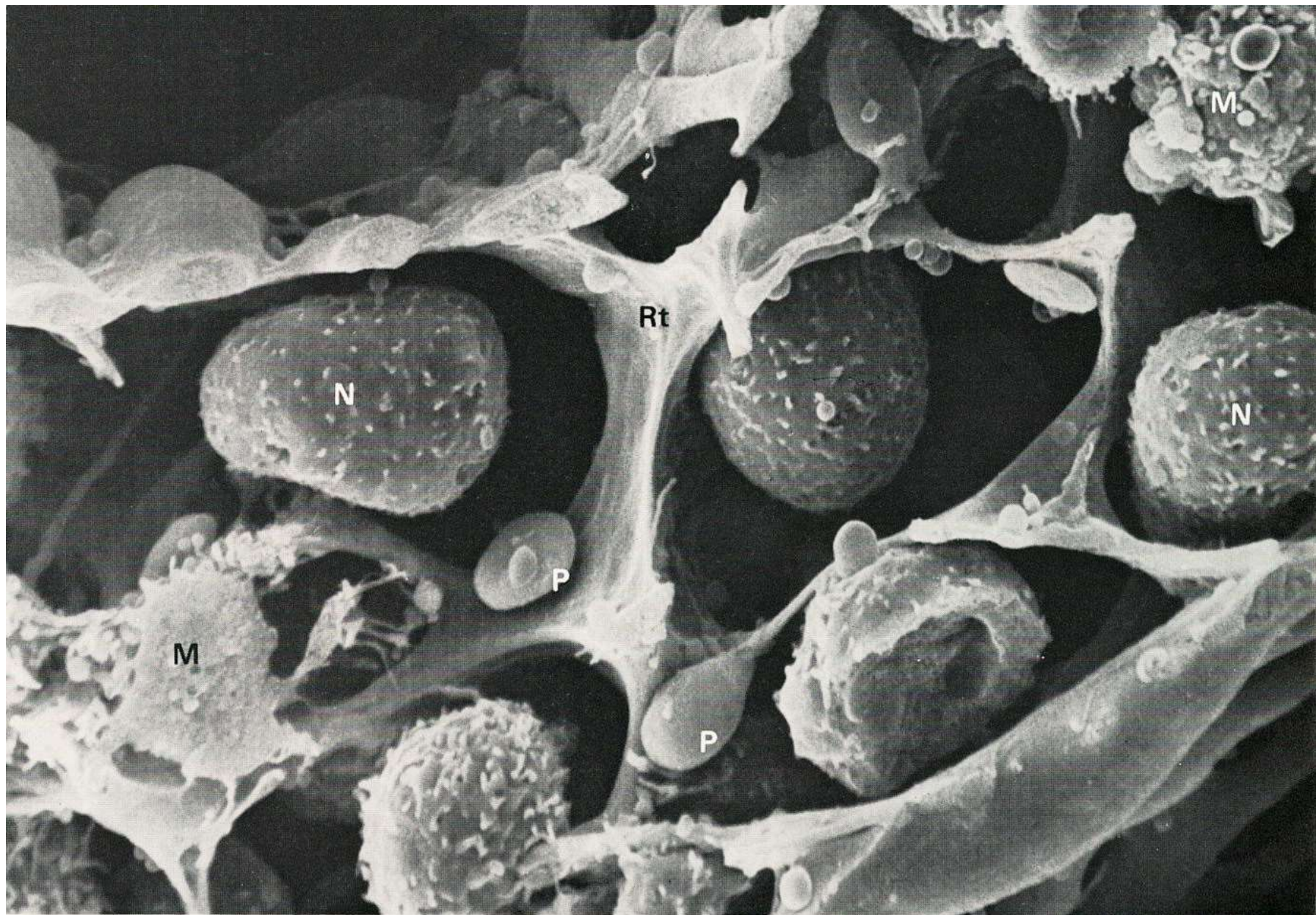
- less abundant than collagen
- polymer – tropoelastin
- minimal tensile resistance, loss of elasticity if overstretched
- reduction of hysteresis = allow return back to original state after mechanic change



## ■ Reticular fibers

- collagen 3D meshwork
- bone marrow, spleen, lymphatic nodules
- microenvironment for e.g. hematopoietic stem cells and progenitors

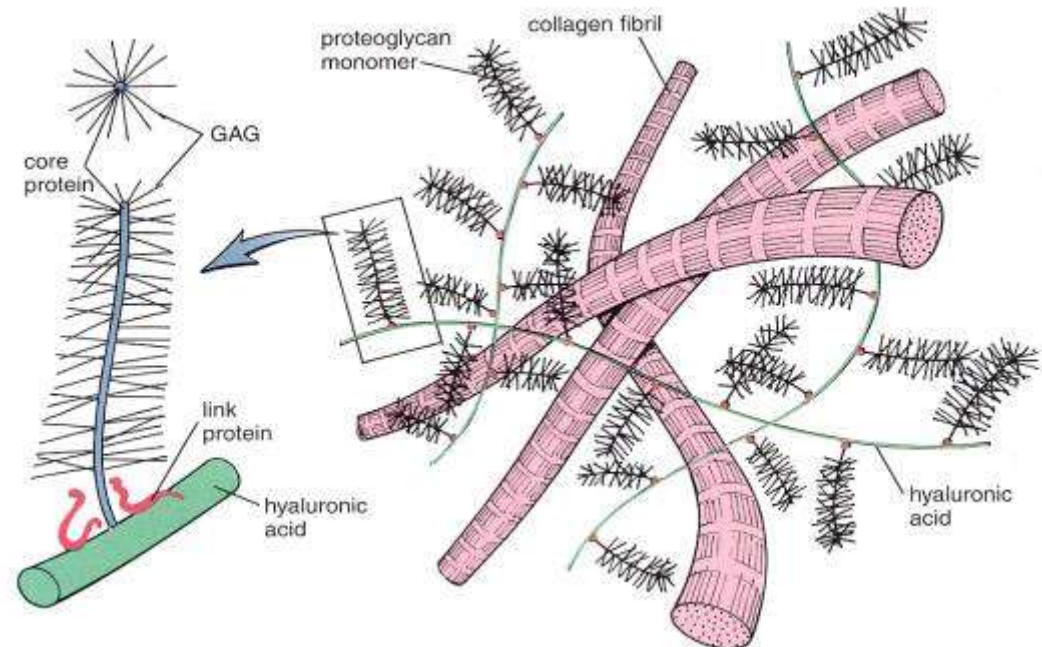
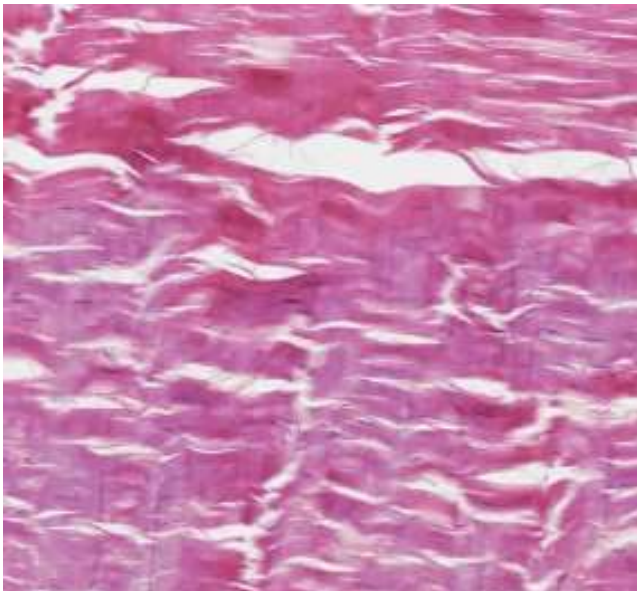




# ■ Extracellular matrix – ground matrix

Amorphous extracellular matrix

Colorless, transparent, homogenous substance consisting of glycosaminglycans, proteoglycans and structural glycoproteins



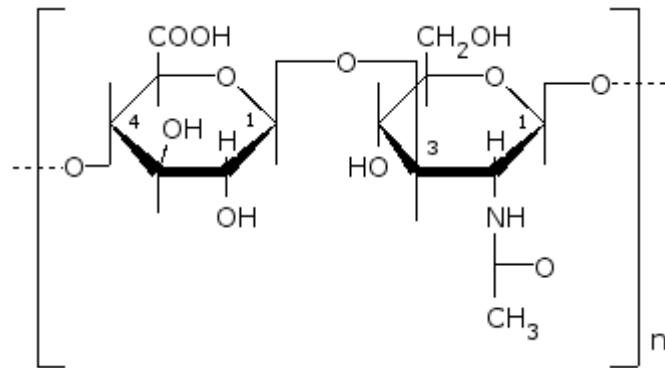
# ■ Glycosaminoglycans

linear polysaccharides composed of two disaccharide subunits

– **uronic acid and hexosamine**

polysaccharides rich in hexosamines = acid mukopolysaccharides

glucuronic or iduronic acid



glucosamin or galactosamin

## ■ Glycosaminoglycans

They bind to protein structures (except for hyaluronic acid)

### **Glycosaminoglycan**

Hyaluronic acid

Chondroitinsulphate

Dermatansulphate

Heparansulphate

Keratansulphate

### **Localization**

Umbilical cord, synovial fluid, fluid of corpus vitreum, cartilage

Cartilage, bone, cornea, skin, notochord, aorta

Skin, ligaments, adventitia of aorta

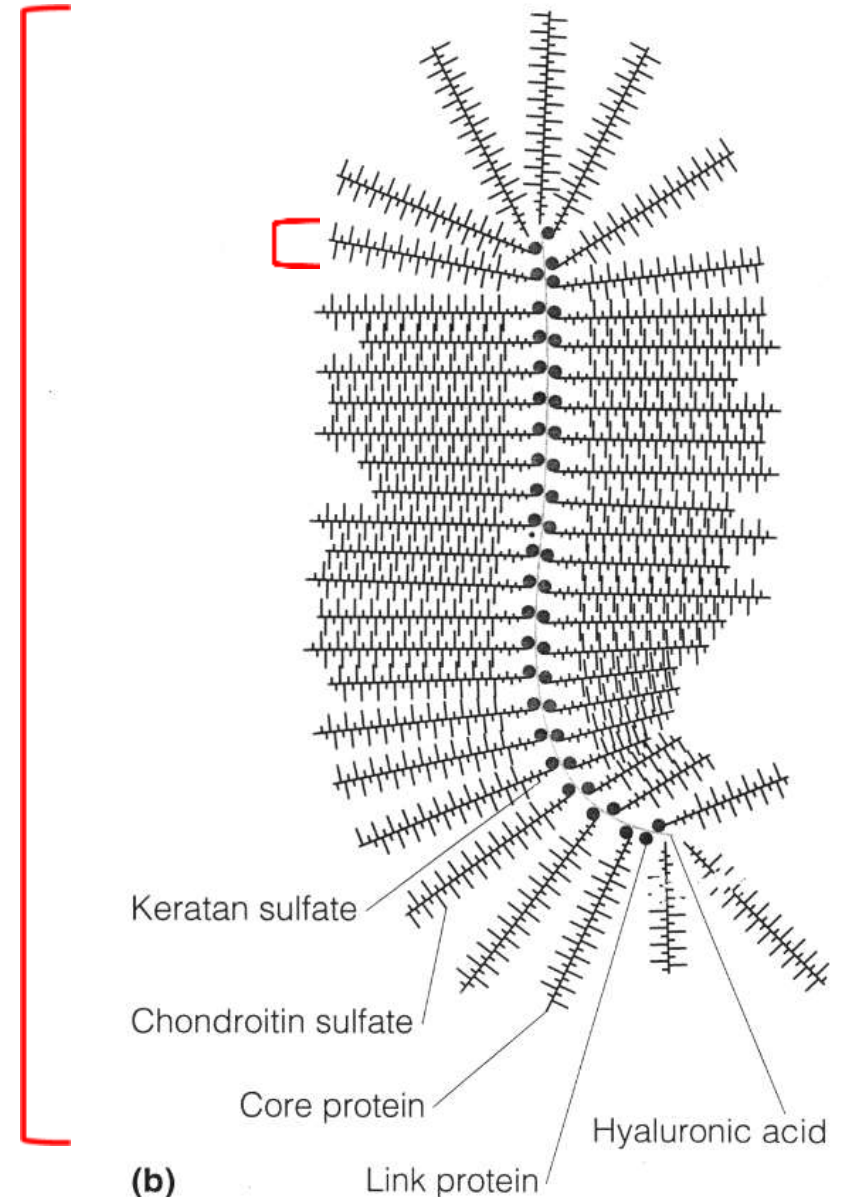
Aorta, lungs, liver, basal membranes

Iris, cartilage, nucleus pulposus, anulus fibrosus

# ■ Proteoglycans

- protein + dominant linear saccharide component
- proteoglycan aggregates
- water-binding, volume dependent of hydration
- aggrecan (cartilage)
- syndecan
- fibroglycan

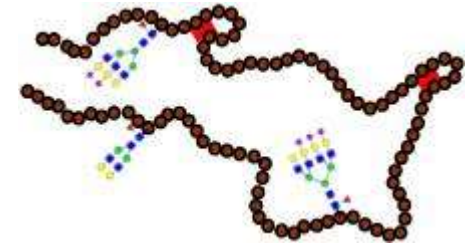
Figure 9.25b Proteoglycan structure in bovine cartilage



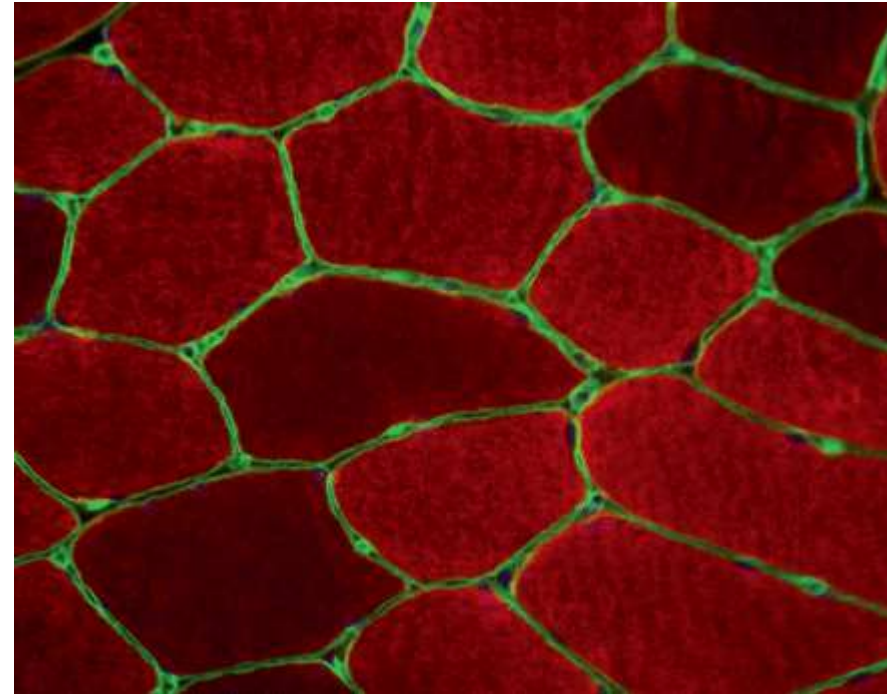


# ■ Structural glycoproteins

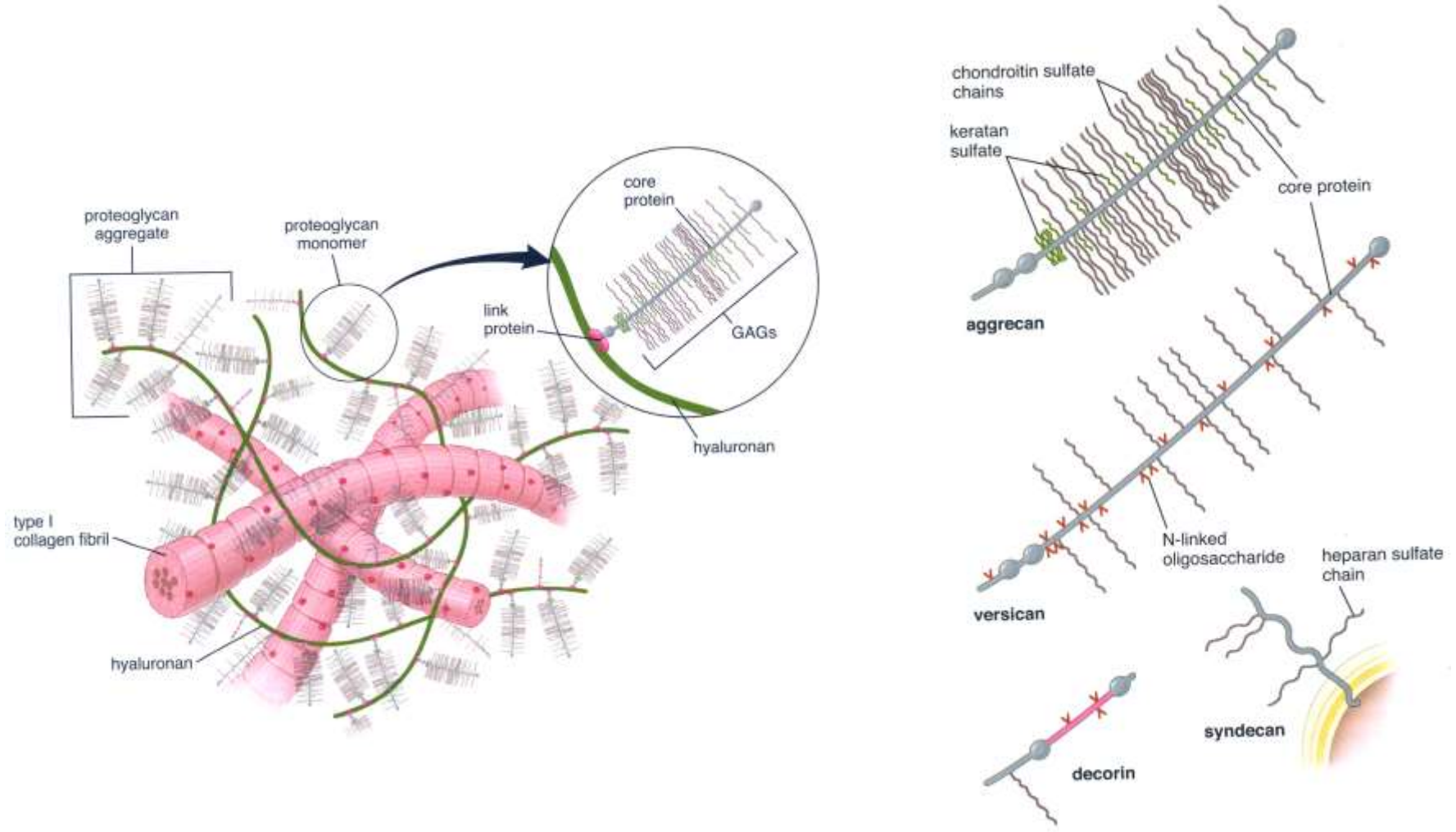
- dominant protein + branched saccharide component
- interaction between cells and ECM



- **fibronectin** – connects collagen fibers and glykosaminoglycans, cell adhesion and migration
- **laminin** – basal lamina – epithelial integrity
- **chondronectin** – cartilage – adhesion of chondrocytes to collagen



# ■ Composition of amorphous ground matrix

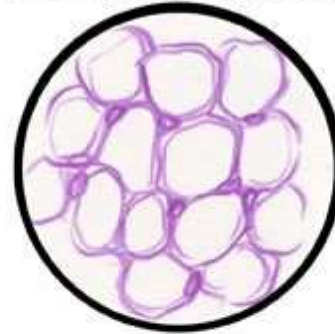


## ■ Classification of specialized connective tissue

**Dense  
Connective Tissue**



**Adipose Tissue  
(Connective Tissue)**



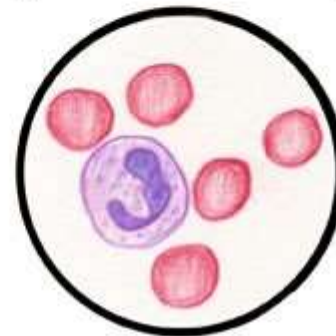
**Areolar Tissue  
(Connective Tissue)**



**Compact Bone  
(Connective Tissue)**

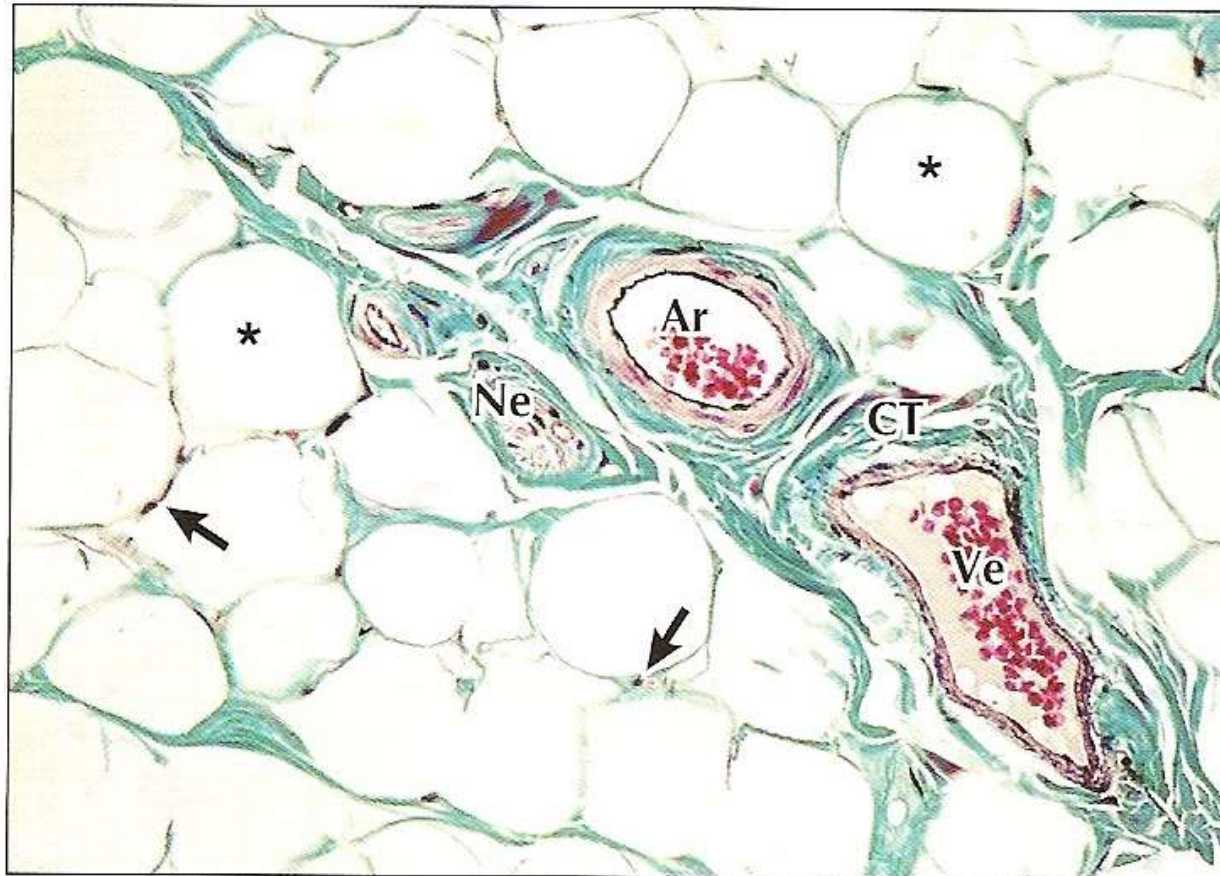


**Blood  
(Connective Tissue)**



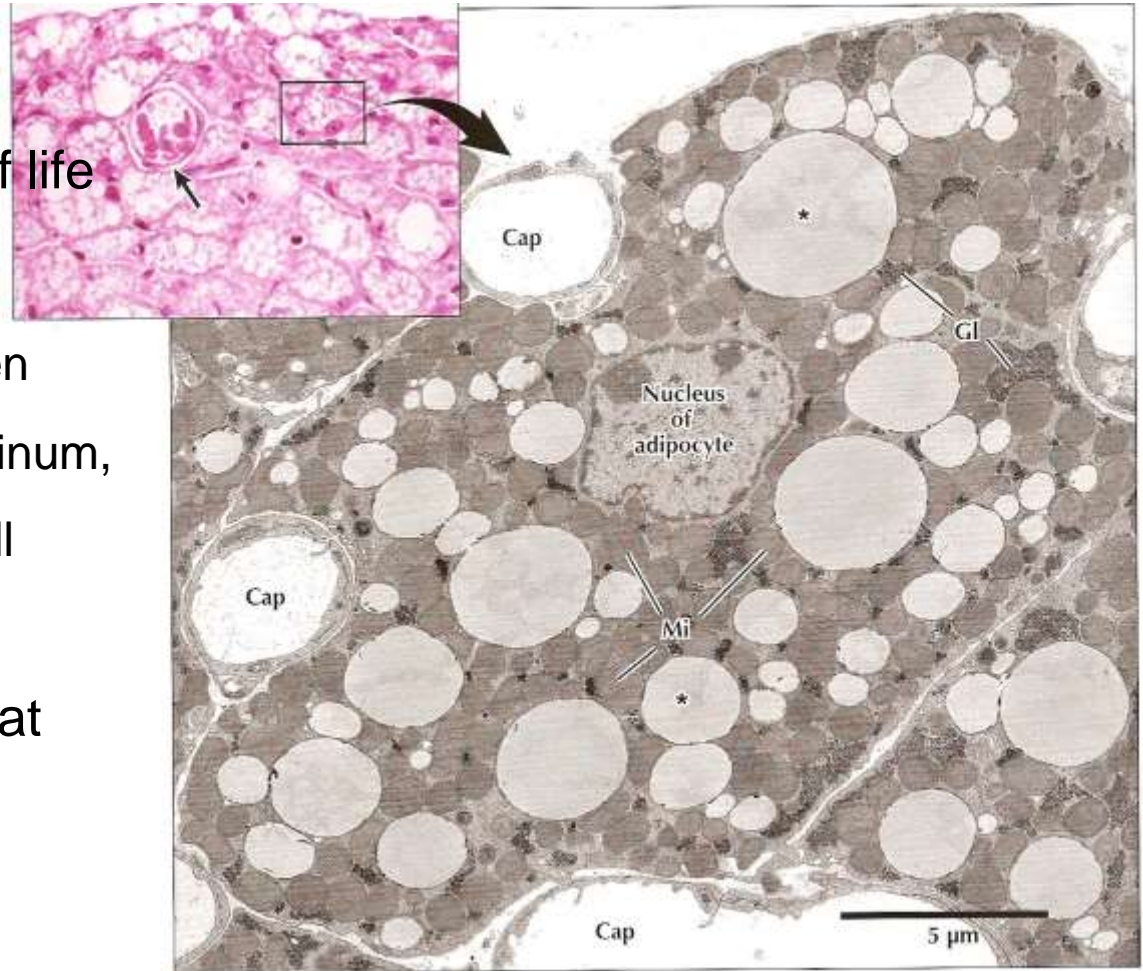
# ■ Adipose tissue

- Adipocytes, fibroblasts, reticular, collagen and elastic fibers, capillarie
- White and brown adipose tissue



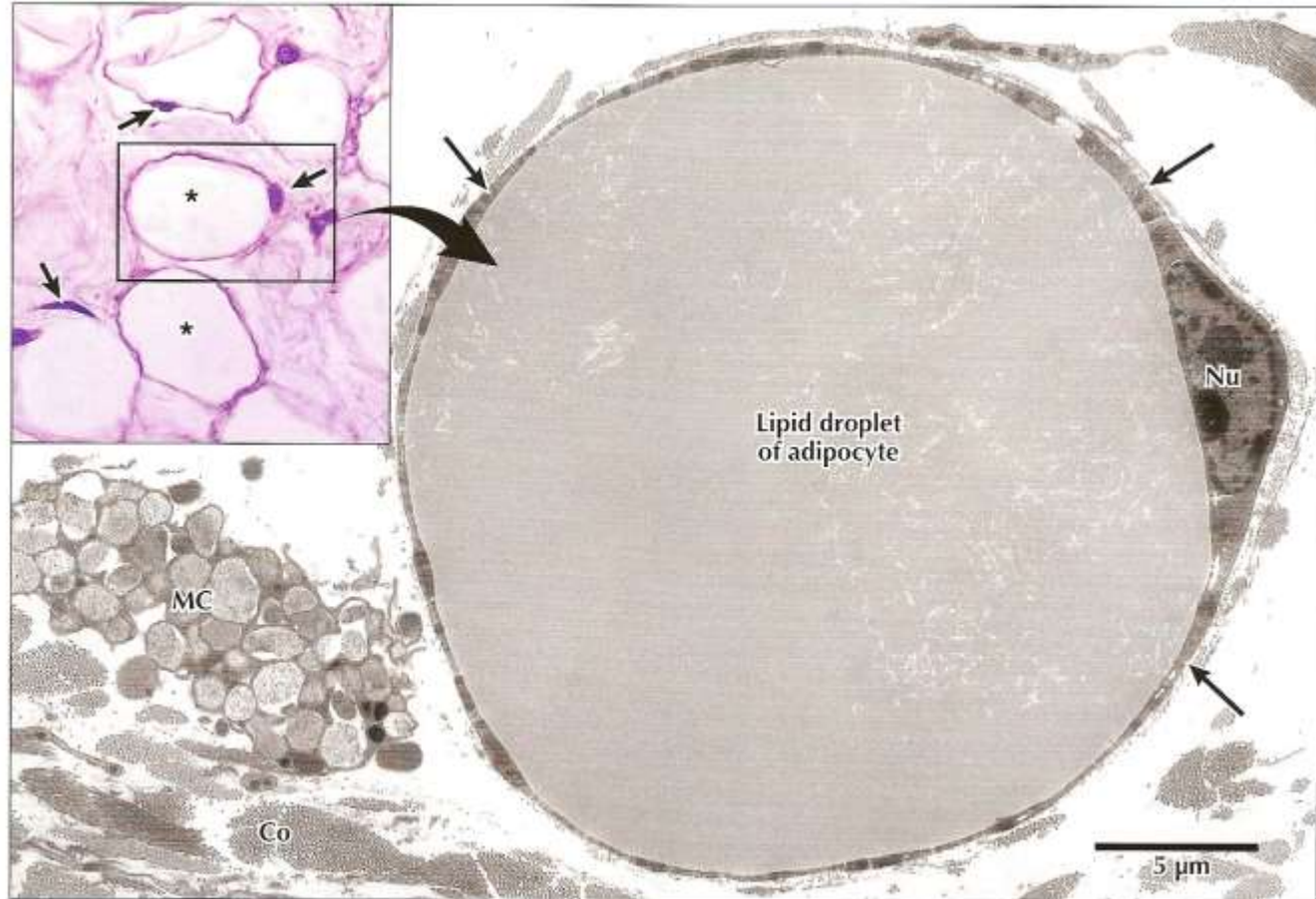
# ■ Brown adipose tissue

- fetus and child to 1<sup>st</sup> year of life
- fast source of energy
- typical localization – between shoulder blades, axilla, mediastinum, around kidneys, pancreas, small intestine
- small cells with numerous fat droplets

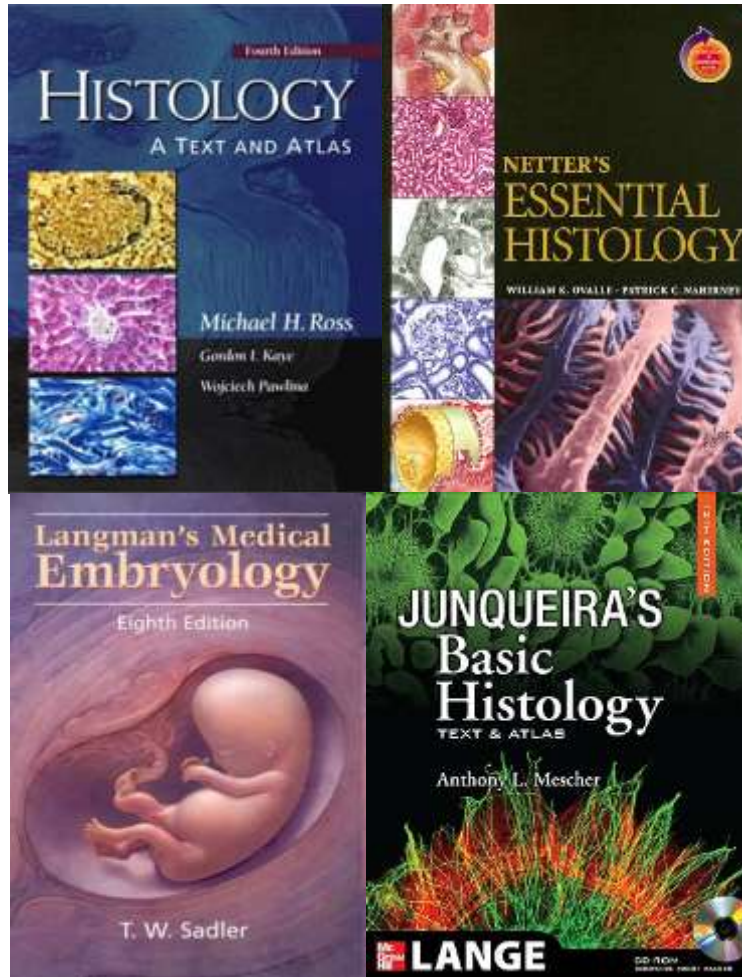


# White adipose tissue

- adipocytes are actively form until 2nd year of life
- no innervations, but rich vascularisation
- adipocytes with only one lipid droplet
- leptin (adipokinins)

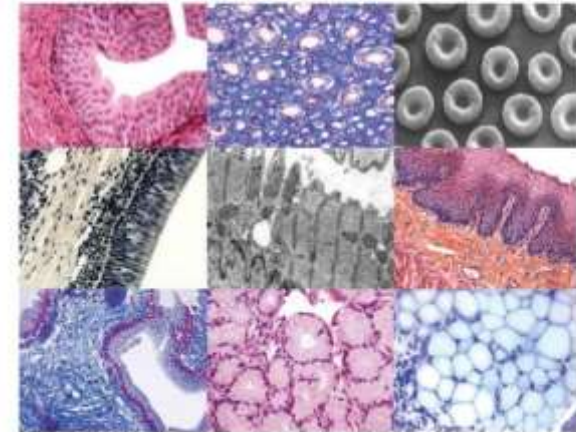


# ■ Further study



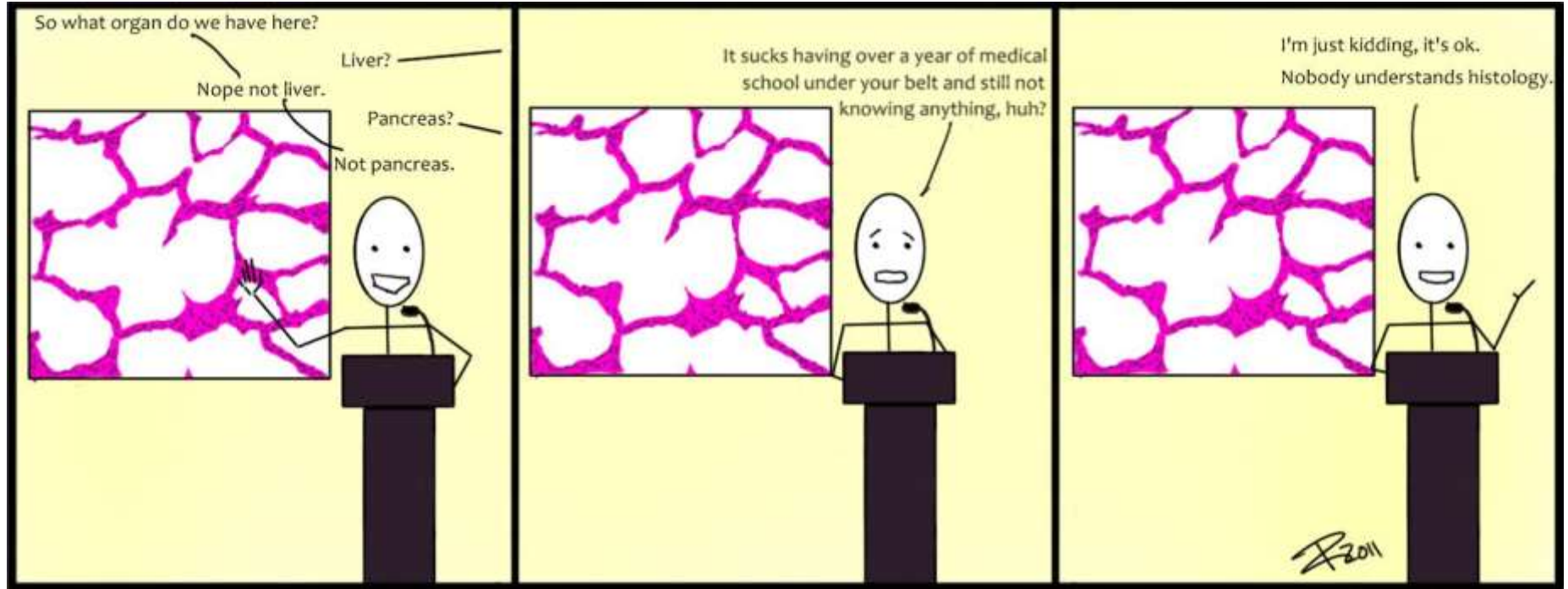
## Guide to General Histology and Microscopic Anatomy

Petr Vaňhara, Miroslava Sedláčková,  
Irena Lauschová, Svatopluk Čech, Aleš Hampel



Masaryk University, Brno 2017

<http://www.med.muni.cz/histology>



Thank you for attention

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