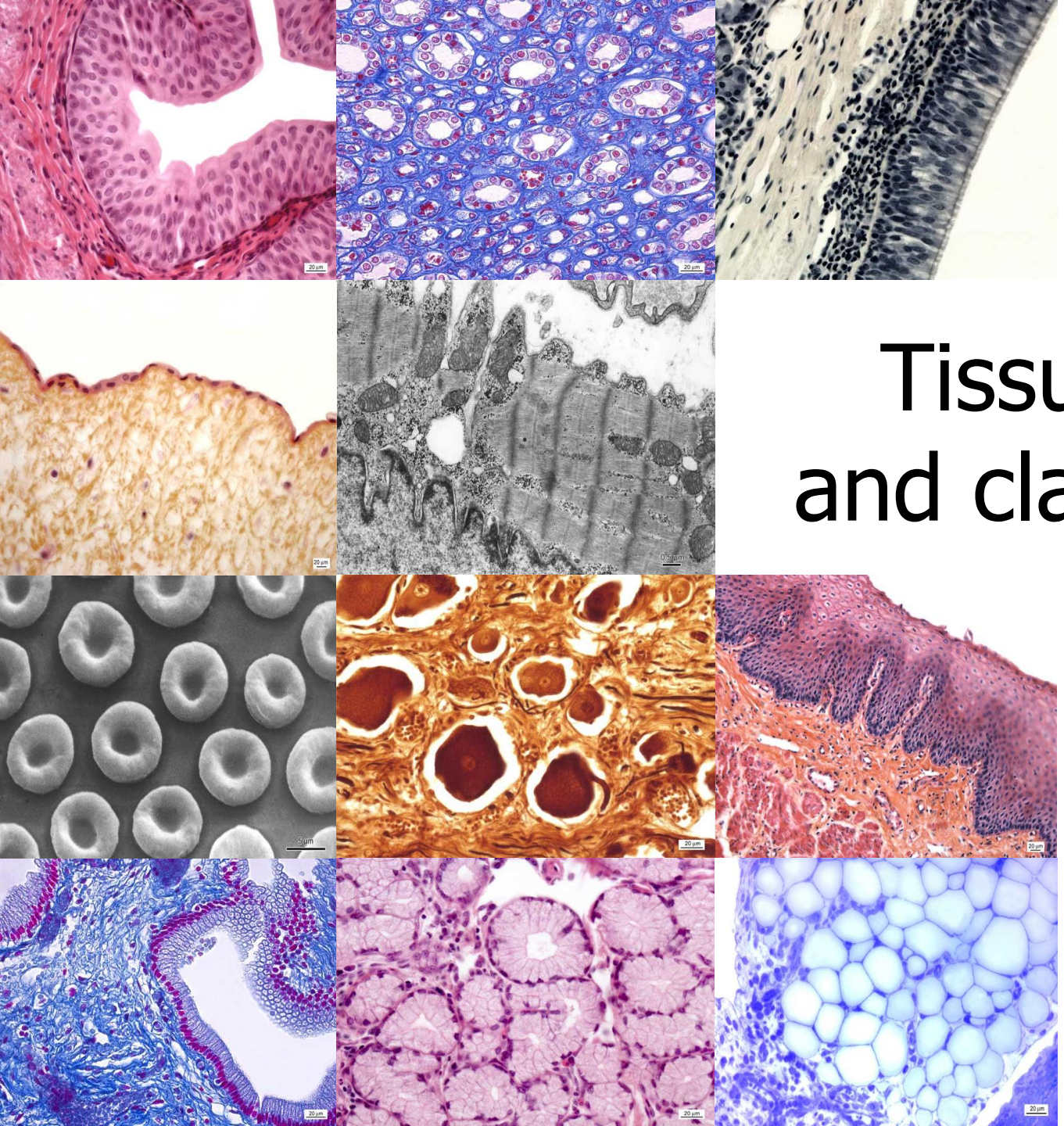

Tissue concept and classification

Petr Vaňhara, PhD

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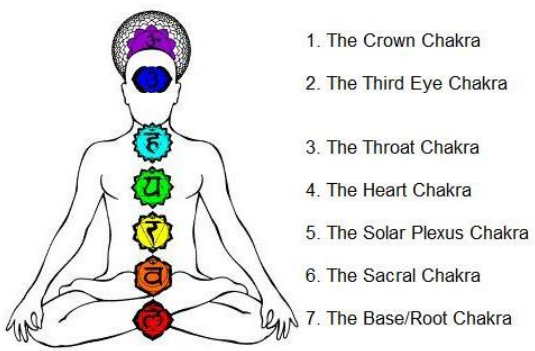
Organization of human body

Hindu

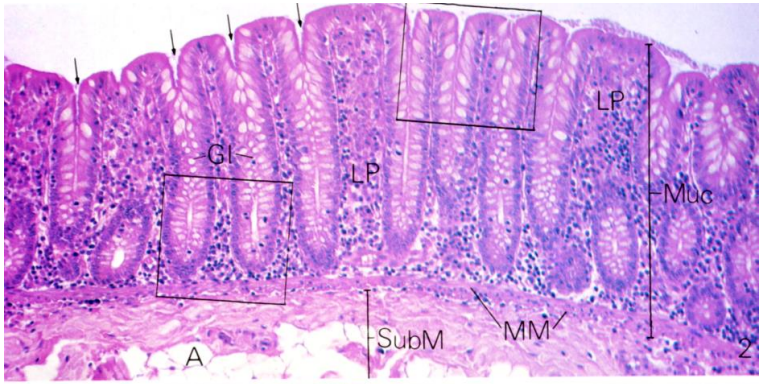


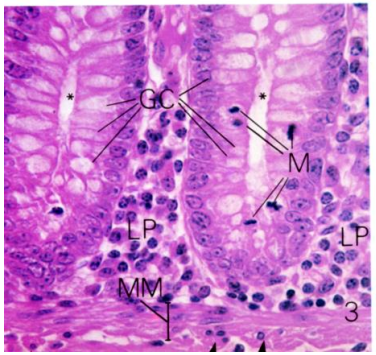
Chinese medicine

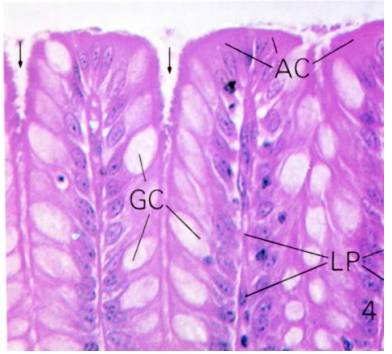
Avicenna

Aristotle
and medieval medicine

Jan E. Purkyně
Matthias J. Schleiden
Theodor Schwann
Robert Remak
Rudolf Wirchow
Camillo Golgi
…
And many others

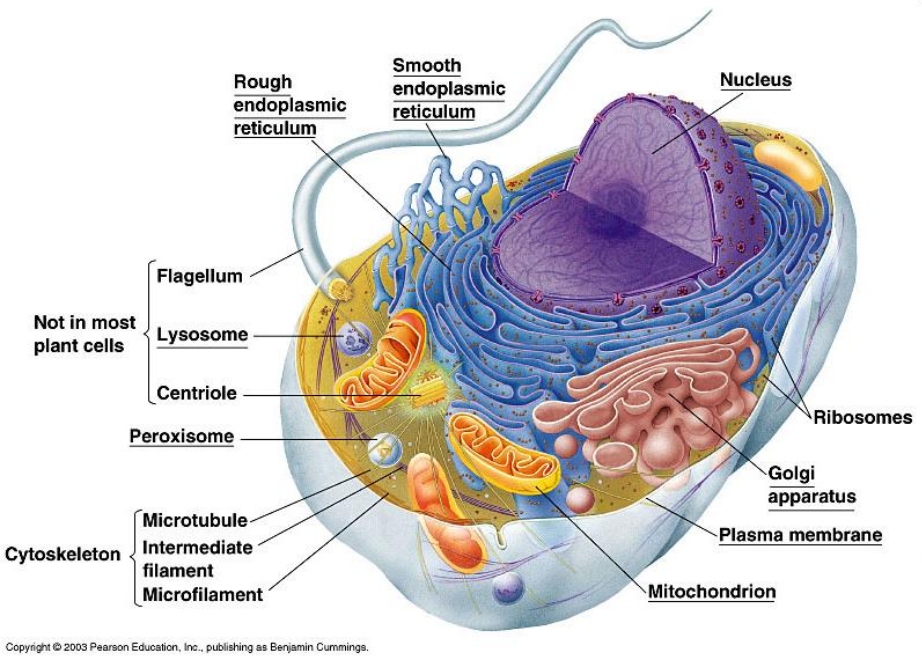


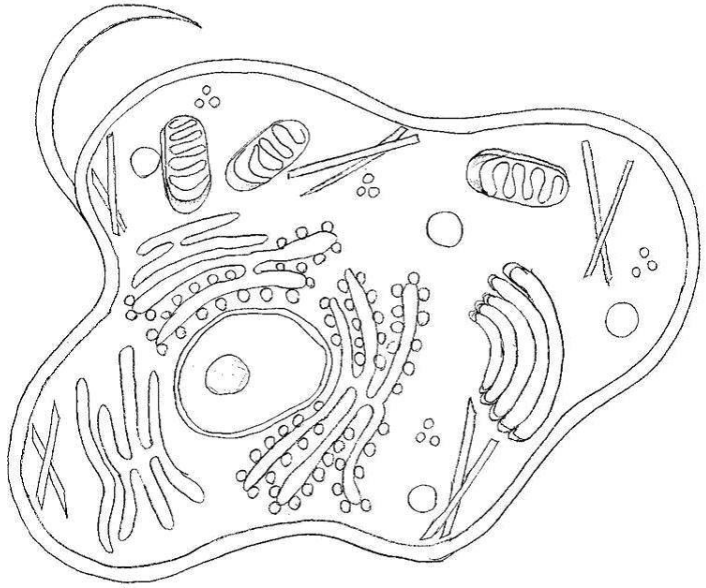


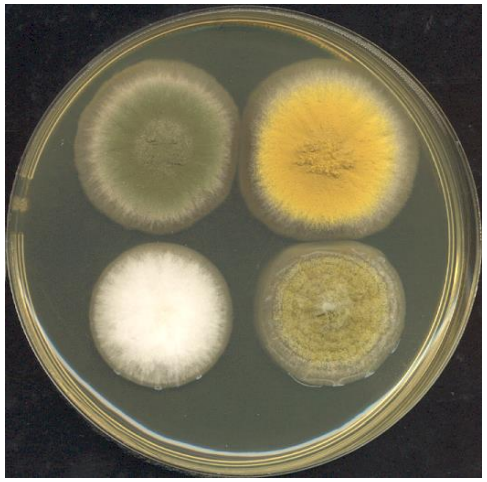


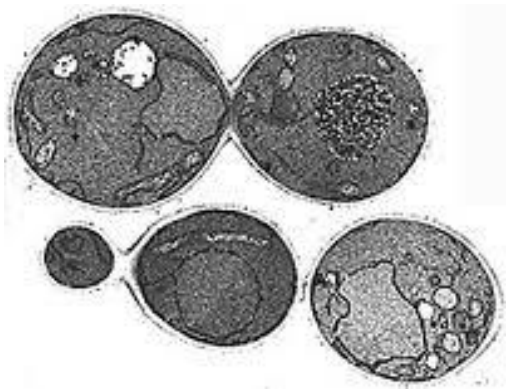
Modern cell theory

- Cells are the **basic units** of any organism
- New cells **origin** only **from other** cells
- Cells **exchange energy** (open thermodynamic system)
- Genetic **information** is **inherited** in new generations
- Chemical and structural composition of cells is generally **identical**





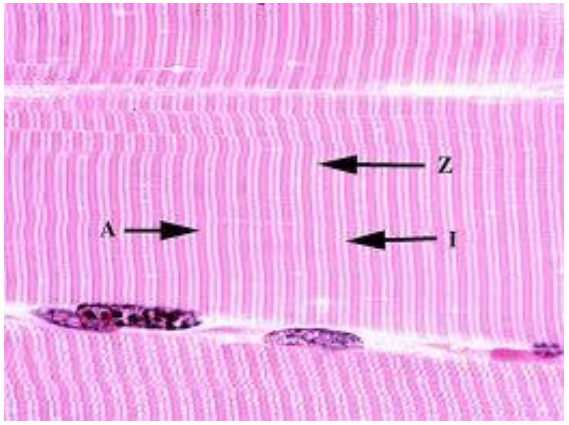


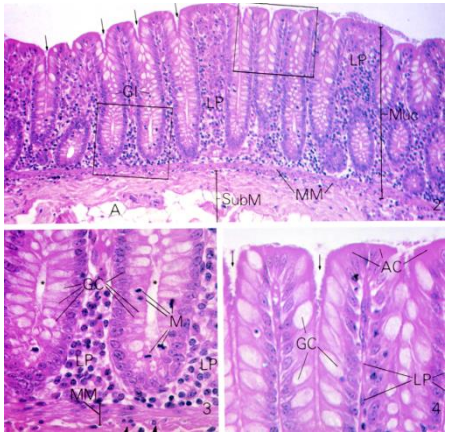


How do these cells differ?

What is the mechanism of tissue formation?

How the variability of a multicellular body develops?





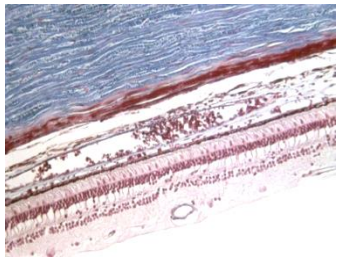
In human body:

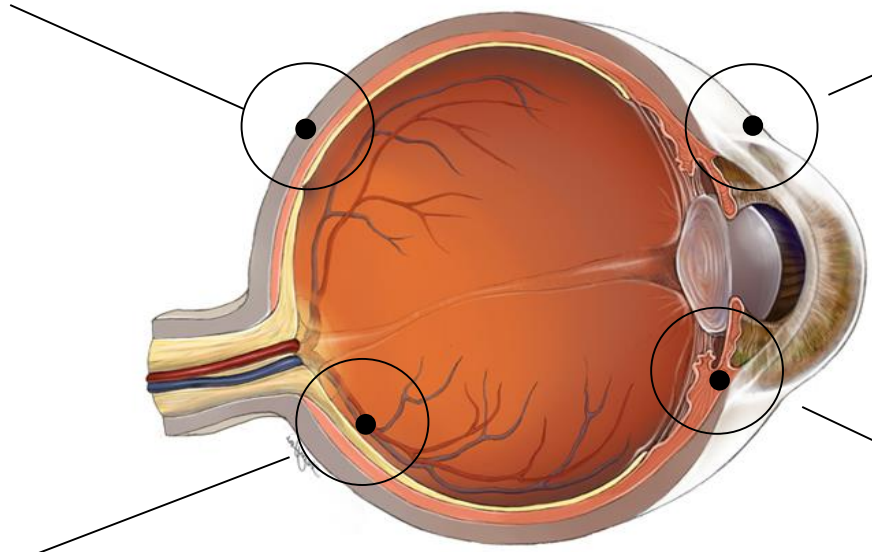
- **6 × 10^{13} CELLS** of **200** different types

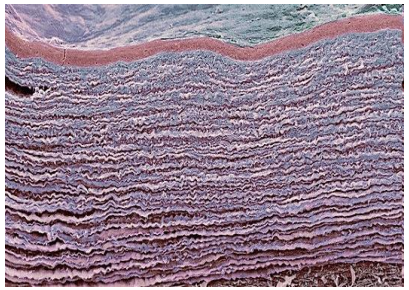
(2 × 10^{11} stars in Milky Way)

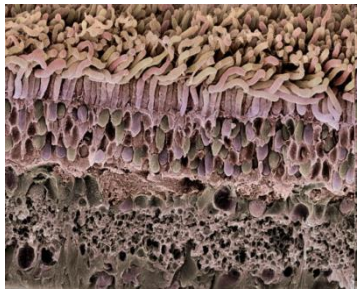
- cells form **functional**, **three-dimensional**, **organized** aggregations of morphologically similar cells and their products or derivatives - **TISSUES**

- tissues constitutes **ORGANS** and organ systems





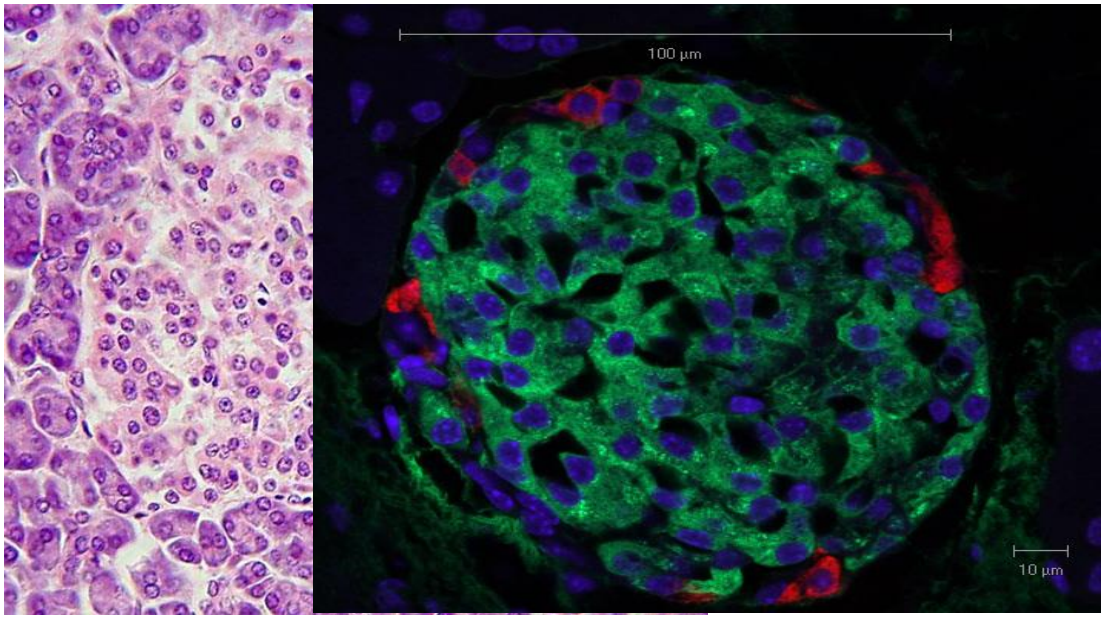




Definition of a tissue

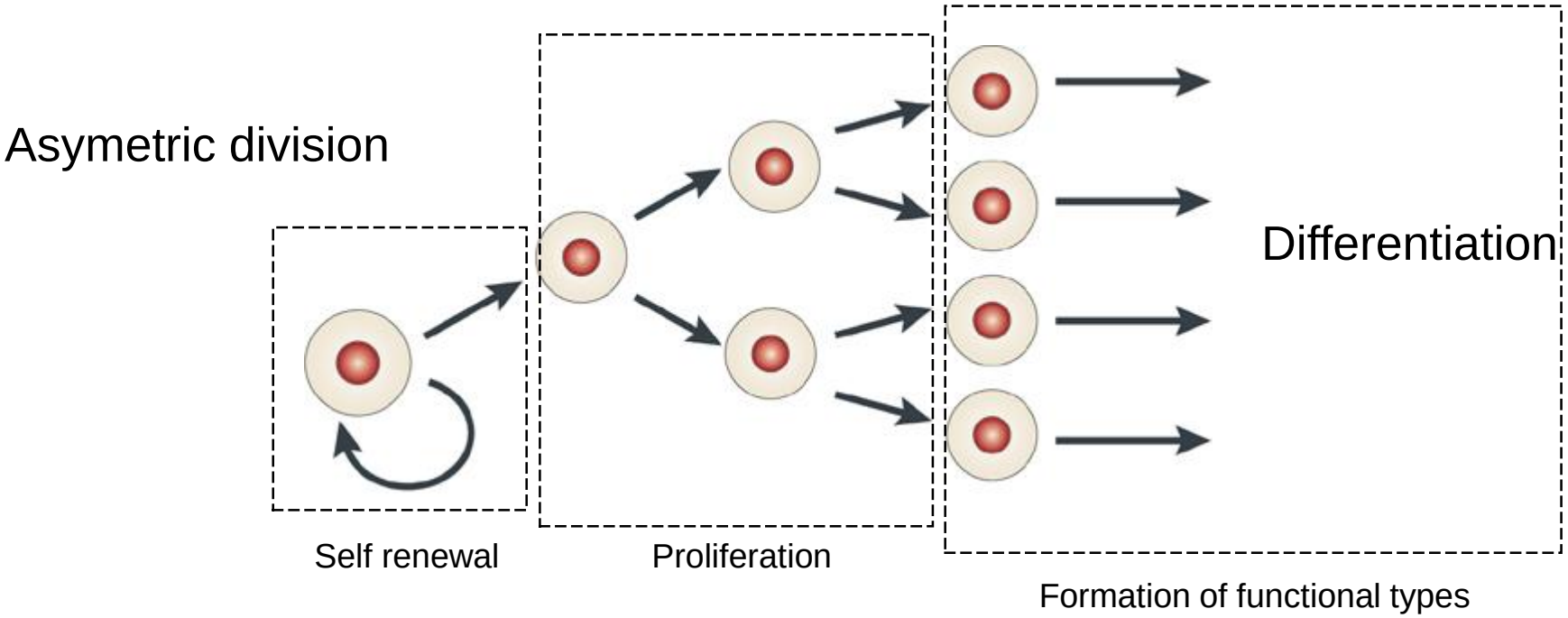
Functional, three-dimensional, organized aggregation of morphologically similar cells, their products and derivatives

- classical histological definition is based on microscopic visualization



- Functional cells of tissues differentiate from stem cells

Stem cells are capable of differentiation and self renewal



Knoblich JA. Asymmetric cell division during animal development. 2001. Nat Rev Mol Cell Biol

Stem cells

Totipotent

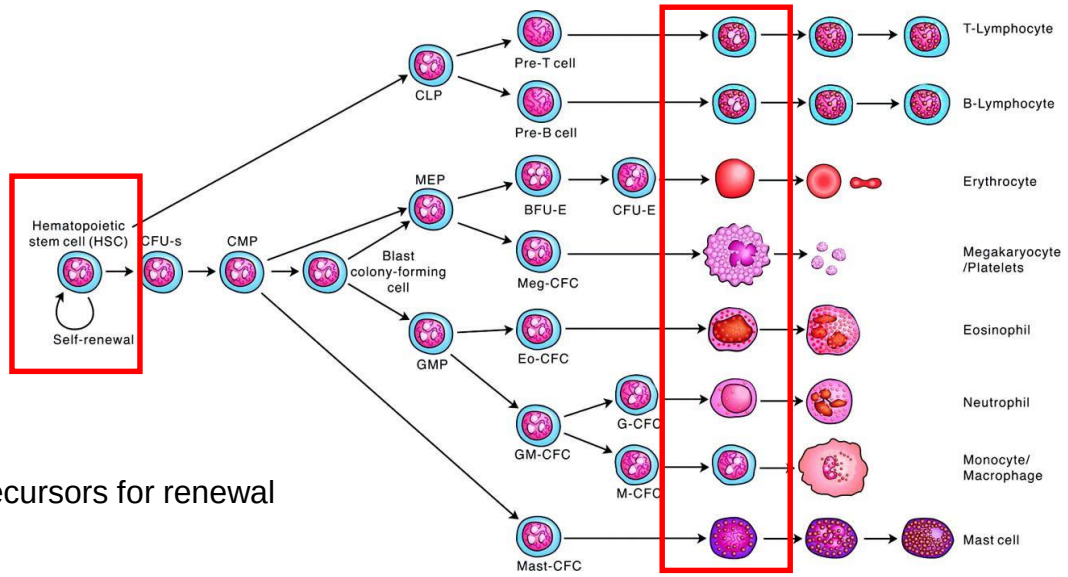
- Constitute all cells of the body incl. extraembryonic tissues
- Zygote and early stages

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

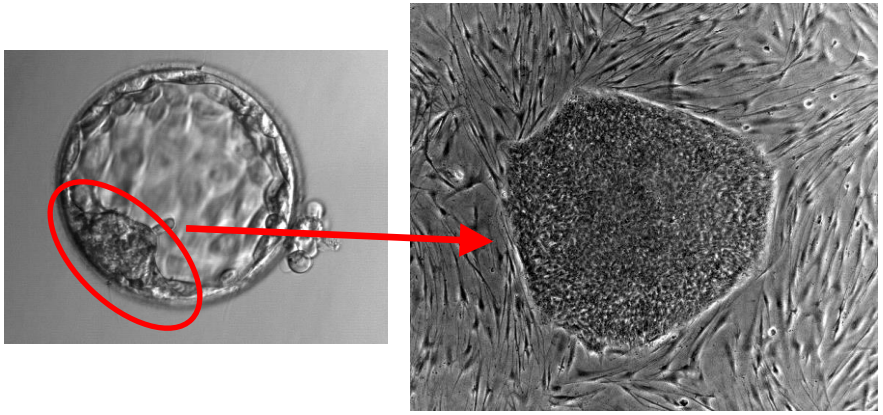
- One or several cell types – hematopoietic, tissue precursors for renewal of intestinal epithelia, etc.

http://www.embryology.ch/anglais/evorimplantation/furchung01.html

Stem cells in human body

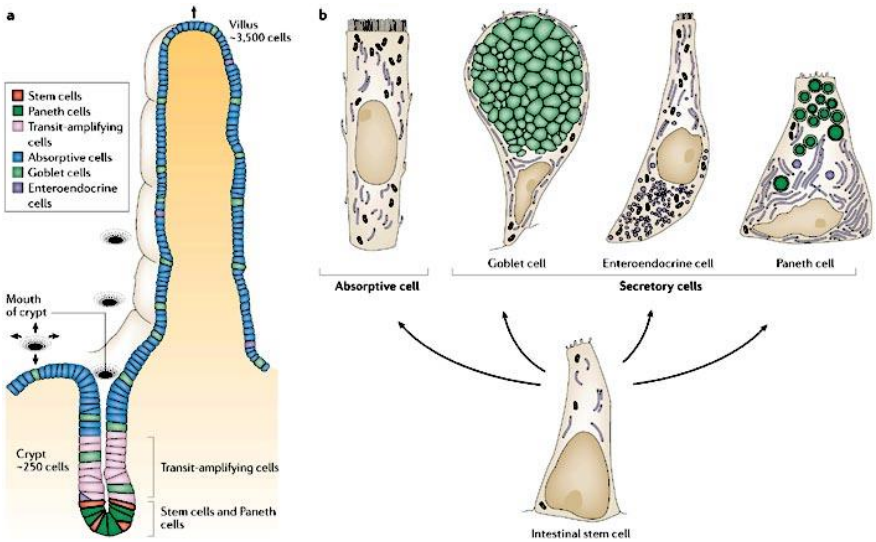
Embryonic stem cells (ESCs)

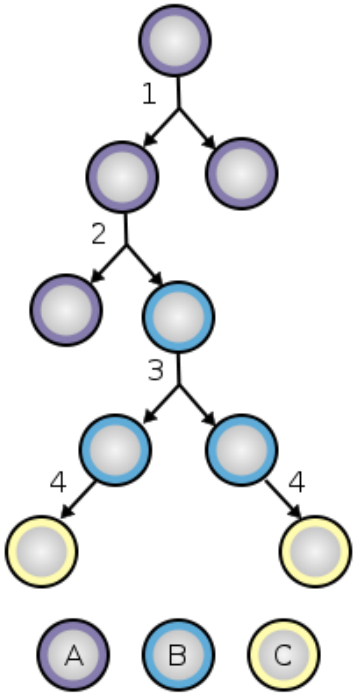
- embryoblast of blastocyst
- pluripotent
- modelling of early embryogenesis, regenerative medicine



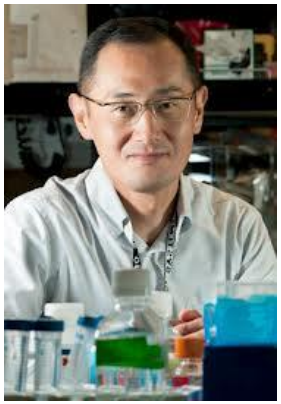
Tissue (adult) stem cells

- regeneration and renewal of tissues
- GIT, CNS, mesenchyme
- regenerative medicine, cancer biology





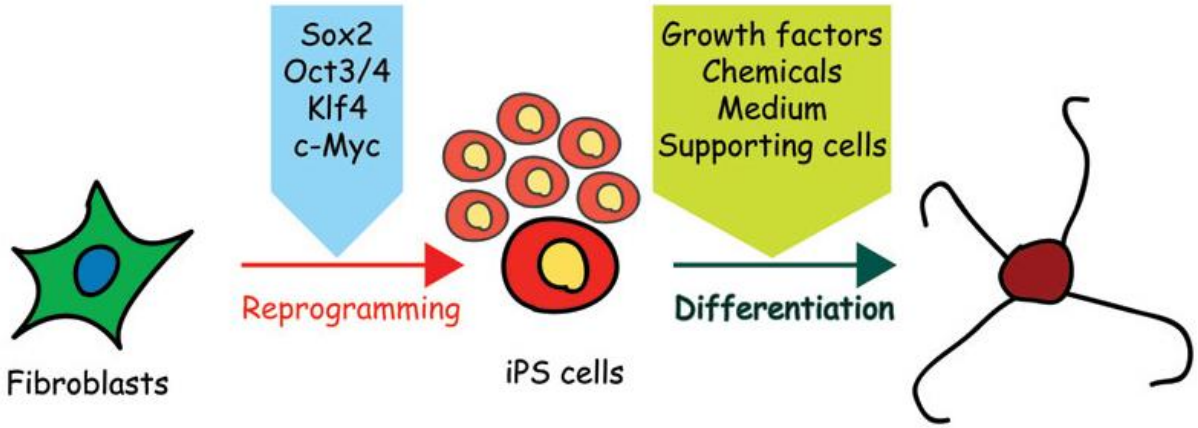
Stem cells as a research tool



Nobel prize 2012

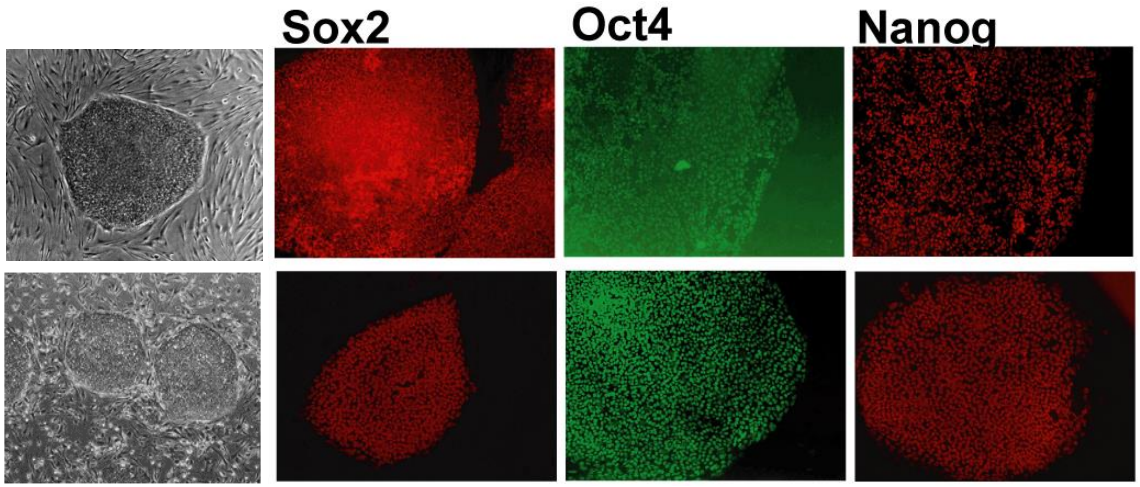
Induced pluripotent stem cells (iPSc)

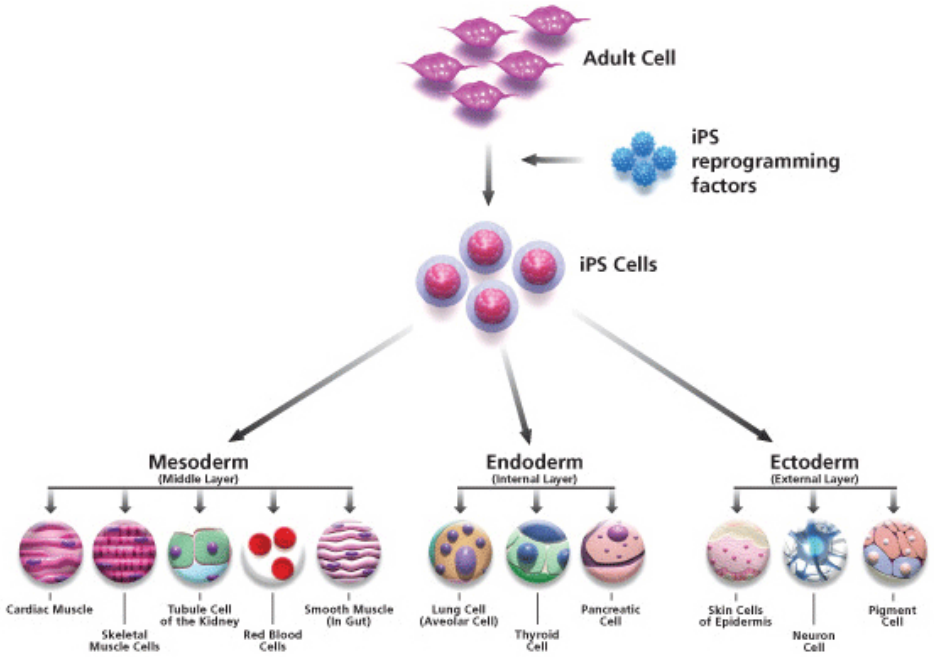
- adult differentiated cell (fibroblast) is reprogrammed into pluripotent state
- differentiation into desired cell type
- regenerative medicine, cell and gene therapy



Disease modelling
Drug testing
Tissue replacement
…

- Induced pluripotent stem cells share biological properties with embryonic stem cells



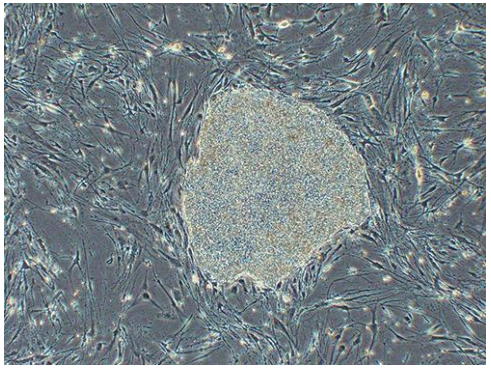


Stem cells as a therapy

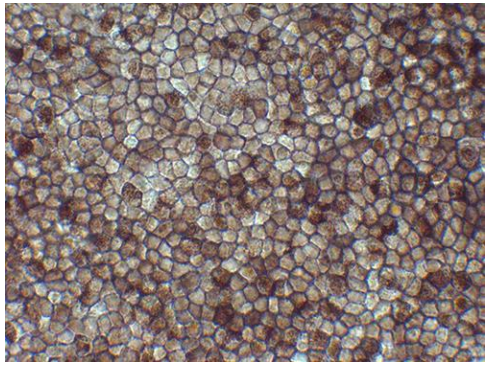
Age-related macular degeneration

neovascularisation

hiPSCs



Retinal pigment epithelium



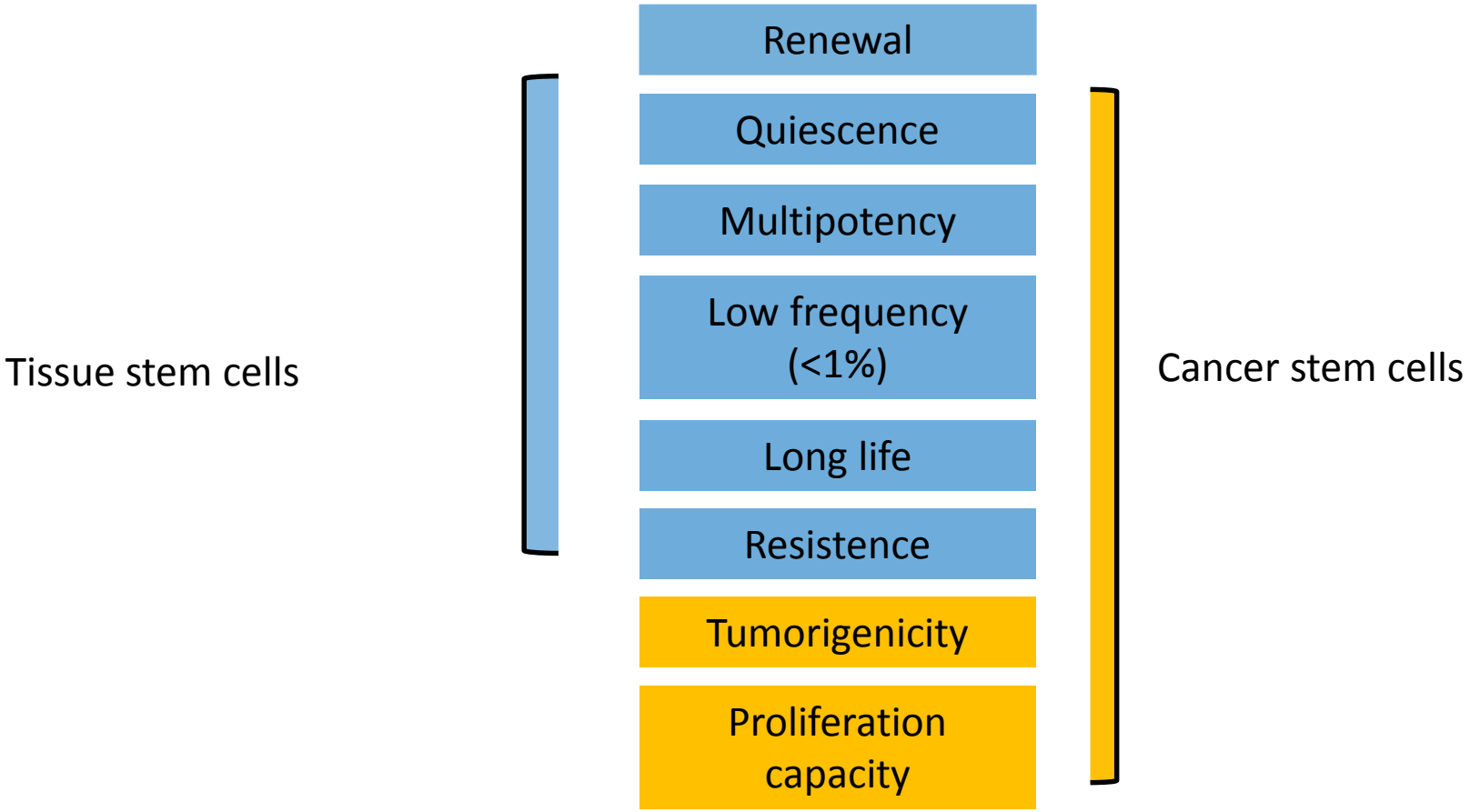
Clinical trial

Stem cells as a foe

Cancer stem cells

- solid tumor is always heterogeneous

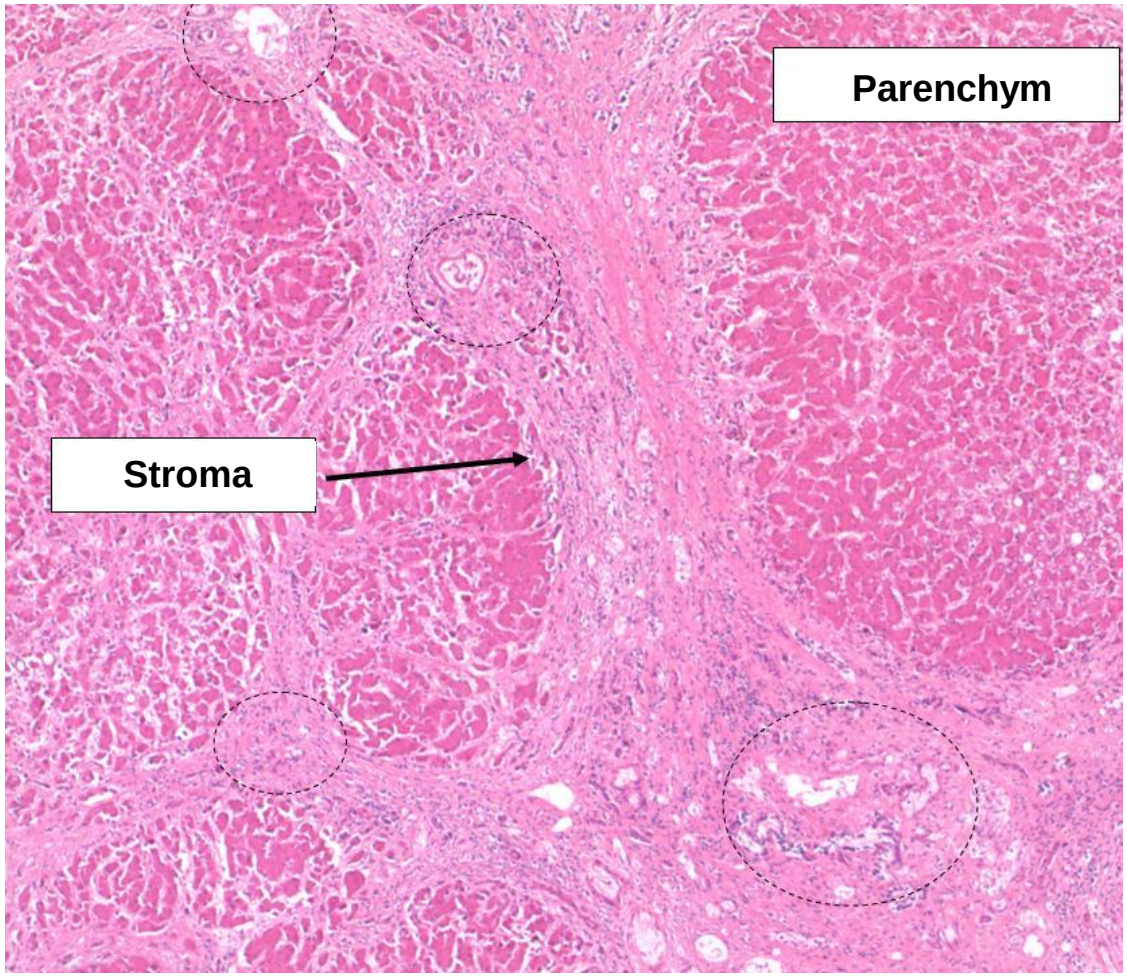
- small population of cells with stem cell character can repopulate tumor tissue after cytotoxic therapy



Tissues are not uniform

Parenchyma: functional tissue of an organ
(liver, lung, pancreas, kidney parenchyma)

Stroma: surrounding, supportive tissue

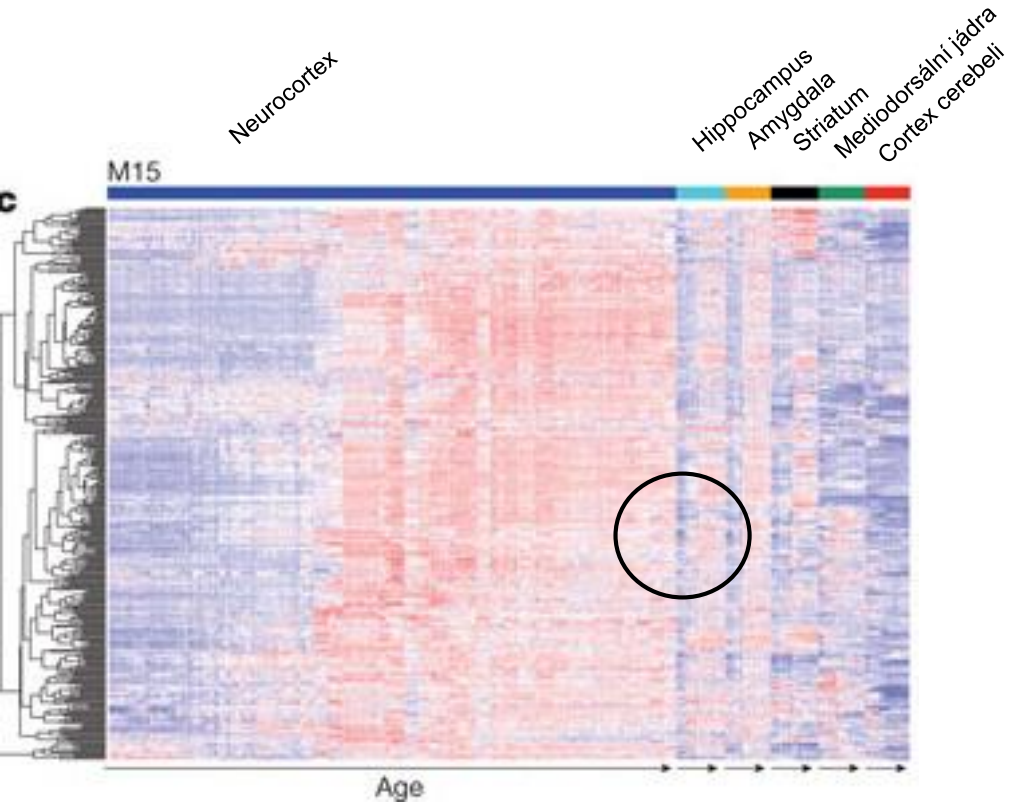


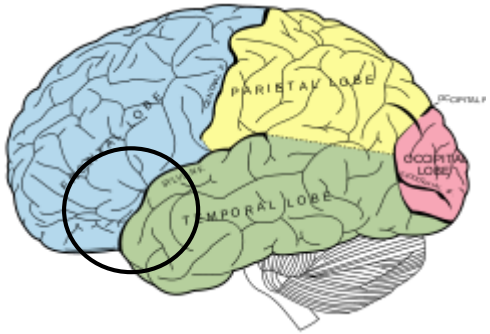
Parenchyma
- Hepatocytes
- Sinusoids and surrounding structures

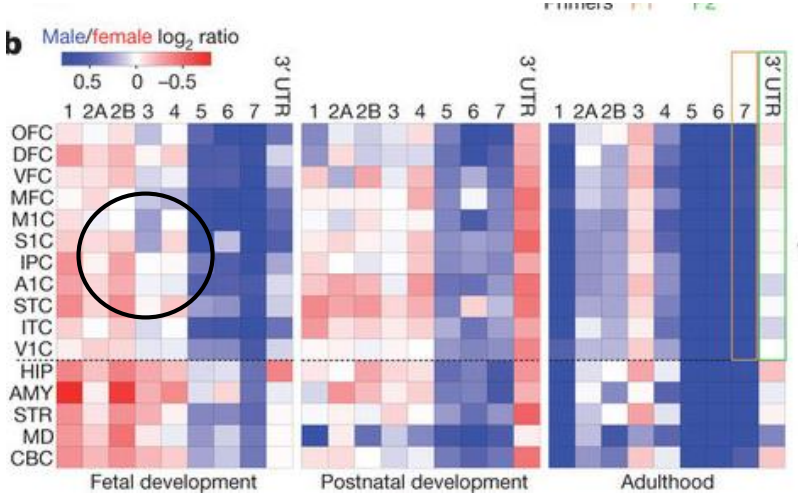
Stroma:

- CT
- Veins
- Nerves
- …

Tissue differ in their genetic and epigenetic profile

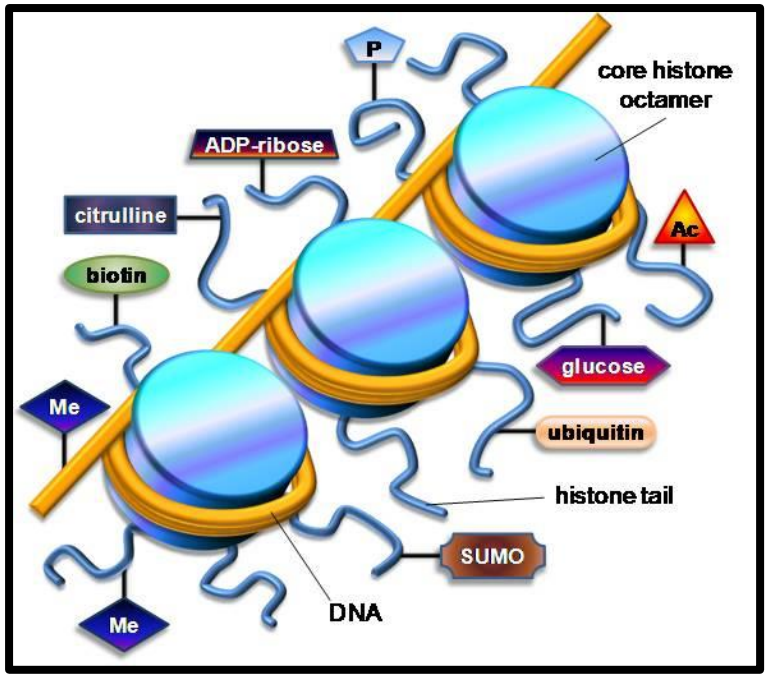


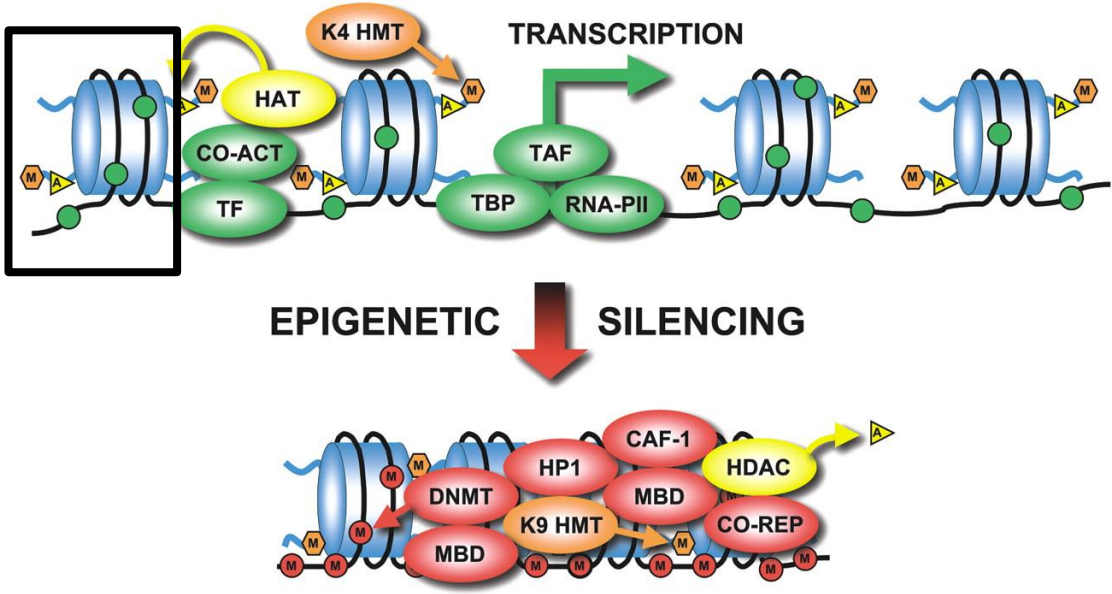




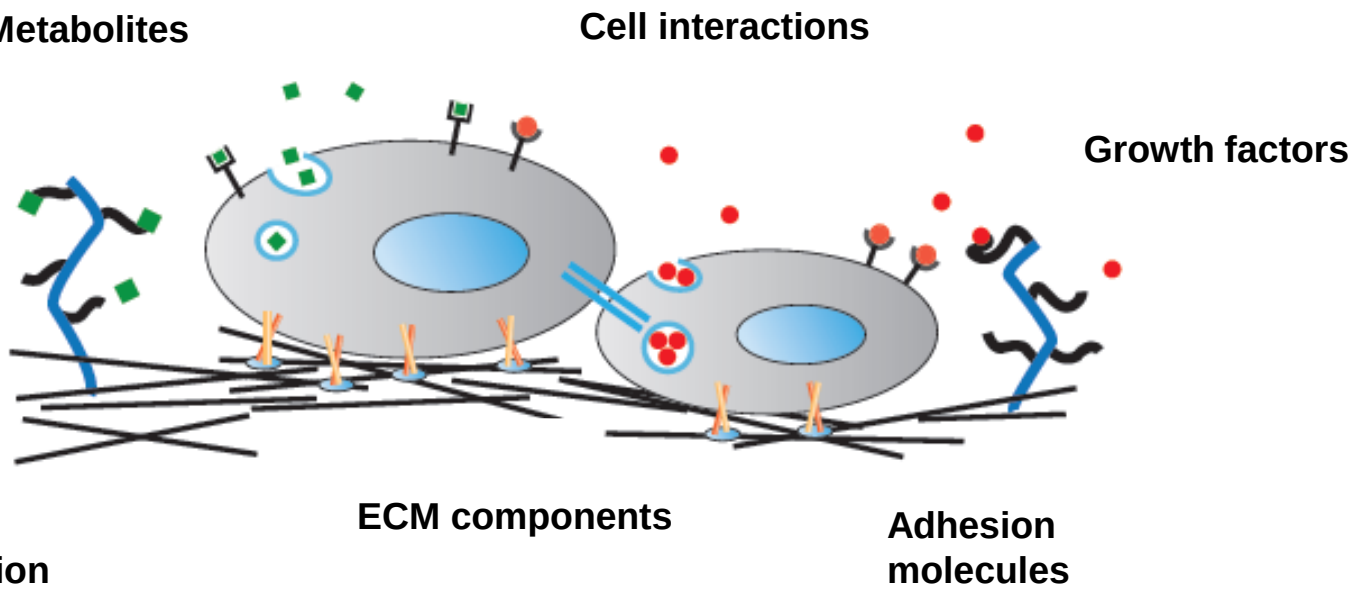
doi:10.1038/nature10523

Tissue differ in their genetic and epigenetic profile





Cells create unique microenvironment

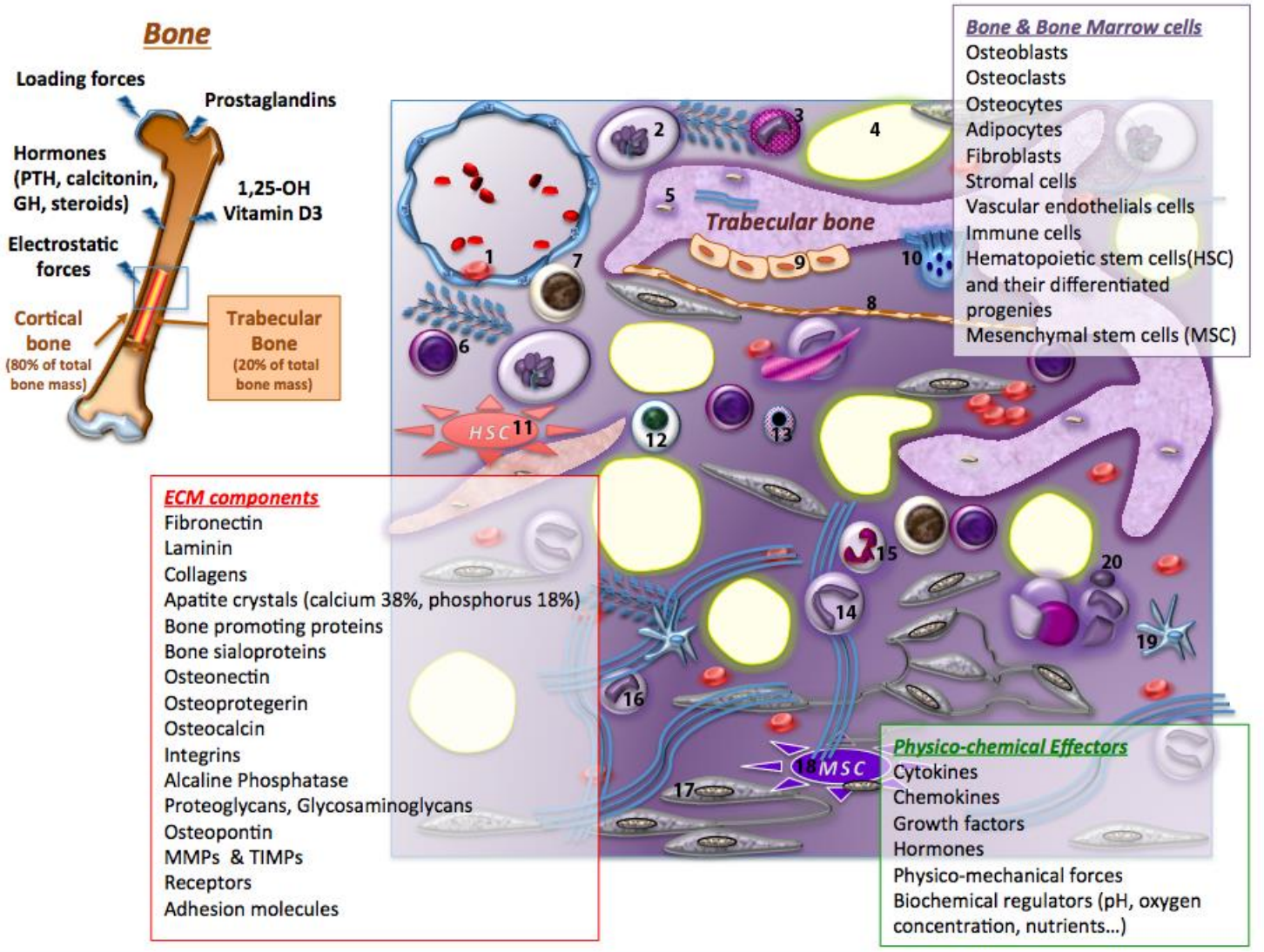


Microenvironment regulates tissue function and reflects its tissue composition

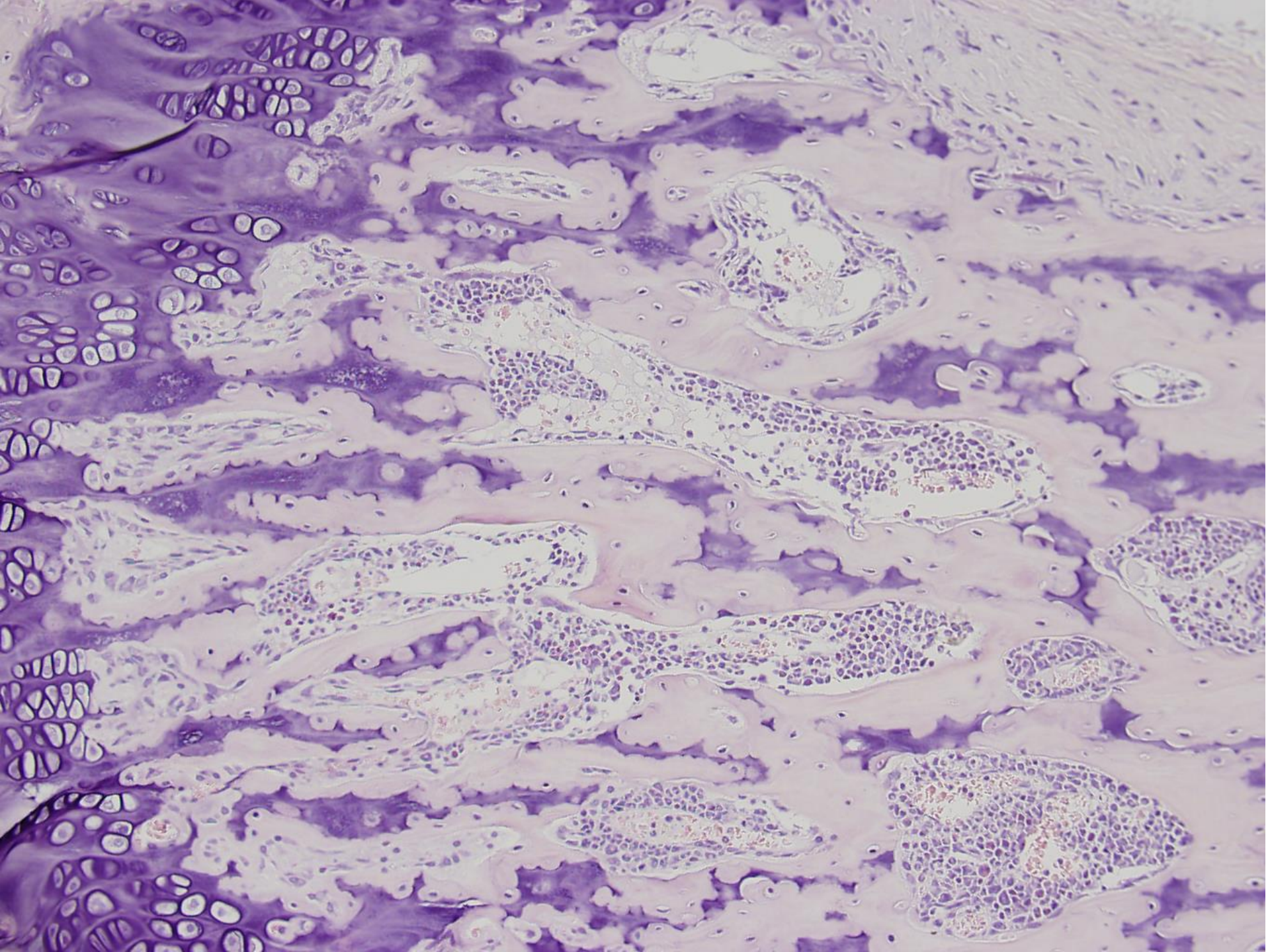
Huge number of **biological** and **physically-chemical** parameters

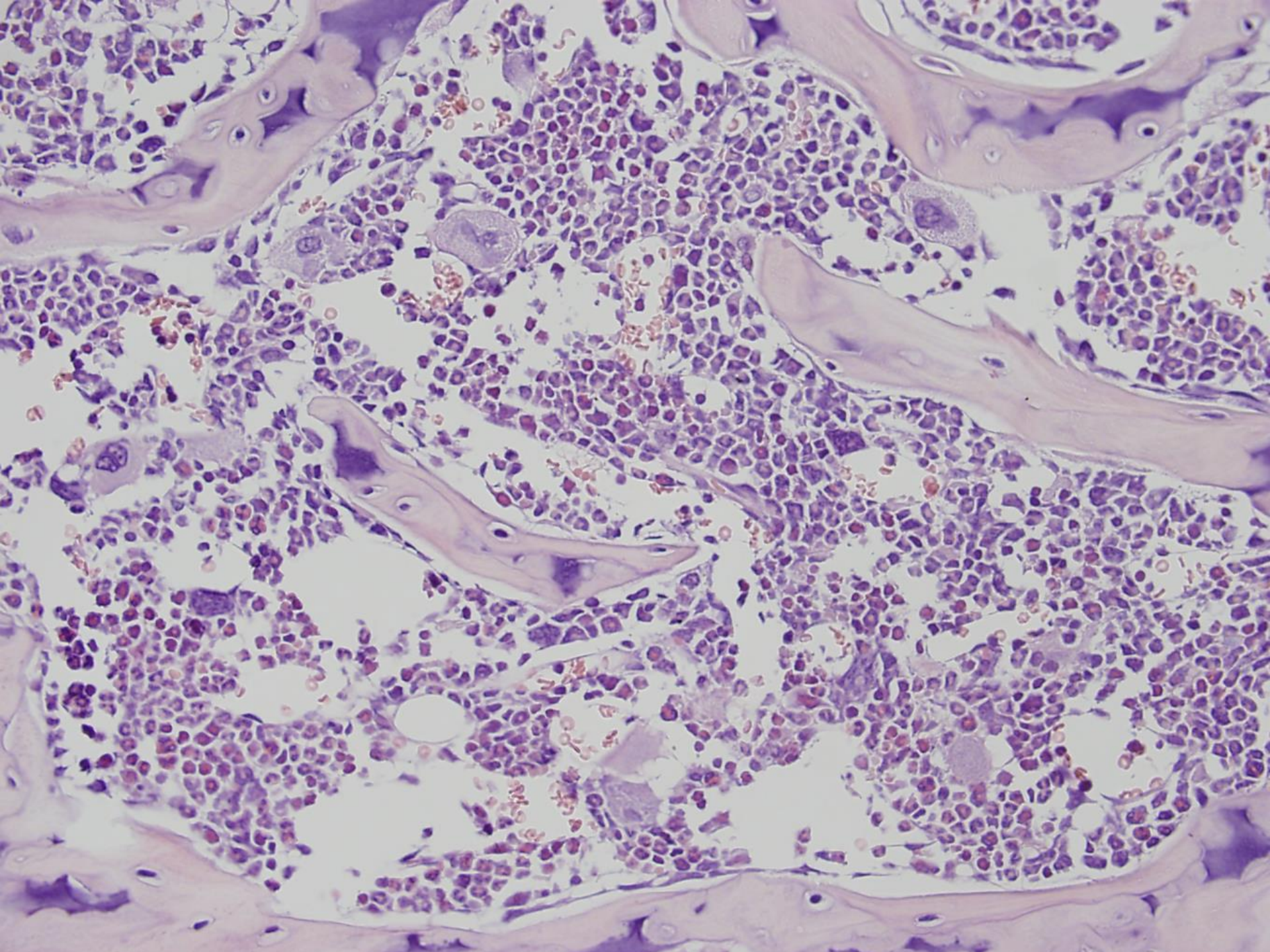
- Embryonic development
- Intercellular interaction
- Space organization (dimensionality)
- Gradient of morphogenes
- Epigenetic profile
- Gene expression dynamics
- Partial pressure of gases
- ECM composition
- Mechanical stimulation
- Perfusion and interstitial flows
- Local immunity response
- Metabolites

Bone marrow microenvironment drives hematopoiesis

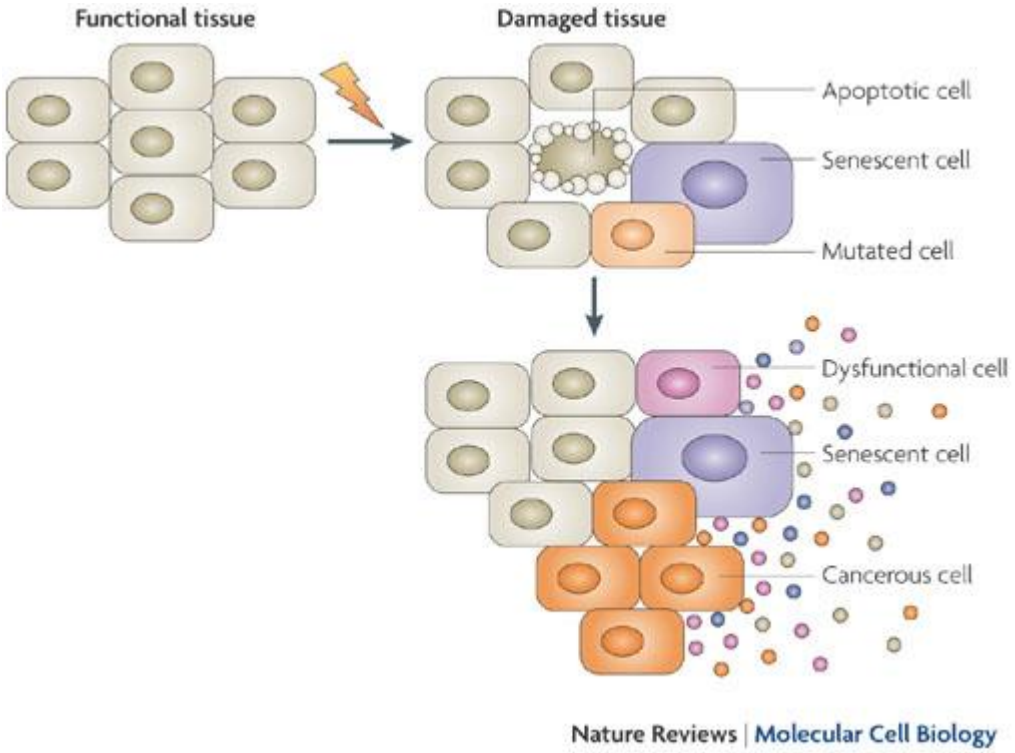


„Stem cell niche“





Microenvironment is necessary for tissue homeostasis



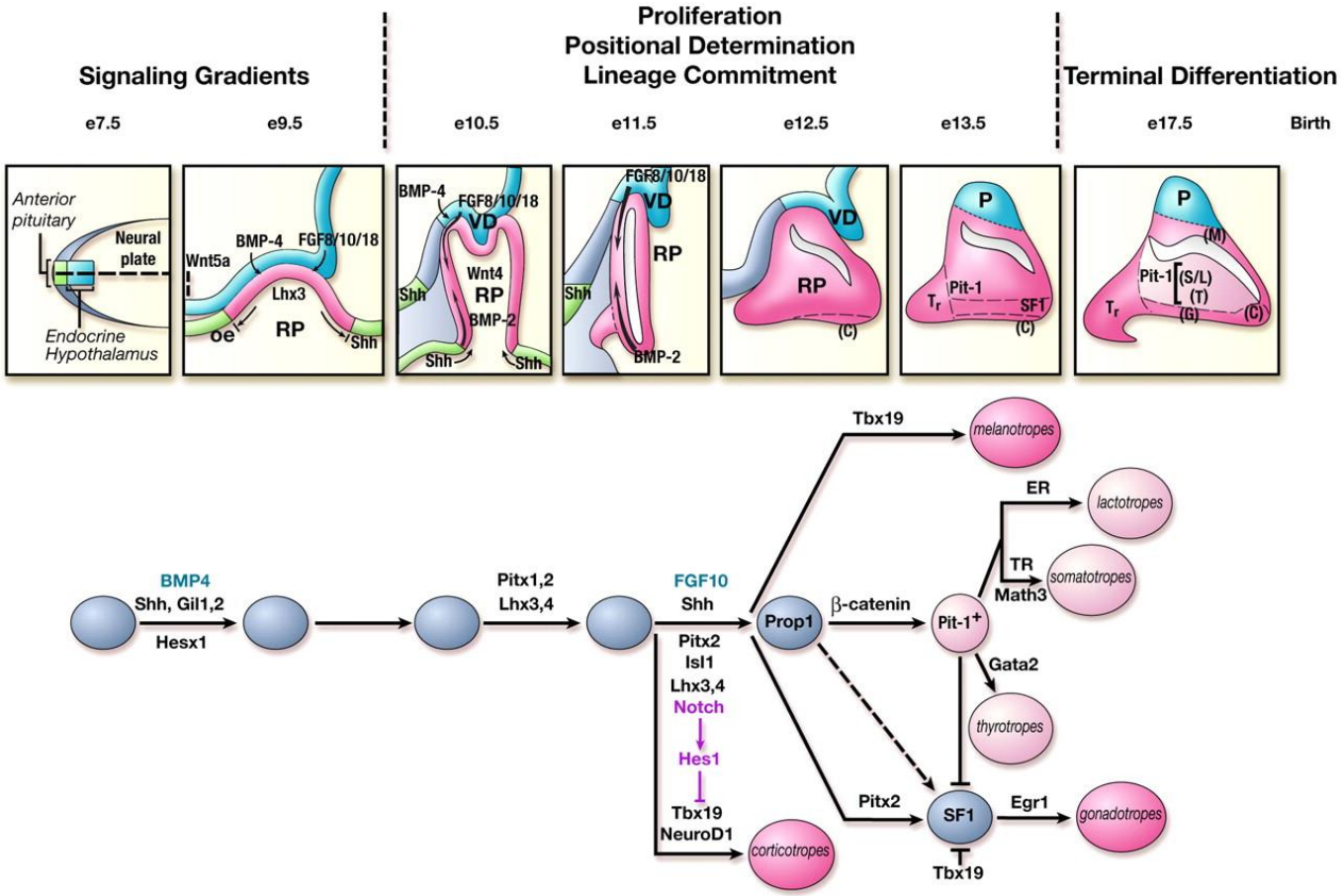
Apoptosis

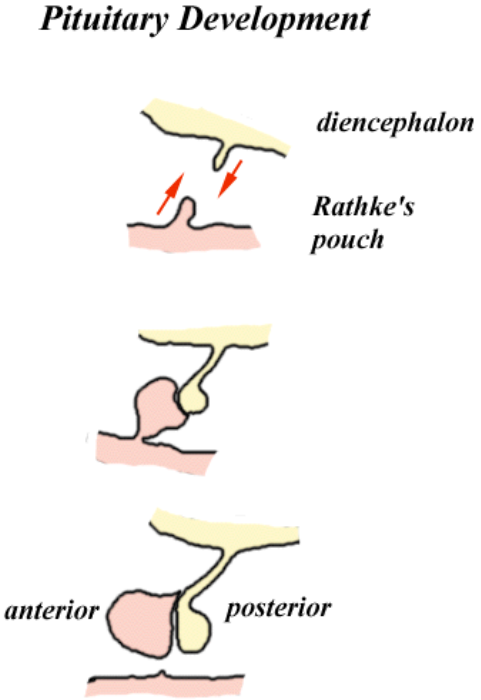
Regeneration

Senescence

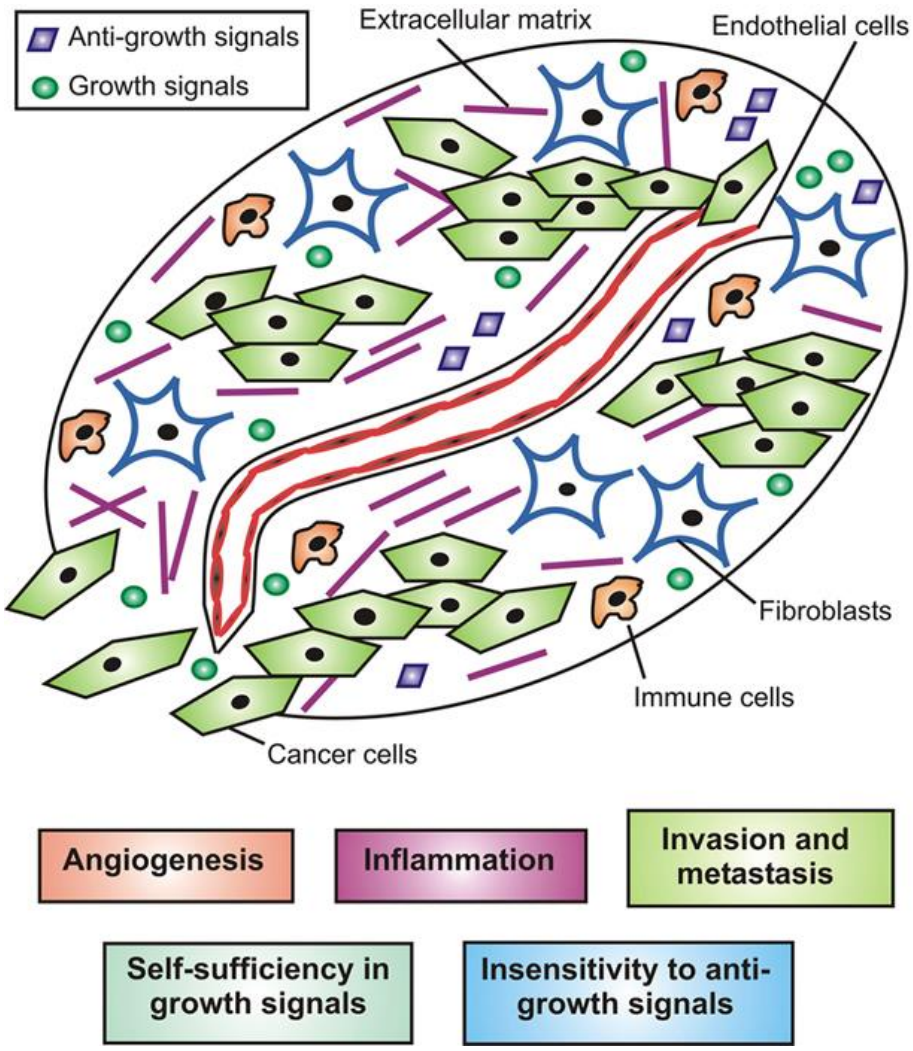
Transformation

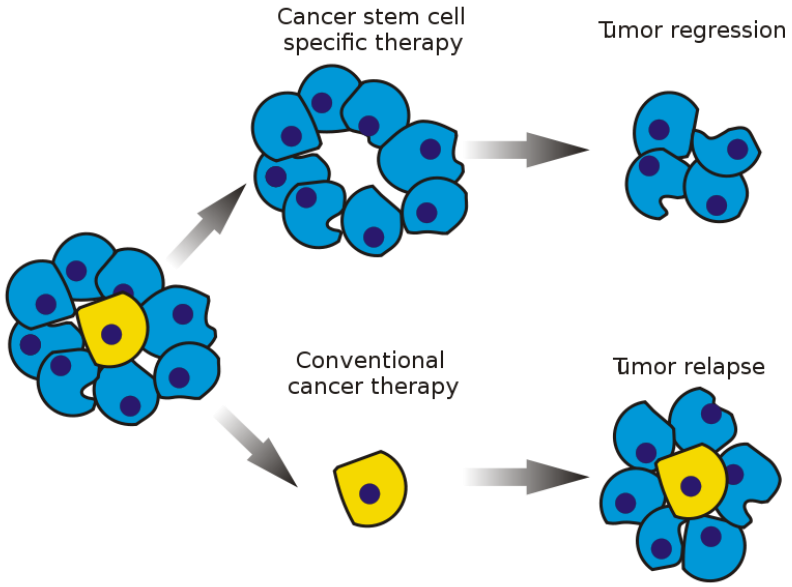
Microenvironment controls embryonic organogenesis



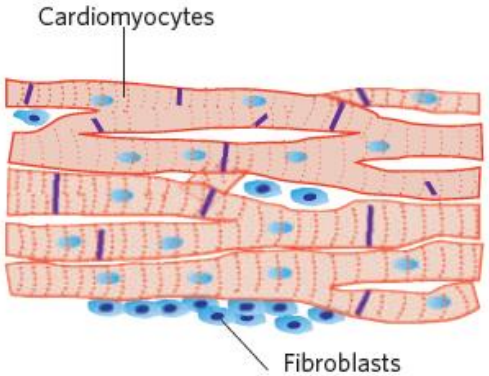


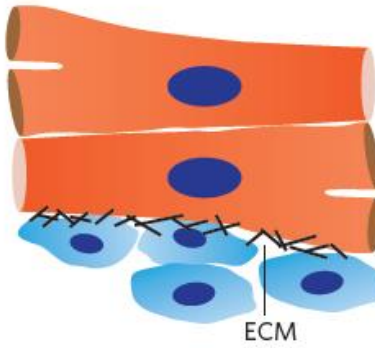
Microenvironment is of clinical importance



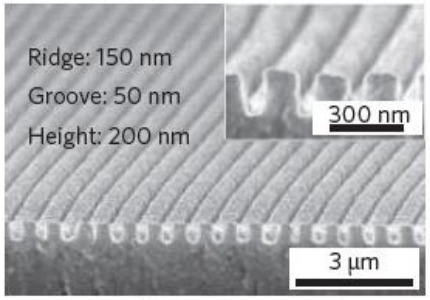


Tissue engineering

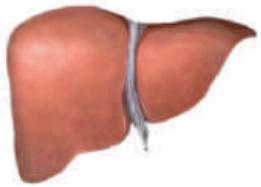


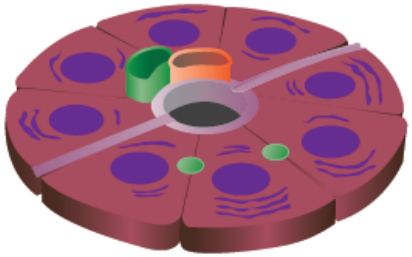


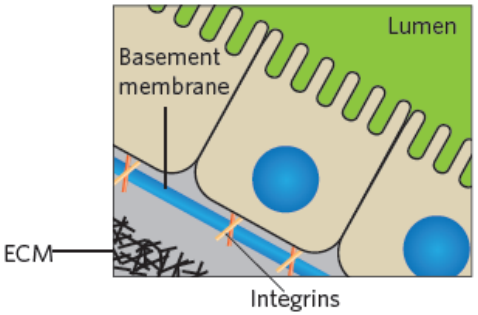
Engineered scaffold

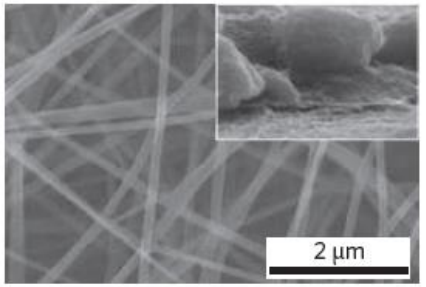


Grooved arrays can promote cardiomyocyte elongation and alignment

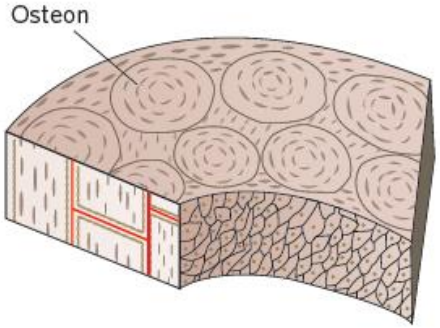


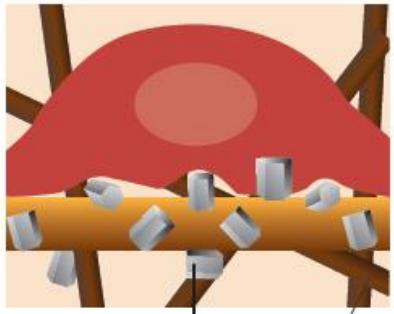


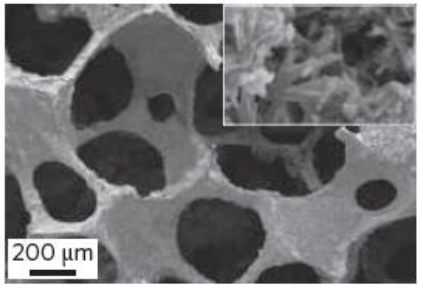




Surface molecules on nanofibres can promote cell polarization

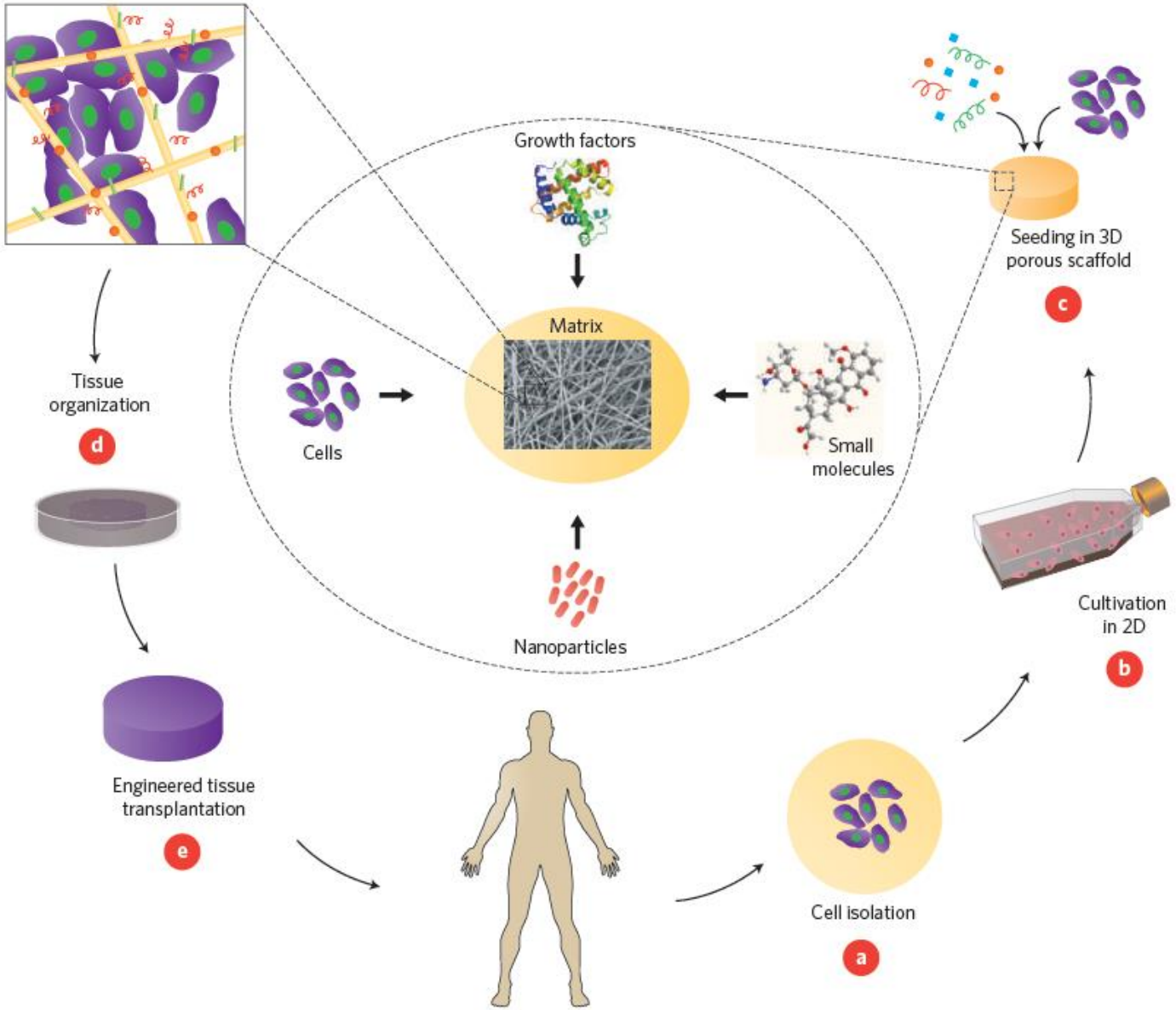






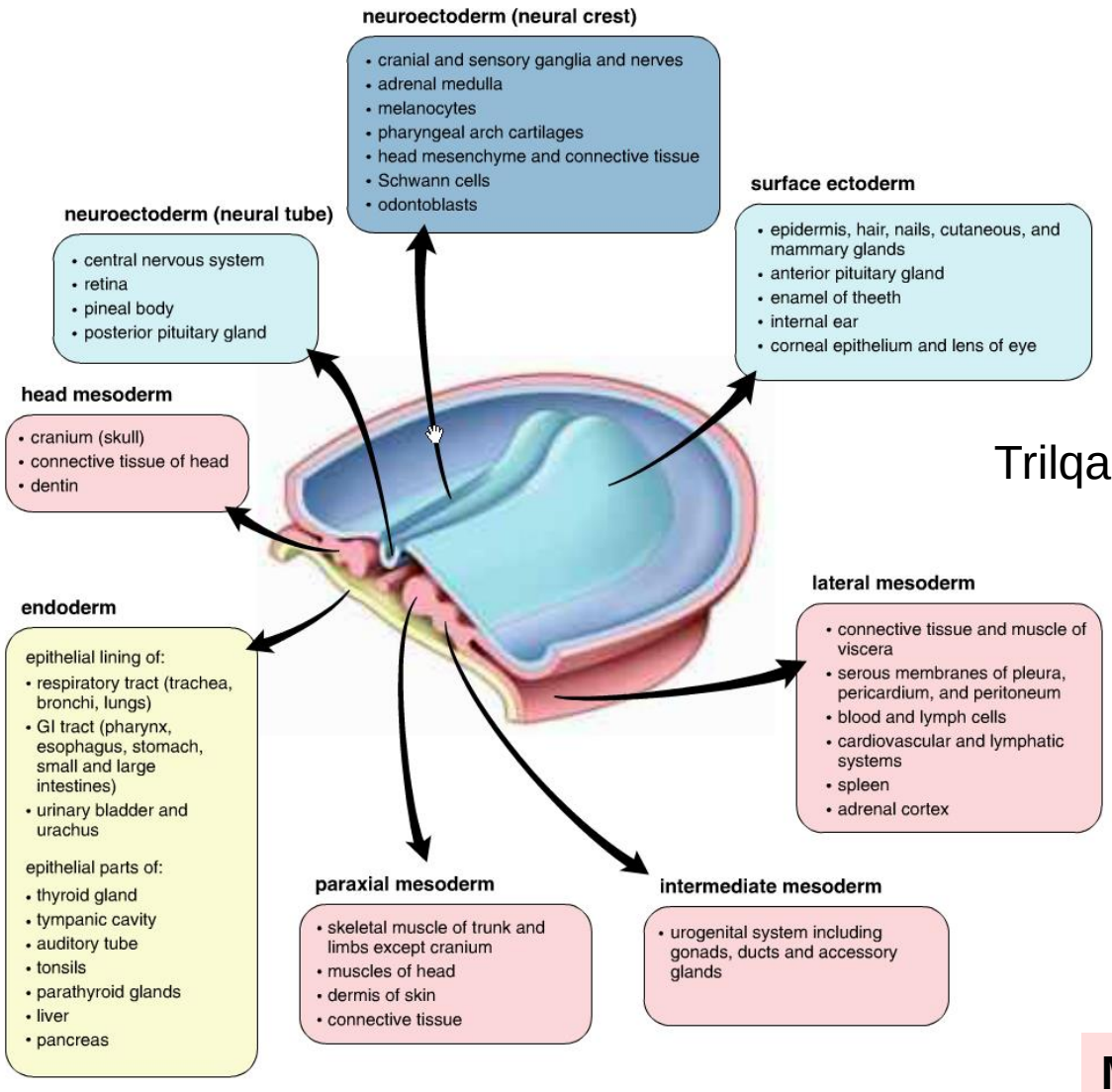
Hydroxyapatite nanostructures can enhance osteogenesis

Tissue engineering



Histogenesis and organogenesis

Ectoderm



Trilqaminar germ disc

(3rd week)

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
  - Enteroendocrinne 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

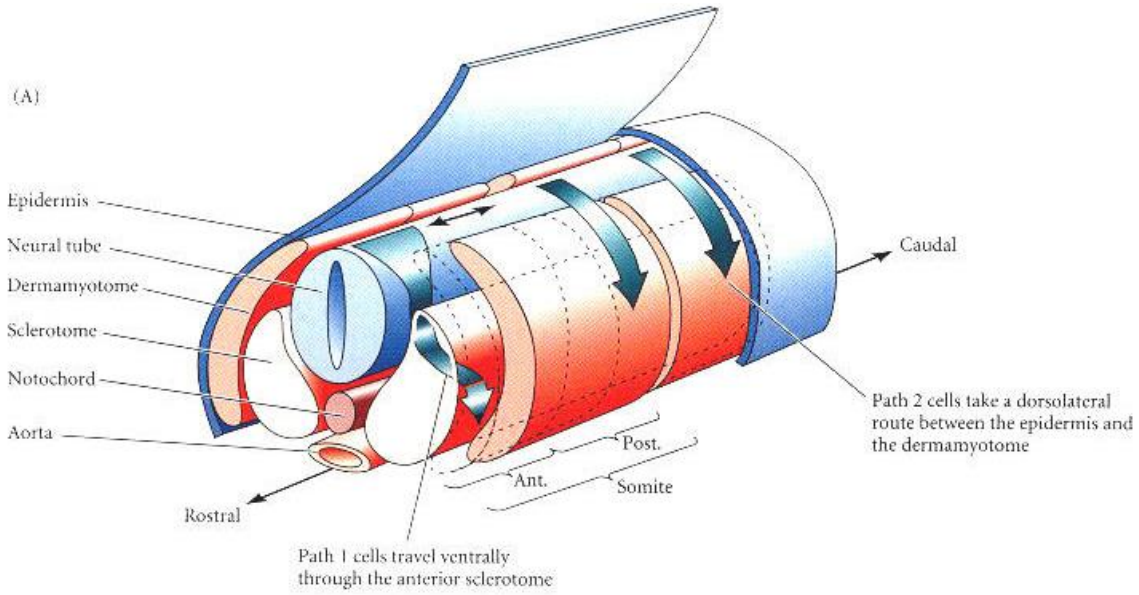
Lateral

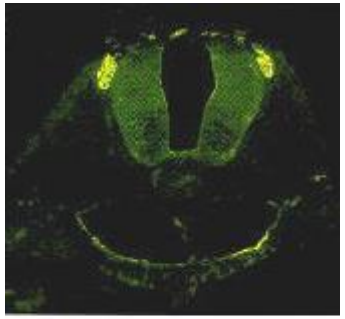
- Visceral muscle and connective tissue
- Serous membranes of pleura, peritoneum and pericardium
- Blood cells, leukocytes
- Cardiovascular and lymphatic system
- Spleen
- Adrenal cortex

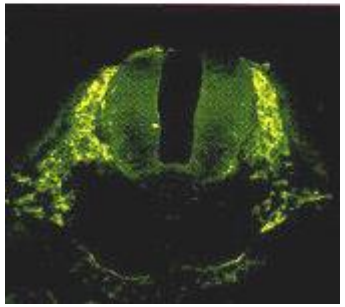
Endoderm

- 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

Neural crest is a „fourth germ layer“





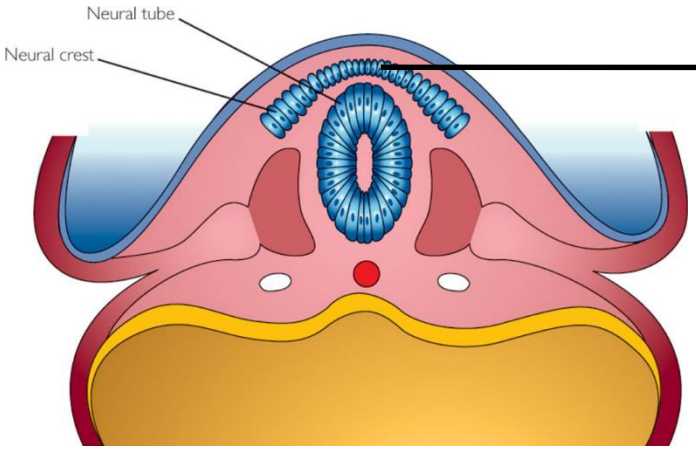


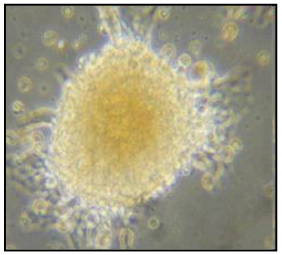
PNS:
Neurons
Sensoric, sympathetic a parasympathetic ganglions and plexuses
Neuroglia and Schwann cells

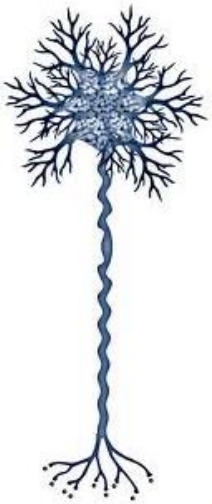
Adrenal medulla
Calcitonin secreting thyroid cells
Pigment cells of epidermis
Viscerocranium

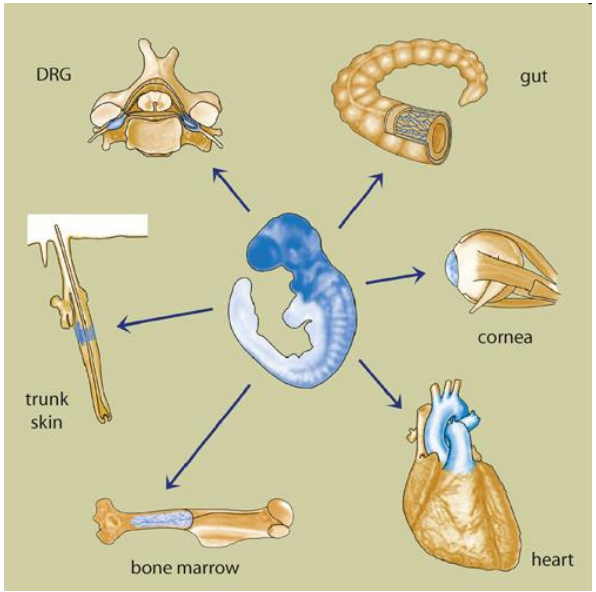
Corneal stroma and endothelium
Tooth papilla
Dermis, smooth muscles and adipose tissue of skin of head
CT of salivary and lacrimal glands, thymus, thyroid and pituitary
…

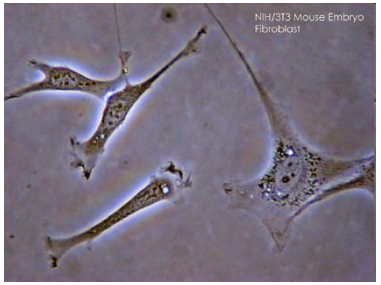
- Neural crest cells are multipotent in vitro

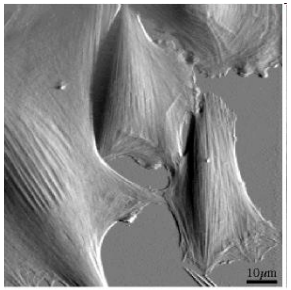


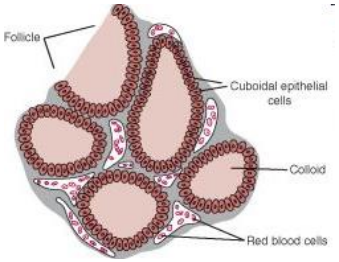






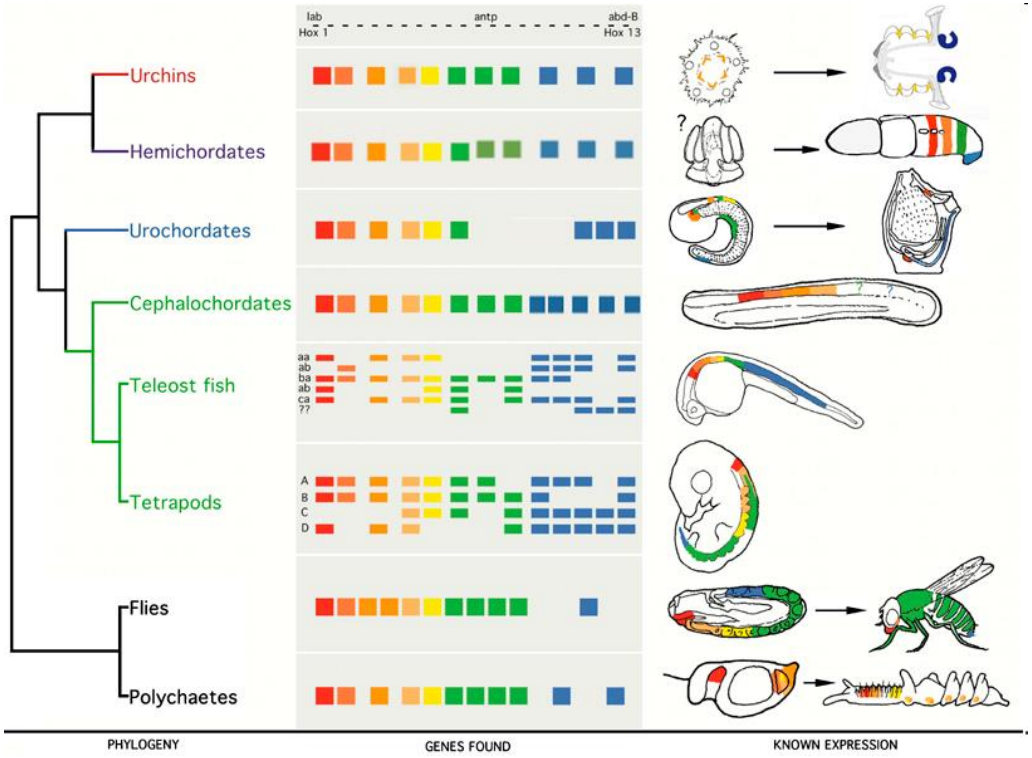






Ref.: Shakhova O., Sommer L. Stem Book 2012. Neural crest-derived stem cells

Molecular principles of histogenesis



doi:10.1038/sj.hdy.6800872

Hox complex

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

Tissue differentiation along anterio-posterior axis

Human (39 genes)

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

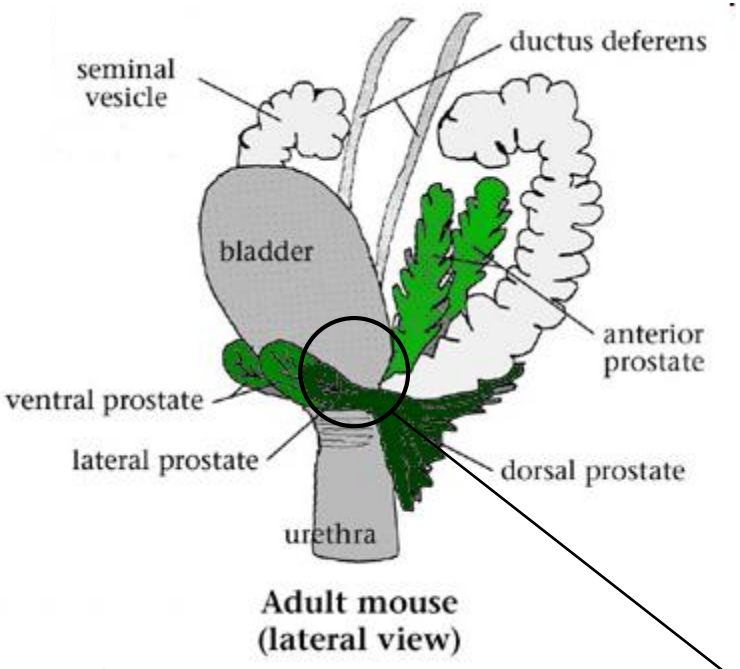
Congenital disorders and HOX genes

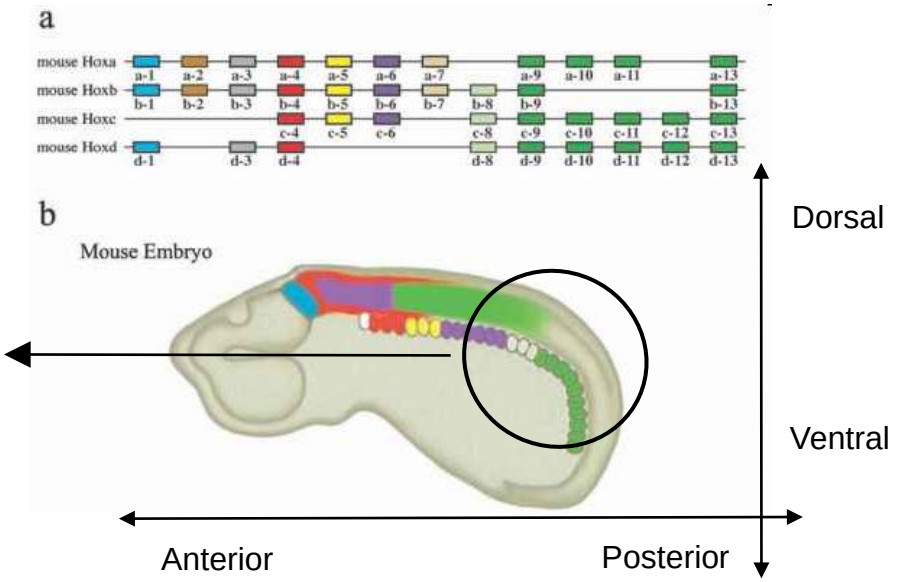
hand-foot-genital syndrome – mutation HOXA13
synpolydaktylia – mutation HOXD13

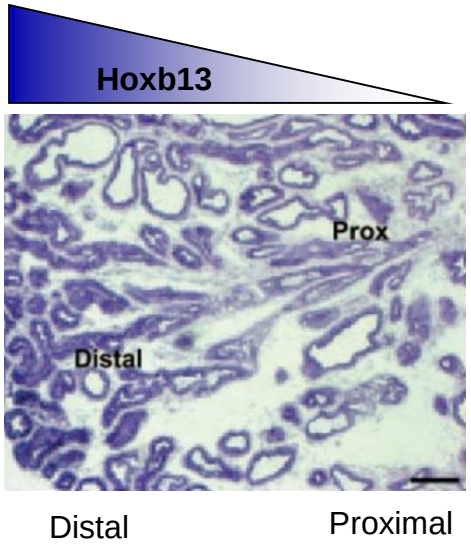
Hox komplex a morphogenetic field

Example: Differentiation of mouse urogenital tract (prostate)

doi: 10.1210/en.2006-1250



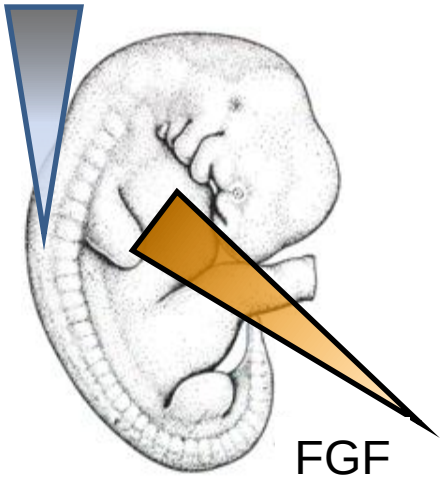




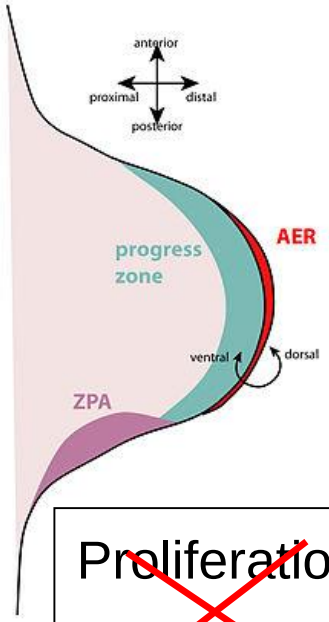
Temporo-spatial **expression** of different regulators determines final **localization**, o**rientation** and **morphology** of a tissue.

Limb formation

HOX

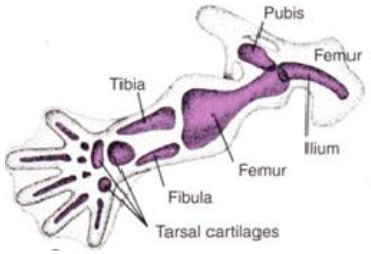


FGF
IGF
…

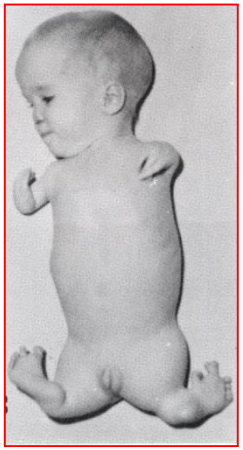


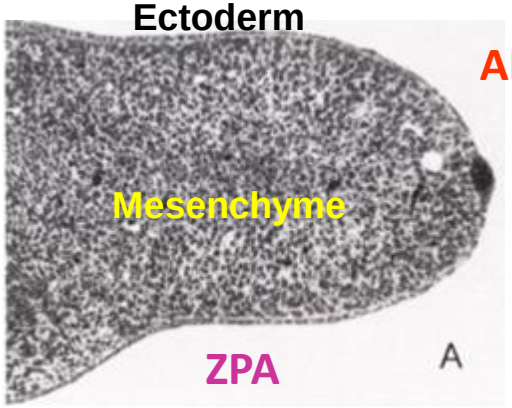
Proliferation

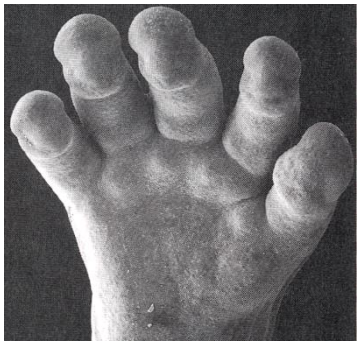
Vascularisation



Thalidomid



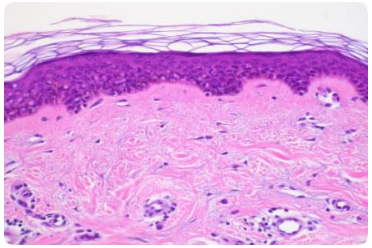




Contemporary tissue classification

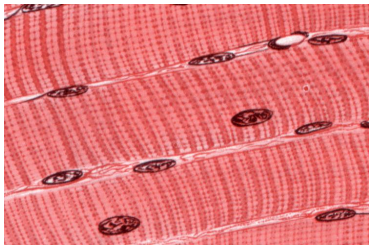
Based on **morphology** and **function**:

Epithelium



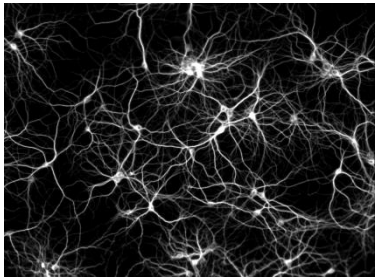
Continual, avascular layers of cells with different function, oriented to open space, with specific junctions and minimum of ECM and intercellular space.
Derivates of all three germ layers

Muscle



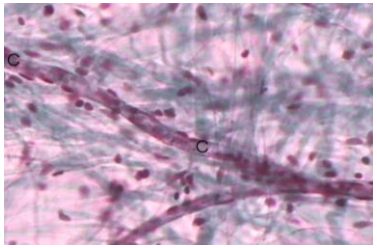
Myofibrils → contraction
Mesoderm – skeletal muscle, myocard, mezenchyme – smooth muscles
Rarely ectoderm (eg. m. sphincter a m. dilatator pupillae)

Nerve

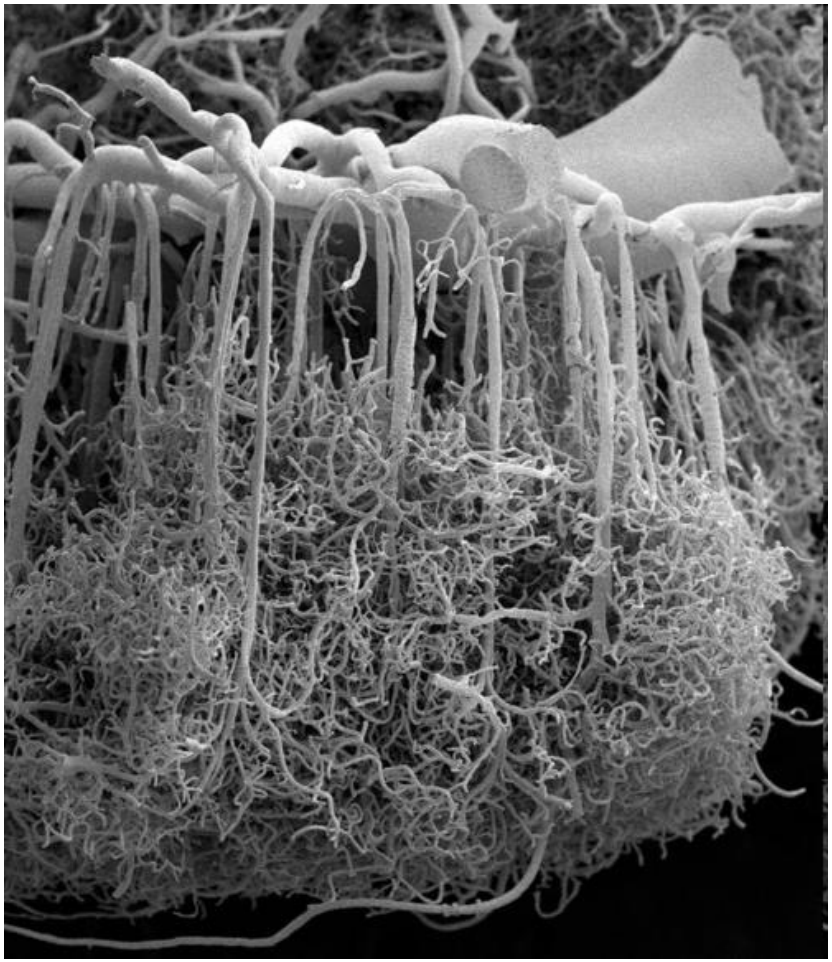


Neurons and neuroglia
Reception and transmission of electric signals
Ectoderm, rarely mesoderm (microglia)

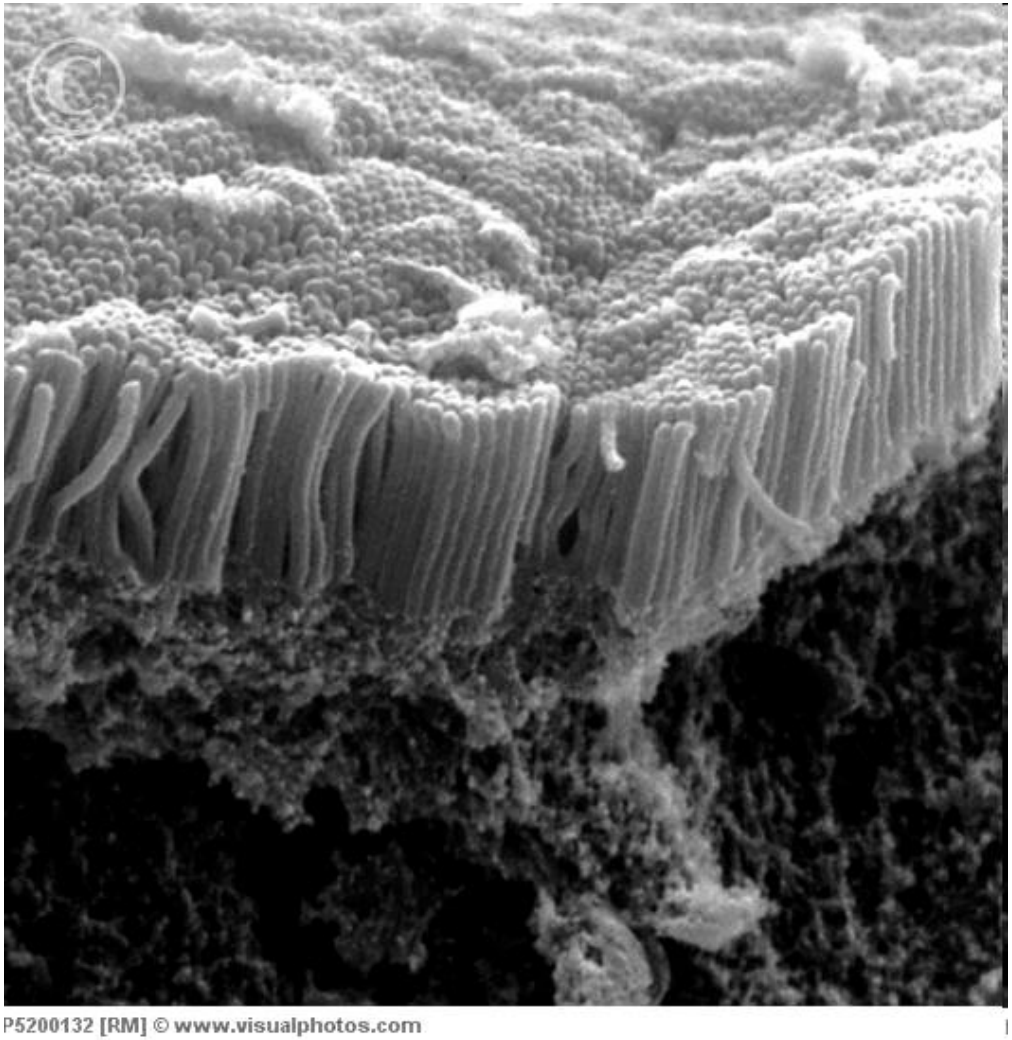
Connective



Dominant extracellular matrix
Connective tissue, cartilage, bone…
Mesenchyme

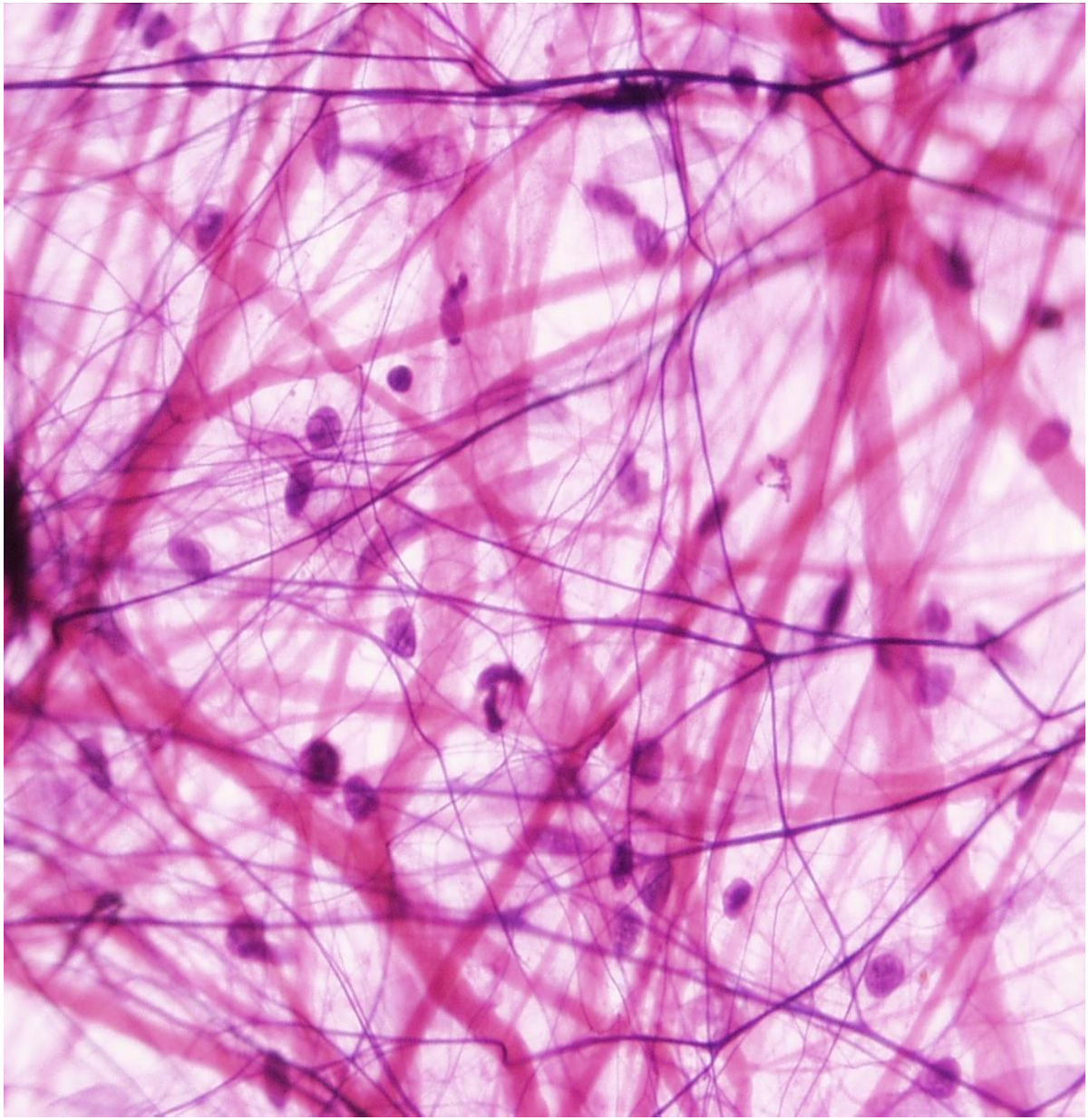


Isocortex vascularisation



Microvilli on surface of small intestine

http://www.livescience.com/14413-brain-images-portraits-mind.html



Connective tissue

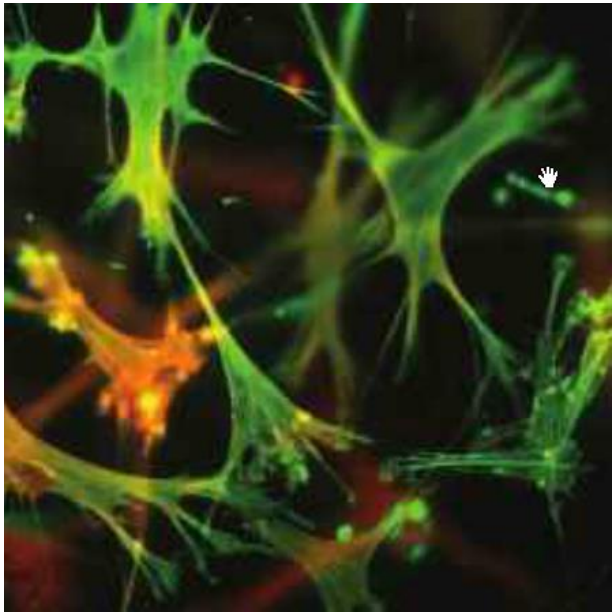
Not only a tissue glue…

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

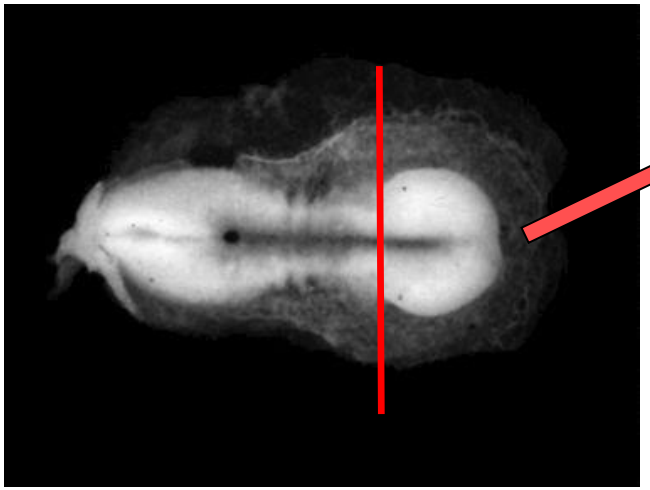
Amorphous component (amorphous ground substance)
- Complex matrix consisting of glycosaminoglycans, glycoproteins and proteoglycans,

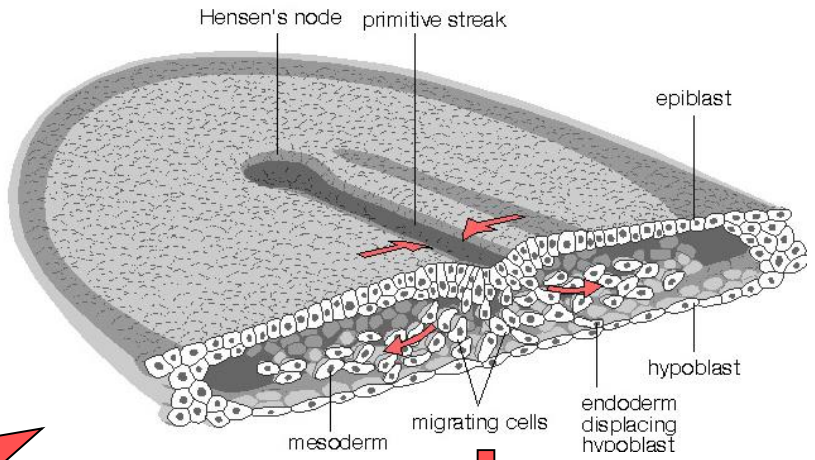
depending on tissue type (connective × ligament × cartilage × bone)

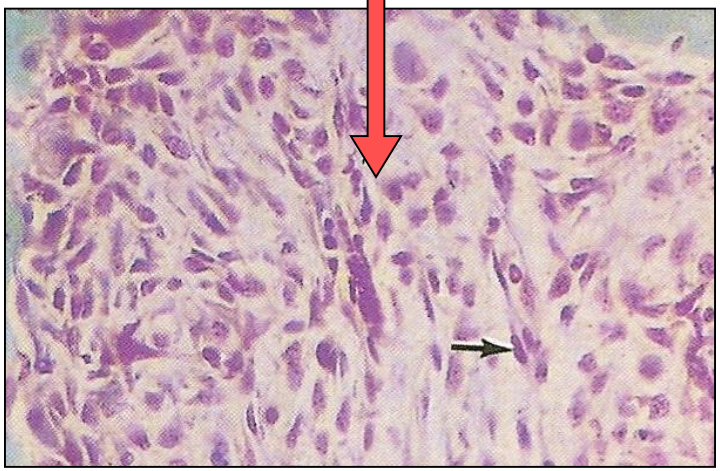
Embryonic origin of CT

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

DAY 12 of embryonic development

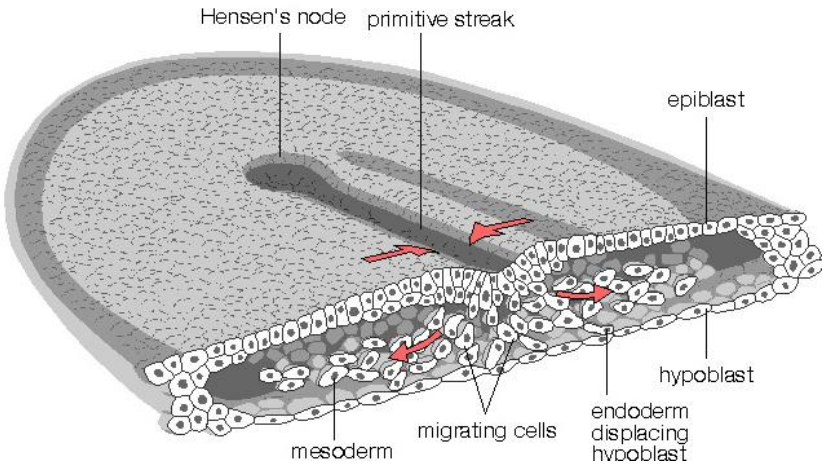


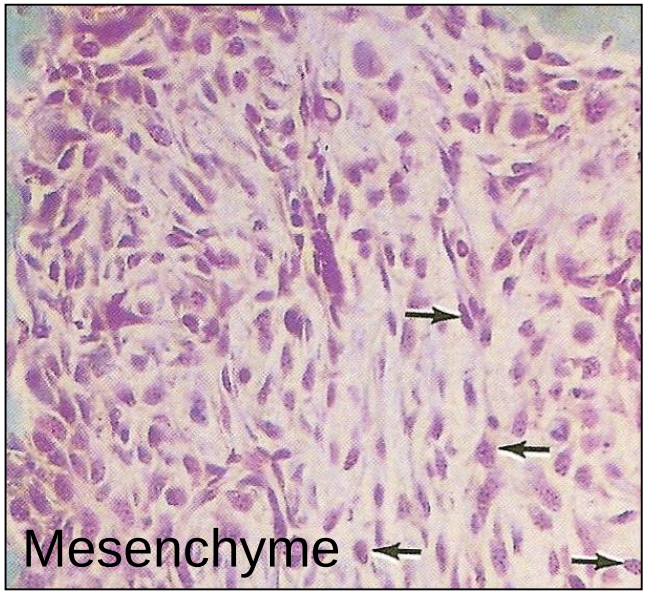


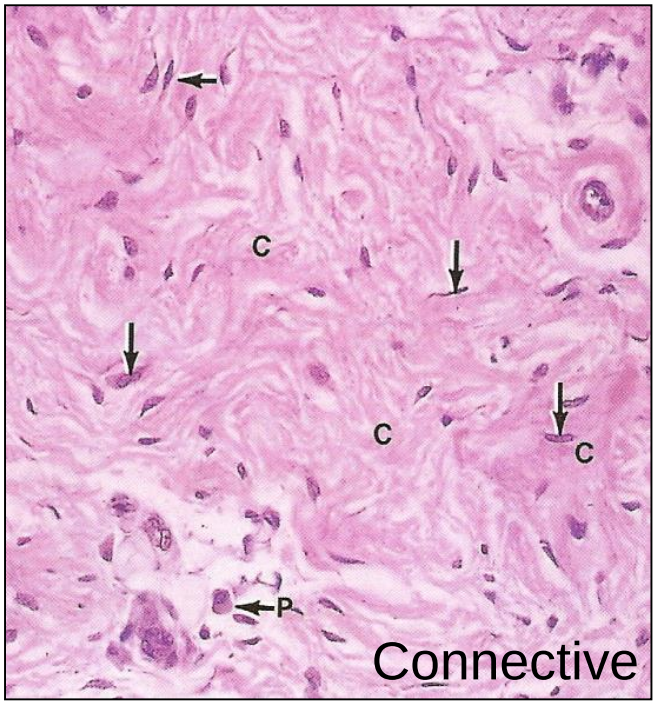


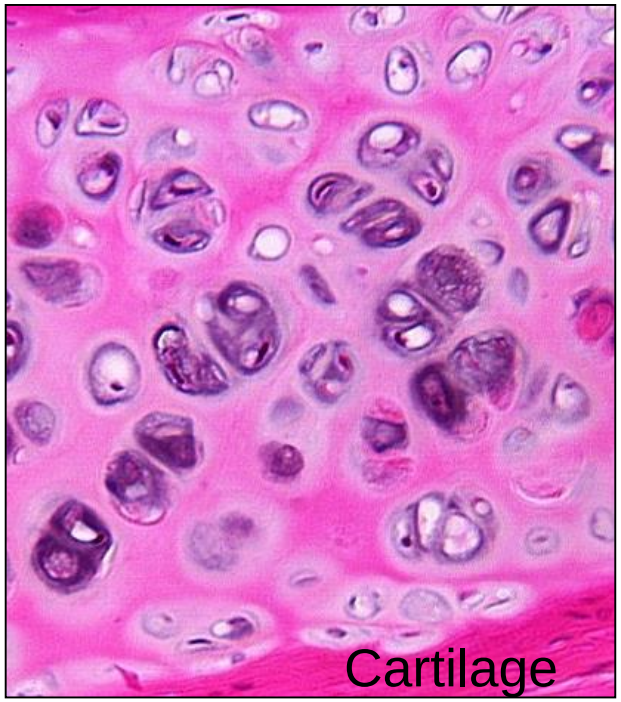
http://www.mun.ca/biology/desmid/brian/BIOL3530/DB_Ch02/DBNModel.html

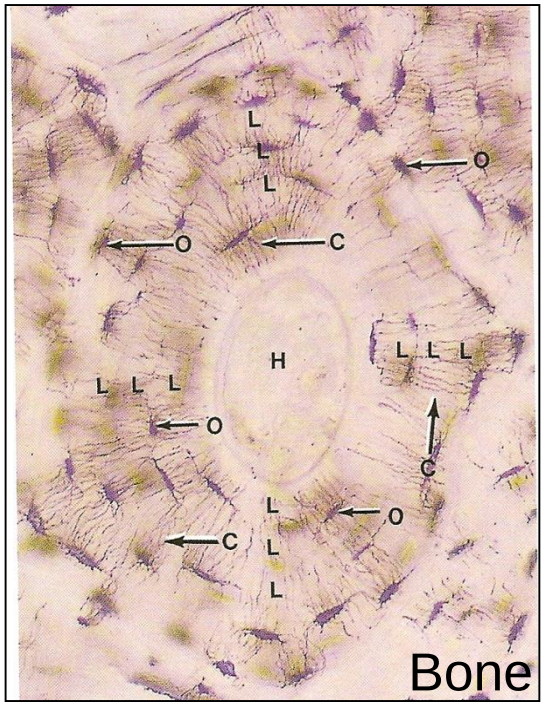
- Basic derivatives of CT











Classification of CT

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

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

} CT

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

} Specialized CT

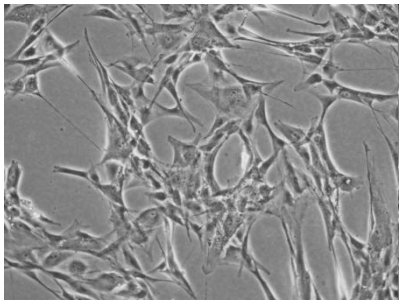
- Blood and hematopoietic tissue
- Lymphatic tissue

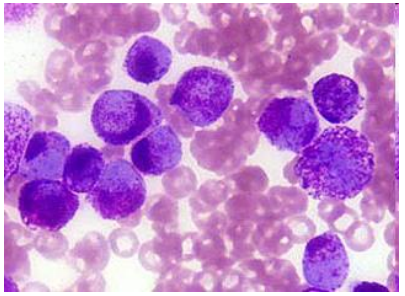
} Trophic CT (body liquids)

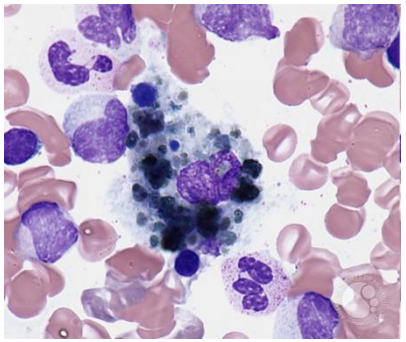
Cells of connective tissue

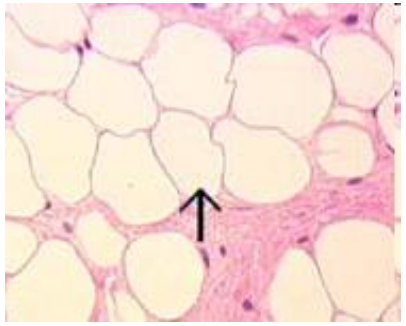
Cells

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



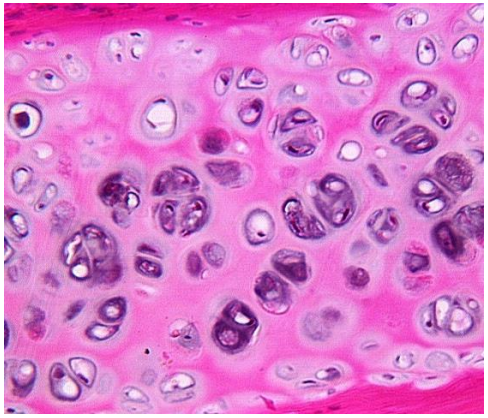


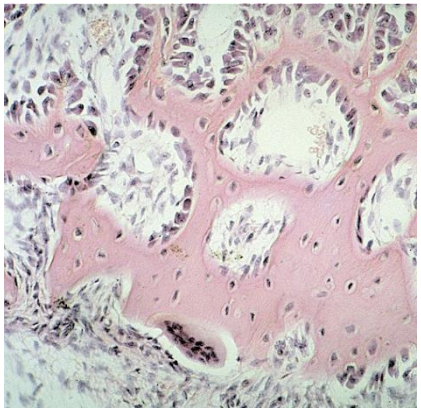


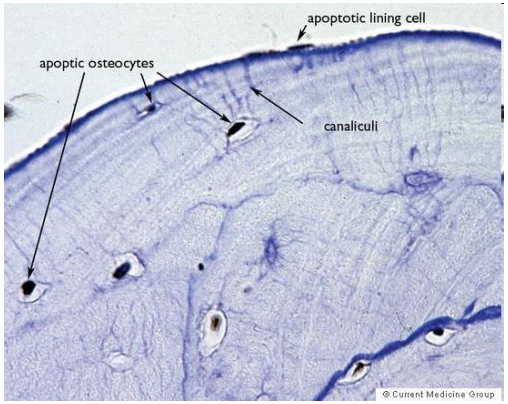


Extracellular matrix

- Fibrous compound
- Amorphous ground substance

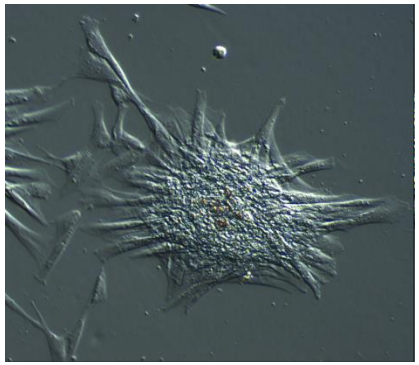


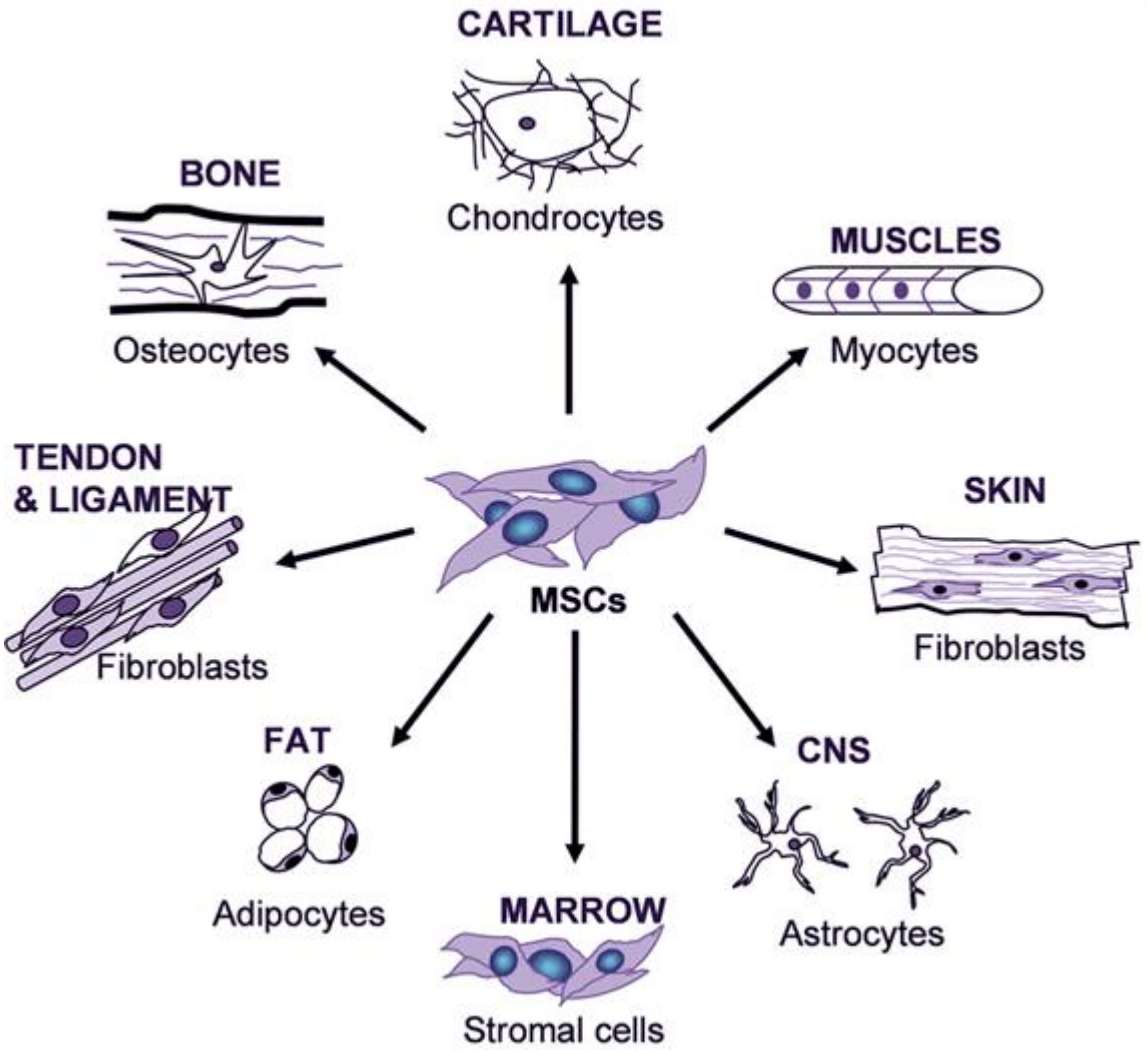




Cells of connective tissue

Mesenchymal (adult) stem cells



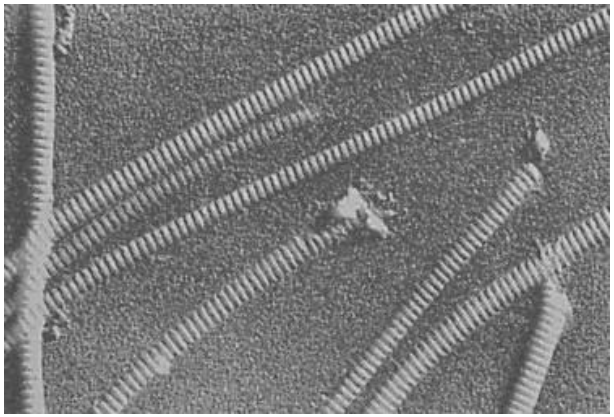


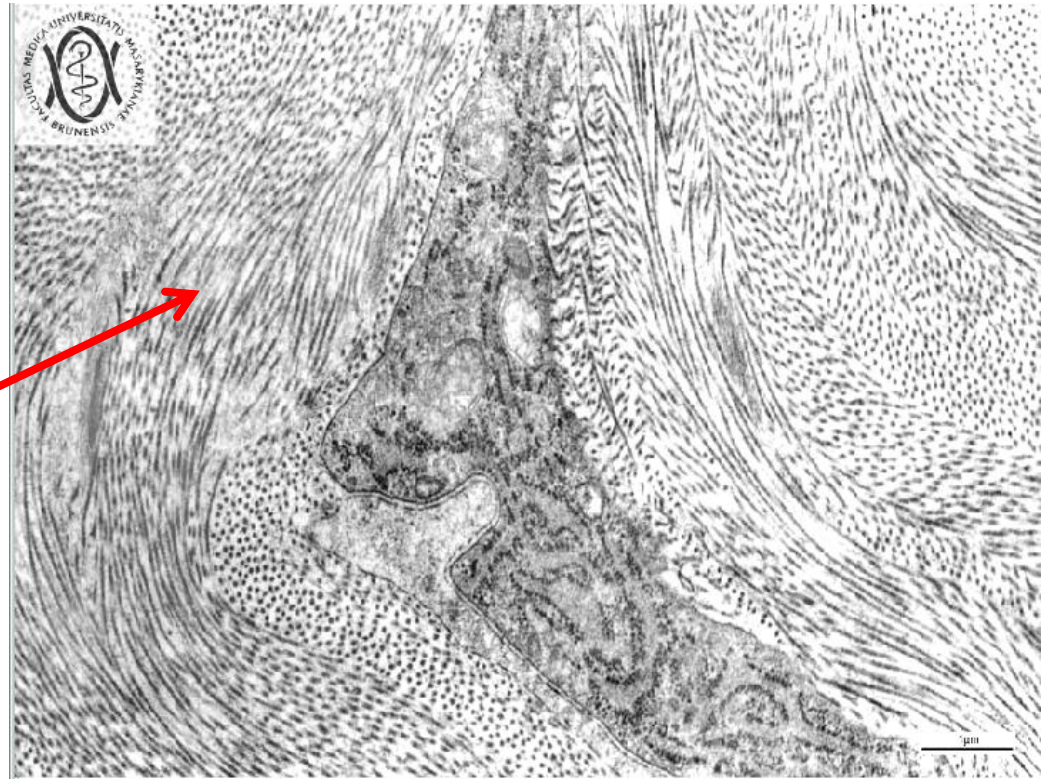
Koch *et al. BMC Biotechnology* 2007 7:26 doi:10.1186/1472-6750-7-26

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)

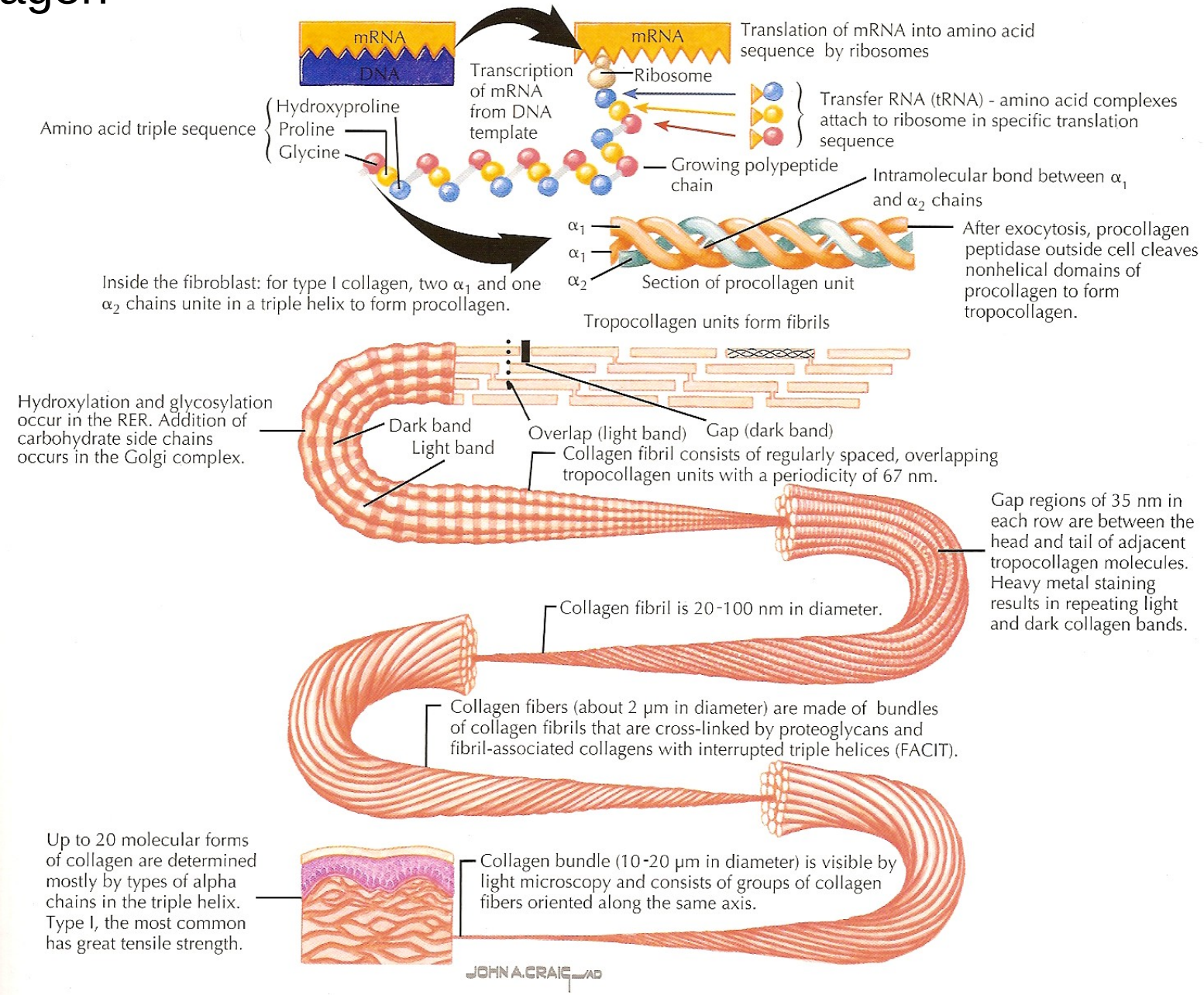




- Collagen

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 glycoprotiens, reticular network	Shape formation
IV	Basal lamina of epithelium and endtohelium, 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


mRNA
DNA
Transcription of mRNA from DNA template
mRNA
Ribosome
Translation of mRNA into amino acid sequence by ribosomes
Transfer RNA (tRNA) - amino acid complexes attach to ribosome in specific translation sequence
Amino acid triple sequence
Hydroxyproline
Proline
Glycine
Growing polypeptide chain
Intramolecular bond between α_1 and α_2 chains
α_1
α_1
α_2
Section of procollagen unit
After exocytosis, procollagen peptidase outside cell cleaves nonhelical domains of procollagen to form tropocollagen.
Inside the fibroblast: for type I collagen, two α_1 and one α_2 chains unite in a triple helix to form procollagen.
Tropocollagen units form fibrils
Hydroxylation and glycosylation occur in the RER. Addition of carbohydrate side chains occurs in the Golgi complex.
Dark band
Light band
Overlap (light band)
Gap (dark band)
Collagen fibril consists of regularly spaced, overlapping tropocollagen units with a periodicity of 67 nm.
Gap regions of 35 nm in each row are between the head and tail of adjacent tropocollagen molecules. Heavy metal staining results in repeating light and dark collagen bands.
Collagen fibril is 20-100 nm in diameter.
Collagen fibers (about 2 μm in diameter) are made of bundles of collagen fibrils that are cross-linked by proteoglycans and fibril-associated collagens with interrupted triple helices (FACIT).
Up to 20 molecular forms of collagen are determined mostly by types of alpha chains in the triple helix. Type I, the most common has great tensile strength.
Collagen bundle (10-20 μm in diameter) is visible by light microscopy and consists of groups of collagen fibers oriented along the same axis.
JOHN A. CRAIG, MD

- Collagen in LM

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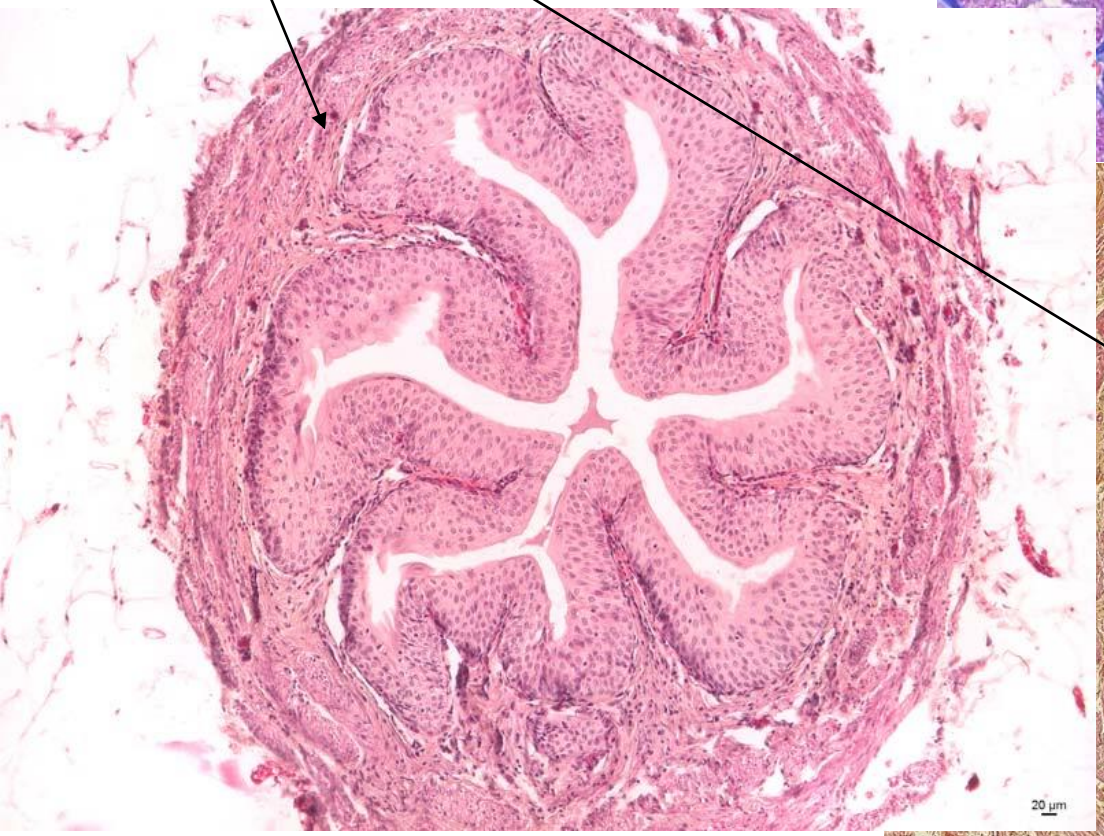
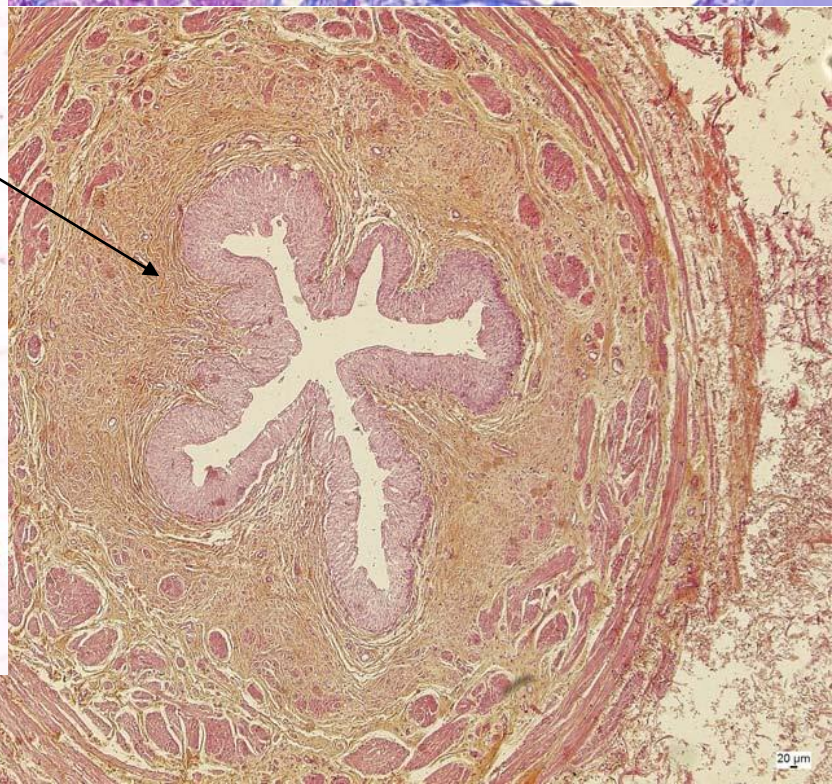




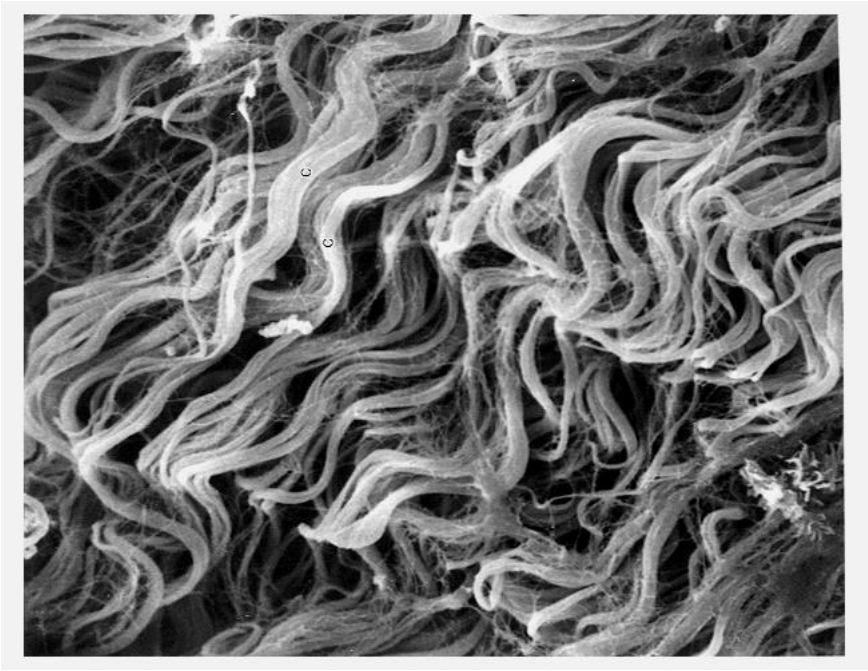
Julian Voss-Andreae "Unraveling Collagen",

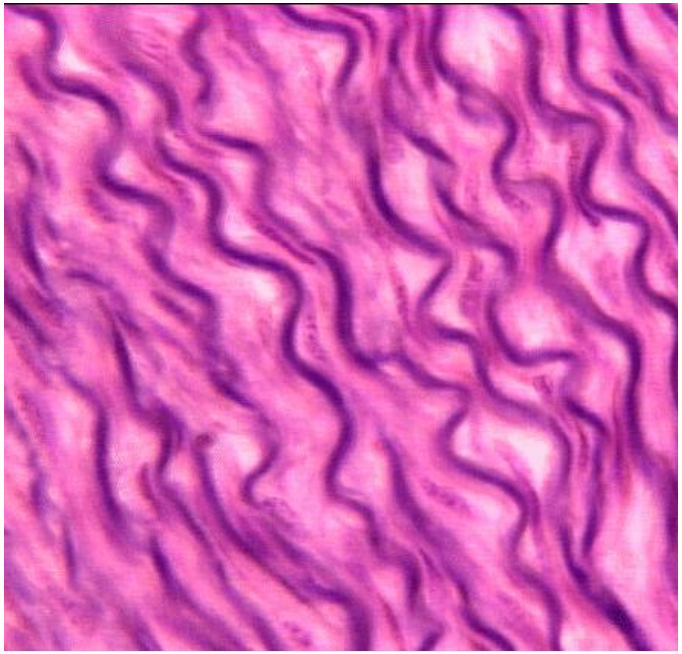
2005

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

Elastic fibers

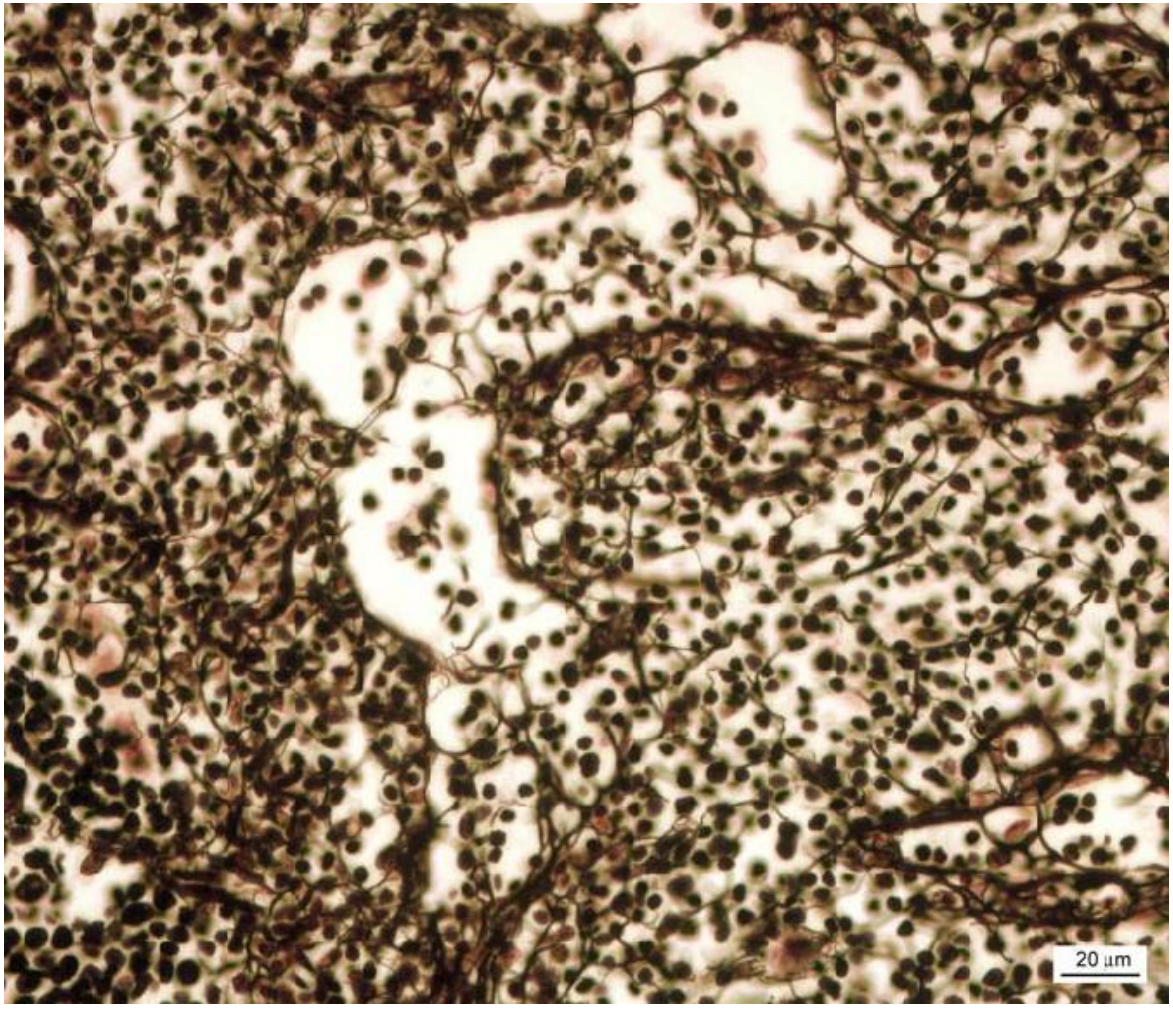
- less abundant than collagen
- polymer – tropoelastin
- minimal tensile resistance, loss of elasticity if overstretched
- reduction of hysteresis = allow return back to original state after mechanic change





Reticular fibers

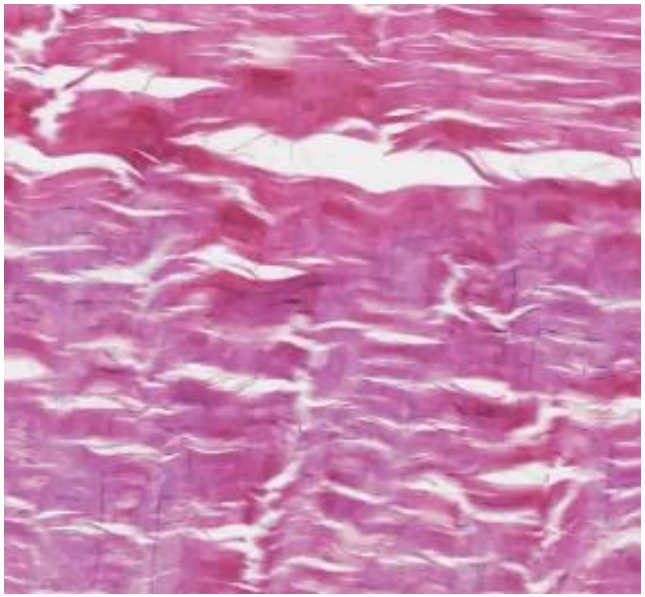
- collagen 3D meshwork
- bone marrow, spleen, lymphatic nodules
- microenvironment for e.g. hematopoietic stem cells and progenitors

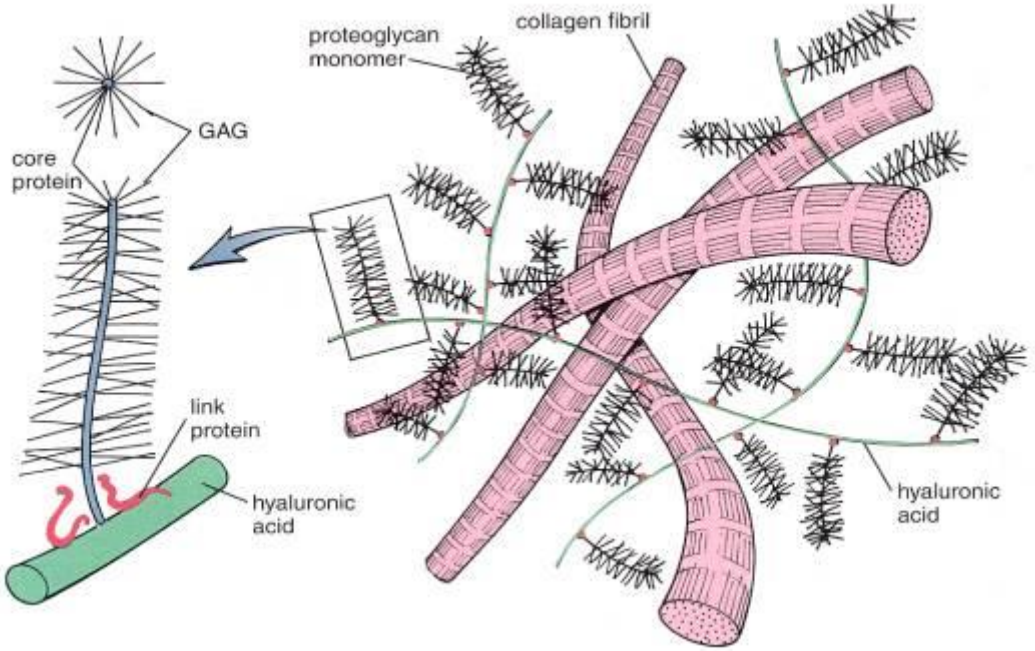


Extracellular matrix – ground matrix

Amorphous extracellular matrix

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



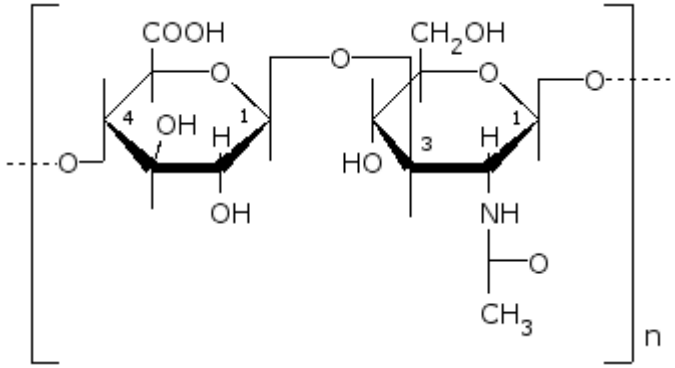


- Glycosaminoglycans

linear polysaccharides composed of two disaccharide subunits – uronic acid and hexosamine

polysaccharides rich in hexosamines = acid mukopolysaccharides

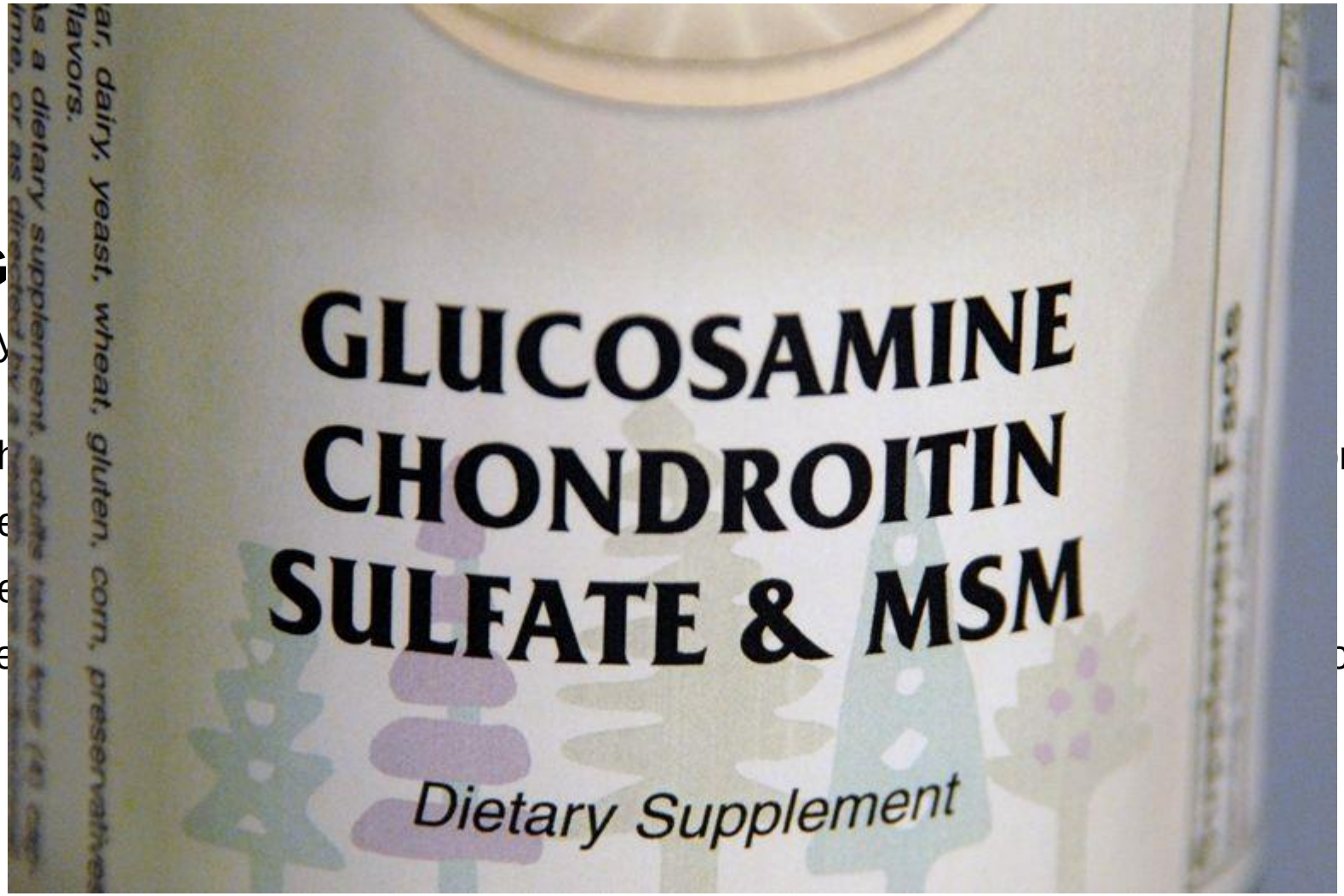
glucuronic or iduronic acid



glucosamin or galactosamin

- Glycosaminoglycans

They bind to protein structures (except for hyaluronic acid)



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Proteoglycans

— protein + dominant <u>linear</u> saccharide component

— proteoglycan aggregates

— water-binding, volume dependent of hydratation

— aggrecan (cartilage)
— syndecan
— fibroglycan

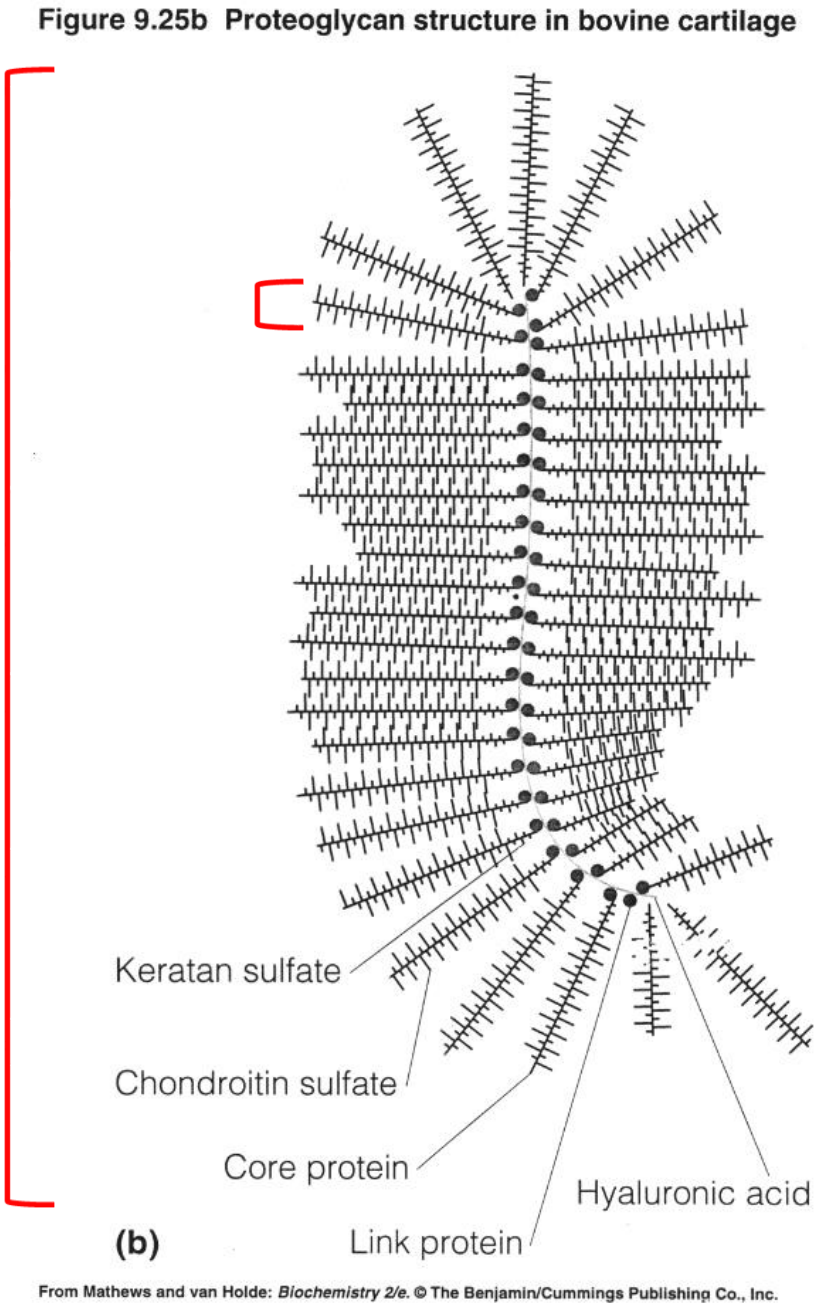
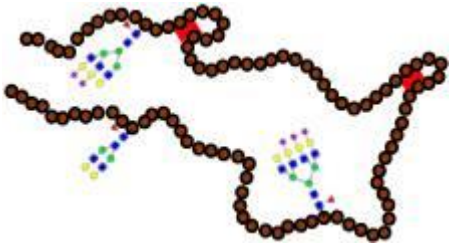


Figure 9.25b Proteoglycan structure in bovine cartilage

From Mathews and van Holde: *Biochemistry 2/e.* © The Benjamin/Cummings Publishing Co., Inc.

Structural glycoproteins

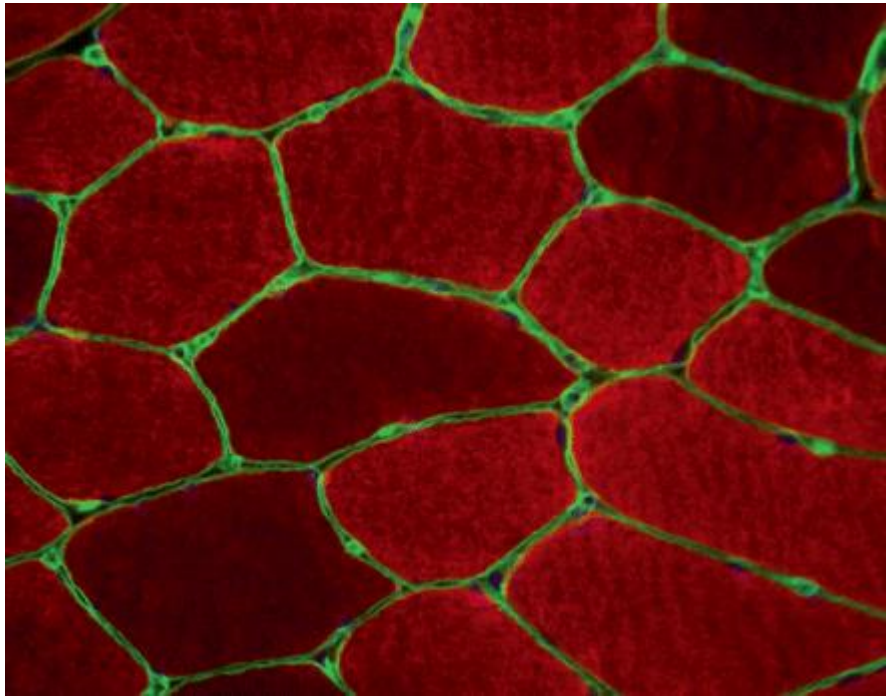


- dominant protein + branched saccharide component
- interaction between cells and ECM

— **fibronectin** – connects collagen fibers and glykosaminoglycans, cell adhesion and migration

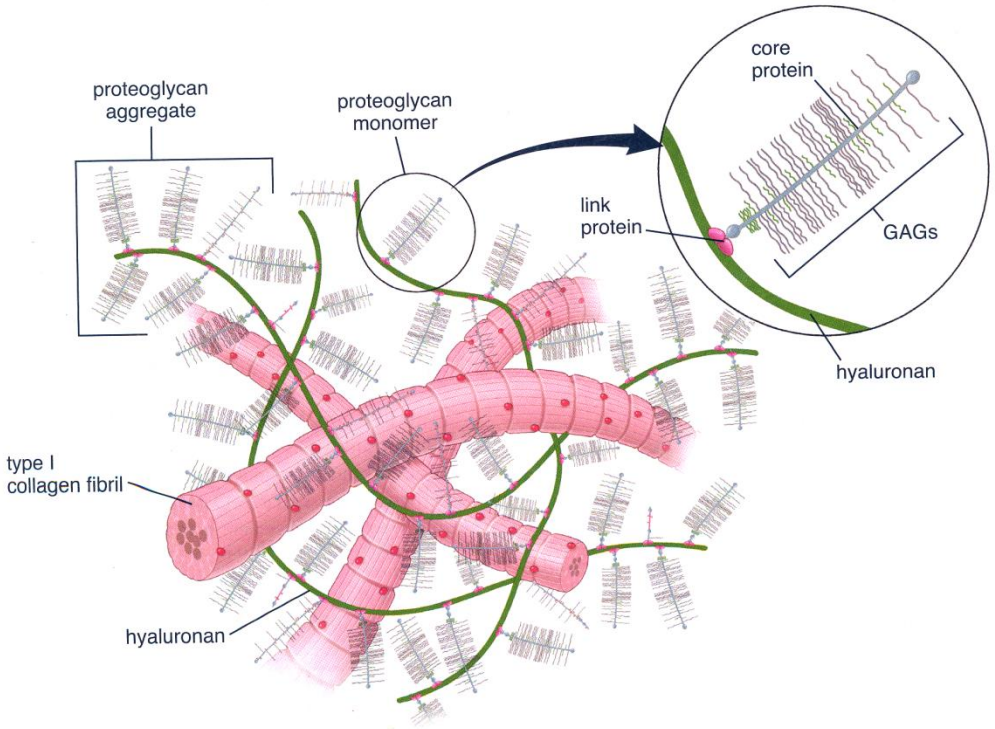
— **laminin** – basal lamina – epithelial integrity

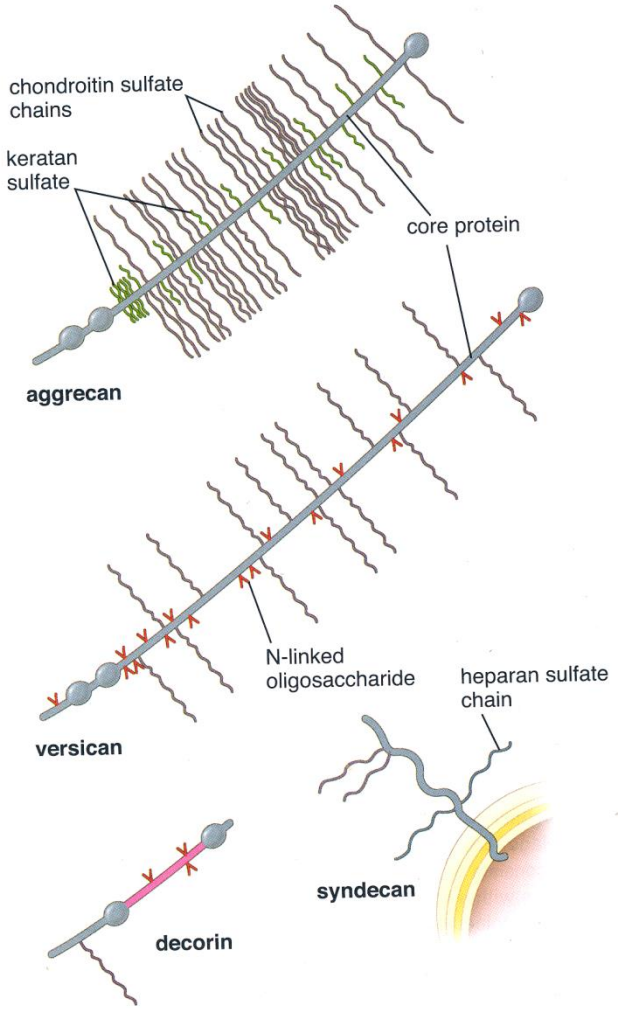
— **chondronectin** – cartilage – adhesion of chondrocytes to collagen



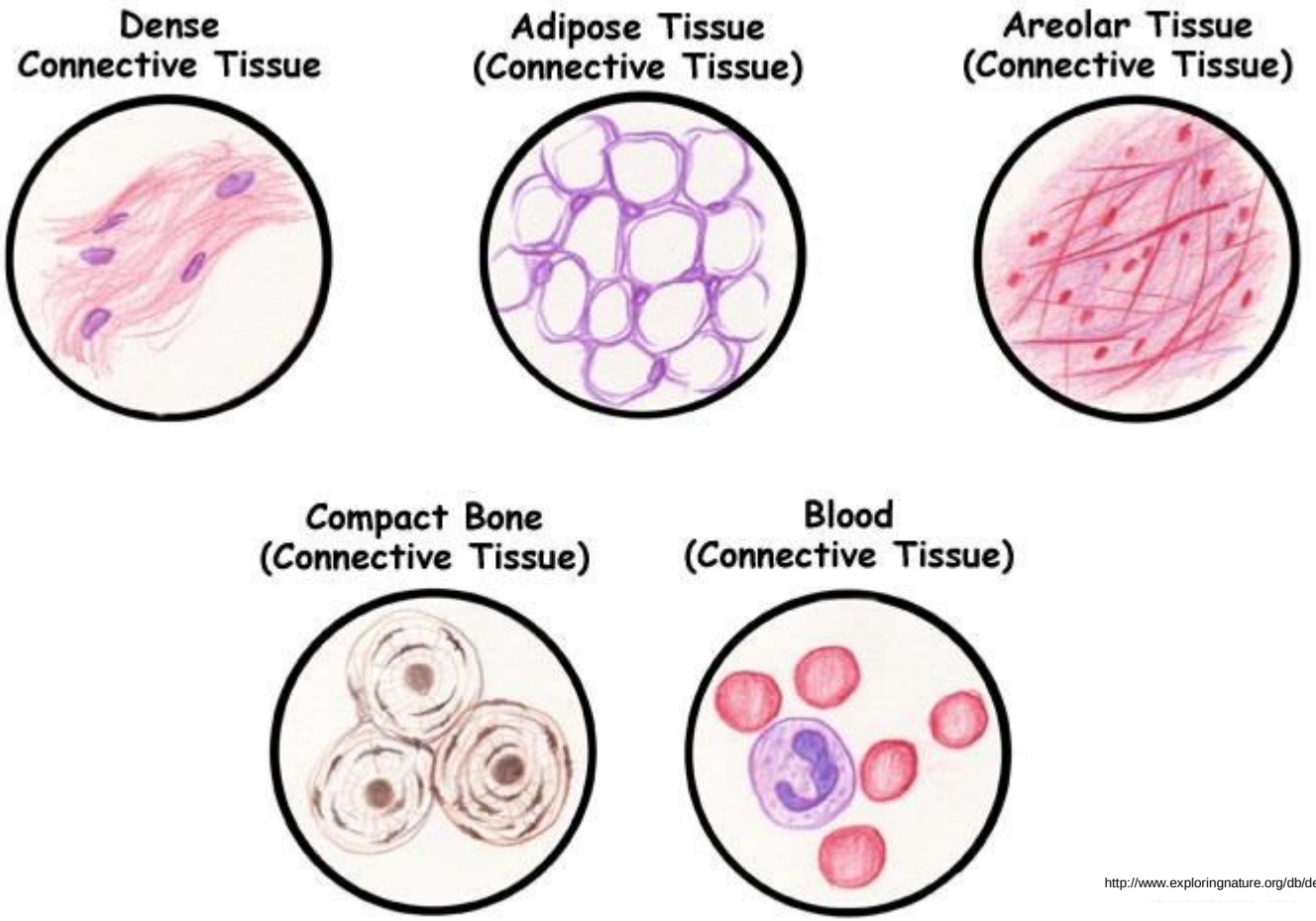
(J. Nutr. 136:2123-2126, 2006)

- Composition of amorphous ground matrix





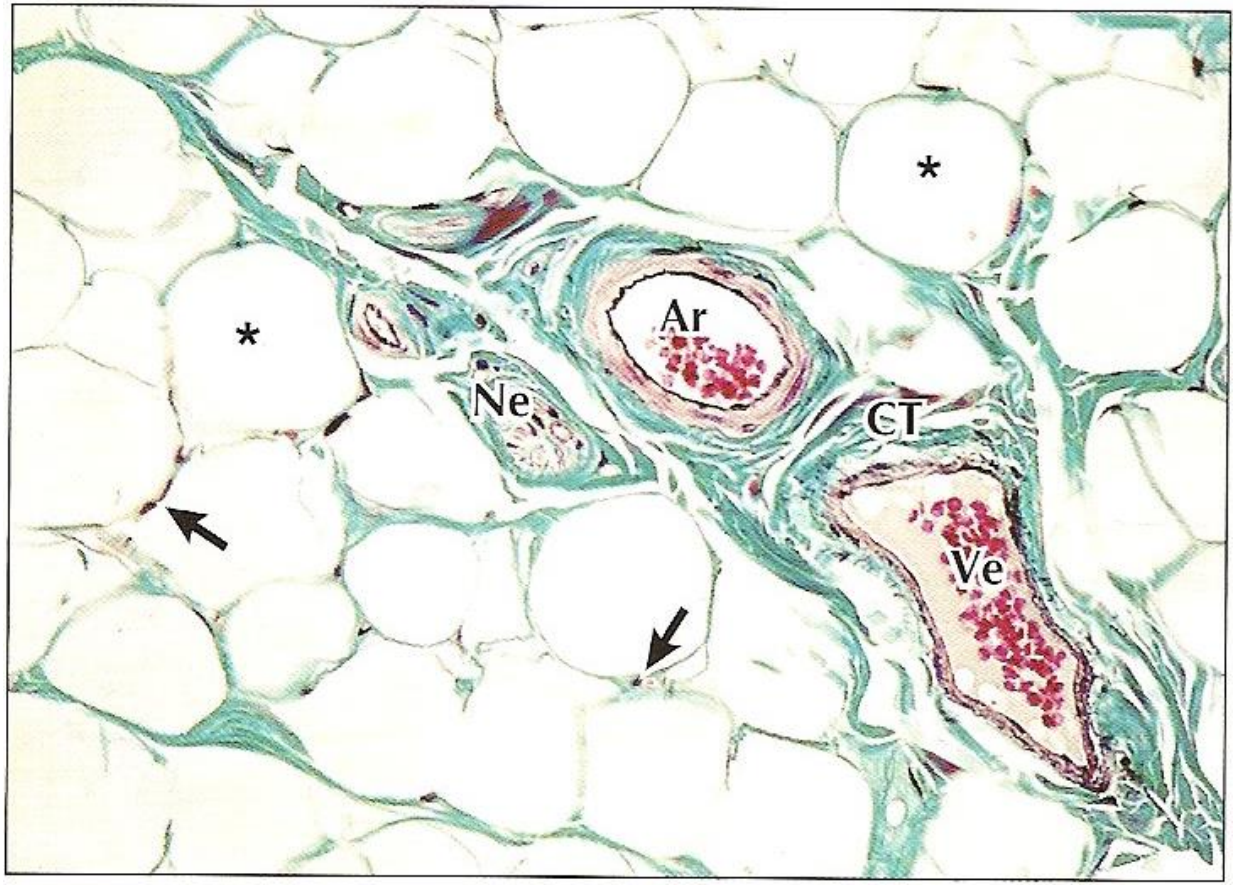
- **Classification of specialized connective tissue**



http://www.exploringnature.org/db/detail.php?dbID=21&detID=691

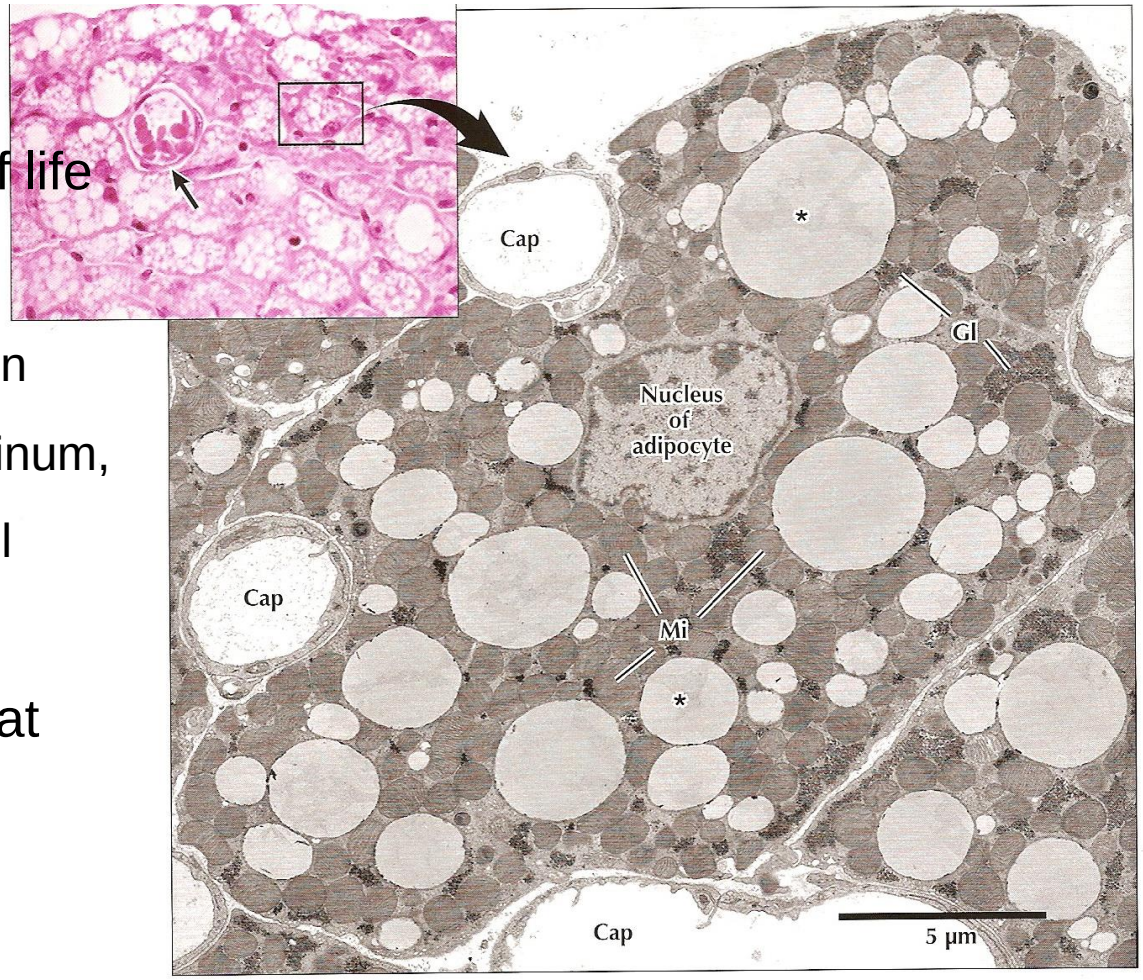
Adipose tissue

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



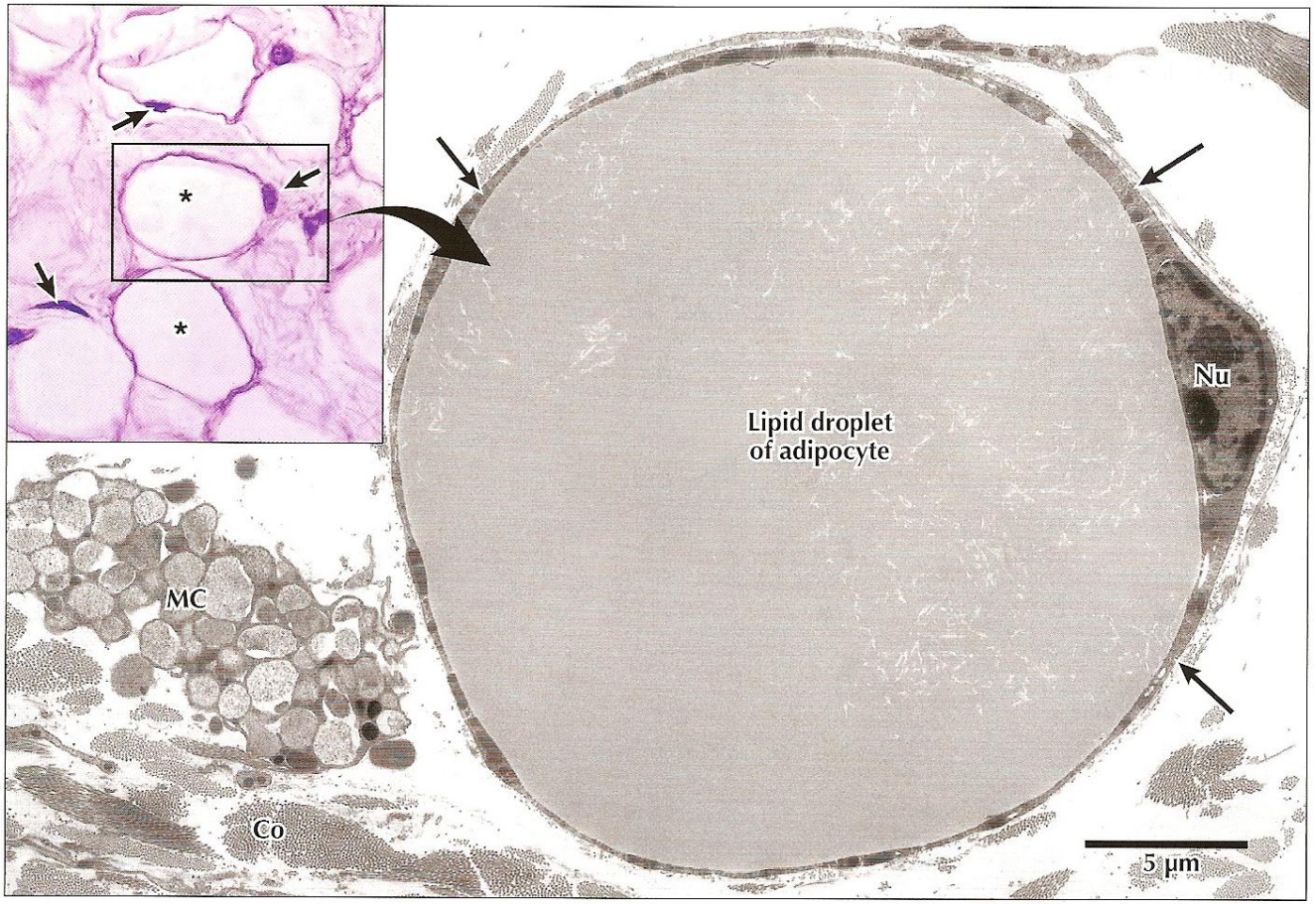
Brown adipose tissue

- fetus and child to 1st 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



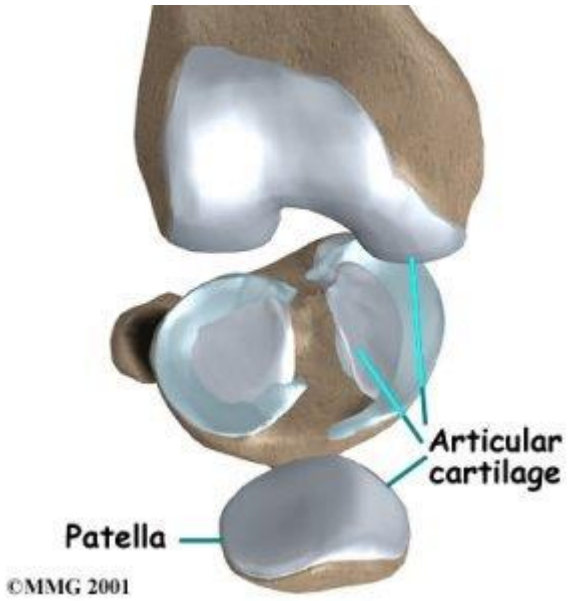
White adipose tissue

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



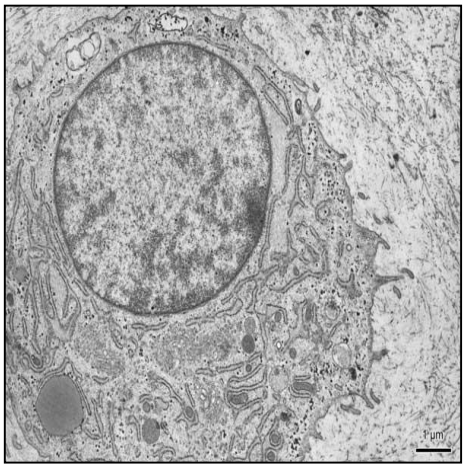
- Cartilage

— specialized connective tissue with continuous ECM
— flexible, mechanically resistant
— avascular, no innervation
— support of soft tissues
— diarthrosis
— growth



Composition and structure

- perichondrium – connective tissue around cartilage (not present in joints)
- chondroblasts, chondrocytes
- extracellular matrix (collagen and elastic fibers, amorphous ground matrix)



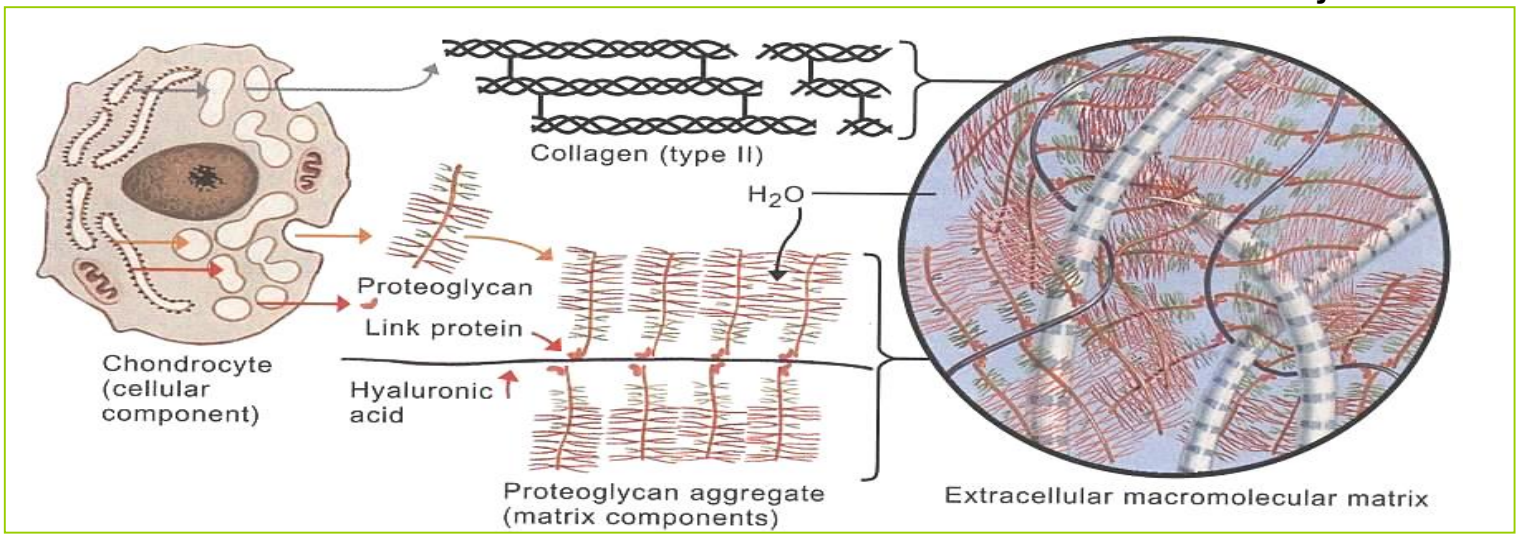
Collagen type II

Glykosaminoglycans

(Hyaluronic acid, chondroitinsulphate, keratansulphate)

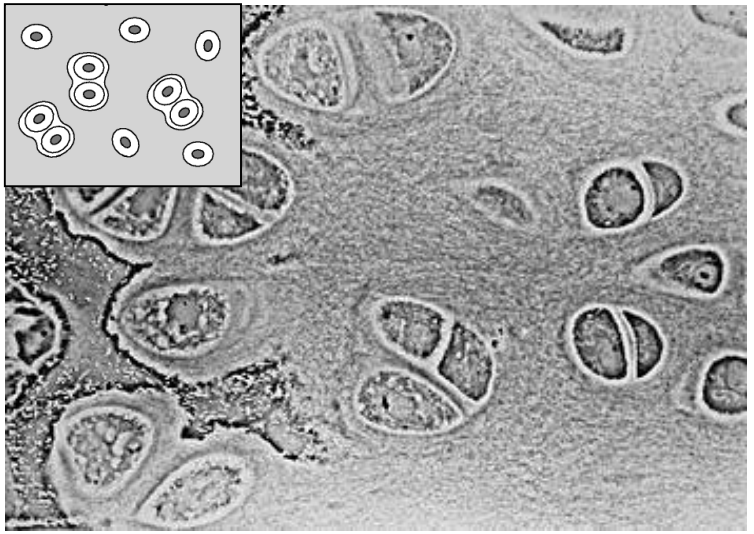
Proteoglycane aggregates

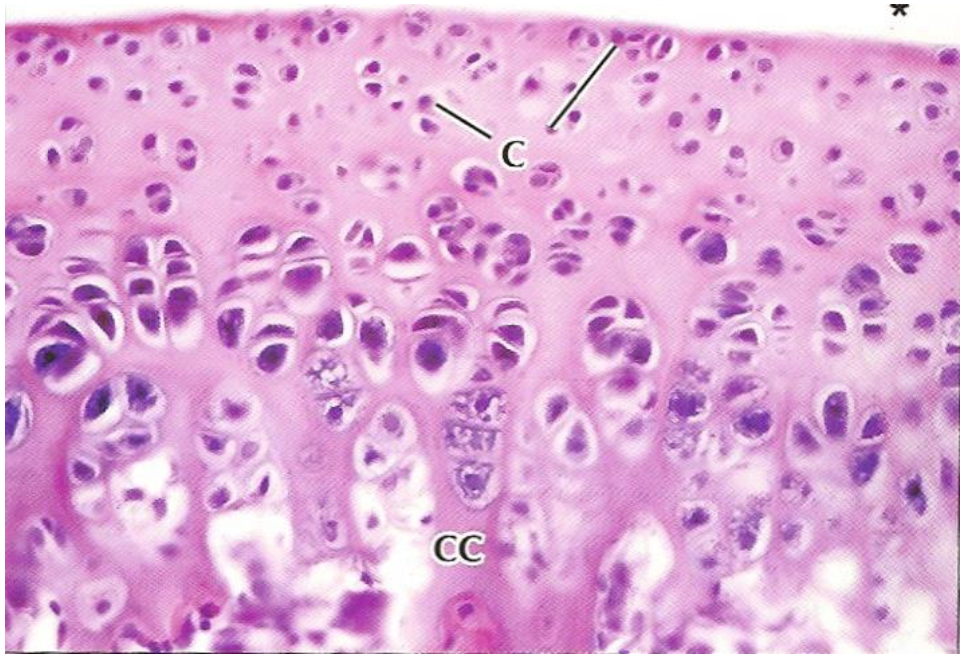
Hydrophilic character – holds water → low friction → smooth movement of joints

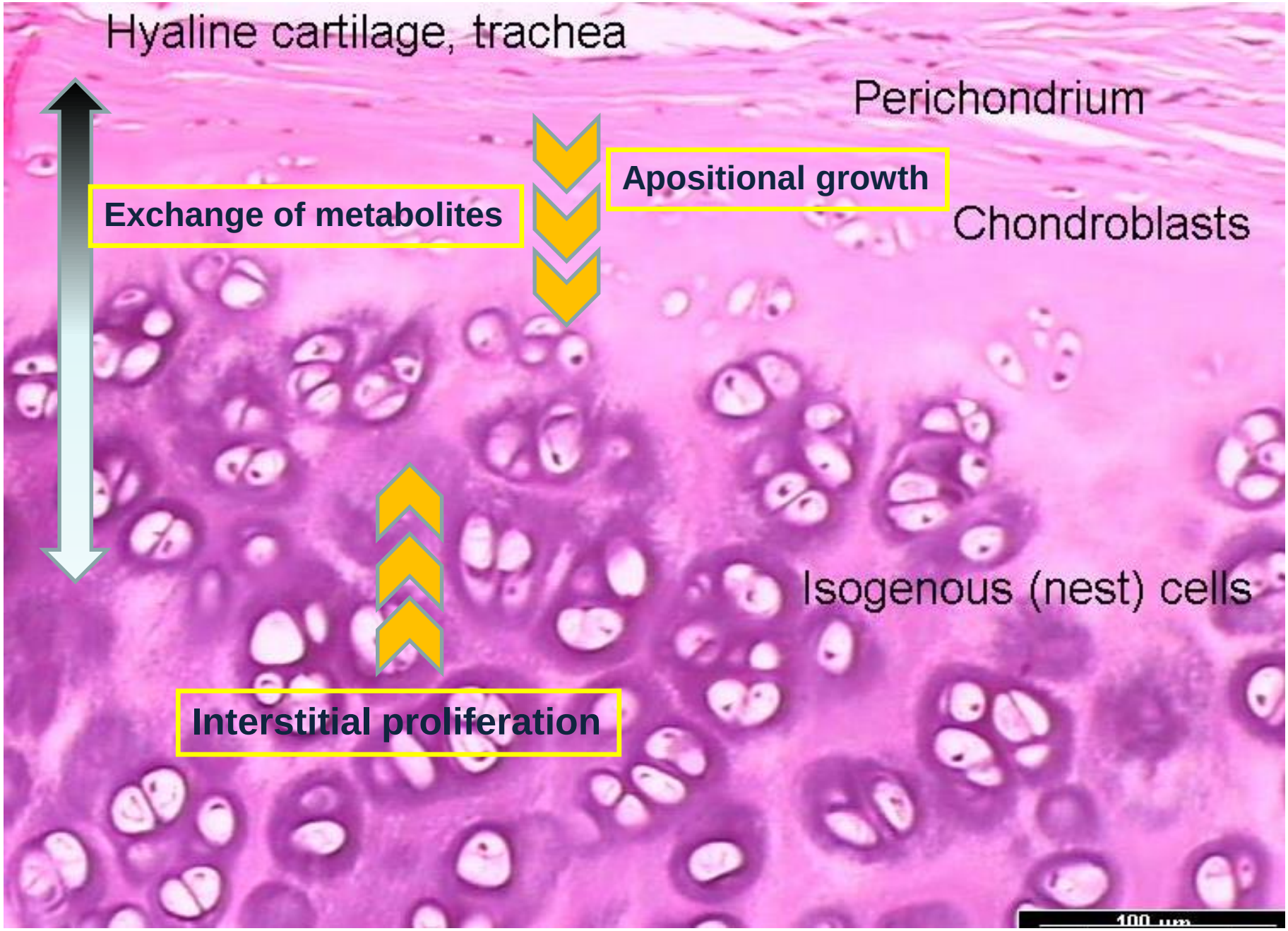


Hyaline cartilage

- most abundant
- temporary embryonal/fetal skeleton
- epiphyseal growth plate
- articulation (joints) respiratory passages
- isogenic groups





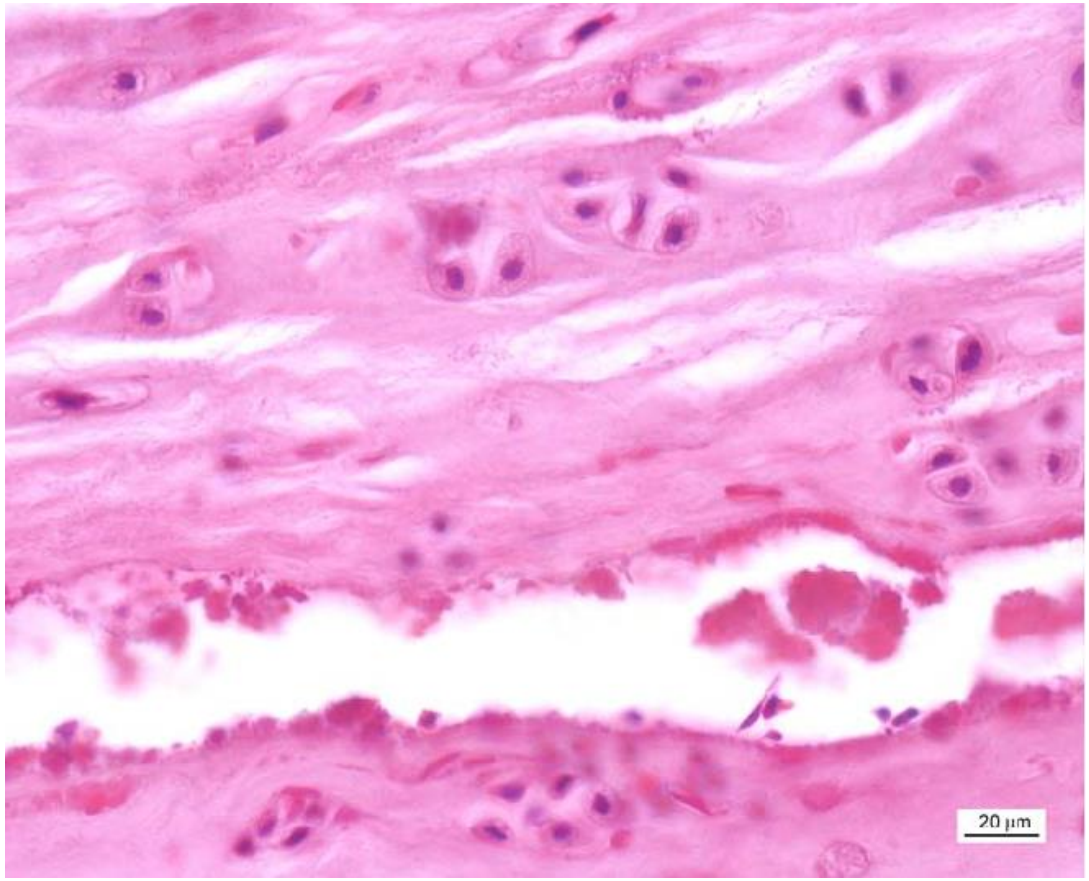

Hyaline cartilage, trachea
Perichondrium
Apositional growth
Exchange of metabolites
Chondroblasts
Isogenous (nest) cells
Interstitial proliferation
100 µm

Elastic cartilage

- Elastic fibers in matrix
- No isogenetic groups
- Auricula, meatus, larynx, epiglottis

Fibrocartilage

- Fibrous compound dominant – collagen I and II – mechanical durability
- Minimum of amoprhous matrix-fibers visible
- Intervertebral discs, symphysis pubis, articular discs, meniscus

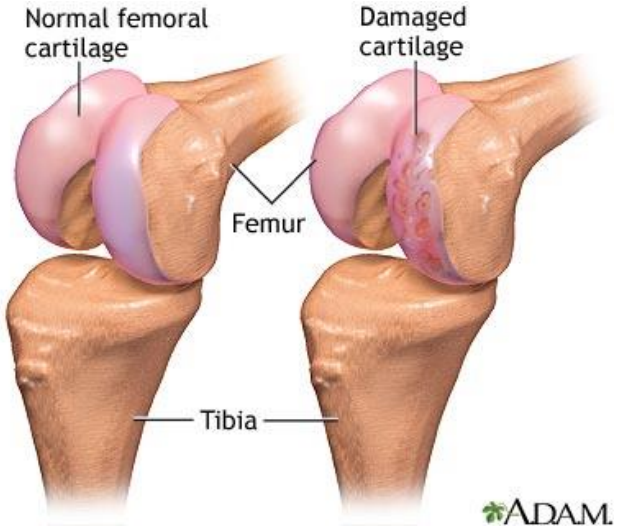


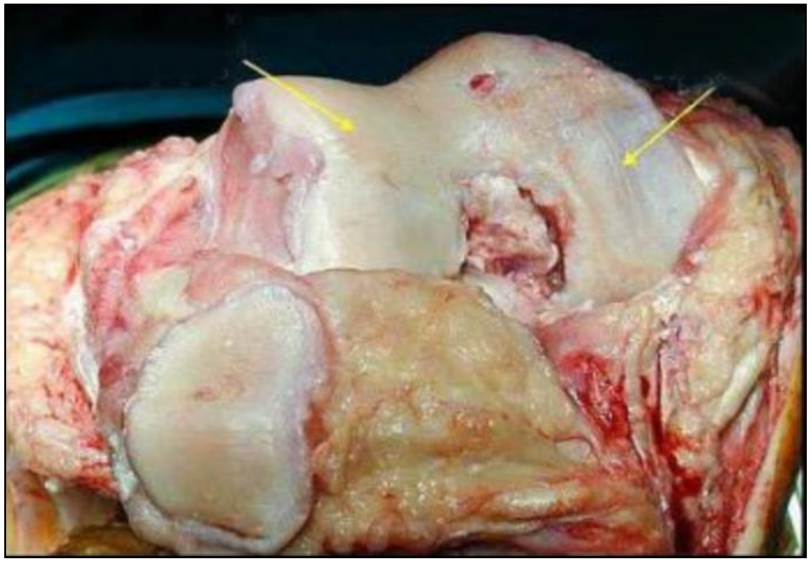
Clinical correlations

Cartilage – no innervation, no vascularization – no spontaneous regeneration

No migration of chondrocytes to site of damage

Initiation of other degenerative events leading to cartilage erosion (arthritis)





Therapy:

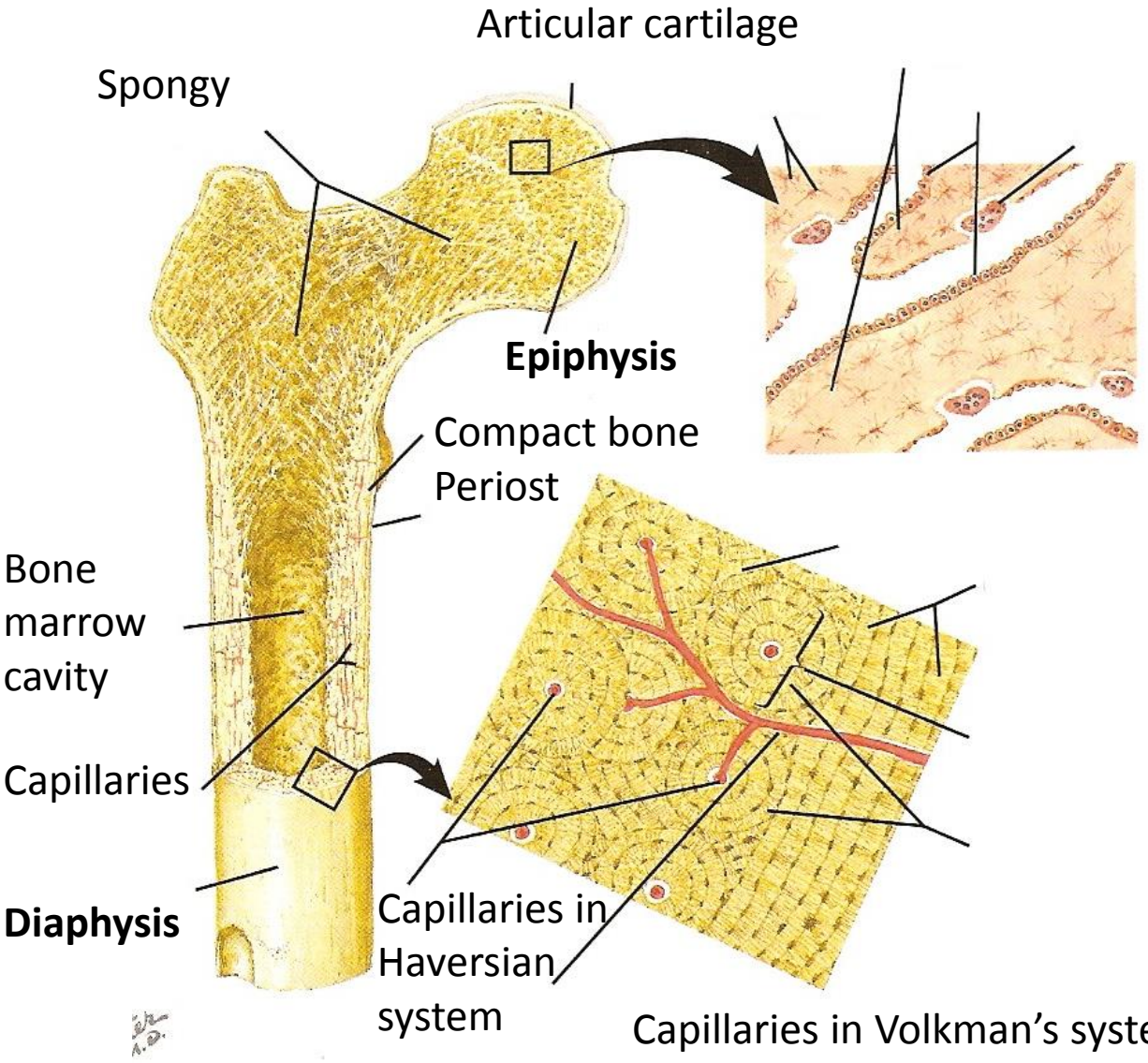
- joint mobility

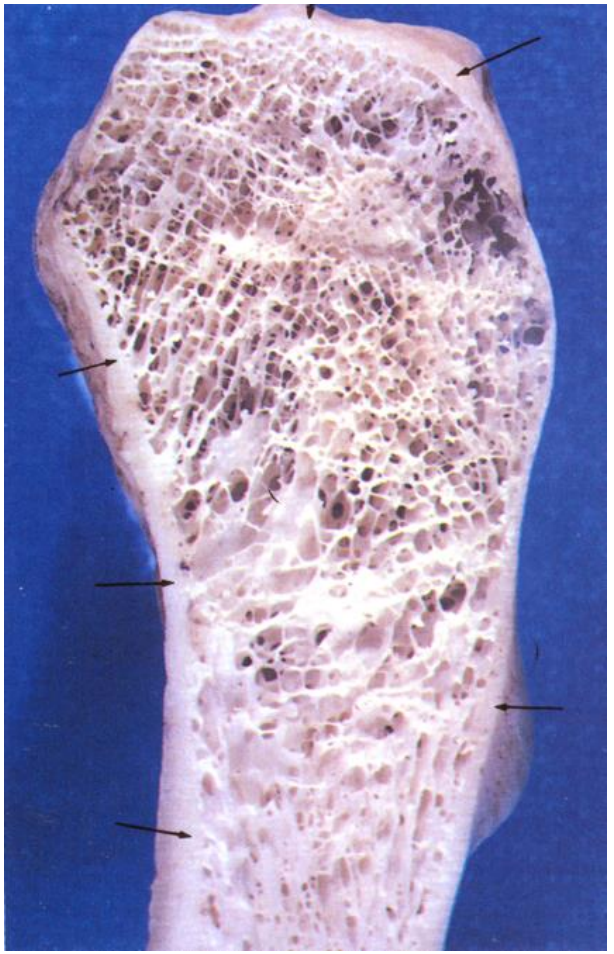
- restoration of biochemical and biophysical parameters of cartilage

- prevention of further damage

- removal of damaged tissue, autologous transplantation, MSCs on biocompatible scaffolds

- Bone

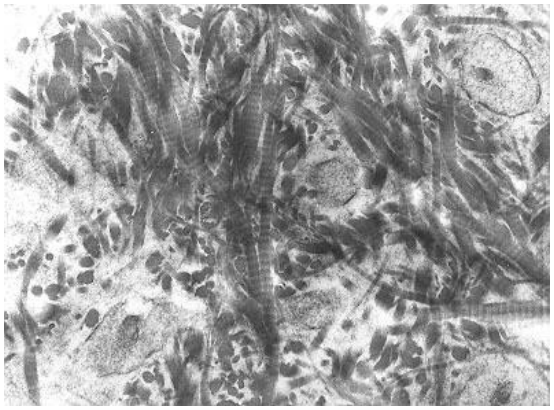




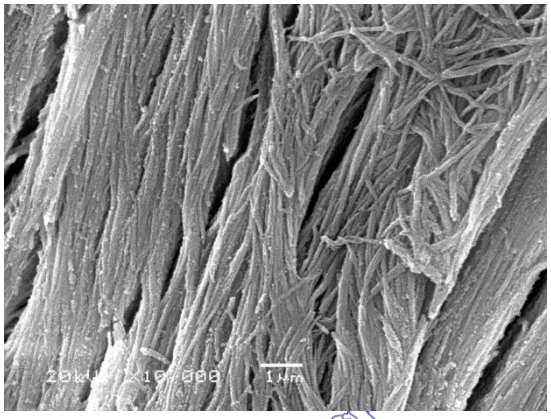
Capillaries in Volkman's system

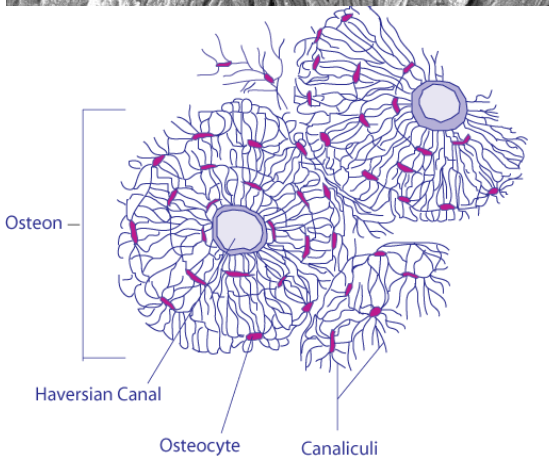
Histological classification of bone tissue

- **Primary (woven, fibrous)**
- Temporary, growth and regeneration of bones, collagen fibrils woven
- Replaced by secondary bone
- Remains only in some parts of body - sutures of skull *tuberositas ossium*, tooth cement



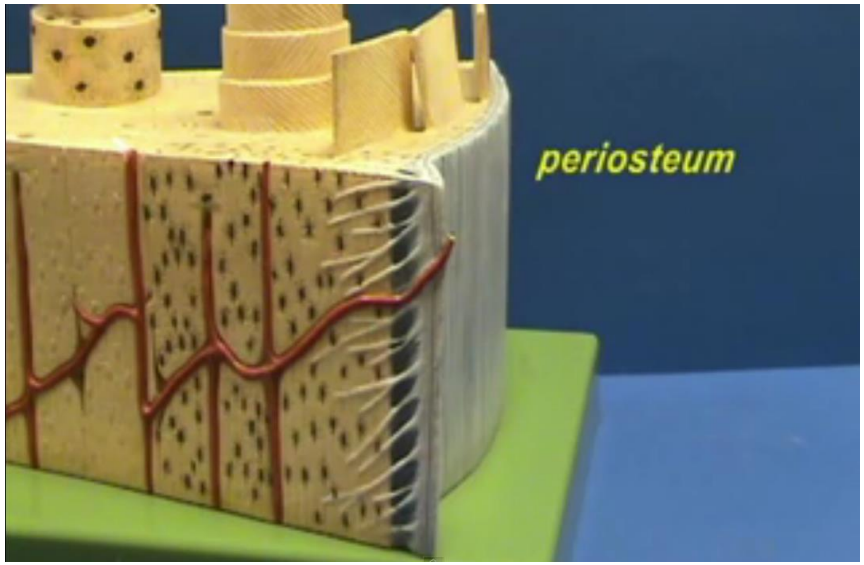
- **Secondary (lamellar)**
- Lamellae – collagen fibers in concentric layers (3-7μm) around a canal with capillaries = Haversian system (osteon)
- Spongy (trabecular)
  - Trabecules, similar to compact
  - Epiphyses of long bones, short bones, middle layer of flat bones of the skull (*diploe*)
- Compact
  - Outer and inner coat lamellae typical Haversian systems
  - Volkmann's canals
  - Interstitial canals

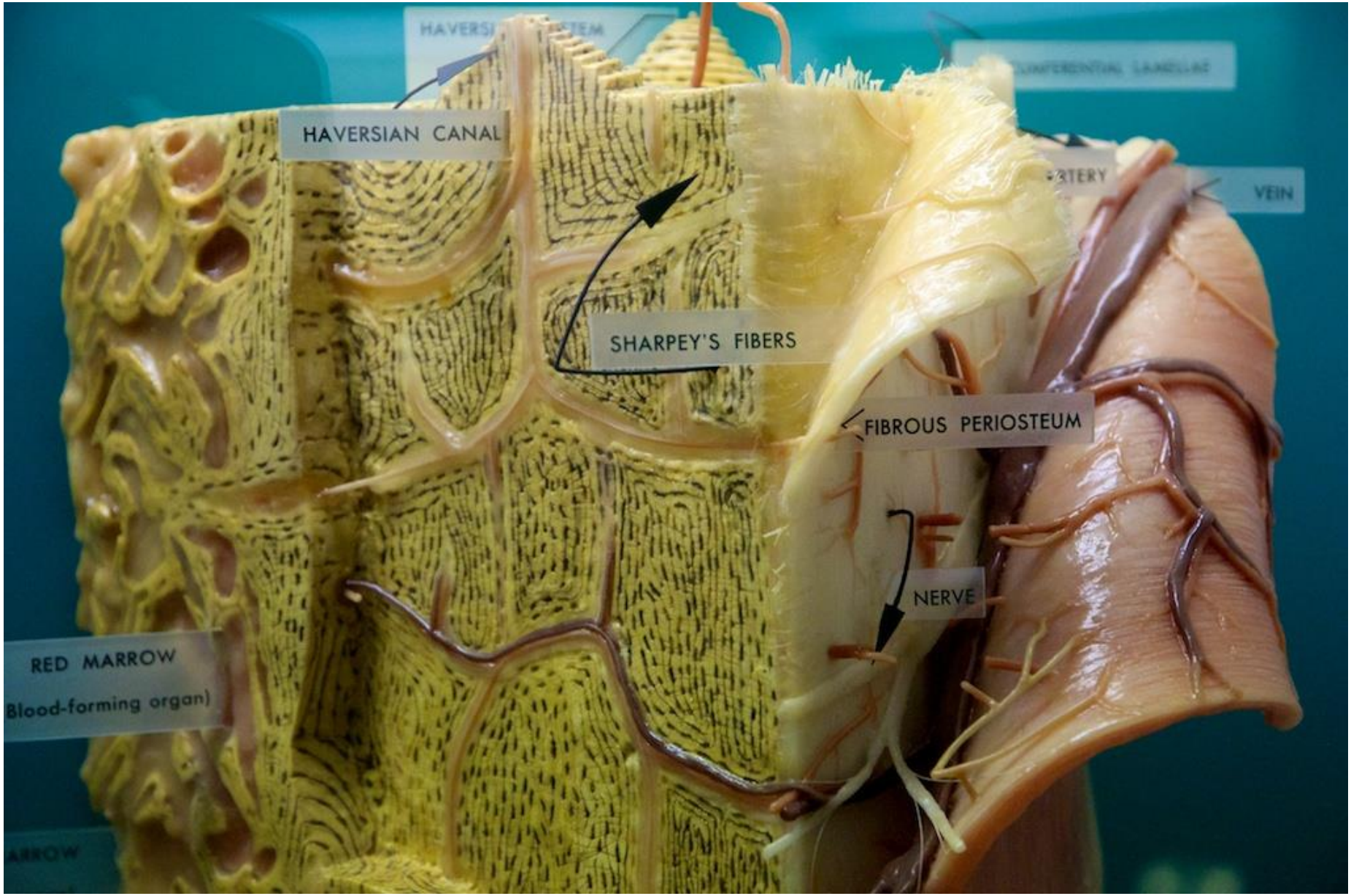




Surface of compact bone

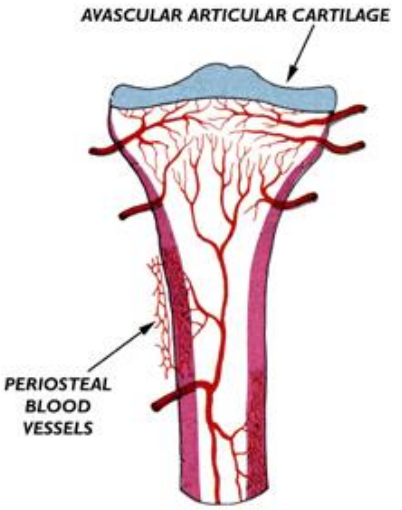
- **Outer surface**
- Synovial joint – hyaline cartilage
- periosteum (periost) – membrane – dense CT, inner layer (osteoblasts) and outer layer (fibrous CT)
- Inactive bone - fibrous CT in periost dominant
- Collagen fibers – parallel to the bone surface
- Sharpey’s fibers fix periost to the bone

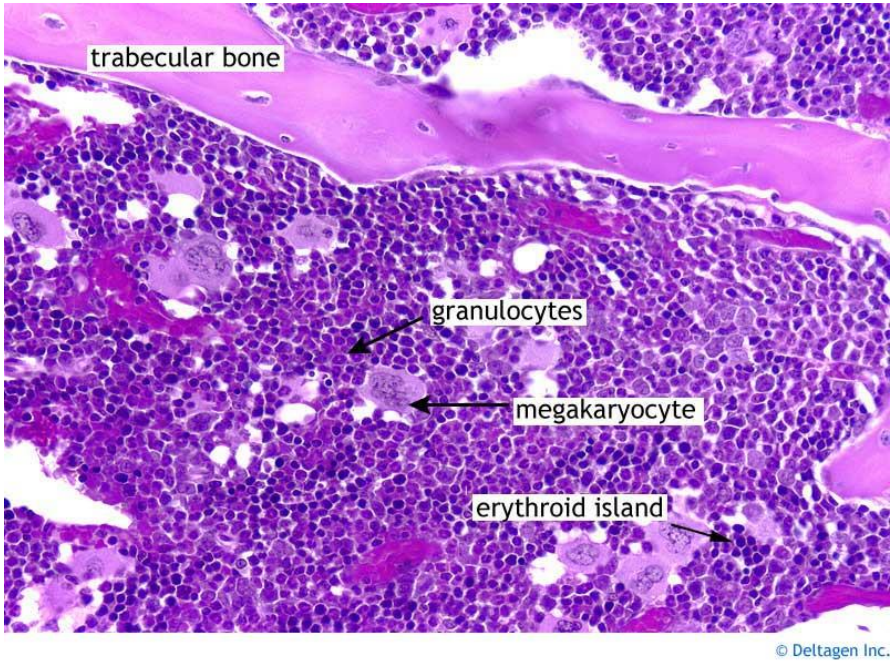


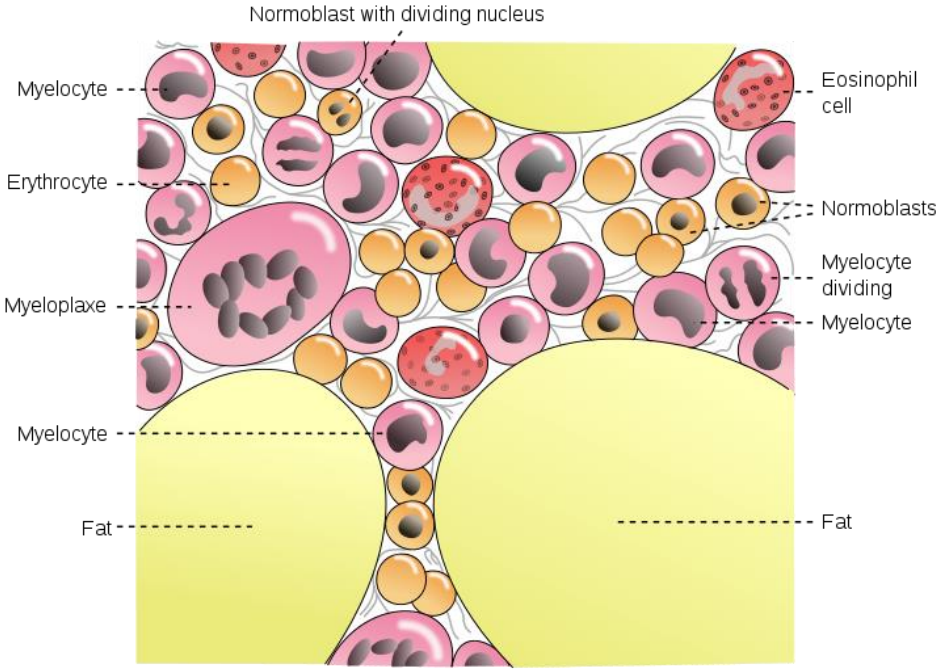


National Museum of Natural History NY, USA

- **Inner surface – cavities lining**
- Medullar cavity
- Endosteum (endost) – single cell lining – bone remodeling
- Red bone marrow – hematopoiesis
- Yellow and gray bone marrow – adipocytes or CT
- Rich vascularisation

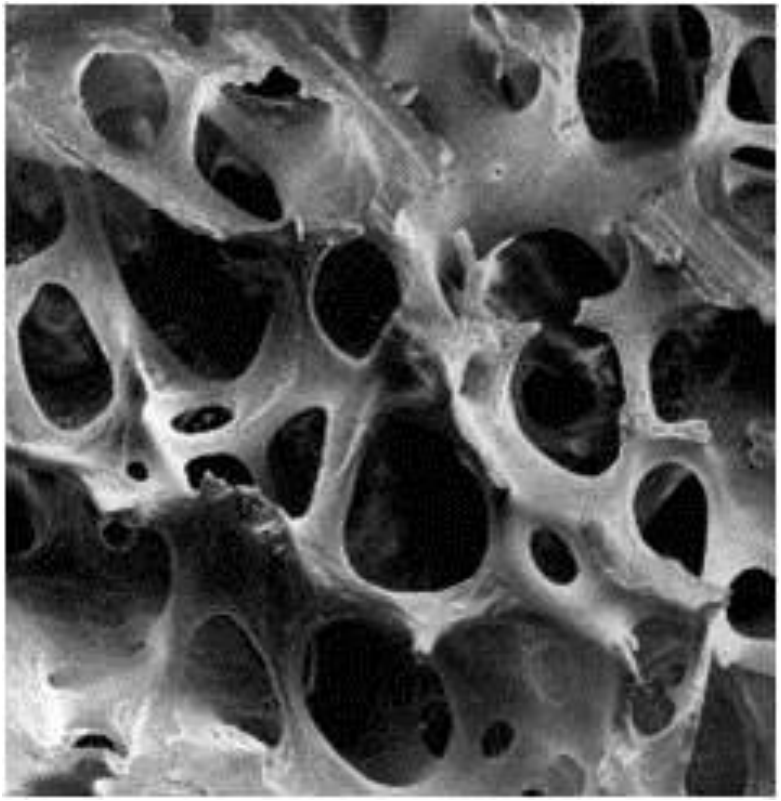


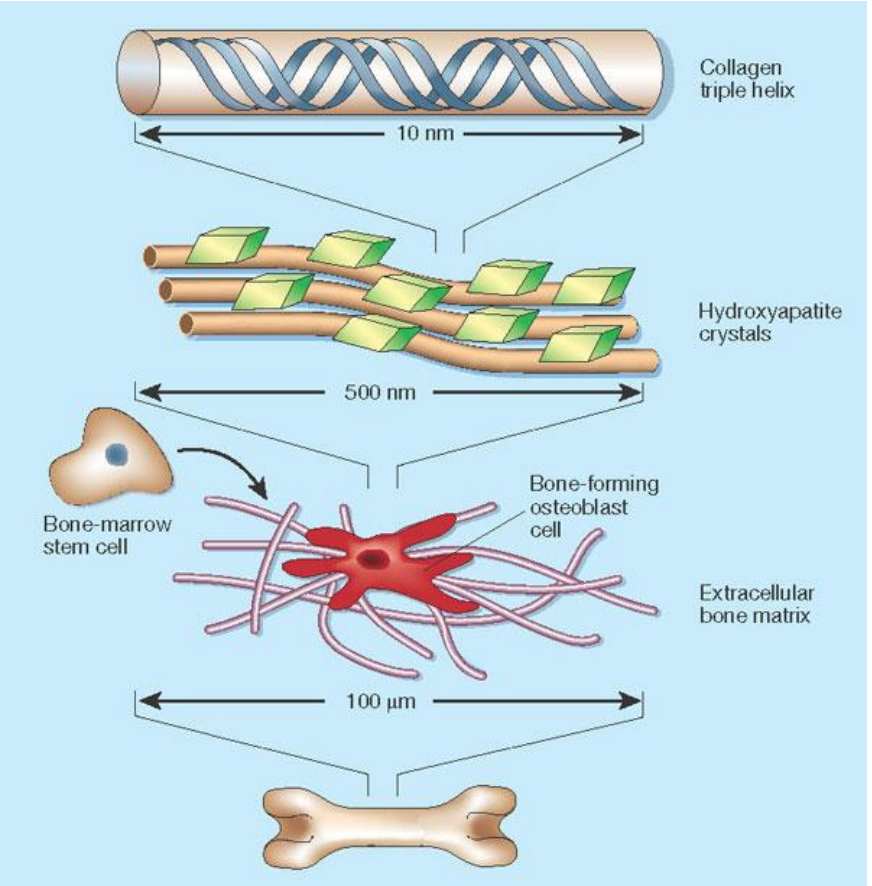




Bone matrix

- 60% mineral compound, 24% organic compound 12% H_20, 4% fat
- Crystals – calcium phosphate, hydroxyapatite

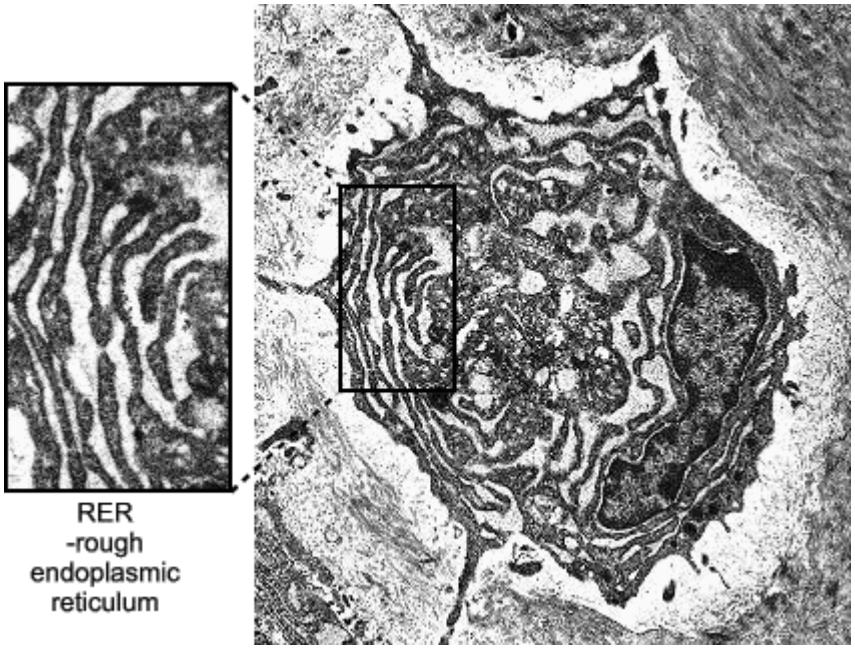


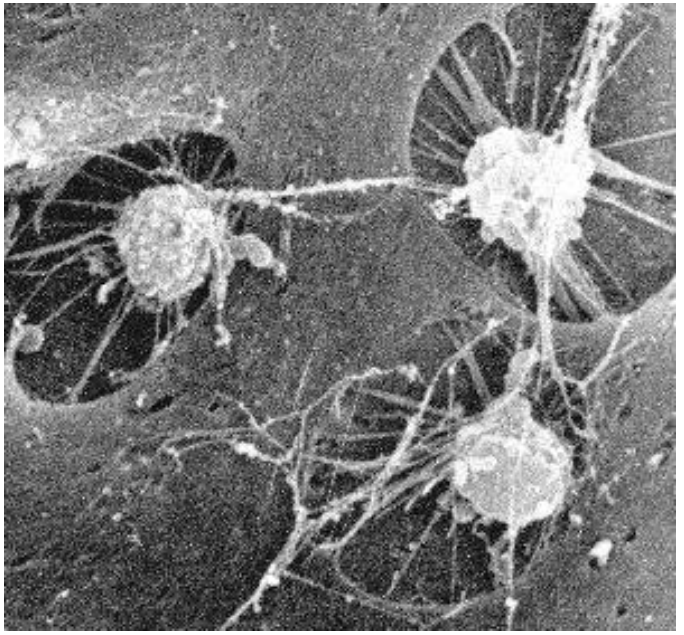


Cells

- **Osteoblasts**

- specialized bone cells
- produce ECM – collagen (I) and noncollagenous proteoglycans, glycoproteins
- osteocytes

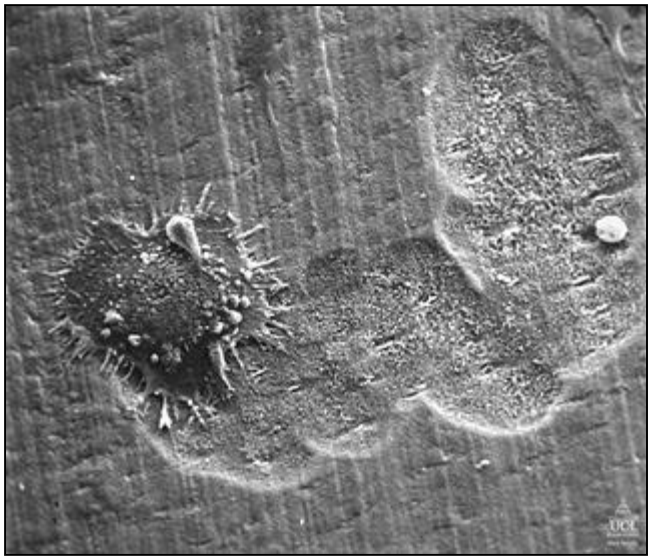


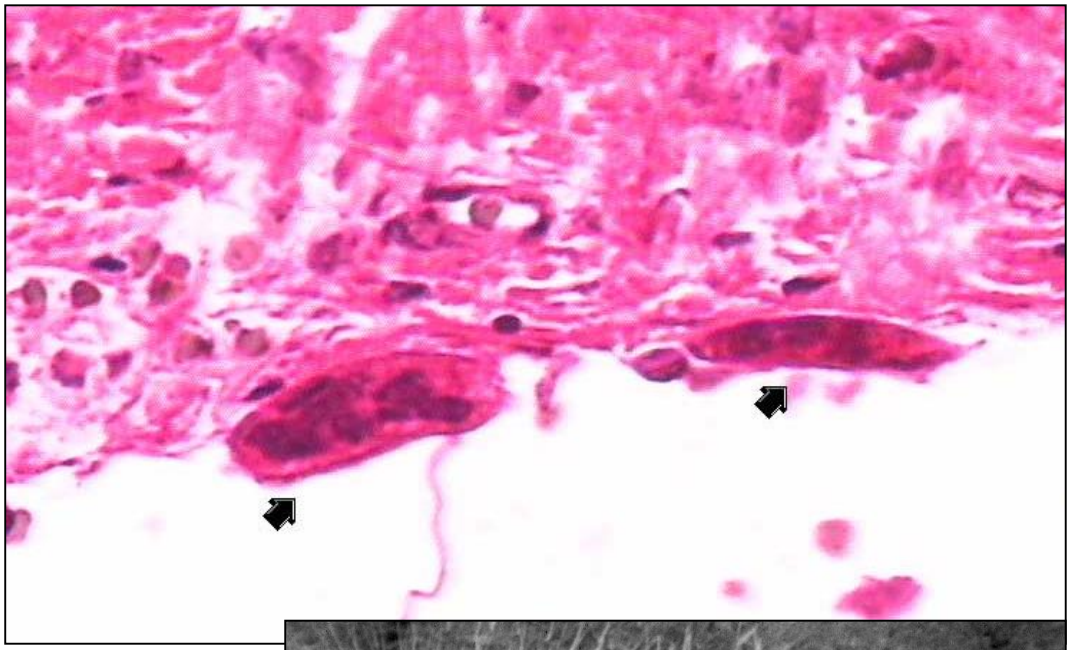


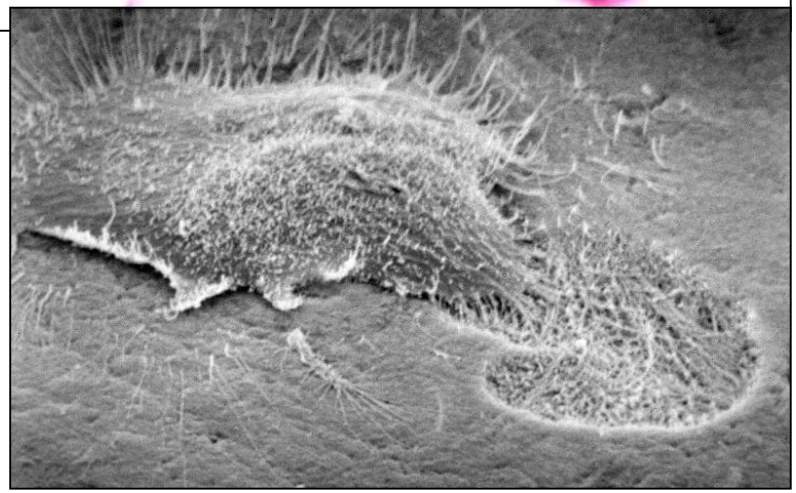
Cells

- **Osteoclasts**

- multinuclear, form by fusion of macrophages
- bone matrix resorption



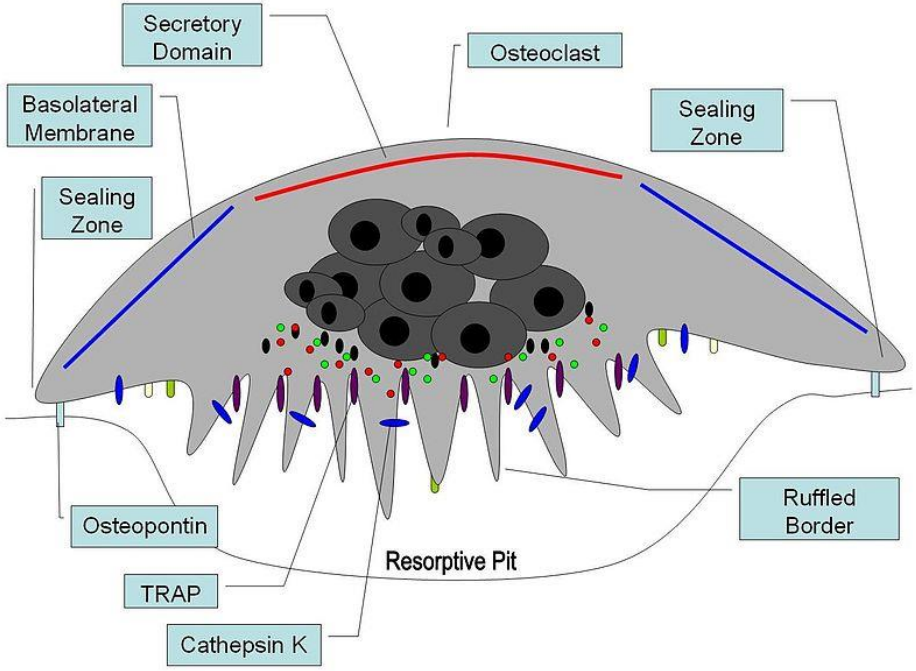


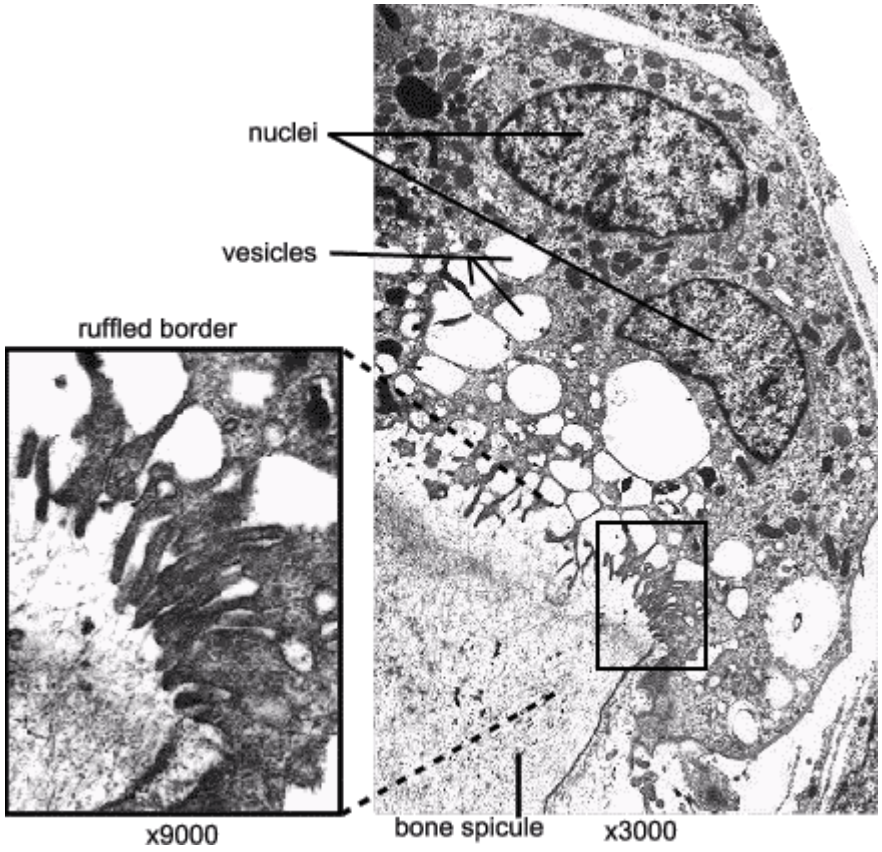


Cells

- **Osteoclasts**

- Complex architecture
- Enzymes degrading organic matrix
- HCl





Ossification

Intramembranoeous

- Mesenychymal cells → osteoblasts

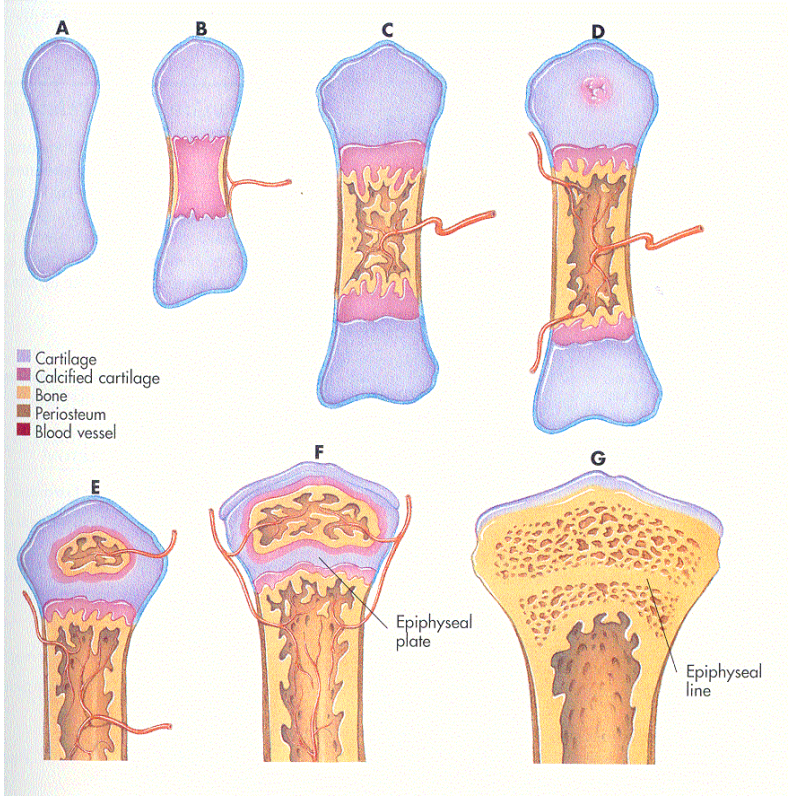
- Ossification center – rich vascularisation, differentiation of osteoblasts, synthesis of primary bone

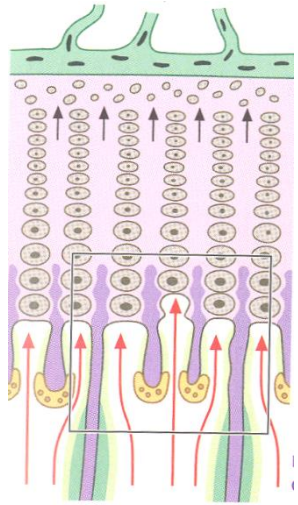
Endochondral

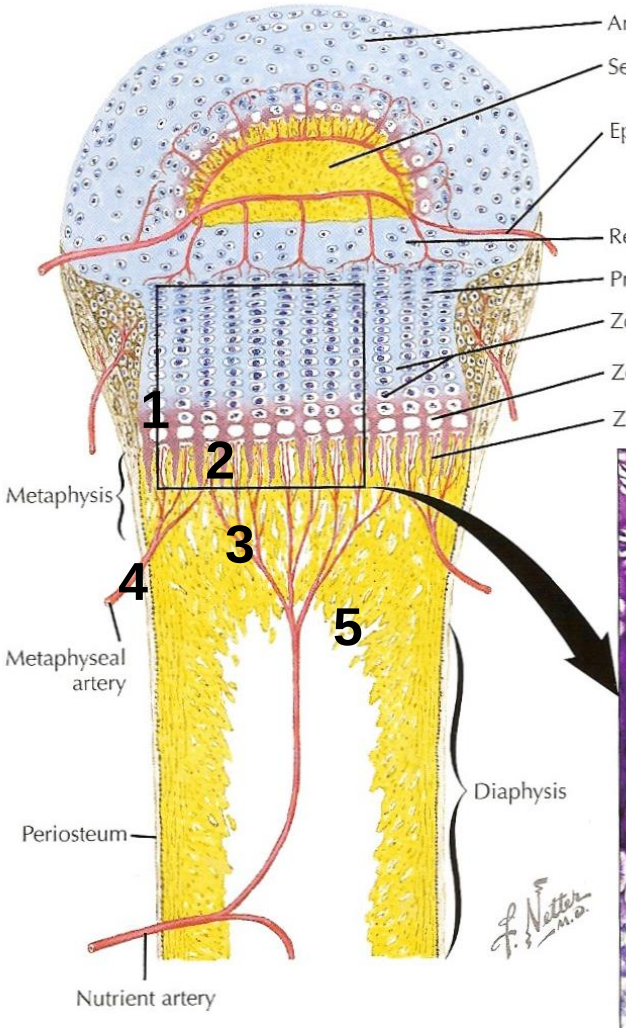
- Cartilage model

- Growth plate

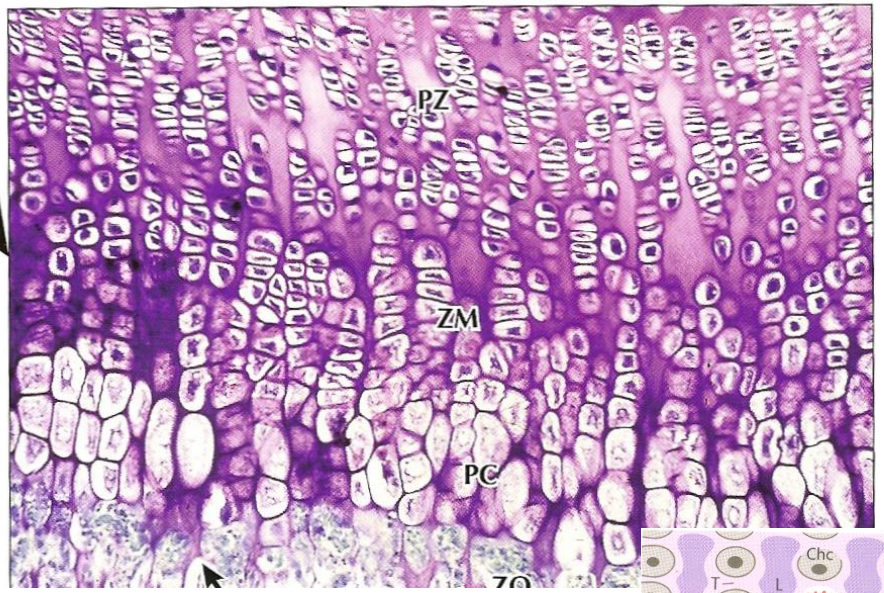
- Primary and secondary ossification centers (diaphyse, epiphyses)

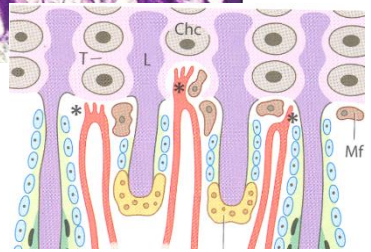




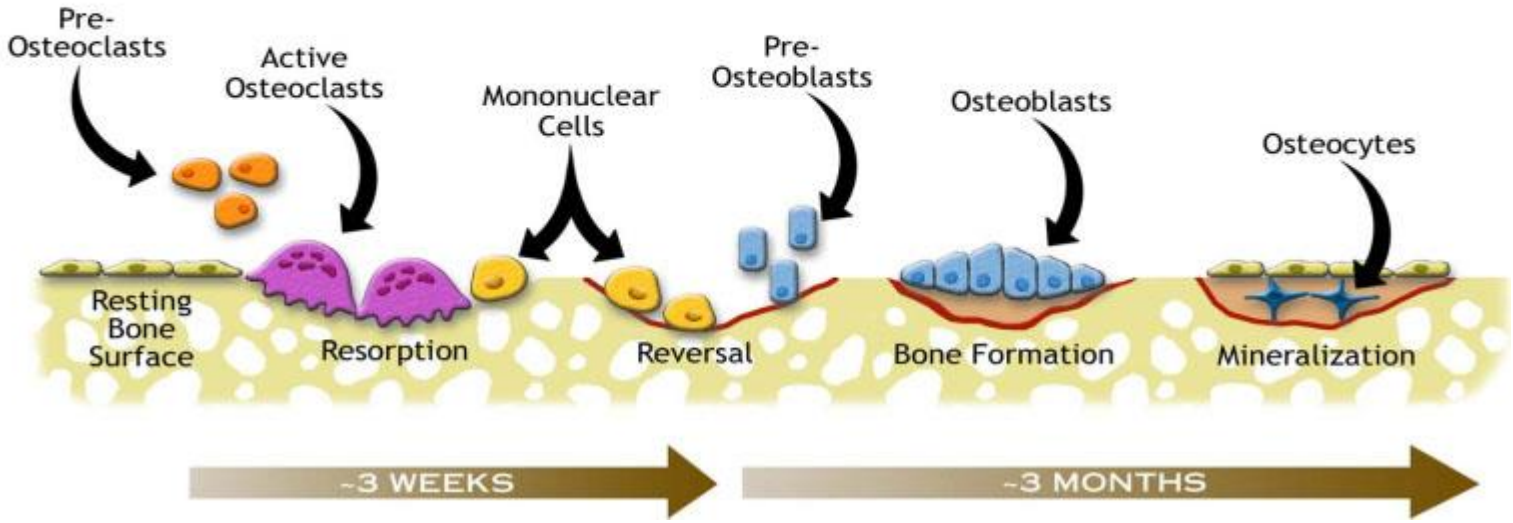

Articular cartilage
Secondary ossification center
Epiphyseal artery
Reserve zone
Proliferative zone
Zone of maturation and hypertrophy
Zone of provisional calcification
Zone of ossification
Metaphysis
Metaphyseal artery
Periosteum
Diaphysis
Nutrient artery
1
2
3
4
5
F. Netter M.D.


Cartilage
Calcified cartilage
Bone


PZ
ZM
PC


Chc
T
L
Mf

Bone Remodeling Cycle



http://ns.umich.edu/Releases/2005/Feb05/img/bone.jpg

- Clinical correlations

- **Fracture healing**

Reactive Phase

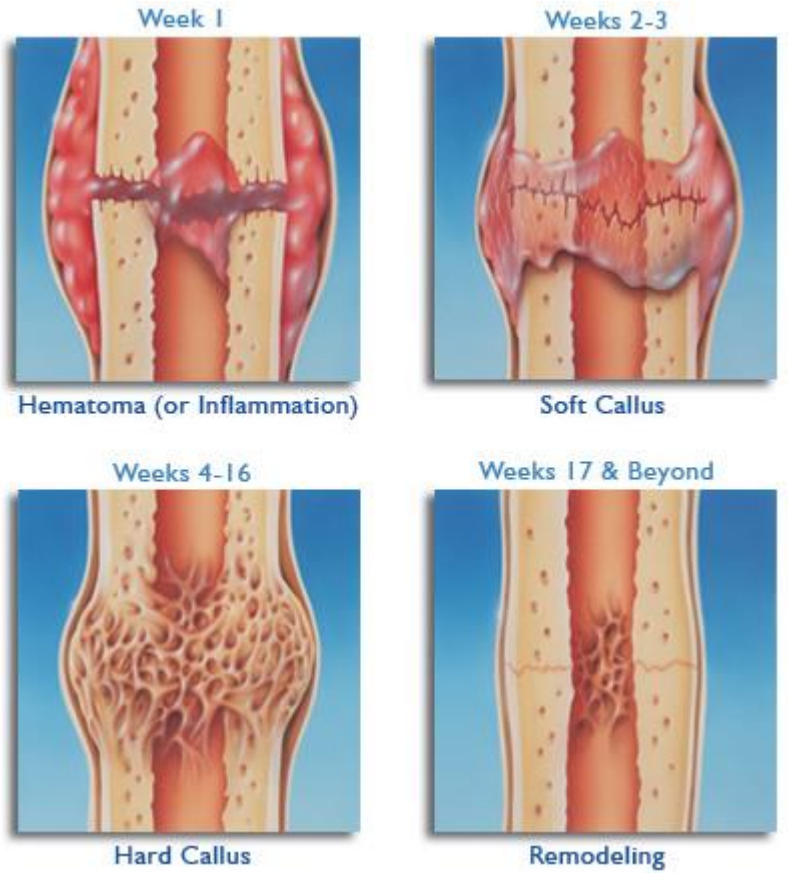
- Fracture and inflammatory phase
- Granulation tissue formation

Reparative Phase

- Cartilage *callus* formation
- Lamellar bone deposition

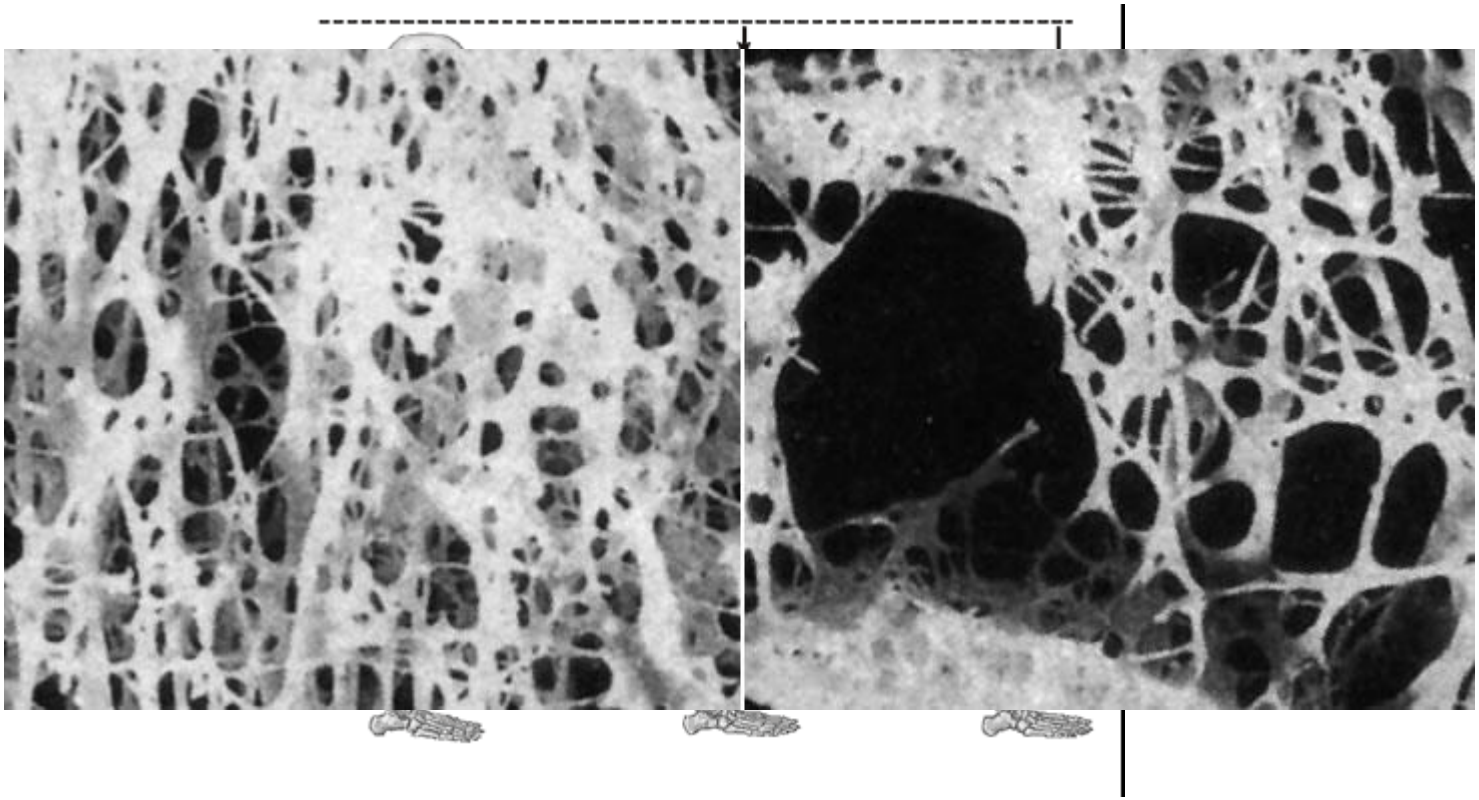
Remodeling Phase

- Remodeling to original bone shape



- Clinical correlations

- **Bone remodelation disorders – OSTEOPOROSIS**



Clinical correlations

- **OSTEOPOROSIS**

- Abnormal activity of osteoclasts
- Low level of estrogens (menopausis)
- Inflammation
- Immobilization
- Nutrition
- Endocrine disorders
- Side effect of therapy with corticosteroids, antiepileptics, anticoagulantia

- treatment: antiresorbing drugs (bisphosphonates, estrogene analogues), stimulation of bone formation, nutrition, exercise
- Osteolytic phenotype – multiple myeloma, breast cancer

Clinical correlations

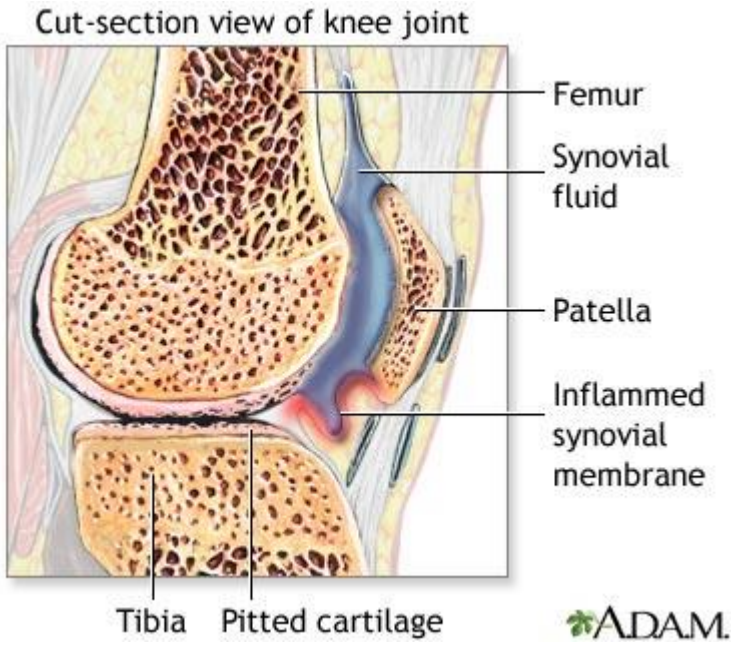
- **Bone remodelation disorders – OSTEOPETROSIS**

- decreased activity osteoclasts
- congenital disease
- various damages (nerve compression, fractures, joint erosion, anemia – closing of medullar cavity)

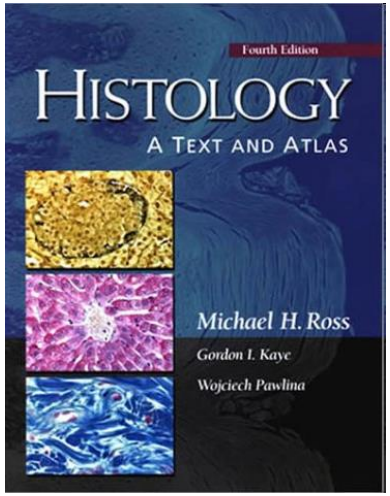
Clinical correlations

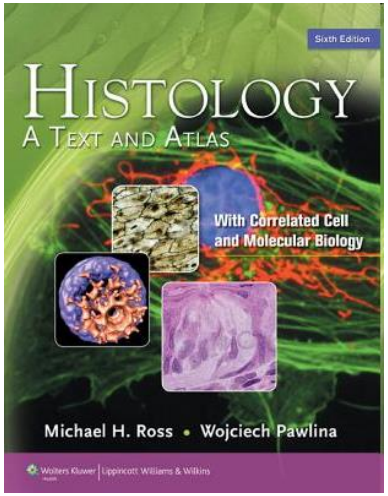
- **Rheumatoid arthritis**

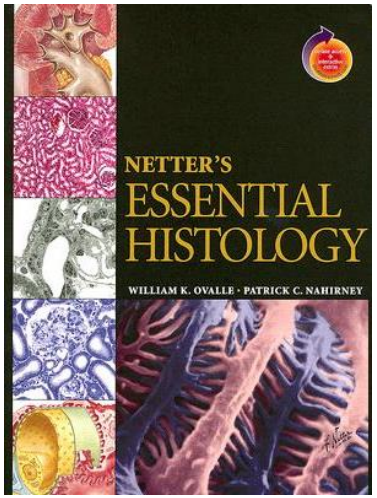
- autoimmune inflammatory disease
- erosion of soft tissue and bone matrix (synovial membrane, cartilage, bone)

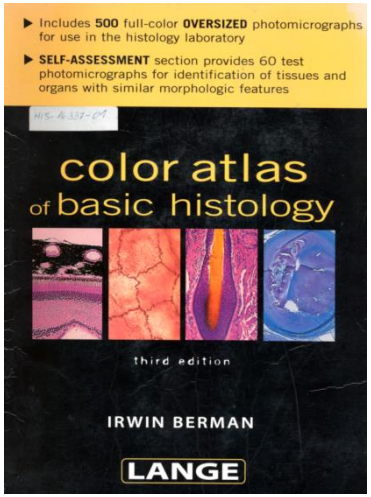


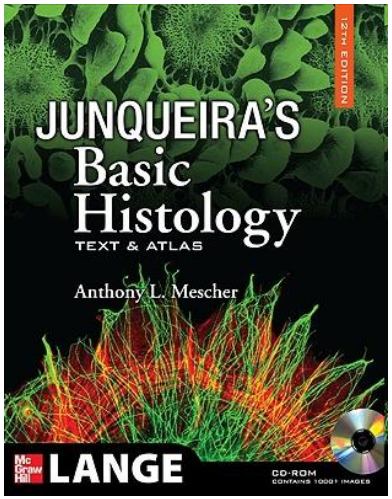
- Further study

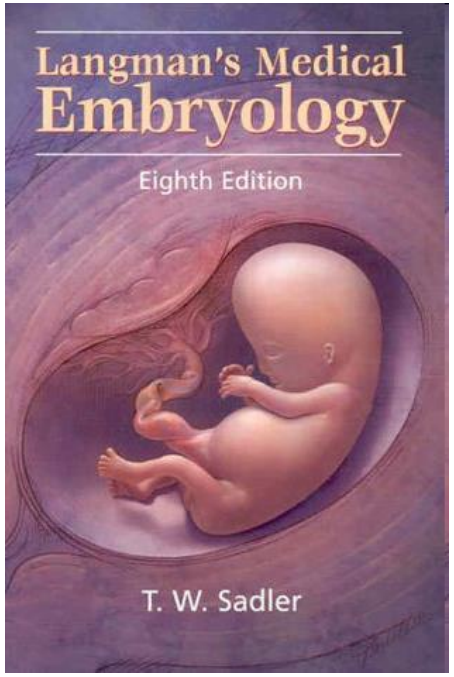












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or visit

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

Thank you for attention