

# Connective Tissue-2

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# Fibers of connective tissue

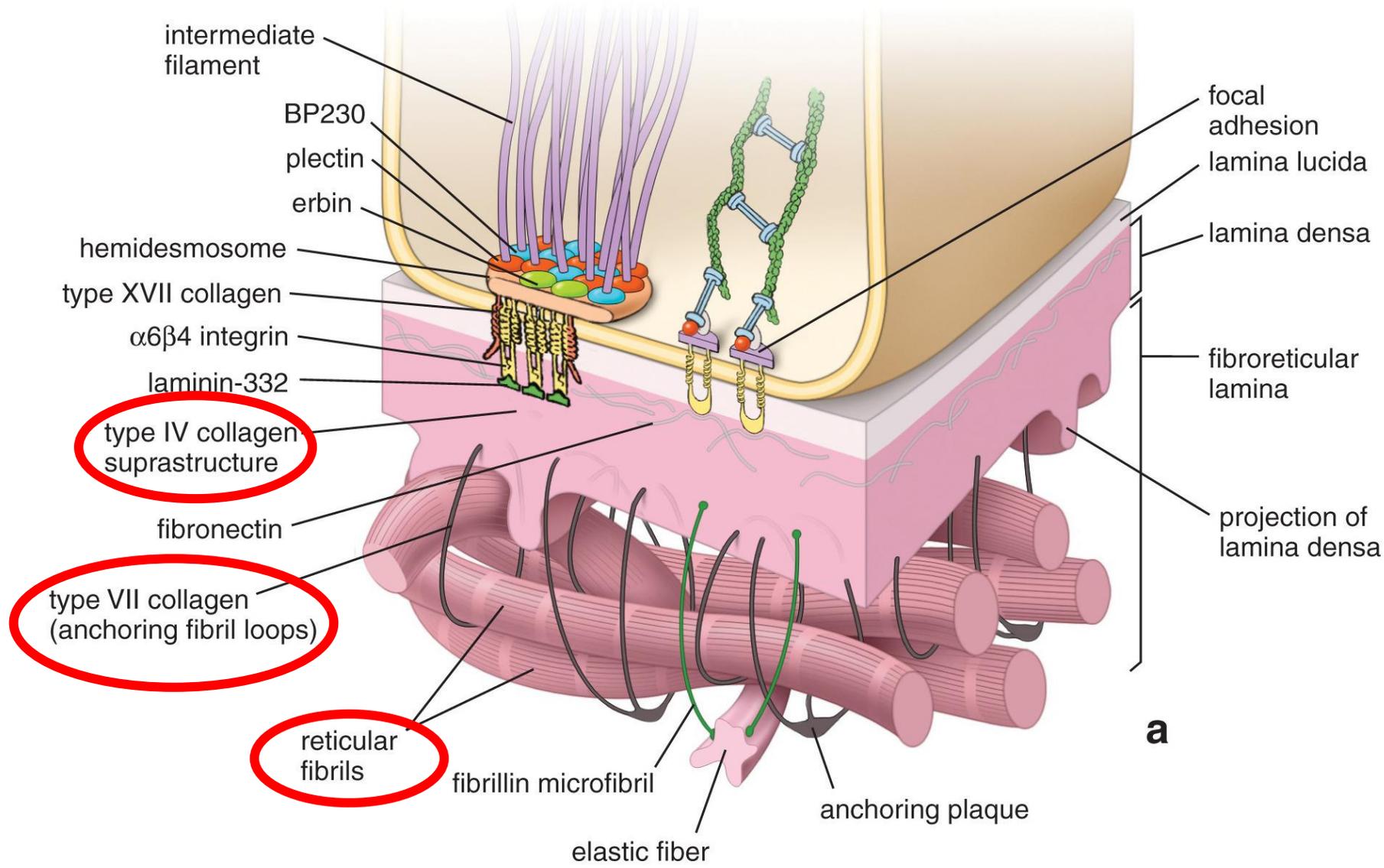
- ▶ The fibrous components of connective tissue are elongated structures formed from proteins that **polymerize after** secretion from fibroblasts
- ▶ The three main types of fibers include **collagen, reticular, and elastic fibers.**
- ▶ Collagen and reticular fibers are both formed by proteins of the collagen family, and elastic fibers are composed mainly of the protein **elastin.**

# Collagen

- ▶ The **collagens** constitute a family of proteins
- ▶ Collagen is the most abundant protein in the human body, representing 30% of its dry weight
- ▶ Produced mostly by fibroblasts

# Collagen subtypes

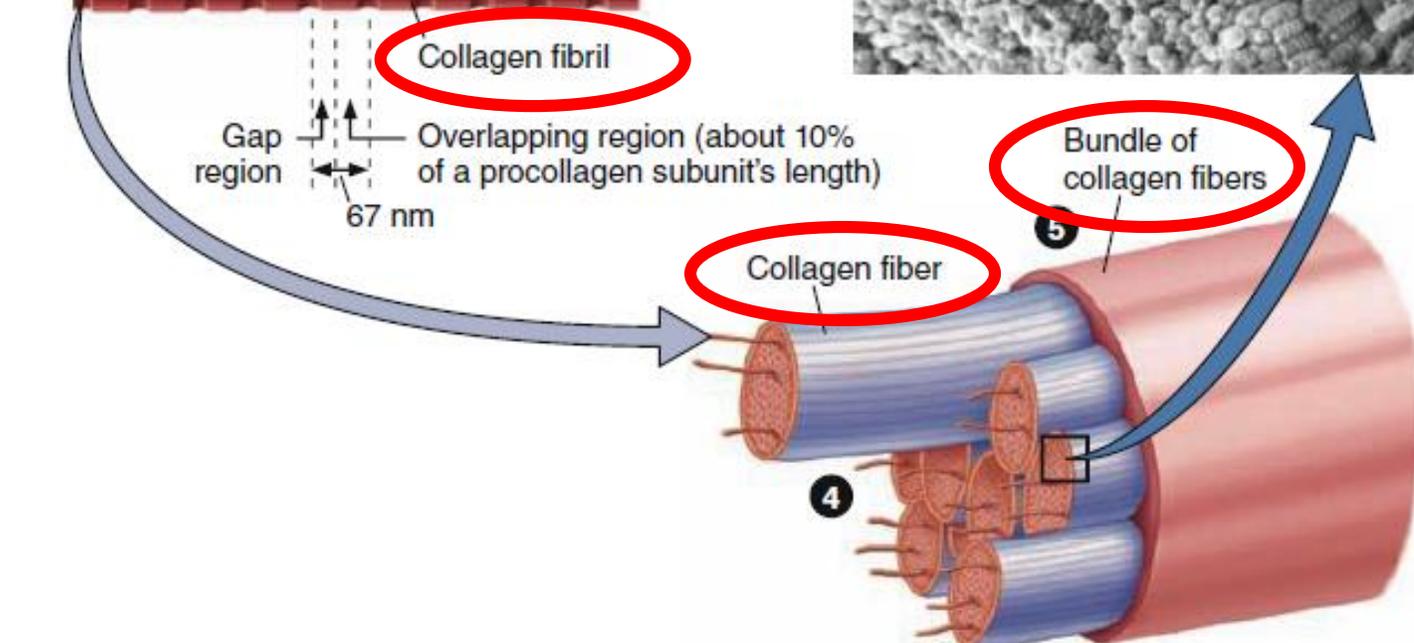
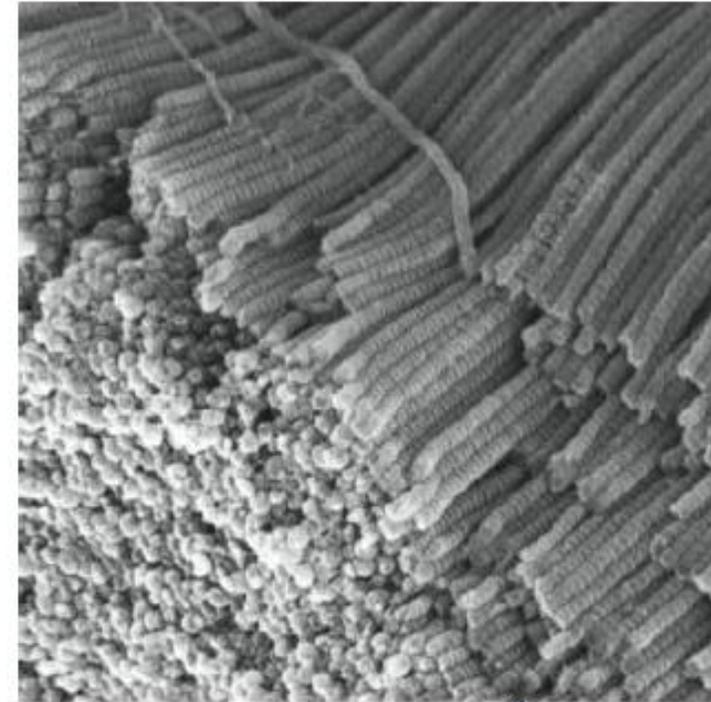
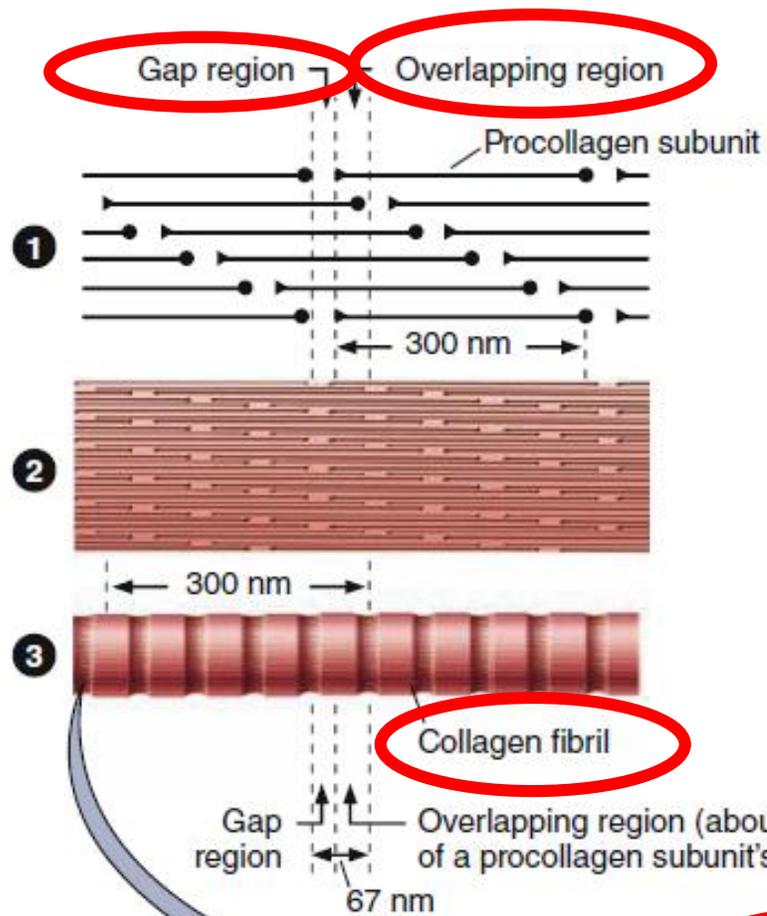
- ▶ **Fibrillar collagens**, such as **collagen types I, II, and III**, have polypeptide subunits that aggregate to form large fibrils clearly visible in the electron or light microscope
- ▶ **Network or sheet-forming collagens**, such as **type IV collagen** have subunits produced by epithelial cells and are major structural proteins all epithelial basal laminae.
- ▶ **Linking/anchoring collagens** are short collagens that link fibrillar collagens to one another (forming larger fibers) and to other components of the ECM. **Type VII collagen** binds type IV collagen and anchors the basal lamina to the underlying reticular lamina in basement membranes



<b>Type</b>	<b>Synthesizing cell</b>	<b>Function</b>	<b>Location</b>
<b>I</b>	Fibroblast, osteoblast, odontoblast, cementoblast	Resist tension	Dermis, tendons, ligament, capsules, bone, dentin, cementum
<b>II</b>	chondroblasts	Resists pressure	Hyaline and elastic cartilage
<b>III</b>	Fibroblasts, reticular cells, smooth muscle, hepatocytes	Form structural framework of organs	Reticuloendothelial system, lung, skin
<b>IV</b>	Epithelium, muscle, Schwann cells	Meshwork of the lamina densa	Basal lamina
<b>VII</b>	Epithelial cells of epidermis	Anchoring fibrils between the lamina densa and reticularis	Derma-epidermal junction

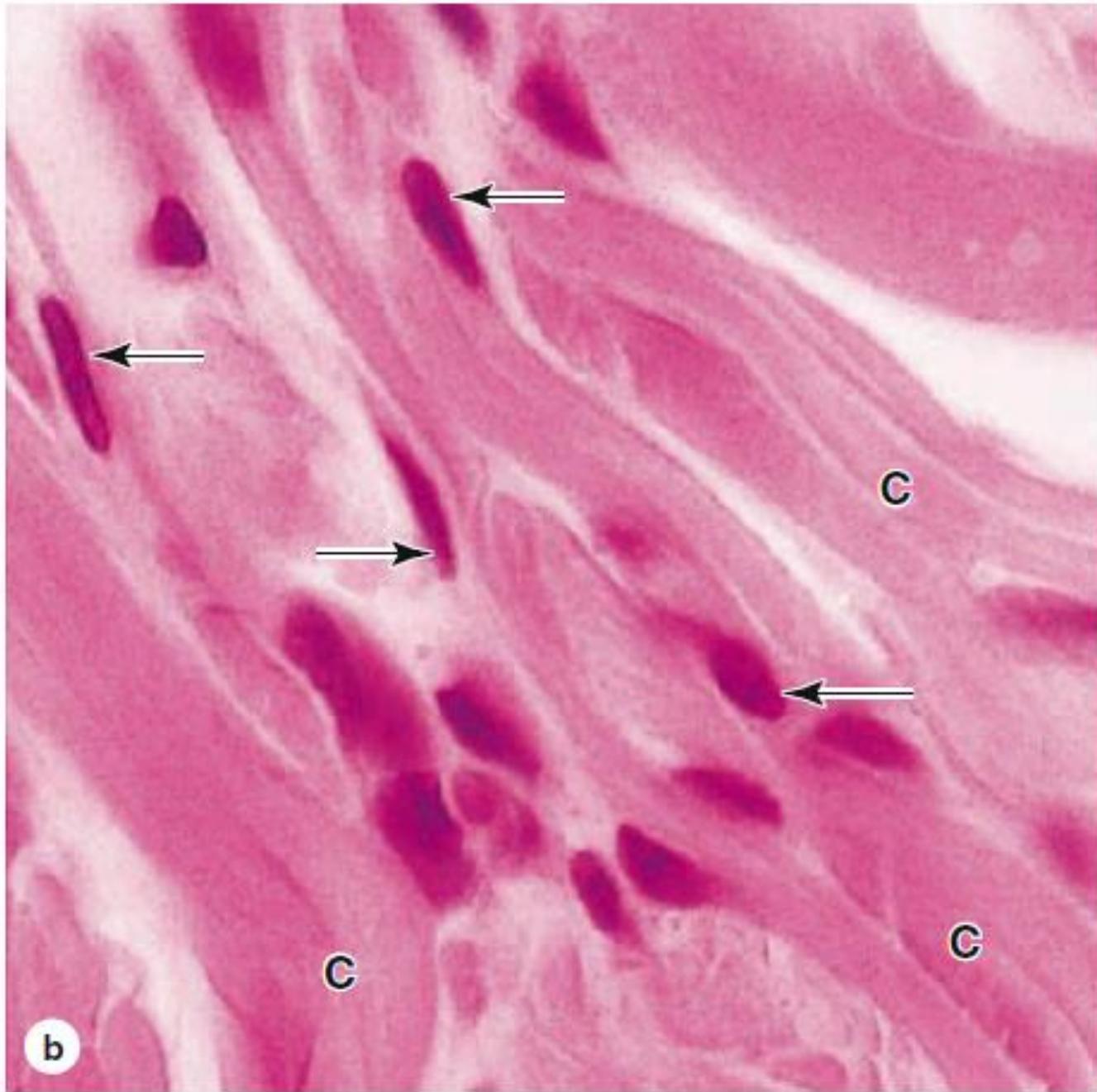
# Collagen Fibers

- ▶ Type I collagen is the most abundant and widely distributed collagen
- ▶ Collagen type I subunits assemble to form extremely strong fibrils
- ▶ Fibrils bundle together further by other collagens into much larger structures called **collagen fibers**.
- ▶ Collagen fibers form structures such as tendons, organ capsules, and dermis



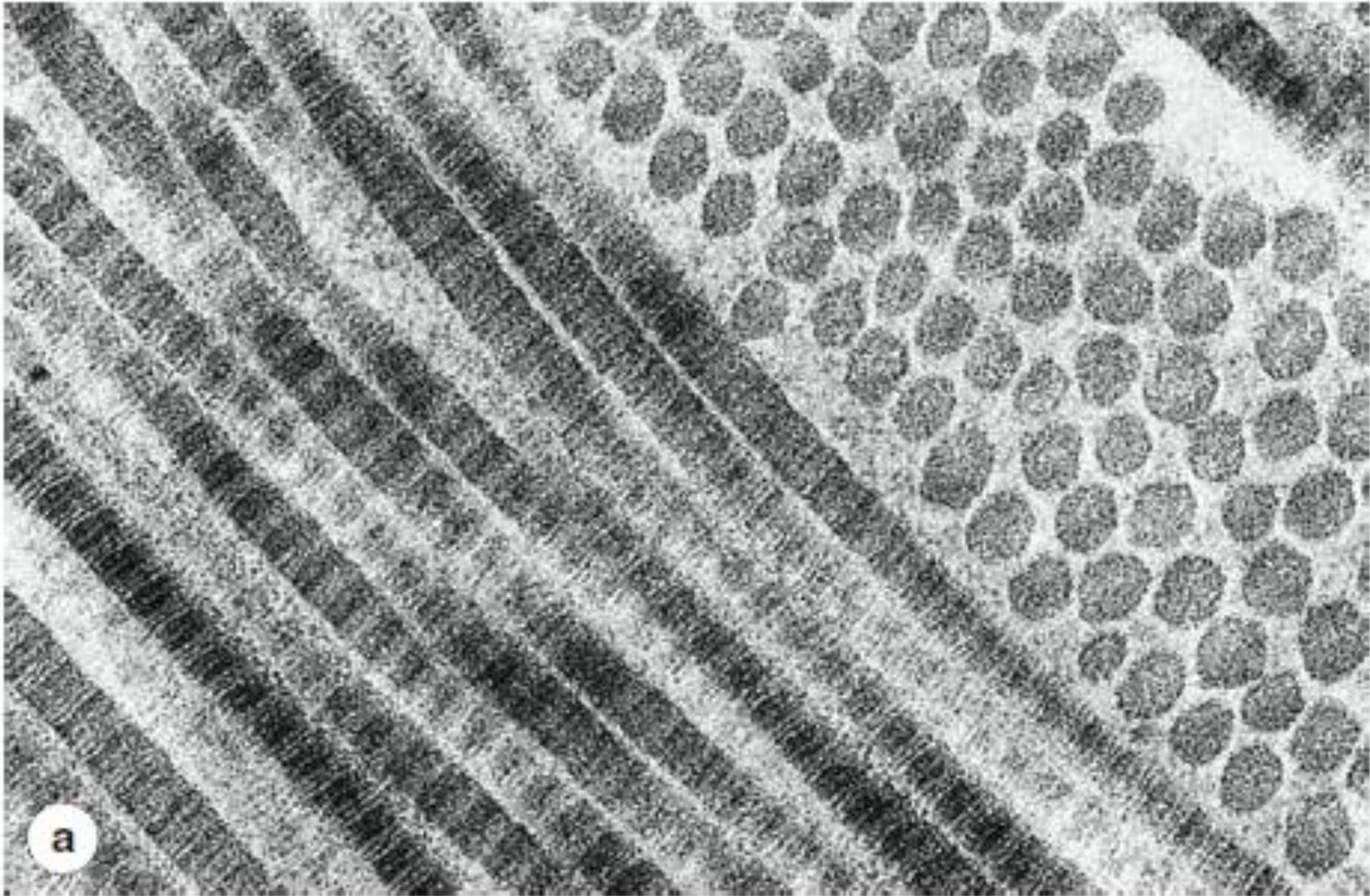
# Collagen fibers in LM

- ▶ Collagen I fibers appear as large eosinophilic bundles
- ▶ They may fill the extracellular space.
- ▶ Subunits for these fibers were secreted by the fibroblasts associated with them.



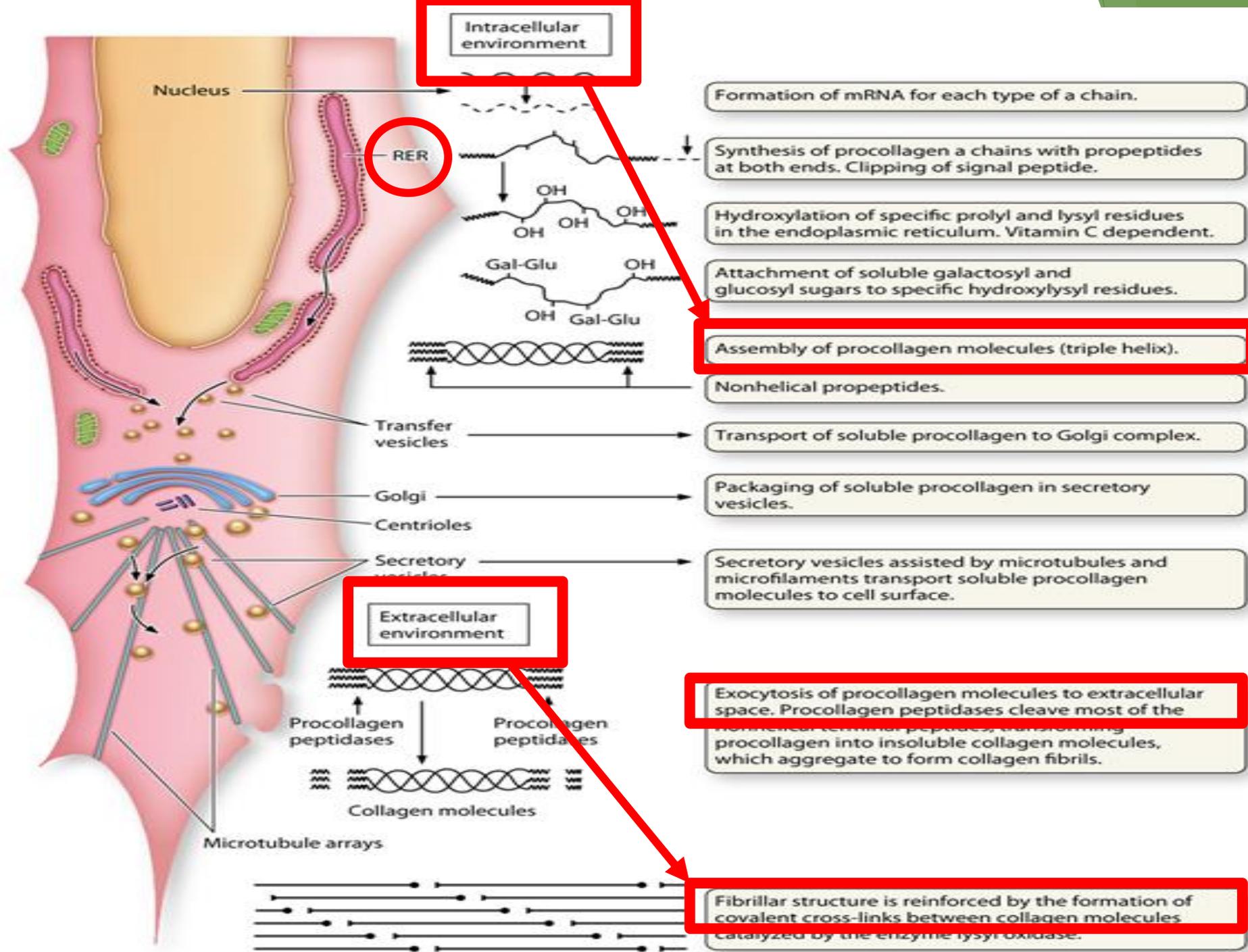
# Collagen fibers in TEM

- ▶ In longitudinal sections fibrils display alternating dark and light bands
- ▶ In cross section the cut ends of individual collagen molecules appear as dots.



# Collagen Synthesis

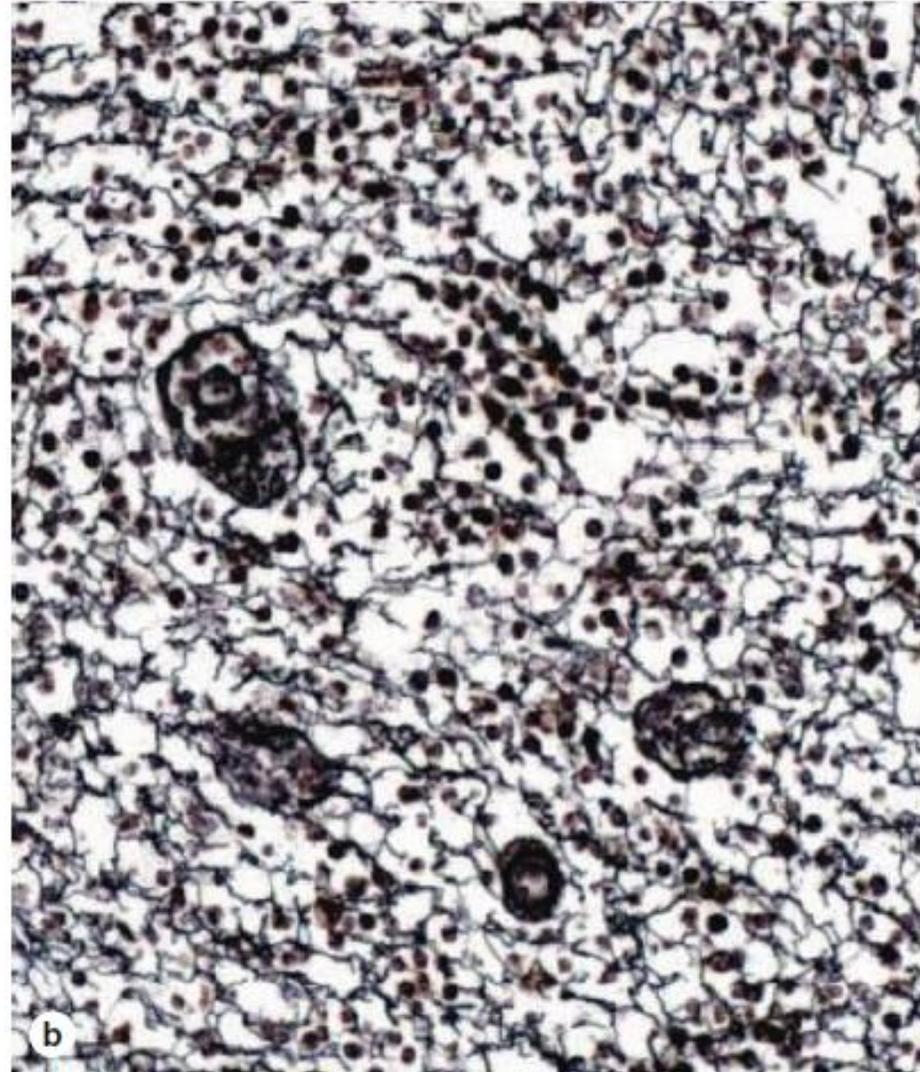
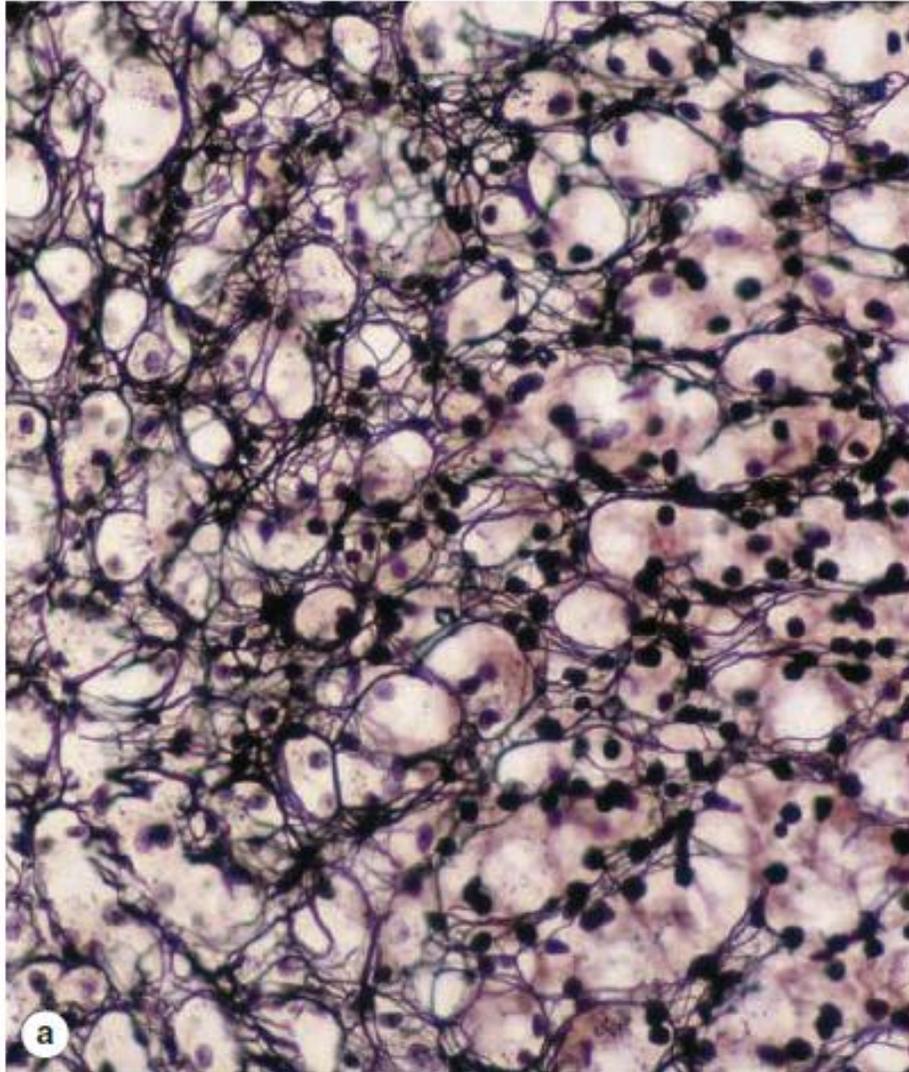
- ▶ **Collagen synthesis** occurs in many cell types but is a specialty of fibroblasts.
- ▶ The initial **procollagen  $\alpha$  chains** are polypeptides made in the RER.
- ▶ In the ER three  $\alpha$  chains are selected, aligned, and stabilized by disulfide bonds at their carboxyl terminals, and folded as a **triple helix**
- ▶ The triple helix undergoes exocytosis and is cleaved to a **procollagen molecule**
- ▶ Procollagen is the basic subunit from which the fibers are assembled.



# Reticular Fibers

- ▶ **Reticular fibers** consist of collagen type III
- ▶ Collagen III forms an extensive network of thin fibers
- ▶ They are found in delicate connective tissue of many organs such as liver, spleen, lymph nodes
- ▶ Reticular fibers are not visible in hematoxylin and eosin (H&E) preparations
- ▶ They stain black after impregnation with silver salts, and are thus termed **argyrophilic**
- ▶ Reticular fibers contain up to 10% carbohydrate and are therefore periodic acid-Schiff (PAS) positive

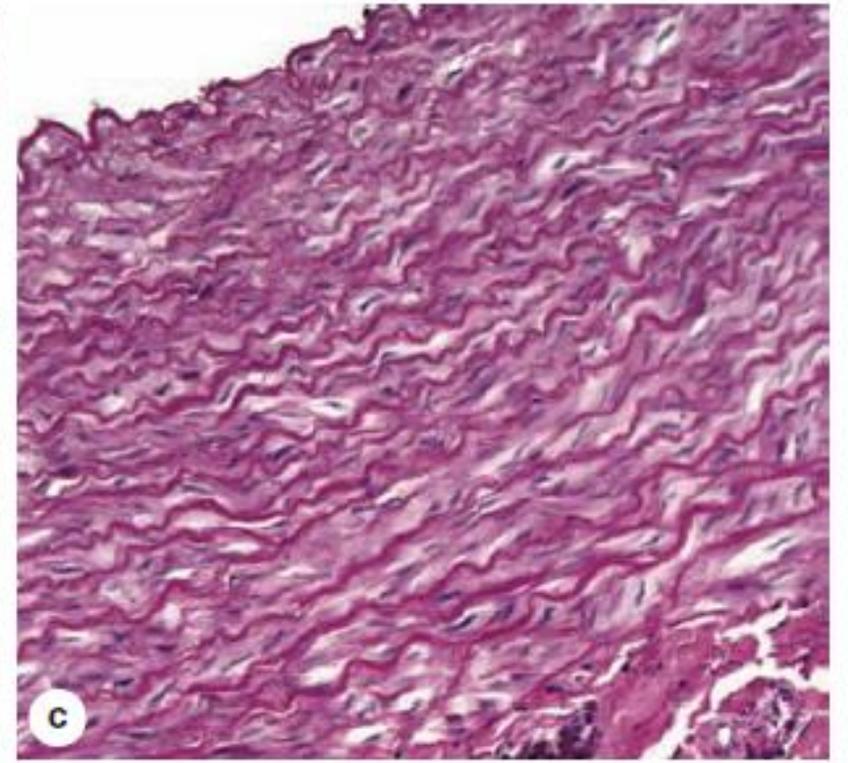
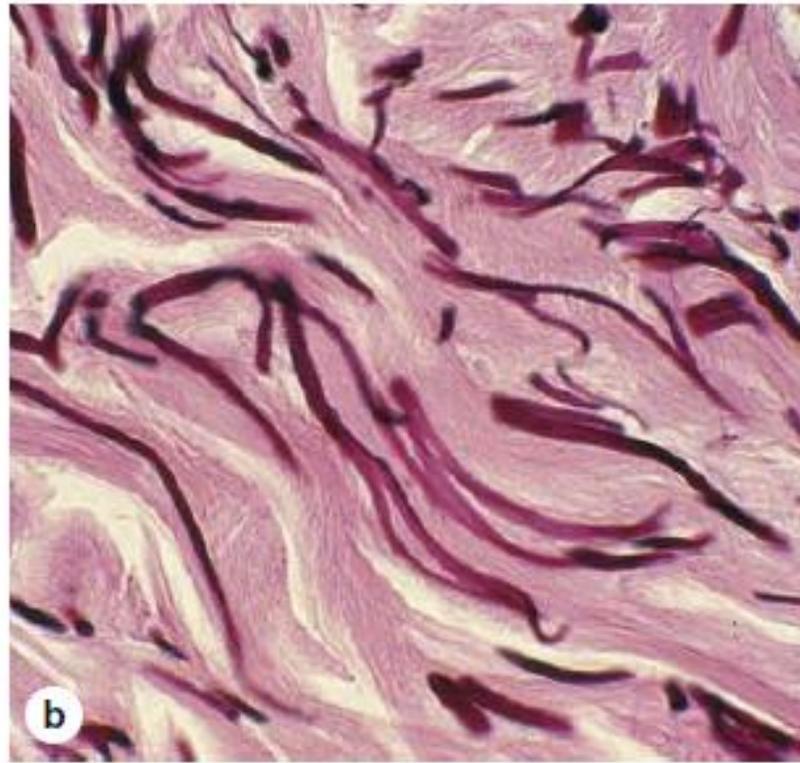
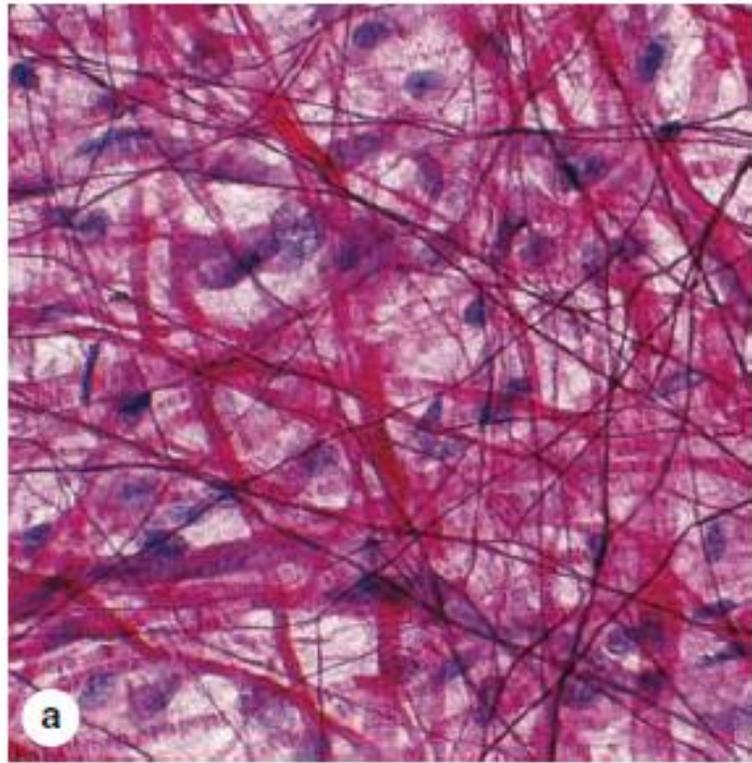
# Reticular fibers-Silver stain



# Elastic Fibers

- ▶ **Elastic fibers** are thinner than the type I collagen fibers
- ▶ They are found between collagen bundles
- ▶ Mainly found in organs subject to regular stretching or bending, such as the stroma of lungs
- ▶ They have rubber-like properties that allow tissue containing these fibers to be stretched and return to their original shape
- ▶ In the wall of large blood vessels, especially arteries, elastin also occurs as fenestrated sheets called **elastic lamellae**.
- ▶ Elastic fibers and lamellae stain poorly with H&E
- ▶ They are stained more darkly than collagen with orcein and aldehyde fuchsin

# Elastic Fibers



Ground substance

# Definition

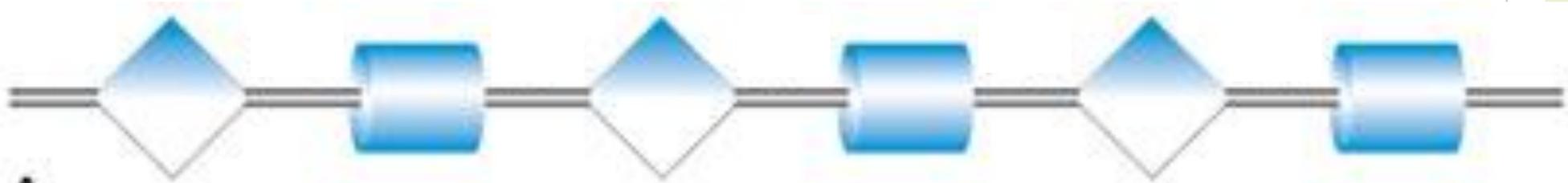
- ▶ The **ground substance** of the ECM is a highly hydrated (with much bound water), viscous, transparent, complex mixture of three major kinds of macromolecules, filling the space between cells and fibers in connective tissue

# Composed of:

- ▶ Glycosaminoglycans (GAGs)
- ▶ Proteoglycans: Responsible for the gel state of the extracellular matrix.
- ▶ Adhesive glycoproteins

# GAGs

- ▶ Also called mucopolysaccharides
- ▶ Long polymers of repeating disaccharide units, usually a hexosamine and uronic acid.
- ▶ The hexosamine can be glucosamine or galactosamine, and the uronic acid can be glucuronate or iduronate.
- ▶ They have a high negative charge
- ▶ GAGs have an extended conformation
- ▶ They have space-filling, cushioning, and lubricant functions.



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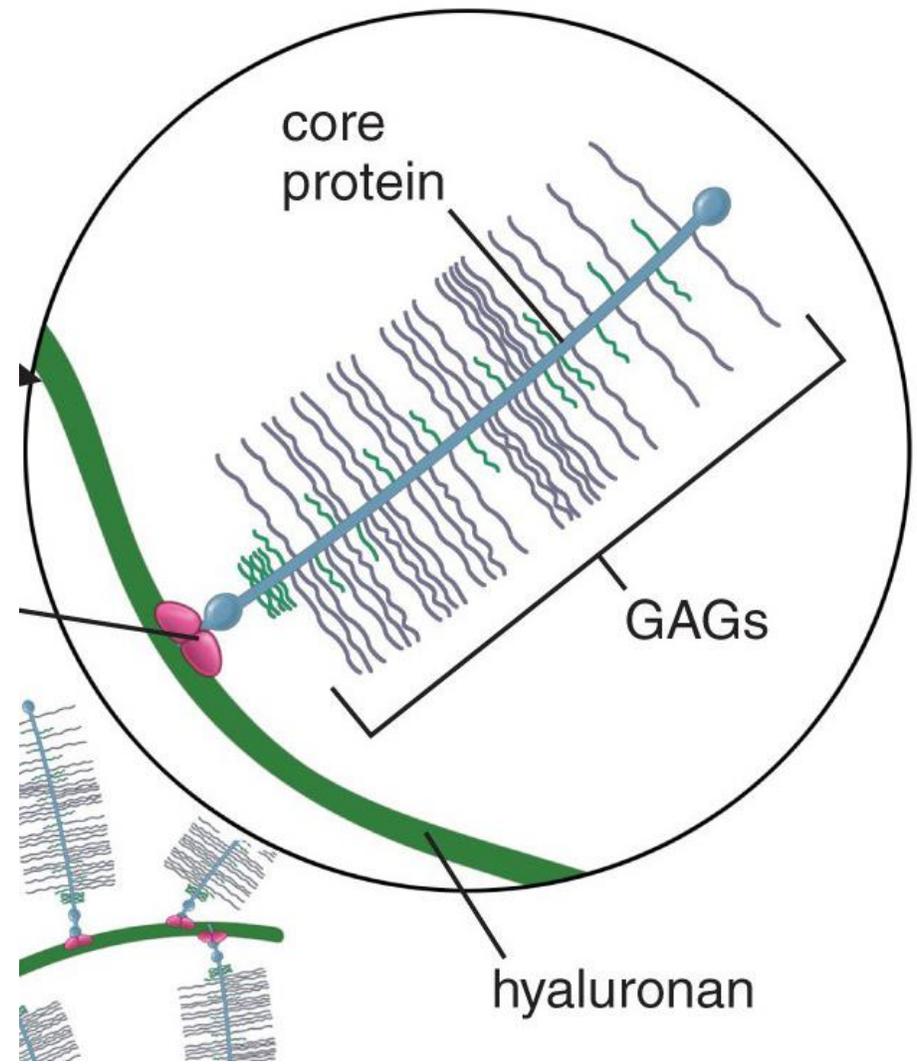
# Other types of GAGs

<b>GAG</b>	<b>Distribution</b>
Hyaluronic acid	<b>Most connective tissue</b> , cartilage, dermis, synovial fluid.
Keratan sulfate	<b>Cartilage</b> , cornea, intervertebral disc.
Heparan sulfate	Blood vessels, lung, <b>basal lamina</b>
Chondroitin 4-sulfate	<b>Cartilage</b> , bone, blood vessels
Chondroitin 6-sulfate	<b>Cartilage</b> , blood vessels, umbilical cord.
Dermatan sulfate	<b>Skin</b> , heart valves, blood vessels
Heparan sulfate (Heparin)	<b>Mast cell granules</b> , basophils, liver lung, skin.

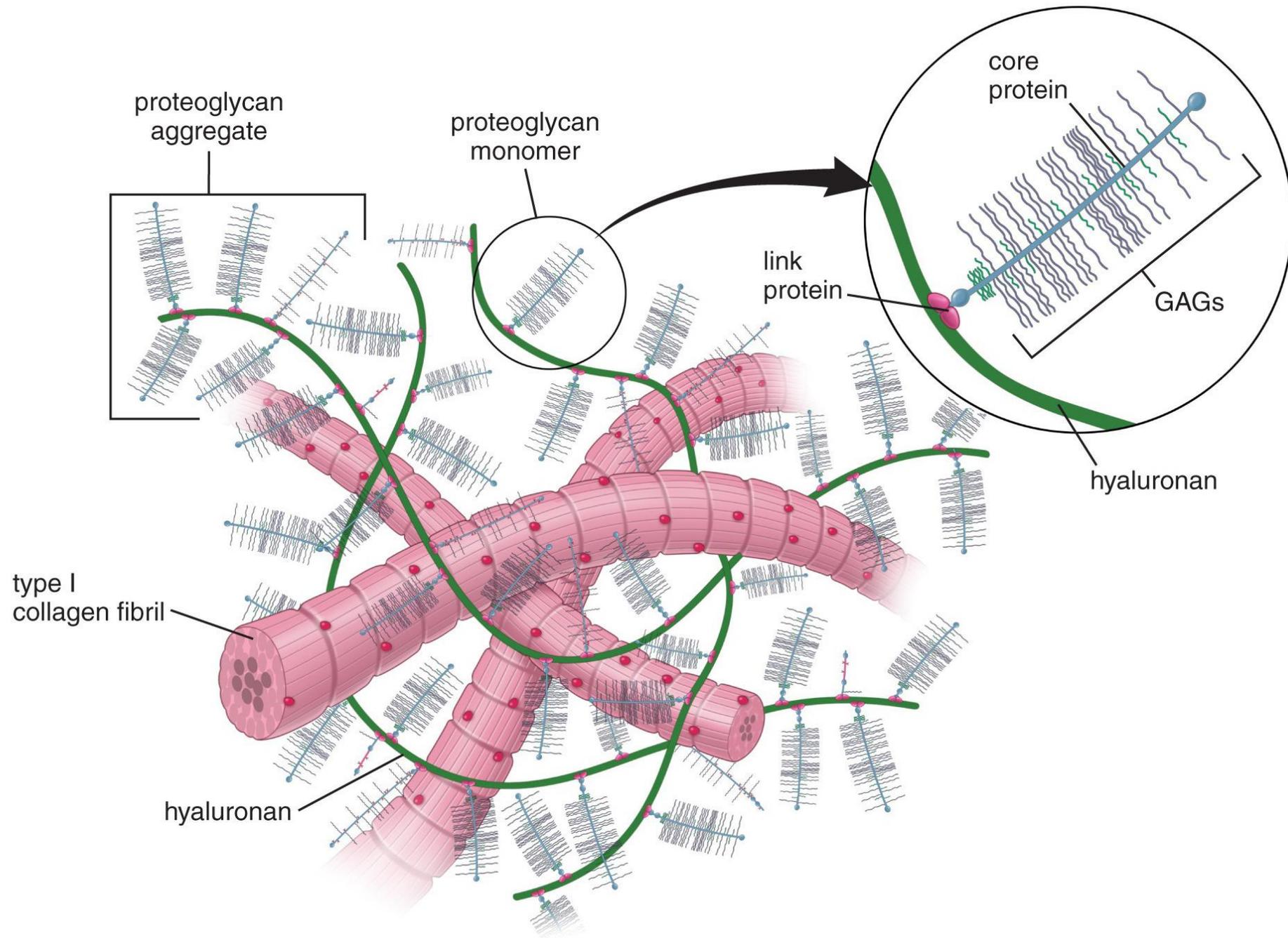
Glycosaminoglycan	Distribution
Hyaluronic acid	Umbilical cord, synovial fluid, vitreous humor, cartilage
Chondroitin 4-sulfate	Cartilage, bone, cornea, skin, notochord, aorta
Chondroitin 6-sulfate	Cartilage, umbilical cord, skin, aorta (media)
Dermatan sulfate	Skin, tendon, aorta (adventitia)
Heparan sulfate	Aorta, lung, liver, basal laminae
Keratan sulfate	Cartilage, nucleus pulposus, annulus fibrosus

# Proteoglycans

- ▶ **Proteoglycans** consist of a core protein to which are covalently attached various numbers and combinations of the sulfated GAGs.
- ▶ Like glycoproteins, they are synthesized on RER, mature in the Golgi apparatus, where the GAG side-chains are added, and secreted from cells by exocytosis.
- ▶ Unlike glycoproteins, proteoglycans have attached GAGs which often comprise a greater mass than the polypeptide core.

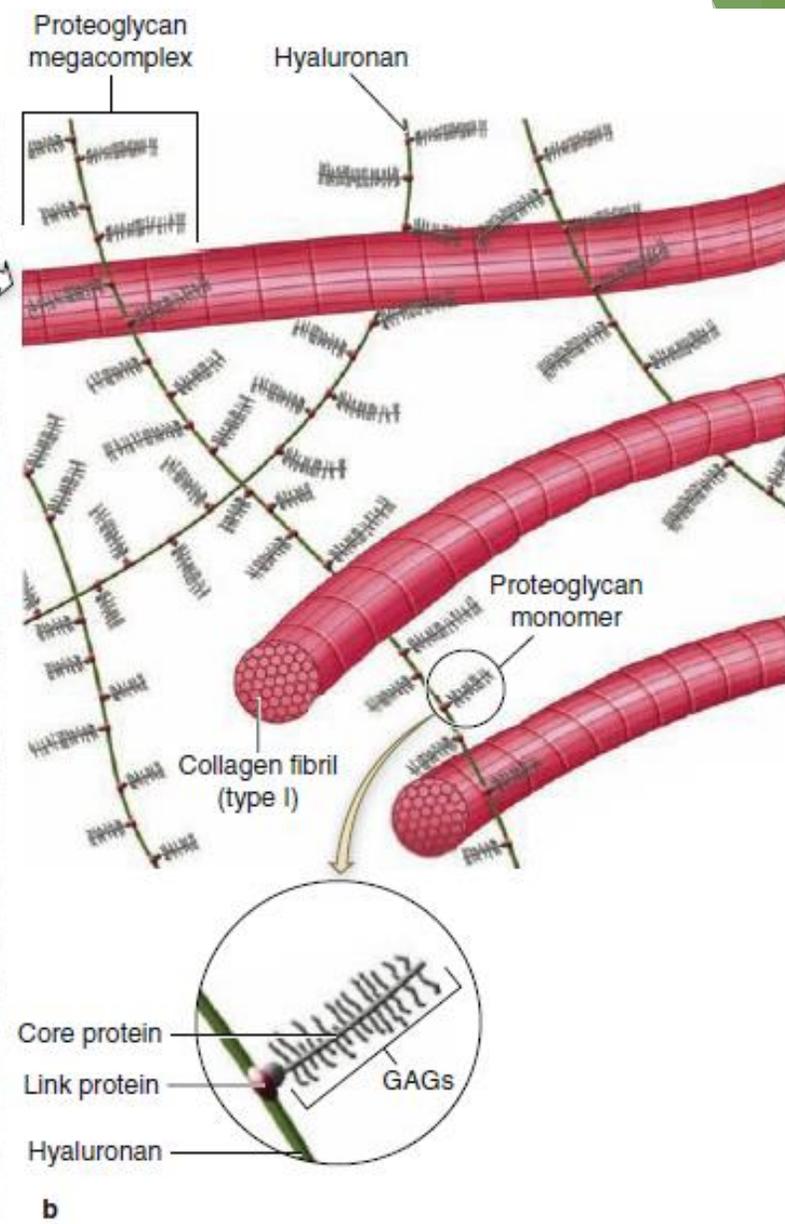
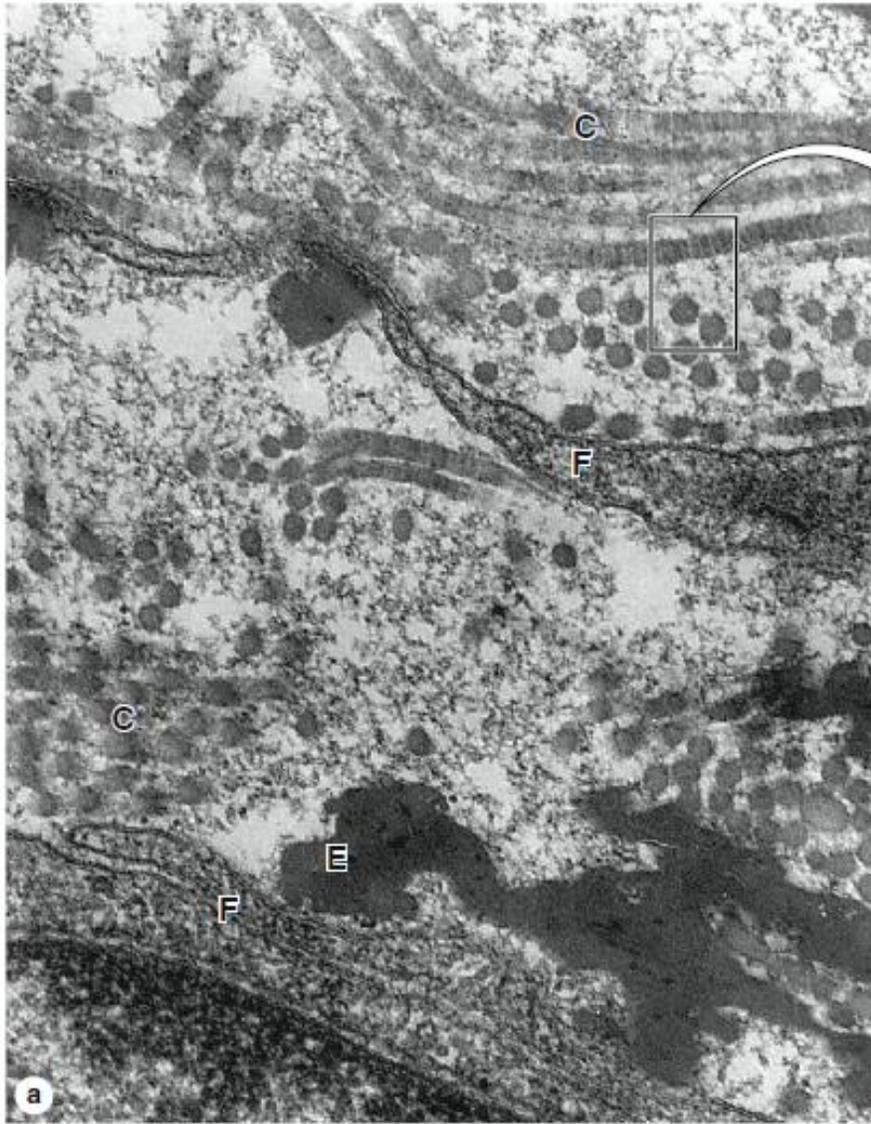


- ▶ After secretion proteoglycans become bound to the hyaluronan by link proteins and their GAG side-chains associate further with collagen fibers and other ECM components



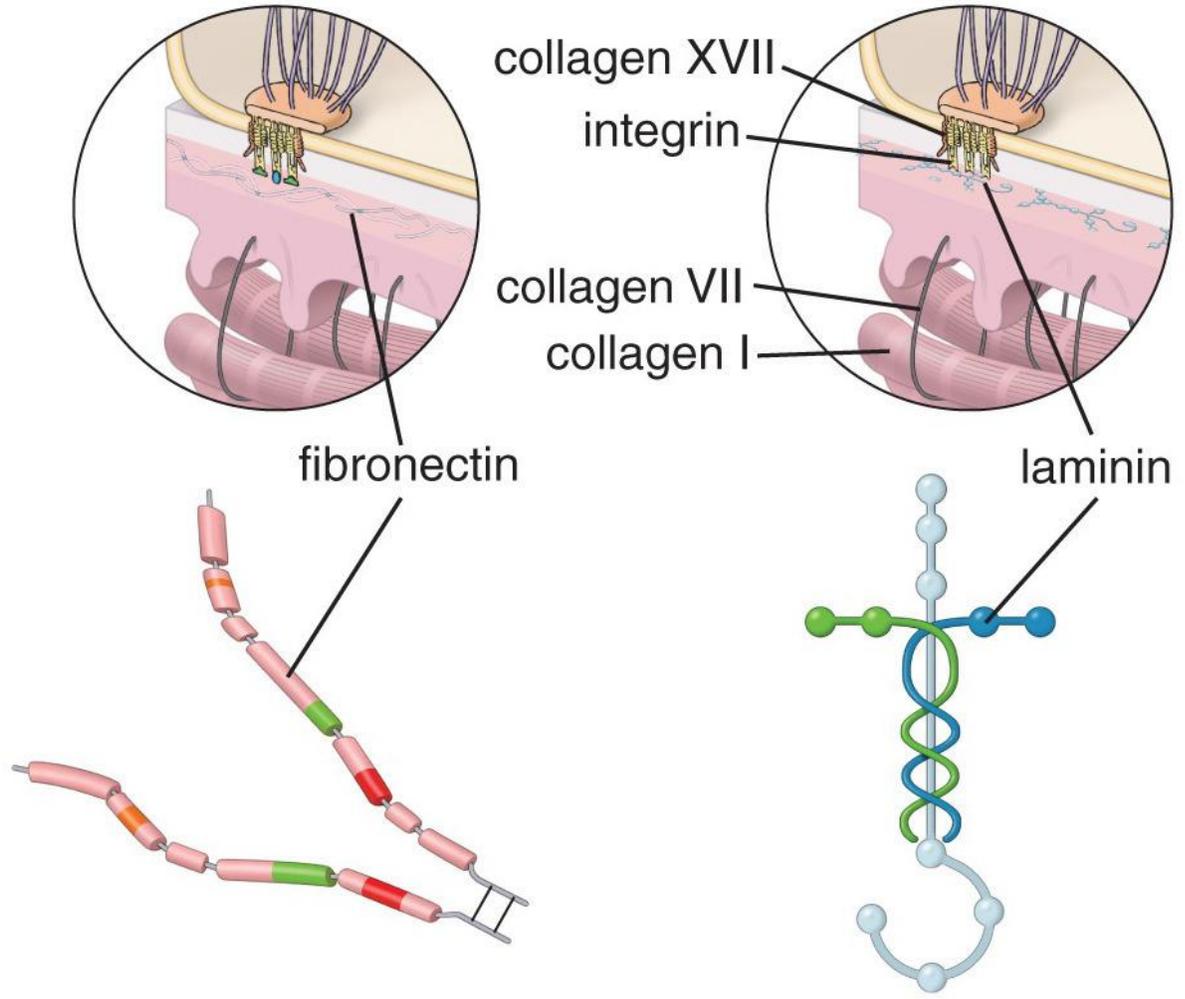
# Hyaluronan

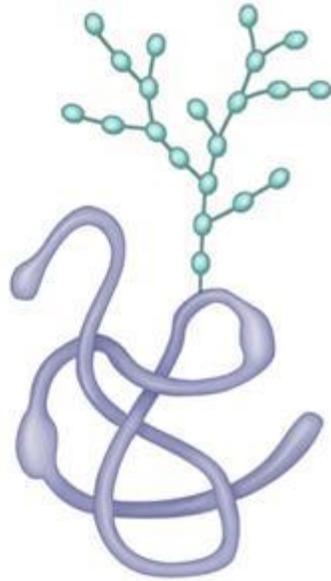
- ▶ The largest and most ubiquitous GAG is **hyaluronan** (also called hyaluronate or hyaluronic acid)
- ▶ Hyaluronan forms a viscous, pericellular network which binds a considerable amount of water
- ▶ It has an important role in allowing molecular diffusion through connective tissue and in lubricating various organs and joints.



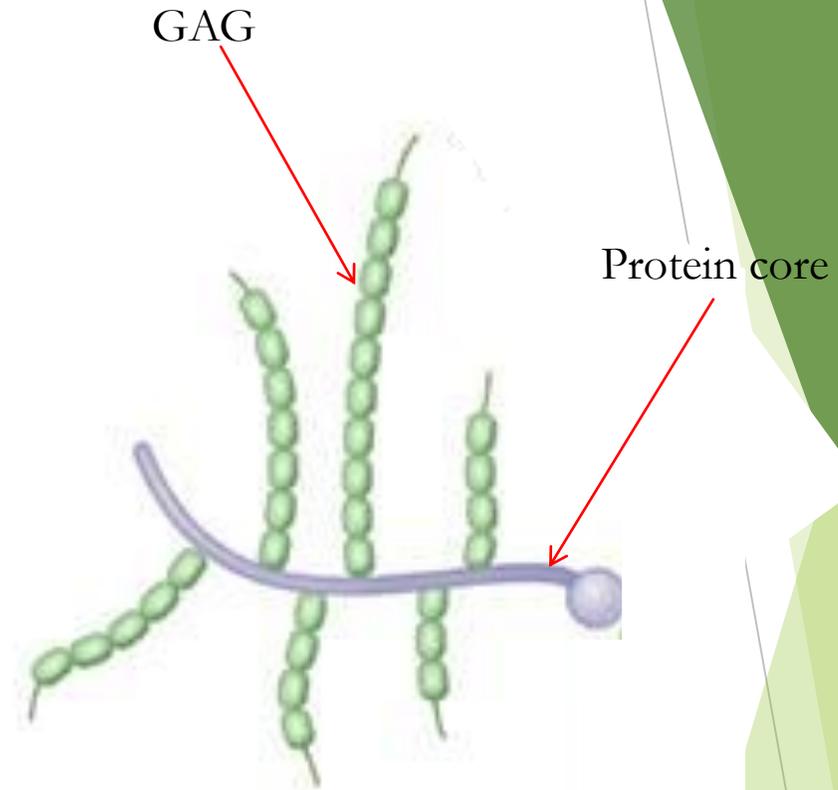
# Adhesive Glycoproteins

- ▶ The adhesive glycoproteins are large molecules with branched oligosaccharide chains and allow adhesion of cells to their substrate
- ▶ They have multiple binding sites for cell surface integrins and for other matrix macromolecules..
- ▶ Examples: Laminin, chondronectin, osteonectin and fibronectin.





Glycoprotein



Proteoglycan

# Classification of Connective Tissue



## ▶ Connective tissue proper:

- Loose (areolar)
- Dense regular
  - Dense irregular
  - Dense regular

## ▶ Special connective tissue:

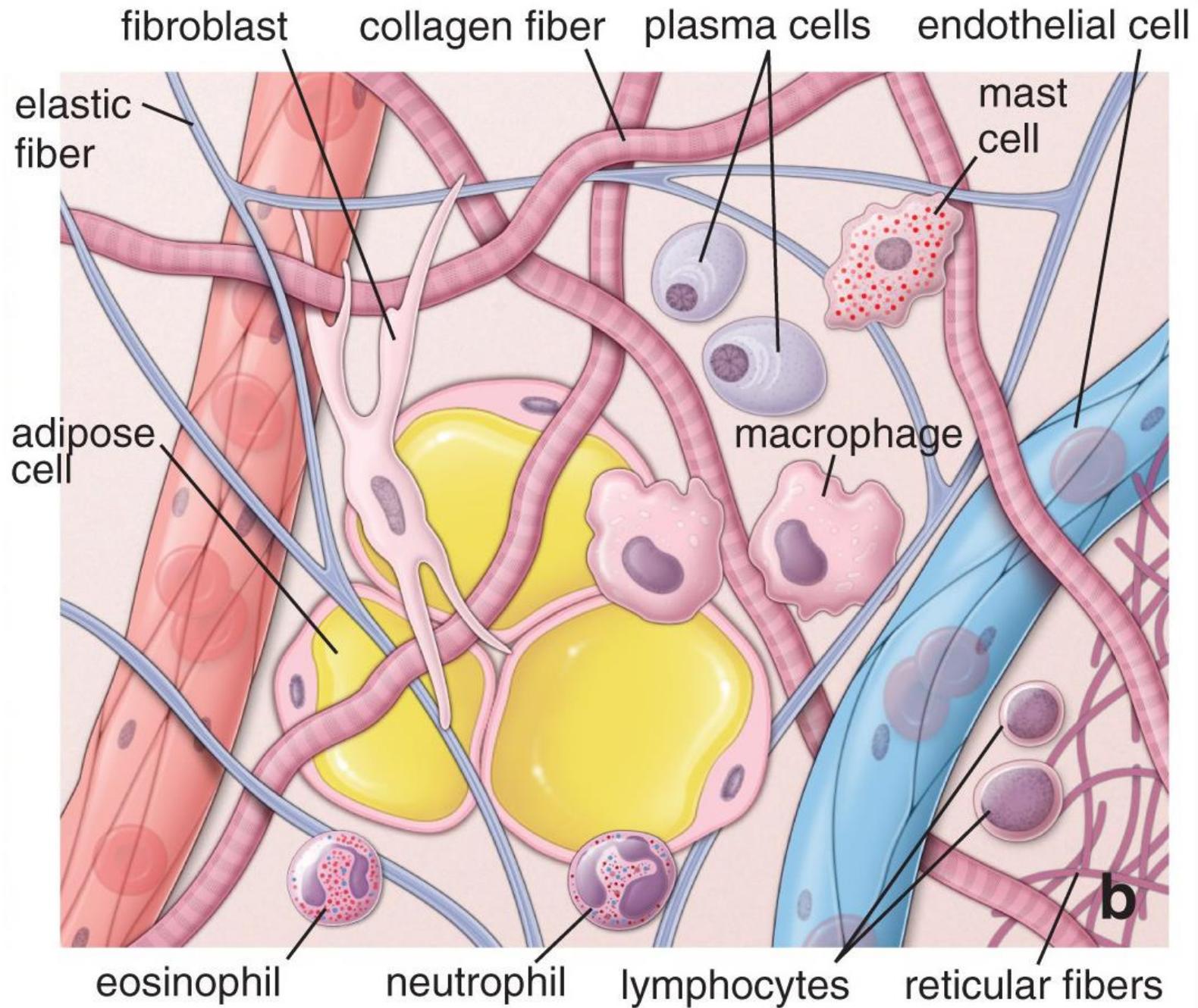
- Reticular
- Elastic
- Adipose
- Bone
- Cartilage
- Blood

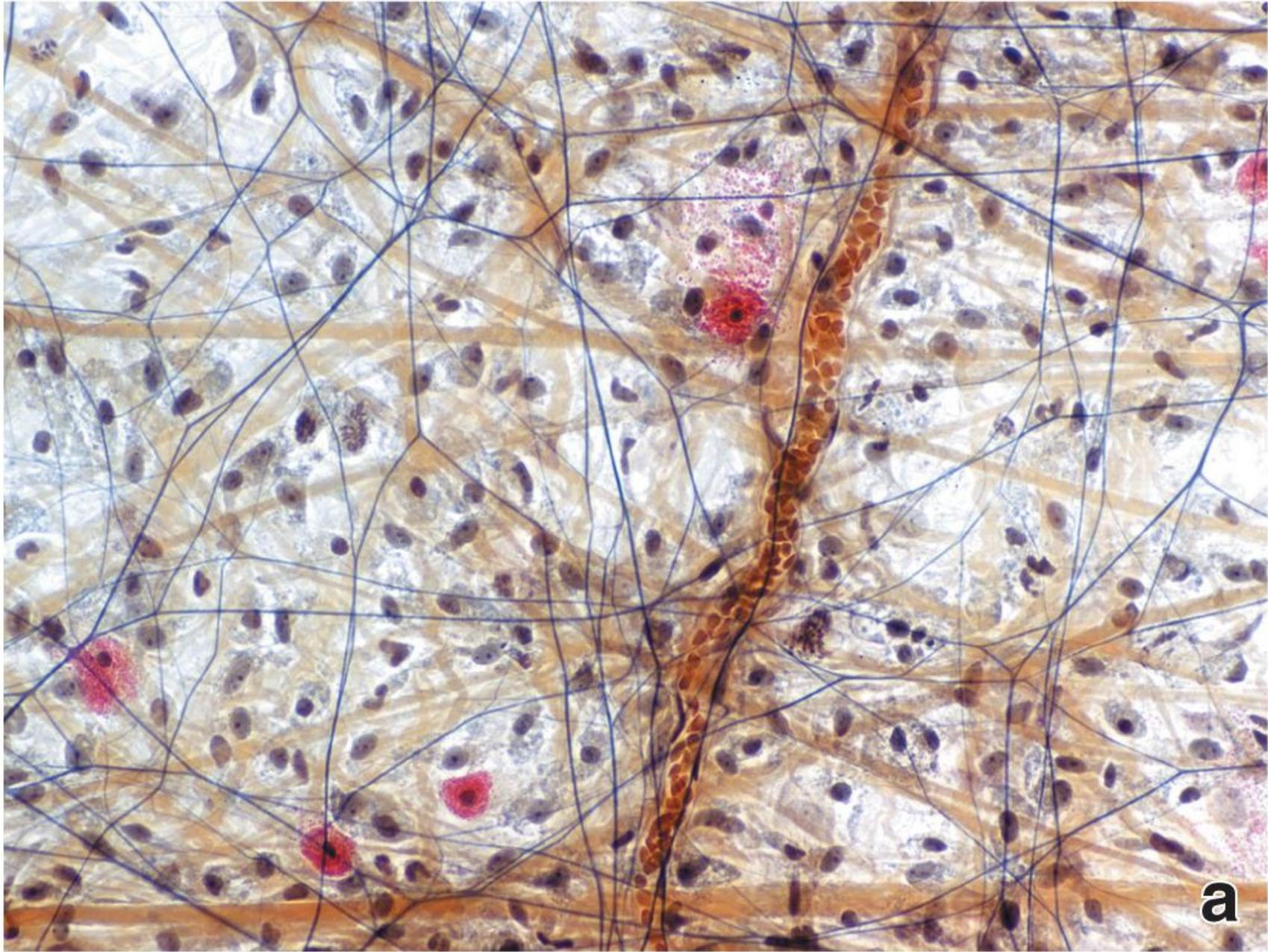
## ▶ Embryonic connective tissue

- Mesenchymal (mucoid) connective tissue

# Loose Connective Tissue

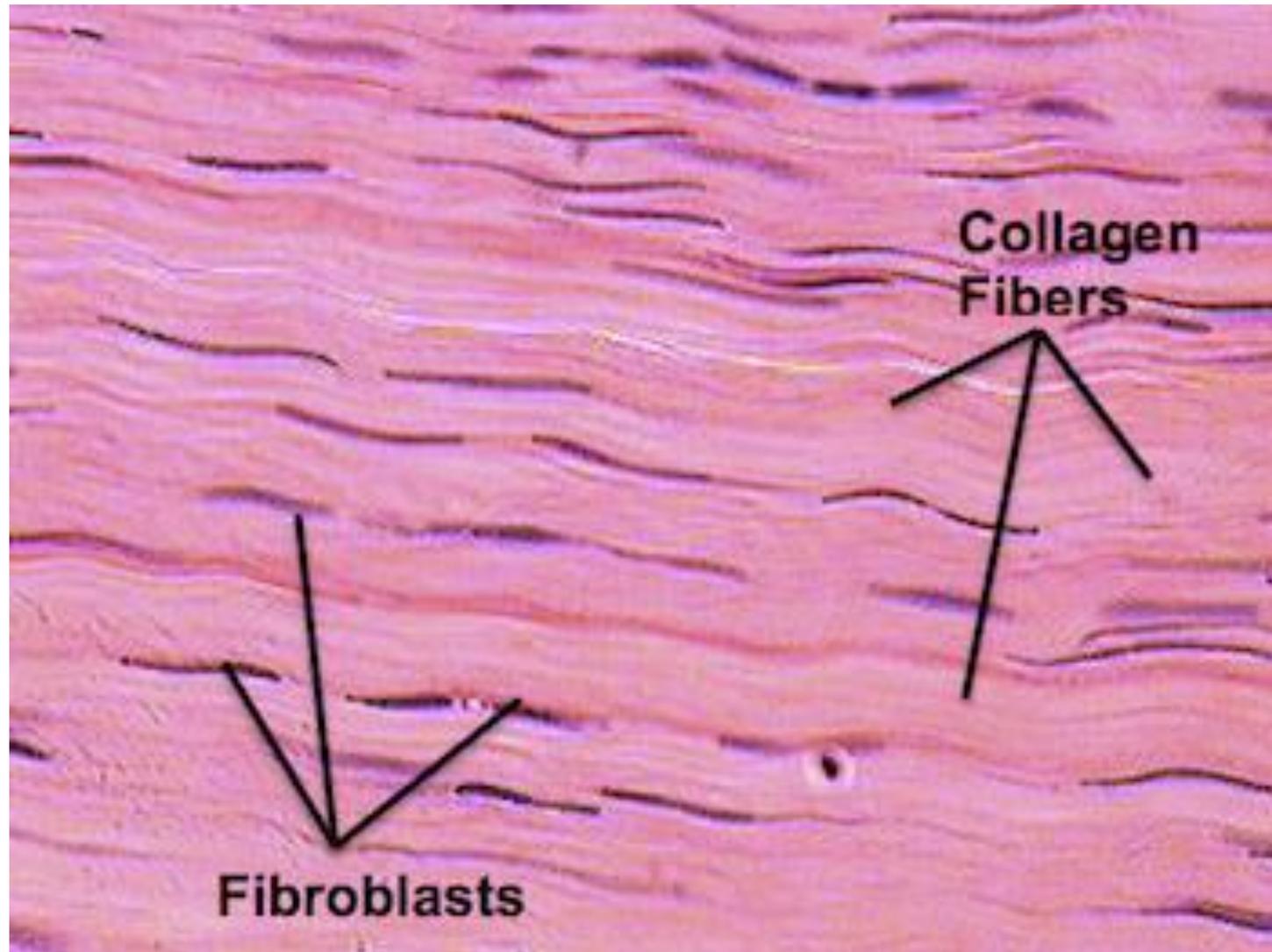
- ▶ Also called areolar connective tissue
- ▶ Typically contains cells, fibers and ground substance in equal amounts
- ▶ Supports epithelium (lamina propria)
- ▶ Surrounds small blood vessels
- ▶ Fills spaces between muscle and nerve cells
- ▶ Mesentery
- ▶ It is flexible but not very resistant to stress





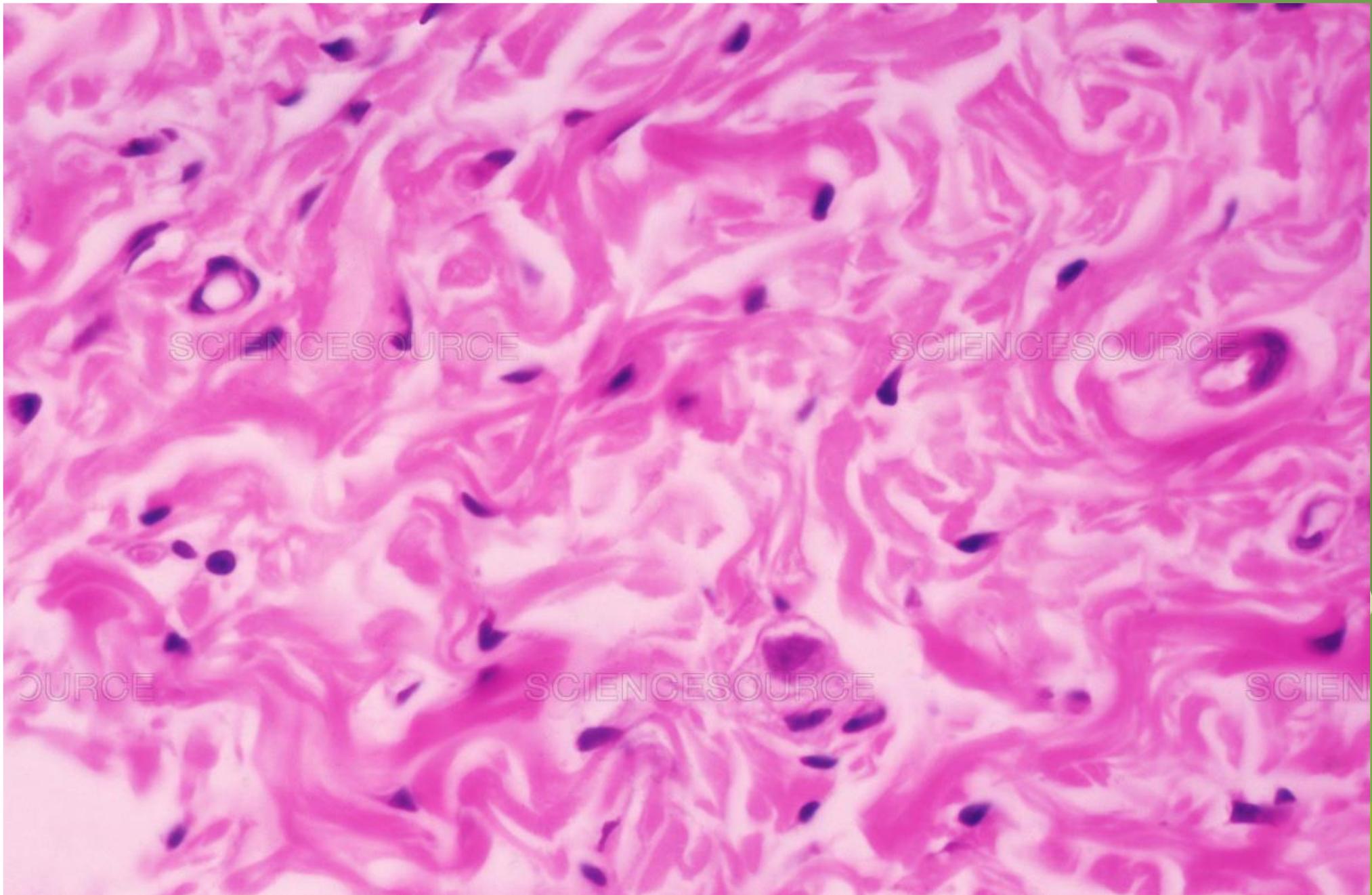
# Dense Regular Connective Tissue

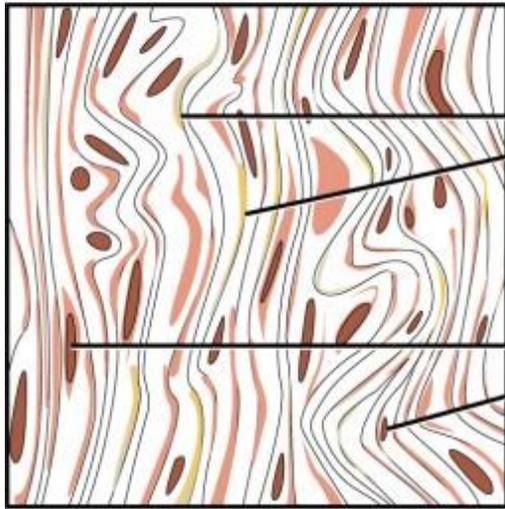
- ▶ Parallel bundles of collagen fibers with few fibrocytes aligned with collagen and separated by very little ground substance
- ▶ Provides resistance to prolonged or repeated stresses exerted in the same direction
- ▶ Ligaments and tendons



# Dense Irregular Connective Tissue

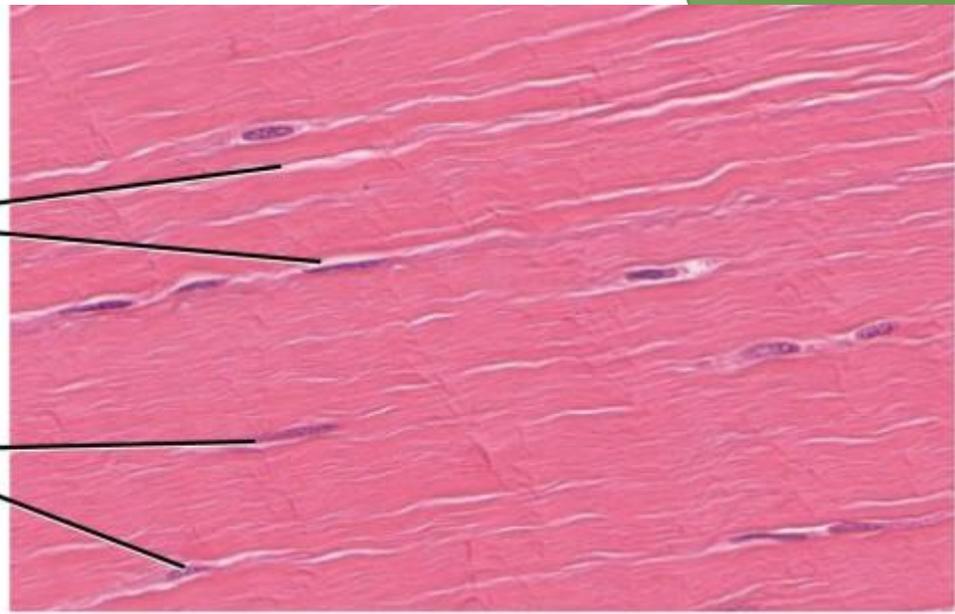
- ▶ Bundles of collagen fibers are randomly interwoven with no definite orientation
- ▶ Provides resistance to stress from all directions
- ▶ Dermis of skin, organ capsules, submucosa



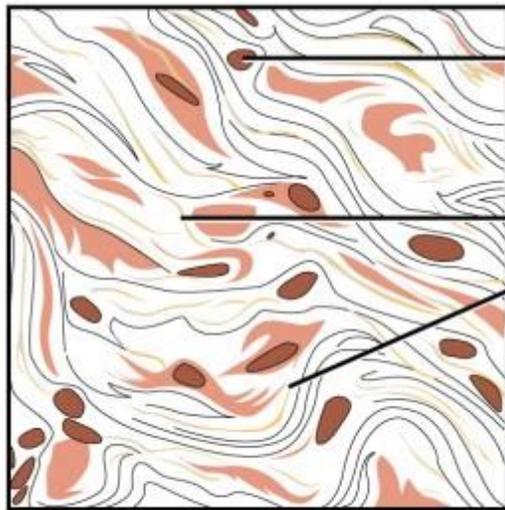


Collagen fibers

Fibroblast nuclei

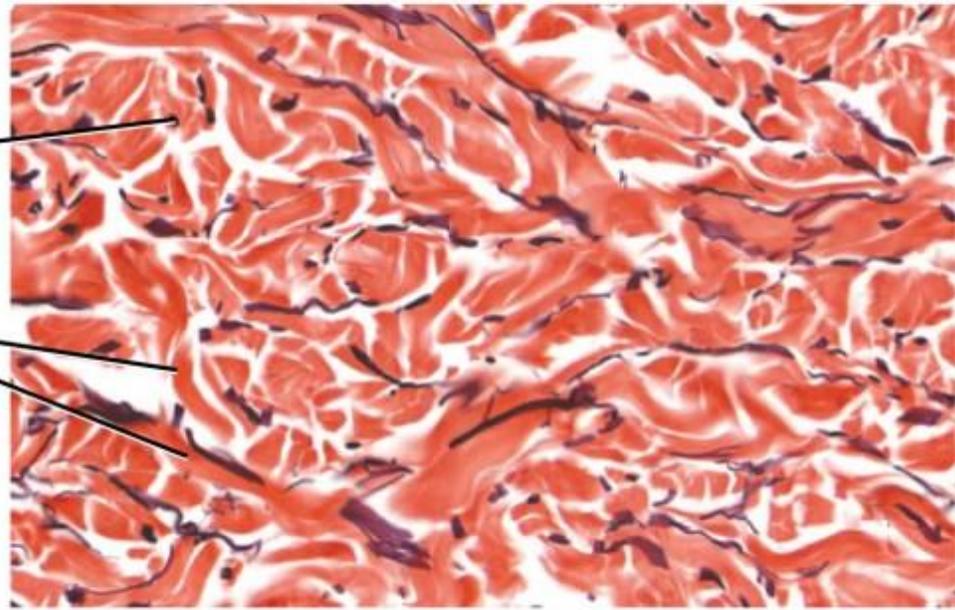


**(a) Regular dense**



Fibroblast nuclei

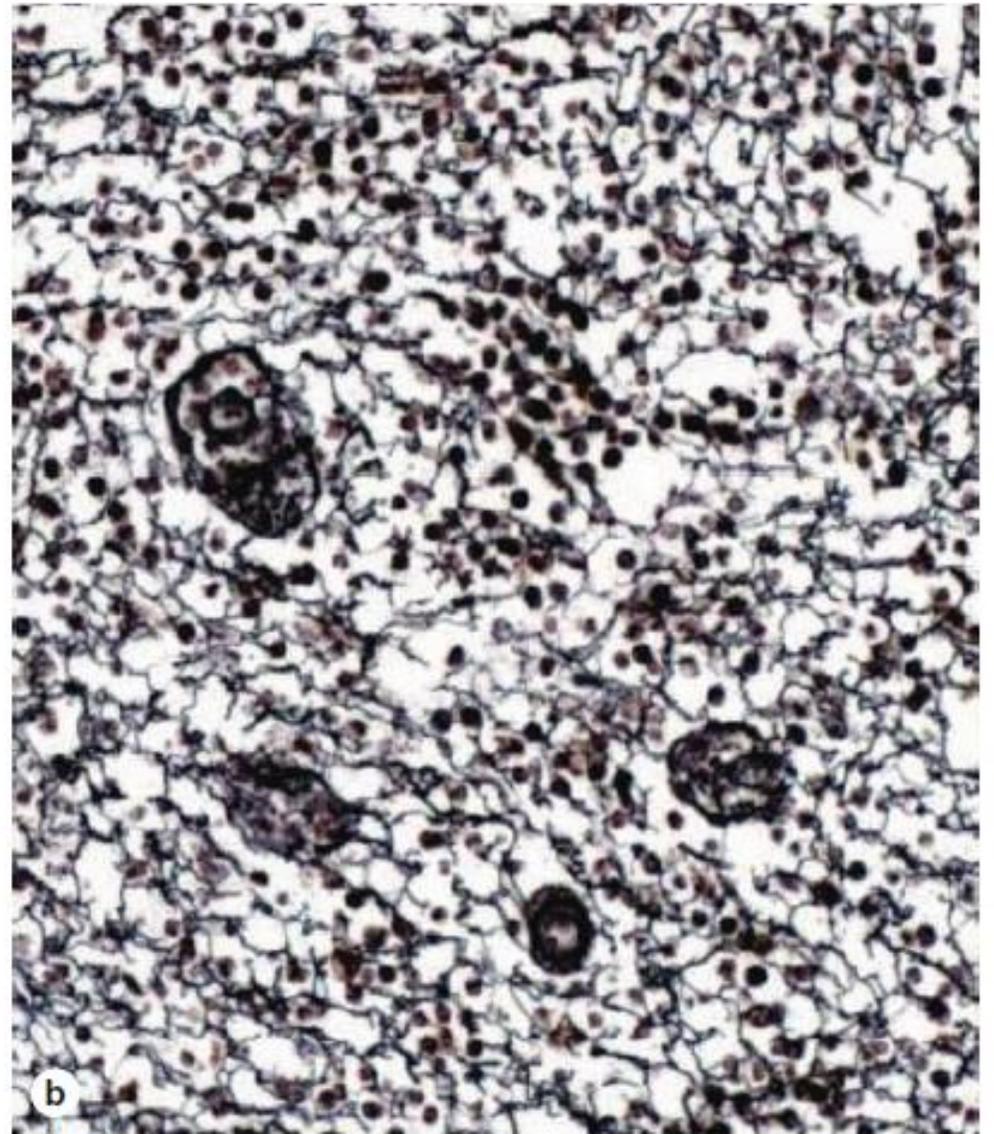
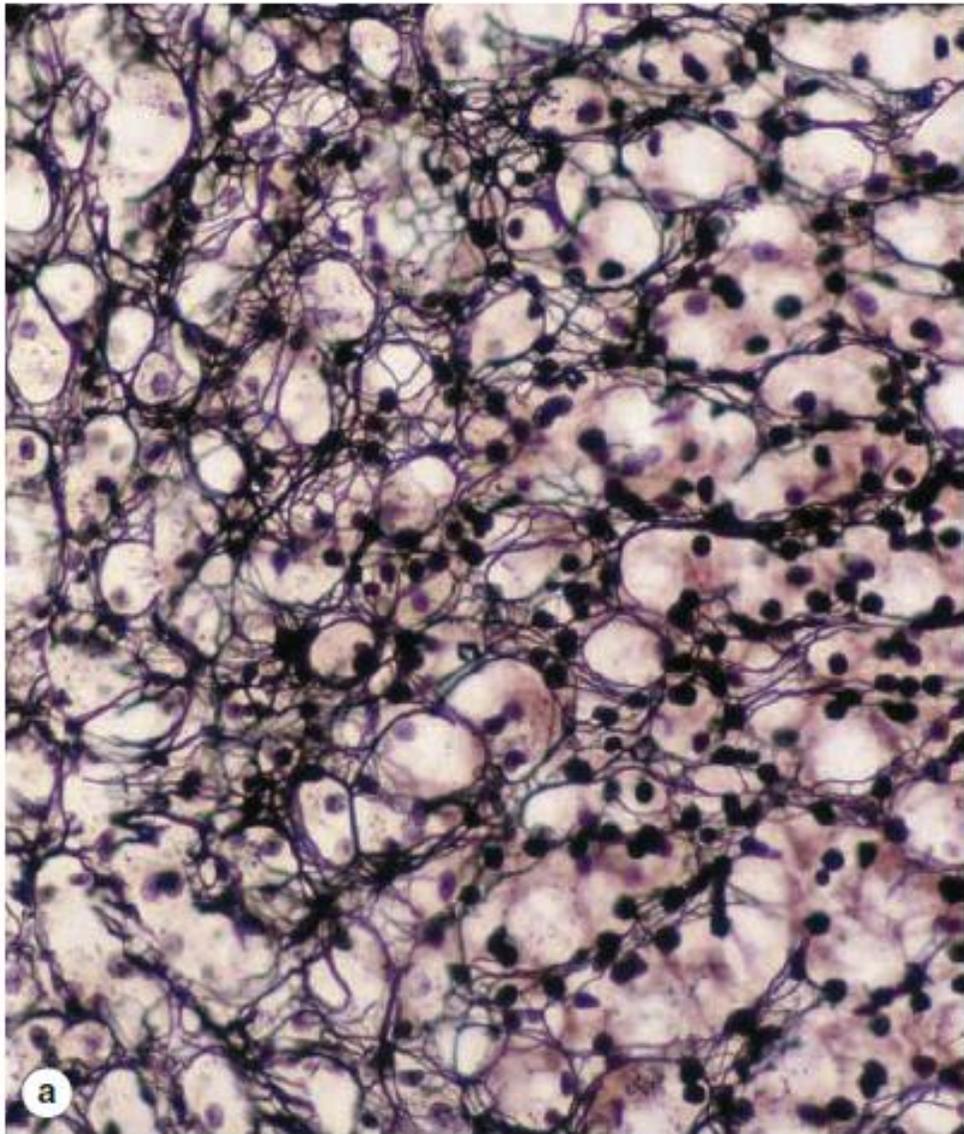
Collagen fiber bundles



**(b) Irregular dense**

# Reticular Connective Tissue

- ▶ Consists of reticular cells (modified fibroblasts) and the network of reticular fibers formed by them
- ▶ Forms the structural framework in which the cells of the organ are suspended
- ▶ In the liver, bone marrow, lymph nodes and the spleen



# Mesenchymal Connective Tissue

- ▶ Mesenchyme forms the undifferentiated "filling" of the early embryo.
- ▶ It consists of mesenchymal cells, which interconnect by slender cell processes.
- ▶ Mesenchymal cells have stem cell properties, i.e. they are able give rise to other cell and tissues types.
- ▶ The wide extracellular space between the mesenchymal cells is occupied by ground substance

