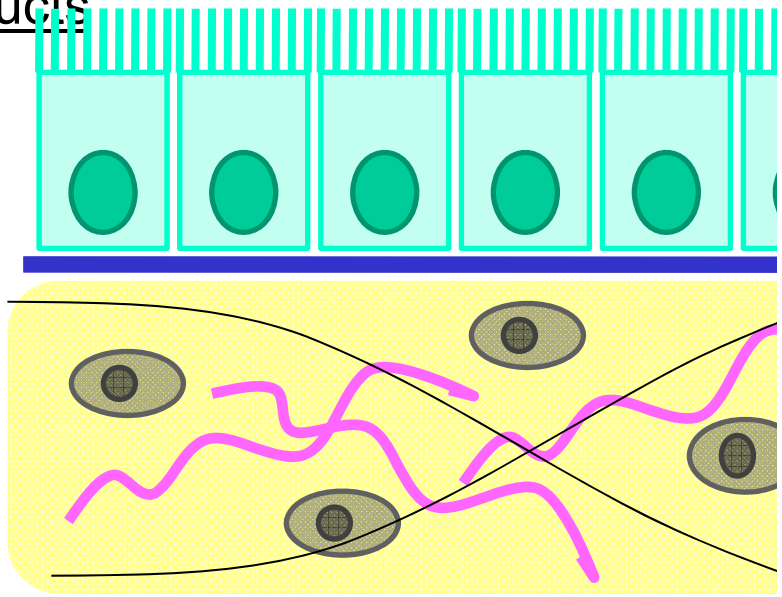
Ordinary Connective Tissue and Cartilage

Images from Human Anatomy 6th ed., © 2009 by Martini, Timmins and Talitsch, denoted by “Ma”.
Images from Basic Histology, Text & Atlas, 11th ed., 2005, by Junqueira & Carneiro denoted by “J”
Images from Wheater’s Functional Histology 5th ed., © 2006 by Young et al. denoted by “W”.
Images from Colour Atlas of Histology 5th ed., © 2009 by Gartner and Hiatt denoted by “GA”.
Images from Colour Textbook of Histology 3rd ed., © 2007 by Gartner and Hiatt denoted by “GT”.

Recall:

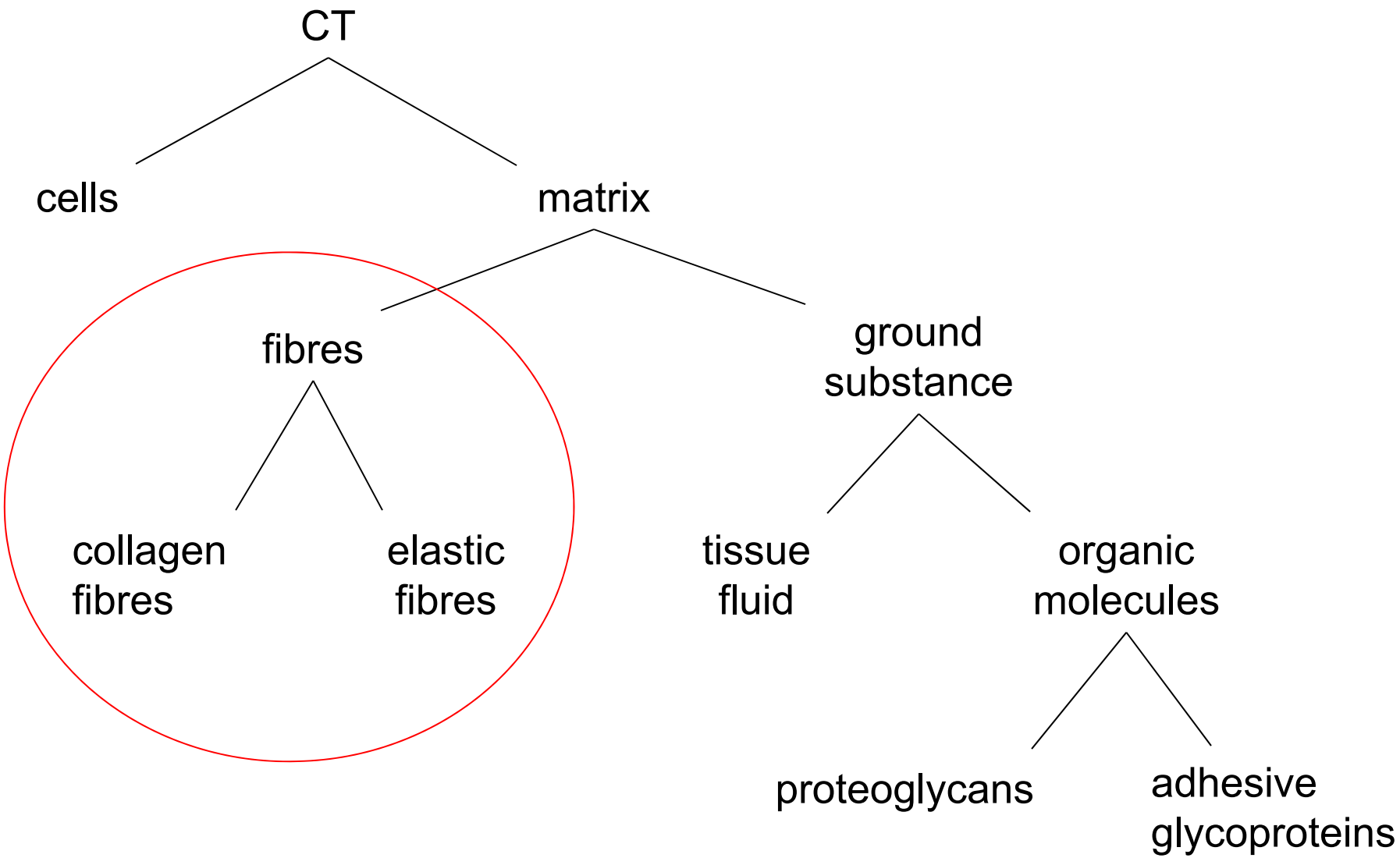
- tissues are composed of cells and cell products
- epithelia is characterised by its *cellularity*



By Contrast:

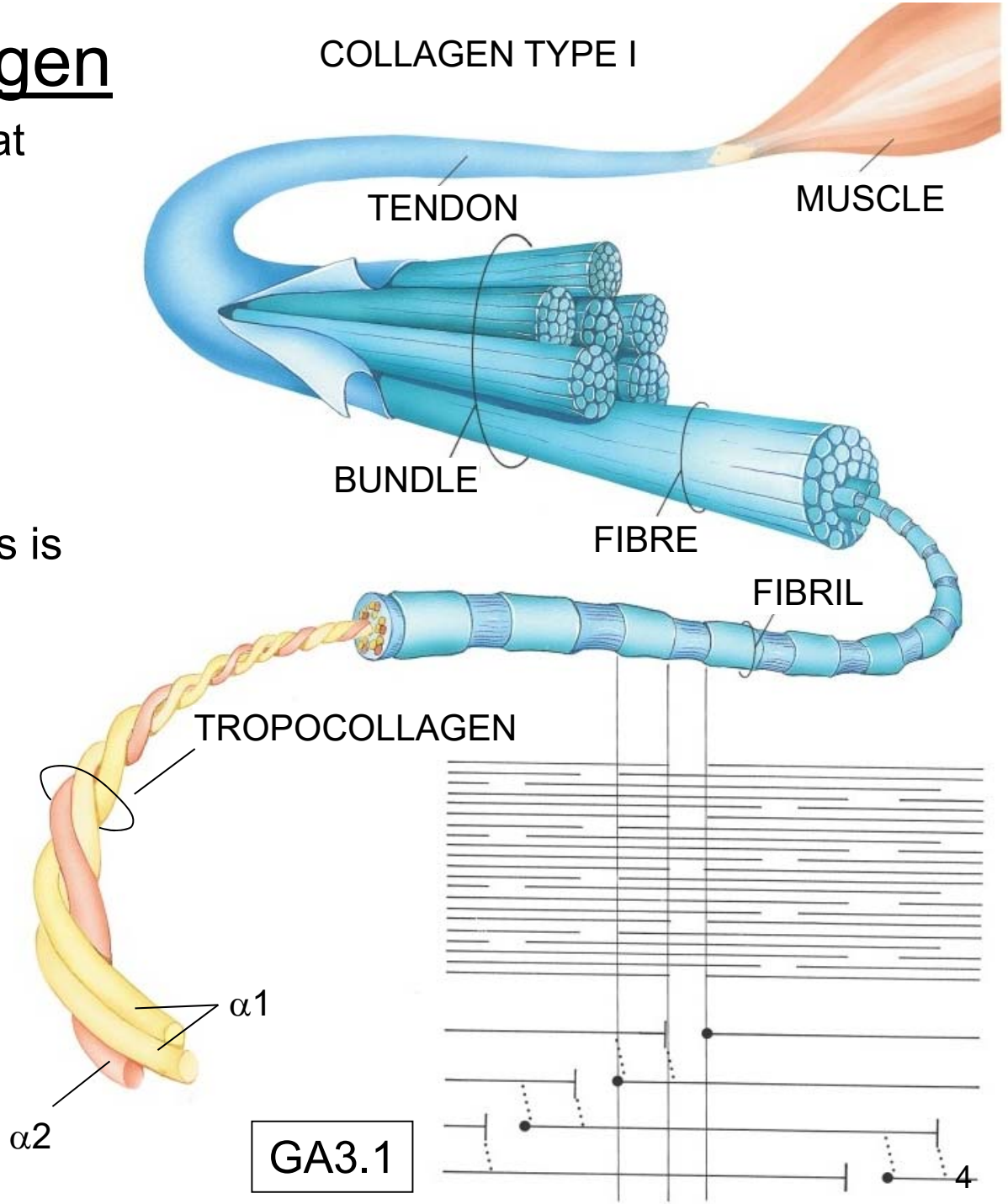
- CT largely cell products, called *matrix*; fewer cells
- matrix = protein fibres + ground substance
- characteristics of matrix largely determine properties and functions of CT
- protein fibres, organic components of GS produced by CT cells; extruded into extracellular space
- consistency of ground substance varies from liquid to solid
- includes CT proper (“ordinary CT”), cartilage & bone
- cells specialized for a given CT type (*fibro-, chondro-, osteo-)*

CT Components

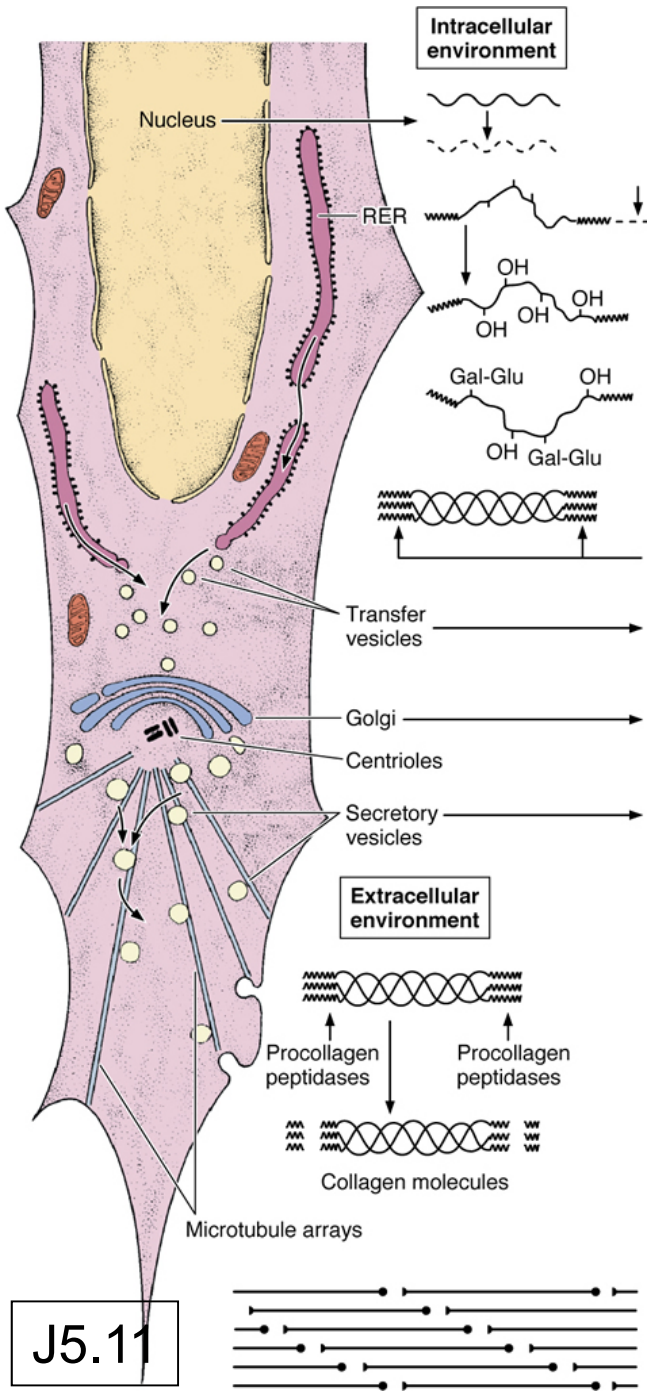


Structure of Collagen

- inelastic protein with great tensile strength
- >20 types of collagen, based on α-chain AA sequence
- fibrillar collagen synthesis is a multistep process:
  - preprocollagen
  - procollagen
  - tropocollagen
  - fibrils
  - fibres



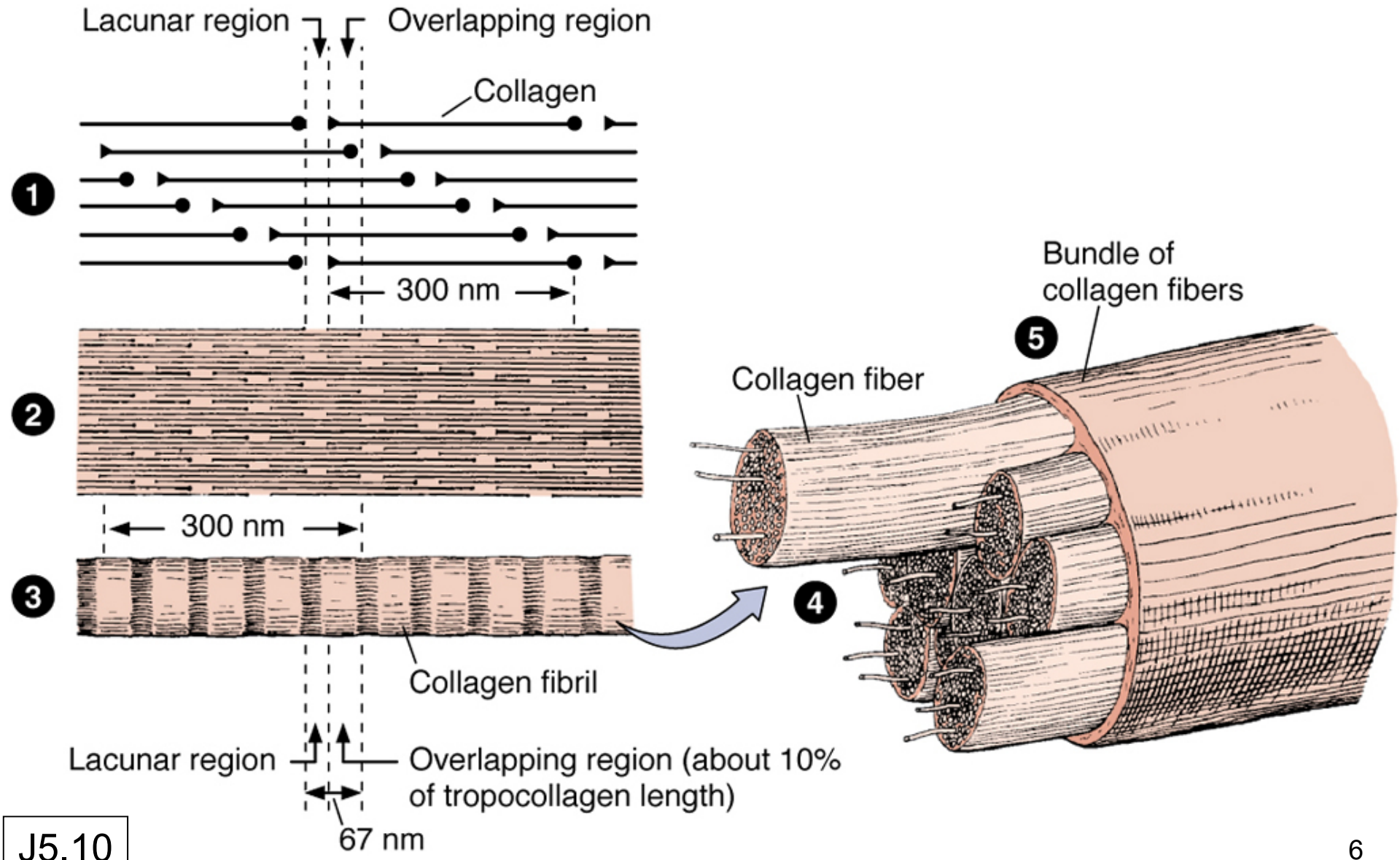
Collagen Biosynthesis



J5.11

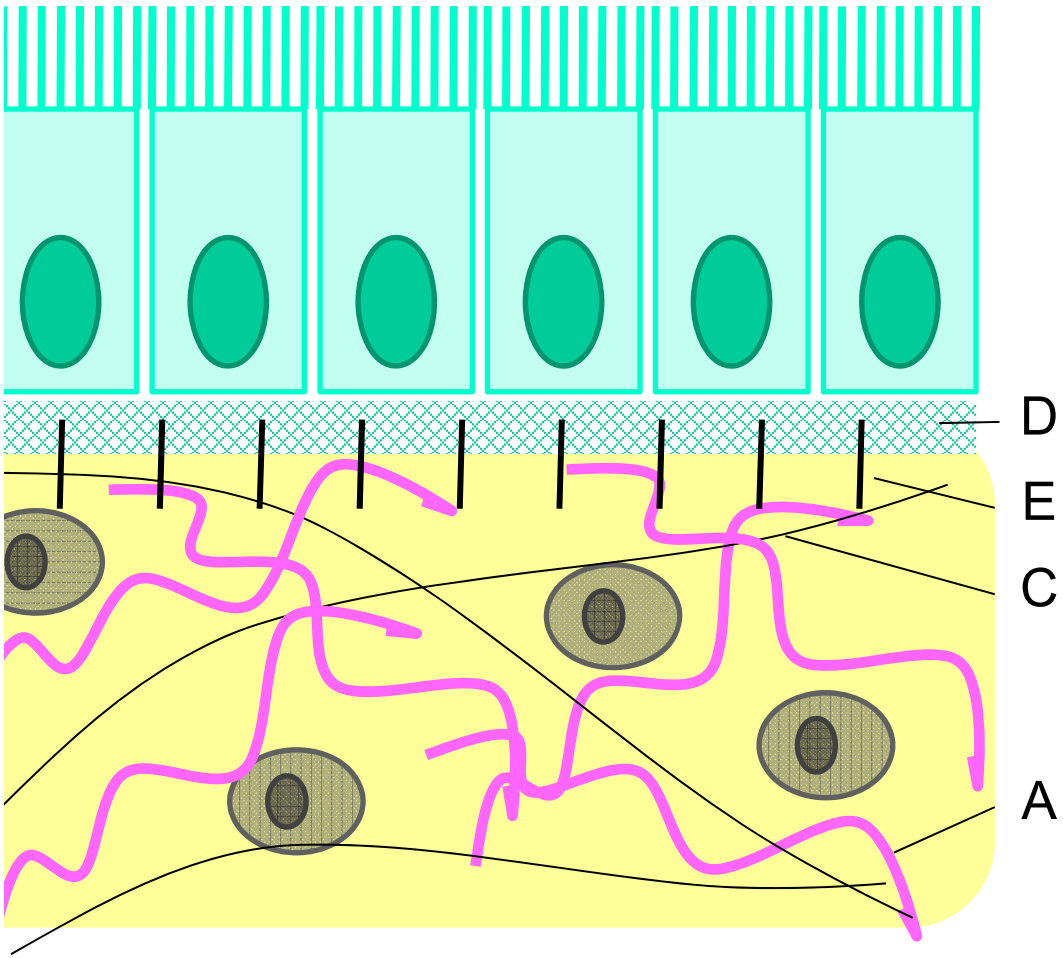
- within nucleus, formation of mRNA for each α chain
- within RER, synthesis of α chains of **preprocollagen**
- post-translational modification & assembly into **procollagen** triple helix with *registration peptides* on both amino- and carboxyl-terminal ends
- registration peptides maintain solubility of procollagen
- transfer of soluble procollagen to Golgi
- in Golgi, further post-translational modification occurs
- soluble procollagen packaged into secretory vesicles
- vesicles transported to cell surface
- during exocytosis, membrane-bound procollagen peptidases remove registration peptides from procollagen, forming insoluble **tropocollagen**
- tropocollagen molecules aggregate: **collagen fibrils**
- covalent cross-links between tropocollagen molecules reinforce fibrilar structure

Extracellular Collagen Assembly



J5.10

Collagen Fibres are Regionally Distributed



A. Type I collagen, most common; CT proper, bone

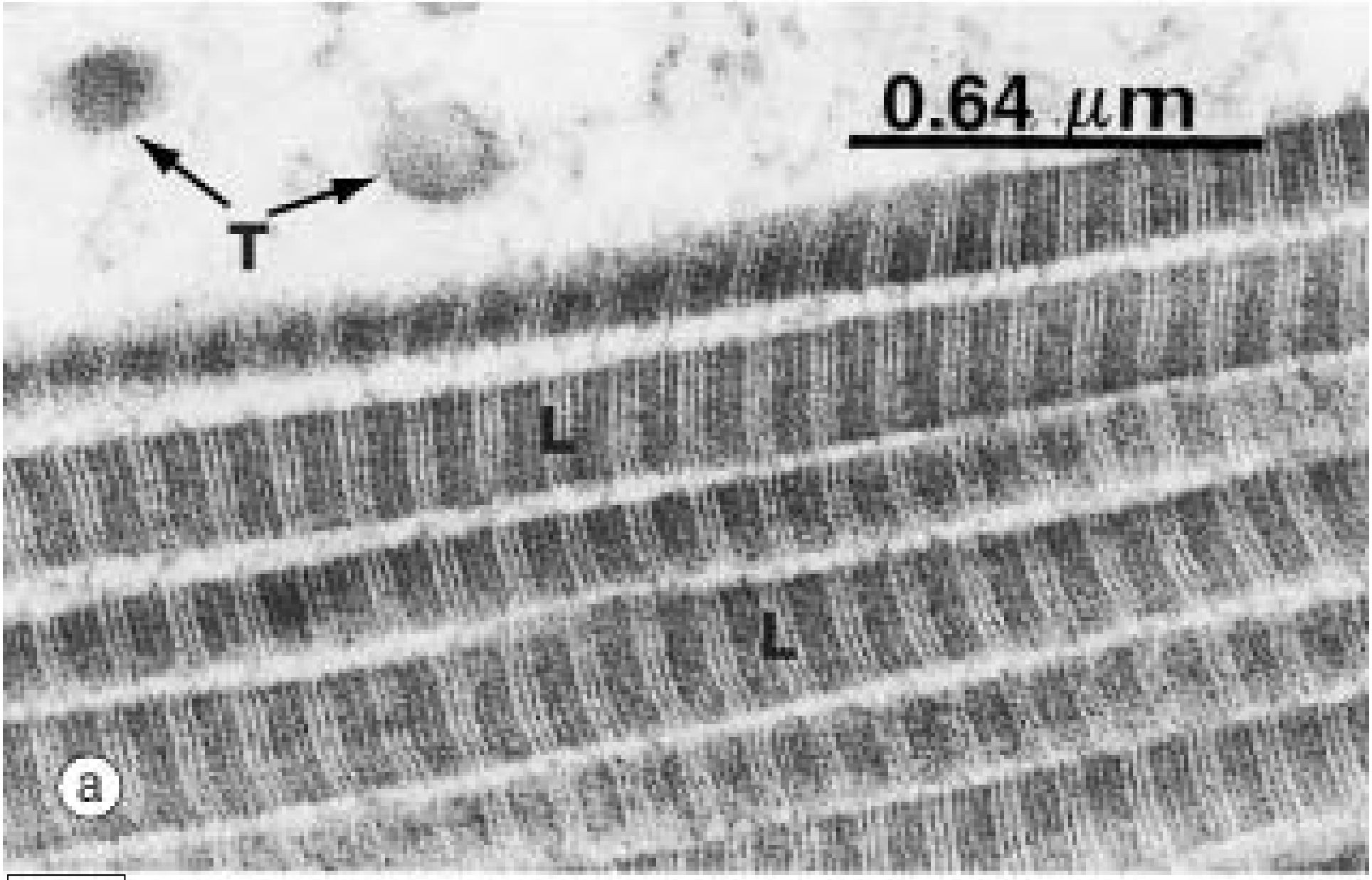
B. Type II collagen, cartilages

C. Type III collagen forms "reticular fibres"

D. Type IV collagen forms a meshwork in the BM

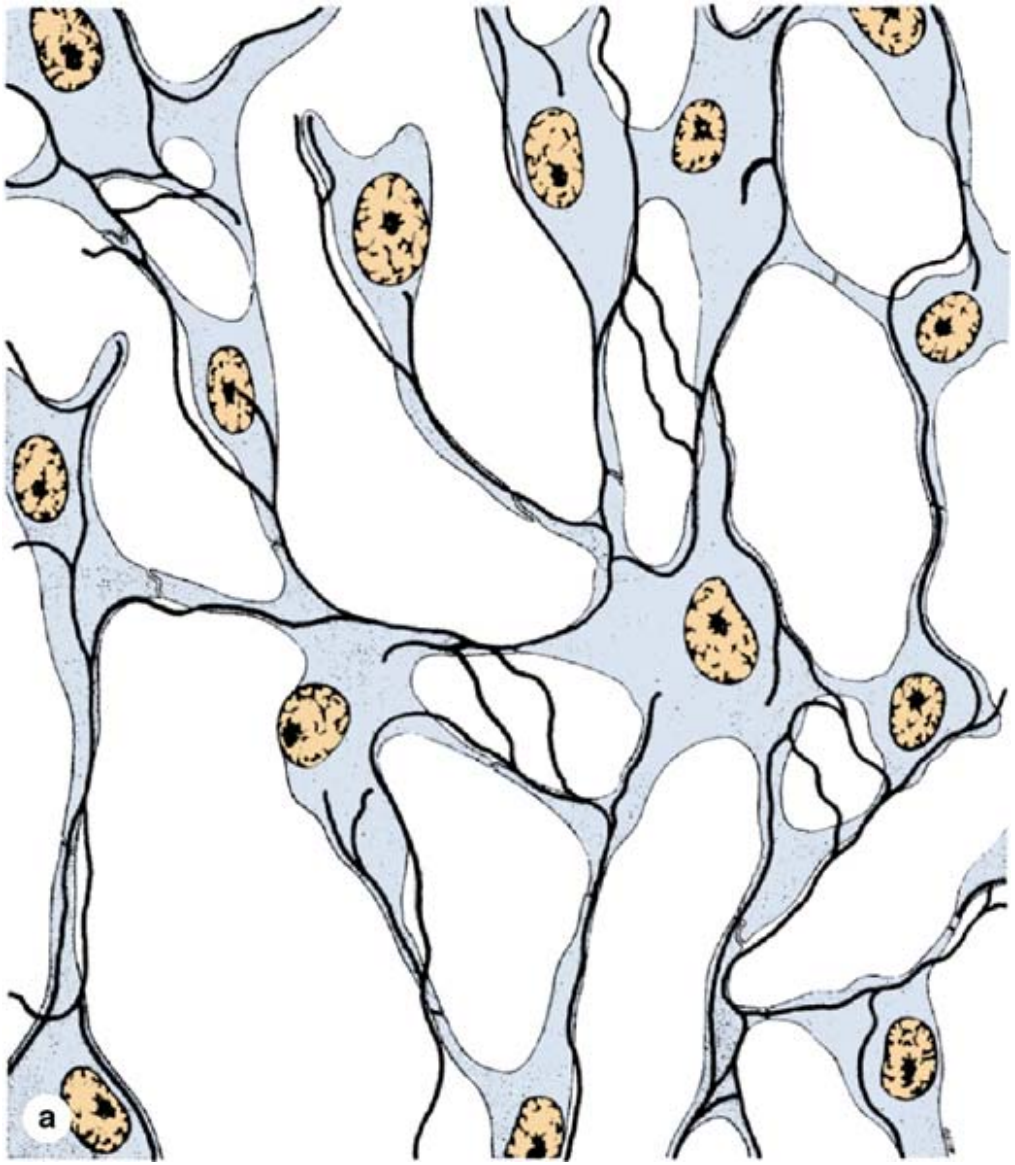
E. Type VII collagen forms *anchoring fibrils*, which bind the BM to underlying type I & type III collagen

Type I Collagen Fibres by TEM



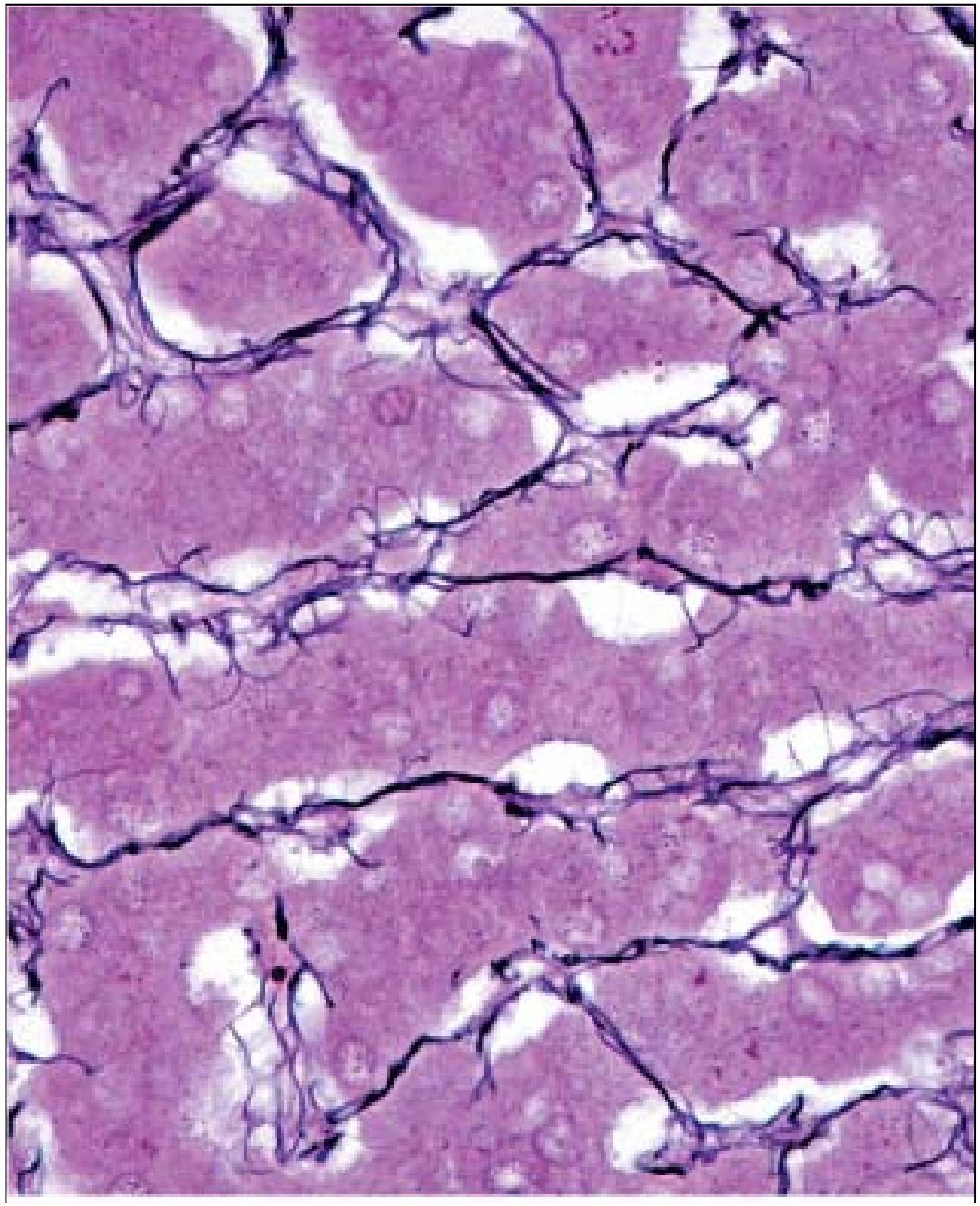
W4.2

Collagen Type III: “Reticular Fibres”



- very fine fibres
- form an extensive network in certain organs
- forms the *stroma* (scaffolding) of highly cellular organs on which they arrange their *parenchyma*, or functional cells

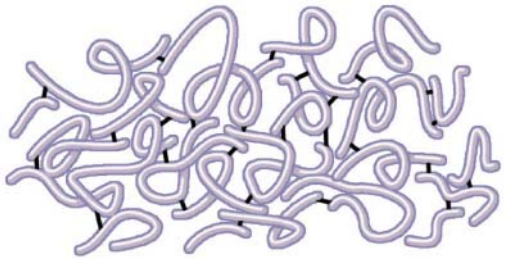
Collagen Type III: “Reticular Fibres”



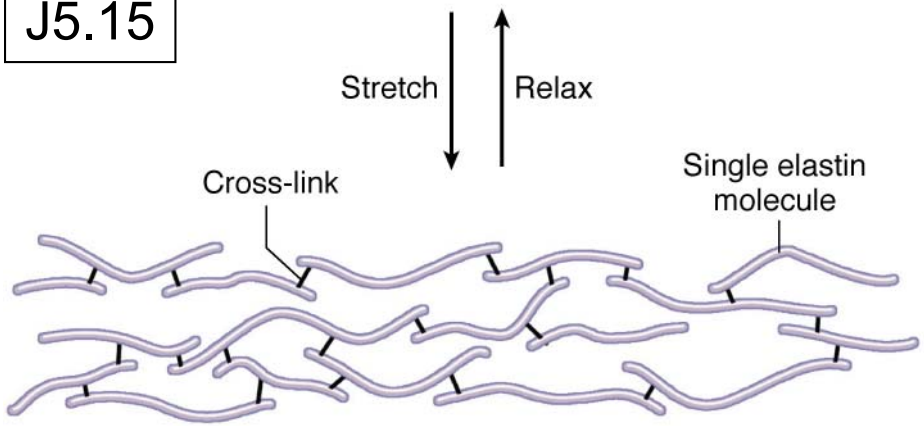
Liver

W4.3

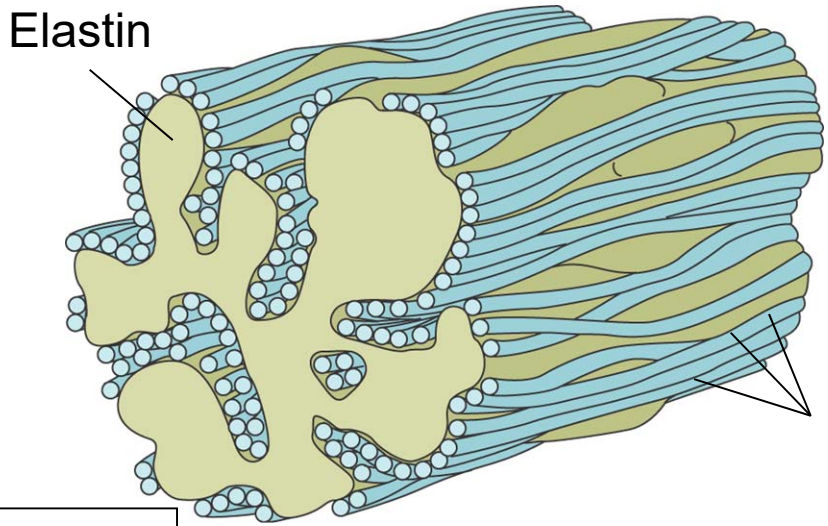
Elastic Fibres



J5.15



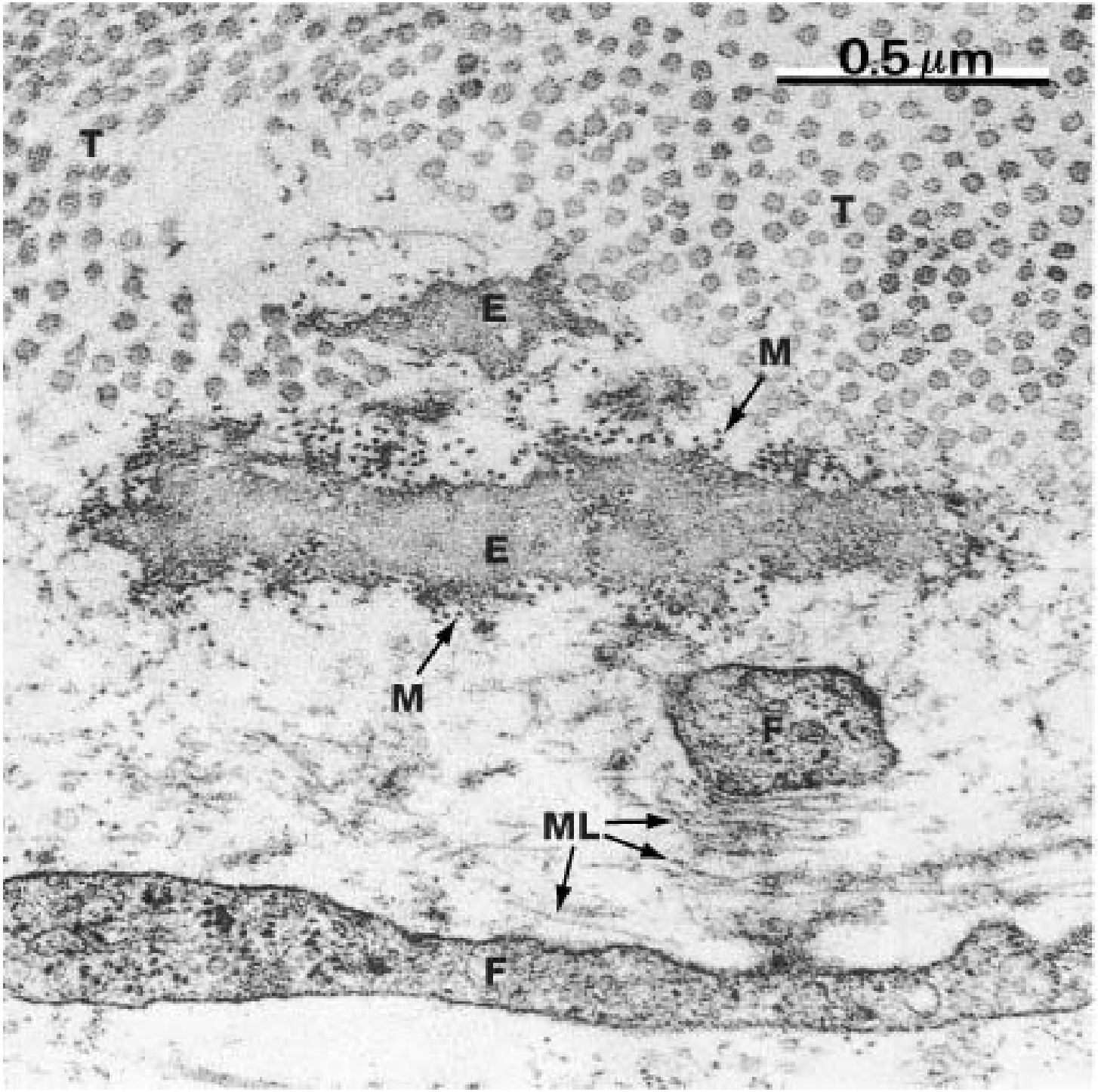
- stretch to 1.5x resting length, then recoil
- esp. certain ligaments, walls of larger BVs



GT4.11

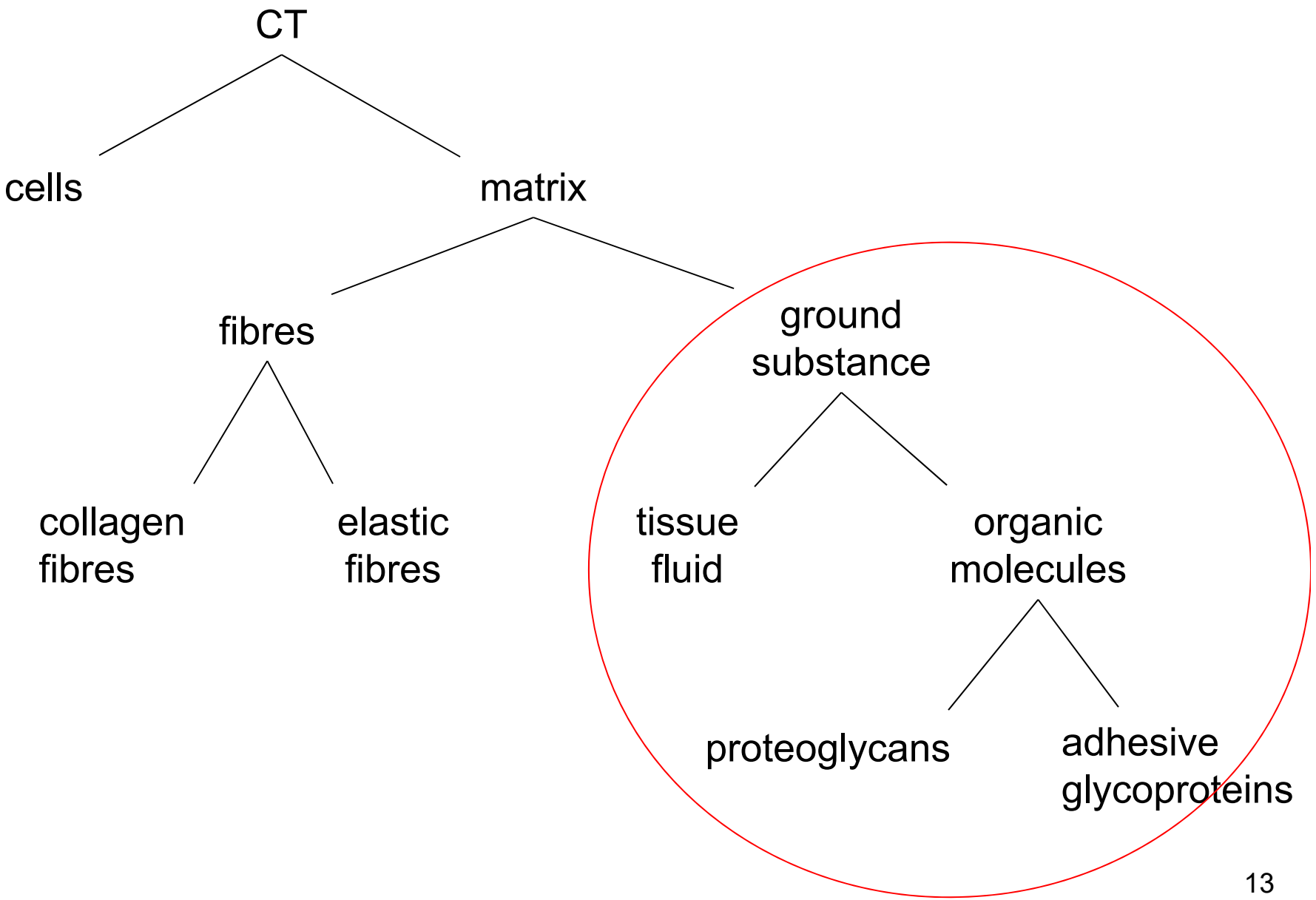
- composed of *elastin* embedded in microfibrils composed of fibrillin

Elastin



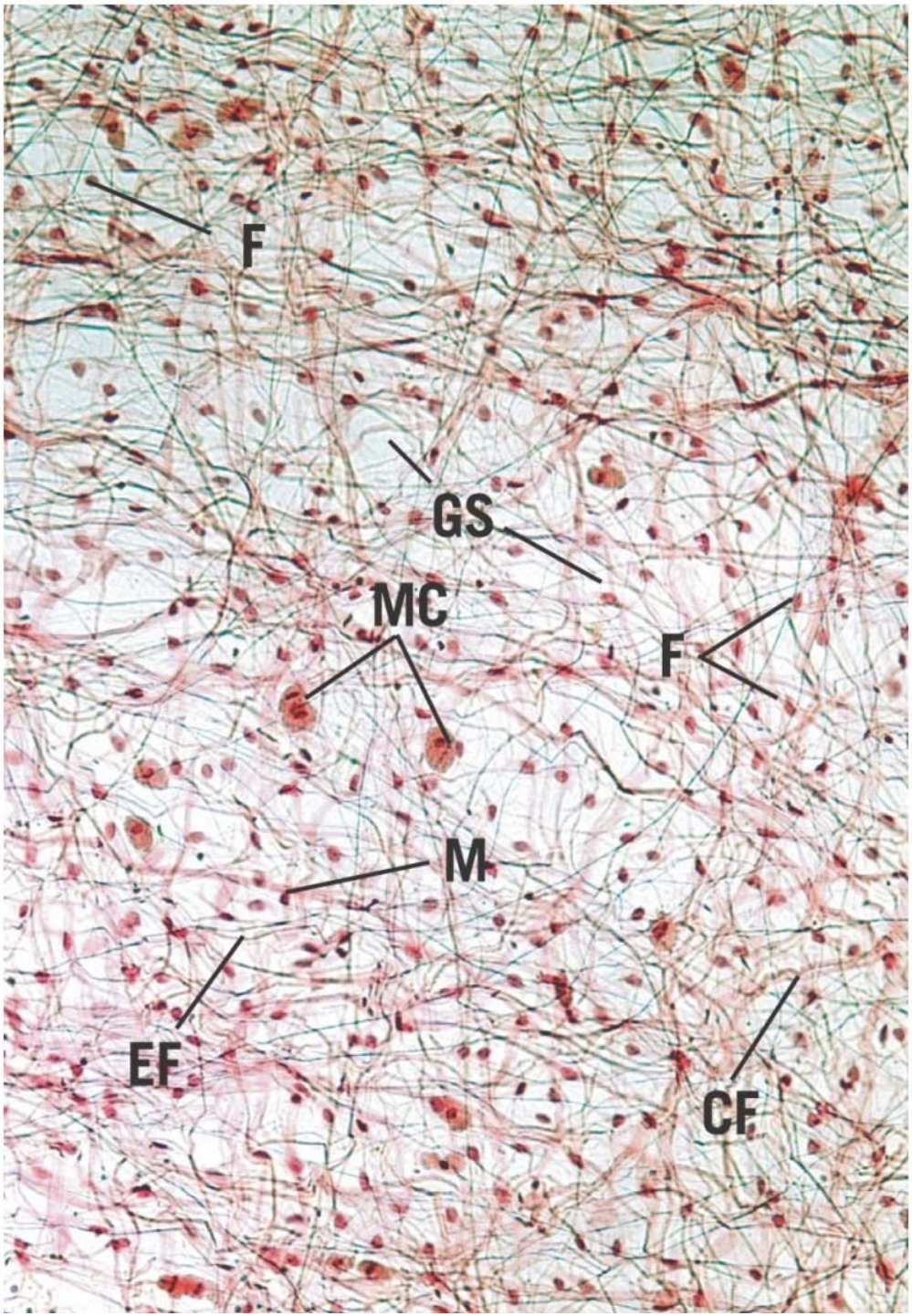
W4.4

CT Components



Ground Substance

Mesentery
spread preparation



GA3-1.1

Now's the time for

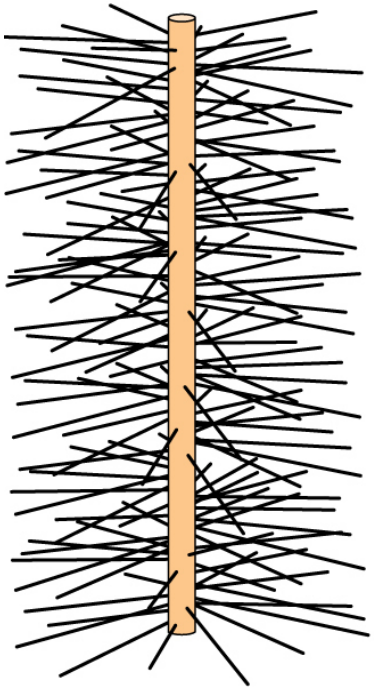
JELL-O

SIX DELICIOUS FLAVORS

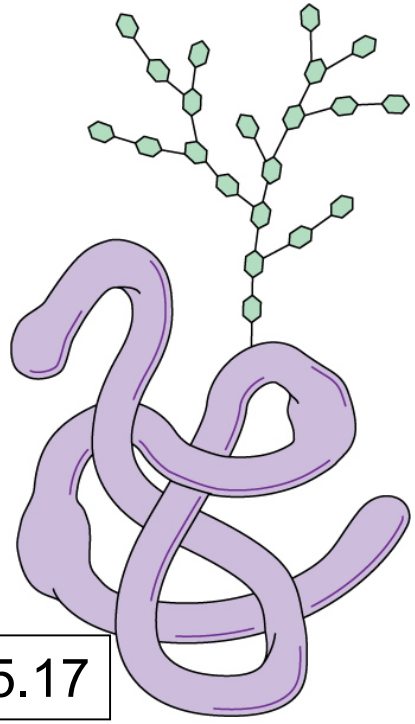
SALADS!

Don't let a week go by without serving one!

A



B



J5.17

Components of CT Proper: Ground Substance

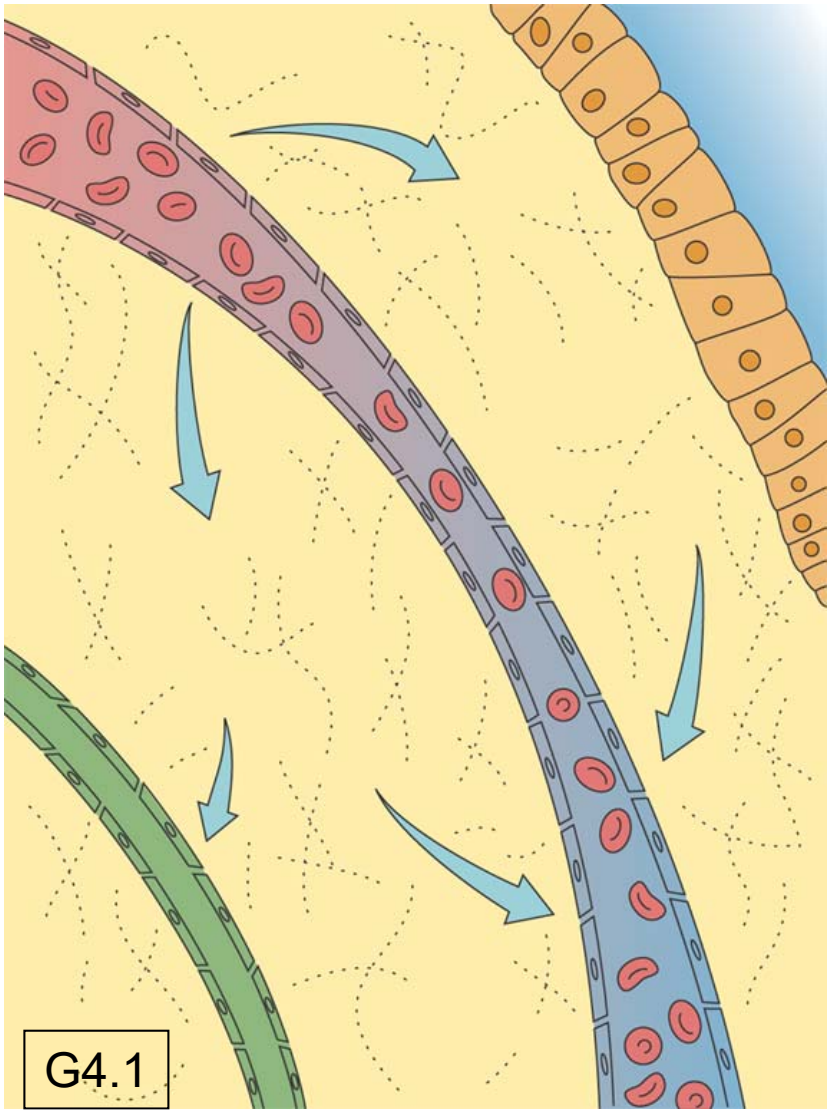
- recall: matrix = fibres + ground substance
- GS a gel-like substance in which cells & fibres are embedded
- GS provides adhesion for tissue components
- GS resists compression; fibres withstand tensile forces
- GS a medium for molecular diffusion btw plasma & ICF
- GS composed of tissue fluid and two classes of molecules
    A. Proteoglycans
    B. Adhesive glycoproteins

Ground Substance: Tissue Fluid

Blood vessels are like irrigation hoses….. in an irrigation hose, hydrostatic pressure forces water out of the lumen and into the surrounding soil.

In BVs, hydrostatic pressure forces fluid from the plasma into the surrounding CT. HOWEVER, this outward fluid movement is offset by an OPPOSING force that simultaneously attracts fluid INTO the lumen of the BVs

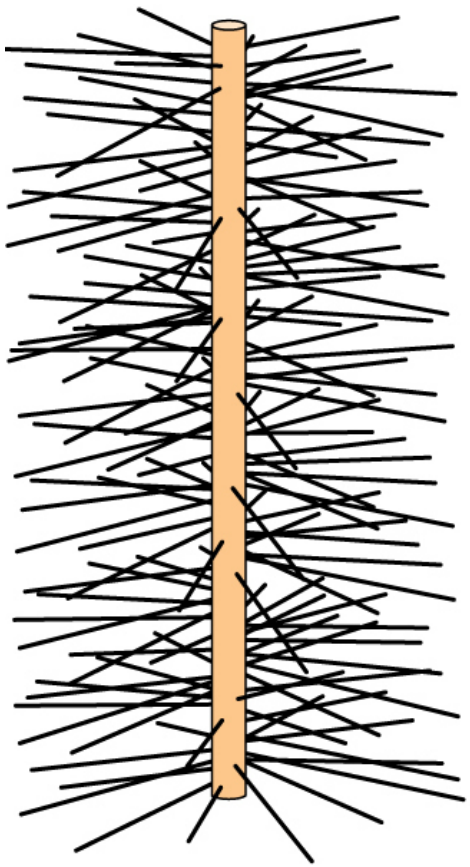
Circulation of Tissue Fluid



- continual exchange of water and solutes between the components of ECF: plasma, interstitial fluid and lymph
- hydrostatic pressure (P_H) (blood pressure) pushes fluid **out of** blood vessels
- osmotic pressure (P_O) due to plasma proteins pulls fluid **into** blood vessels
- summed P determines overall direction of fluid movement at any point along vessels
- lowest P_H within lymphatic vessels, so excess interstitial fluid becomes lymph
- edema: excess tissue fluid
  - disruption of normal gradients of hydrostatic or osmotic Ps of blood or fluid
  - excess production
  - reduced venous clearance
  - reduced lymphatic clearance

Ground Substance: Proteoglycans

A



glycosaminoglycans (GAGs): inflexible unbranched polysaccharides composed of repeating disaccharide units

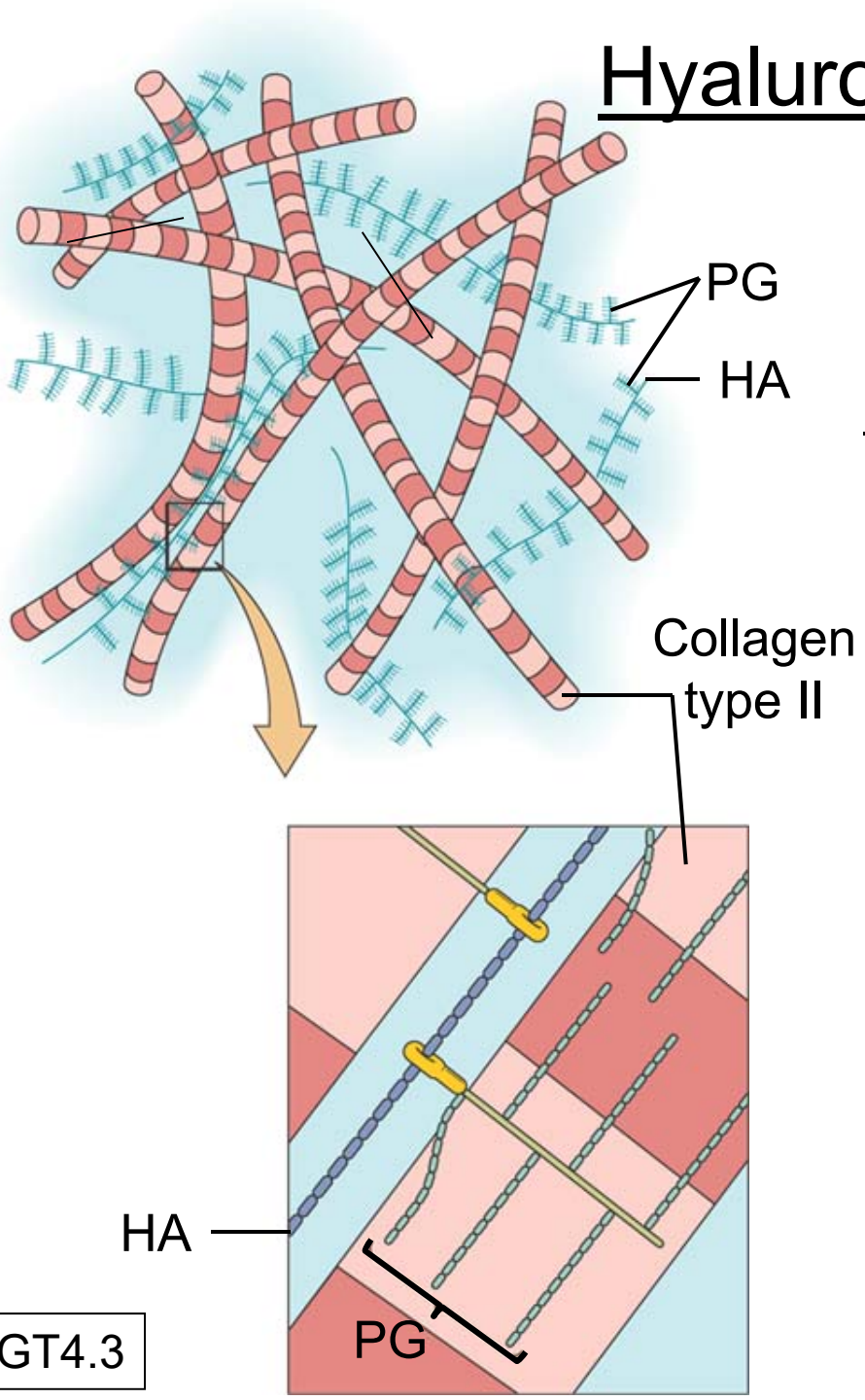
- intensely hydrophilic; imparts viscous, slippery texture to ground substance

A. most GAGs link to a core protein, forming ***proteoglycans***

- chemistry of proteoglycans are tissue-specific

J5.17

Hyaluronic Acid: A Different GAG



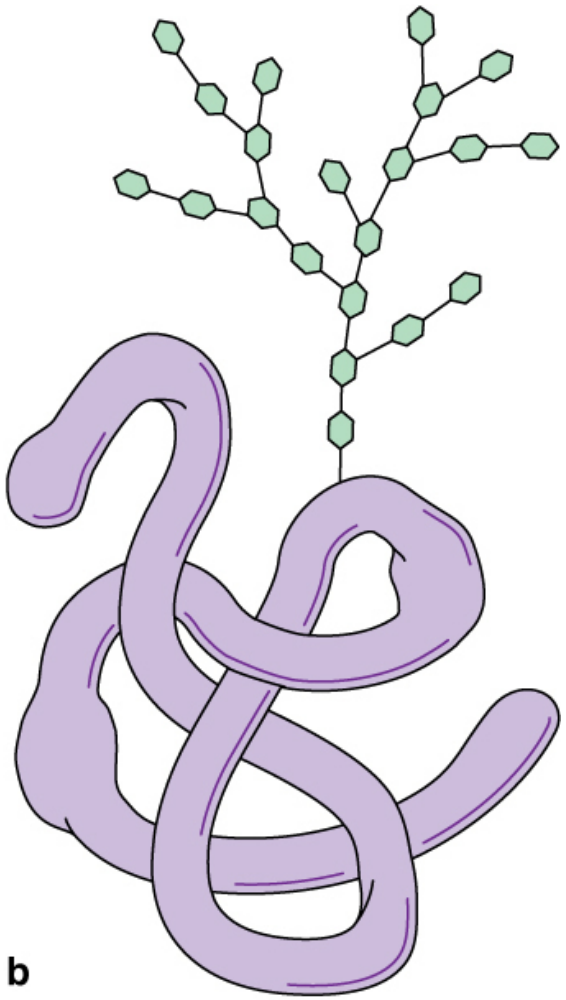
In cartilage, proteoglycans link with hyaluronic acid forming *agreccan.*

<u>proteoglycans responsible for</u>:

- gel-like consistency of matrix
- turgidity & ability of CT to resist compression
- molecular filter of varying pore size, charge distribution
- slow diffusion of substances, cells, pathogens through interstitial fluid

GT4.3

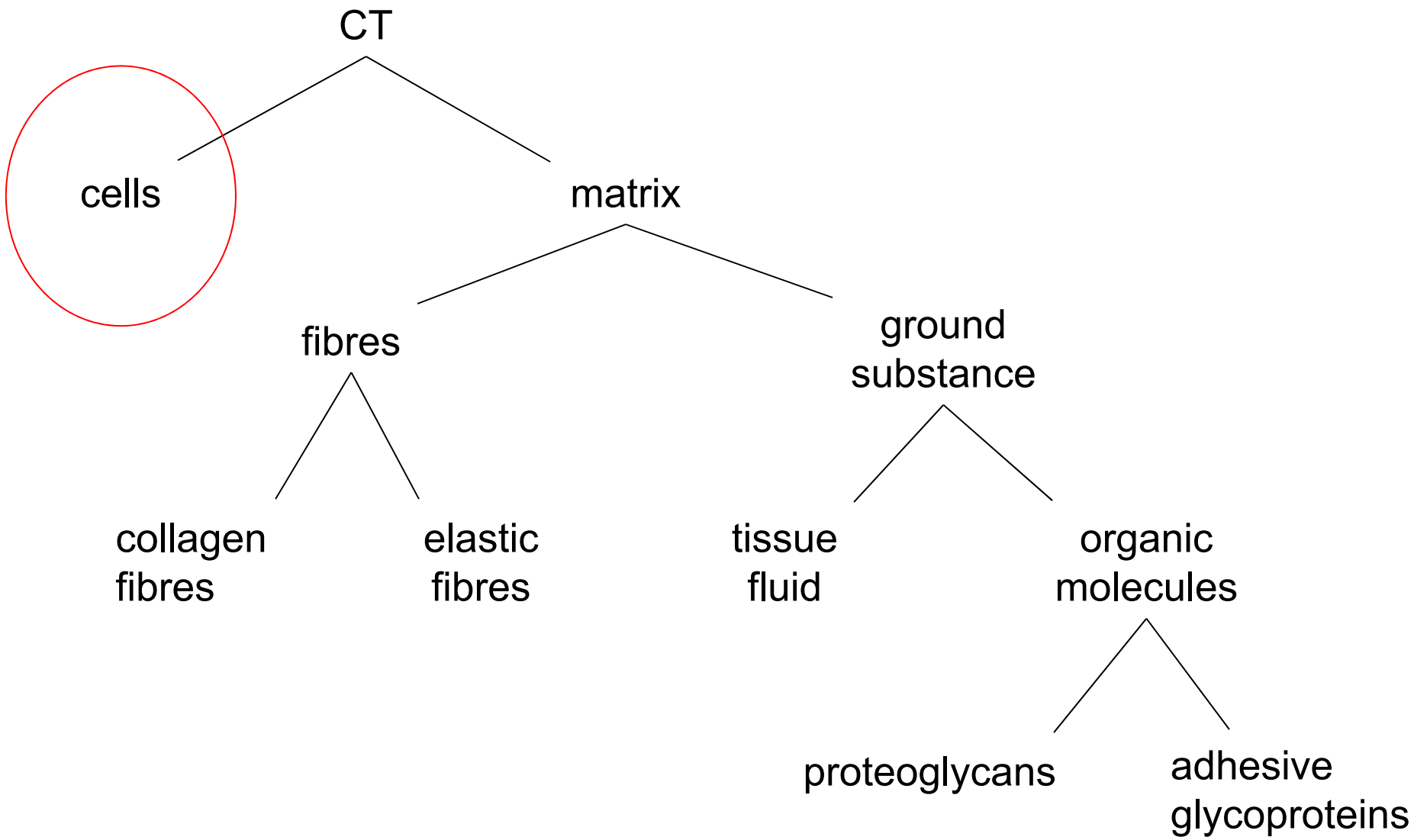
Ground Substance: Adhesive Glycoproteins



- inc, fibronectin, laminin
- binding sites for collagen, GAGs & *integrins* of the cell membranes
- integrins are transmembrane link glycoproteins

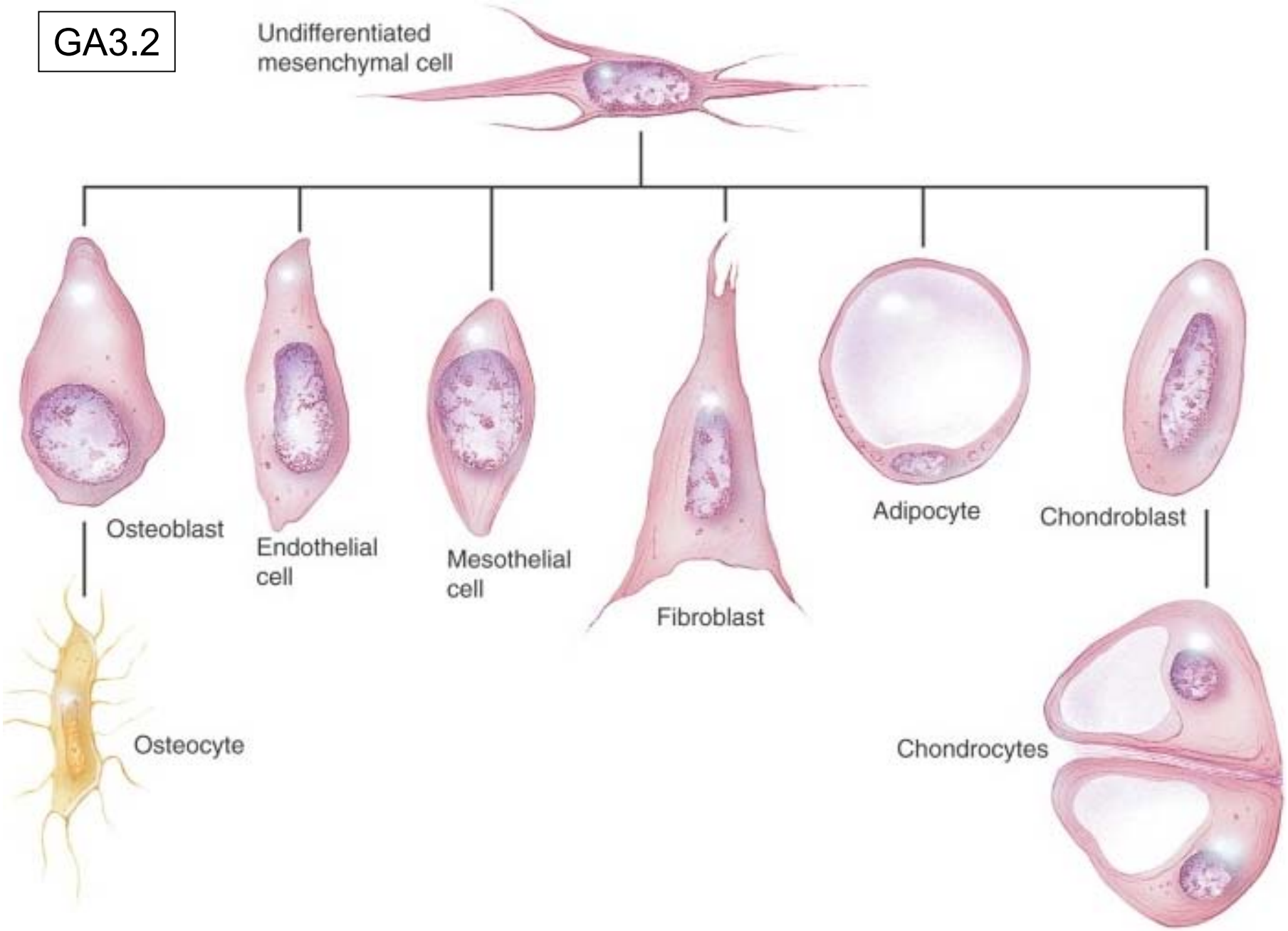
J5.17

CT Components



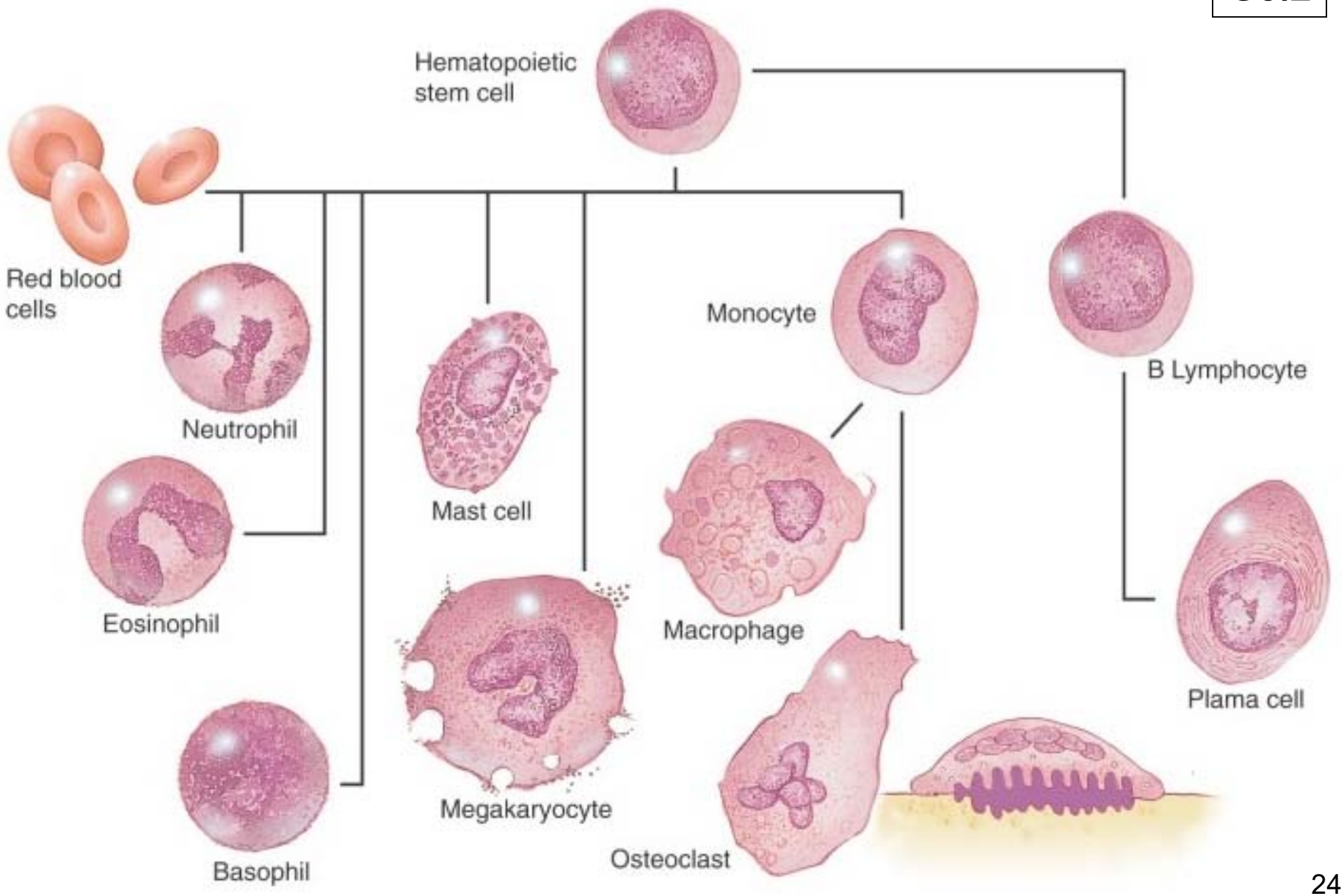
All CT Cells are Derived from Mesenchyme

GA3.2



All Blood Cells are Derived from Mesenchyme

G3.2



CT Proper: Cells

- type, proportion of cells varies with CT type

Fixed cells primarily function locally:

- fibroblasts: produce fibres, GS
- fixed macrophages: avidly phagocytic
- adipocytes: store lipids
- mast cells: involved in mediating inflammation, hypersensitivity reactions
  - activated by trauma, antigen exposure to release histamine, etc.
- mesenchymal cells: multipotential stem cells

Wandering cells ↑ # with tissue damage or infection:

- monocytes drawn in by chemotactic signals differentiate into macrophages
- lymphocytes: become antibody-producing *plasma cells* with antigen exposure
- microphages (neutrophils and eosinophils): drawn by chemotactic signals

Fibroblasts

G3.2

- produce fibres, proteoglycans and glycoproteins of the matrix
- abundant RER, well-developed Golgi
- oval nucleus
  - pale in active fibroblasts
  - darker in quiescent “fibrocytes”

Fat Cells

G3.2

Adipocyte

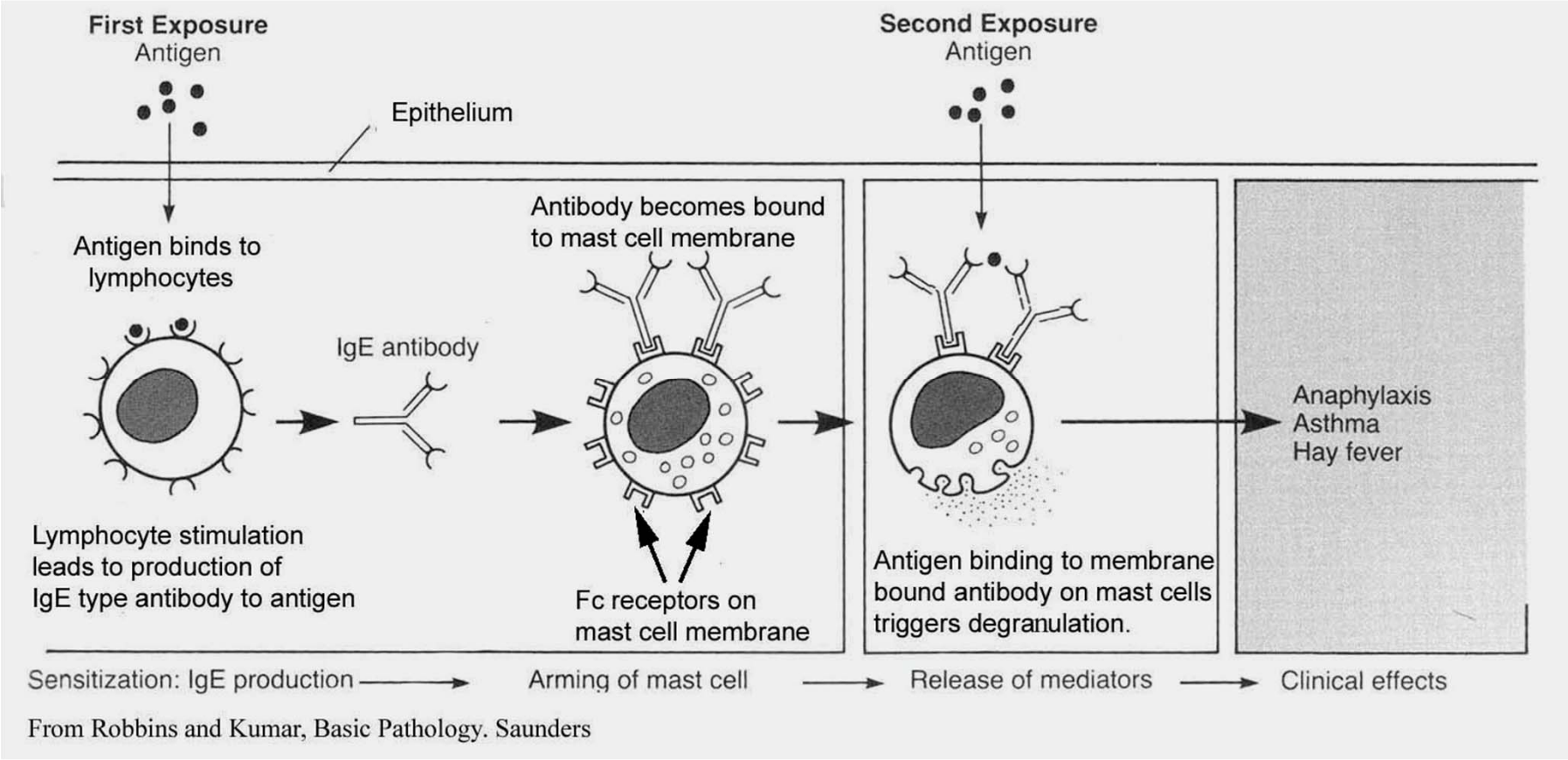
- lipid storing cells
- “signet ring” shape with thin rim of cytoplasm and flattened nucleus surrounding large droplet of stored lipid.
- lipid extraction during preparation makes the cell appear empty.
- when adipocytes predominate in certain areas, tissue is referred to as adipose.

Mast Cells

G3.2

- store chemical mediators of inflammation and hypersensitivity reactions
- oval cells with granular cytoplasm and round, central nucleus
- granules are metachromatic, i.e. certain stains that bind with the granules change their colour (eg. toluidine blue stains the granules purple or magenta)
- activated by trauma or by presence of antigen
- become sensitized to specific antigens when antibodies made against that antigen become bound to receptors on the mast cell membranes

Mast Cell Sensitization and Degranulation



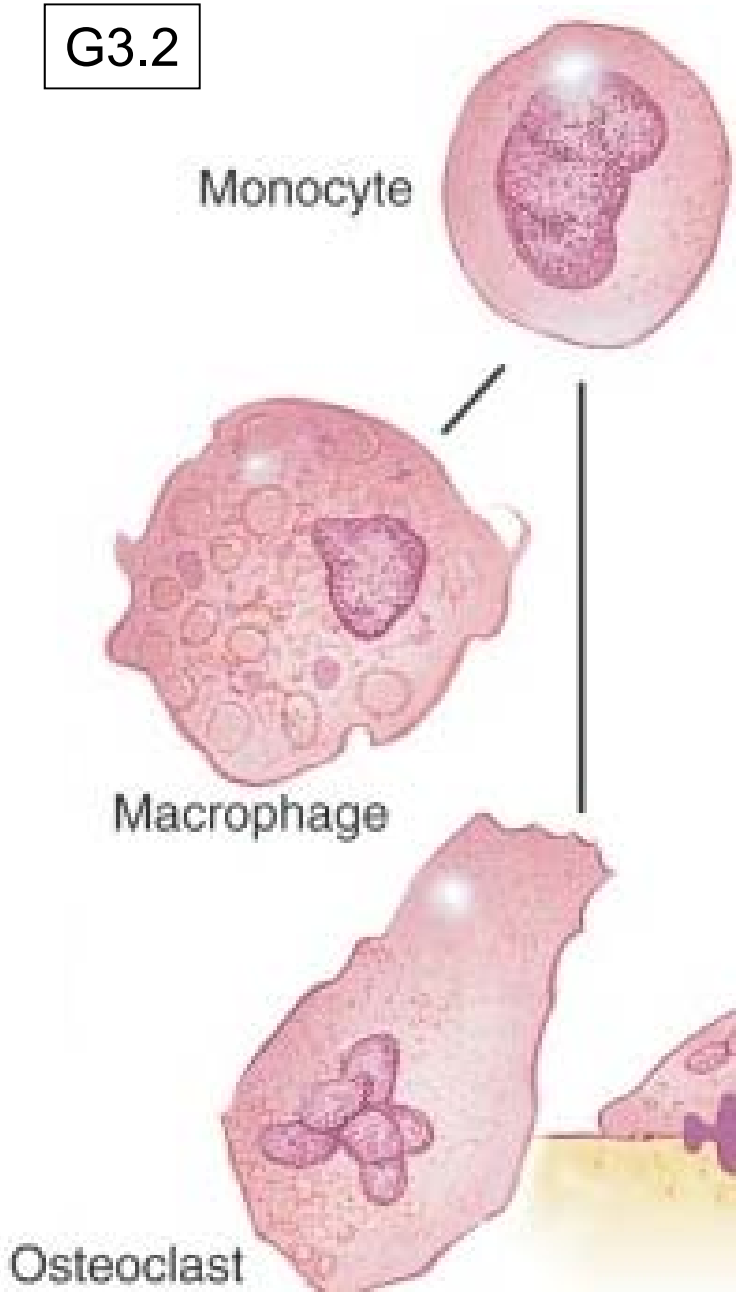
From Robbins and Kumar, Basic Pathology. Saunders

Activated mast cells immediately release:

1. Histamine
   - Vasodilatation increases blood flow
   - Increased vascular permeability (esp. post-capillary venules) increases production of protein-rich tissue fluid and slows blood flow.
2. NCF attracts neutrophils
3. ECF attracts eosinophils

Macrophages

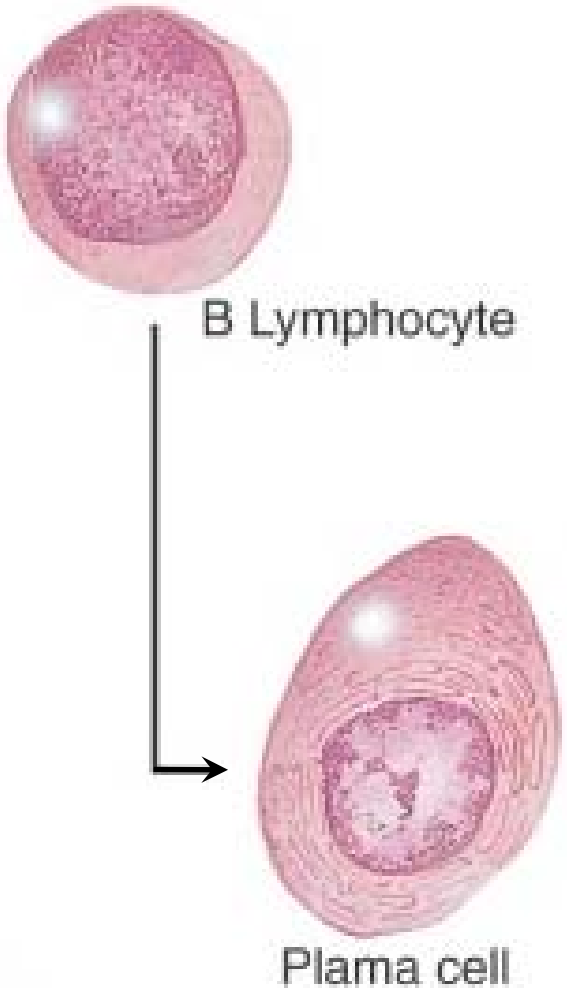
G3.2



- derived from blood monocytes
- mature in tissue spaces
- can proliferate locally
- avidly phagocytic cells
- antigen presenting cells
- relatively small and inconspicuous unless they have been active in phagocytosis
- are the Kupffer cells of the liver, microglial cells of the CNS, Langerhans cells of the skin, osteoclasts of bone tissue

Plasma Cells

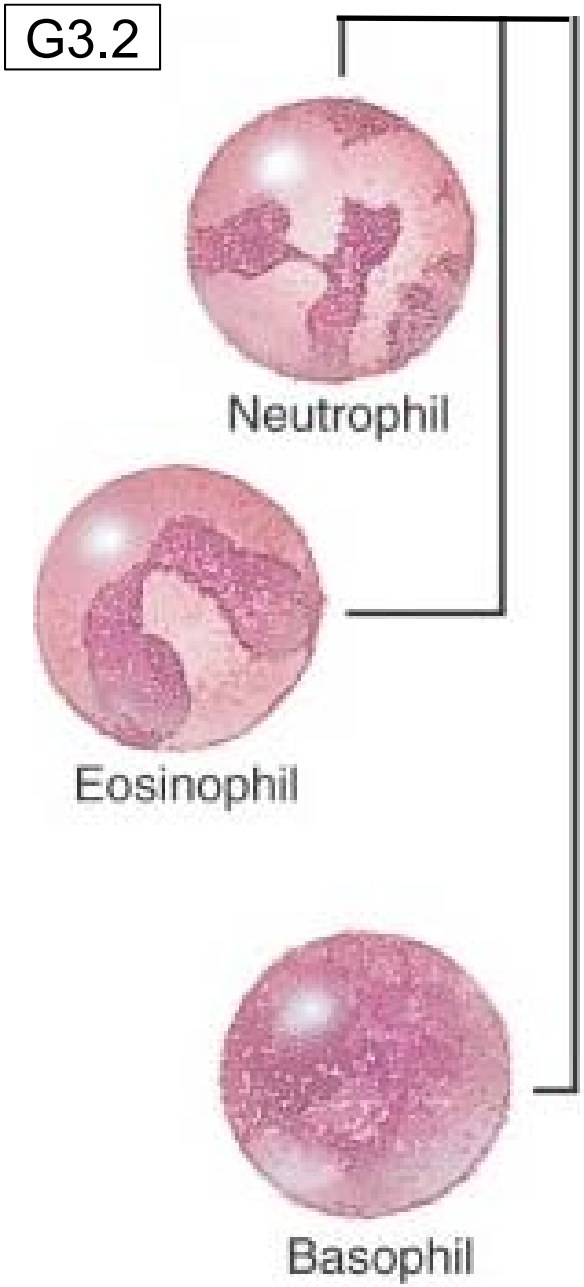
G3.2



- derived from B-lymphocytes
- antibody-producing
- relatively small, round cells with basophilic cytoplasm (filled with RER)
- round, eccentric nucleus, like a “clock face”, ie. prominent nucleolus and clumps of peripheral heterochromatin
- juxtanuclear Golgi forms pale “halo” around nucleus

Leukocytes aka WBCs

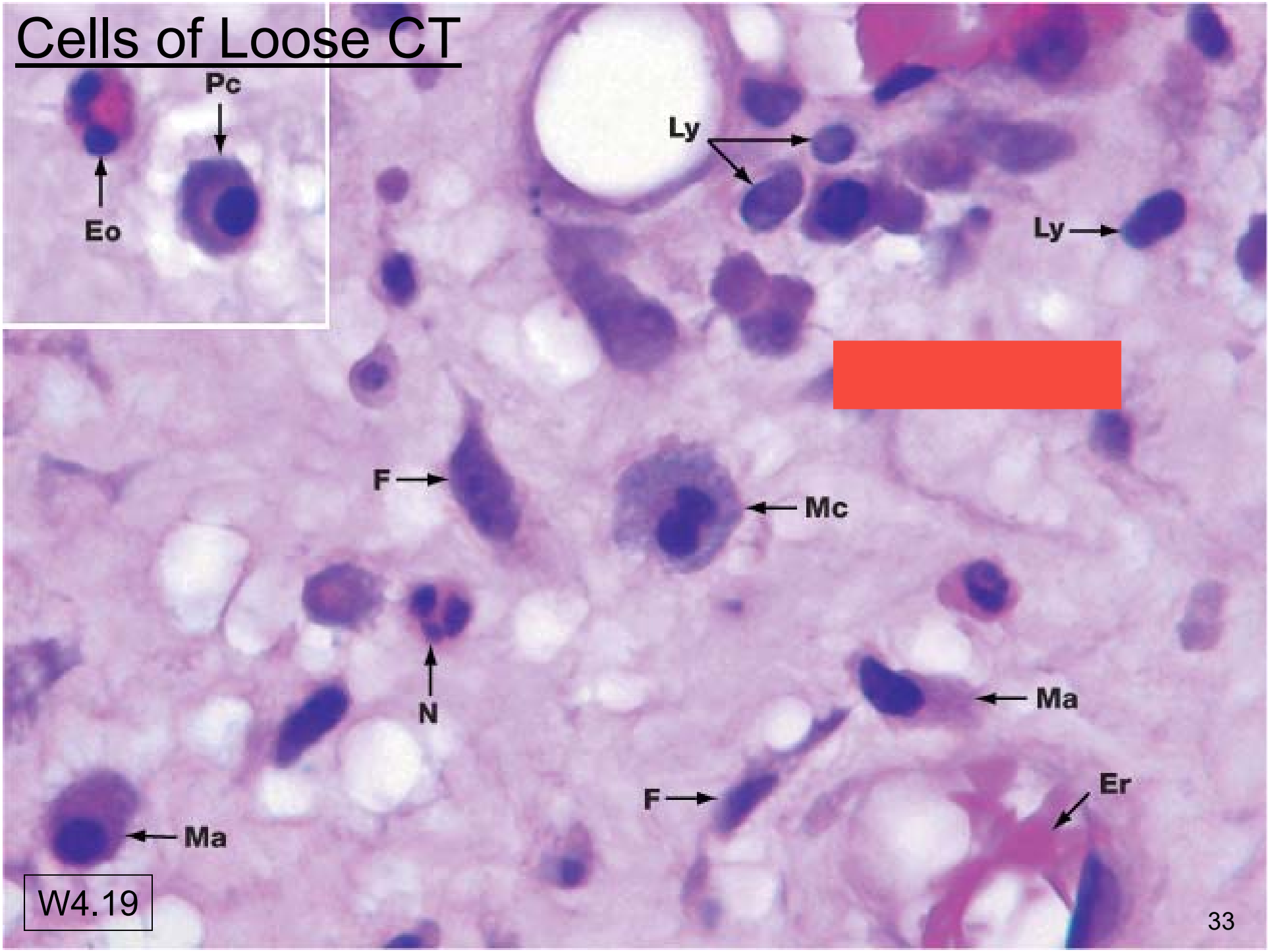
G3.2



- carried in the circulation, but function in connective tissue

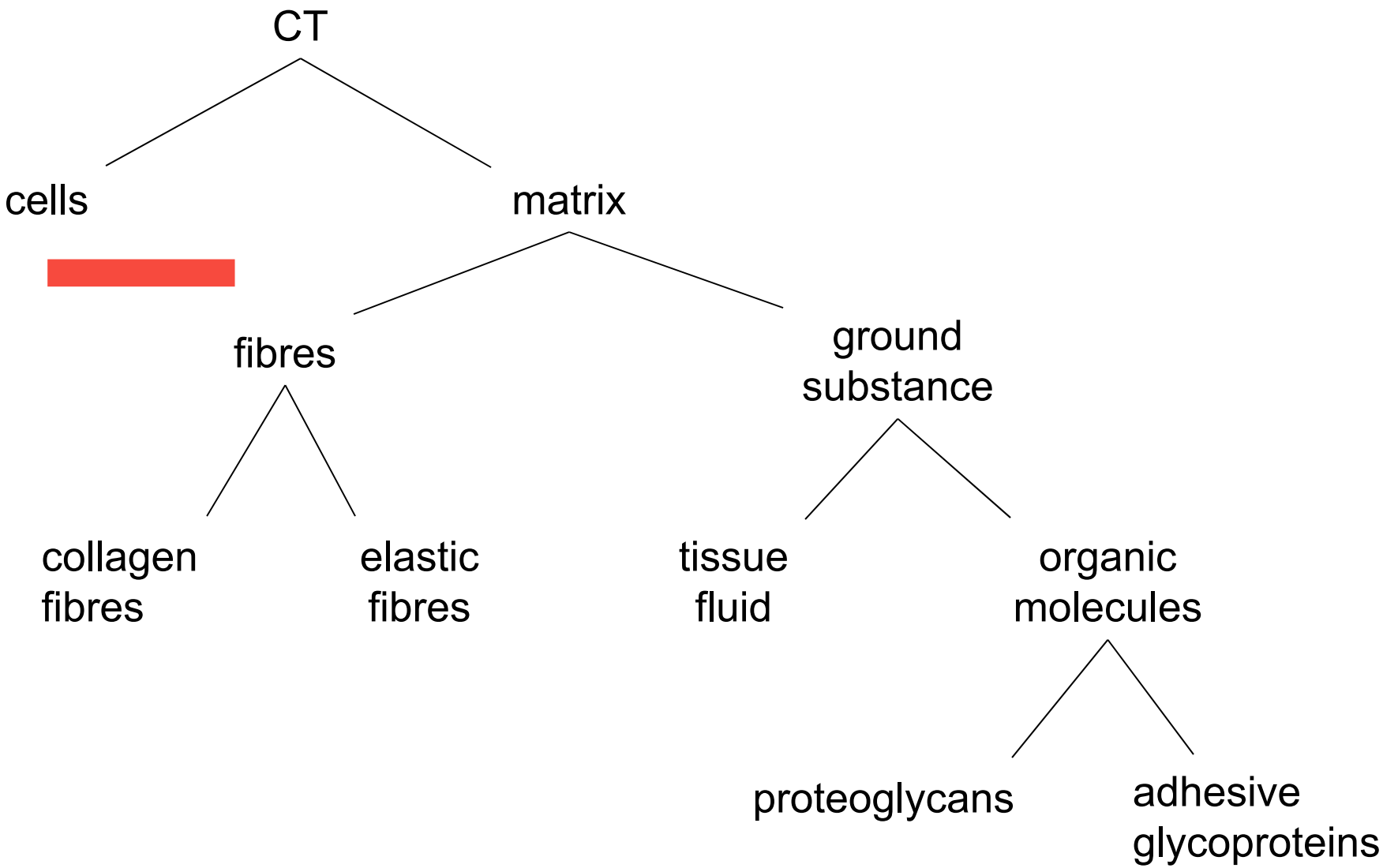
- an increased number in connective tissue is indicative of inflammation

Cells of Loose CT



W4.19

CT Components



A Classification of Connective Tissue

- all develops from embryonic *mesenchyme*

Connective Tissue Proper

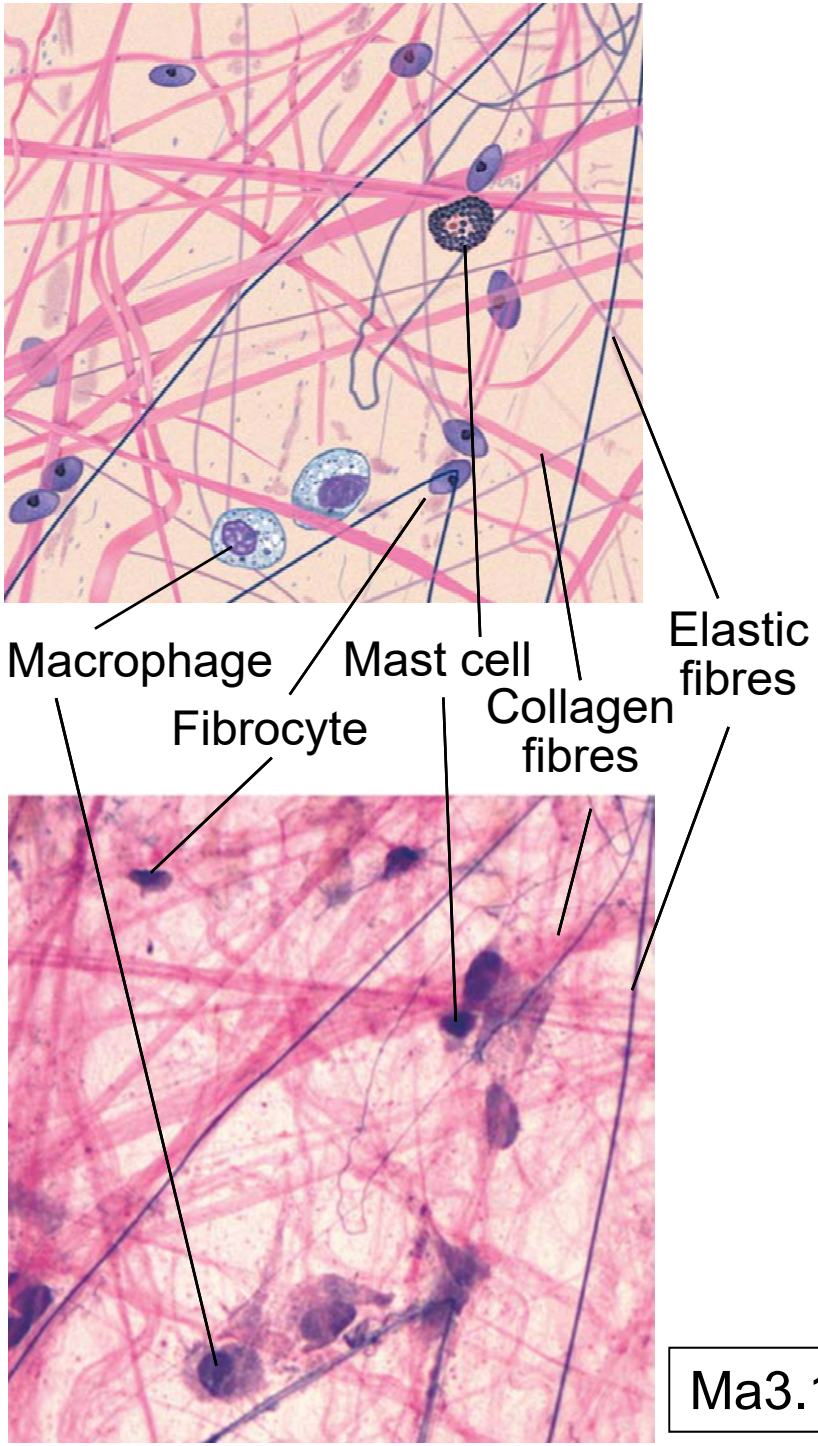
1. Loose CT: fewer fibres, more GS by volume
    a. areolar CT
    b. reticular CT
    c. adipose tissue
2. Dense CT: dominated by densely-packed fibres, fewer cells, less GS
    a. dense regular CT
    b. dense irregular CT
    c. elastic tissue

Supporting Connective Tissue

3. Cartilage
    a. hyaline cartilage
    b. elastic cartilage
    c. fibrocartilage
4. Bone

Connective Tissue Proper:
1. Loose Connective Tissue

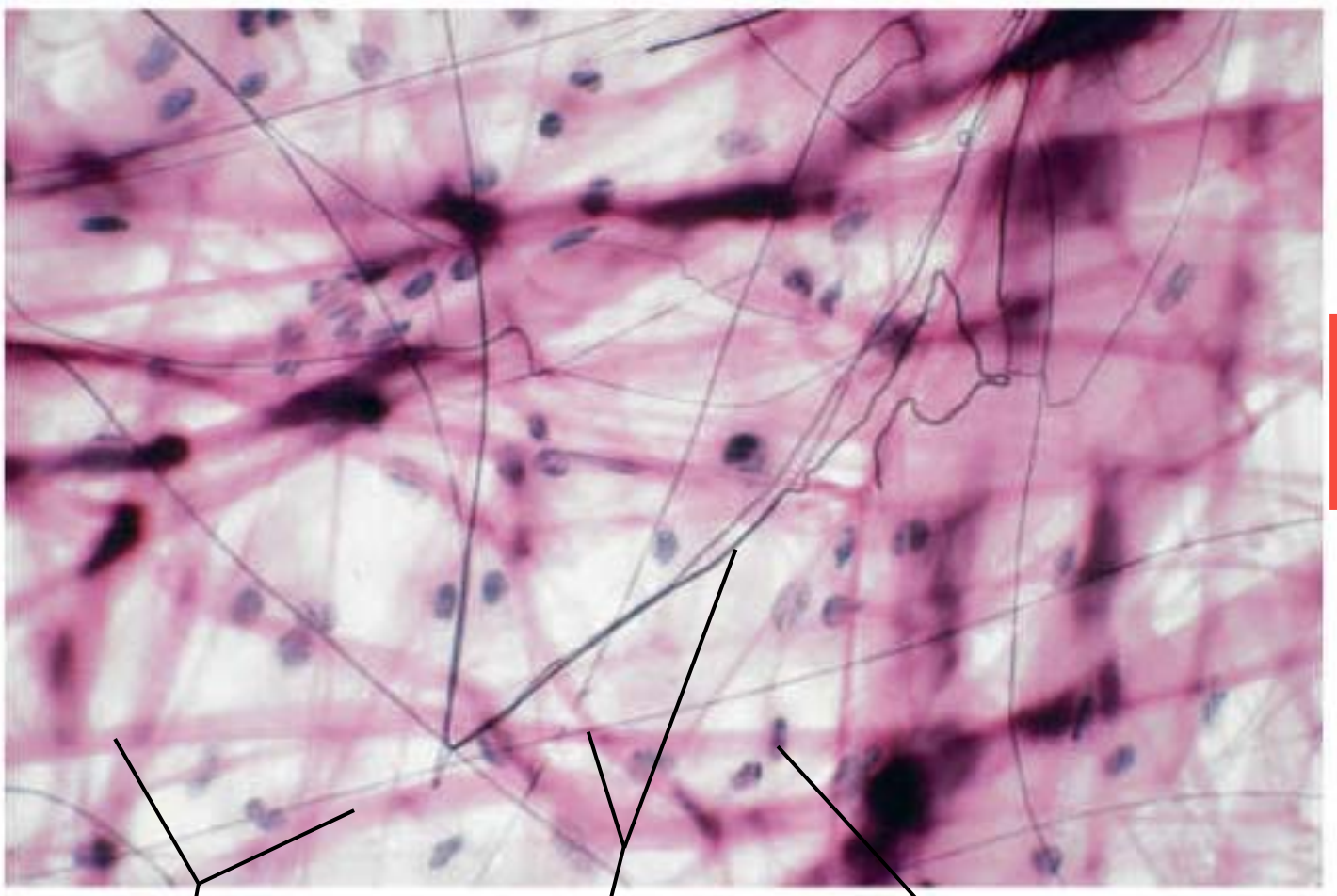
1. Loose CT a) Areolar CT



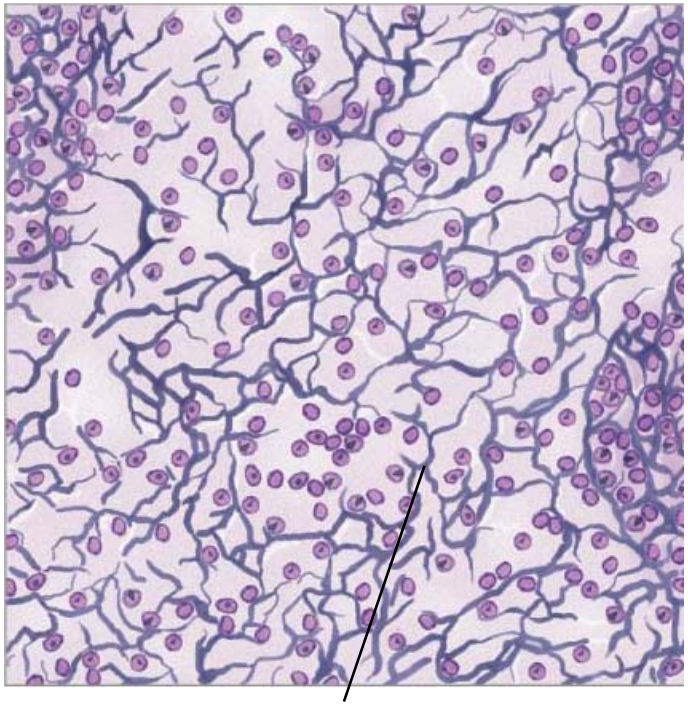
- least specialized; all cell & fibre types
- mostly ground substance by volume
- eg. superficial
  muscles, BVs, Ns, around joints
- provides support but allows independent movement
- provides defence against pathogens

Ma3.14

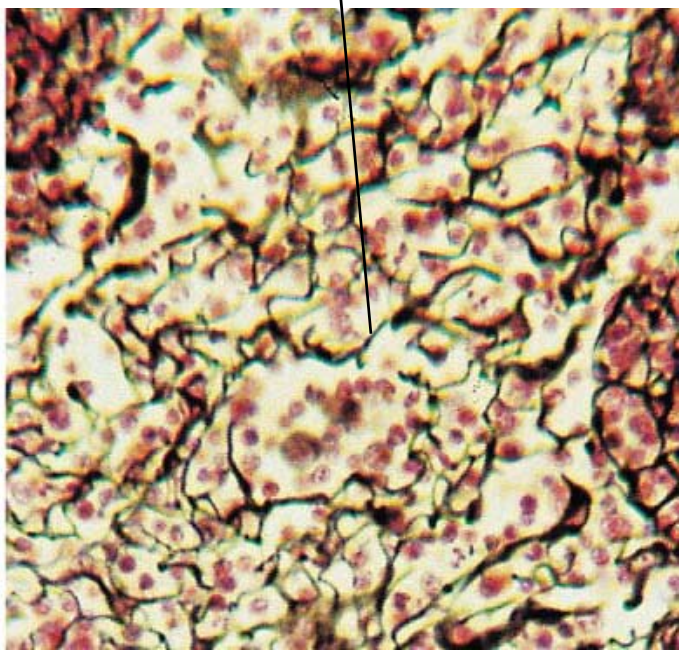
Areolar CT by LM



PAL



Reticular fibers



1. Loose CT: b) Reticular CT

- dominated by delicate reticular fibres

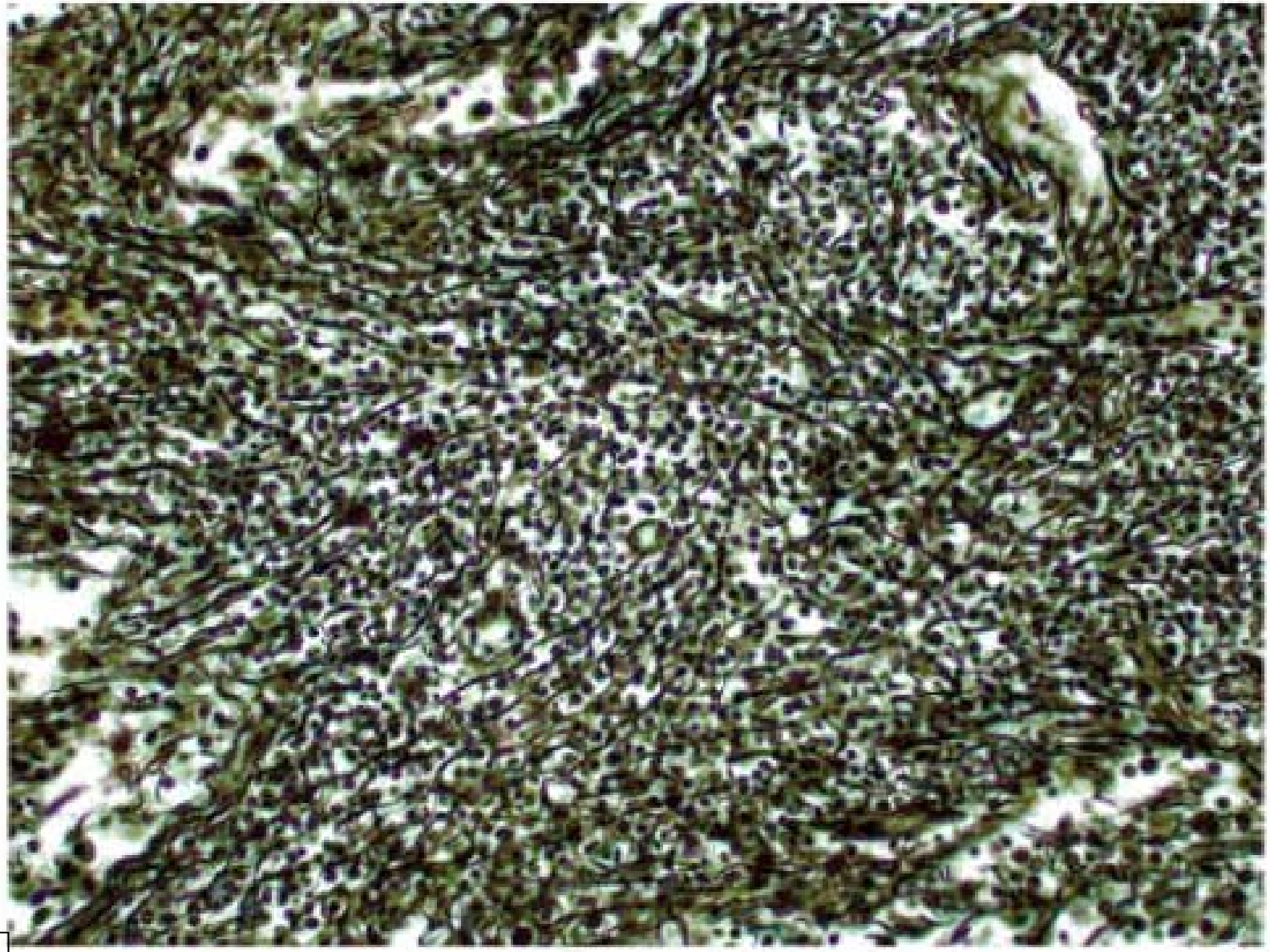
- liver, kidneys, spleen, lymph nodes, smooth muscle and bone marrow

- forms the *stroma* (scaffolding) of these highly cellular organs on which they arrange their *parenchyma*, or functional cells

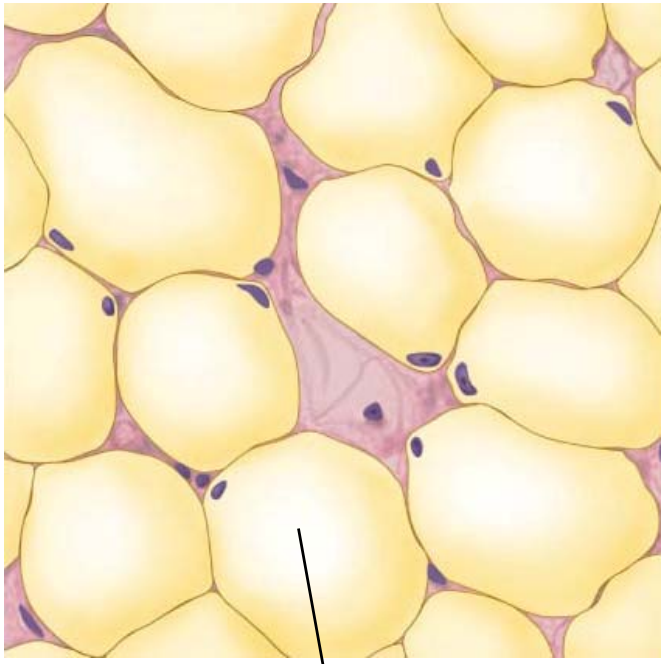
Ma3.14

Reticular CT by LM

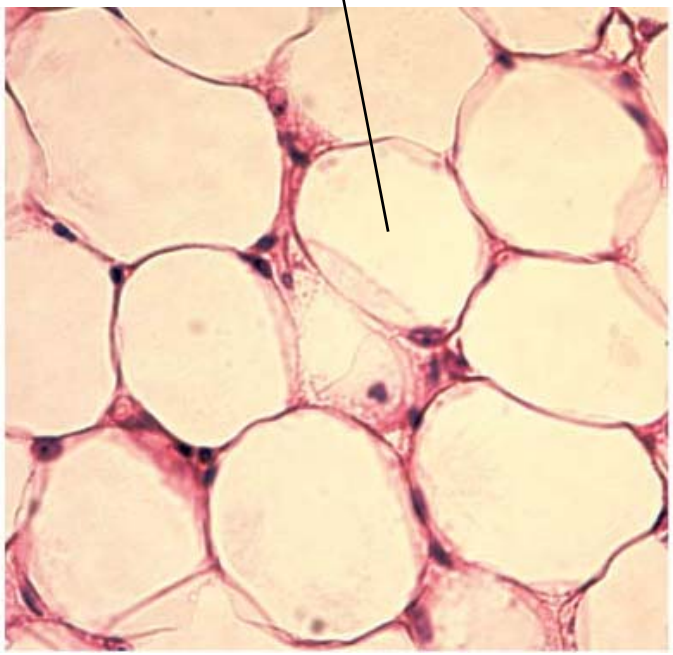
Lymph node



PAL



Adipocytes



1. Loose CT: c) Adipose CT

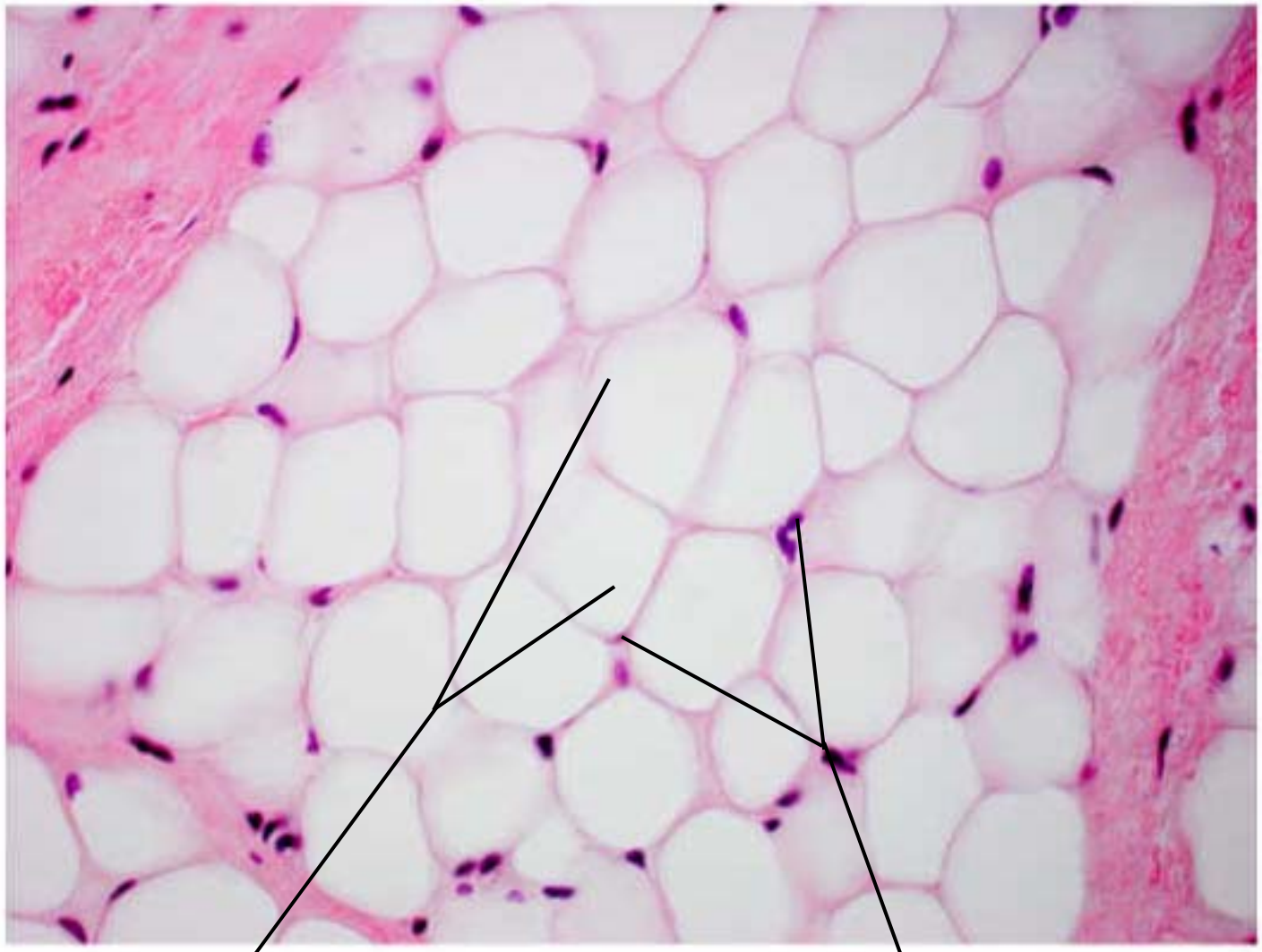
- mostly adipocytes by volume

- with areolar CT; amount, distribution varies with age, sex, activity level

- particularly abundant deep to skin, behind eyes, around kidneys

Ma3.14

Adipose CT by LM

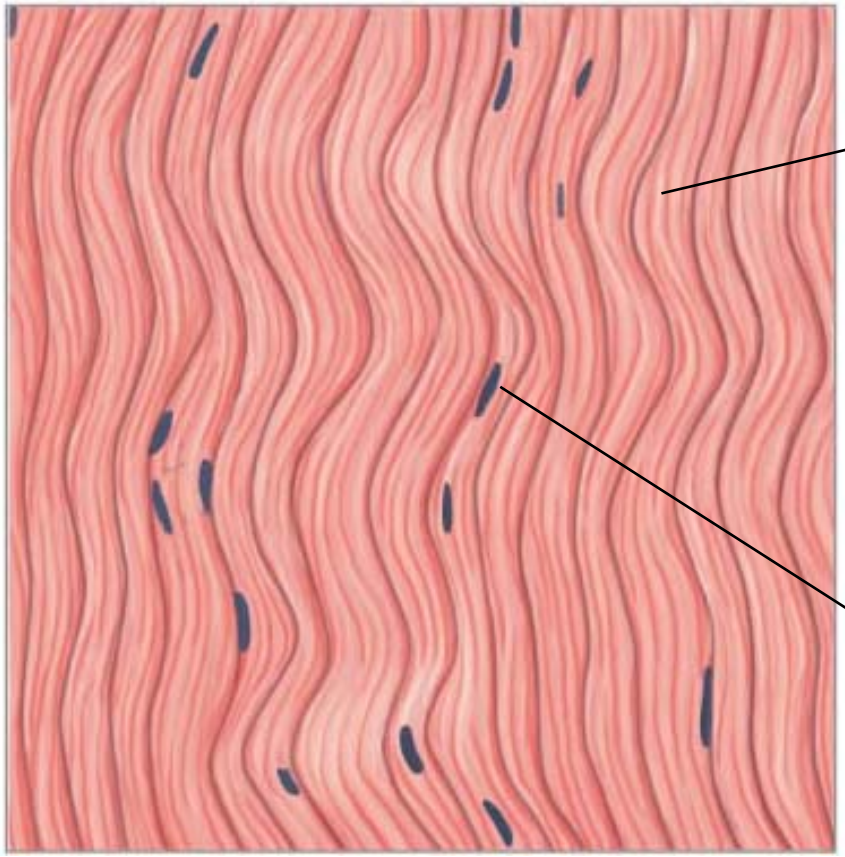


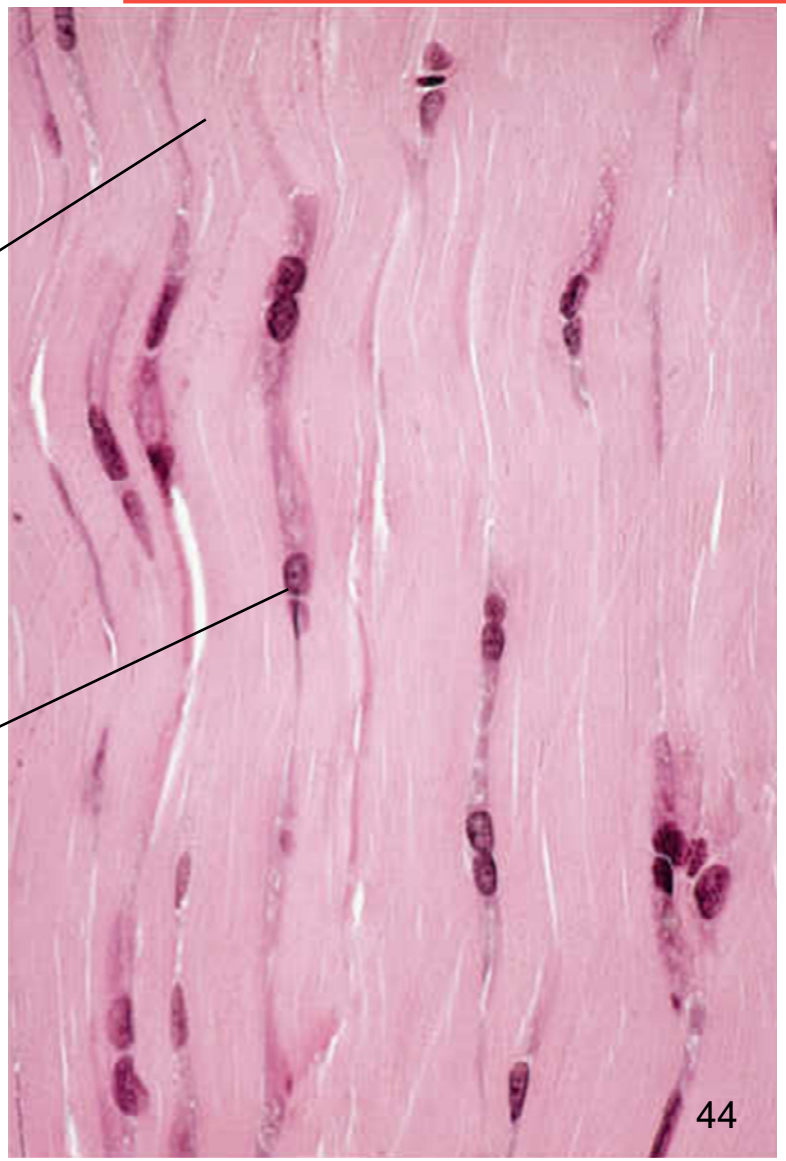
PAL

Connective Tissue Proper:
2. Dense Connective Tissue

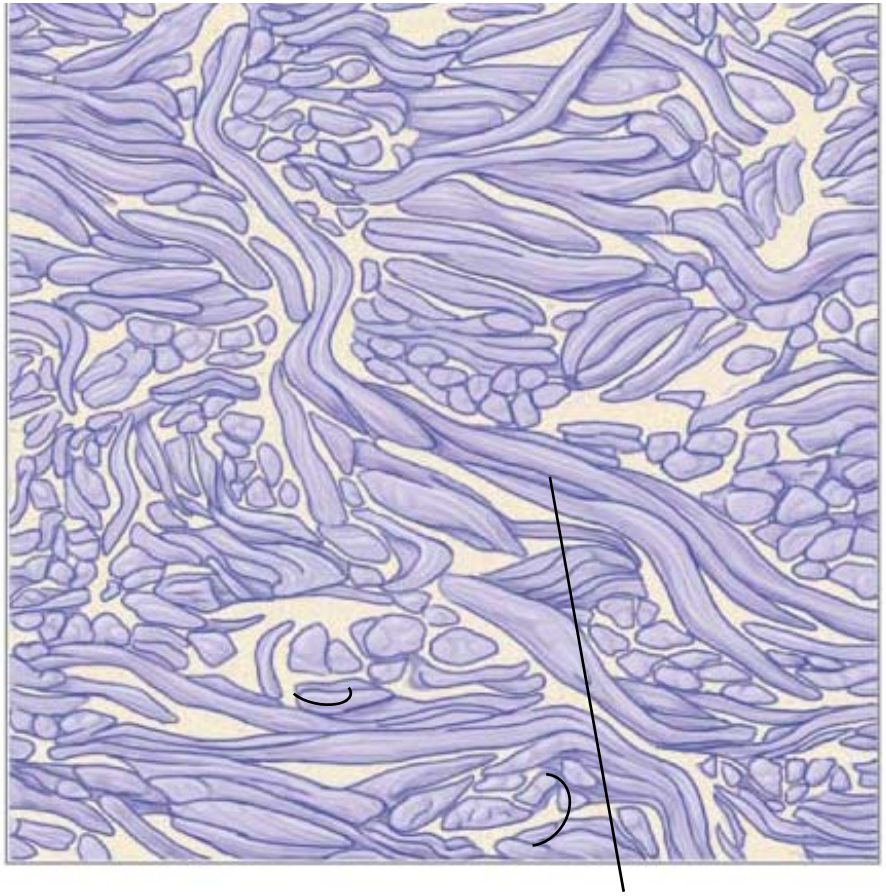
2. Dense CT: a) Dense Regular

- largely collagen type I fibres arranged in parallel arrays; ∴ imparts tensile strength in one direction
- eg. tendons, aponeuroses, ligaments





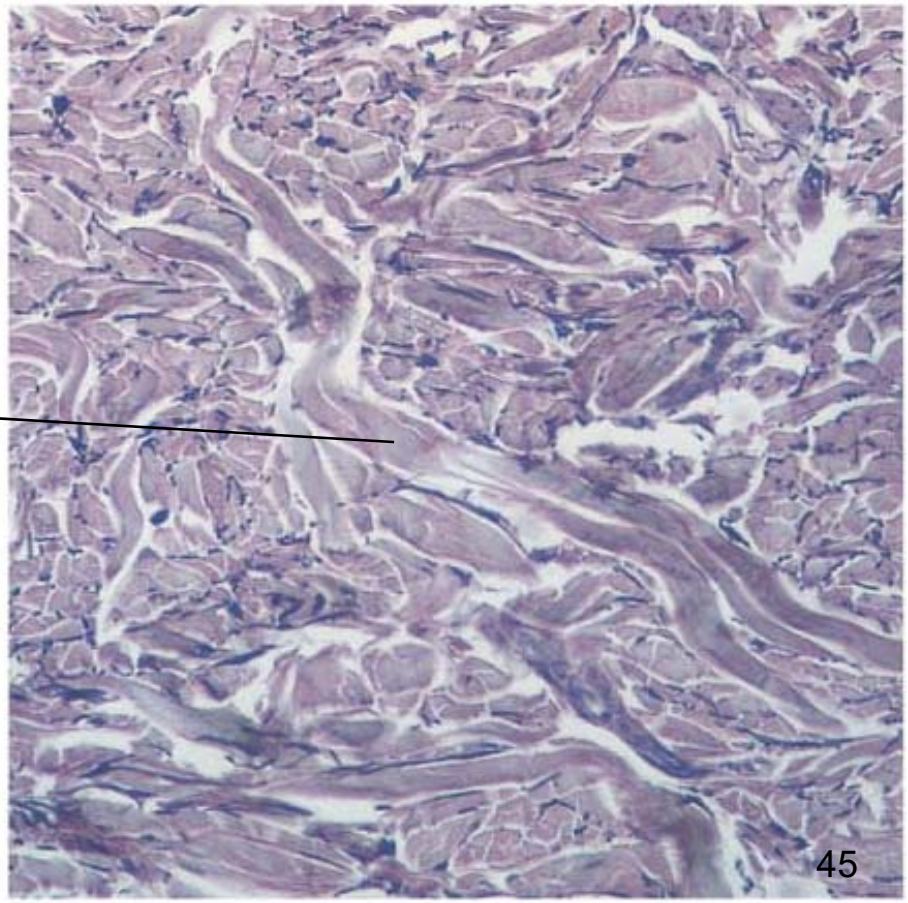
Ma3.15



Collagen fiber bundles

2. Dense CT:
b) Dense Irregular CT

- largely collagen type I fibres arranged in a meshwork sheet; ∴ imparts tensile strength in >1 direction

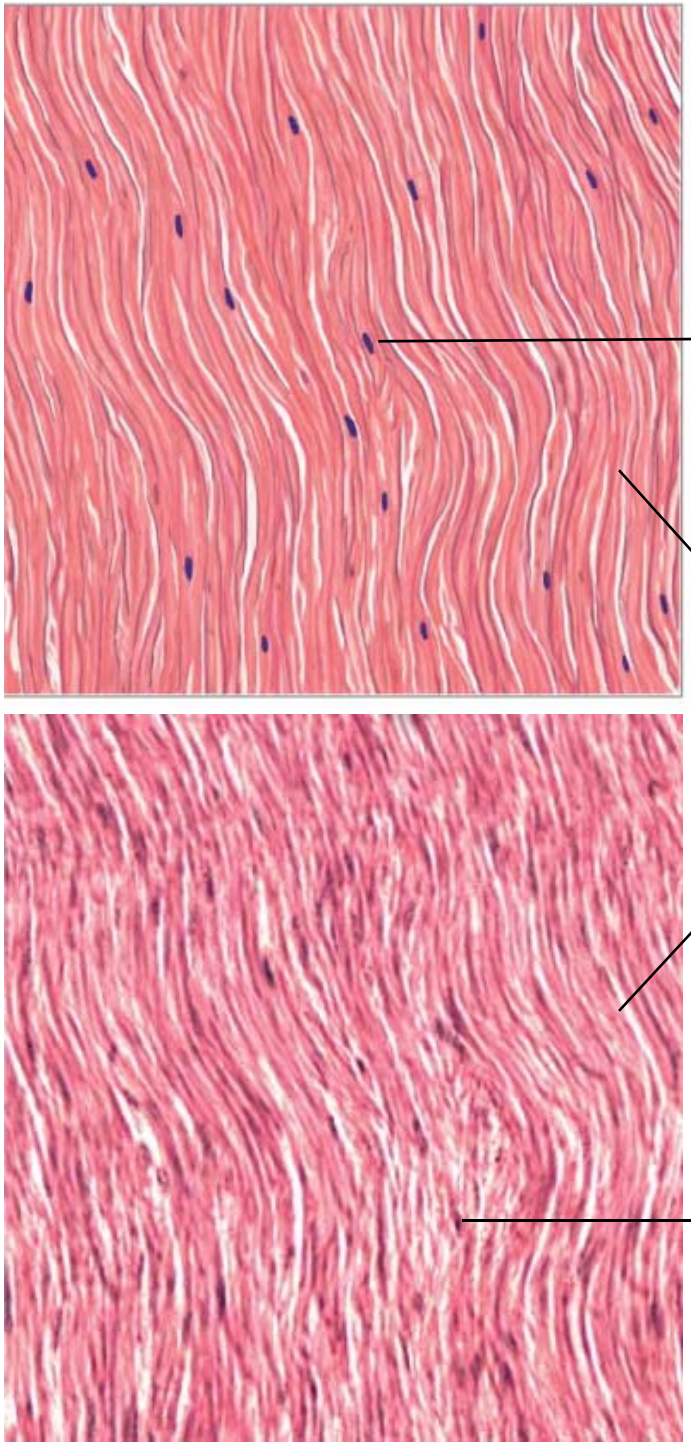


dermis

- eg. reticular layer of dermis, periosteum, perichondrium, organ capsules, joint capsules, submucosa of GI tract

Ma3.15

2. Dense CT: c) Elastic Tissue



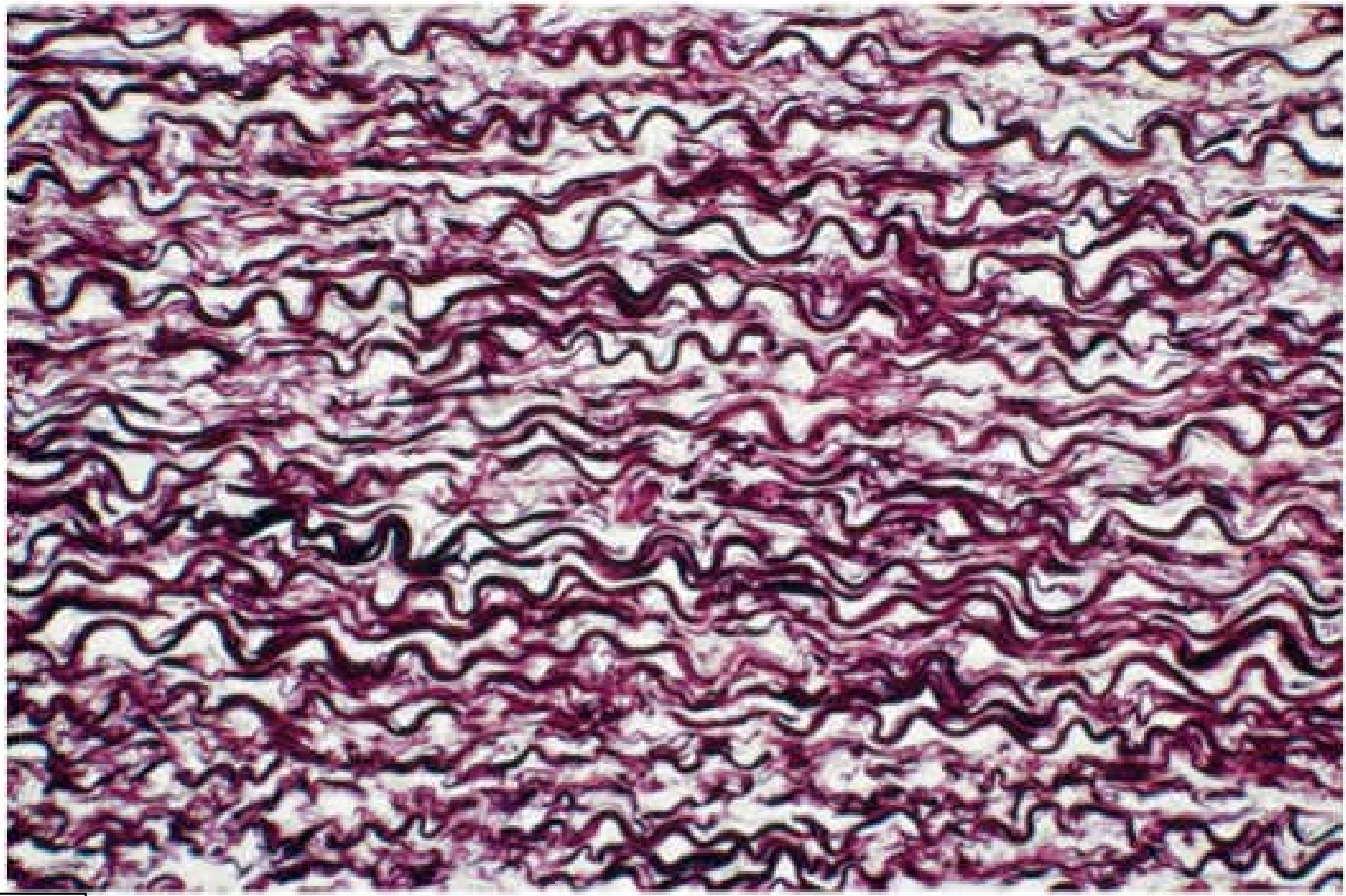
- high concentration of elastic fibres ↑ *resiliency*
- found in structures that must stretch & recoil
- certain ligaments, eg. *ligamentum flavum*, supporting transitional epithelium, blood vessels

Ma3.15

Ligamentum flavum

Elastic Tissues by LM

aorta



PAL

Supporting Tissue Proper:
3. Cartilage

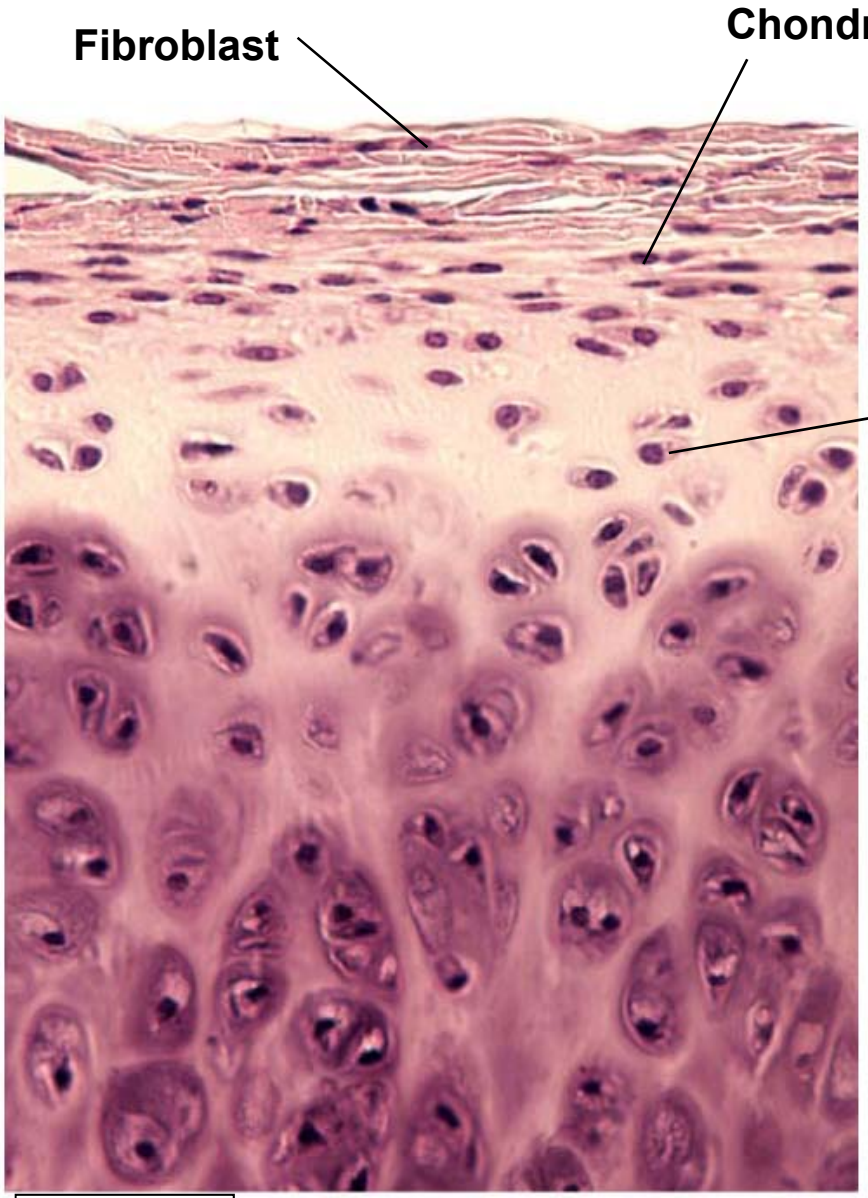
Cartilage: Characteristics & Functions

- EC matrix abundant, firm, gel-like, resilient & smooth
- gives structure to soft tissues
- fxn. in development & growth of long bones (covered under bone)
- most cartilages surrounded by *perichondrium*
- all types: avascular, no lymphatic vessels, no nerves
  - ∴ chondrocytes metabolize glucose mainly by anaerobic glycolysis
  - nourished by diffusion through the ground substance from vessels in the surrounding perichondrium and/or ordinary CT

Matrix Defines the Cartilage

- composition of the matrix determines the physical properties of a cartilage
- ground substance:
  - rich in proteoglycans linked to hyaluronic acid forming aggrecan
  - high water content resists compression
  - adhesive glycoproteins binds cells with components of the matrix
- fibres: most cartilage rich in collagen type II
- components & proportions vary between cartilage types, determine characteristics
- cells: chondrocytes in lacunae within the matrix
  - fxn to produce, maintain fibres and organic components of the GS

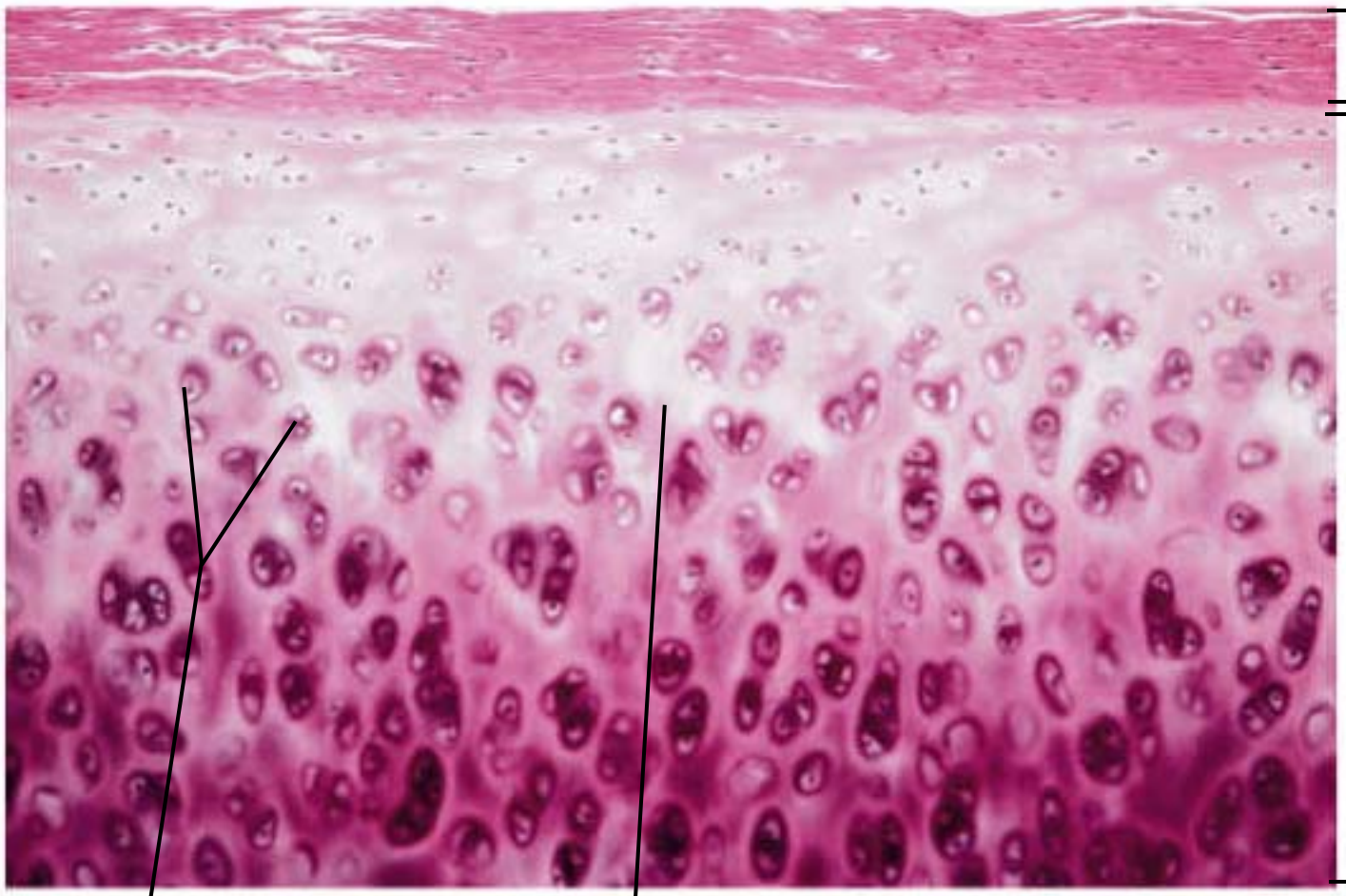
Perichondrium & Cartilage



Ma3.17

- perichondrium is dense irregular CT
- has BVs, Ns, Ls
- fxn. in cartilage growth and attachment
- consists of 2 layers:

1. outer fibrous layer
   - contains mainly collagen fibres, fibroblasts
2. inner cellular layer
   - contains *chondroblasts*: synthesize the organic components of the matrix
   - contributes to cartilage growth; ∴ ↓ prominence with maturity



PAL

The Formation of Cartilage

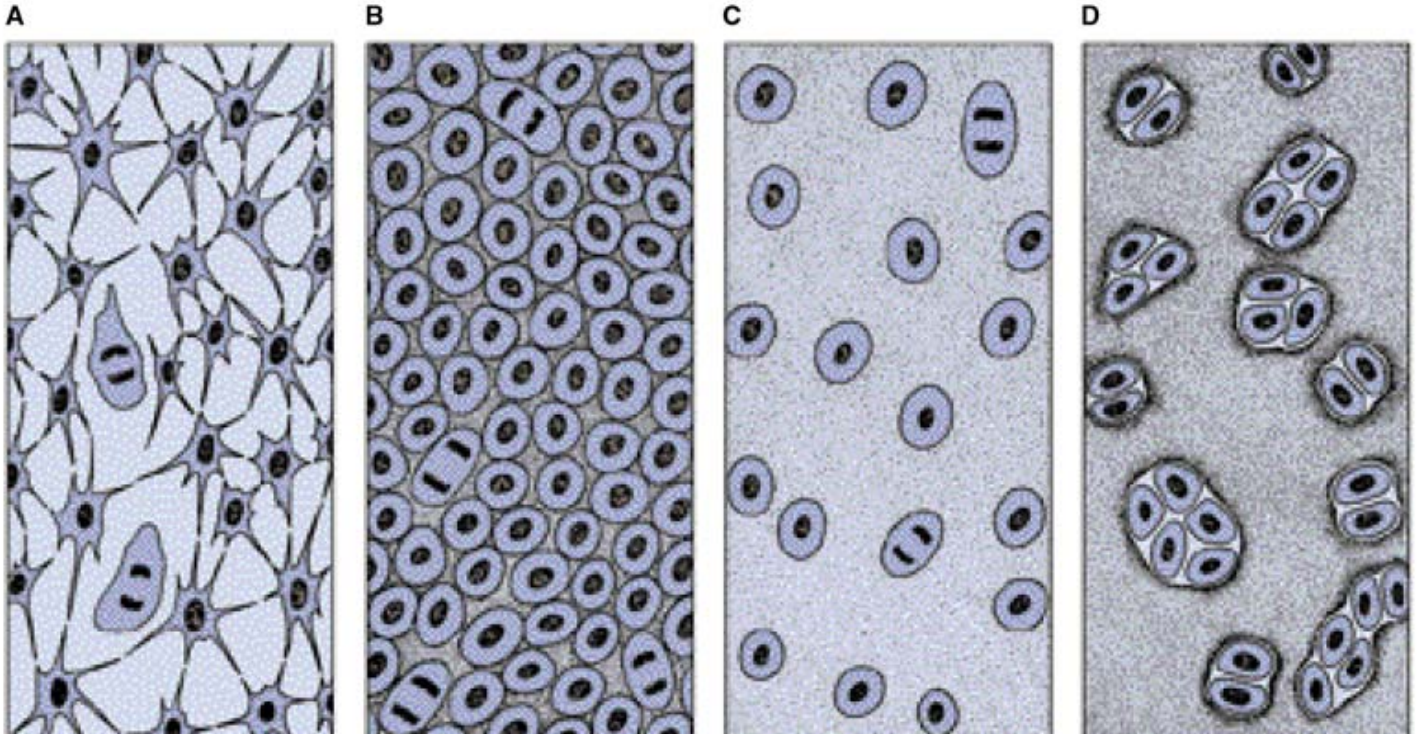
A. cartilage develops from condensations of embryonic mesenchyme

B. mesenchymal cells differentiate into *chondroblasts,* which secrete the organic components of the matrix

C. chondroblasts ultimately surround themselves with matrix, thus becoming isolated in their lacunae

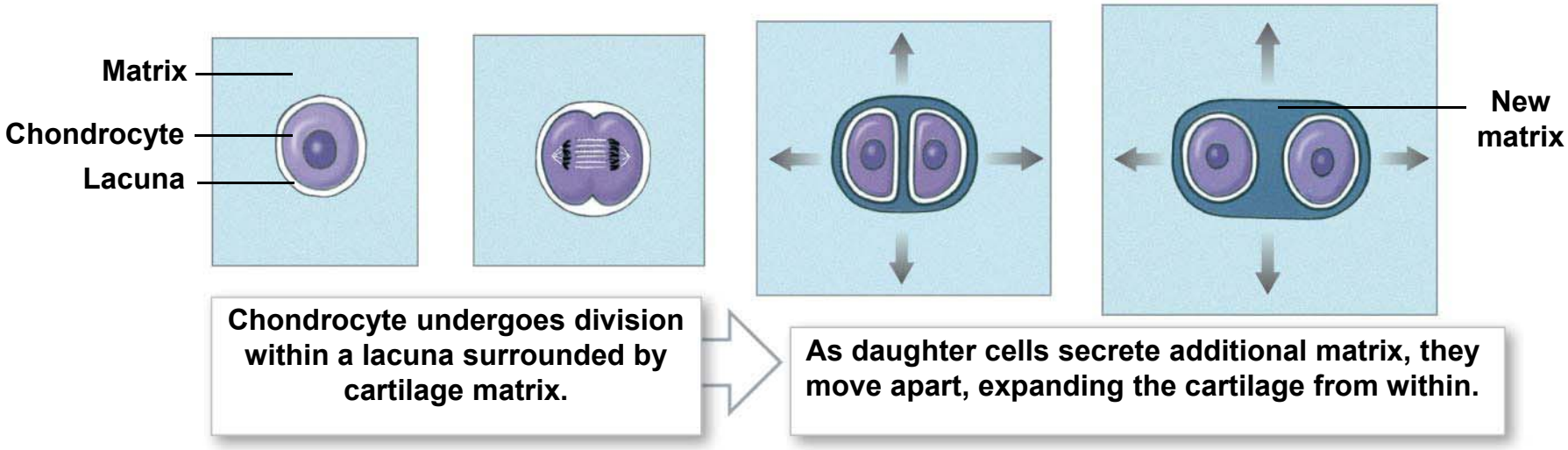
D. these chondroblasts may divide, thus causing the cartilage to grow from within in a process called *interstitial growth*

- isolated chondroblasts become quiescent, maintain matrix as *chondrocytes*



J7.6

Interstitial Growth of Cartilage



Interstitial Growth. The cartilage expands from within as chondrocytes in the matrix divide, grow, and produce new matrix.

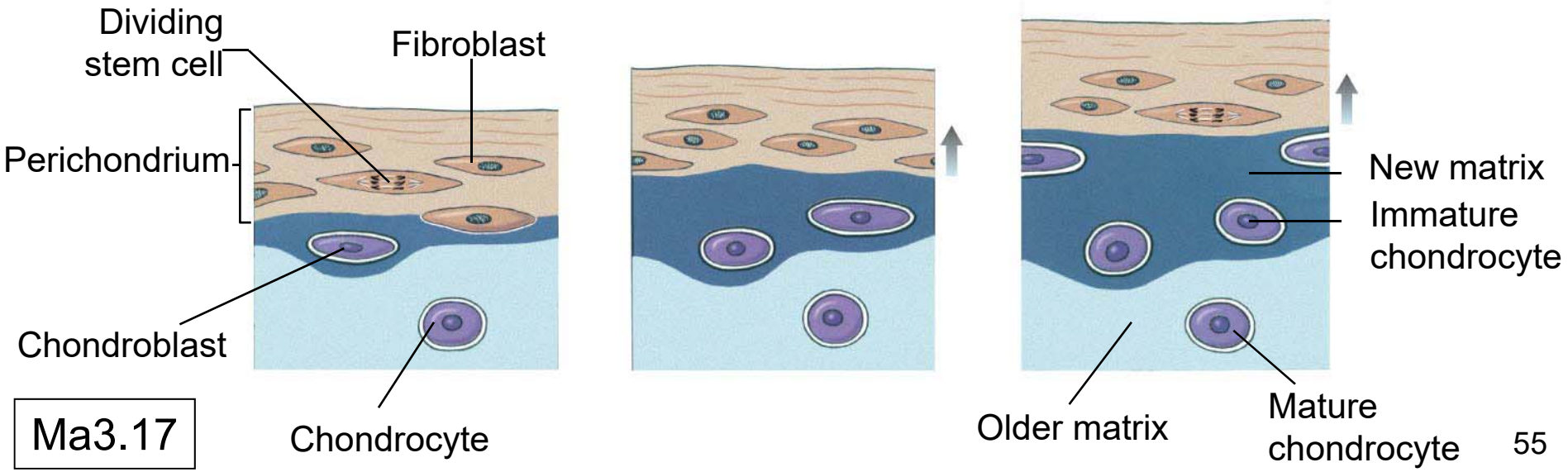
Ma3.17

Appositional Growth of Cartilage

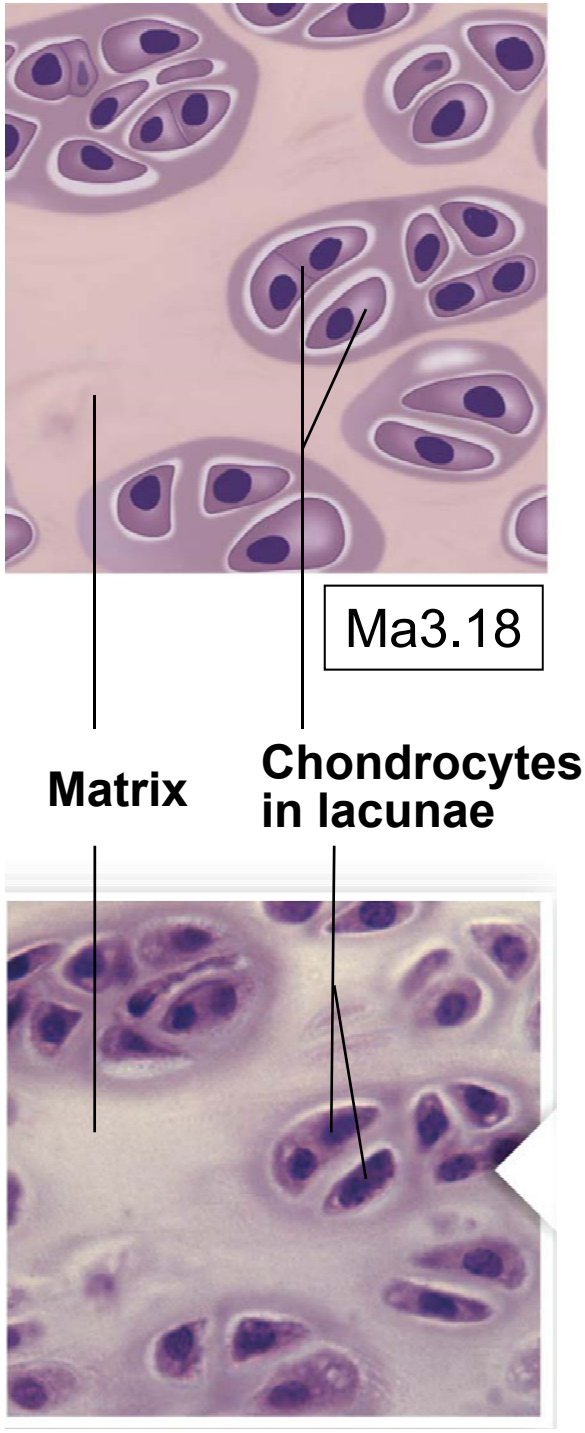
- mesenchymal cells at the surface of the newly formed cartilage differentiate into fibroblasts, which form the fibrous layer of the perichondrium

- mesenchymal cells deep to this fibrous layer differentiate into chondroblasts forming the cellular layer of the perichondrium

- these cells secrete matrix onto the surface of the newly forming cartilage in a process called *appositional growth*



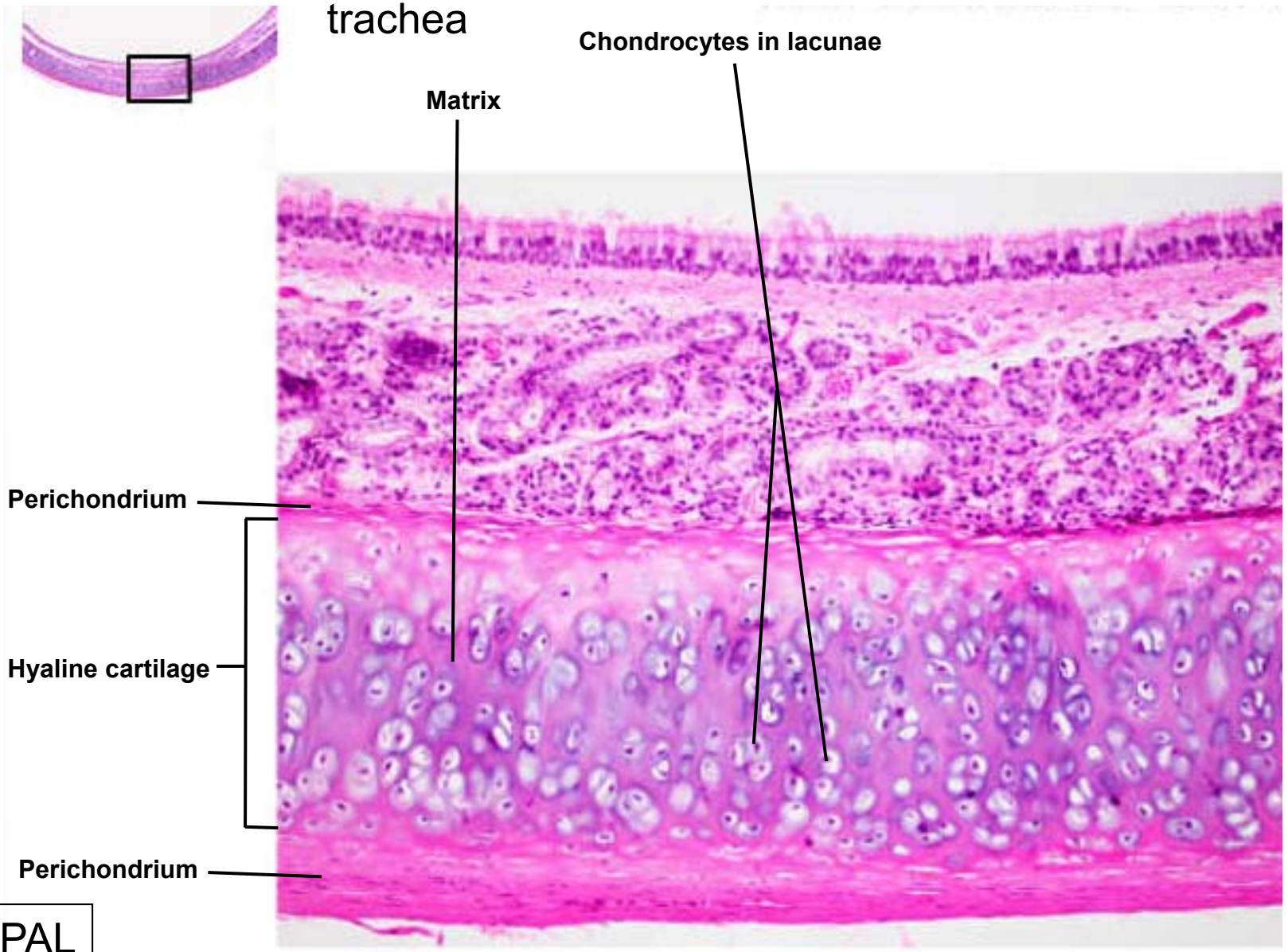
Ma3.17



3.a) Hyaline Cartilage

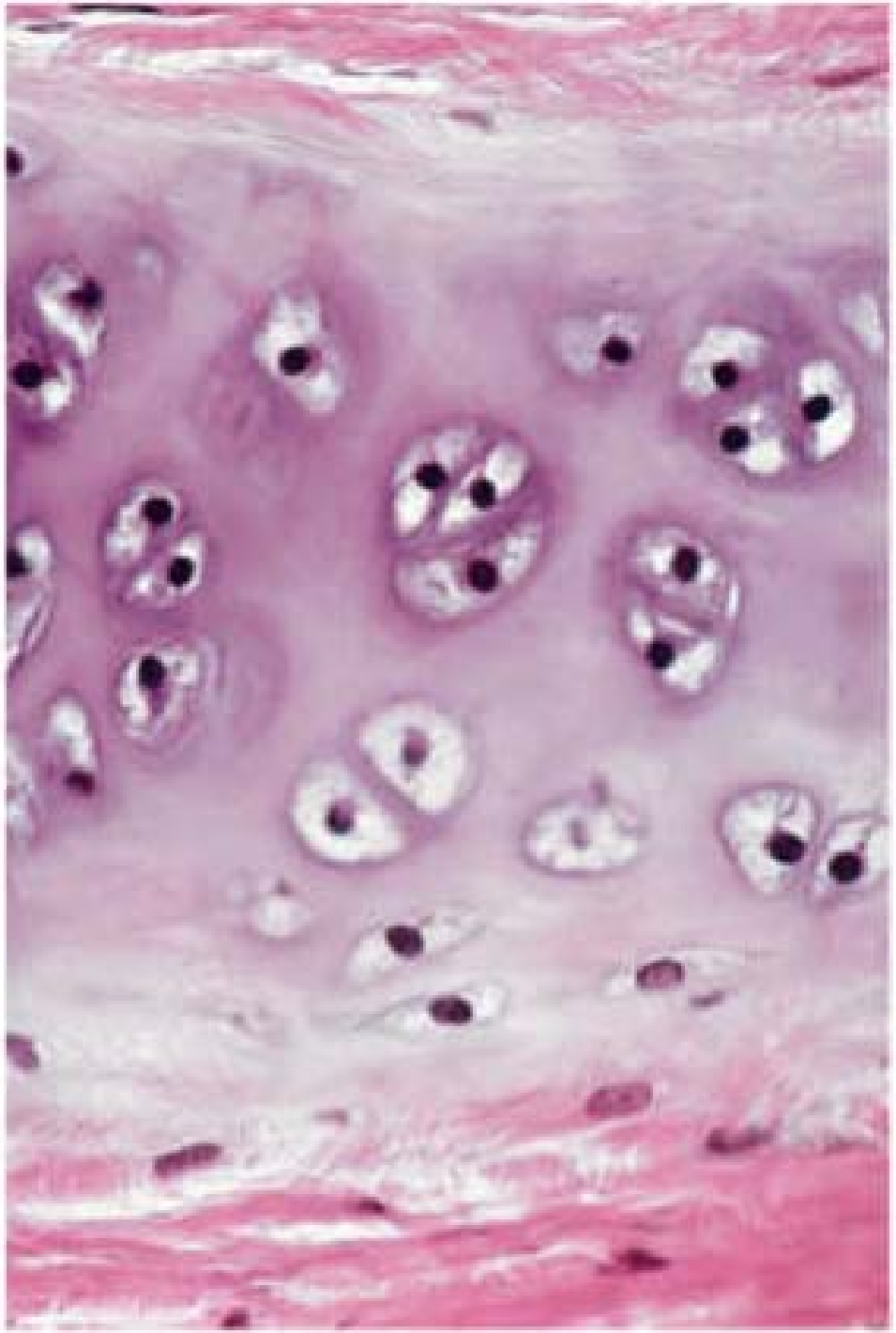
- most common and weakest cartilage
- closely packed collagen type II fibrils in a firm gel-like GS
- articular cartilage*, tracheal rings, costal cartilage, immature skeleton, nasal cartilages
- fxn. resists compression; provides tough, flexible support; reduces friction between bony surfaces in articulations

Hyaline Cartilage

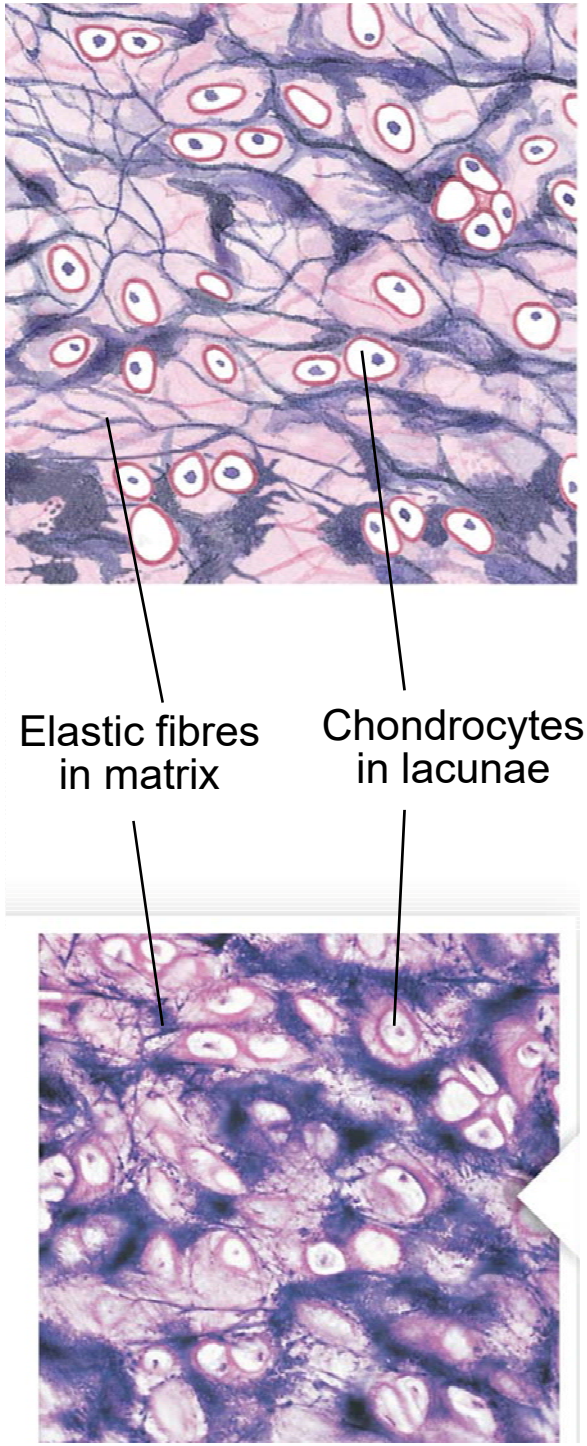


Hyaline Cartilage

trachea



PAL



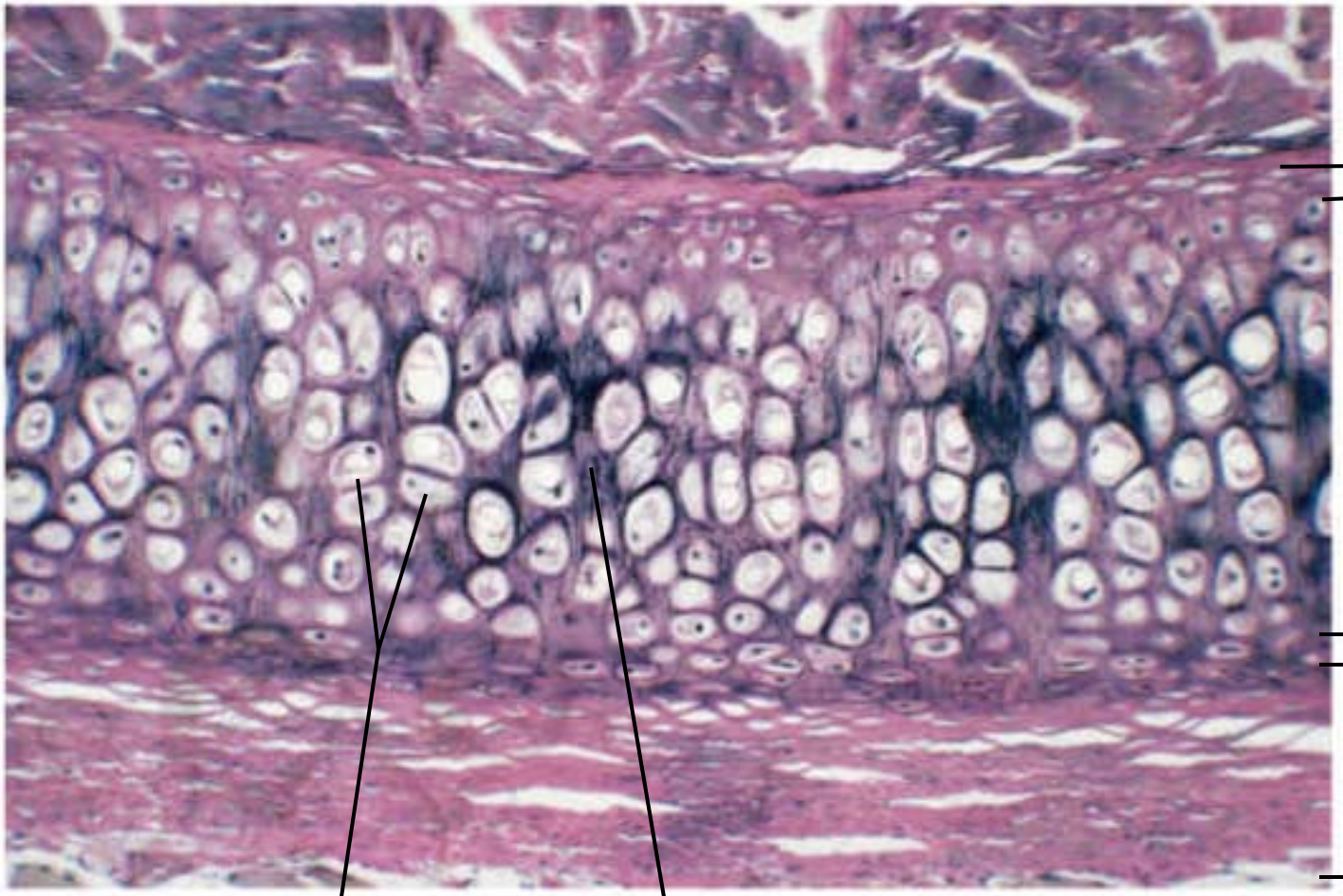
3.b) Elastic Cartilage

- like hyaline, but with a higher proportion of elastic fibres
- pinna of external ear, epiglottis, pharyngotympanic tube
- fxn. provides greater flexibility and *resiliency*, i.e. it "bounces back"

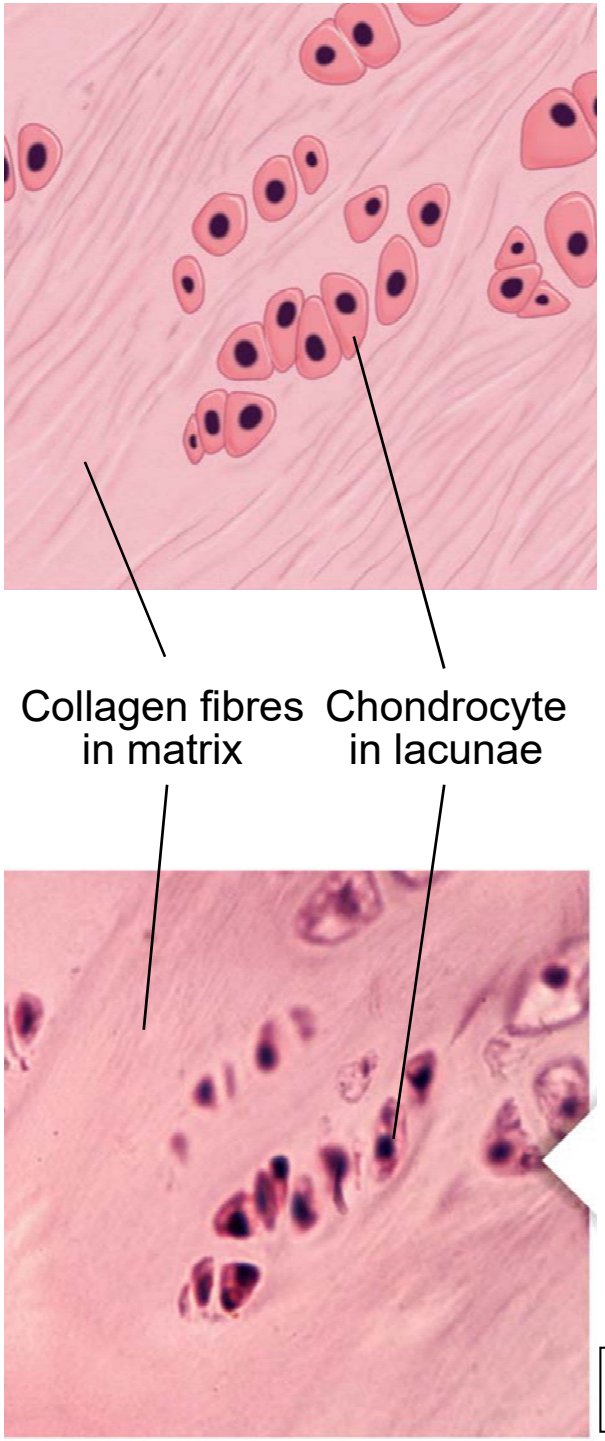
Ma3.18

Elastic Cartilage

epiglottis



PAL



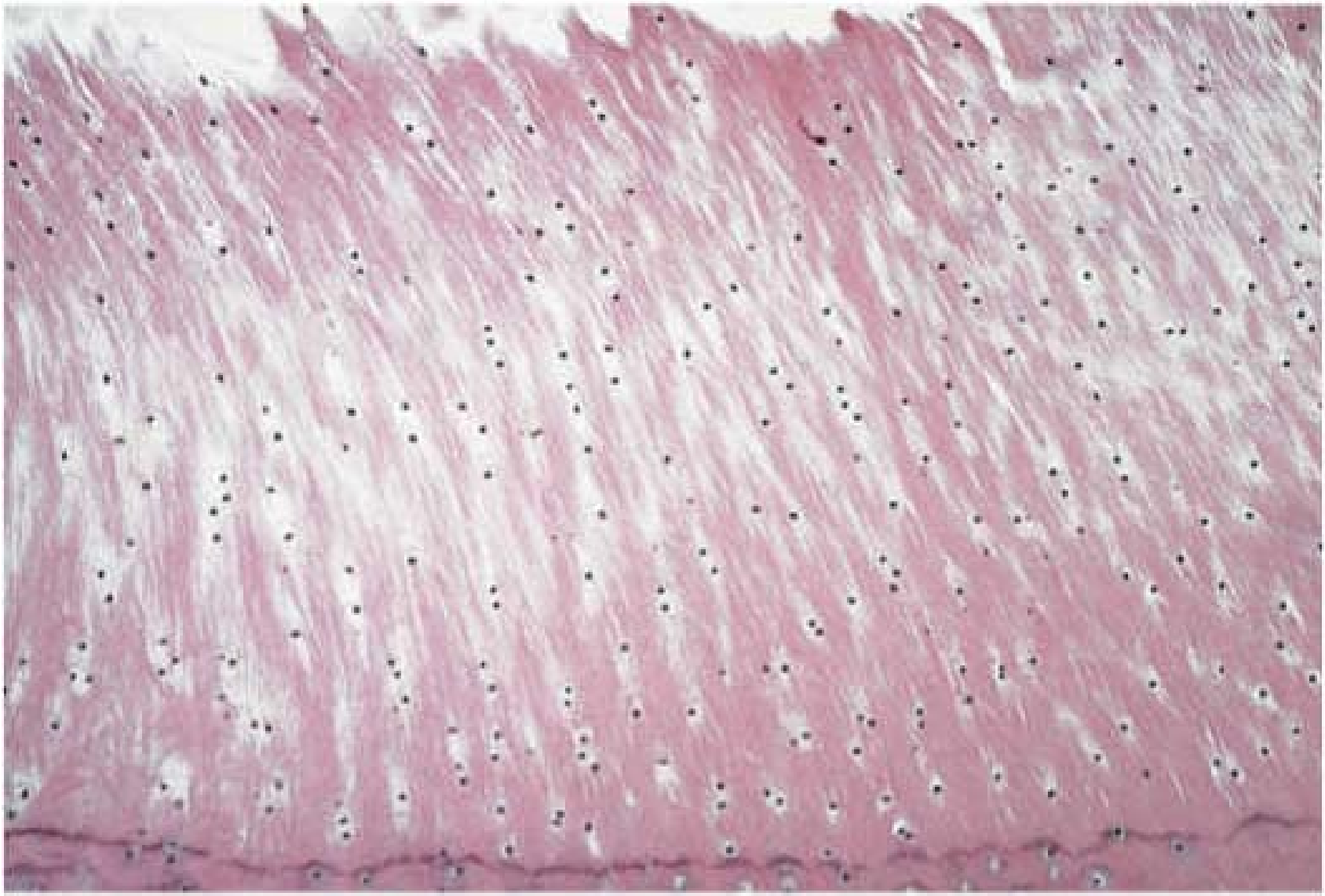
3.c) Fibrocartilage

- little ground substance; high proportion of densely interwoven collagen type I fibres arranged in perpendicular arrays
- intermediate in strength between hyaline cartilage and dense regular CT
- chondrocytes arranged in rows between bundles of collagen type I fibres
- anulus fibrosis of intervertebral disks, pubic symphysis, intra-articular disks, tendon & ligament insertions
- fxn. resists both compression & tension

Ma3.18

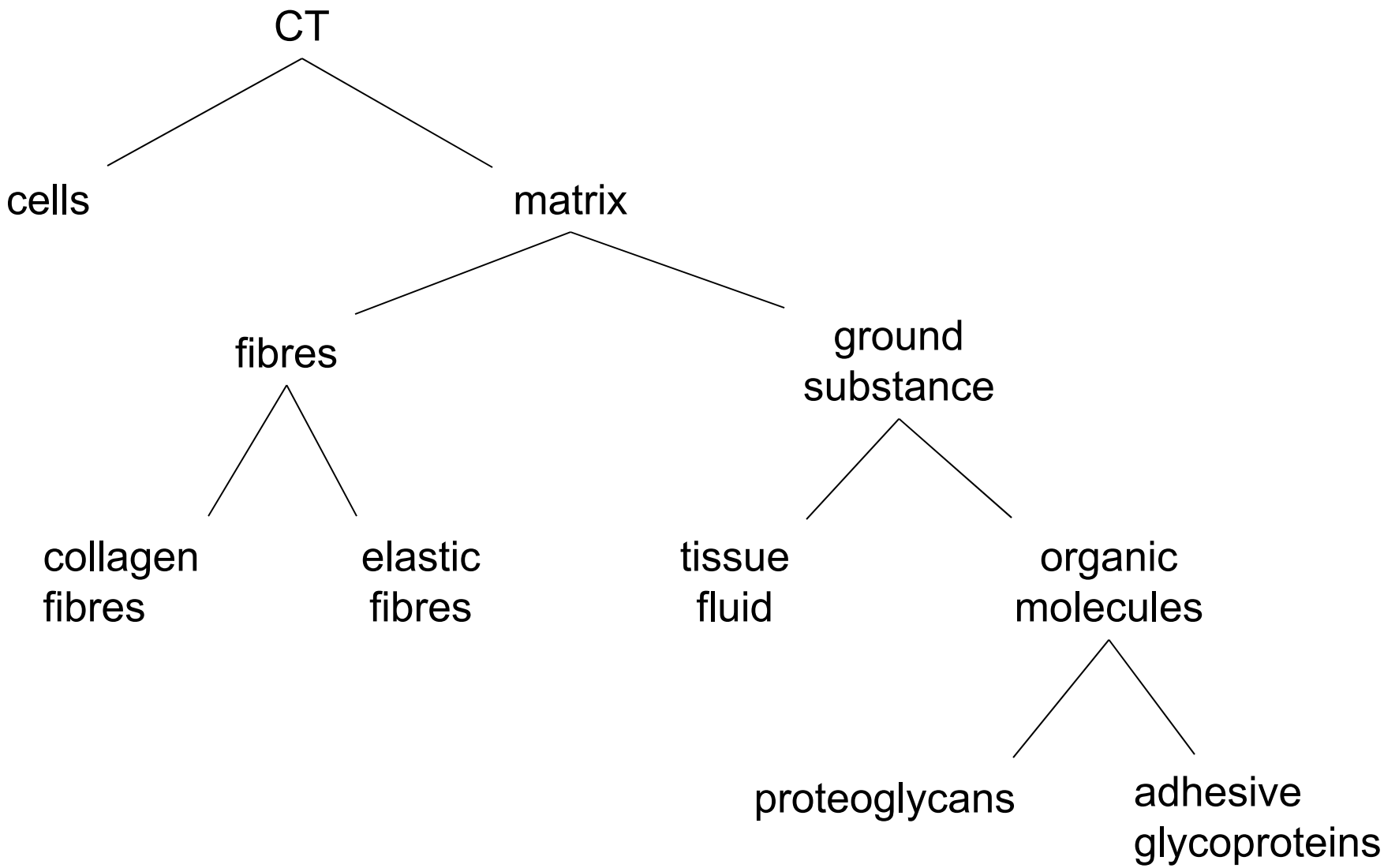
Fibrocartilage

Intervertebral disc



PAL

A Summary of CT Components



A Summary of Connective Tissues

Connective Tissue Proper

1. Loose CT: fewer fibres, more GS by volume
    a. areolar CT
    b. reticular CT
    c. adipose tissue
2. Dense CT: dominated by densely-packed fibres, fewer cells, less GS
    a. dense regular CT
    b. dense irregular CT
    c. elastic tissue

Supporting Connective Tissue

3. Cartilage
    a. hyaline cartilage
    b. elastic cartilage
    c. fibrocartilage
4. Bone (next……)