Connective Tissue

By

Dr. Heba Sharaf Eldin

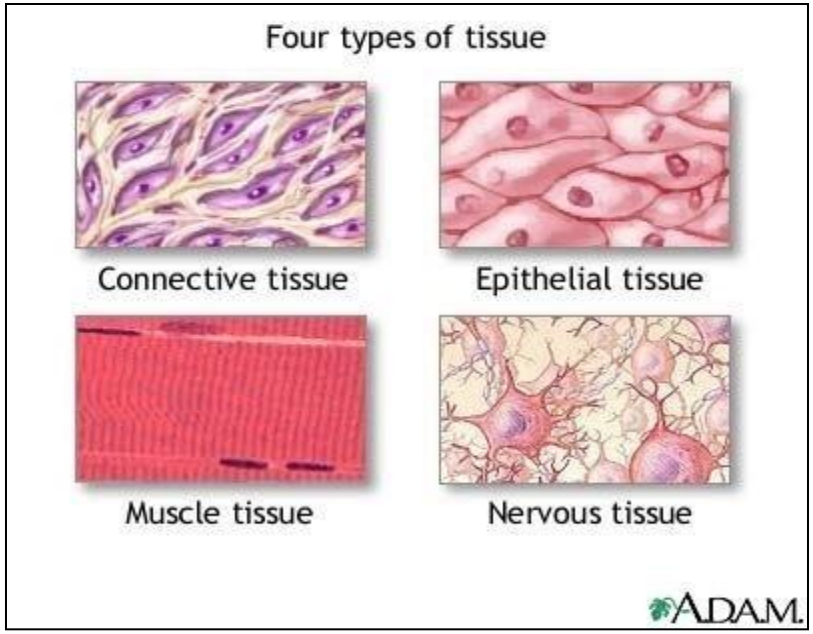
Associate Professor of Histology & Cell Biology

ILOs

1. Know the structural characteristics of the connective tissue.
2. Identify different types of connective tissue.
3. Differentiate between different types of connective tissue.
4. Relate the composition of connective tissue to its specific function.
5. Predict the special type of connective tissue from its components.

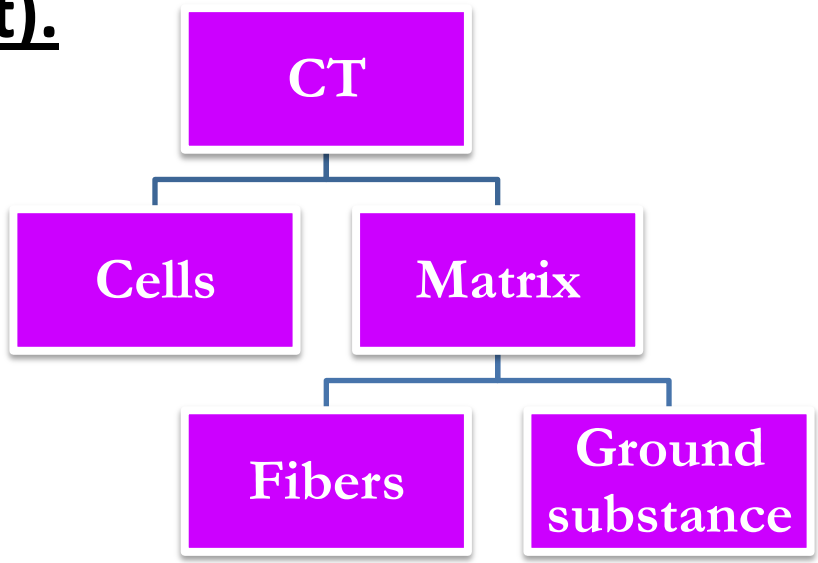
Definition

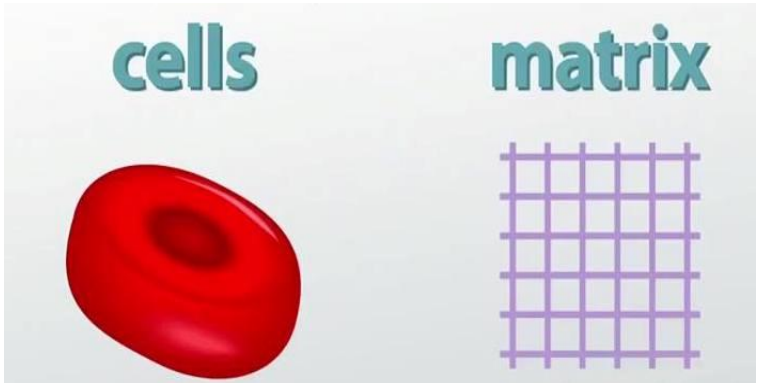
- It is one of the four basic tissues of the human body.
- The name "connective" is related to the function of *connection* and *binding cells* and organs together

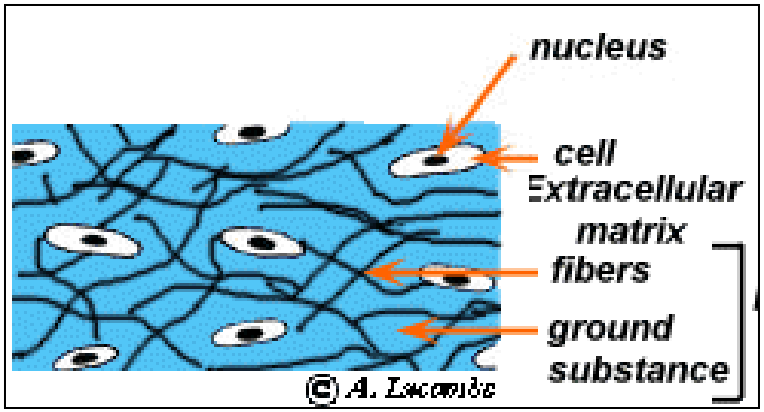


Composition of C.T.

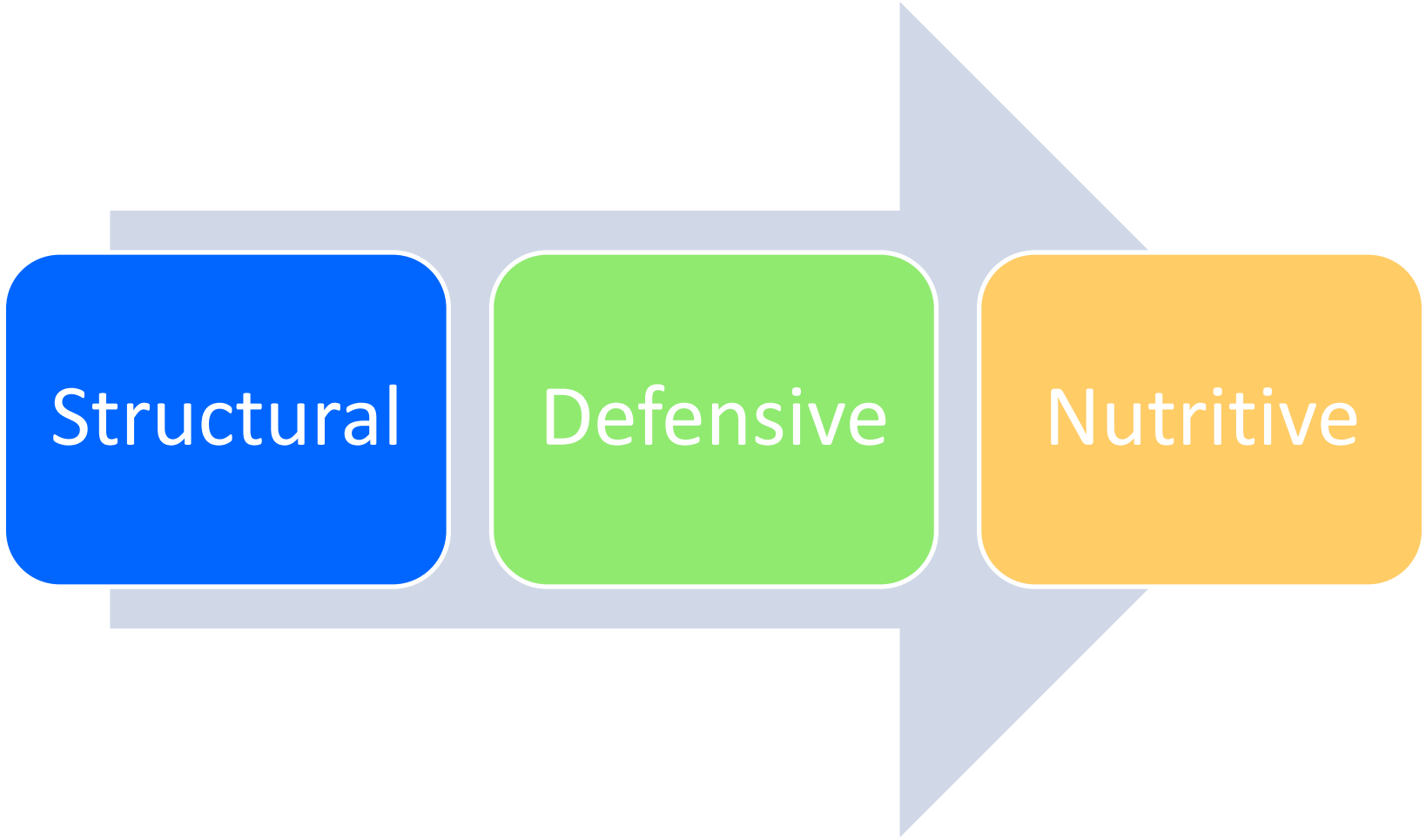
- **Connective tissue cells (less-widely separated)**
- **Extracellular substance (Matrix) (More- the major constituent).**



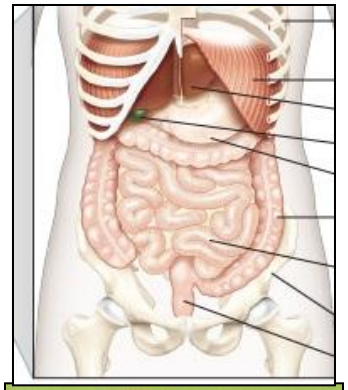


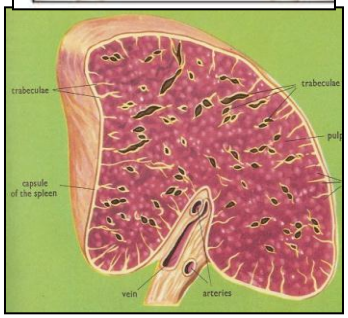


Functions of connective tissue

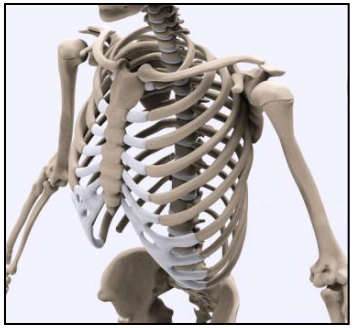


Structural function





1-Loose CT fills spaces between organs 2-Form the capsule & internal architecture of the organs



3-Bone and cartilage support soft tissues.

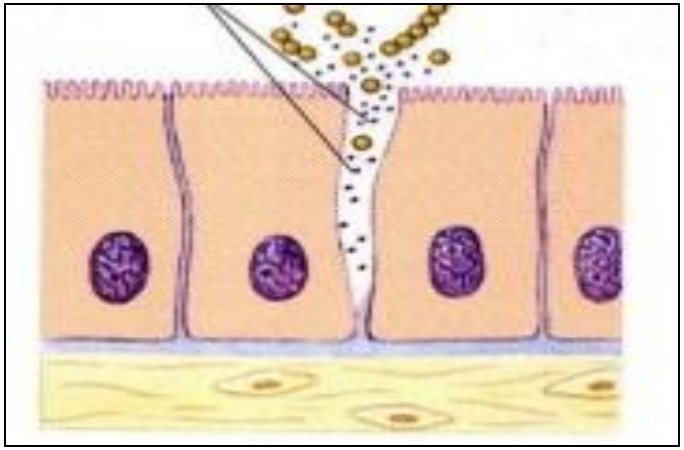
4-Dense CT make up tendons and ligaments

5-Adipose CT stores fat.

Defense function

1-Physical barriers:

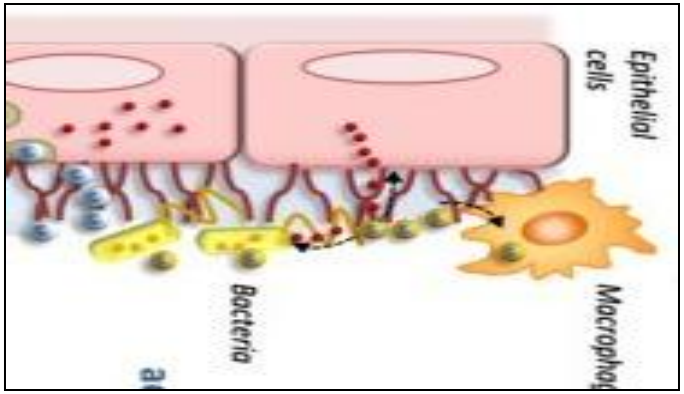
Prevent spread of microorganisms that pass through *epithelia.*



2-Contains immune cells:

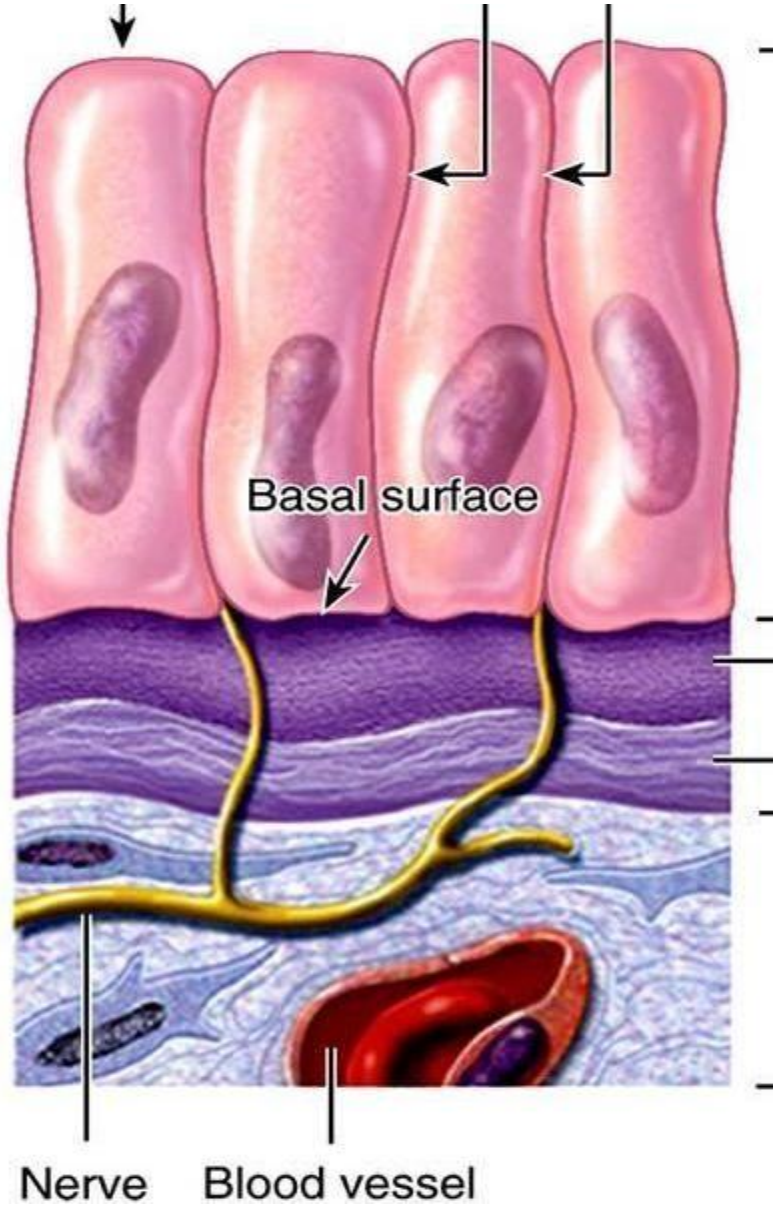
*Phagocytic cells

*Plasma cells



Nutritive Function

Ground substance of C.T. serves as ***a medium*** through which *nutrients* and *metabolic wastes* can be exchanged between epithelial cells and blood supply.



Functions of connective tissue

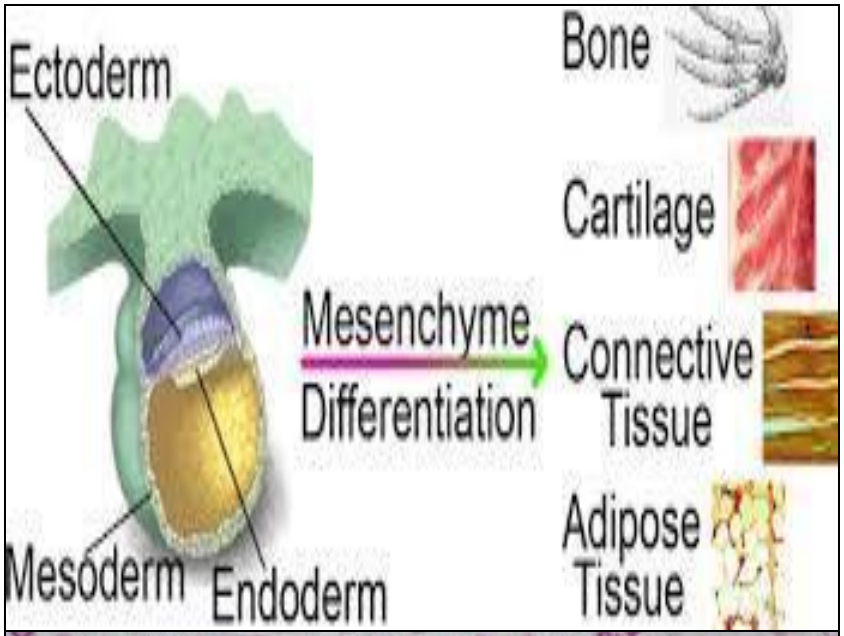
Structural

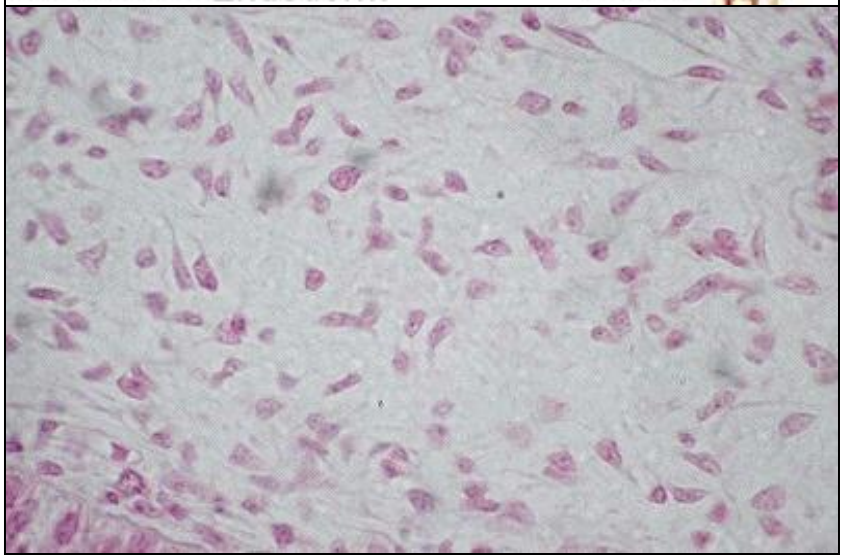
Defensive

Nutritive

Development

- **C.T. develops from the mesenchyme (*embryonic tissue).***
- **The mesenchyme developed from the mesoderm.**
- **The mesenchyme is formed by *mesenchymal cells.***

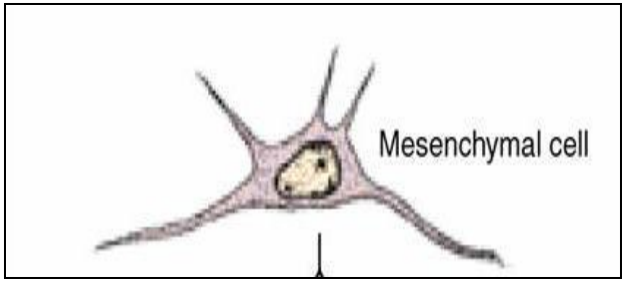




Undifferentiated mesenchymal cell

Shape

Spindle shaped cell having many processes



Size

small

Nucleus

- Oval
-pale
-with prominent nucleoli and fine chromatin.

→ **Active cell**

Cytoplasm

L.M : Small in amount
- Basophilic

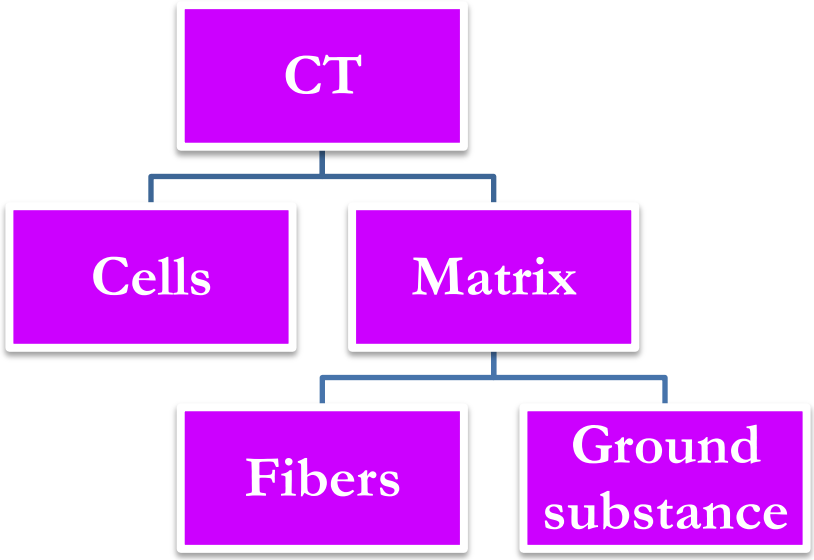
E.M:
- Free ribosomes
-Mitochondria

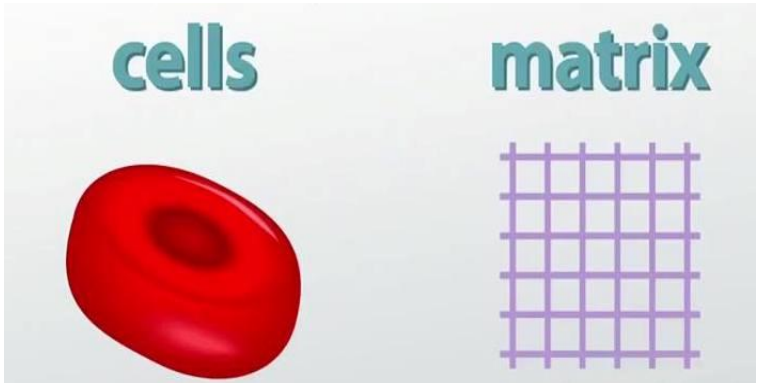
→ **Protein synthesizing cell**

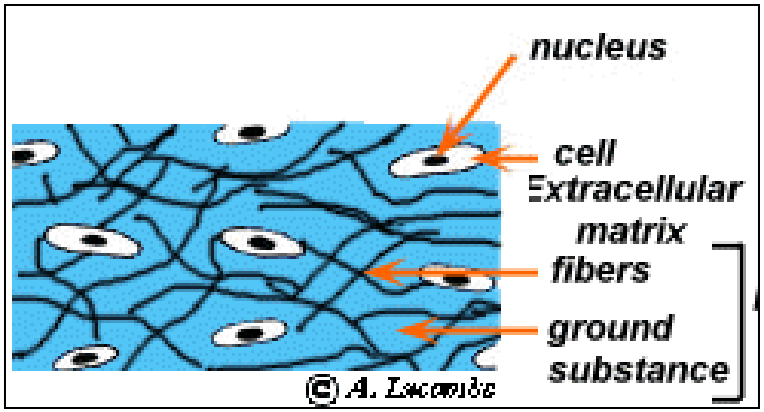
Function

It is the stem cell (Mother cell) of most connective tissue cells.

Composition of C.T.







Extracellular matrix (ECM)

I- Ground amorphous substance

Resist compression

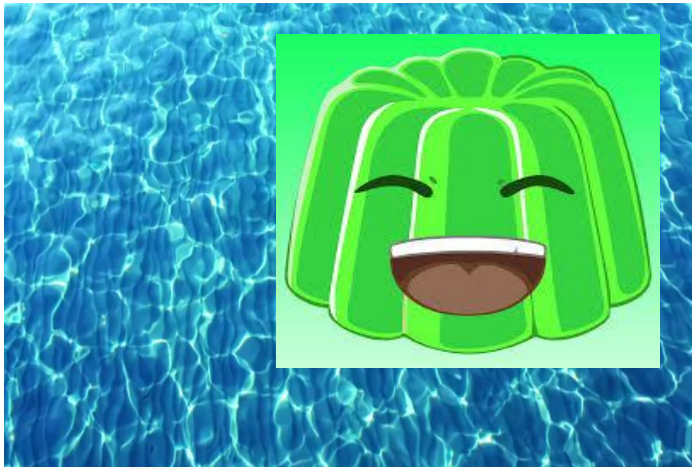
II- Connective tissue fibers

Resist tension

Ground substance

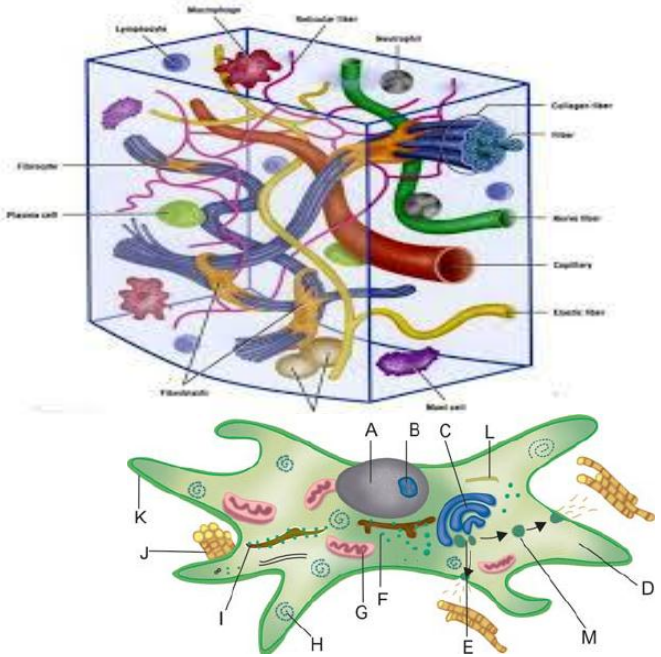
Character:

- Abundant **(Major constituent of C.T.)**
- Amorphous
- Colorless
- Transparent
- Homogenous substance
- Jelly Like
- Hydrated



Site:

- Present *inbetween* the connective tissue cells.
- Connective tissue fibers are in it.



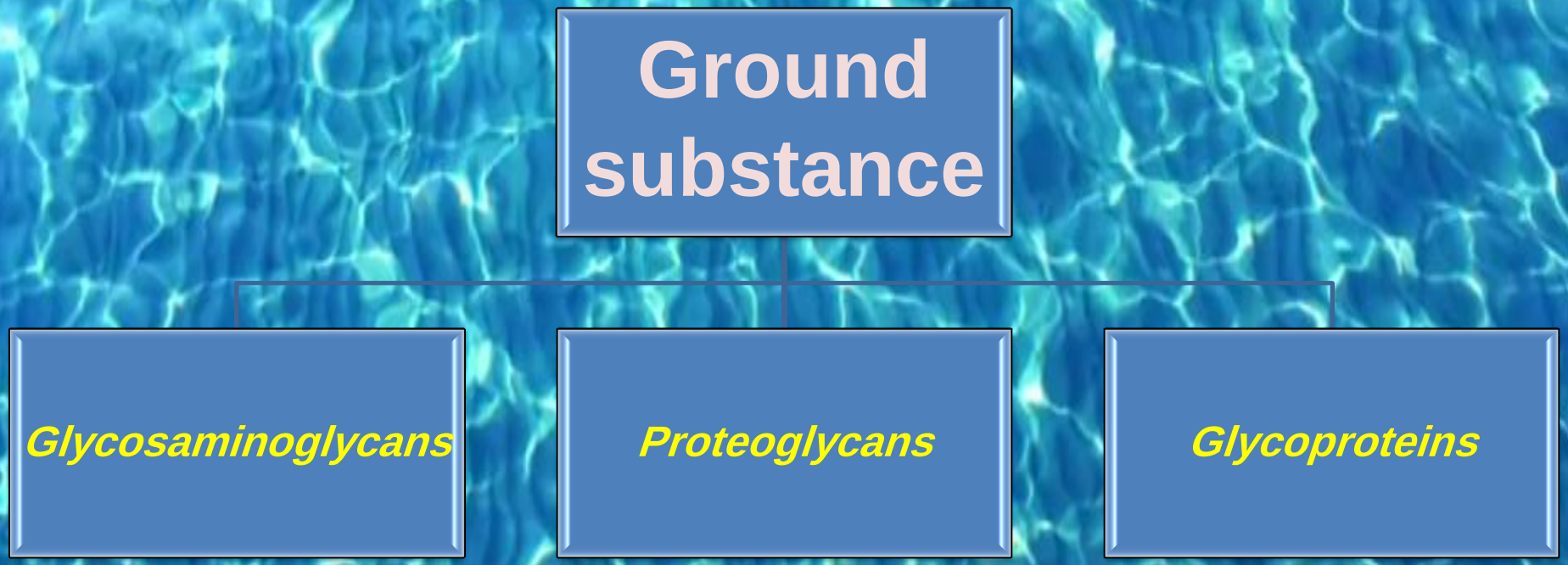
Formation:

1. *Glycosaminoglycans*
2. *Proteoglycan*
3. *Glycoproteins*

secreted by:

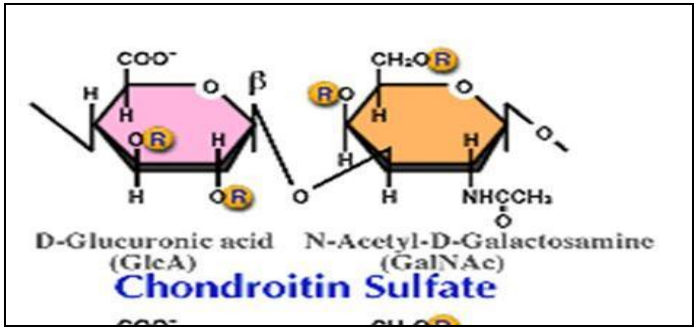
Fibroblasts.

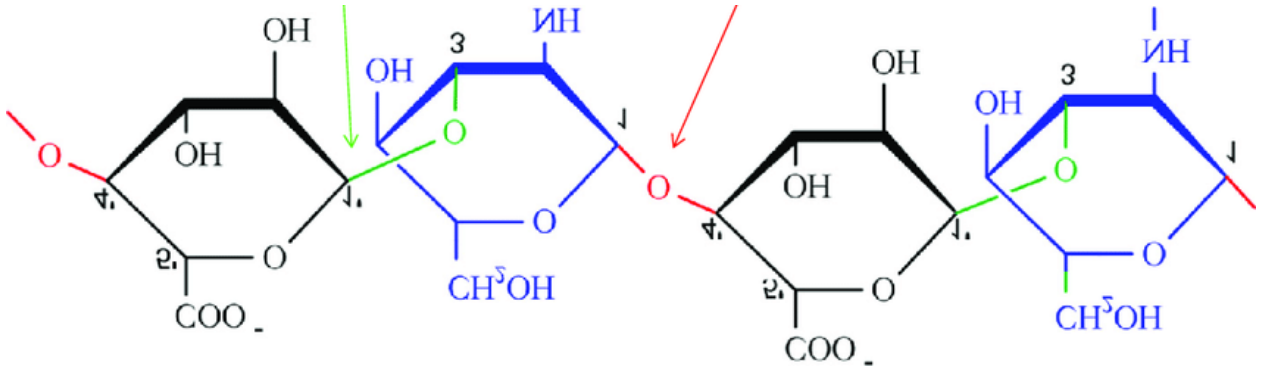
I- The ground substance

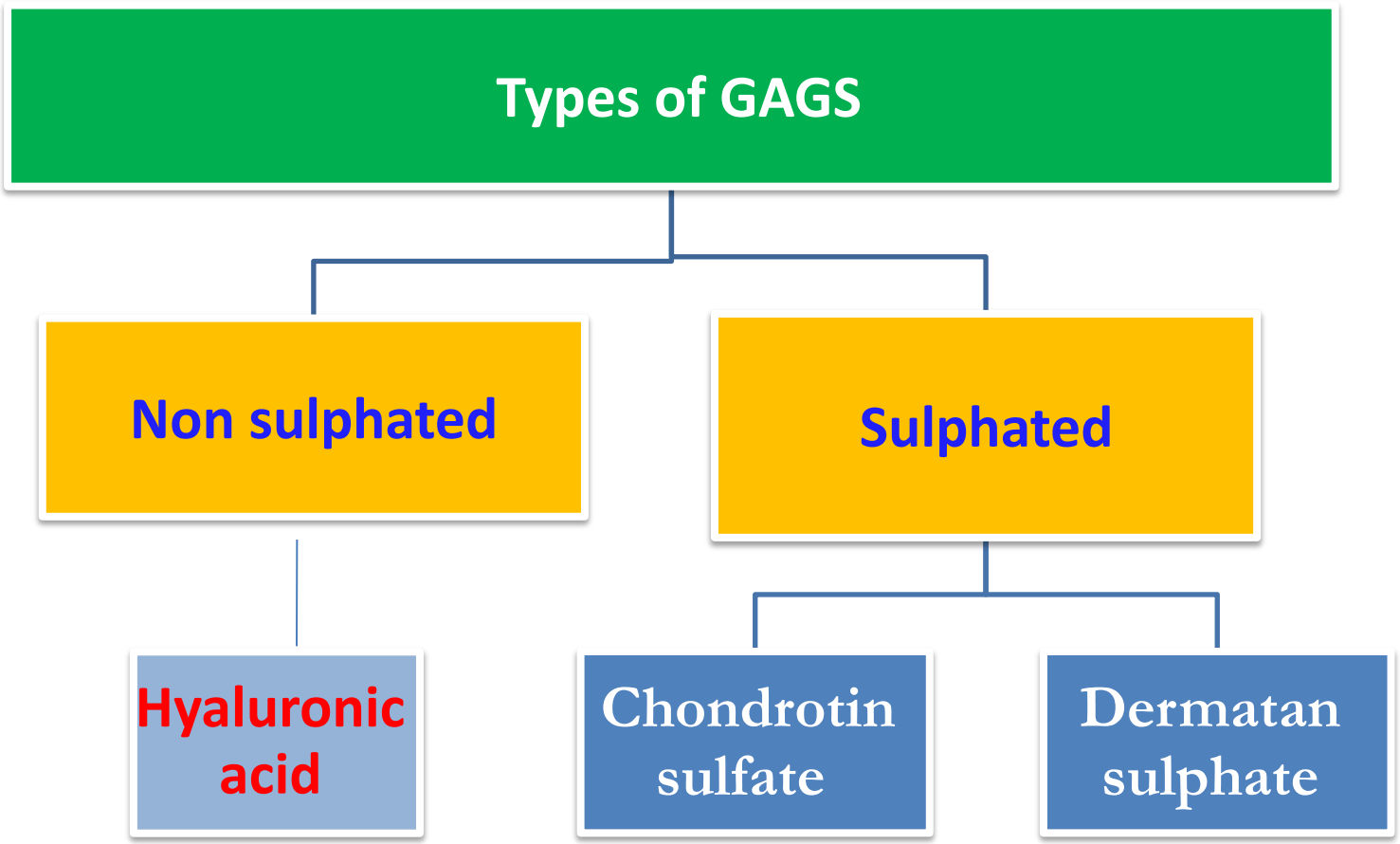

Ground substance
Glycosaminoglycans
Proteoglycans
Glycoproteins

A- Glycosaminoglycans

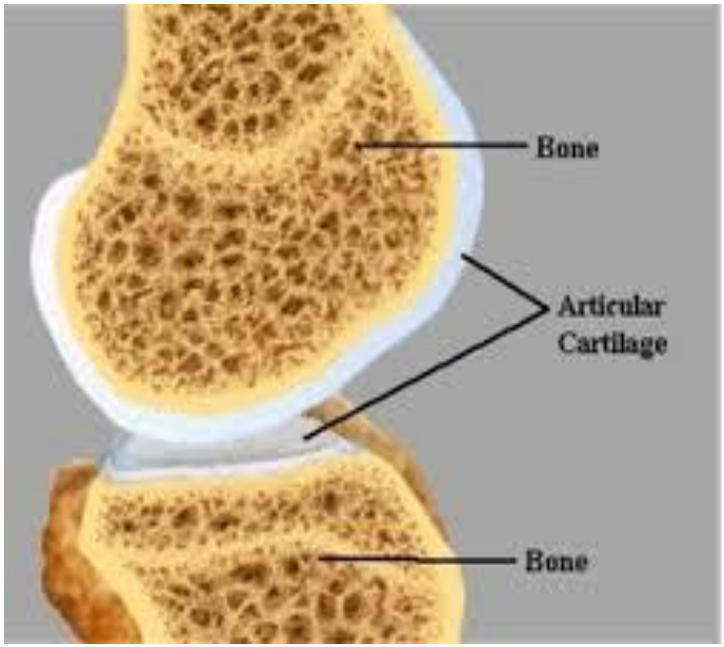
- **Linear unbranched molecules**
- Formed of repeating ***disaccharide units.***






Types of GAGS
Non sulphated
Sulphated
Hyaluronic acid
Chondrotin sulfate
Dermatan sulphate

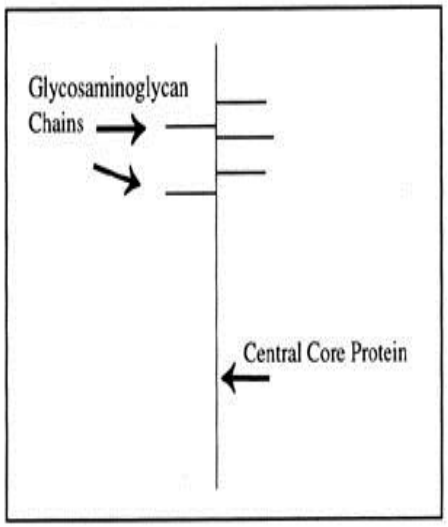
Glycosaminoglycans are negatively charged ⟶ attract Na^+ ⟶ attract H_2O ⟶ hydrated matrix ⟶ resist compression



GIycosaminoglycans are negatively charged ⟶ repeal each other ⟶ slippery texture (Jelly like)

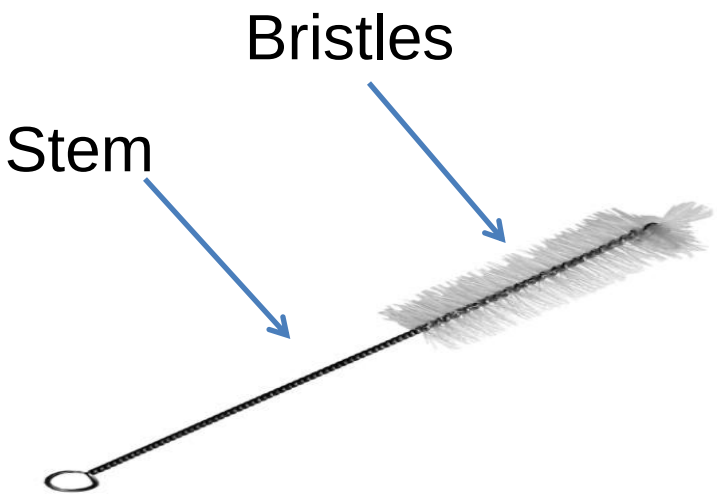
B- Proteoglycans

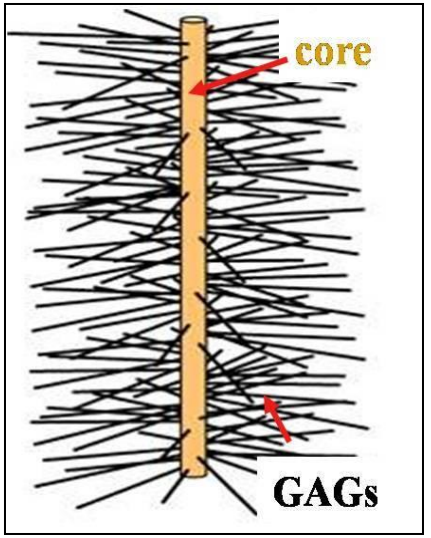
Sulphated GAGs + Protein core → proteoglycan



Proteoglycan molecule is similar to *test tube brush*.

- **The wire stem represents the protein core and the bristles represent the GAGS**

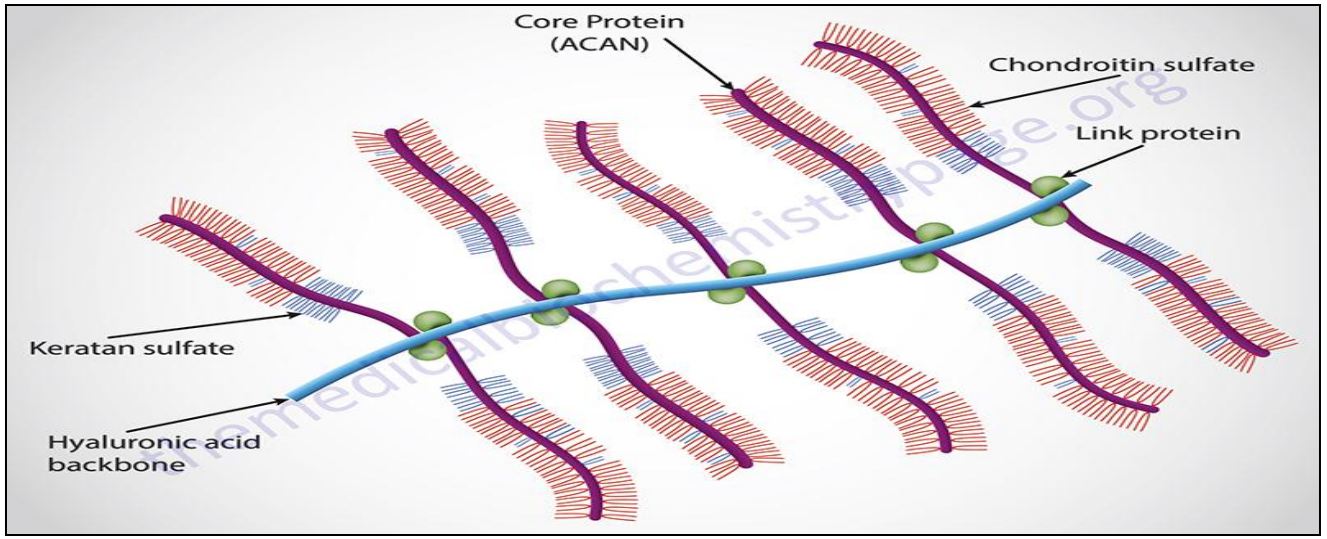




Proteoglycan- hyaluronate complex

When several proteoglycans are bound to *hyalouronic acid* (aggrecan)→ **proteoglycan- hyaluronate complex**

(cartilage)

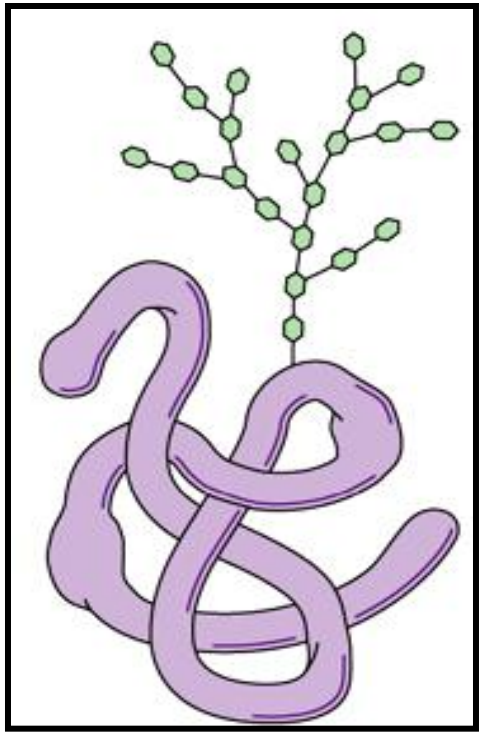


C- Glycoproteins

- **Structure:**

Macromolecules are formed mainly of:

protein conjugated with ***branched oligosaccharides*** (few sugars)



- **Examples:**

1-Fibronectin: present in CT.

2- Chondronectin:present in cartilage.

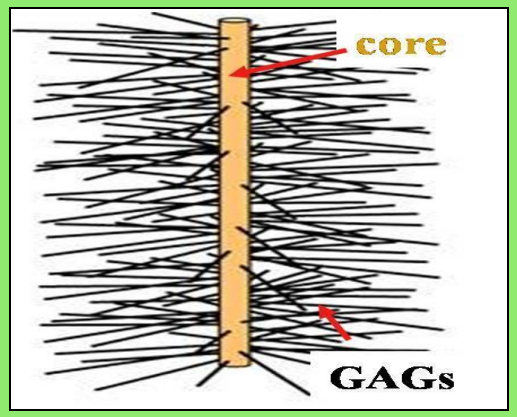
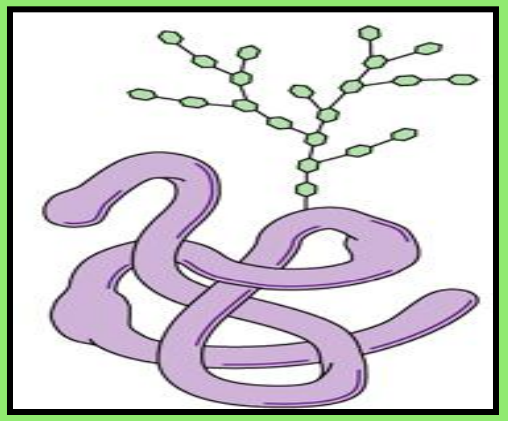
3-Laminin: present in basal laminae.

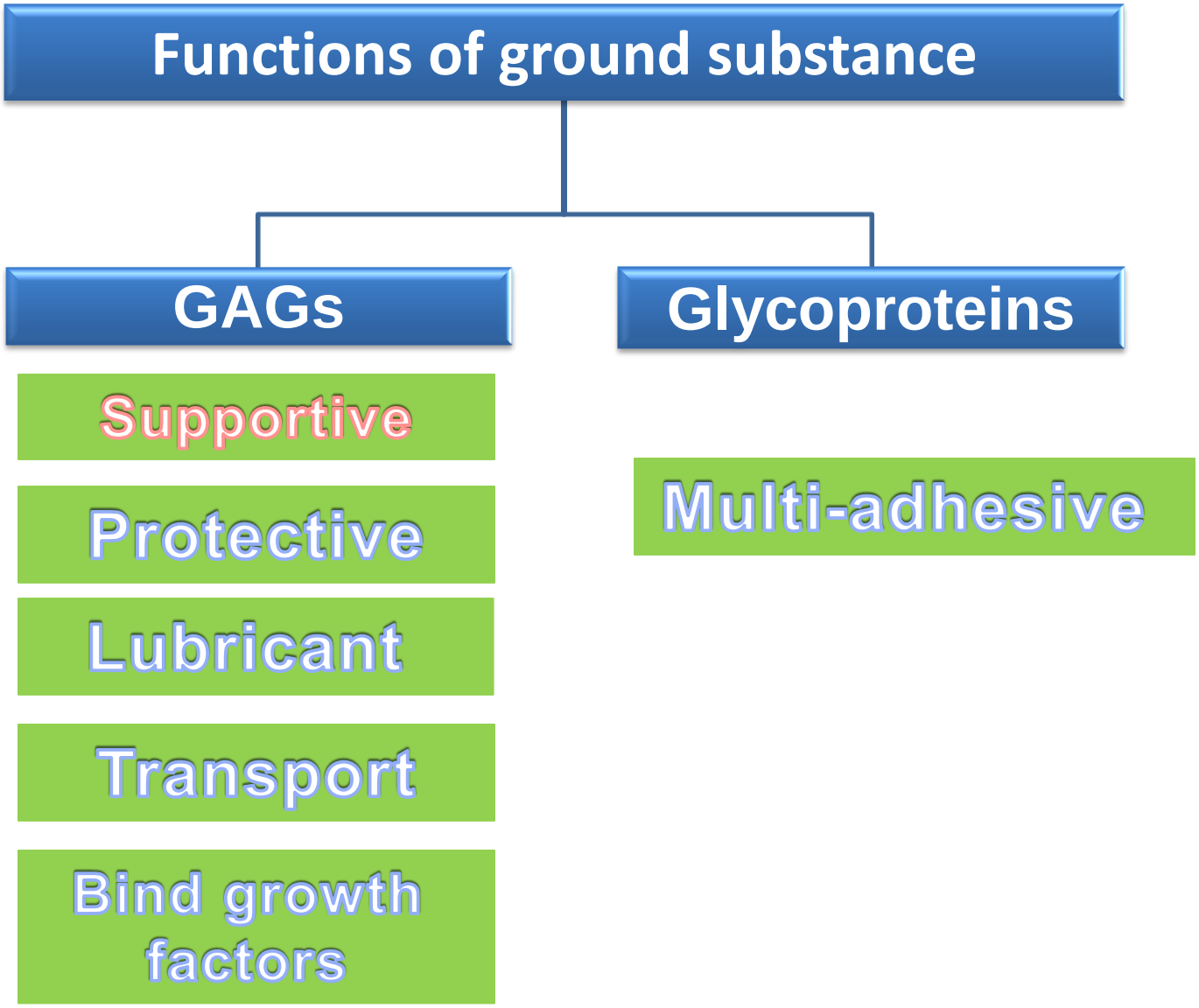
In contrast to ***Proteoglycans***, **glycoproteins** are characterized by:

The *protein moiety* predominates.

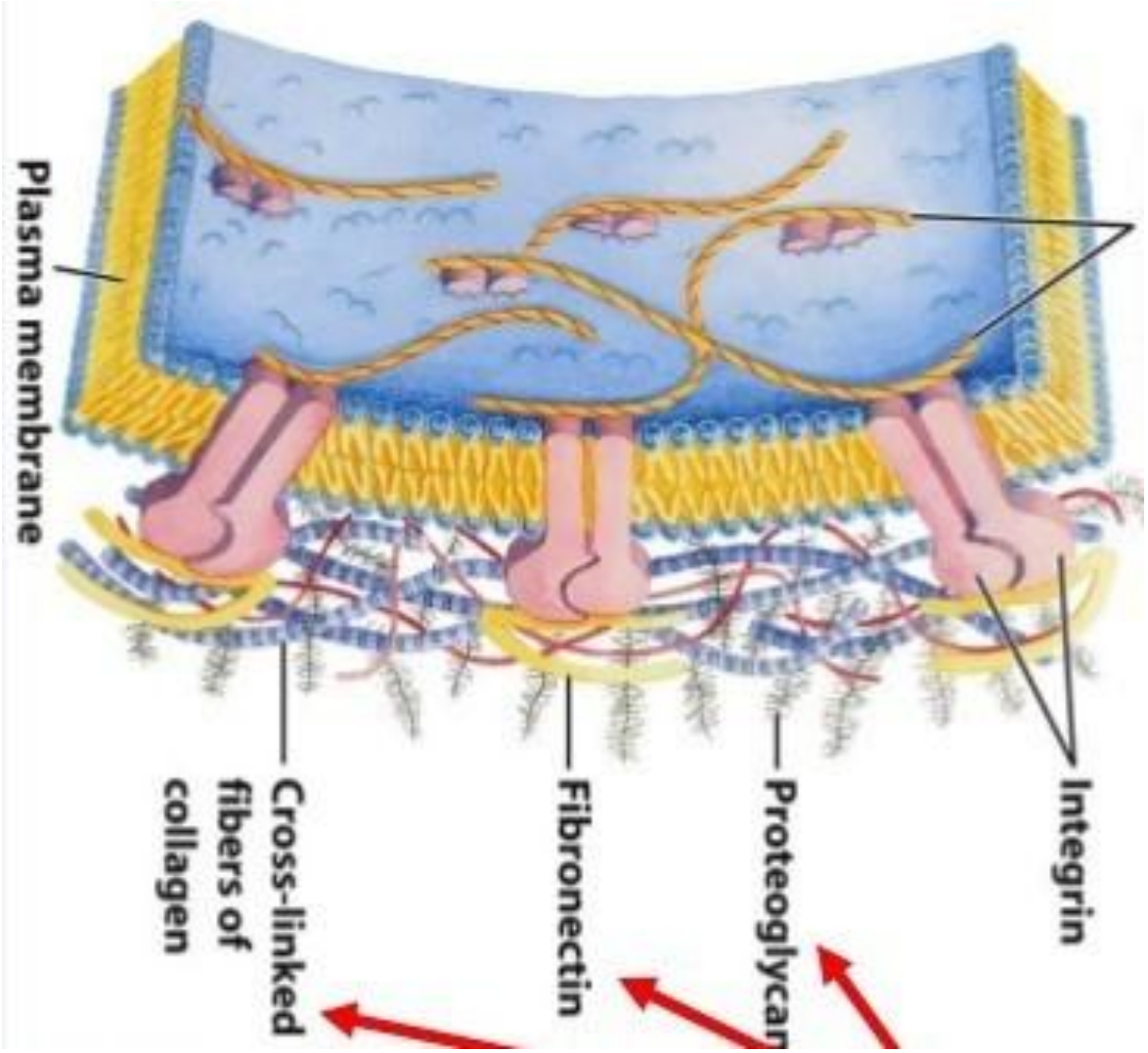
The carbohydrates are *branched.*

Comparison between proteoglycan and glycoproteins

Proteoglycan (Sulphated GAGs)	Glycoproteins
Carbohydrates moiety predominates	Proteins moiety predominates
Linear polysaccharides	Branched oligosaccharides
Repeated disaccharides	oligosaccharides
Sulphated	----------
	


Functions of ground substance
GAGs
Glycoproteins
Supportive
Protective
Lubricant
Transport
Bind growth factors
Multi-adhesive

Multia-dhesive glycoproteins (fibronectin)



Have *binding sites* for:

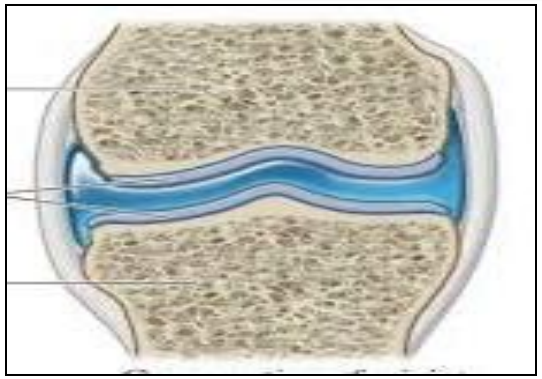
-C.T. Fibers

-GAGS

-Cell membrane proteins

so connect the component of GS together.

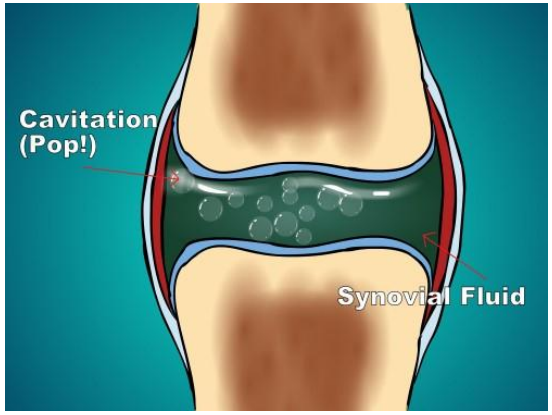
Functions of ground substance



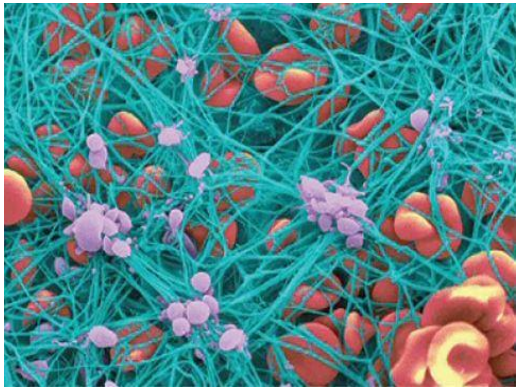
Supportive

Protective

Bind growth factors



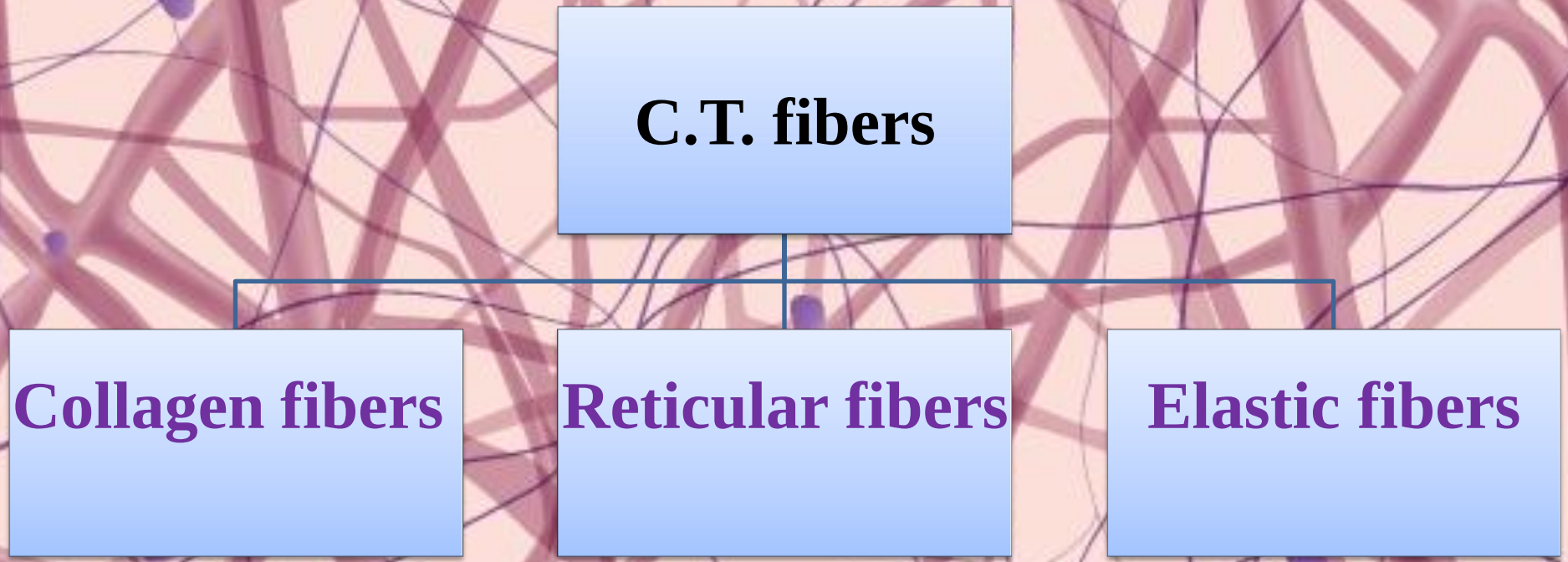
Lubricant



Transport

Multiadhesive

2-Connective tissue fibers

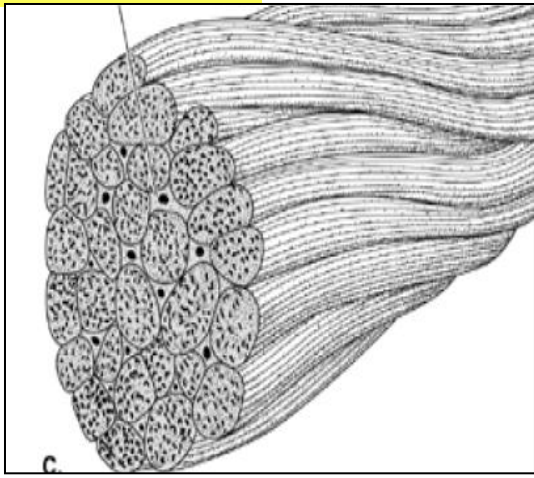


Connective tissue fibers

- Structure & form
- Character
- Formation
- Stain

Collagen fibers

Most numerous fibers of connective tissue



Structure & form

Fibrils form fibers (Wavy) arranged into bundles

Character

-Inelastic, but highly resistant to stretch

-When present in great amount, they give the tissue a white color e.g .(Tendon)

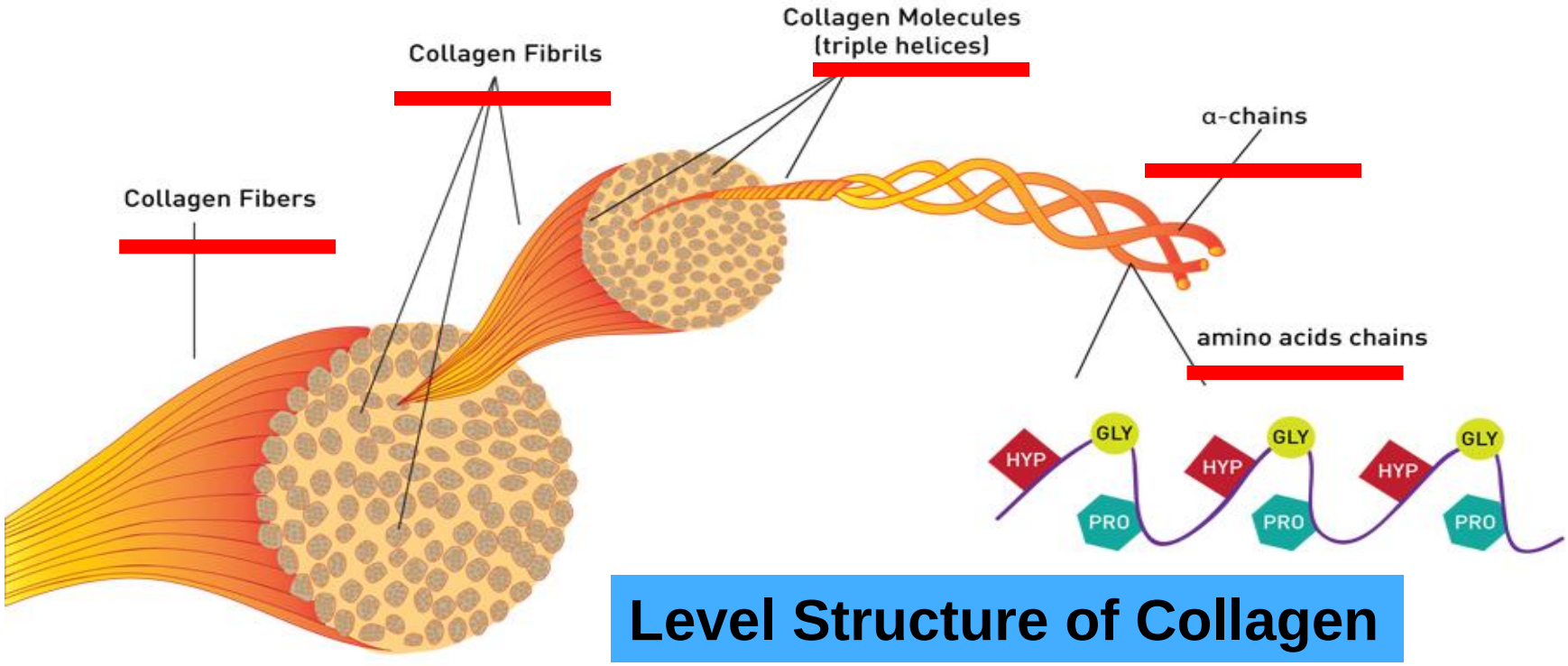
Formation

-protein called collagen.

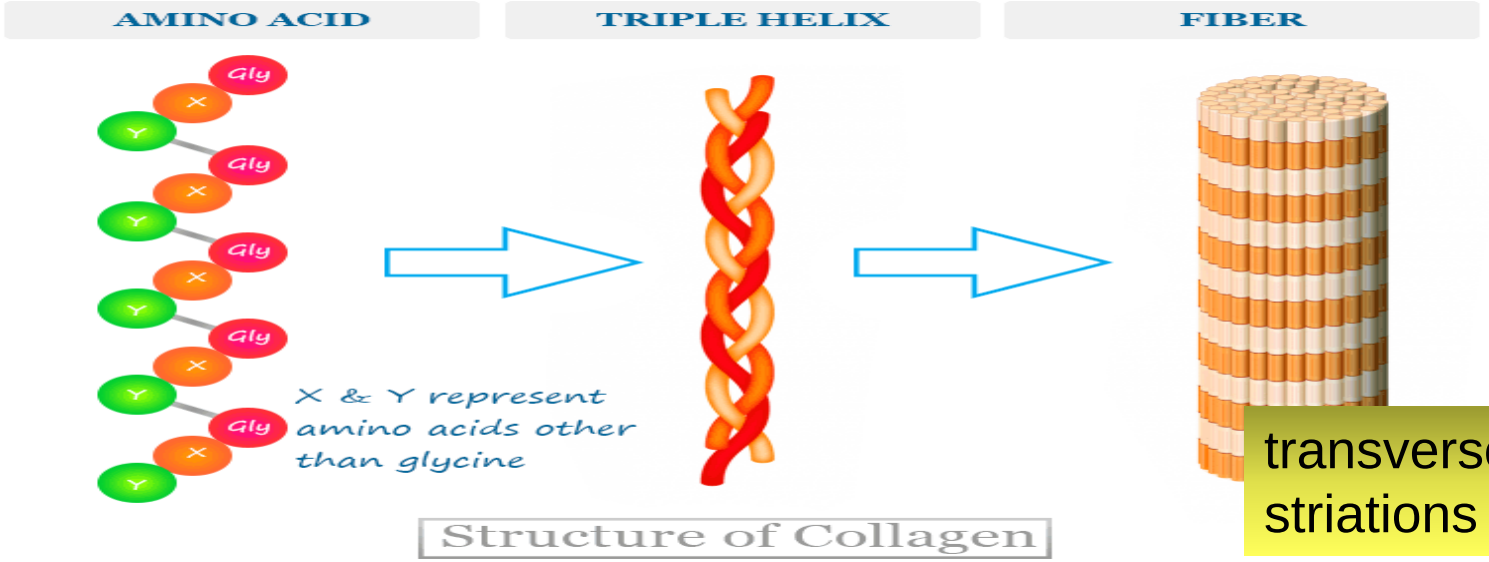
-most abundant protein in human body representing 30% of its dry weight

Stain

- Red with eosin .
- Sirius red



Level Structure of Collagen

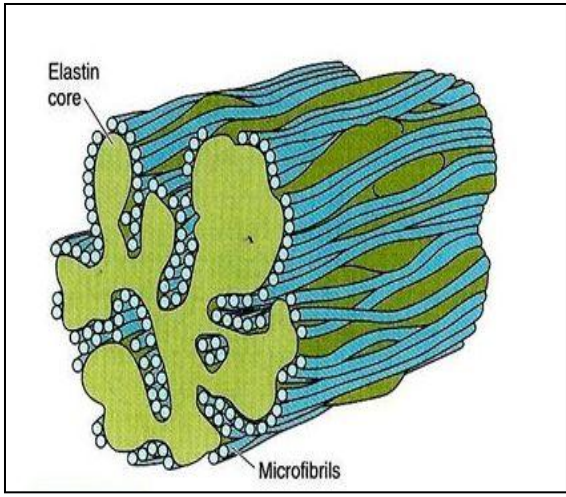


Collagen type	Tissue distribution	Cells synthesize it	Function
I	*CT proper *Fibrocartilage *Bone *Dentin	*Fibroblast *Chondroblast *Osteoblast *Odontoblast	**Resists tension**
II	*Hyaline, Elastic cartilage	*Chondroblast	**Resists pressure**
III	* Reticular CT * Blood vessels * Liver * Endoneurium	* Fibroblast and reticular cells. * Smooth muscle cells *Hepatocytes * Schwann cell	**Supportive**
IV	*Basal lamina	*Epithelial cells *Endothelial cells	Acts as a **filter**

Elastic fibers

Structure

Fibers, Branched



Form

Usually present singly

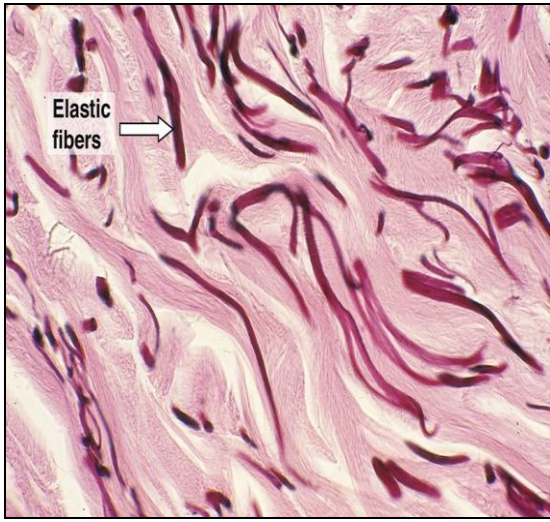
Character

- Rubbery.
- When present in large amounts, they give the tissue a yellow color .

Formation

-Elastin

-Fibrillinis (microfibrils that form a scaffold upon which elastin is deposited and *is present around and inside the elastic fibers*



Stain

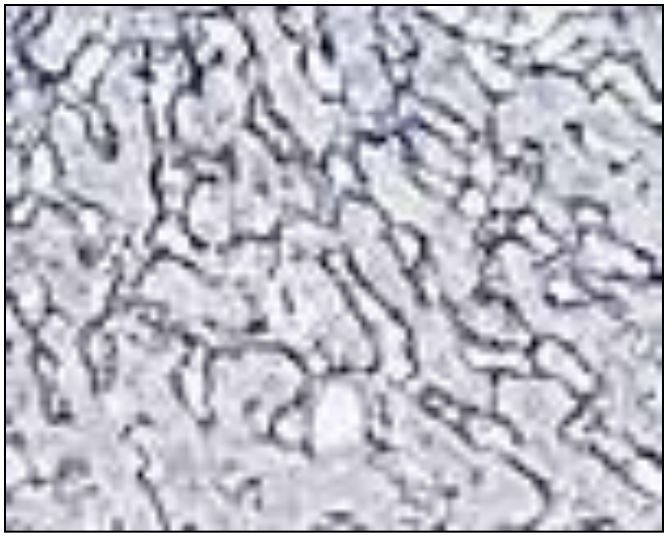
Orcein (Brown)

Reticular fibers

Structure — Formed of fibrils, branch and reunite.

Form — Network

Formation — Composed mainly of collagen Type III .



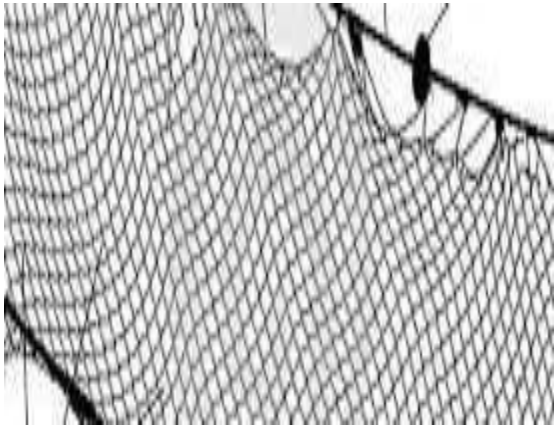
Stain — Black with silver

Comparison between connective tissue fibers

Type of fiber	Collagen fibers	Elastic fibers	Reticular fibers
structure	Fibrils that form fibers	Branched rubbery fibers	Fibrils
Form	Bundles	Single	Network
Protein	Collagen	-Elastin -Fibrillinis	Collagen Type III
Stain	-Red with eosin -Sirius red	Brown with Orcein	Black with silver

Collagen fibers

Elastic fibers



Reticular fibers

Connective tissue cells

A- Fixed cells

Developed & remain in CT.

They ***originate locally*** from undifferentiated mesenchymal cells and spend their life in C.T.

- **Fibroblasts**
- **Adipocytes**
- **UMC**

B- Transient cells

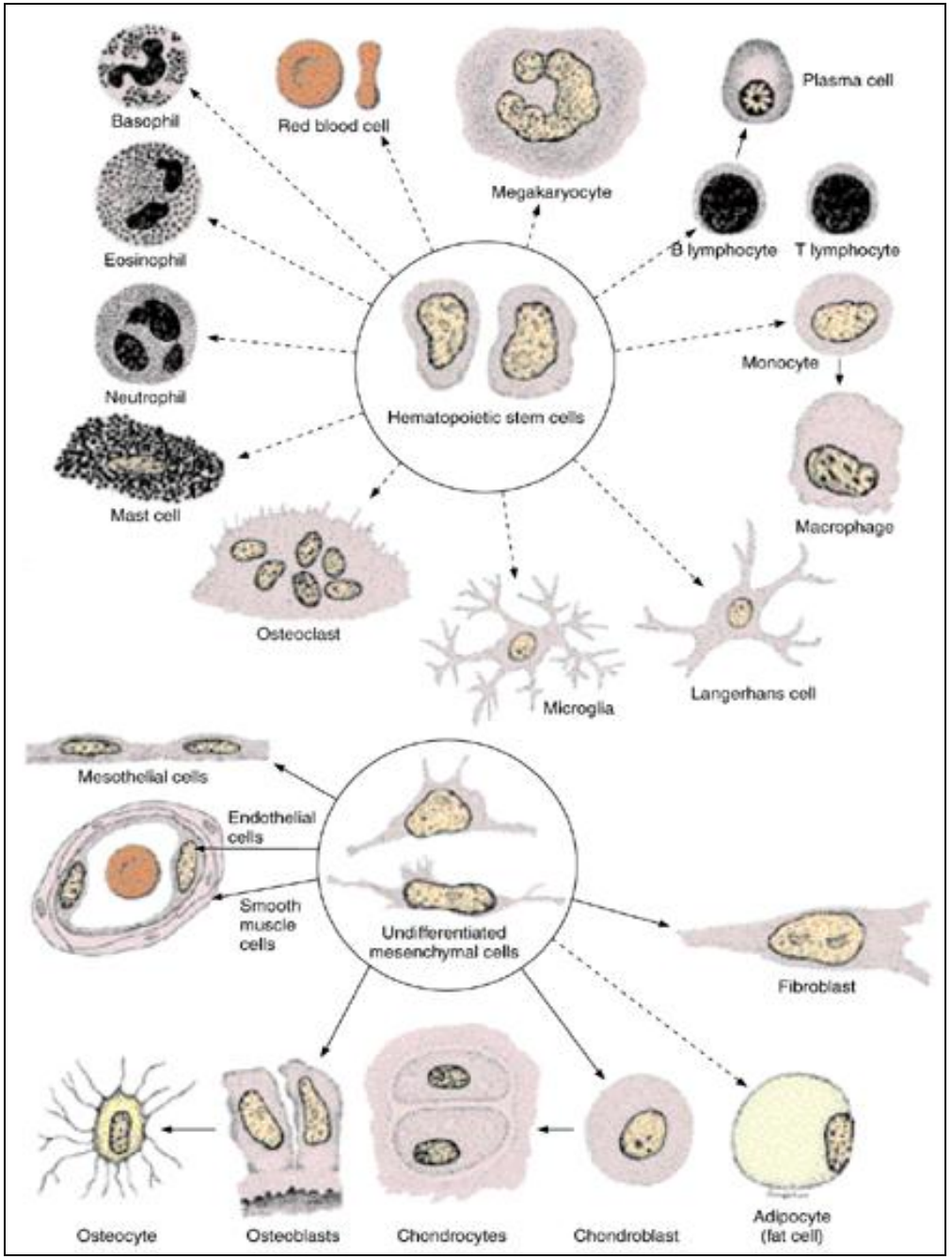
- Cells coming ***from outside***
- Come from hematopoietic stem cells in bone marrow
- Circulate in blood and then move into C.T (wondering)

- **Plasma cells**
- **Macrophage**
- **Mast cells**
- **Leukocytes**

Transient

Connective tissue cells

Fixed



Cell types

Macrophage

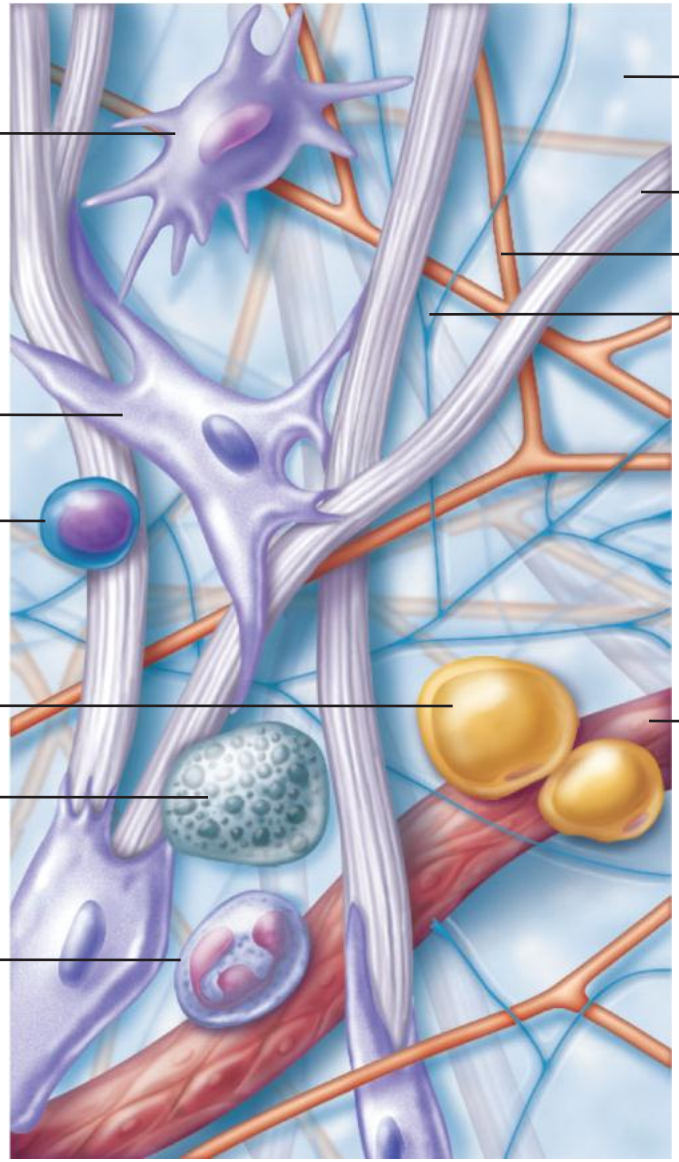
Fibroblast

Lymphocyte

Fat cell

Mast cell

Neutrophil



Extracellular matrix

Ground substance

Fibers

- Collagen fiber
- Elastic fiber
- Reticular fiber

Capillary

Connective tissue cells

Shape

Size

Nucleus

Cytoplasm

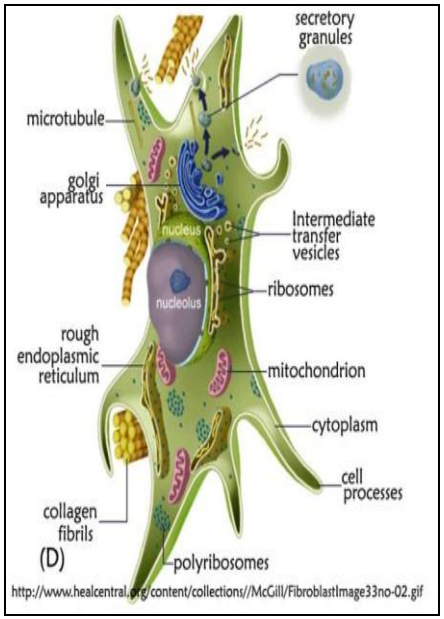
Function

Fibroblast

Most common cell in C.T.

Shape

Branched cells with long processes



Size

larger than fibrocyte

Nucleus

-Large ovoid
- Pale staining with fine chromatin
- Prominent nucleolus

Active cell

Cytoplasm

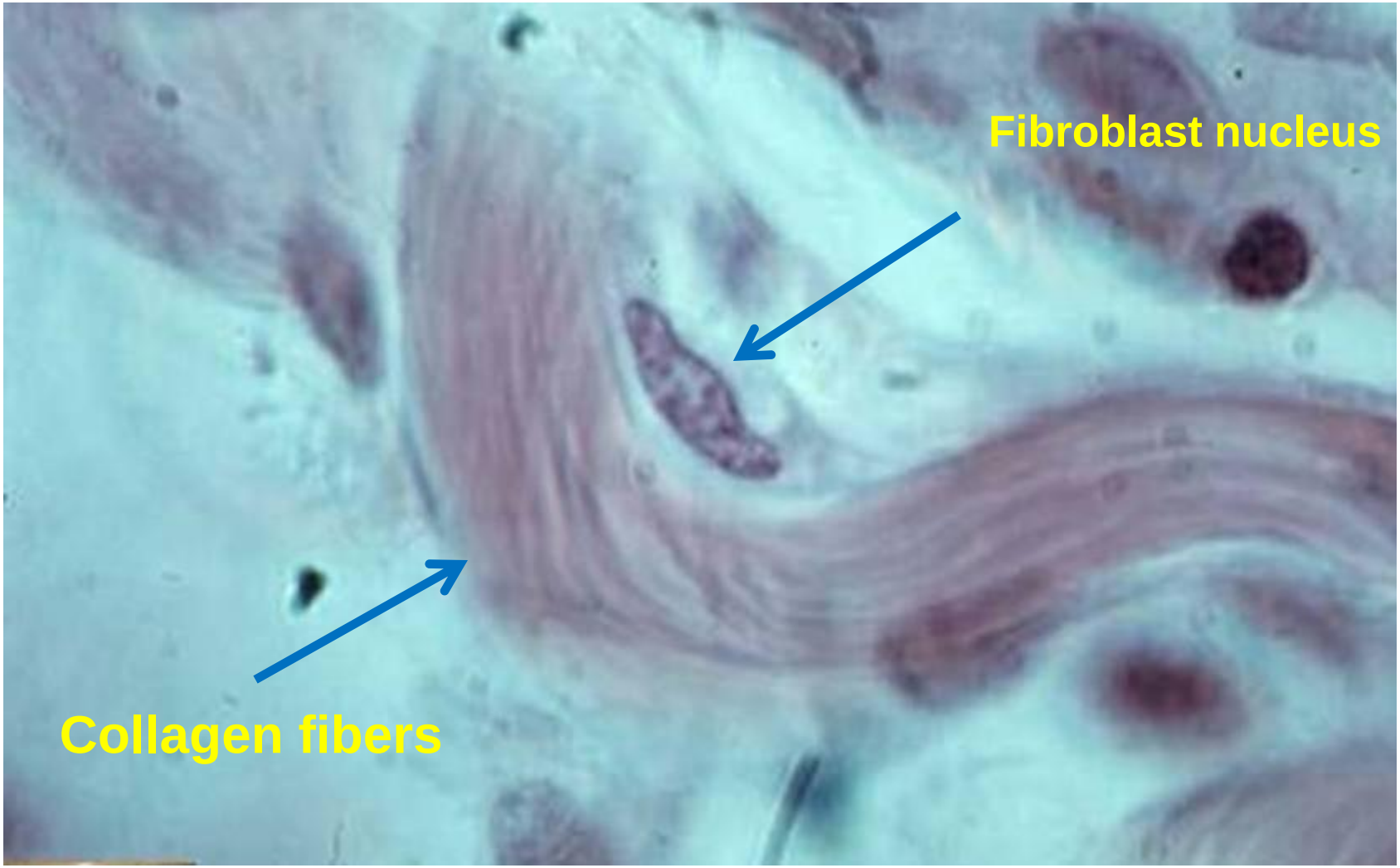
L.M: Basophilic

E/M:
- Rich in RER
-Well developed Golgi

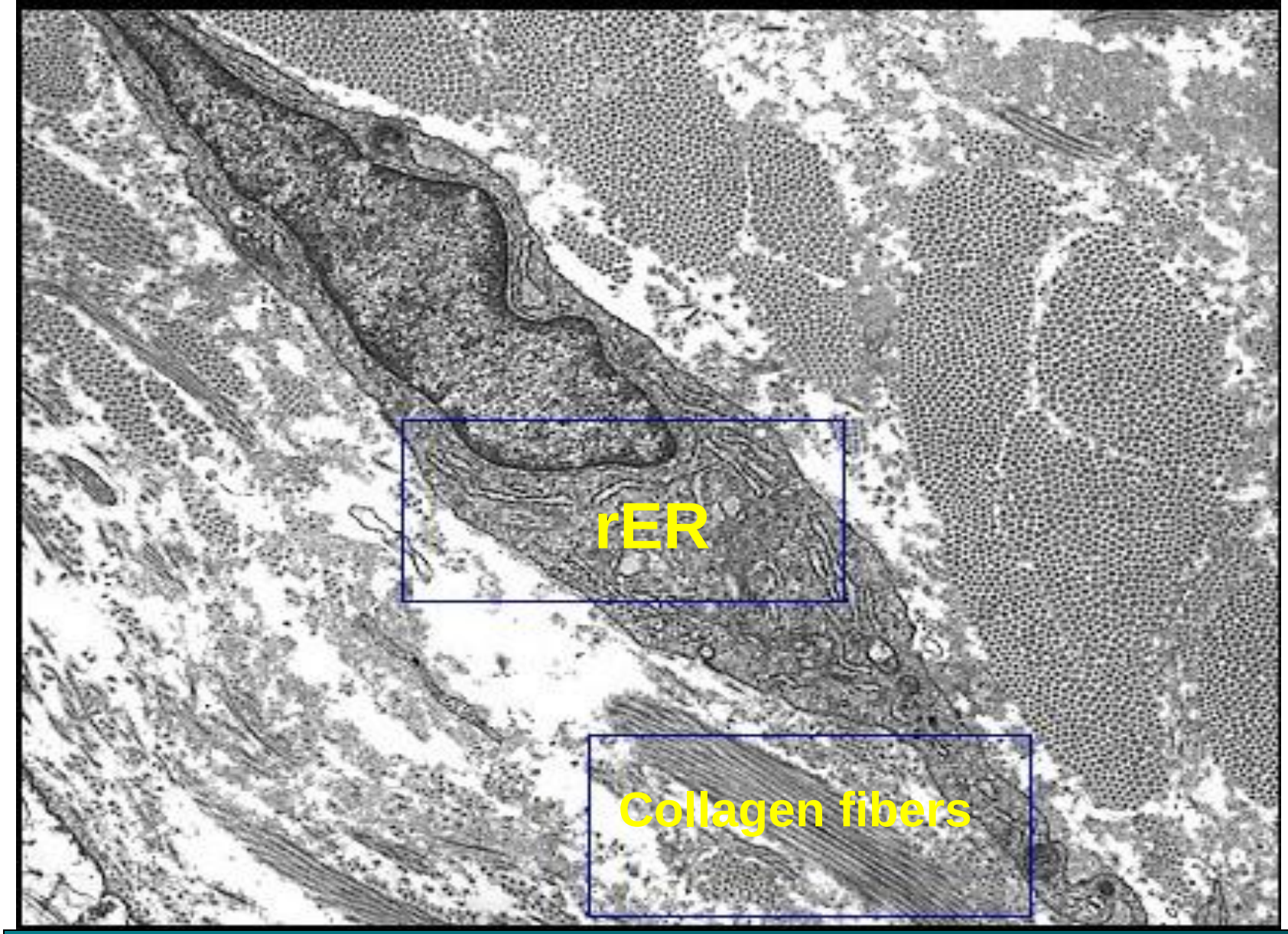
Function

Formation of:
- Components of connective tissue matrix
- Collagenic, elastic and reticular fibers.

Protein synthesizing cell



Fibroblast and collagen fibers



Fibroblast and collagen fibers


FIBROBLAST
Collagen fibrils
Enzymes
Elastin
Extracellular matrix
Growth factor
Hyaluronic acid

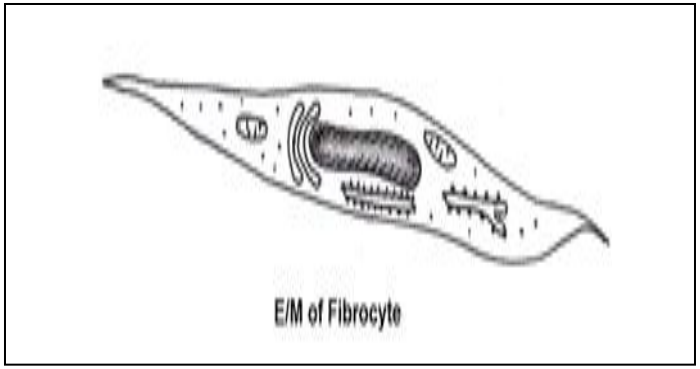
Fibrobocyte

Old or inactive fibroblast

Shape — Spindle shaped with fewer processes.

Size — Smaller than fibroblast

Nucleus — Smaller, dark elongated



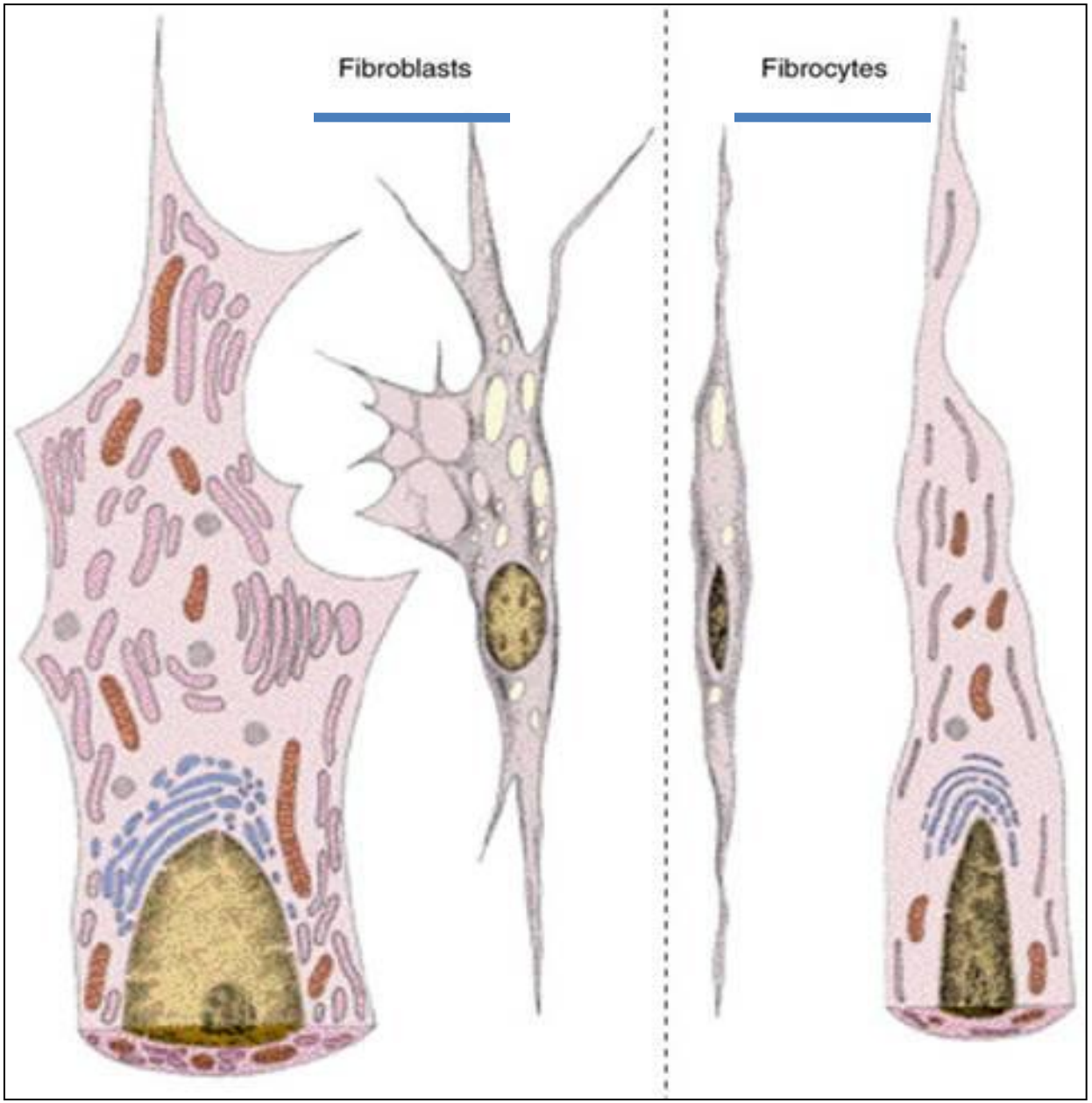
Cytoplasm — ***L.M:*** Less basophilic (nearly acidophilic) ***E/M:*** - Few RER

Function — It **maintains** components of connective tissue

Branched

Many rER

Ovoid pale nucleus

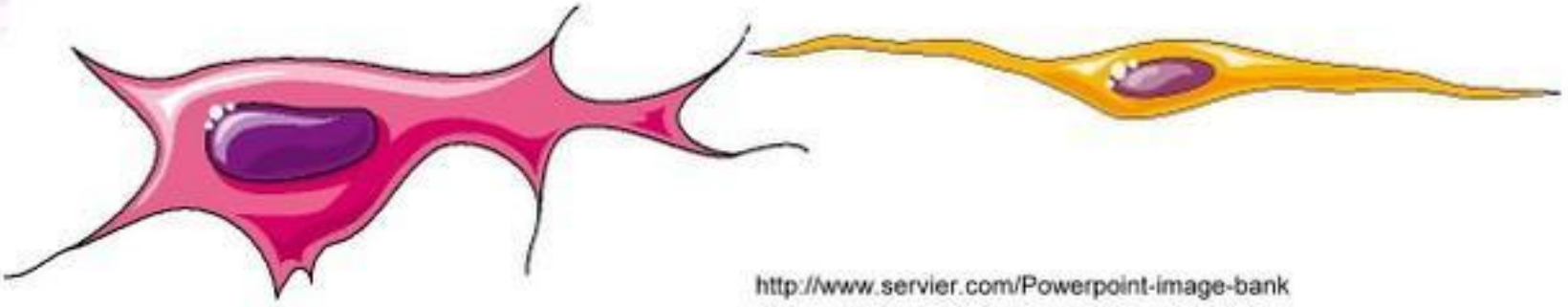


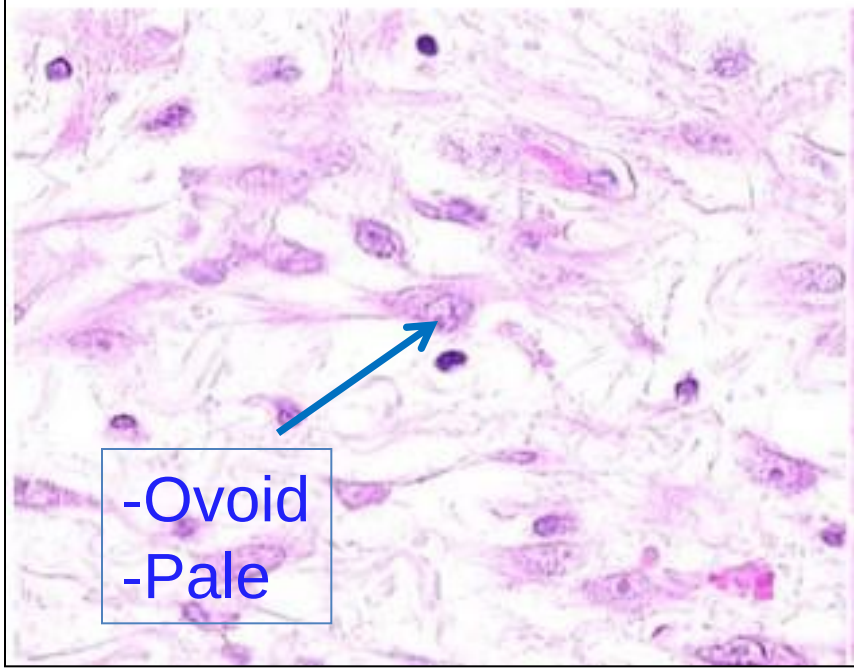
Spindle

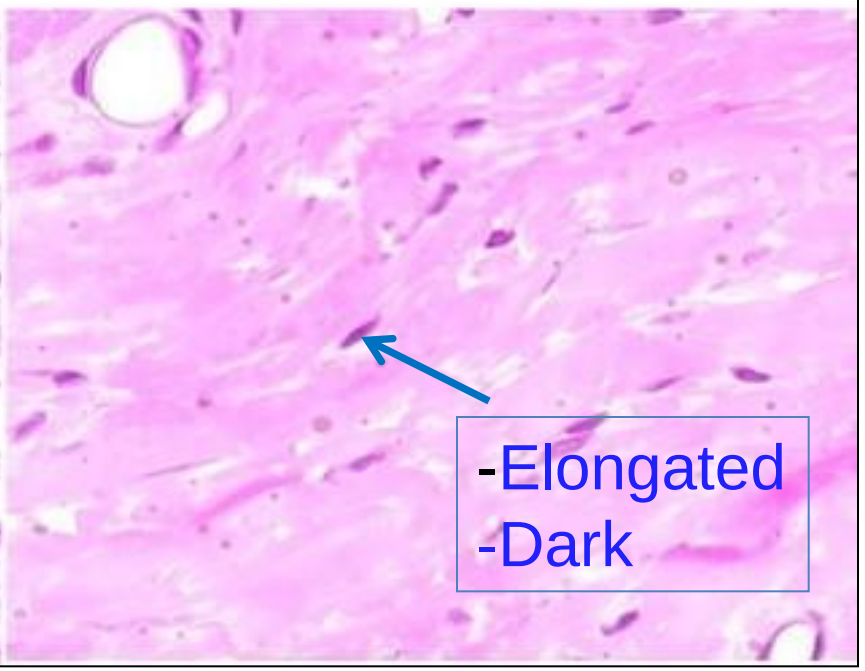
Few rER

Elongated dark nucleus

Fibroblast Fibrobocyte





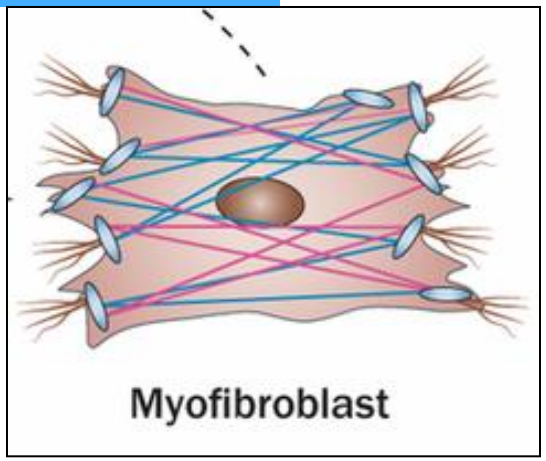


Myofibroblast

They are cells with features of fibroblast and smooth muscle cells.

Cytoplasm

E/M: It contains increased amount of actin and myosin microfilaments.



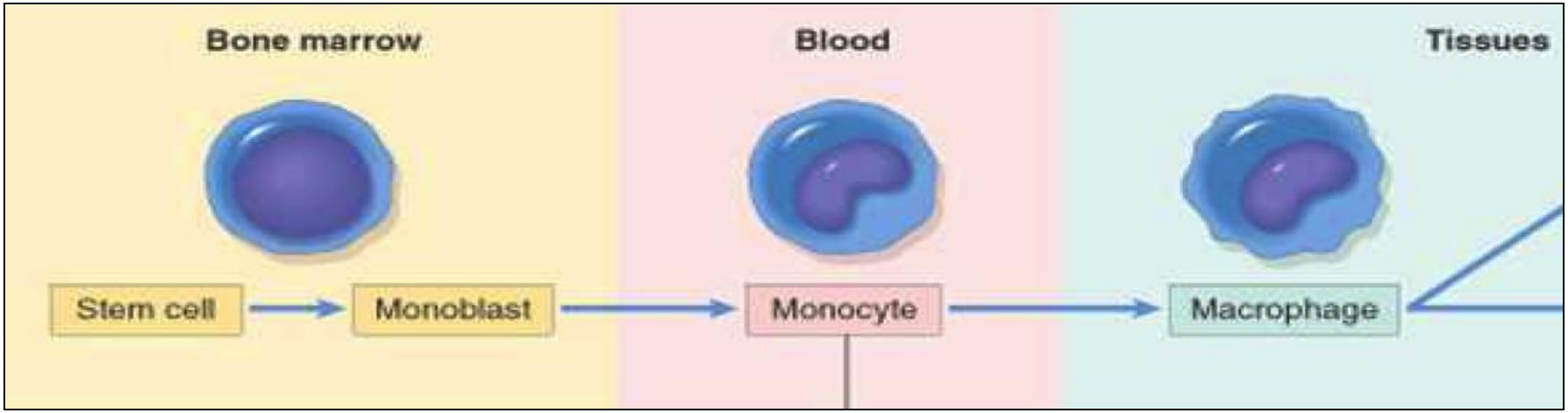
Function

t is responsible for wound closure (wound contraction).

Macrophage

Origin

- Derived from bone marrow precursor cell that divide, producing monocyte that circulate in the blood.
- Then, these cells cross the wall of capillaries to penetrate the connective tissue, where they mature and acquire morphological features of macrophages.



Macrophage

- ***Shape:***

Irregular surface with protrusions and indentations

- ***Nucleus :***

- Eccentric

- Oval or kidney shaped.

- ***Cytoplasm:***

L.M:

- Basophilic

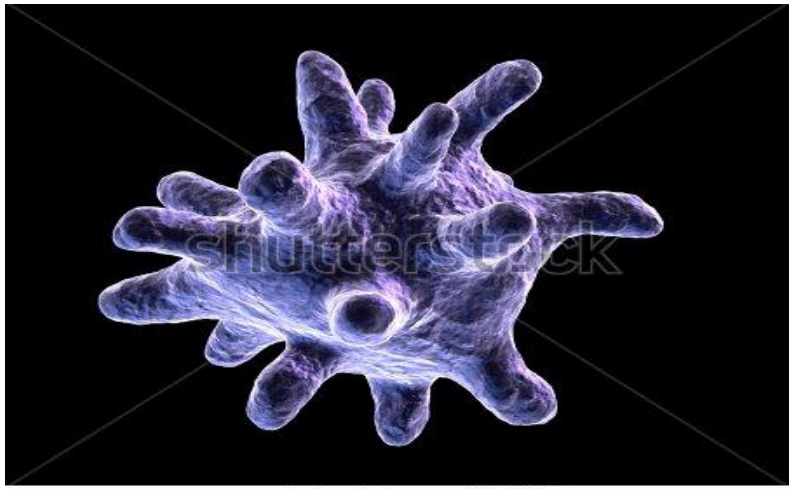
- Contains many small vacuoles.

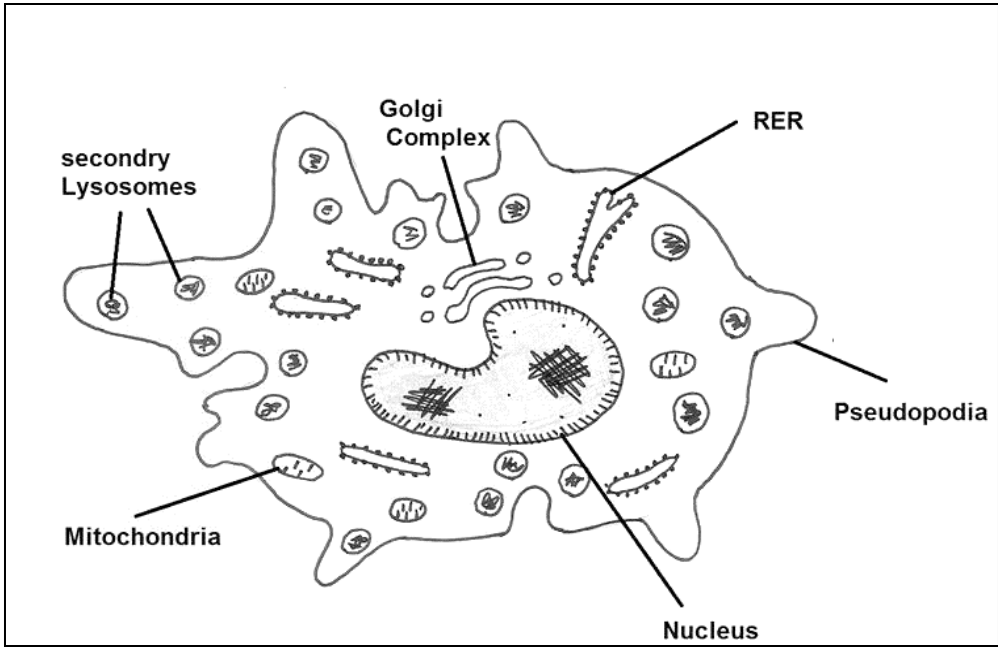
E.M :

- Many lysosomes.

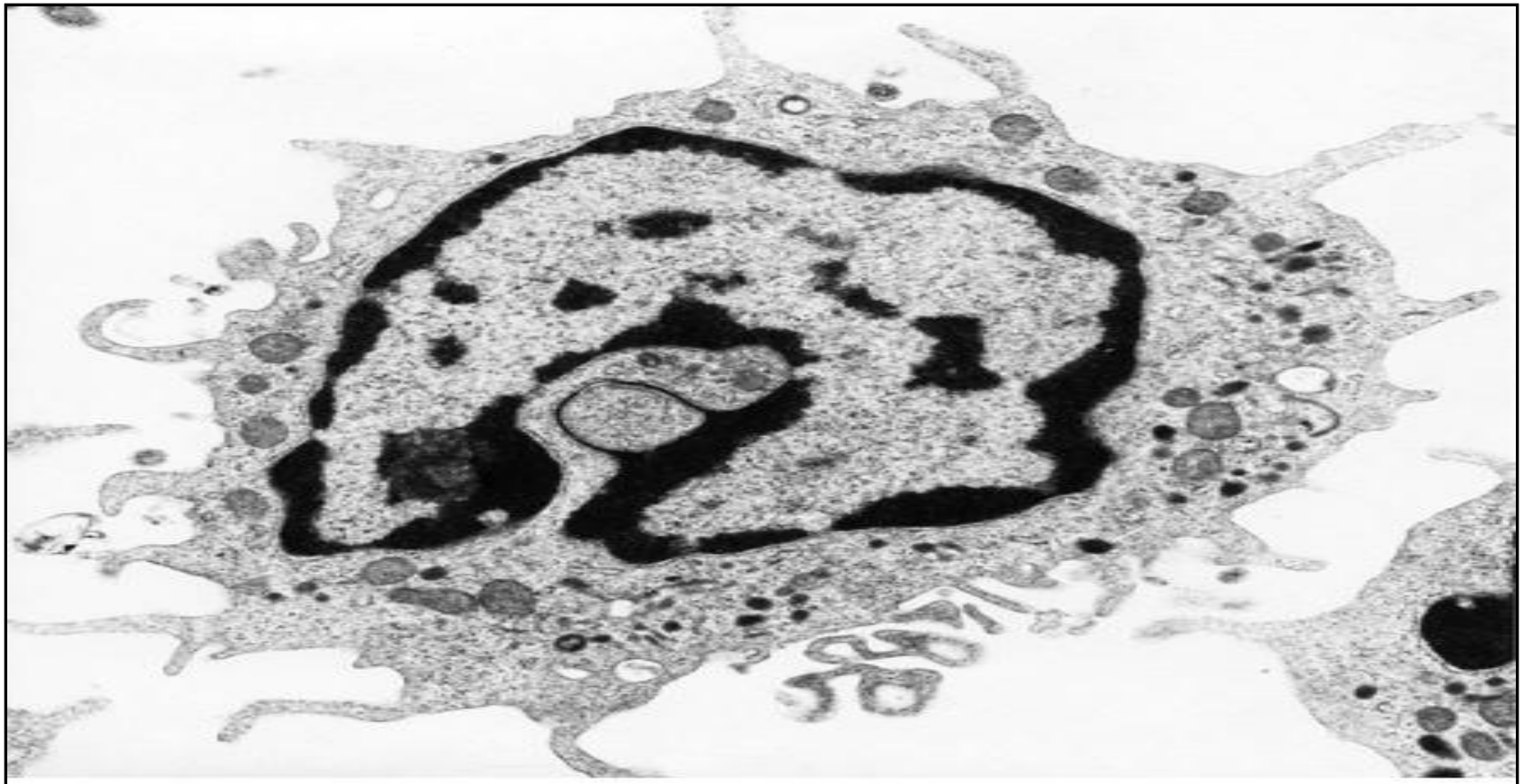
- Well-developed Golgi.

- Prominent RER.



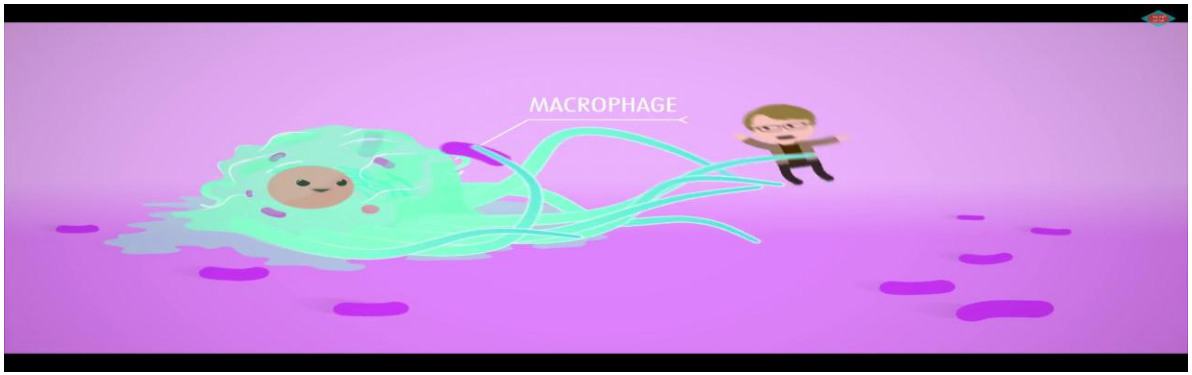


Macrophage (E.M)



:Function

1. Ingestion of foreign particles (phagocytosis).
2. Digestion of foreign particles by lysosomes.
3. Destruction of old red blood cells.
4. Antigen processing and presentation.
5. Secretion of substances that participate in defensive functions.



Mast cell

- ***Origin***:
  From stem cells in bone marrow.

- ***Sites:***

- Mast cells are widely distributed in the human body
- Abundant in dermis near to small blood vessels (perivascular mast cell),
mucosa of GIT and respiratory tract (mucosal mast cell).

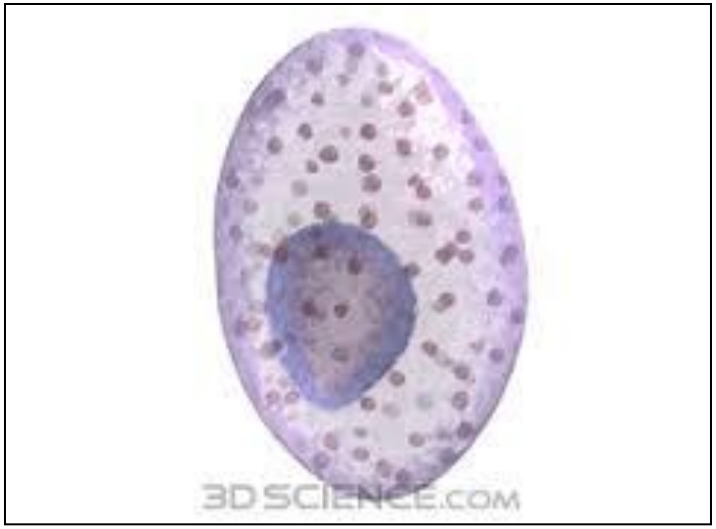
- ***Shape :***
  Oval to round
- ***Nucleus :***

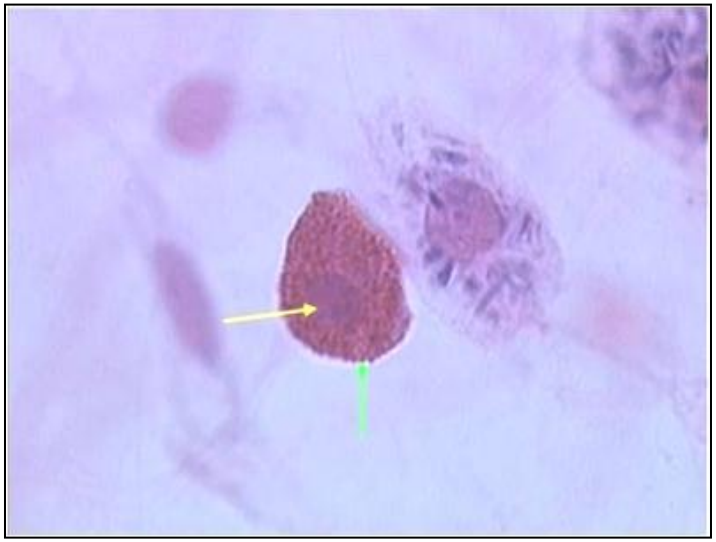
- Small, spherical
- centrally located.
- Obscured by cytoplasmic granules.

- ***Cytoplasm:***

:L.M
coarse granules

Staining:
The granules are metachromatic granules because they are stained red with toluidine blue..





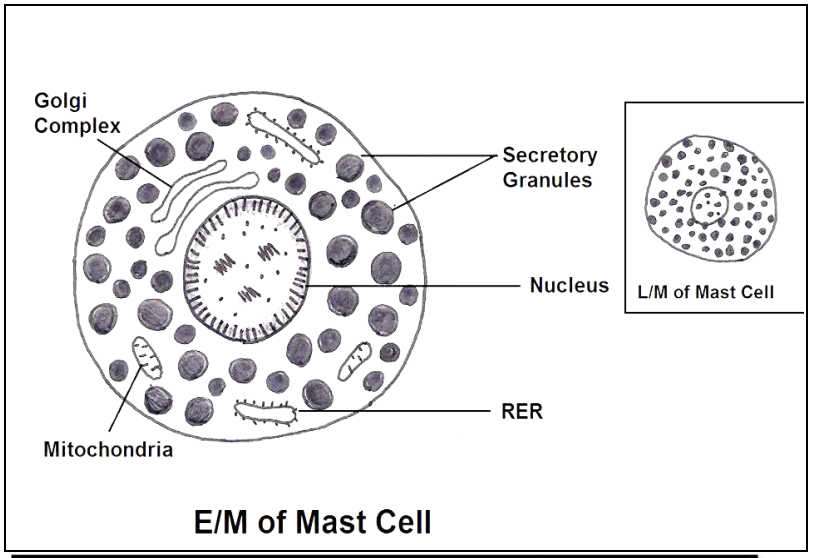
E/M:

-Well - developed Golgi.

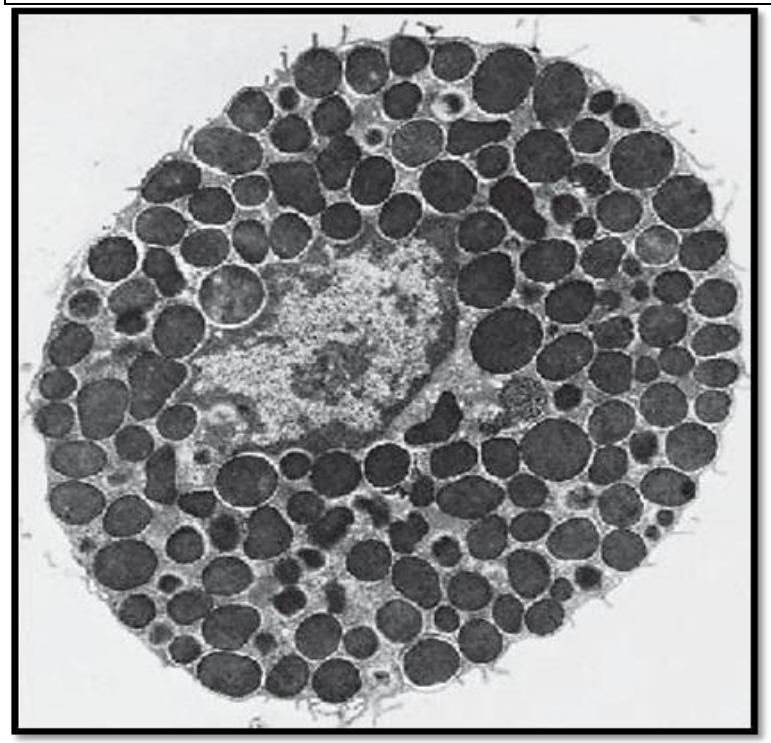
-Heterogeneous granules which are membrane limited.

- Few mitochondria.

-RER



E/M of Mast Cell



Function of Mast cell:

- **Initiate allergic and local inflammatory responses by release of their granules (degranulation)**
- **Synthesis and storage of chemical mediators of inflammation.**

-Histamine:

a- Dilates blood capillaries and increases their permeability.

b- Causes contraction of smooth muscle (mainly bronchioles).

-Leukotriens:

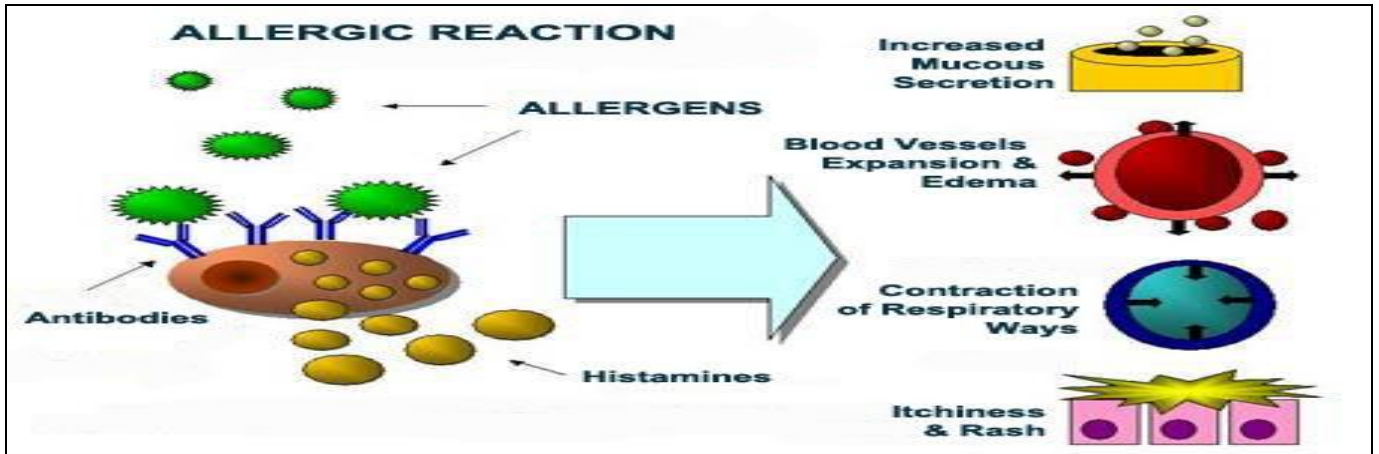
produce slow contraction of smooth muscle.

-ECF-A:

attracts blood eosinophils.

-Heparin:

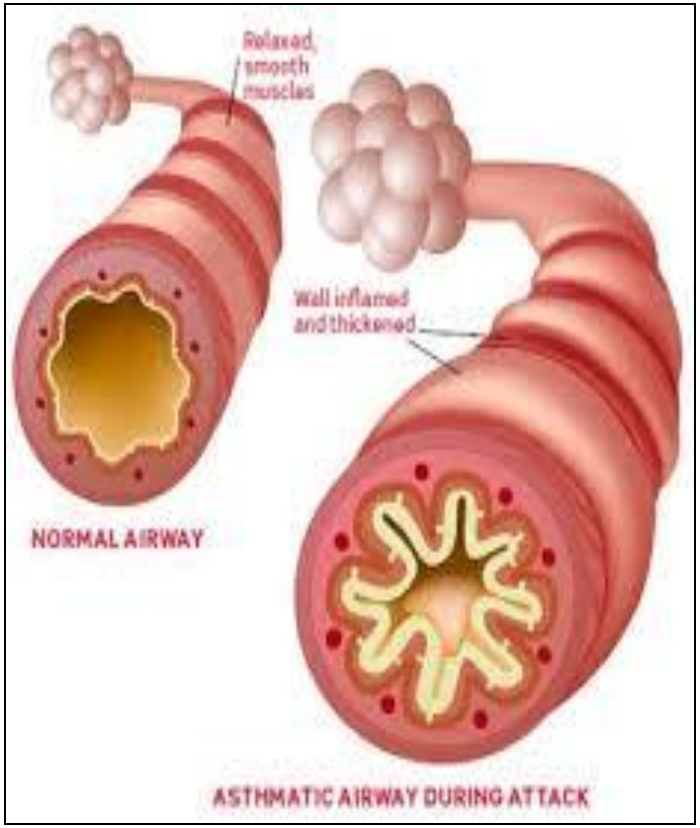
is blood anticoagulant, but blood clotting remains normal in human during anaphylactic shock.



Bronchial asthma

Allergic condition occurs due to secretion of large amount of histamine by mast cells triggered by subsequent exposure the same allergen.

-Leads to bronchospasm and *difficulty in breathing*.



Plasma cell

- ***Origin:***

  B-lymphocyte

- ***Shape :***

  large and oval

- ***Nucleus :***

- Spherical

- Eccentrically placed.

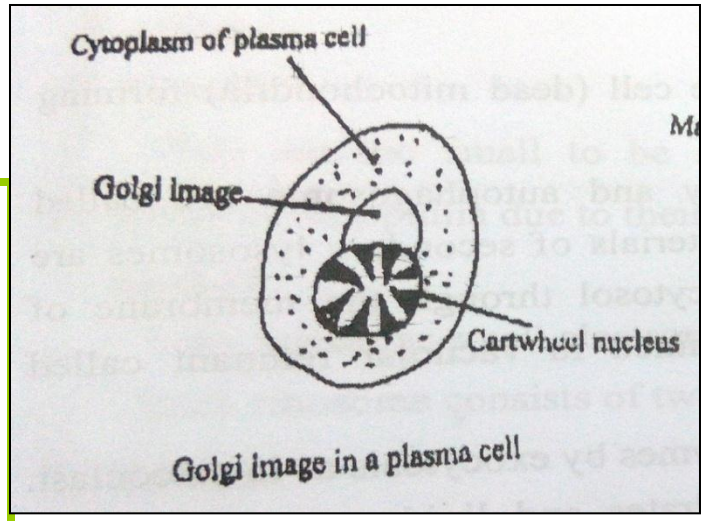
-Contains compact coarse chromatin alternating with light-areas of equal size that gives (clock-face appearance) or (cartwheel)

- ***Cytoplasm :***

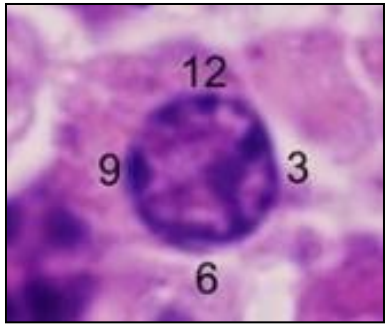
-L.M:

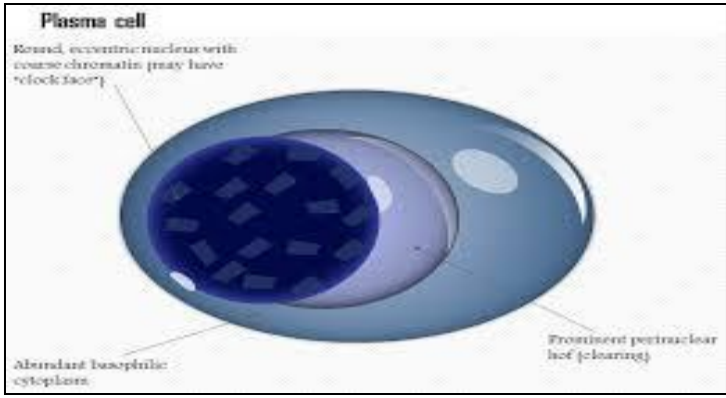
- Basophilic

- Contains pale area near the nucleus (- ve Golgi image

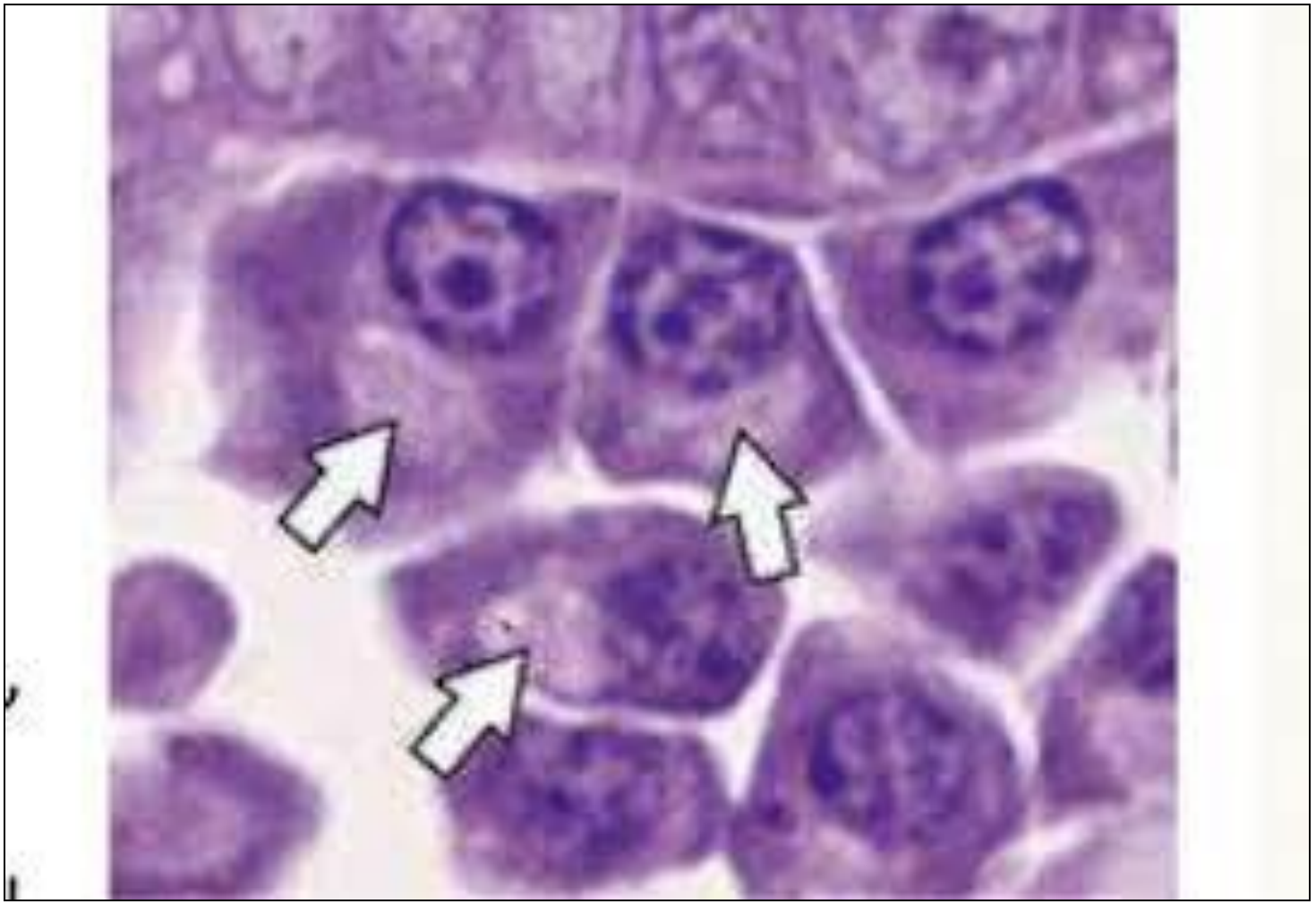


Golgi image in a plasma cell



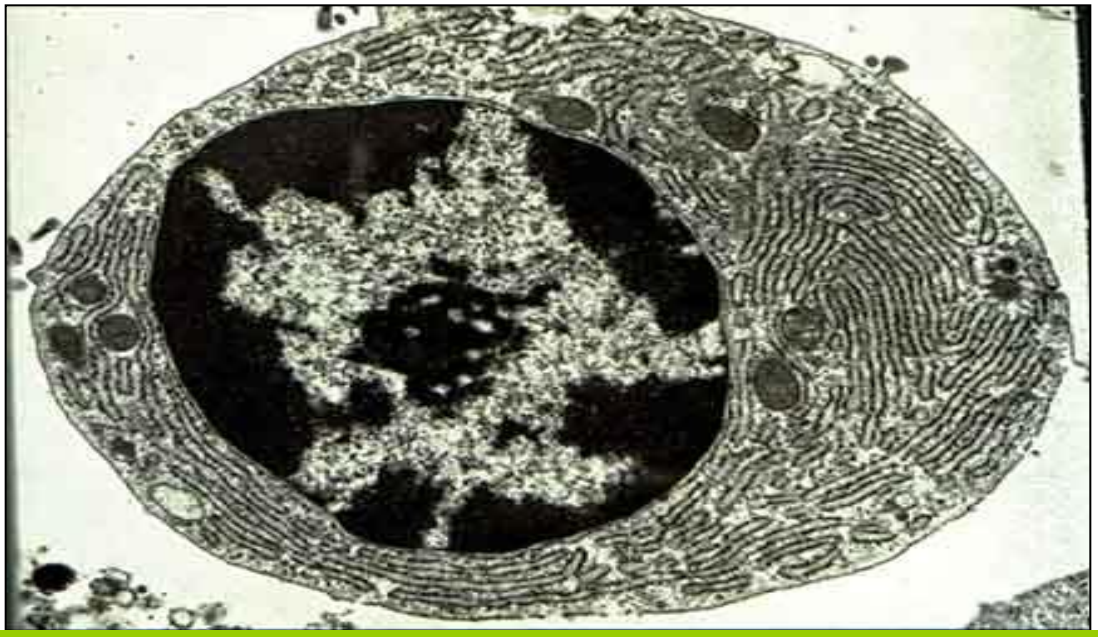


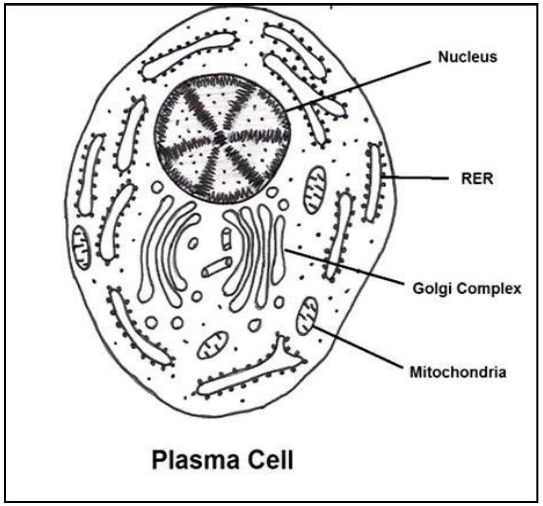
Negative Golgi image



E/M:

- Rich in RER
- Well developed Golgi
- centriole are present at the juxtanuclear region.





Plasma Cell

Antigen presenting:

Most antigens are partially digested in macrophages then transferred to B-lymphocytes that becomes Plasma cell

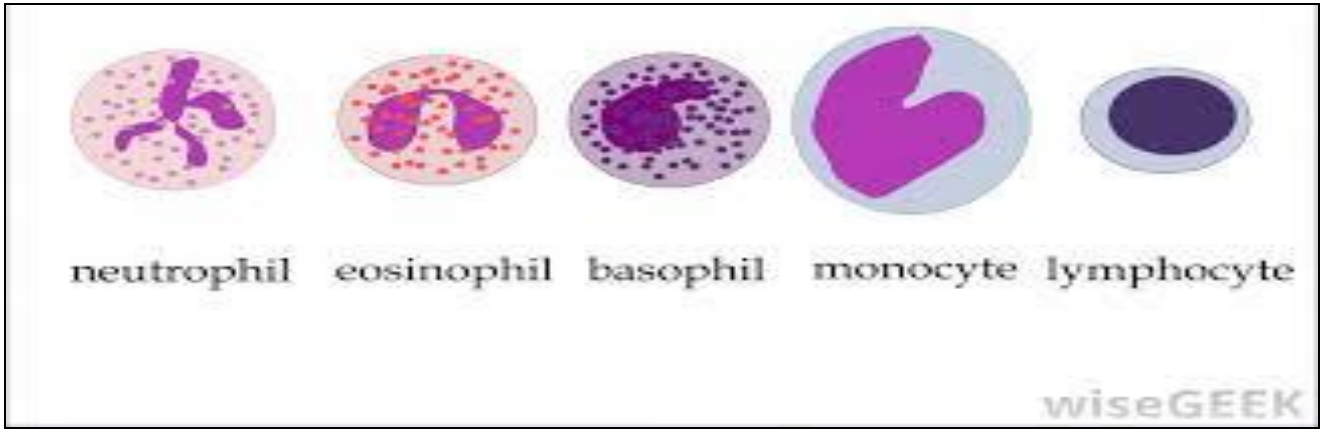
Function:

Production of antibodies

- Specific globulins produced in response to penetration by antigen.
- Each antibody is specific for one antigen that gives rise to its production

Blood leucocytes

-White blood cells migrate to connective tissue where they perform their functions e.g. lymphocytes and eosinoplils .

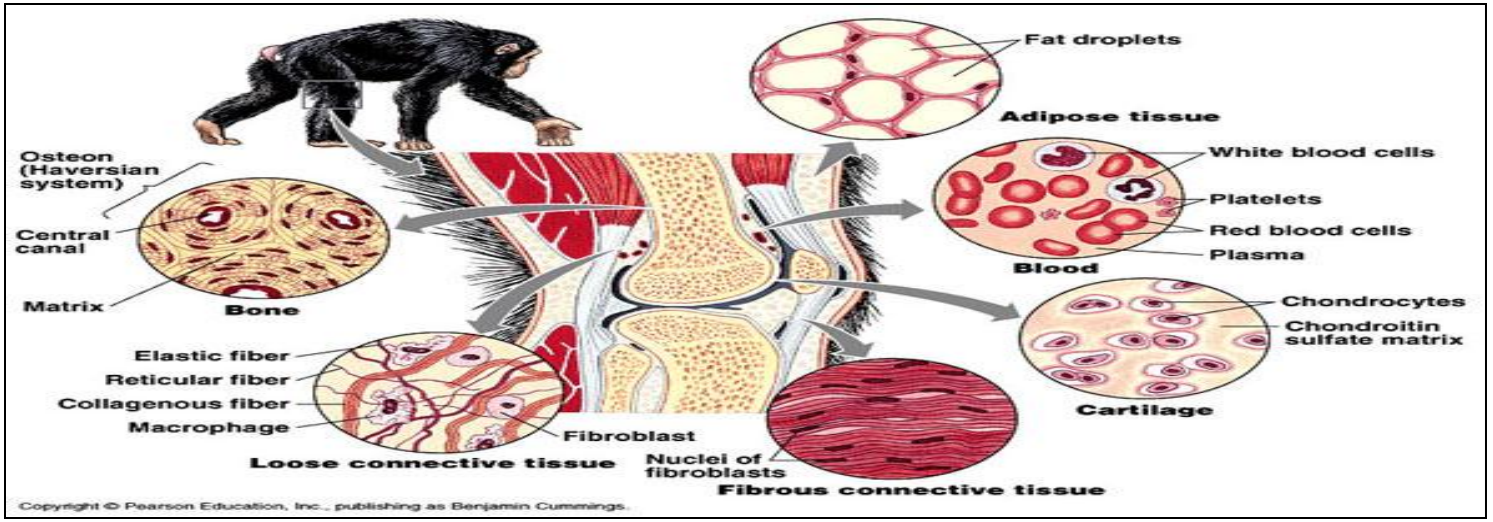


Classification of C.T.

C.T. proper
-Loose C.T.
-Dense C.T

Specialized C.T.
-Adipose
- Reticular
- Mucous
- Elastic

Supporting C.T.
- Bone
- Cartilage



Types of connective tissue

- Structure
  - Cells
  - Fibers
  - GS
- Character
- Sites

I- Connective tissue proper

1-Loose (areolar) connective tissue

- **Structure:**

- **Cells:**

Contains all the cells (*fibroblasts and macrophages are the most numerous cells*) –dispersed

- **Fibers:**

Contains all the fibers that are loosely arranged.

- **GS:**

Contains Large amount of ground substance.

- **Character:**

-it is the most widely distributed connective tissue in the body.

-It binds body parts together while allowing them to move freely over one another.

-Highly vascular (allow nutrients diffusion)

- Does not resist stress.

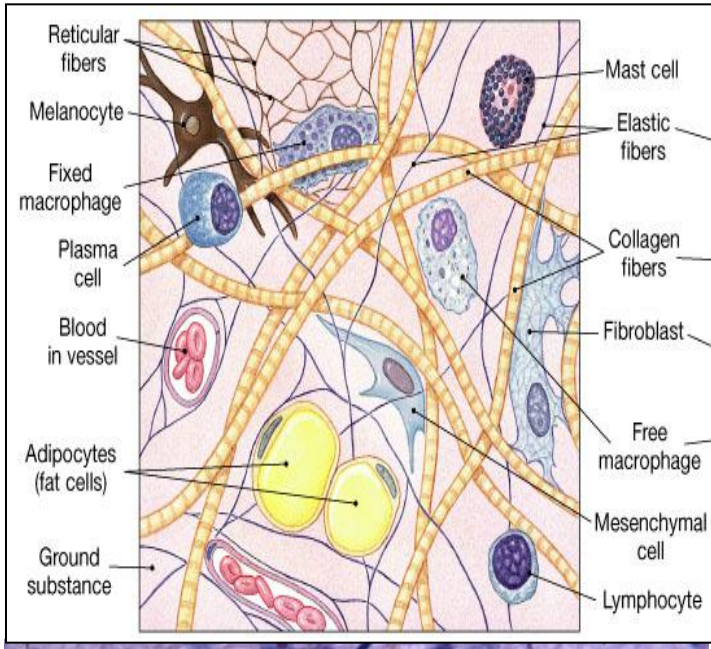
- **Sites**

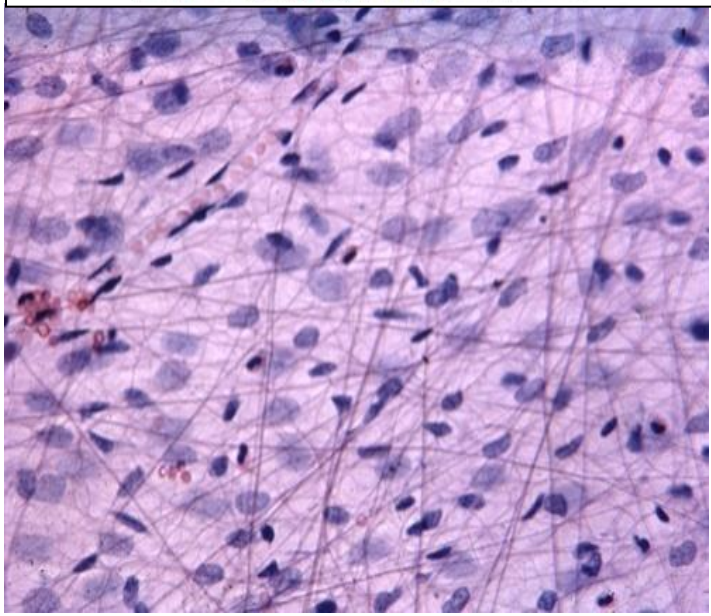
- It fills the spaces between fibers and muscle sheaths.

- It supports epithelial tissue of serous and mucous membranes.

- It is present in papillary layer of dermis.

- It ensheathes the blood and lymphatic vessels.





2- Dense connective tissue

- **Structure:**

Cells:

- few cells

Fibers:

It is mainly formed of **collagenous fibers**

GS:

Little ground substance

- **Character:**

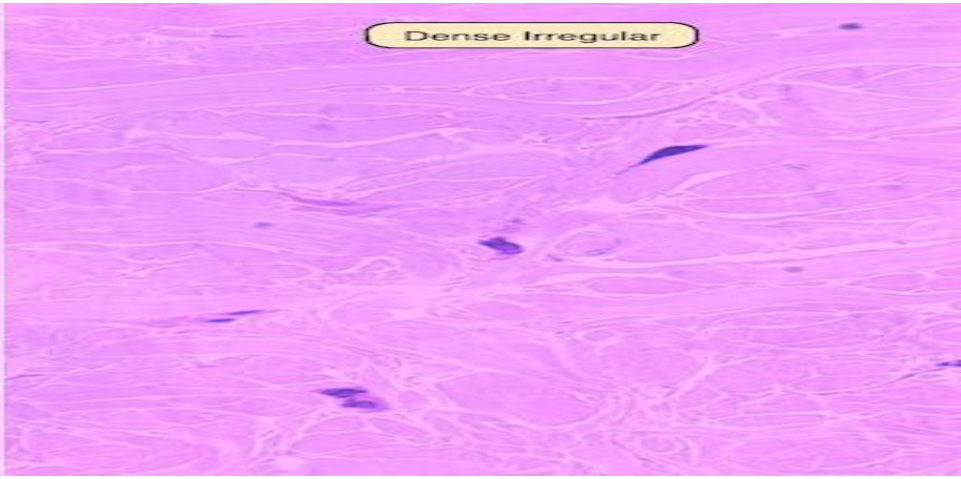
- It is less flexible

-Resist stress

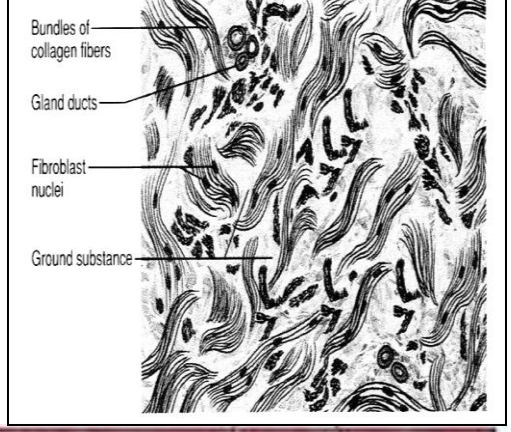
- **Types:**

a**) Dense regular connective tissue**

b) Dense irregular connective tissue



Types of dense connective tissue



1. Dense irregular connective tissue:

Structure:

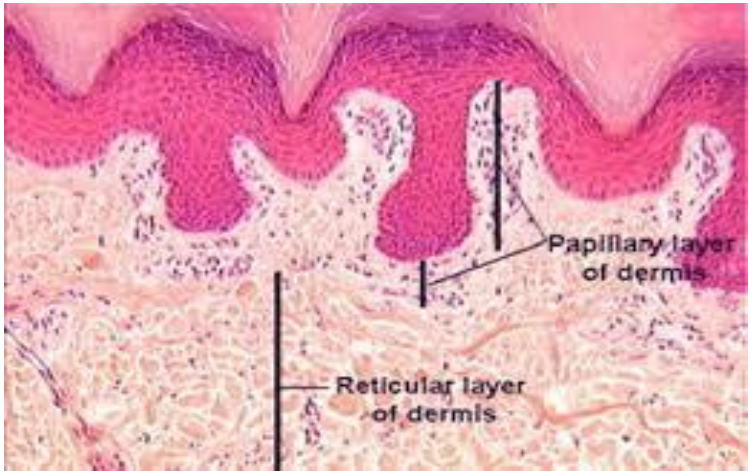
- The collagenous bundles are irregularly arranged without definite orientation and run in different directions.
- Few C.T cells mainly fibroblasts.
- little amount of ground substance.

Function:

It withstands stress from all directions.

Sites:

- Reticular layer of Dermis of the skin
- Capsules of spleen, lymph nodes and liver.
- perichondrium and periosteum.



2)Dense regular connective tissue:

Sturcture:

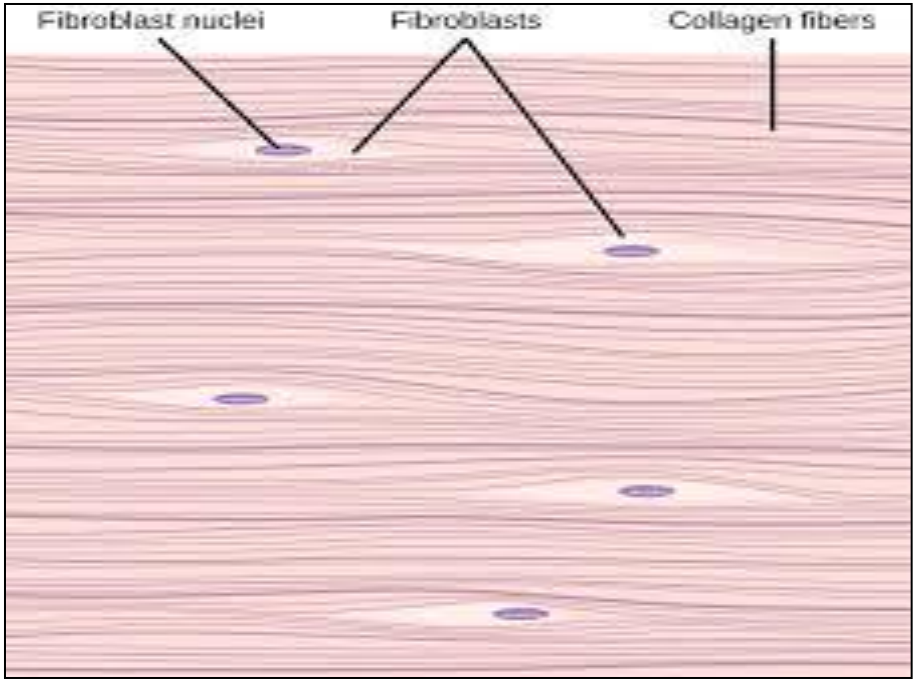
- The collagen bundles are arranged in regular pattern .
- Fibroblast are located between the collagen bundles with their long axis parallel to the bundles
- Little amount of ground substance.

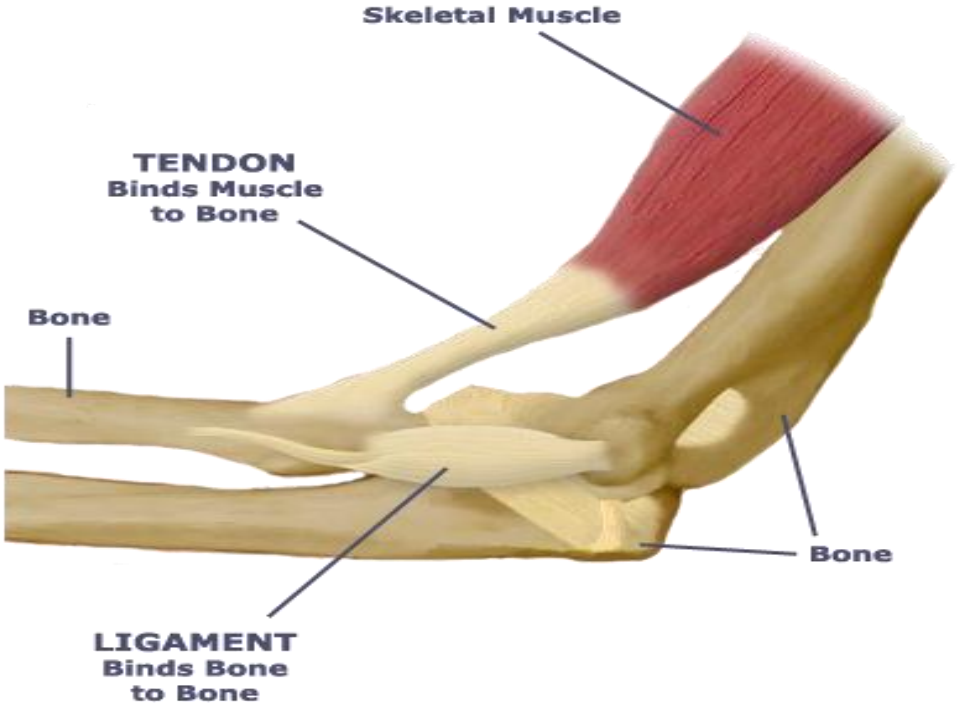
Function:

- It withstand prolonged stress in one direction

Site:

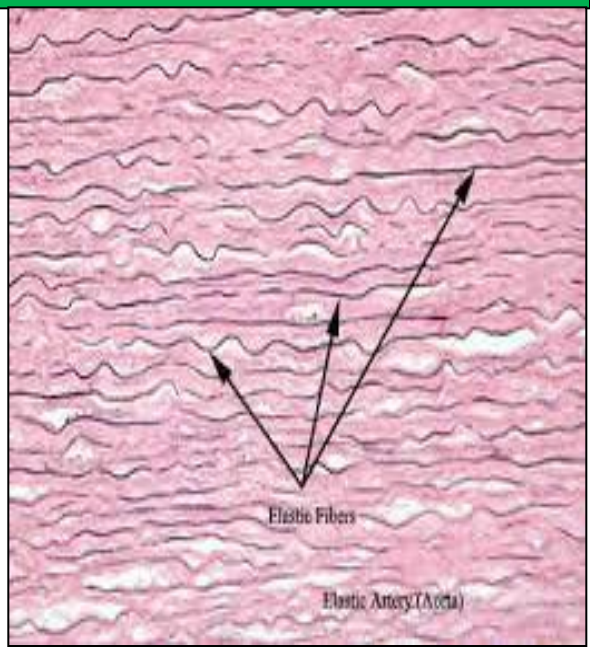
- **Tendons**
- **Ligaments**





II- Connective tissue with special proporties

Yellow elastic tissue



- **Structure:**
- **Cells:**

Flattened fibroblasts

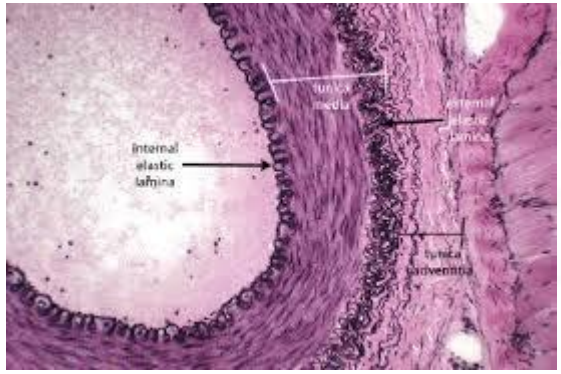
- **Fibers:**

Large number of bundles of thick parallel elastic fibers

and thin collagenous fibers

- **GS:**
- **Character :**
- The abundance of elastic fibers gives the tissue great elasticity and the yellow colour
- **Site:**

- Ligaments of vertebral column
- True vocal cords.
- Elastic lamina of arteries.



Reticular connective tissue

- **Structure:**

1- **Reticular cells**

- They are fibroblasts with cytoplasmic processes.
- Specialized for the secretion of reticular fibers.
- Their nuclei are large with fine chromatin and one or more visible nucleoli.

2- **Reticular fibers**

- Enveloped by the cytoplasm of the reticular cells but the fibers are extracellular being separated from the cytoplasm by the cell membrane.
- Reticular cells and fibers create **spongy like structure** within which cells and fluids are mobile. It slows flow of material along the **sinus like spaces**.

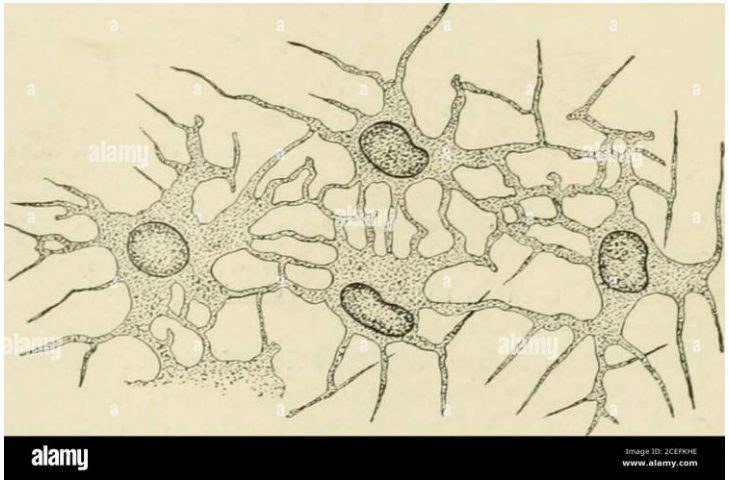
3- **Ground substance**.

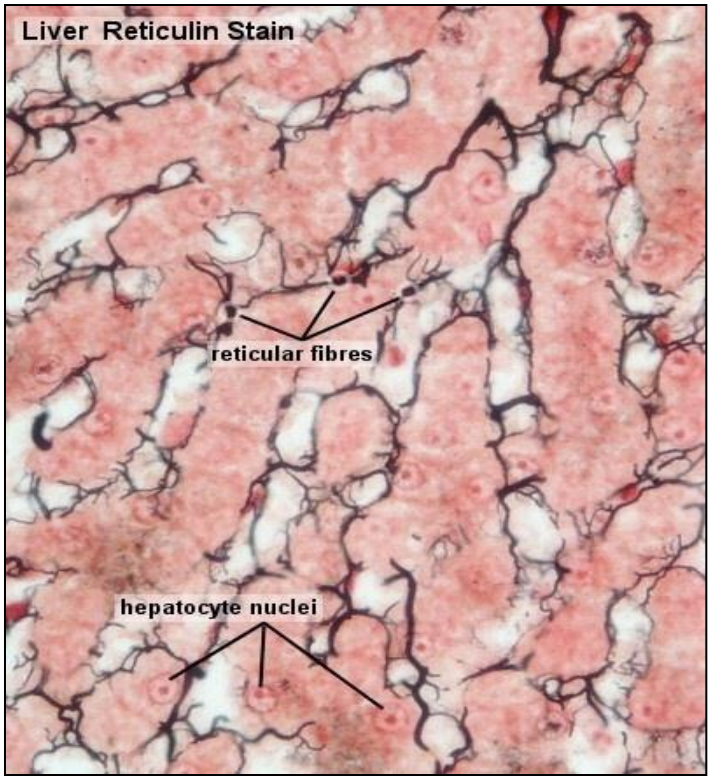
4- **Mononuclear macrophages**

- **Site:**

It forms the framework of all parenchymatous tissues:

- Myeloid tissue (bone marrow)
- Hematopoietic organs.
- Lymphoid organs (lymph node, lymph nodules, spleen)
- Liver.





Mucoid connective tissue

- **Structure:**

- **Cells:**

Mainly fibroblasts.

- **Fibers:**

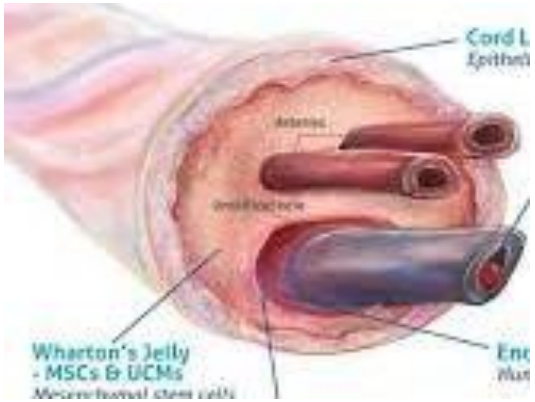
Few collagen, elastic and reticular fibers

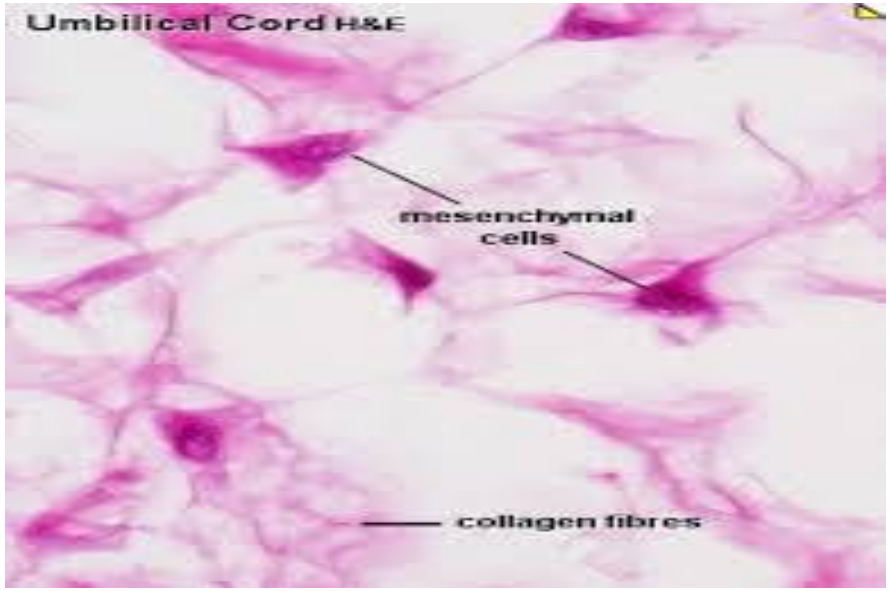
- **GS:**

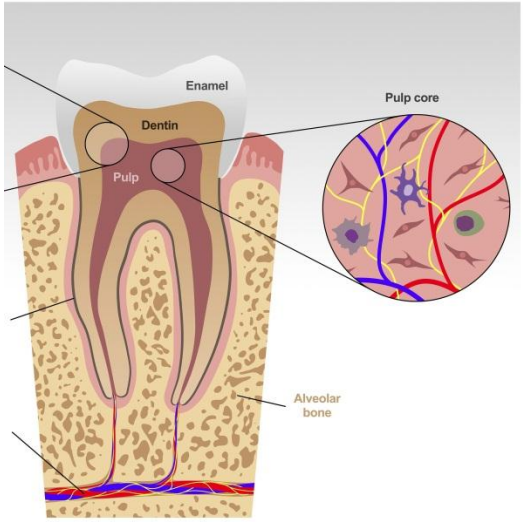
It has *abundant jelly like matrix* composed mainly of hyaluronic acid

- **Site:**

- Umbilical cord ***(Wharton's jelly).***
- Pulp of young tooth.
- Vitreous humor of the eye.







Adipose connective tissue

- It is a special type of connective tissue in which *adipocytes predominate*.
- **Functions**

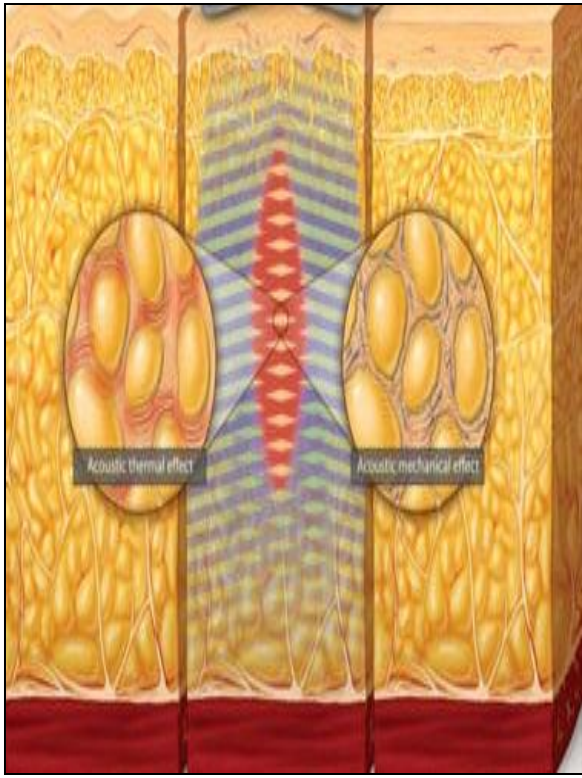
1- Store energy in the form of triglycerides.

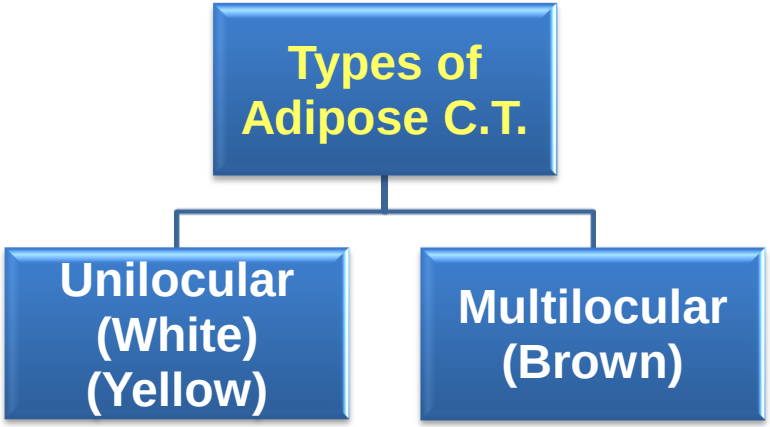
2- Shape the surface of the body.

3- Shock absorbers chiefly in soles and palms.

4- Thermal insulators.

5- Fills the spaces between other tissues and keep some organs in position





1- Unilocular (White) adipose tissue

- It is the common type.
- it is the almost only type in adult.

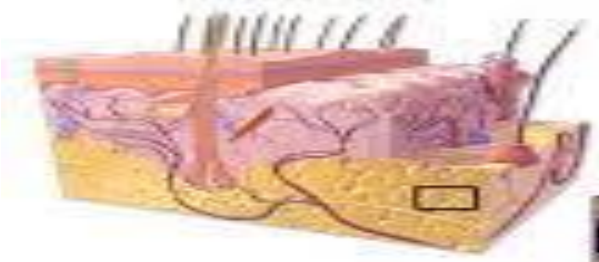
- ***Function:***

Unilocular adipose tissue is the main energy depot for the organism.

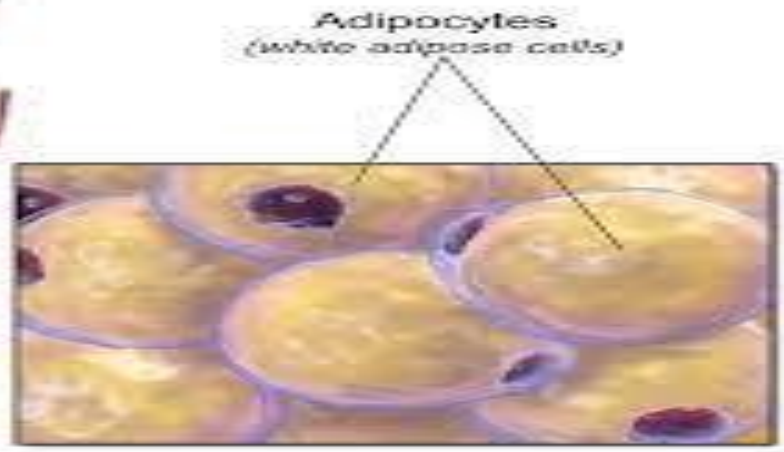
- ***Sites:***

It is present throughout the human body except eyelids, penis, scrotum and auricle of external ear.

- ***Color:*** **depends on diet, varies from white to yellow due to the dissolved carotenoid in fat droplets.**



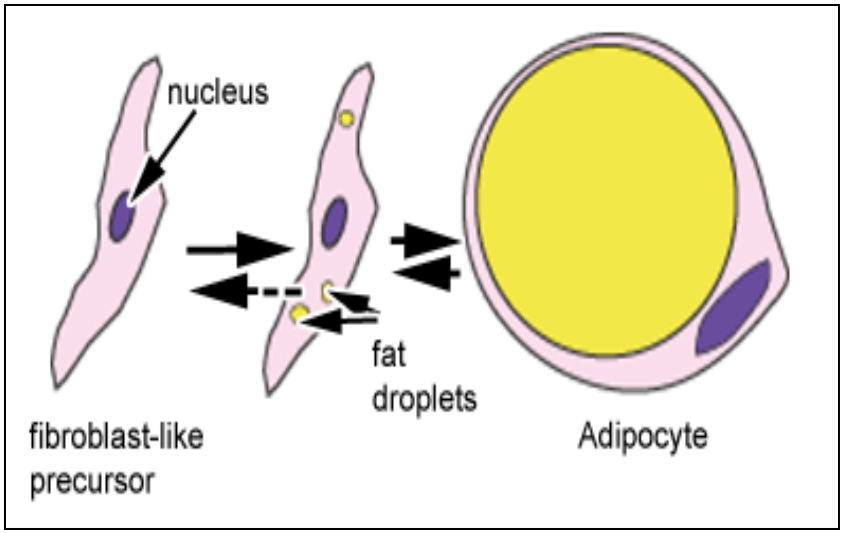
Adipose Tissue



Histological structure

Adipocytes

- Develop from lipoblasts that originate from U.M.C.
- Found isolated or in small groups within the C.T.
- If found in ***large aggregates***, they make up adipose C.T.
- It represents 15-20% of body weight in men and 20-25% of body weight in women.



Adipose (fat) cell

L.M:

- ***Shape :***

- Spherical when single
- Polyhedral in adipose C.T.(closely packed).

- ***Nucleus :***

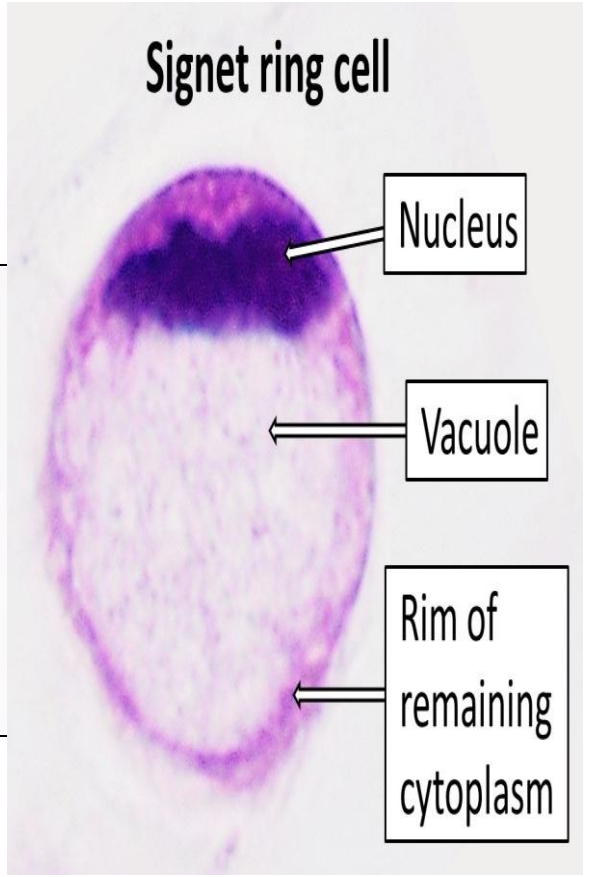
peripheral and flattened (signet ring appearance).

- ***Cytoplasm:***

- Hx & E staining.

Appears as thin ring surrounding a dissolved fat vacuole

- Sudan III: orange



E/M:

- Each cell is surrounded by a basal lamina.

- The fat appears as :

minute droplets in addition to the single large one, the droplets are not surrounded by a membrane.

- *The thickest potion of the cytoplasm surrounding the nucleus contains:*

1-Golgi complex

2- Filamentous and ovoid mitochondria

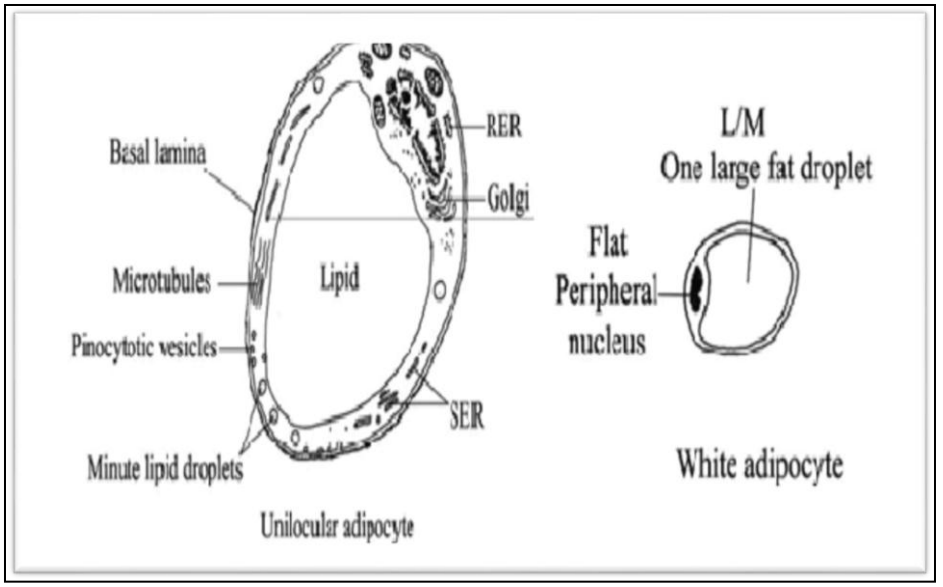
3- Few RER and free polyribosome.

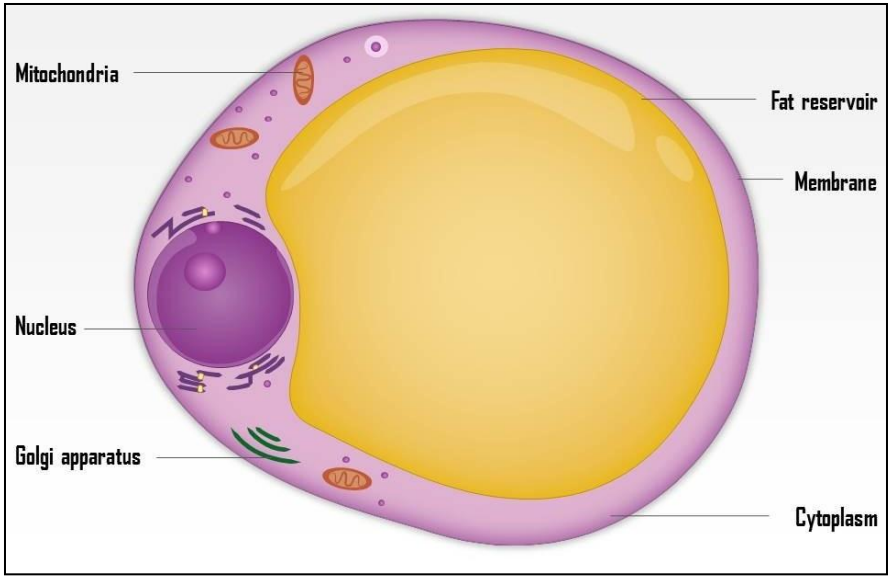
- *The rim of cytoplasm surrounding the lipid droplet contains:*

1-Vesicles of SER

2- Occasional microtubules

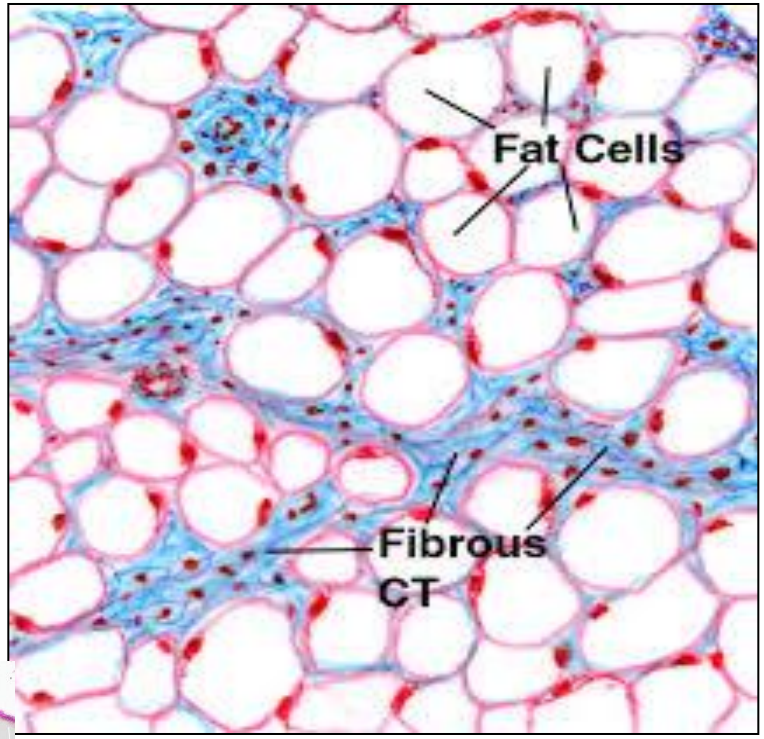
3- Numerous pinocytic vesicles

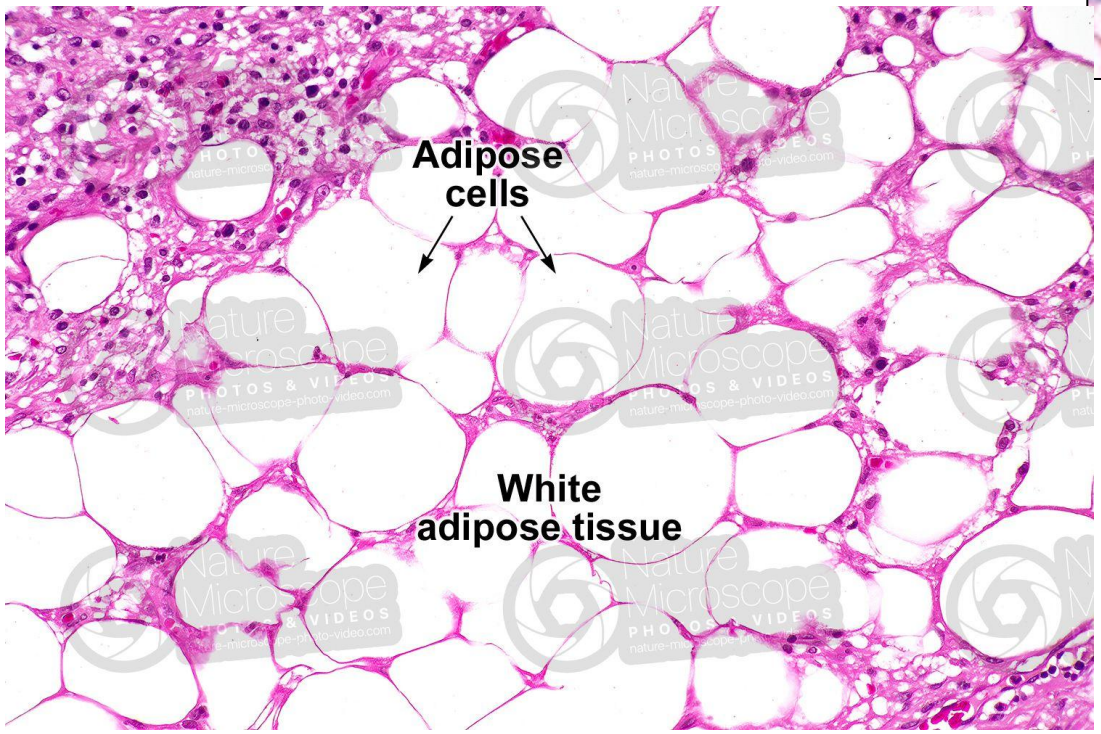




Characteristics of the unilocular adipose tissue:

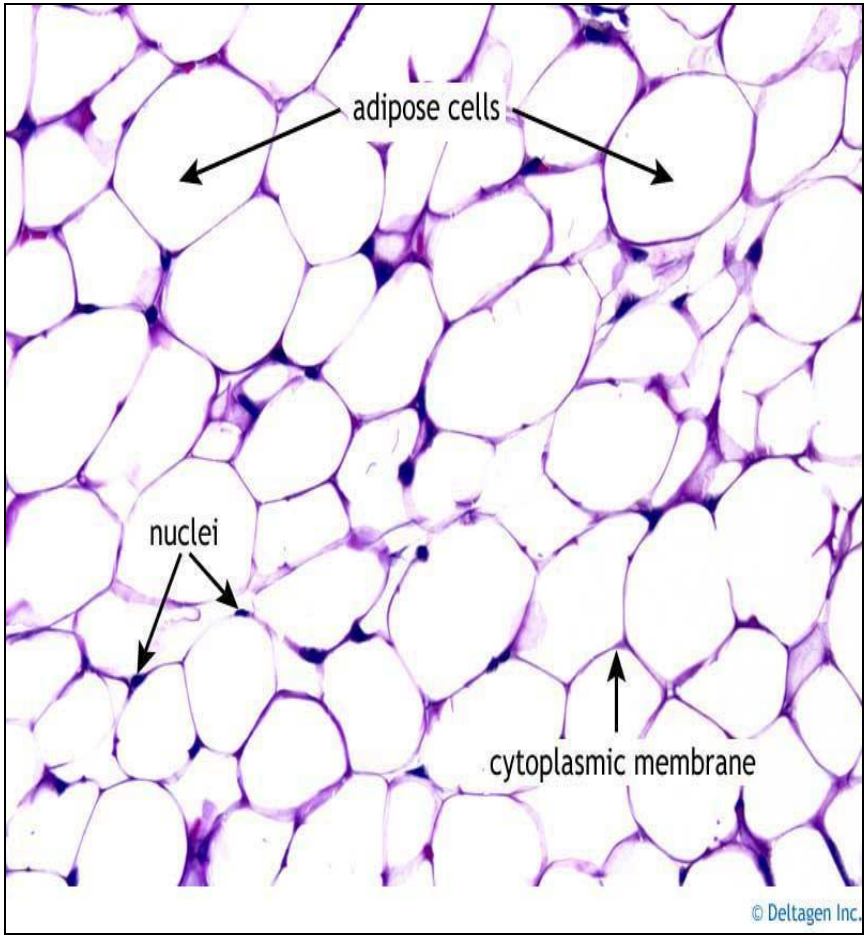
- It is subdivided into incomplete lobules by connective tissue partitions. C.T. is rich in blood vessels and sympathetic nerves.
- Reticular fibers form a fine network that supports individual fat cells.



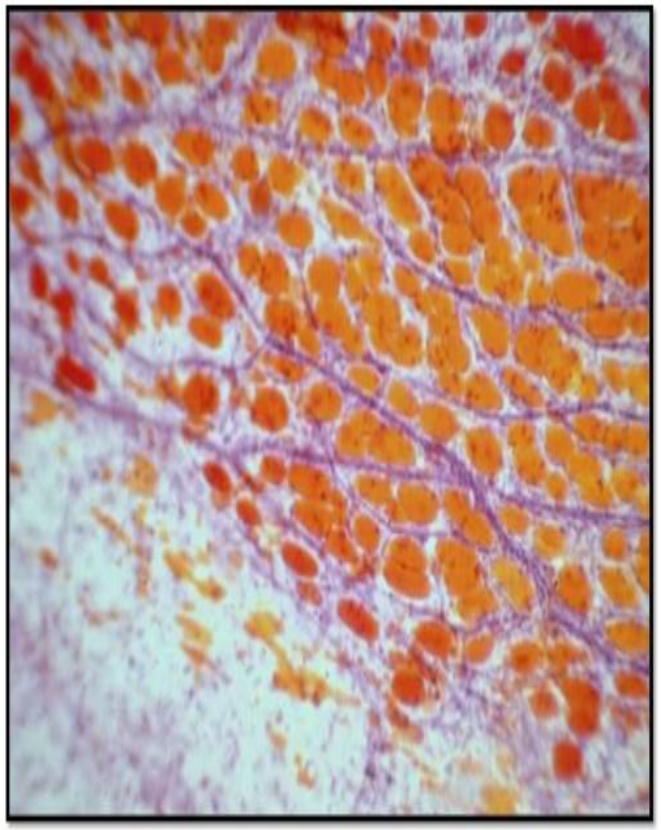


Unilocular adipose C.T.

H&E



L.M. Adipocytes stained with Sudan III



Histology Department / Faculty of Medicine / Cairo University

2 - Multilocular adipose tissue (brown fat)

- It is greatly reduced in adult.
- ***Sites:*** - In hibernating animals.
  - In human embryo and newborn, it is found in several areas and remains restricted to these locations after birth (e.g. neck, axilla, and mediastinum).

- ***Functions:***

-In animals It transforms the stored chemical energy to heat when stimulated.

-In human it is important in the first months of postnatal life as it produces heat that protects newborn against cold.

Histological structure:

L/M:

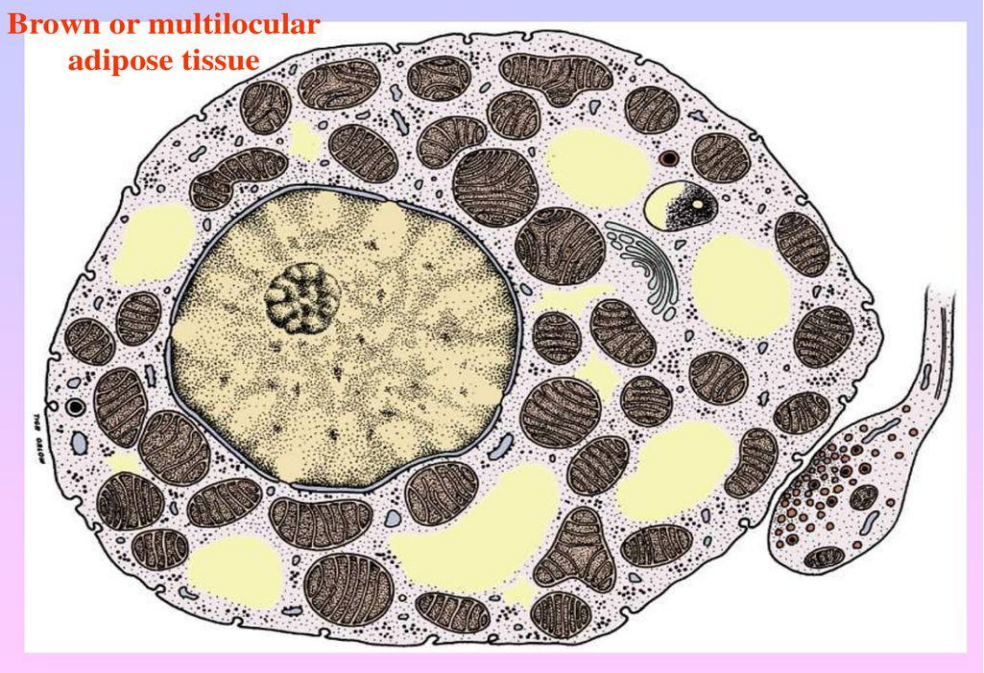
- **Cell shape:**
- Polygonal.
- Diameter: smaller than those of unilocular adipose tissue.
- **Cytoplasm:** Several fat vacuoles in Hx & E staining.
- **Nucleus:** spherical and eccentric.

E/M:

- Numerous lipid droplets of different sizes.
- The mitochondria are numerous with abundant long cristae.

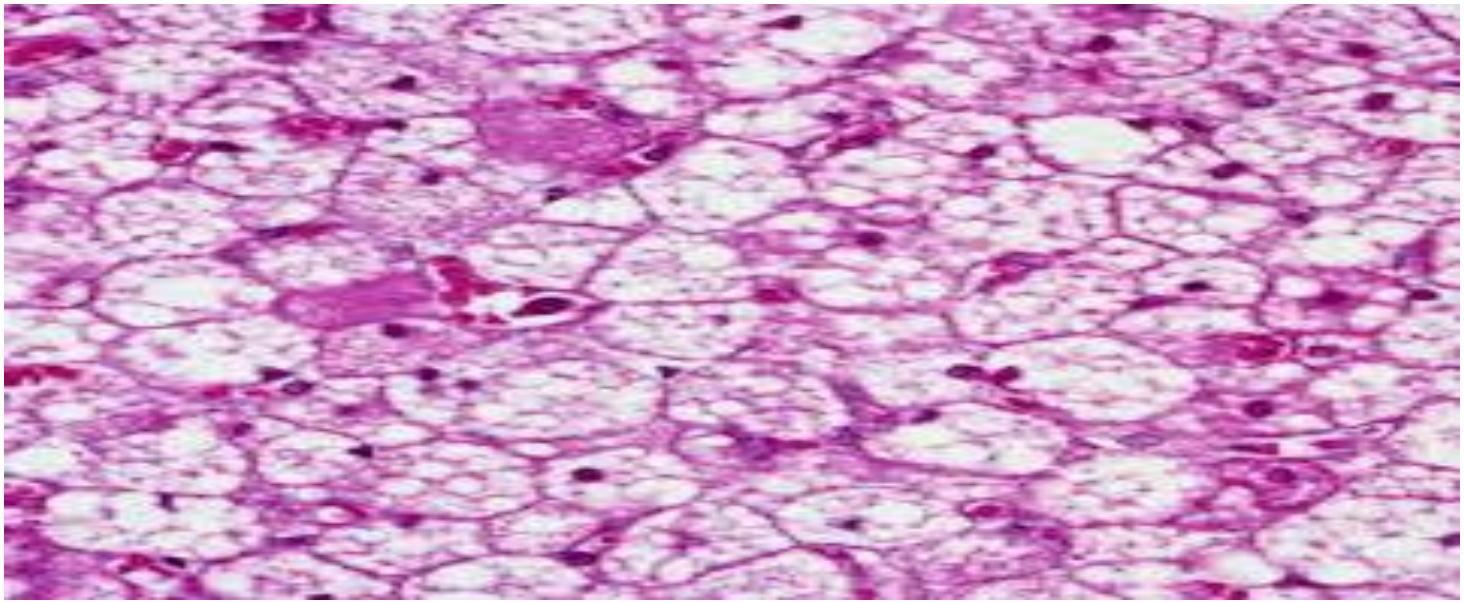
Its color is brown due to:

- Large number of blood capillaries.
- Numerous mitochondria that contain colored cytochrome.



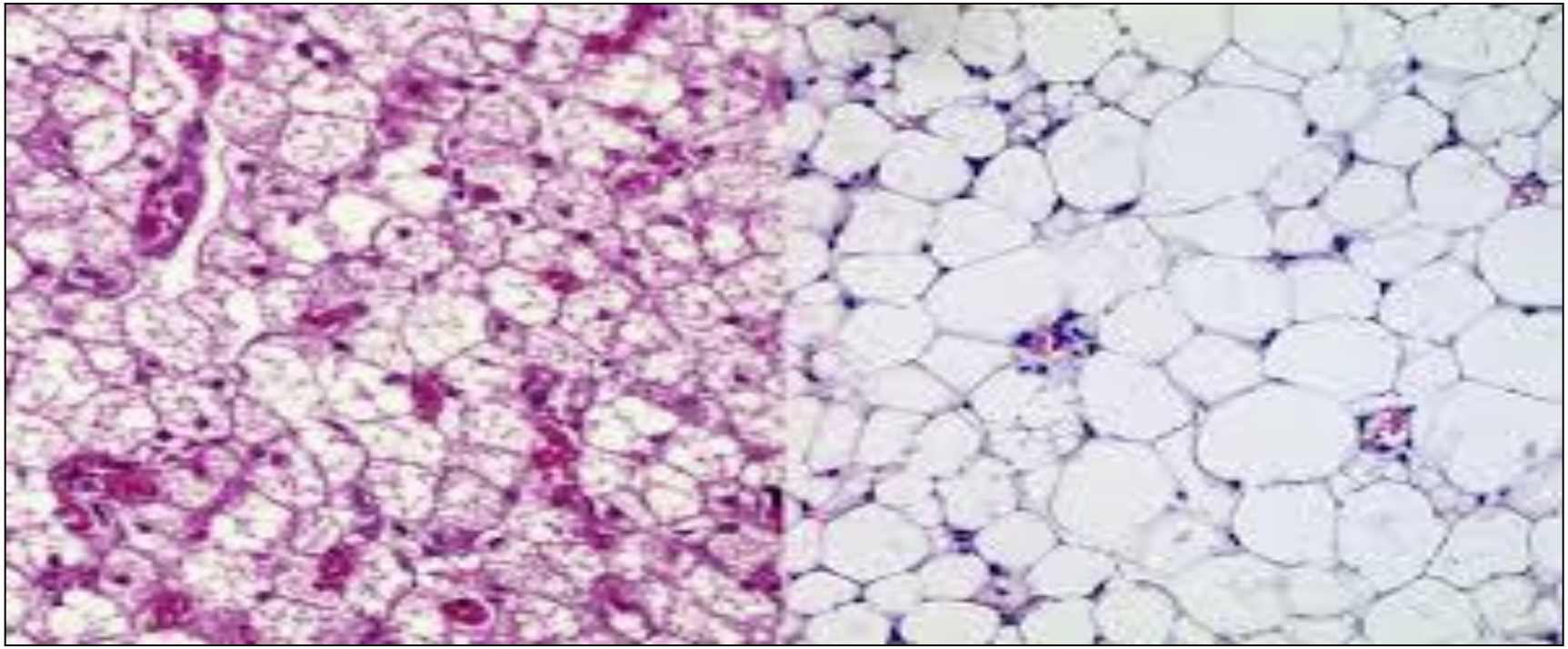
Characteristics of the brown adipose tissue:

- It is subdivided by connective tissue into prominent lobules.
- It is abundant in hibernating animals and resembles endocrine organs as its cells aggregate into closely packed masses associated with blood capillaries.
- Receives direct sympathetic innervation



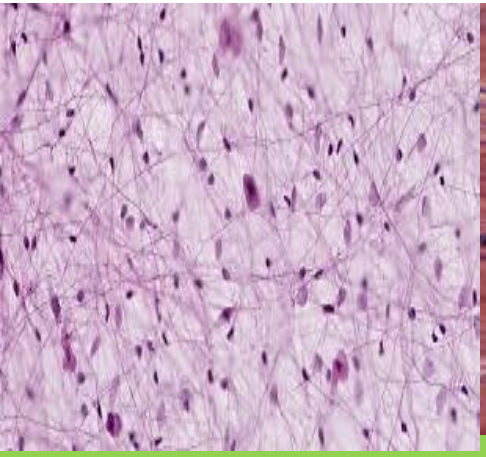
Brown fat

White fat

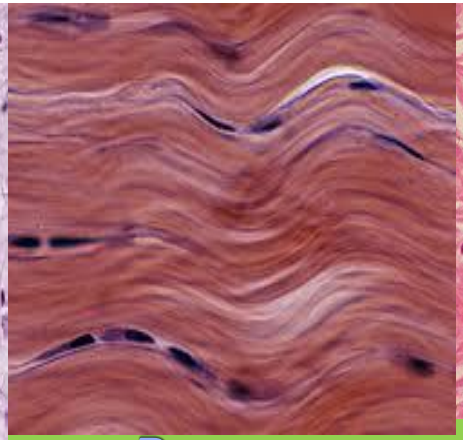


Type of connective tissue	Loose C.T.	Dense regular C.T.	Dense irregular C.T.	Mucoid C.T.	Elastic C.T.	Adipose C.T.
cells	-All	-All -Few	-All -Few	-All -Mainly fibroblasts	- fibroblast	-Mainly adipocytes
Ground substance	-Large amount	-Few	-Few	-Large abundant -Jelly like(Wharton's)	-Few	-Few amount
fibers	-All -Less	- Mainly collagen	-Mainly collagen	-All -Few	-Mainly elastic fibers	-Few amount
Sites in the body	-Dermis -Mucous membranes -pleura	-Tendon -Ligaments	-Dermis -Capsules of spleen	-Umbilical cord -Pulp of young tooth	- ligaments of vertebral column -true vocal cords	

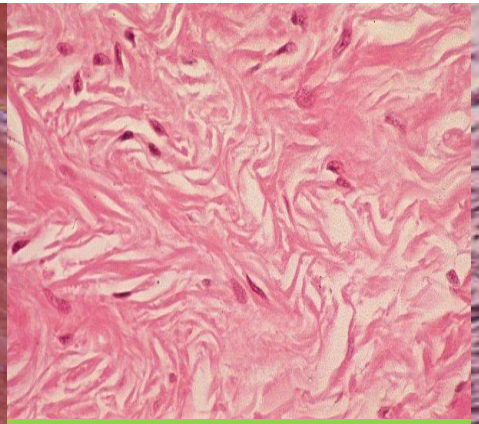
Types of C.T.



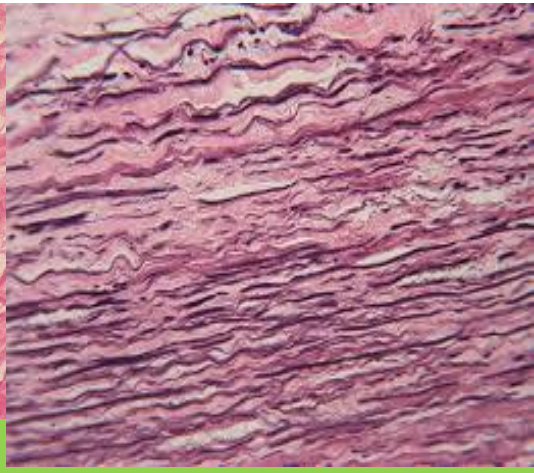
Loose C.T



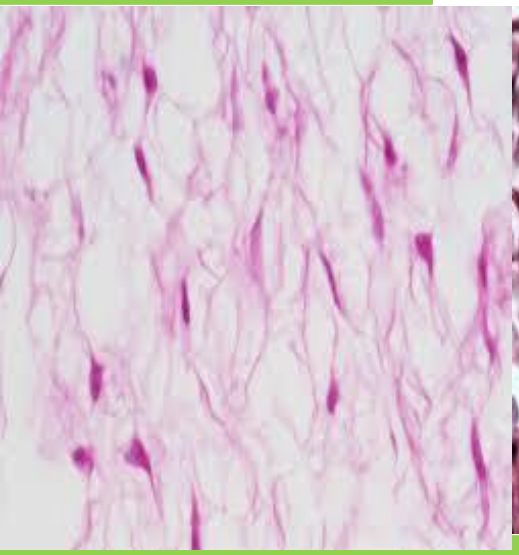
Dense regular C.T.



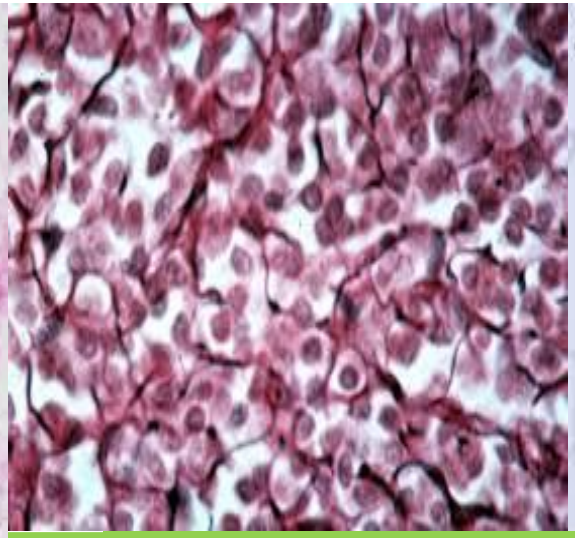
Dense irregular C.T.



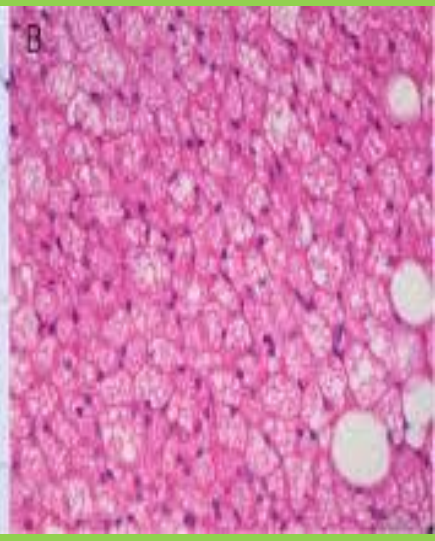
Elastic C.T.



Mucoid C.T.



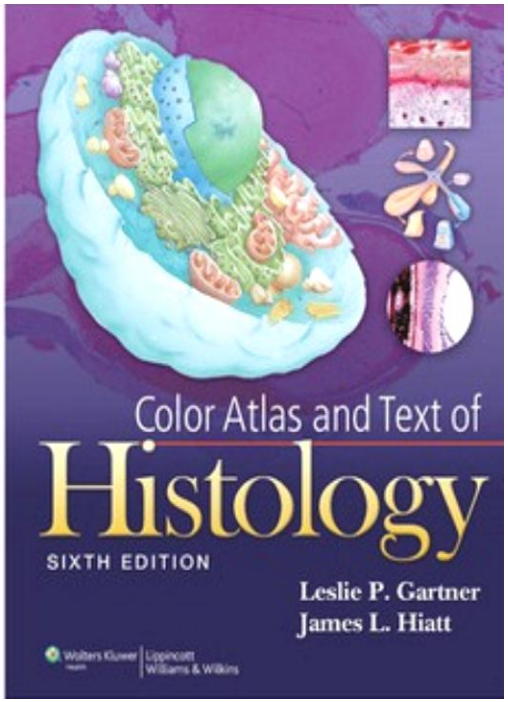
Reticular C.T.

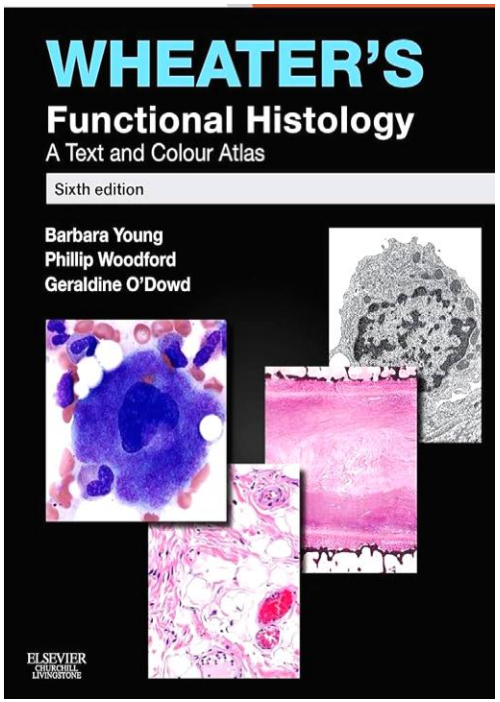


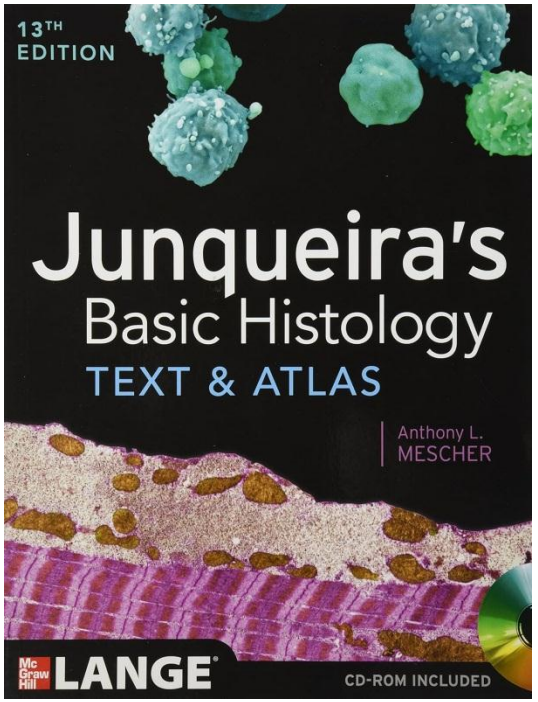
Adipose C.T.

References

Text books







Web sites

www.histology-world.com

Thank you