

Histology

Modified n. 10



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Connective Tissue

General Features

- Connective tissue provides a matrix that supports and physically connects other tissues and cells together to form the organs of the body.
- The interstitial fluid(found in the spaces between cells outside of blood vessels-part of ECF) of connective tissue gives metabolic support to cells as the medium for diffusion of nutrients and waste products.
- Composed of cells (fixed and wandering), fibers and ground substance(**Matrix**)

these cells (some is fixed and can always be seen in CT and others are seen depending on the physiological state of the tissues)

fibers differ in connective tissues by nature example: loose connective tissues have less amount of fibers

Ground substance → fillings between cells and fibers

Ground substance + Fibers = Matrix

General Features

- Variable vascularity.

it's vascular but not all the time → for CT vascularity is reflected in regeneration unlike epithelium is Avascular with a good generation capacity → example on CT: bones are very well vascular while cartilage is Avascular → any damage in the bones can be healed immediately unlike cartilage

- Variable regenerative power. **Depends on vascularity**

Functions

1. Structural framework for the body. → bones, and associated cartilage
2. Transportation of fluids and dissolved substances → blood
3. Protection of delicate organs. → Gland and kidney surrounded by capsule
4. Supports, surrounds, and connects other tissues. → like ligaments and fascia
5. Storage of energy in the form of lipids. → (adipose tissues)
6. Defend the body against microorganisms. → White blood cell

Origin

- All connective tissues originate from **embryonic mesenchyme**, a tissue developing mainly from the middle layer of the embryo, **the mesoderm.**
- Mesenchyme consists largely of viscous ground substance with few collagen fibers.
- Mesenchymal cells are undifferentiated and have large nuclei, with prominent nucleoli and fine chromatin.
- Mesenchymal cells are spindle-shaped **with a few amount of cytoplasm**---- with their scant cytoplasm extended as two or more thin cytoplasmic processes
- The location and amount of such cells depend on the stage of the embryo

Origin

All the types of connective tissue arise from mesenchyme (with different differentiation pathways)

Application :

Mesenchyme cells are used frequently in stem cell applications and (stemness: the ability to differentiate to something more advanced)
Embryo → comes from fertilized ovum and gives rise to many cells which differentiate to create more specialized cells

More differentiation = more specialized

Until it reaches its final differentiation which won't give rise to new cells → example: bone cells

*The paragraph from the textbook on stem cells :
Medical application page 96*

Some cells in mesenchyme are multipotent stem cells potentially useful in regenerative medicine after grafting to replace damaged tissue in certain patients. Mesenchyme-like cells remain present in some adult connective tissues, including that of tooth pulp and some adipose tissue, and are being investigated as possible sources of stem cells for therapeutic repair and organ regeneration.

Note: adipose tissues are used because they are rich in fat which causes the least complications when used in such applications

Components

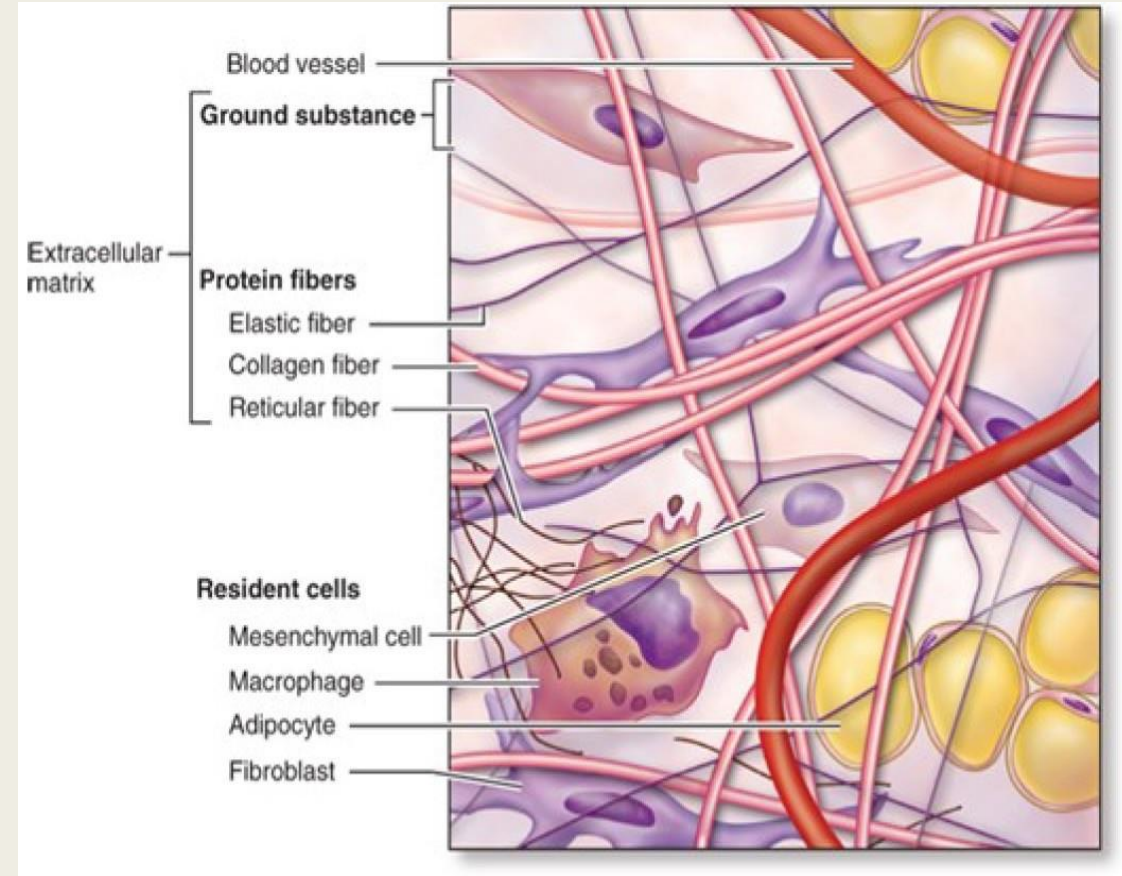
- Cells
- Fibers
- Ground substance

Matrix → significantly differs between different types of CT

Ground substance

- Ground substance is a complex of anionic, hydrophilic proteoglycans, glycosaminoglycans (GAGs), and multiadhesive glycoproteins (laminin, fibronectin, etc.)

It differ bas on the type of connective tissues



It's the mother of connective tissue which means this cell is the one in charge of synthesizing and secreting fibers and ground substance and is present in all types of connective tissues

Cells of Connective Tissue

- Fibroblast
- Mast cell
- Macrophage
- Plasma cell
- Adipocyte

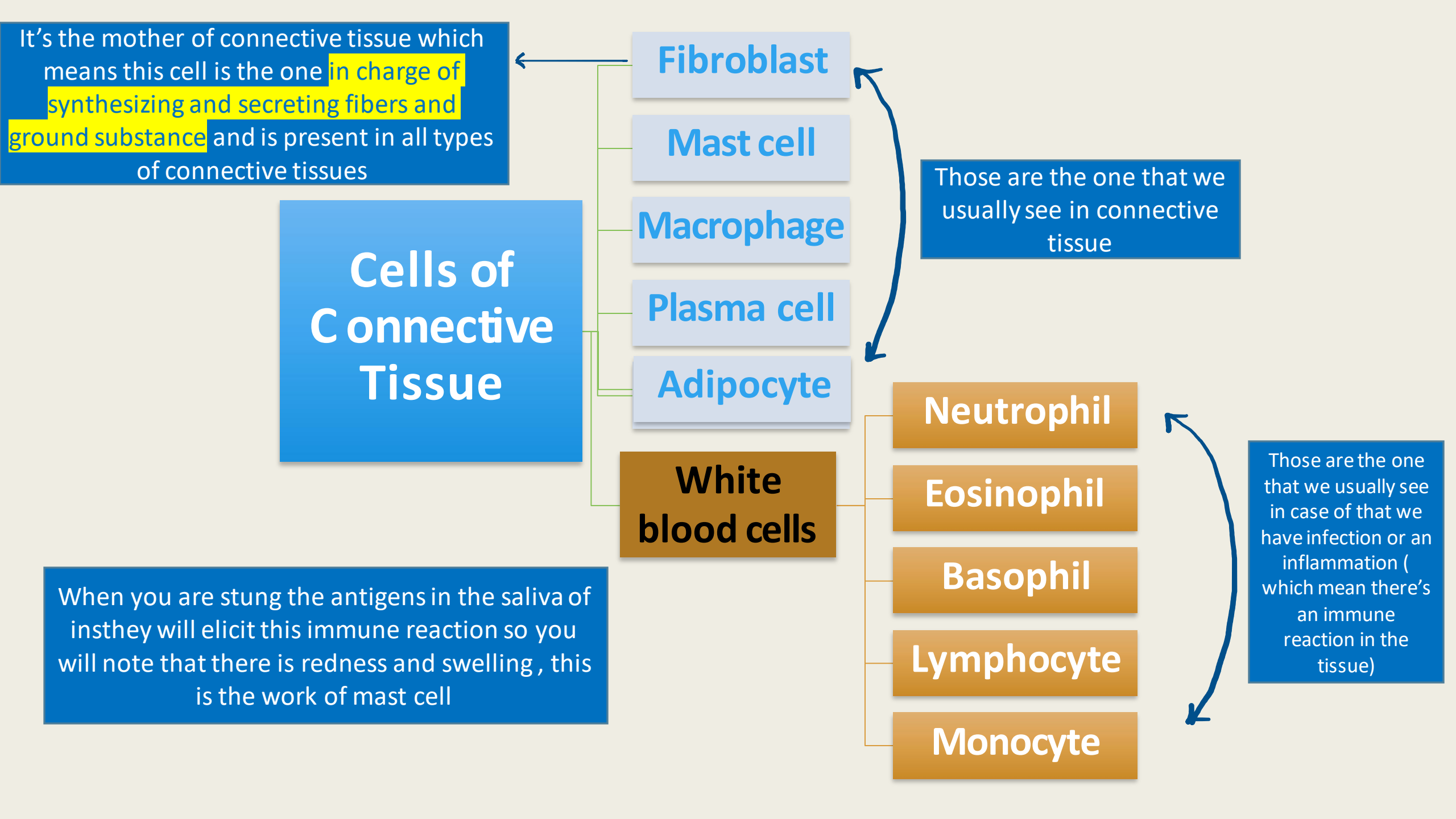
Those are the one that we usually see in connective tissue

White blood cells

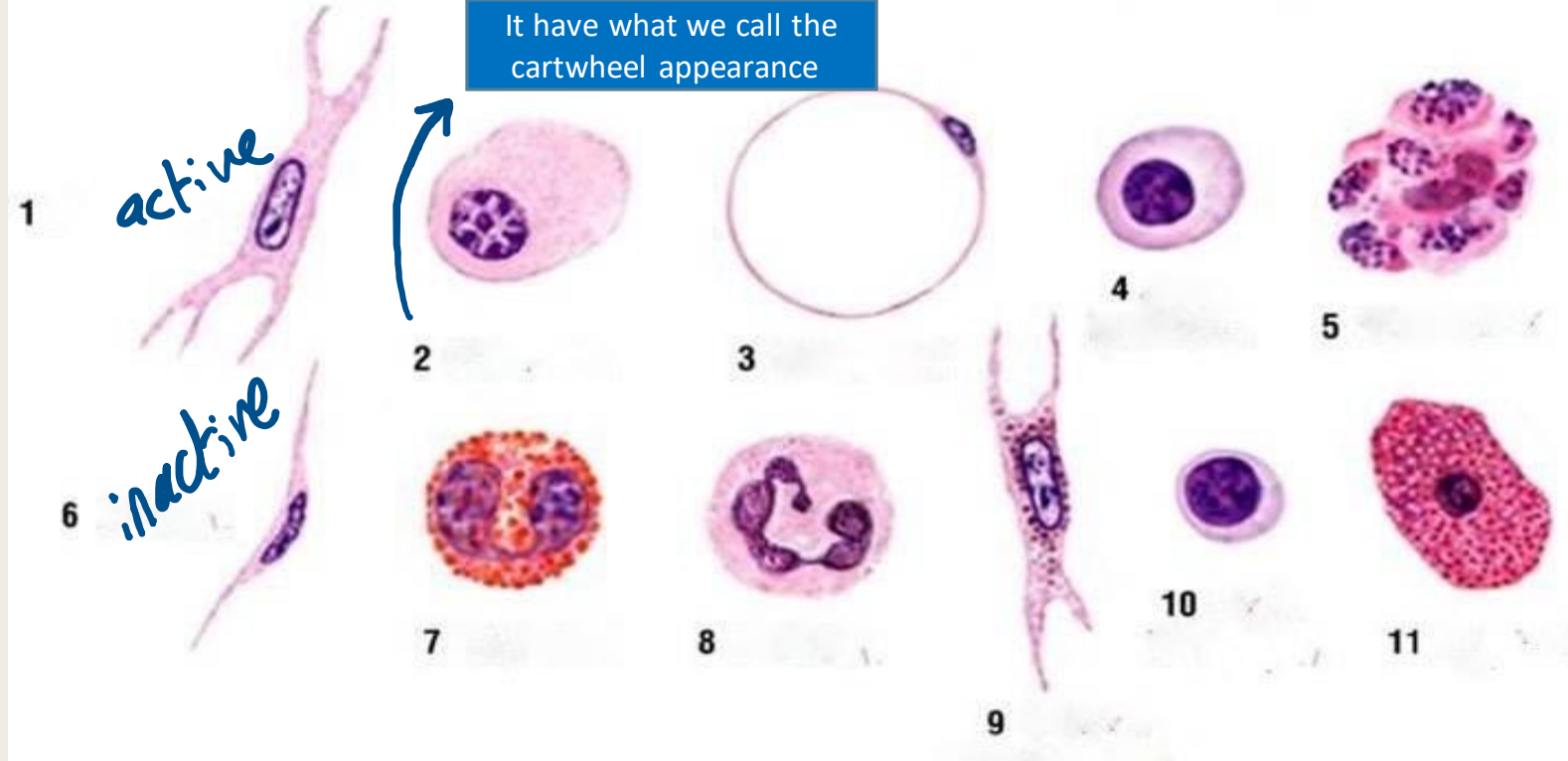
- Neutrophil
- Eosinophil
- Basophil
- Lymphocyte
- Monocyte

Those are the one that we usually see in case of that we have infection or an inflammation (which mean there's an immune reaction in the tissue)

When you are stung the antigens in the saliva of insthey will elicit this immune reaction so you will note that there is redness and swelling, this is the work of mast cell



How can we recognize active form from in active form cells?
 By the size of the nucleus and the amount of cytoplasm and the amount of processes (يلي) processes
 بتكون طالعاه من الخليه)



1. **Fibroblast**

2. Plasma cell

3. Adipocyte

4. large lymphocyte

5. Macrophage

6. Fibrocyte(

7. Eosinophil

8. Neutrophil

9. Cell with pigment granules

10. Small lymphocyte

11. Mast cell

Relatively large in comparison to other types of white blood cells

Connective tissue cells

Cell Type	Major Product or Activity
Fibroblasts (fibrocytes)	Extracellular fibers and ground substance
Plasma cells	Antibodies
Lymphocytes (several types)	Various immune/defense functions
Eosinophilic leukocytes	Modulate allergic/vasoactive reactions and defense against parasites
Neutrophilic leukocytes	Phagocytosis of bacteria
Macrophages	Phagocytosis of ECM components and debris; antigen processing and presentation to immune cells; secretion of growth factors, cytokines, and other agents
Mast cells and basophilic leukocytes	Pharmacologically active molecules (eg, histamine)
Adipocytes	Storage of neutral fats

It's first line responders, it's emergency cell

First line responders are seen if we have infections and will take over the fight until more specialized cells appear

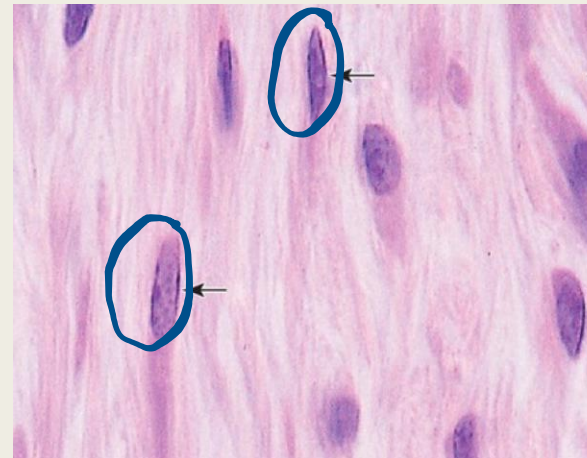
Fibroblast

- The most common cells in connective tissue proper
- Produce and maintain most of the tissue's extracellular components.
- Most of the secreted ECM components undergo further modification outside the cell before assembling as a matrix.
- **Important for regeneration and repair**
why it's present in all CT

برضو لاحظوا
the amount of
cytoplasm
around the
nucleus

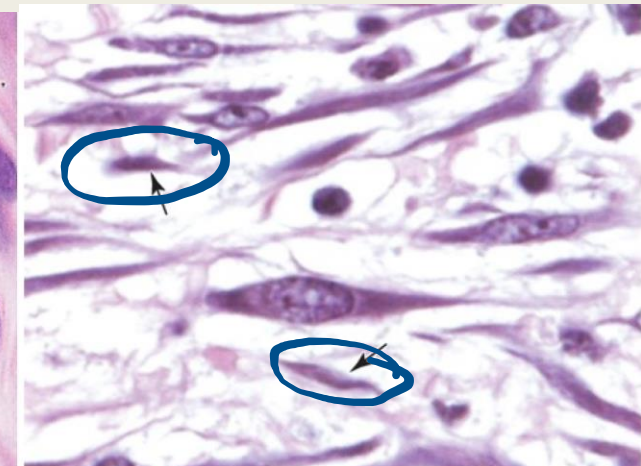
Euchromatic when the genetic material is free, accessible so we can easily get copies and messengers RNA which will go to the cytoplasm so we can translate this into proteins

Fibroblast



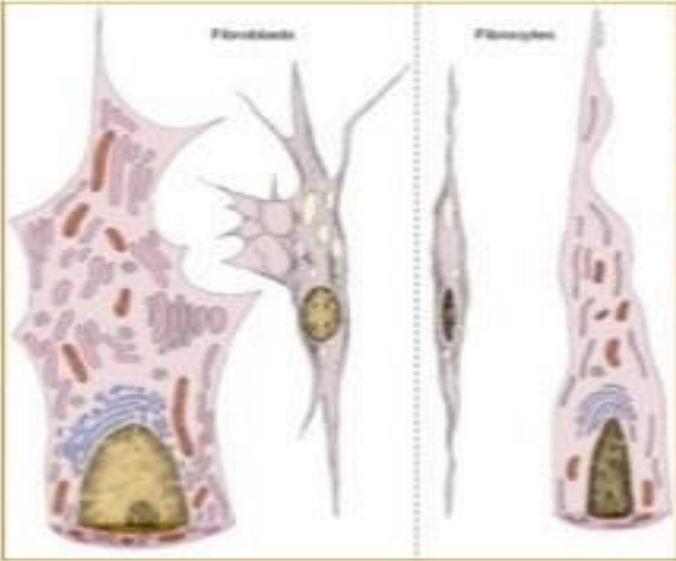
Heterochromatic, the chromatin will clump on itself and it will be highly folded versus the chromatin in the fibroblast. transcriptionally silent

Fibrocyte

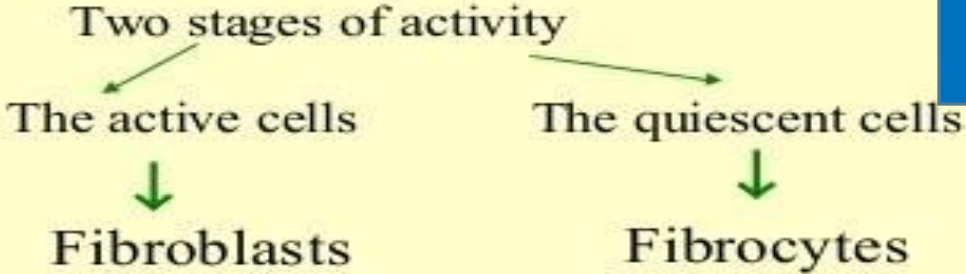


Fibroblasts _ Fibrocytes

- ✓ Fibroblasts
 - the most common cells in connective tissue
 - cells responsible for the synthesis of extracellular matrix components
 - an abundant and irregularly branched cytoplasm
 - ovoid, large and pale staining nucleus with nucleolus
 - rich in RER and well developed Golgi complex
 - produce the growth factors → influence growth and cells differentiation
 - proliferate when the additional fibroblasts are required



- ✓ Fibrocytes
 - smaller than fibroblasts
 - fewer processes
 - smaller, darker, elongated nucleus
 - small amount of RER



Rich in RER as it's in charge of synthesizing and releasing proteins

Fibroblast has many processes as it can actively move between the other elements of the tissues

This also applies to bone and cartilage :
 Bone : osteoblast and osteocyte
 Cartilage : Chondroblasts and chondrocyte

Fibrocytes can reverse into the active form(fibroblast) if needed → it's not a dead cell but a dormant sleeping cell

Macrophage

When they are in the blood they called monocytes , when they are in connective tissue they called macrophages and when it leaves it acquire new features(different shape and function)

Those are white blood cells but they have left the blood and (موجودين تقريبا في كل مكان بجسمنا) resided somewhere else (

لما تنتقل الخلية monocytes من الدم وتروح لهاي الأماكن رح يصير لها بعض التغيرات رح تظل immune related function ولكن بطريقه مختلفه



- Macrophages have highly developed phagocytic ability and specialize in turnover of protein fibers and removal of apoptotic cells, tissue debris, or other particulate material
- Being especially abundant at sites of inflammation.
- Size and shape vary considerably, corresponding to their state of functional activity.
- A typical macrophage measures between 10 and 30 μm in diameter and has an eccentrically located, oval or kidney-shaped nucleus.
- They generally have well-developed Golgi complexes and many lysosomes.

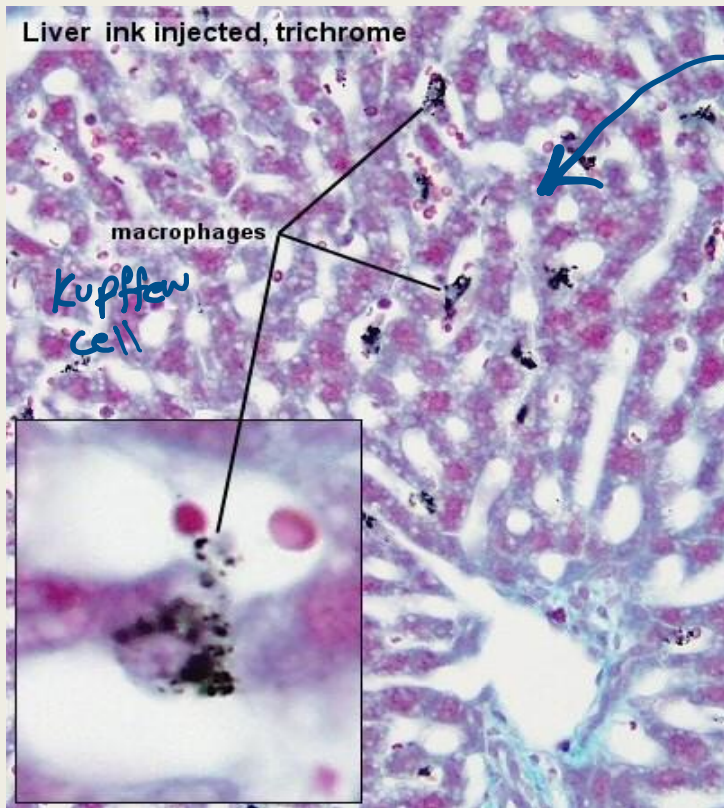
Mononuclear phagocyte system → precursor is monocyte

Cell Type	Major Location	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow, pleural and peritoneal cavities	Production of cytokines, chemotactic factors, and several other molecules that participate in inflammation (defense), antigen processing, and presentation
Kupffer cell	Liver (perisinusoidal)	Same as macrophages
Microglial cell	Central nervous system	Same as macrophages
Langerhans cell	Epidermis of skin	Antigen processing and presentation
Dendritic cell	Lymph nodes, spleen	Antigen processing and presentation
Osteoclast (from fusion of several macrophages)	Bone	Localized digestion of bone matrix
Multinuclear giant cell (several fused macrophages)	In connective tissue under various pathological conditions	Segregation and digestion of foreign bodies

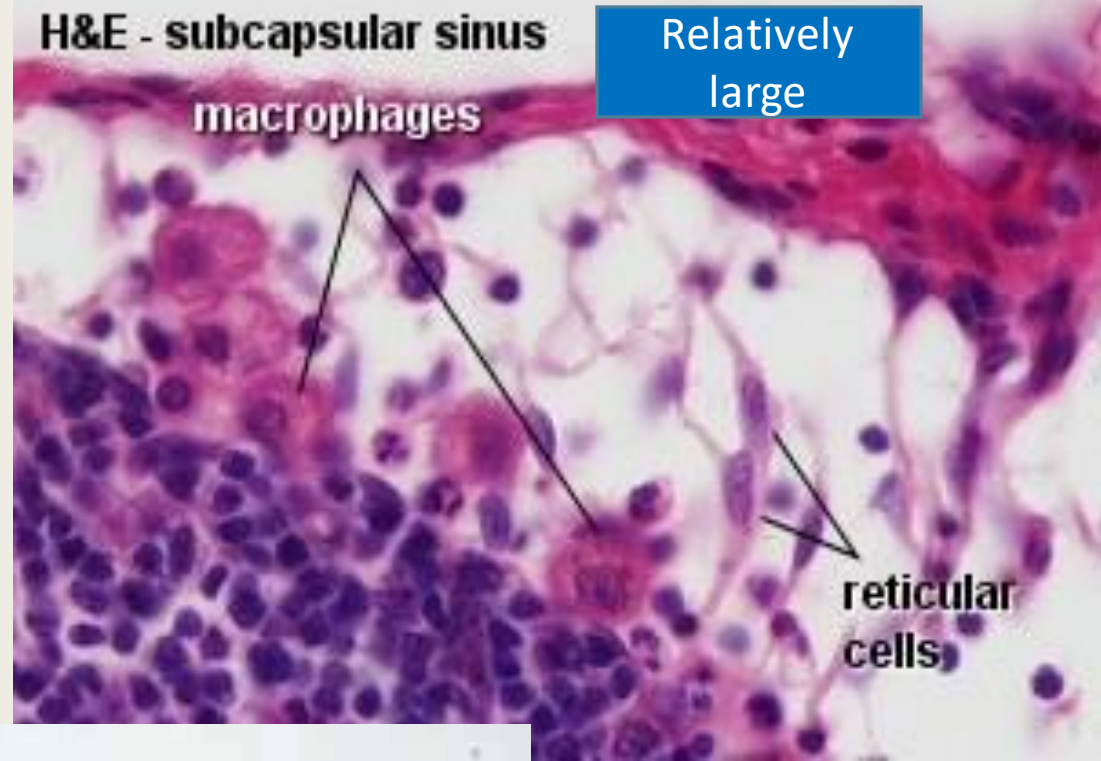
Bones are in a constant state of remodeling

not immune related function , in this process we help liberate calcium and pump it back into the blood so we can restore the calcium level

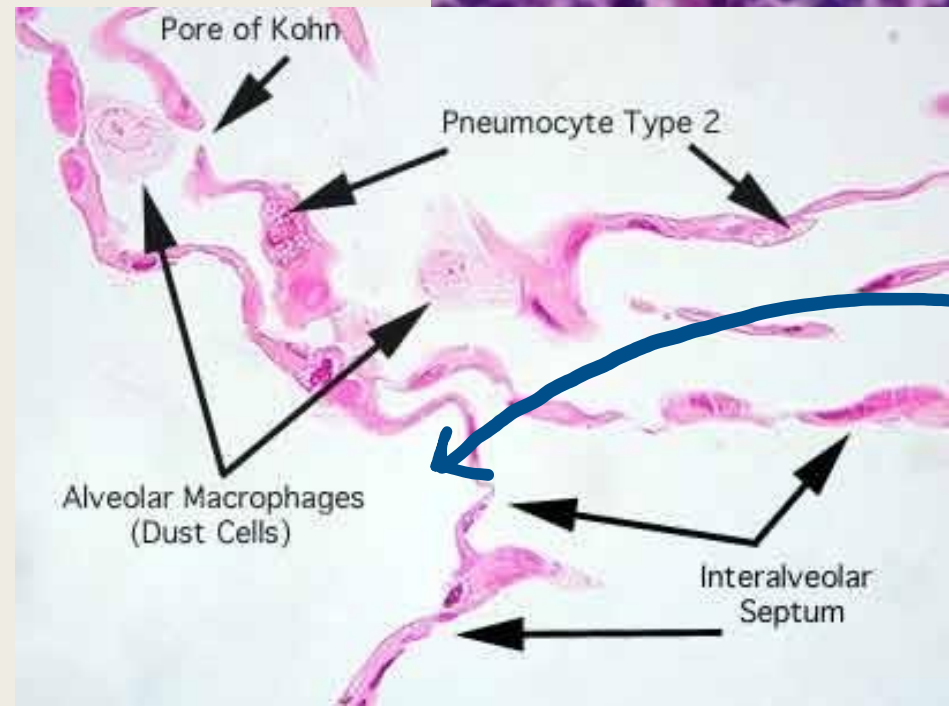
Will see many nuclei inside the cytoplasm



When anything runs in the blood and needs to be picked up, they will pick it and store it



كيف قدرنا نلاقي هذه الخلايا و عرفنا مواقعهم
 We give an animal (mouse) ink ? and the blood will circulate , the blood will reach the liver where there is macrophages, and they will recognize the ink as foreign material so they will engulf it and bring it inside



We can see inside the lungs (they engulf the particles that we inhale) to clean the interior of the lungs

Mast Cell

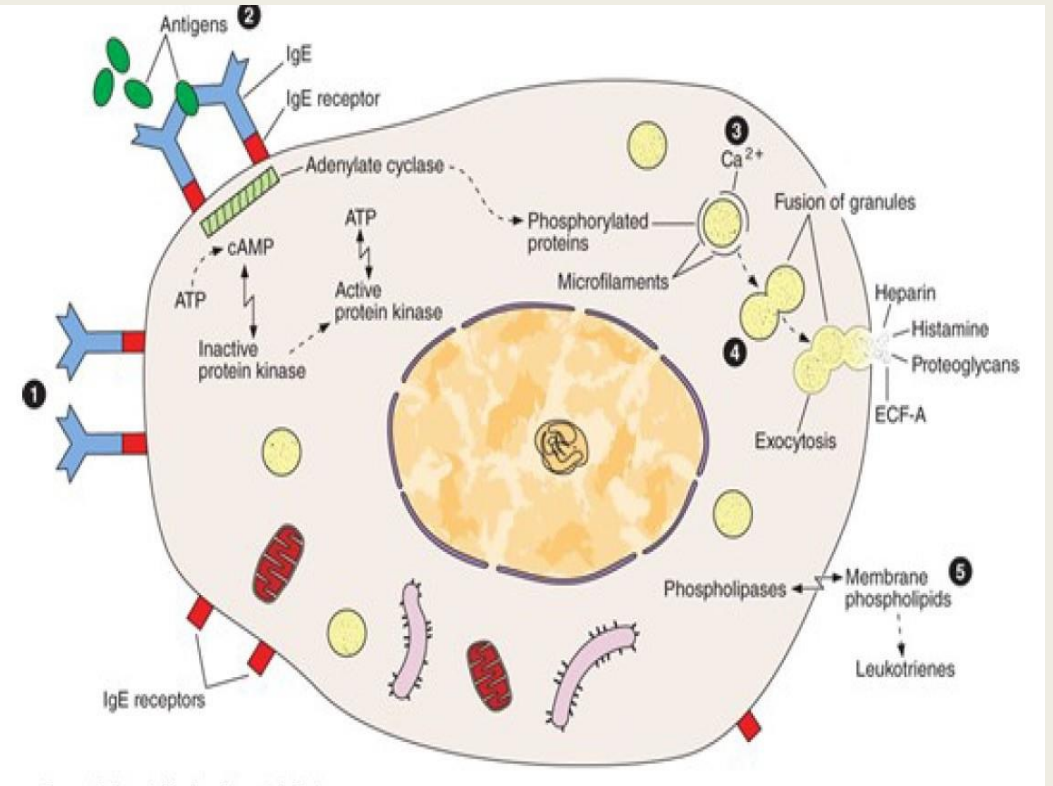
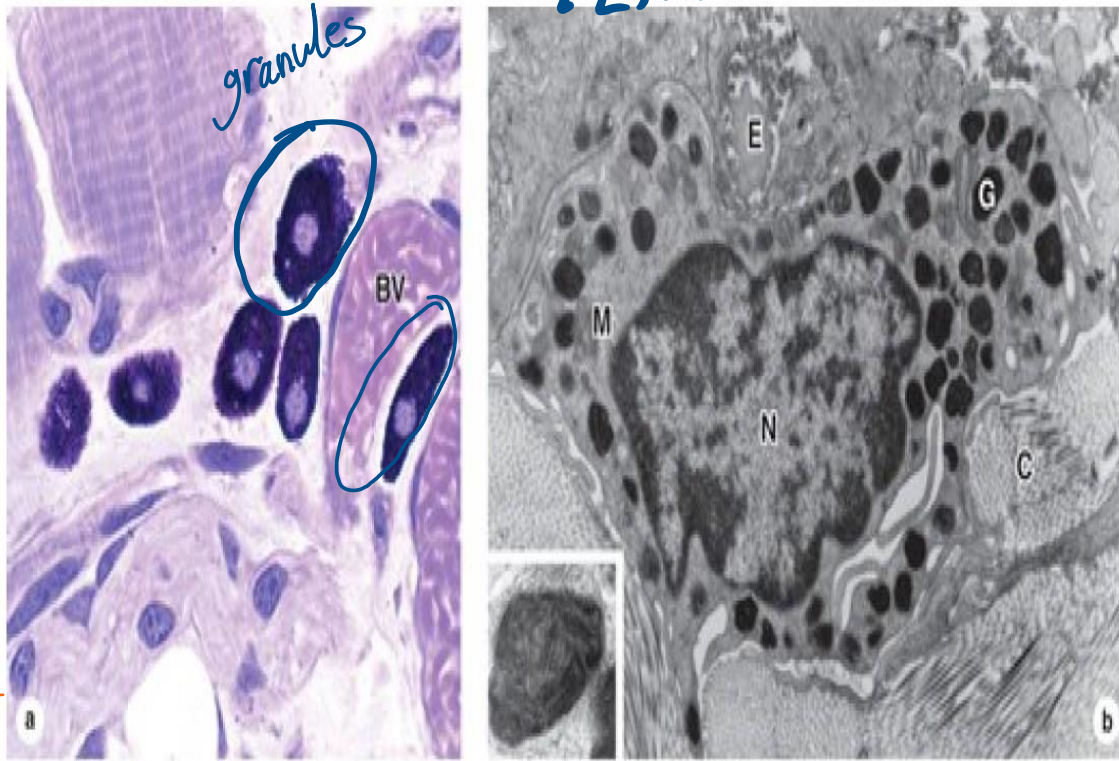
Resident cells → seen regularly in CT and vary in amount → more mast cells means that there is an immune reaction

- Mast cells are oval or irregularly shaped cells of connective tissue,
- Filled with basophilic secretory granules that often obscure the central nucleus
- Mast cells function in the localized release of many bioactive substances, includes the following:
 1. Heparin, a sulfated GAG that acts locally as an anticoagulant
 2. Histamine: promotes increased vascular permeability and smooth muscle contraction
 3. Serine proteases: activate various mediators of inflammation
 4. Eosinophil and neutrophil chemotactic factors: attract those leukocytes
 5. Phospholipid precursors: converted to other important lipid mediators of the inflammatory reaction.

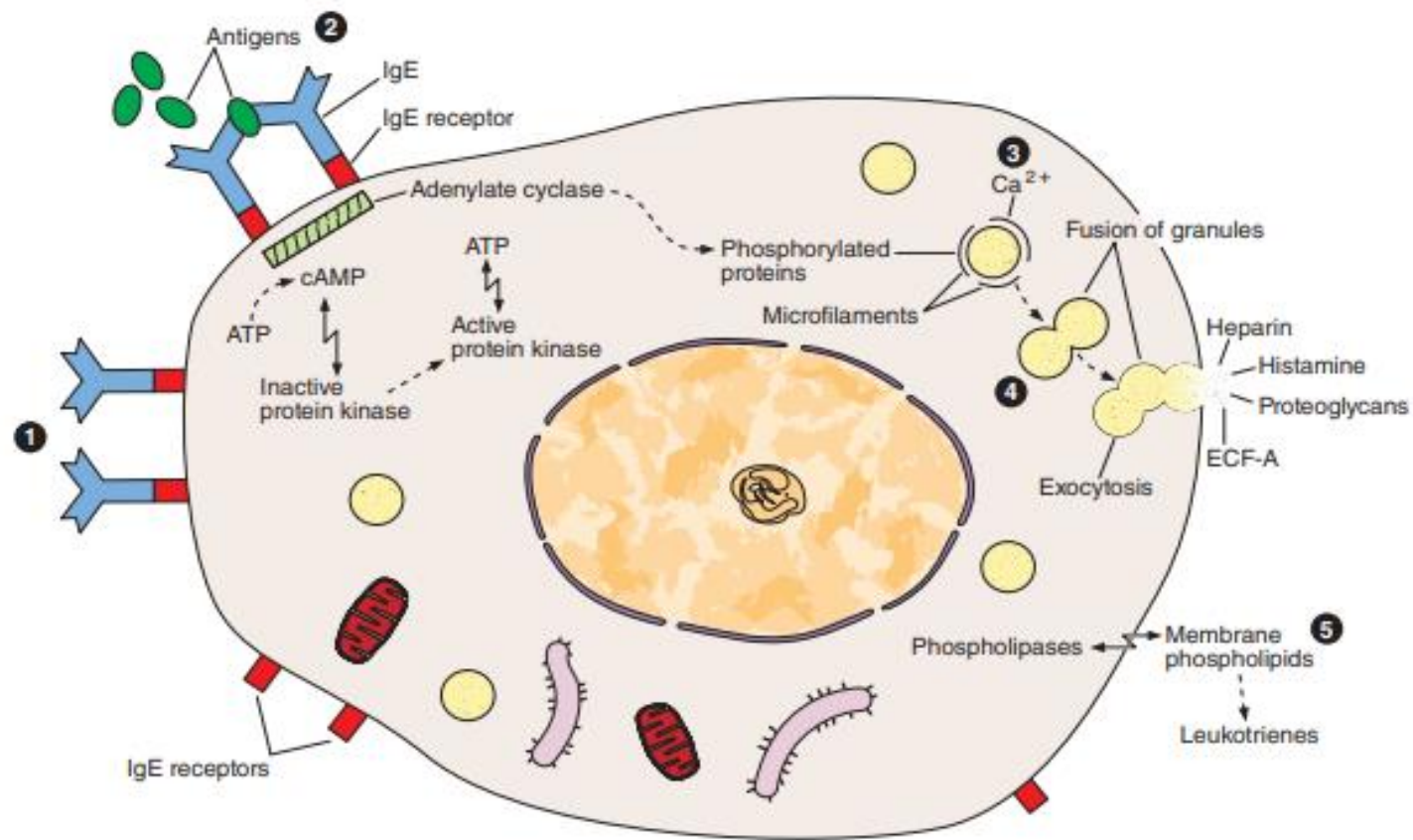
Blood vessels they are usually not permeable, when we have lots of histamine that make the capillaries more leaky, so when it's bigger the blood that's coming will be more — more red in the region — the temperature will rise — the size of stung will be bigger

Mast cell

TEM



Toluidine blue → cells are filled with granules containing bioactive material and this stain recognises these granules



Mast cell secretion is triggered by reexposure to certain antigens and allergens. Molecules of IgE antibody produced in an initial response to an allergen such as pollen or bee venom are bound to surface receptors for IgE (1), of which 300,000 are present per mast cell.

When a second exposure to the allergen occurs, IgE molecules bind this antigen and a few IgE receptors very rapidly become cross-linked (2). This activates adenylate cyclase, leading to phosphorylation of specific proteins (3), entry of Ca²⁺ and rapid

exocytosis of some granules (4). In addition, phospholipases act on specific membrane phospholipids, leading to production and release of leukotrienes (5).

The components released from granules, as well as the leukotrienes, are immediately active in the local microenvironment and promote a variety of controlled local reactions that together normally comprise part of the inflammatory process called the **immediate hypersensitivity reaction**. "ECF-A" is the eosinophil chemotactic factor of anaphylaxis.

Plasma Cell

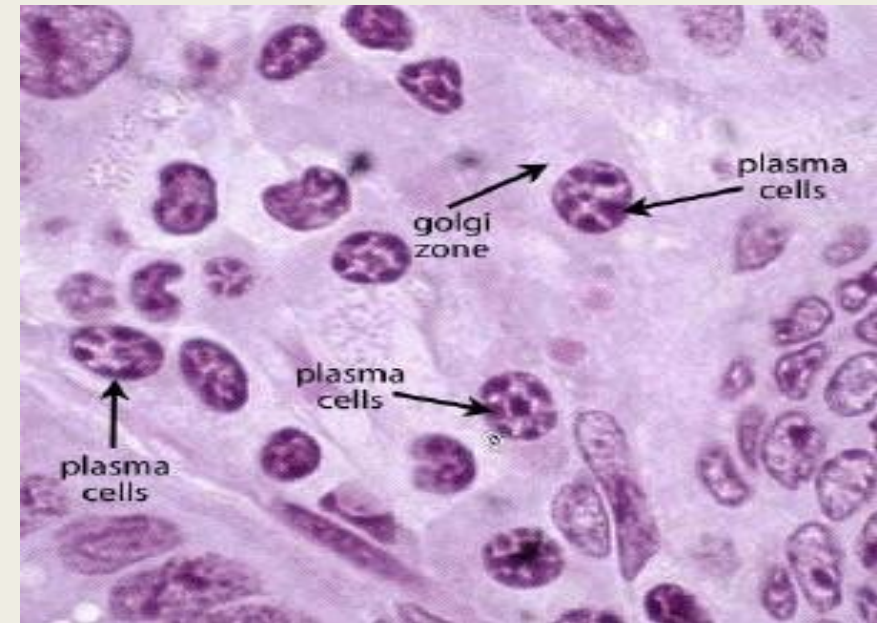
In the blood we have cell that's called lymphocytes and they are two major family: B lymphocytes and T lymphocytes

- Plasma cells are B lymphocyte-derived, antibody- producing cells.
- Relatively large, ovoid cells have basophilic cytoplasm rich in RER.
- Large Golgi apparatus near the nucleus that may appear pale in routine histologic preparations

مقارنة مع الام (B lymphocyte it's small) طيب ليش ال plasma كبيره ؟ because those are antibody secreting so the need golgi , ribosomes so I need a good amount of cytoplasm

When they encounter a pathogen part of them eventually will store code for this pathogen will give us plasma cell and another one memory cell

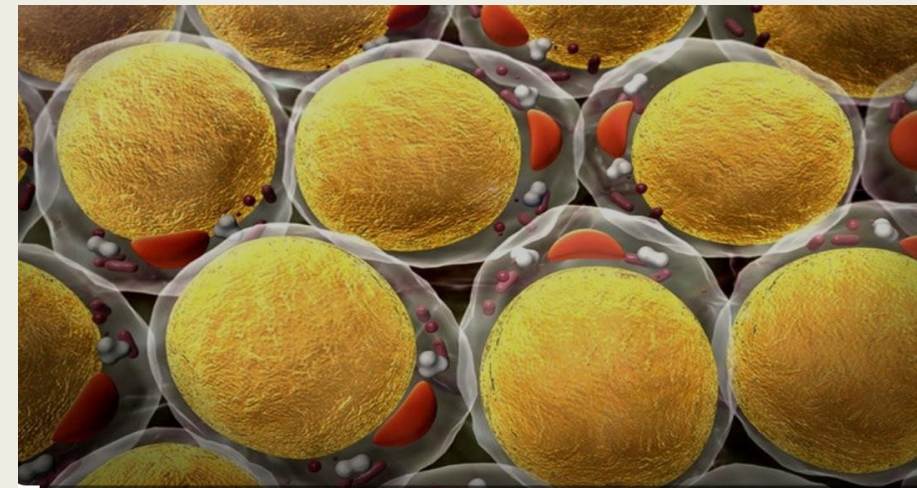
The base of immunization, if we encounter this pathogen in the future They will alert the human Body and then they can fight that antigen quite easily



Adipose Cells

Usually they are found in the glands

- Fat cells
- Found in the connective tissue of many organs.
- Large, mesenchymal-derived cells are specialized for cytoplasmic storage of lipid as neutral fats, or less commonly for the production of heat.
- Tissue with a large population of adipocytes, called adipose connective tissue, serves to cushion and insulate the skin and other organs.
- **Appear as rings with empty white space because after undergoing tissue processing fat will be dissolved leaving an empty white space with flattened nuclei**



Connective tissue Fibers/Collagen

- Form various extracellular fibers, sheets, and networks.
- Extremely strong and resistant to normal shearing and tearing forces.
- Collagen is a key element of all connective tissues, as well as epithelial basement membranes and the external laminae of muscle and nerve cells.
- Most abundant protein in the human body, representing 30% of its dry weight.
- A family of 28 collagens exists in vertebrates.

three types → collagen, elastic and reticular fibers (can be considered two as reticular fibers are collagen type 3)

These fibers have different arrangement in different types of CT for example loose connective tissues have less fibers and more ground substance

While ligaments have an extensive amounts of fibers aligned well around each other with a lower amount of ground substance