



Connective Tissue

Basic tissues are :

- 1- Epithelium
- 2- Connective tissue
- 3- Nervous tissue
- 4- Muscle tissue

CT proper means they are more dominant in our body .

CONNECTIVE TISSUE :

- the tissue that connects + provides support to other tissues in the body .
- most abundant tissue in our body

ORIGIN :

- Mesoderm + Ectomesenchyme (which has the properties of mesoderm)
- **All CT is derived from EMBRYONIC MESENCHYME .**

Q: the origin of CT is :

- a- Ectoderm
- b- Ectomesenchyme
- c- Endoderm
- d- Mesoderm
- e- **B+D**

Mesenchyme : (is embryonic tissue regardless of the origin)

Found in the embryo

Embryonic CT with multipotential cells (cells that can differentiate into other types of cells)

Note : mesenchymal cells are : elongated with an oval nucleus and many cytoplasmic processes.

Extracellular Substance : has less fibers and more ground substance .

CT is composed of :

- 1- Cells
- 2- Fibers
- 3- Ground substance



EMBRYONIC ORIGIN OF CT CELLS :

HEMATOPEOTIC STEM CELLS (HSC)	
Basophil	Langerhans cells
Eosinophil	Microglia
Neutrophil	Mast cells
Megakaryocyte	Osteoclasts
Red blood cell	
B lymphocyte -> plasma cell	
T lymphocyte	
Monocyte -> macrophage	

UNDIFFERENTIATED MESENCHYMAL CELLS (UMC)
Osteoblast -> osteocyte
Mesothelial cells
Endothelial cells
Smooth muscle cells
Chondroblast -> chondrocyte
Adipocyte (fat cell)
Fibroblast

NOTE :

- Mesothelial cells line body cavities ex : pleura
- All cells coming from HSC go through many cells to give the final product (dots)
- Only adipocytes coming from UMC go through many cells o give final product , all other cells originate almost directly except osteocytes and chondrocytes .

Q: are all bone cells derived from UMC ? no osteocytes are from HSC , while osteoblast and osteocyte are from UMC.

Q: If they ask for origin you go one step back ex : the origin of macrophage is monocyte , origin of osteocyte is osteoblast .

Q: the origin of osteoblast :

- Mesoderm
- Ectoderm
- Ectomesenchyme
- Endoderm
- Undifferentiated mesenchymal cells

GENERAL CHARACTERISTICS OF CT :

- 1- Variety of cell types
- 2- Varying degree of vascularity +lymphatics+ nerves
- 3- Extracellular matrix (ECM) = GS + fibers
 - In calcified CT (bone , cementum and dentin) ECM is mineralized .

CT FUNCTIONS :

- 1- providing an maintaining the form of the body.
- 2- providing the matrix the binds and connects the cells + organs .



- 3- protection of organs
- 4- had nerves and BV .
- 5- transport of substances (nutrients + wastes)
- 6- special functions according to different types.

TYPES OF CT :

- 1- CT proper (loose , dense regular , dense irregular)
- 2- Elastic CT
- 3- Adipose CT (white , brown)
- 4- Reticular CT
- 5- Mucous CT
- 6- Fluid CT (lymph + blood)
- 7- Supportive CT (osseous CT – bone + cartilage)

SOFT CT COMPONENTS :

- 1- Ground substance (GS) : molecular material that fills the space between cells and fibers
 - 2- Fibers : (reticular , collagen , elastic)
 - 3- Cells : (fibroblast , fibrocyte , macrophage , mast cells , inflammatory cells [neutrophils +lymphocytes])
 - 4- BV : Arteries , arterioles , lymphatic vessels , veins , capillaries .
 - 5- Nerves : peripheral nervous tissue
-

EXTRA –CELLULAR MATRIX [ECM]

Composed of : ground substance + Fibers

A.GROUND SUBSTANCE : gel of variable viscosity – contains :

- 1- WATER +++
- 2- Adhesion proteins (glycoproteins + proteoglycans + glycosaminoglycans GAGS)

FUNCTIONS OF GS :

- 1- Structural : can contribute to the shape and form of the organ or tissue .
- 2- Adhesion + binding b/w cells and fibers
- 3- Molecular sieve through which nutrients diffuse b/w blood + cells
- 4- Reservoir for growth factors + hormones .

NOTE :

- H&E stain : cell nuclei + collagen fibers are visible but not GS (appears as unstained spaces)
- TEM : collagen fiber + parts of cell appear , GS appears as a FUZZY material b/w cells and collagen + b/w collagen fibers .



ADHESION PROTEINS :

1-GYLCOPROTEINS : GP

- Protein core with attached , brached saccharide [sugars]
- EX : (fibronectin + laminin)
- Mostly protein with some attached sugar molecules .
- Variety of function (their function determines there molecular structure and appearance)

LAMININ : part of basement membrane promotes adhesion of cells to basal lamina .

FIBRONECTIN : glycoprotein that has binding sites for (collagen + cells + GAGs) -> func: assists in binding. (mostly associated with CT)

- 1- ECM components together
- 2- ECM components to cells .

NOTE : cell receptors called **integrins** recognize specific binding sites of **fibronectin** molecules .

2-PROTEOGLYCANS : PG

- Protein core with attached GAGS

GAGs are carbohydrate molecules with repeating units of disaccharides of a particular type (Uronic acid or galactose)

- Distribution and type of PG varies according to the tissue type (bone , tendon , skin , cartilage)

3-GAGs : Glycosaminoglycans

TYPES OF GAGs :

NAME	CHONDROITON SULFATE (TYPE 4 &6)	KERATAN SULFATE	HYALURONIC ACID	DERMATAN SULFATE	HEPARAN SULFATE
LOCATION	Cartilage Skin bone Aorta Developing pulp	Cartilage Corneal	Cartilage Umbilical cord Pulp	Tendon Skin Pulp Aorta	Lung Liver Pulp Basal lamina
NOTES	Interact with collagen type 2		Can exist by itself as a GAG rather than a PG	Interact with collagen type 1	Interact with collagen type 3 and 4.



NOTES :

- Different PG molecules are formed according to the quantity and combinations of particular GAGs .
 - 1- **Aggrecan** : cartilage matrix
 - 2- **Syndecan** : cell surface PG -> assists in cell to ECM adhesion.
- GAGs + PG are hydrophilic (attract water and swell filling the spaces b/w components of CT)
- Cartilage has : chondroitin sulfate + keratin sulfate + hyaluronic acid
- Pulp has : dermatan sulfate + hyaluronic acid + heparin sulfate
- Developing pulp has only chondroitin sulfate

Collagen type 1 interacts with Dermatan sulfate

Collagen type 2 interacts with chondroitin sulfate

Collagen type 3 and 4 interacts with heparin sulfate

B. FIBERS : [remember - REC]

1-Collagen >25 types

2- Reticular fibers (very thin collagen fibers that are mainly type 3)

3- Elastic fibers

1- COLLAGEN FIBERS :

- Most abundant protein in our body
- Main amino acids forming collagen are (proline , hydroxyproline , glycine)
- Produced by : fibroblasts , chondroblast , cementoblasts , osteoblasts , odontoblasts

COLLAGEN FORMS :

NAME	TYPE	FUNCTION /DESCRIPTION
Long-fibril forming collagens	1,2,3,5,7,11 (type 1 is most common)	Forms fibrils
Fibril associated collagens	9 , 12 , 14	Short structures that bind collagen fibrils together and to the ECM
Collagens that form networks	Type 4 (basal lamina)	Forms meshwork – smaller than fibrils that forms the basal lamina
Collagens that form anchoring fibers	7	Present in fibrils that bind collagen fibers to basal lamina



COMMON TYPES OF COLLAGEN

Type	Structure	Location	Function
1	Fibrils fibers bundles	Dermis Tendons Ligaments Dentin Skin Fibrocartilage	Resistance to tension
2	Fibrils only	Hyaline + elastic cartilage	Resistance to pressure
3	Fibrils + fibers	Reticular fibers Uterus Liver Spleen Kidney Lungs + Blood vessels	Delicate flexible framework + structural support
4	Network sheet	Basal lamina	Filtration + support of delicate structures

Q: what are the types of cells that secrete dental structure collagens in the crown ?

a-odontoblast

b-cementoblast

c-fibroblast

d- A +C (crown has pulp)



COLLAGEN SYNTHESIS :

Subunits of collagen are **tropocollagen** .

Composed of 3 chains (2 alpha 1 + 1 alpha 2 peptide chains) the 3 chains intertwined together and form a triple helix held by **hydrogen bonds**.

STEPS : (INTRACELLULAR)

- 1-Formation of mRNA for each type of alpha chain .
- 2-Synthesis of alpha chains of procollagen.
- 3-assembly of procollagen molecules to form the triple helix at the RER.
- 4-transport of procollagen to Golgi Complex
- 5-packing of procollagen in secretory vesicles.
- 6-secretory vesicles transport collagen to cell surface

_____END OF INTRACELLULAR STEPS _____

STEPS : (EXTRACELLULAR)

- 7-Discharge of procollagen to extracellular space
 - * **procollagen peptidase** transforms procollagen to tropocollagen which aggregates to form collagen fibrils.
- 8-fibrillar structure is reinforced by the formation of covalent cross links b/w tropocollagen molecules .
- 9-Aggregation of tropocollagen to form fibrils – fibers – bundles
 - a- Arrangement of rod like tropocollagen subunits
 - b- Cross striations (64 nm) periodicity of dark and light bands (seen by EM)
[64 nm is the distance b/w the bands] – if u see the bands then the collagen is normal
Those bands are due to specific arrangement of tropocollagen above each other
 - c-fibrils aggregate to fibers
 - c- Fibers aggregate to form bundles

NOTE : collagen type 3 does not form bundles .



Disorder	Defect	Symptoms
<i>Ehlers – danlos type 4</i>	Faulty transcription or translation of collagen 3	Aortic or intestinal rupture
<i>Ehlers – danlos type 6</i>	Faulty lysine hydroxylation	Increase of skin elasticity , rupture of eye ball
<i>Ehlers – danlos type 7</i>	Decrease in procollagen peptidase activity	Increase in articular mobility + frequent luxation (displacement of bone from a joint)
<i>scurvy</i>	Lack of vitamin c which is a cofactor for prolyl hydroxylase	Ulceration of gums + hemorrhage
<i>Osteogenesis imperfect</i>	Change in 1 nucleotide in genes for collagen 1	Spontaneous fracture + cardiac insufficiency

Note : bone is mostly collagen type 1 and 3 .

2-RETICULAR FIBERS :

- Very fine type 3 collagen fibers
- Form scaffold (meshwork)of fibrous CT in certain organs and tissues
- Similar banding to collagen type 1 but the triple helix has only alpha 1 chains .
- Can't be seen in H & E stain
- Needs Argyrophilic (silver stains) to identify them with a microscope.

LOCATIONS OF RETICULAR FIBERS :

- 1- Smooth muscles
- 2- endoneurium (CT of nervous tissue)
- 3- bone marrow
- 4-lymph nodes
- 5- spleen
- 6- liver

Q: why are reticular fibers called argyrophilic?

Because they need silver stain to be seen (appear black)

3-ELASTIC FIBERS :

Synthesis : Proelastin is a globular molecule formed by fibroblast cells In CT + smooth muscle cells

- 1- Proelastin polymerizes to form elastin
- 2- The AA of elastin are similar to collagen + they have **desmosine & isodesmosine** (which are responsible for the elasticity of elastic fibers)



ELASTIC FIBER SYS:

1-Oxytalan fibers :

- Bundle of microfibrils -10 nm
- GP mainly fibrillin forms a scaffold to hold elastin.
- Resist stretching (since no elastin protein)
- Found in dermis (near basal lamina) + PDL

2-Elaunin fibers :

- oxytalan microfibrils + some elastin
- Seen around sweat glands

3-Elastic fibers :

- Most numerous part of this sys
 - Fully stretchable and recoverable
 - Rich in elastin (occupies center of fiber bundles + surrounded by microfibrils)
-

NOTES:

- Elastic fibers are present in high amounts in the walls of arteries .
 - Elastin molecules are joined together by bonds to form a network , each elastin can expand and contract so the whole network can strength + recoil.
 - Elastin appears e- dense in TEM.
-

Q: this type of fiber present in PDL , not stretchable , composed of desmosine AA .

Oxytalan fibers



Types of connective tissue cells :

Cell name	Fibroblast	Fibrocyte	Myofibroblast	Adipose cells (fat cells)	
				unilocular adipose cells (more common)	multilocular adipose cells
Shape	many branched processes with abundant cytoplasm, rich in rER-mitochondria - Golgi	Spindle shape with few processes, less rER		rounded cells that show a narrow rim of cytoplasm larger than multilocular	polygonal cells
Nucleus / nucleolus	has an ovoid, large nucleus with prominent nucleolus.	Nucleus is dark& elongated.		eccentric nucleus squeezed to the periphery due to the fat droplet	Central nucleus
Characteristics		inactive fibroblast	Features of smooth muscle Cells have Contractile actin filaments& myosin in the cytoplasm allowing them to contract	1-They contain a single fat droplet. In H&E, cells show a vacuole due to dissolved lipid droplet 2-White color	1-numerous small lipid droplets and 2-abundant mitochondria 3-mitochondria are rich in cytochromes, Which account for the brown color + help in oxidative energy
Embryonic origin	Undifferentiated mesenchymal cells	Undifferentiated mesenchymal cells	Undifferentiated mesenchymal cells	Undifferentiated mesenchymal cells	
Main function	Synthesize+breakdown all the components of ECM	During wound healing, fibrocyte reverts to fibroblast,showing same appearance+ functions.	Wound healing , responsible for closing the wound after tissue injury	Store fat + provide energy	
Other functions	produce growth factors.				



Cell name	Mast cell	Macrophage	Plasma cell
Shape	Oval to round	round with irregular cell outlines - cytoplasm filled with many phagosomes & residual bodies. +cytoplasmic extensions	Large, ovoid cells , basophilic cytoplasm , rich with rER
Nucleus / nucleolus	Central spherical nucleus	large kidney or oval shaped	Nucleus is spherical & eccentric, clockface appearance.
Characteristics	<p>1-cytoplasm filled with basophilic granules</p> <p>2-granules contain heparin, histamine, & ECF-A</p> <p>3- granules are metachromatic; takes on a different color (red) from that of the applied dye (Toluidine blue).</p> <p>Note : Special technique must be used in histological sections since it's difficult to identify mast cells due to the water solubility of their granules which lost during preparation.</p>	<p>Monocytes cross the B.V. to tissues to be as macrophages.</p> <p>Note :</p> <p>macrophage networks exist throughout the body in organs such as the lungs, liver (Kupffer cells), spleen, lymph nodes, brain (microglial cells)</p> <p>*long living cells and might survive for months.</p>	
Embryonic origin	Hematopoietic stem cells	monocyte-Hematopoietic stem cells	
Main function	Granules contain a chemical mediators (histamine) – initiate vascular and other changes seen in inflammation.(vasodilatation, increased permeability, cell recruitment)	<p>1-Phagocytosis (main function)</p> <p>2-Antigen processing & presentation to other cell (langerhans cells in lining epithelia –epidermis + oral epithelium)</p> <p>3- Cell recruitment (they release cytokines that attract other inflammatory cells to the area)</p> <p>4- Storage of wastes in residual bodies (wastes include tars and carbons – mostly in macrophages in lungs of smokers)</p>	Produce antibodies
Other functions	Mast cell-bound IgE: Mediate Immune hypersensitivity reactions such as anaphylaxis, 'hay fevers' and aspects of asthma .		



- ECF-A= Eosinophil Chemotactic Factor A (recruitment of eosinophil in the area- eosinophils also secrete histamine) / heparin is an anticoagulant.
- Macrophages have an irregular outline since it has many cytoplasmic process to engulf foreign particles

LIPID STORAGE & RELEASE BY ADIPOCYTES :

- 1- Triglycerides are transported in the blood from intestine and liver by lipoproteins .
- 2- In BV, these lipoproteins are broken by **lipoprotein lipase** enzyme to give free fatty acids
- 3- Free fatty acids diffuse from capillary to adipocyte cell then then combine with **Glycerol phosphate** forming triglycerides (stored in droplets until needed)
- 4- Stored lipids are mobilized by neurgenic mechanism that will liberate fatty acids +glycerol into the blood .
- 5- Free fatty acids are bound to albumin

Q: what are the structures that the free fatty acids pass through until they reach the adipocyte ?

Capillaries (triglycerides changed to free fatty acids – by lipoprotein lipase) then the free fatty acids pass through the capillary wall - endothelium) - the basement membrane - the GS – another basal laina – cell wall – cytoplasm of cell – sER (glycerol phosphate) – forms triglycerides (stored inside the cell)

FIBROCYTES – FIBROBLASTS :

- There is no such thing as fibroblast
- In wound healing you need myofibroblast + fibrocytes

MAST CELLS

secretion :

- 1- Mast cell surface has IgE receptors.
- 2- IgE (produced by plasma cells at the first exposure to an antigen)
- 3- Re-exposure to the antigen at a later time results in antigen binding to the IgE on the mast cells, this activates adenylate cyclase and phosphorylates certain proteins
- 4- Ca²⁺ enters the cell
- 5- Intracellular fusion of granules +exocytosis of their contents (histamine, heparin & ECF-A, PGs)
- 6- Phospholipases act on membrane phospholipids to release leukotrienes.

Notes :

- leukotrienes ->contraction of smooth muscles (this explains the difficulty in breathing in anaphylactic shocks)
- Histamine -> inc. bv permeability , vasodialation.
- First stage (first exposure) there is no reactions , second stage (2nd exposure) there is a reaction due to the binding of the antigen and the receptors.



MACROPHAGES

In normal fibrous C macrophages are referred to histiocytes , but in cases of inflammation monocytes that cross BVS to CT are called macrophages.

INFLAMMATORY / IMMUNE CELLS :

1. Lymphocytes : (B & T cells)
2. Plasma cells : type of b-lymphocyte – produces antibodies
3. Phagocytic cells (neutrophils)
4. Cells that contain chemical mediators (basophils + eosinophils)

those cells are not normally found in CT Except in : Gingival cervice fluid + mucosal CT of GIT & resp tracts

Functions :

- Immune sys function
- Phagocytosis
- Inflammatory reactions
- Role in healing

Q : which type of inflammatory cells present in acute inflammation ? Neutrophils

Q: which type of inflammatory cells present in chronic inflammation ? monocytes

Q: acute pulpitis : neutrophils macrophage

Q:Chronic pulpitis : lymphocytes

Q: cells that are involved in allergic reactions – plasma cells + mast cells



TYPES OF CT

Name	Loose (alveolar) CT	Dense CT		Elastic CT	Reticular CT	Mucous CT	Adipose CT
		Regular	Irregular				
Description	Less fiber , more GS , more cells	Collagen +++ in dense bundles	Collagen ++ in dense bundles	Bundles of thick parallel elastic fibers	Very delicate + specialized	Mainly GAGs +few cells like fibroblasts + meshwork of collagen fibers	
Location	Beneath lining epithelia b/w muscle bundles around BVS and nerves	Tendons + ligaments	Dermis of skin + capsules	Walls of BVS (aorta)	Lymph node Spleen Liver	Umbilical cord beneath skin of embryo	Unicellular:throughout the body Multiocular : newborn babies and animals and around adrenal glands and neck region
Function	Supportive	Great resistance to pulling forces along one direction	Support +resist to forces from different directions	Expand and recoil - elasticity	Framework that provides support to tissue and organs		Lipid storage + metabolism Insulation under skin Cushioning pads around organs Multiocular : temp regulation
Histology	Mixture of all CT components	Fibroblasts are aligned along the bundles	Bundles are in random direction		Reticular fibers (collagen type 3) secreted by reticular cells similar to fibroblasts		Adipocytes + vascular loose CT



DENTISCOPE.ORG



ASK@DENTISCOPE.ORG



DENTISCOPE