

Done by:

HISTICS Team

Special thanks:

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Table of Contents

1.	Introduction	1
2.1	The Nucleus	2
2.2	The Cytoplasm	3
2.2.1	The Cell Membrane	4
2.2.1	Gap Junctions	5
2.2.2	Mitochondria	6
2.2.3	Endoplasmic Reticulum	6
2.2.4	Glogi Apparatus	6
2.2.5	Lysosomes	6
2.2.6	Proteasomes	7
2.2.7	Ribosomes	7
2.2.8	Centrioles	7
2.2.9	Cytoskeleton	7

1. Introduction

Histology: Microscopic anatomy, the study of tissues.

When studying any tissue, consider:

- 1) Appearance under light microscope (colored). Resolution power (R.P.): 0.25µm
- 2) Appearance under electron microscope (black & white). It differentiates electron-dense structures from electron-lucent structures.
 - R.P. of transmission E/M: 0.2 nm.
 - R.P. of scanning E/M: 10 nm

Resolution Power (R.P): The least distance between 2 particles at which they will appear separated.

Tissue Preparation:

Fixation	• By formalin			
Dehydration	• By alcohol			
Clearing	• By xylene			
Embedding	• By paraffin			
Sectioning	• By microtome to 5 -10 µm			
Mounting & Staining the Section				

<u>Staining</u>: Tissues are stained by water-soluble stains to differentiate the various cellular components. Types of stains for light microscope:

- 1) Hematoxyline: A base. It stains the acidic components of the cell dark blue. So they are called basophilic structures. Such as: DNA & RNA.
- 2) Eosin: An acid. It stains the basic components of the cell pink. So they are called acidophilic structures. Such as: regions of the cytoplasm.

2. The Cell Components:

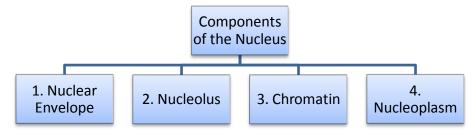
2.1 The Nucleus (Interphase):

It is the largest organelle in the cell. Usually, cells have 1 nucleus, but they could have 2 or more nucleuses.

- <u>Position</u>: It could be central, eccentric, peripheral or basal.
- Functions:
 - 1) The control center of the cell and it contains DNA.
 - 2) Synthesis and processing of RNA.
- Can be divided into several kinds according to shape, number, size, position or color.

• Blue-colored when stained with H&E and viewed under light microscope. It is basophilic due to the acidic structures within it.

• Doesn't produce protein, but contains protein imported from cytoplasm.



2.1.1 The Nuclear Envelope:

The nuclear envelope is composed of two unit membranes that fuse together at certain regions to form nuclear pores.

• Inner Nuclear Membrane: It is 6 nm thick and it faces the nuclear contents.

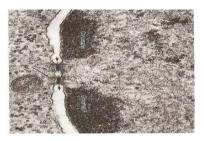
- It is in close contact with the nuclear laminas, which are intermediate filaments that organize and provide support to the lipid bilayer membrane.
- Perinuclear cisternea: The space between the inner and outer nuclear membranes.
- Outer nuclear membrane: It faces the cytoplasm and is continuous with the RER.

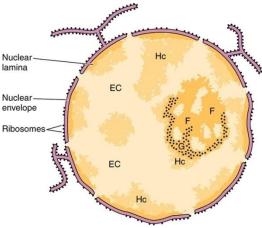
• <u>Nuclear Pores</u>: Interruptions in the nuclear envelope where inner and outer membrane fuse with each other. Their number depends on the activity of the cell.

- Pores are surrounded by non-membranous structure (glycoprotein).
- Nuclear pore + glycoprotein = Nuclear pore complex.
- The nuclear pore complex selectively guards passage through the pore.

• The envelope is surrounded by vimentin (intermediate filaments) and usually has ribosomes.

<u>Vimentin</u>: A thin, loose meshwork of intermediate filaments.





2.1.2 The Nucleolus:

The nucleolus is a dense non-membranous, basophilic structure within the nucleus.

- Synthesize rRNA.
- Contain: Proteins, rRNA and a small amount of inactive DNA.
- Contain a densely staining nucleolus-associated chromatin which is being transcribed into rRNA.
- Number, size, and shape relate to the activity of the cell.
- Have four distinctive areas (can be seen under E/M).

2.1.3 Chromatin:

Chromatin is a complex of proteins and DNA that represents uncoiled chromosomes of the interphase nucleus.

• <u>Euchromatin</u>: An active form of chromatin, representing DNA that is being transcribed into RNA. It is scattered through the nucleus.

- Invisible under L/M, but it appears under E/M as an unwound thread like material.
- <u>Heterochromatin</u>: condensed, inactive, peripheral.
 - Stain deeply & visible under L/M and appears under E/M as coarse granules.

2.1.4 Nucleoplasm (Nuclear Matrix):

- Consists of:
 - 1- <u>Interchromatin granules</u>: Located in clusters scattered among chromatin material and connected with each other by thin fibrils. They contain ribonucleoproteins (RNPs) and enzymes.
 - 2- Perichromatin granules: RNPs at the margins of heterochromatin.

2.2 The Cell Cytoplasm:

A) Inclusions:

Inclusions are non-living components that do not possess metabolic activity and are not bounded by membranes.

Glycogen	Lipids	Pigments	Crystals
•Carbohydrate storage, abundant in muscle cells.	•Triglyceride storage, in adipocytes.	•Hemoglobin, melanin, lipofuscin	•In sertoli cells and macrophages.

• Lipofuscin: In neurons and cardiac muscle cells. Membranous inclusions formed from the fusion of several residual bodies.

B) Organelles:

A. Membranous:

1. Cell membrane. 2. Mitochondria. 3. Endoplasmic Reticulum. 4. Golgi Apparatus. 5. Lysosomes. 6. Peroxisomes. 7. Preoteasomes. 8. Endosomes.

B. Non-membranous:

- 1. Ribosomes 2. Centrioles.
- 3. Cytoskeleton:
- 3.b. Intermediate filaments.
- 3.a. Microfilaments. 3.c. Microtubules

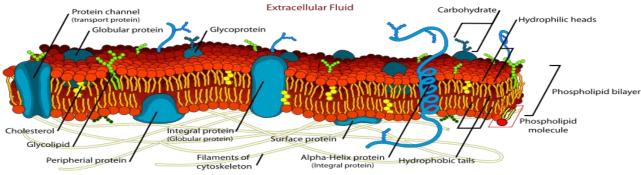
2.2.1 The Cell Membrane:

- Under L/M: Invisible.
- Under E/M: Trilaminar structure: two thin lines with intervening light area.
- It is formed of two leaflets: inner & outer. Each leaflet is a single layer of phospholipids and associated proteins (1:1).
- Types of proteins in cell membrane:
 - Integral proteins: Span the entire lipid bilayer.
 - Peripheral proteins: Loosely attached to cytoplasmic aspect of cell membrane.

• Glycocalyx (cell coat): Carbohydrate chains that are attached to proteins (glycoprotein) or phospholipids molecules (glycolipid). Could be seen by E/M.

• Functions:

- Protection of the cell. 0
- 0 Cell to cell recognition.
- Functions of cell membrane:
 - Endocytosis (Phagocytosis (cell eating) and pinocytosis(cell drinking)). -
 - Control the transport of materials in and out of cell. _
 - Cell to cell recognition. -
 - Protection of the cell.
 - Formation of cilia, flagella and microvilli.



2.2.1.1 Microvilli:

- Cylindrical, membrane-bound cytoplasmic projections of the striated border of the intestinal absorptive cells (invisible by L/M) and the brush border of the kidney proximal tubules (visible by L/M).
- Function: Increase surface area for transport and absorption.
- Contain core of actin filaments (microfilaments).
- Stereosilia: Long microvilli found in epididymis and hair cells of cochlea. They are not motile.

2.2.1.2 Cilia:

- Motile hair-like projections (visible with L/M) surrounding cell membrane.
- <u>Function</u>: Propelling mucus and other substances over the surface.
- The core of the cilia consists of microtubules (axoneme).
- Composed of 9 doublets of microtubules (9+2) and two centrally placed microtubules (singlets).
- Cilia is attached to the basal body which is similar to centrioles (9 triplets) and no singlets.
- Pairs are attached by dynein molecules.

Lateral Membrane Specialization (Junctional Complex):

1. Occluding or tight junctions (Zonulae Occludentes):

- Formed by the fusion of transmembrane proteins of adjacent cell membranes.
- Forms impermeable barrier, apically located, belt-like junctions.
- Functions:
 - 1. Prevents the movement of membrane proteins.
 - 2. Fuse membranes to prohibit water-soluble molecules from passing.

2. Zonulae Adherentes:

• Just basal to tight junctions & encircle the cell.

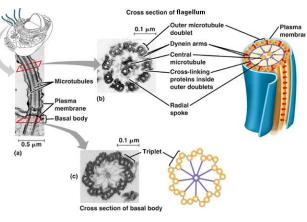
• The intercellular space between joining cells is occupied by the extracellular cadherins (Ca dependent integral proteins) that attach to intracellular actin filaments.

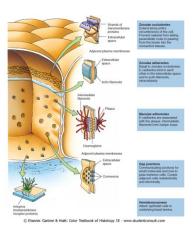
3. Desmosomes (Maculae Adherents):

- Weld-like junctions that appear randomly along the lateral cell membrane.
- They are formed of attachment plaques on the cytoplasmic aspect of adjoining cells.
- The intermediate filaments of both cells are inserted in these plaques forming hairpin turn to disperse the shearing forces on the cell.
- The intercellular space contains filamentus materials (a family of cadherins).

Gap (nexus or communicating) junctions:

- Widespread in epithelial tissues, cardiac muscle, smooth muscle and neurons.
- They are narrow gaps (2nm) to communicate with adjacent cells.
- They are built by transmembrane proteins that have aqueous pores (connetion).
- They are regulates (can open or close).
- Function: Cellular sharing of molecules.







2.2.2 The Mitochondria:

Flexible, rod-shaped organelles (L/M: visible with stain).

• <u>Function</u>: Produce ATP through oxidative phosphorylation.

• Composed of two membranes: <u>Inner folded membrane</u> and <u>outer smooth membrane</u>, between them is the intermembrance space.

- <u>Inner membrane</u>: Composed of folds (cristae) that increase the surface of the area, number of cristae is related to the energy requirement of the cell.
- Inner membrane encloses a space called matrix or intercristal space.
- Matrix: A space filed with a dense fluid composed of at least 50% proteins.
- Components of the matrix: Circular DNA, tRNA, mRNA.
- They are self-replicating.

2.2.3 The Endoplasmic Reticulum (ER):

The ER is system of interconnected tubules and vesicles whose lumen is called cistern.

- Largest membranous system of the cell.
- It has two components:
 - 1. Smooth Endoplasmic Reticulum (SER):
 - Smooth surfaced tubules and occasional flattened membrane-bound vesicles.
 - Abundant in cells active in synthesis of fats and cells that do detoxification.
 - In skeletal muscle cells (SR) known as sarcoplasmic reticulum which regulates calcium in cytoplasm.
 - 2. Rough Endoplasmic Reticulum (RER):
 - Rich in cells that synthesis proteins.
 - Continuous to perinuclear cistern.
 - Ribosomes bind to the surface of RER at integral proteins.
 - Function: Performs post-transitional modifications of these proteins.

2.2.4 Glogi Apparatus:

• Composed of one or more series of flattened, slightly curved membrane-bounded cisternae (golgi stack) and it has three levels of cisernae:

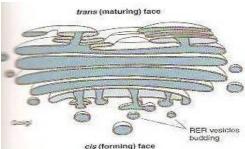
- 1. Cis face: Closest to RER, convex in shape and is the entry face.
- 2. Medial face (intermediate face).
- 3. Trans face : Concave in shape, considered to be the exit face.
- Functions:
 - 1. Synthesis of carbohydrates.
 - 2. Modification and sorting of protein.
 - 3. Formation of lysosomes.

2.2.4 Lysosomes:

• Small membrane-bounded organisms that contain acid hydrolases as sulfatases, proteases, nucleases, lipases and glycosidases.

• <u>Function</u>: Digest macromolecules, phagocytosed microorganism, cellular debris, excess of senescent organelles (mitochondria, RER).

• The small, soluble end products are either reused by the cell or exported into the extracellular space (Form lipofucin pigment in long-living cells).



2.2.5 Peroxisomes:

- Contain 40 oxidative enzymes such as urate oxidase & catalase.
- Function: Catabolism of long fatty acids.

2.2.6 Proteasomes:

Proteasomes are small organelles composed of enzyme complexes that are responsible for proteolysis (protein digestion).

2.2.7 Ribosomes:

Ribosomes are small non-membranous particles, composed of proteins and rRNA, which are responsible for protein synthesis.

- They are formed of 2 subunits (small and large), individually until synthesis begins.
- Found freely in the cytoplasm (free ribosomes), or attached to RER (attached ribsomes)
 - Free ribosomes form proteins that are used within the cell.
 - Attached ribosomes form proteins that are expelled from the cell or used within the cell membrane.
- Few ribosomes can join together by mRNA forming polyribosomes.

2.2.8 Centrioles:

Centrioles are cylindrical, non-membranous structures located near the nucleus. (2 perpendicular in each cell).

- Formed of 9 triplets, each formed of 1 complete and 2 incomplete microtubules fused together.
- Important during cell division and for the formation of cilia and flagella.

2.2.9 Cytoskeleton:

- Three-dimensional meshwork of protein filaments.
- <u>Functions</u>: Maintenance of cellular morphology and participation in cellular motion.
- Consist of:
 - 1. Thin Filaments (microfilaments):
 - Contractile.
 - 6nm thick.
 - Myosin filaments are thicker (15nm) and are usually attached to actin especially in muscles.
 - 2. Intermediate Filaments:
 - \bullet Between thin and thick filaments (8 to 10 nm).
 - Non-contractile.
 - Functions: Provide structural support to for the cell and anchor the nucleus in place.
 - Examples: keratin, desmin, vimentin.
 - 3. <u>Microtubules:</u>
 - Long straight, rigid, hollow cylinder structural (25nm).
 - Dynamic structures.
 - <u>Functions</u>: Provide rigidity, establish intercellular compartments and form the core of cilia and flagella.