The Cell

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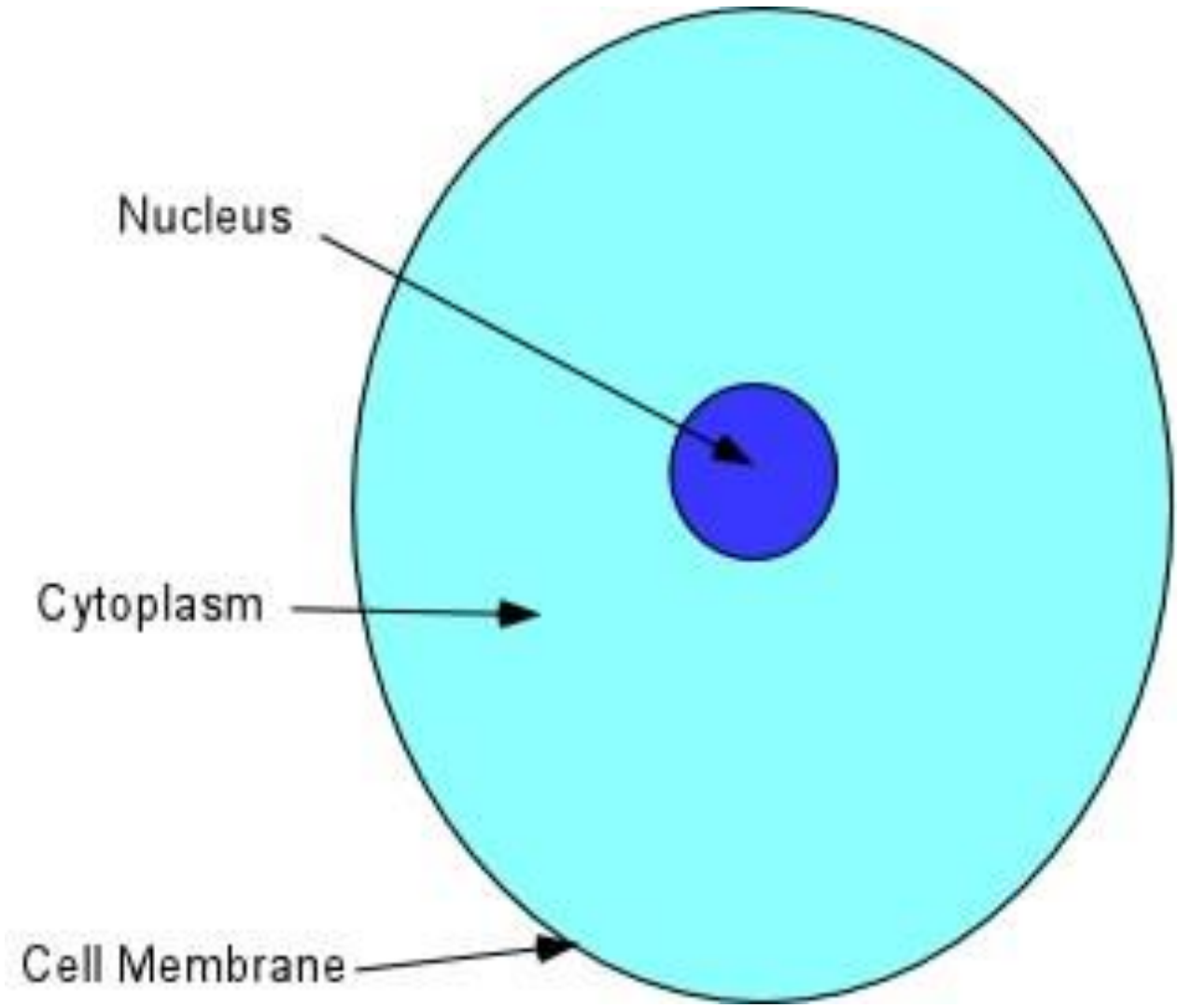
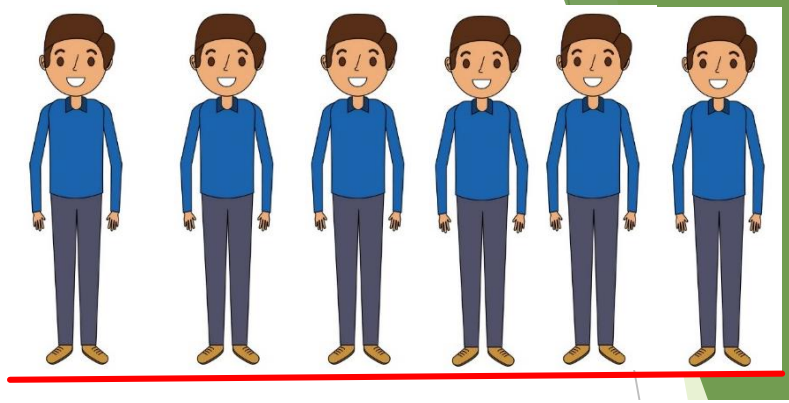
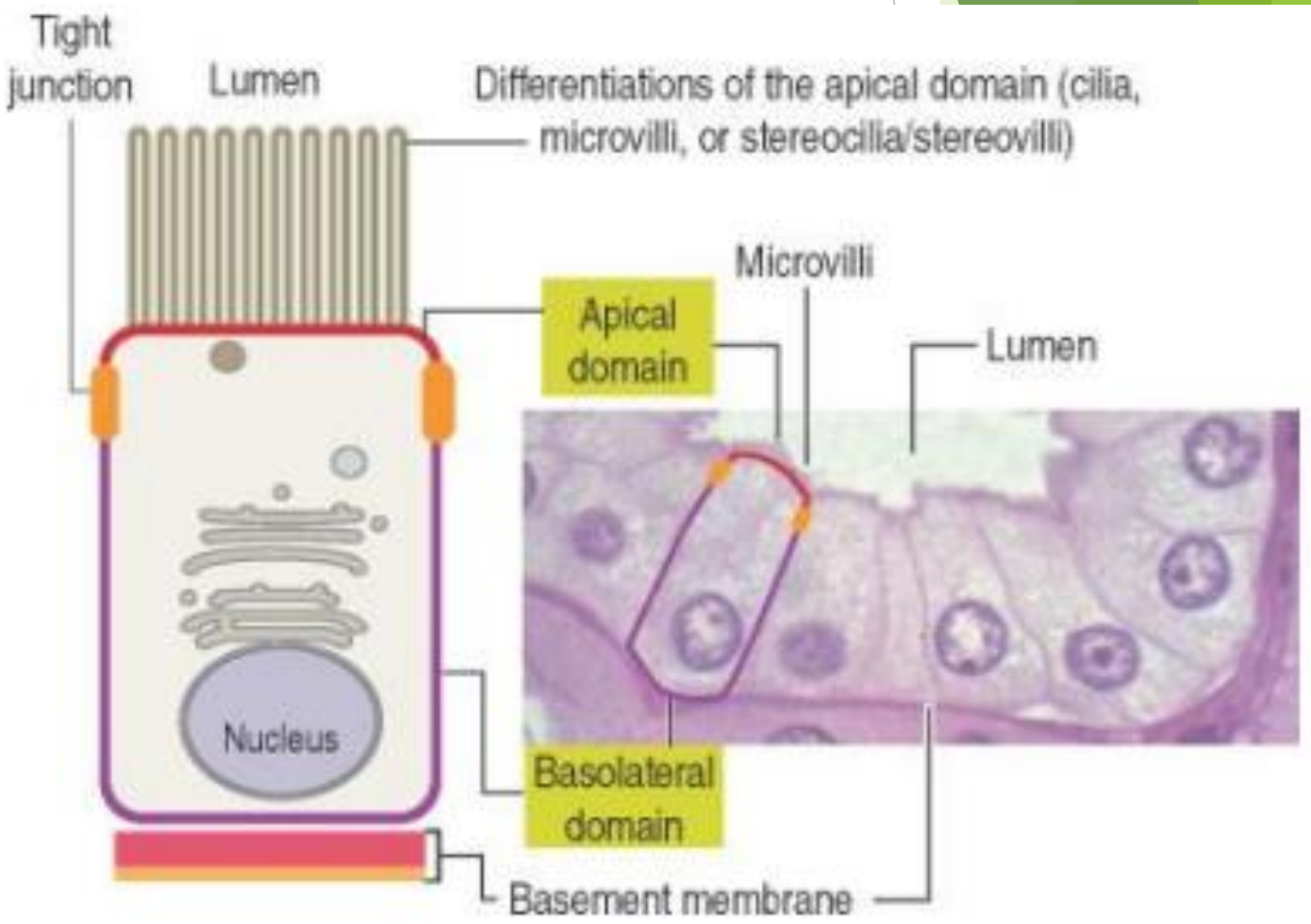

Nucleus
Cytoplasm
Cell Membrane

Cell polarity



- Many cells show polarity, meaning different areas of the cell have different structures
- The most-studied polarity is in epithelial cells, they have
  - Apical domain
  - Basal (basolateral) domain



The Plasma Membrane

What is the plasma membrane?

- The **plasma membrane** (**cell membrane** or plasmalemma) that envelops every eukaryotic cell.

- It functions as a selective barrier regulating the passage of materials into and out of the cell and facilitating the transport of specific molecules.

IMPORTANT

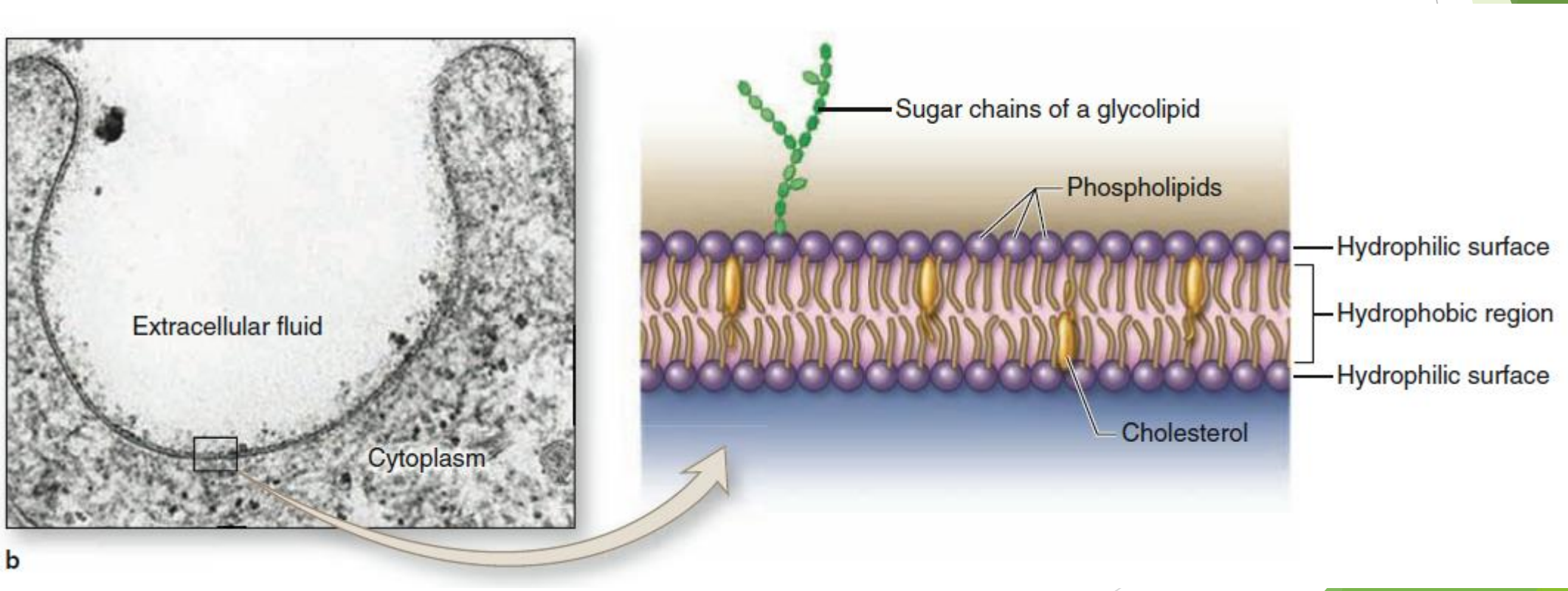
- Membranes range from 7.5 to 10 nm in thickness and consequently are visible only in the electron microscope (can NOT be resolved by the light microscope). They appear as a trilaminar unit in TEM.
- The line between adjacent cells sometimes seen faintly with the light microscope consists of plasma membrane proteins plus extracellular material, which together can reach a dimension visible by light microscopy.

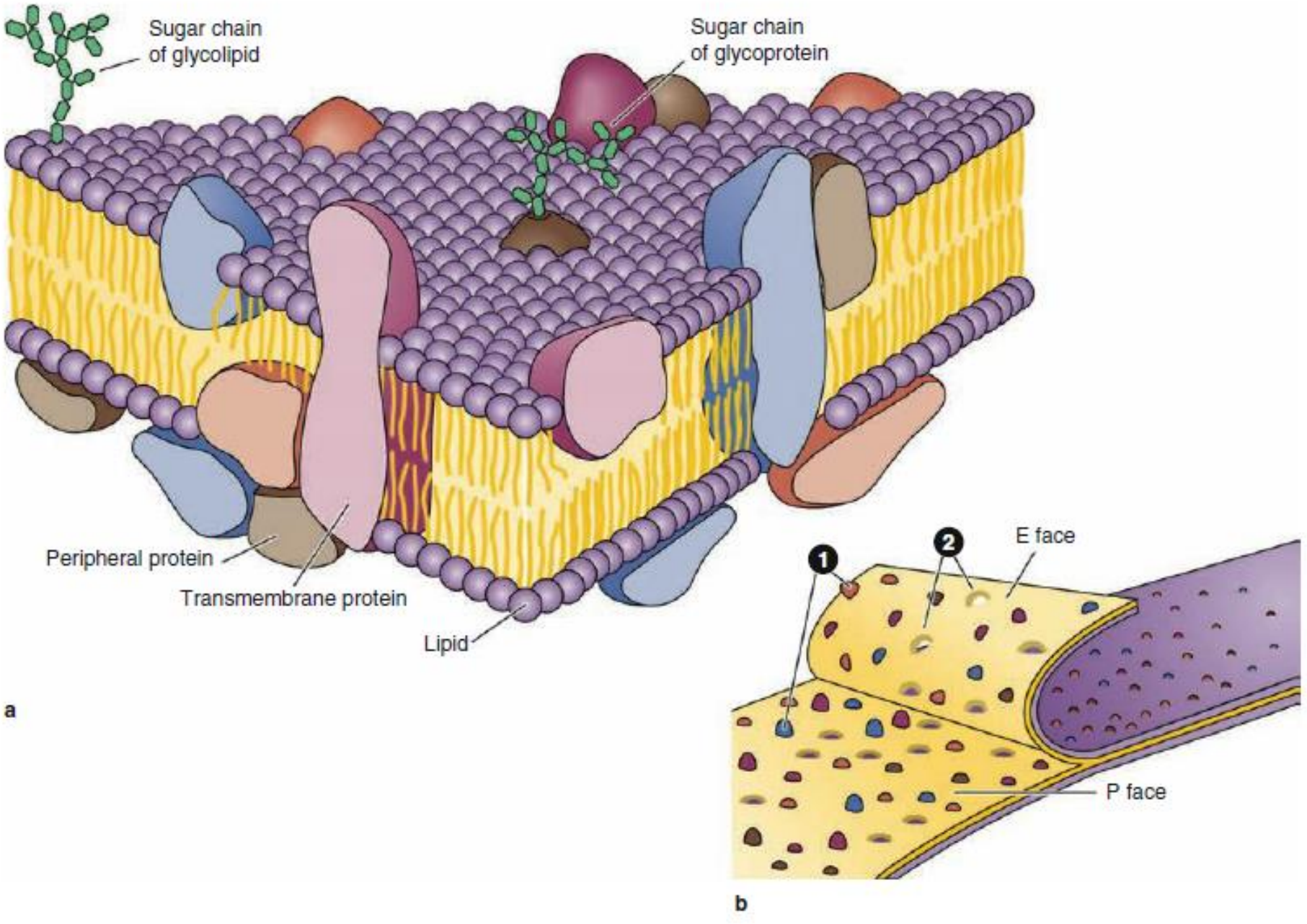
Components of plasma membrane

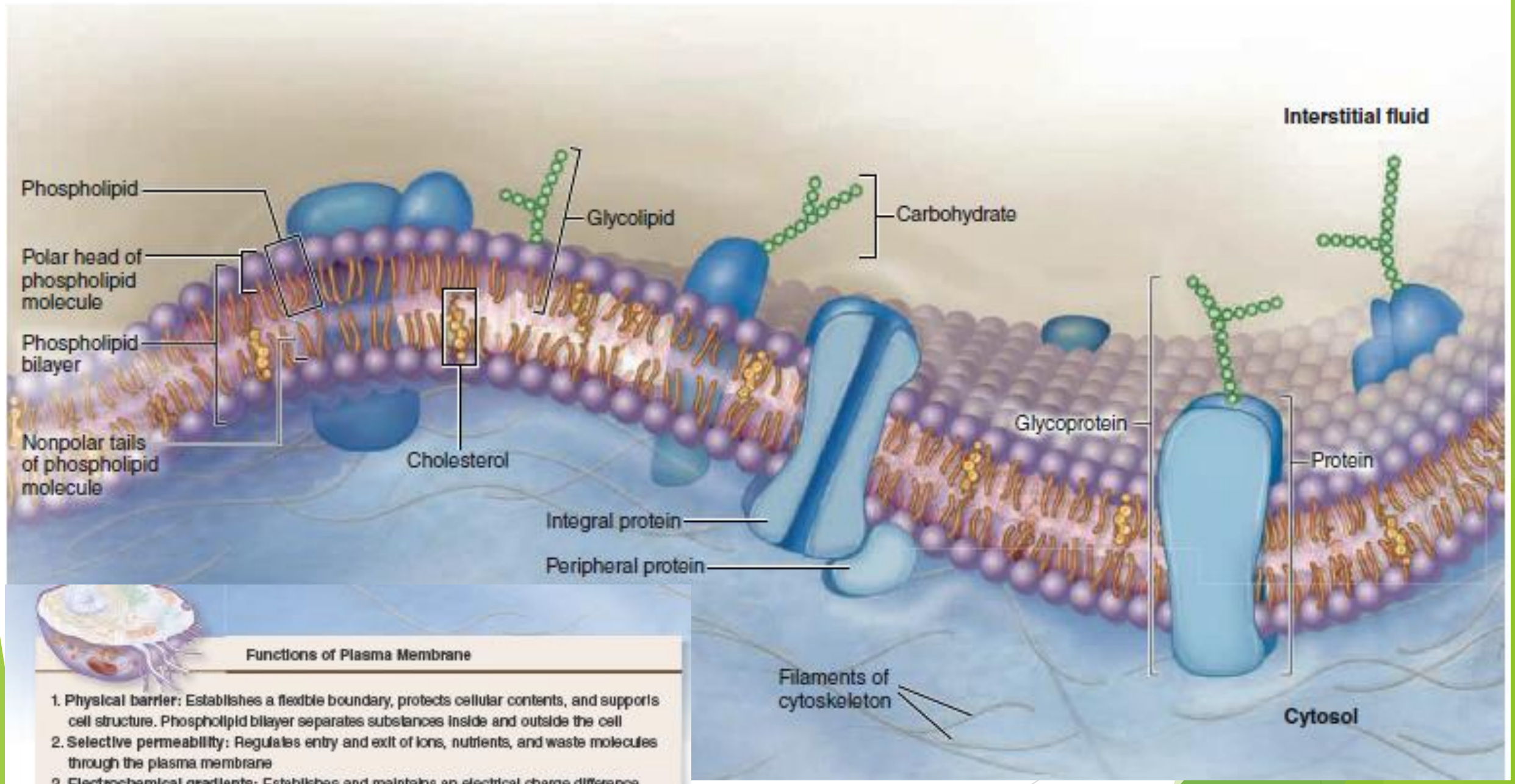
- Phospholipids
- Cholesterol
- Proteins
  - Integral: incorporated directly within the lipid bilayer
  - Peripheral: bound to one of the two membrane surfaces, particularly on the cytoplasmic side
- Oligosaccharide (carbohydrate) chains linked to many of the phospholipid (to form glycolipids) and protein (to form glycoproteins) molecules.

Structure of plasma membrane

- Model: Mosaic phospholipid bilayer

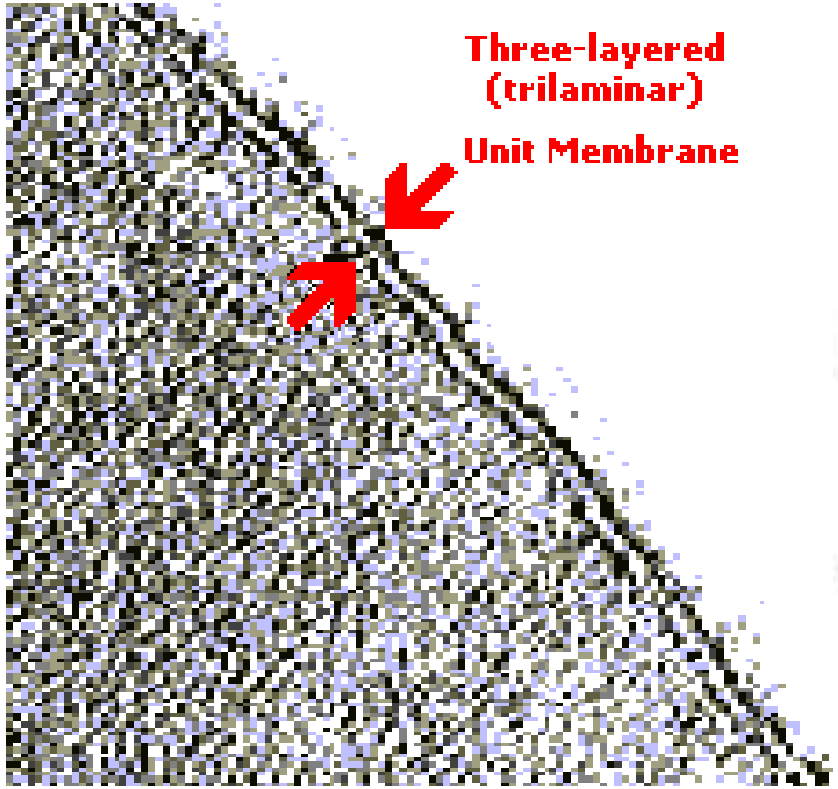


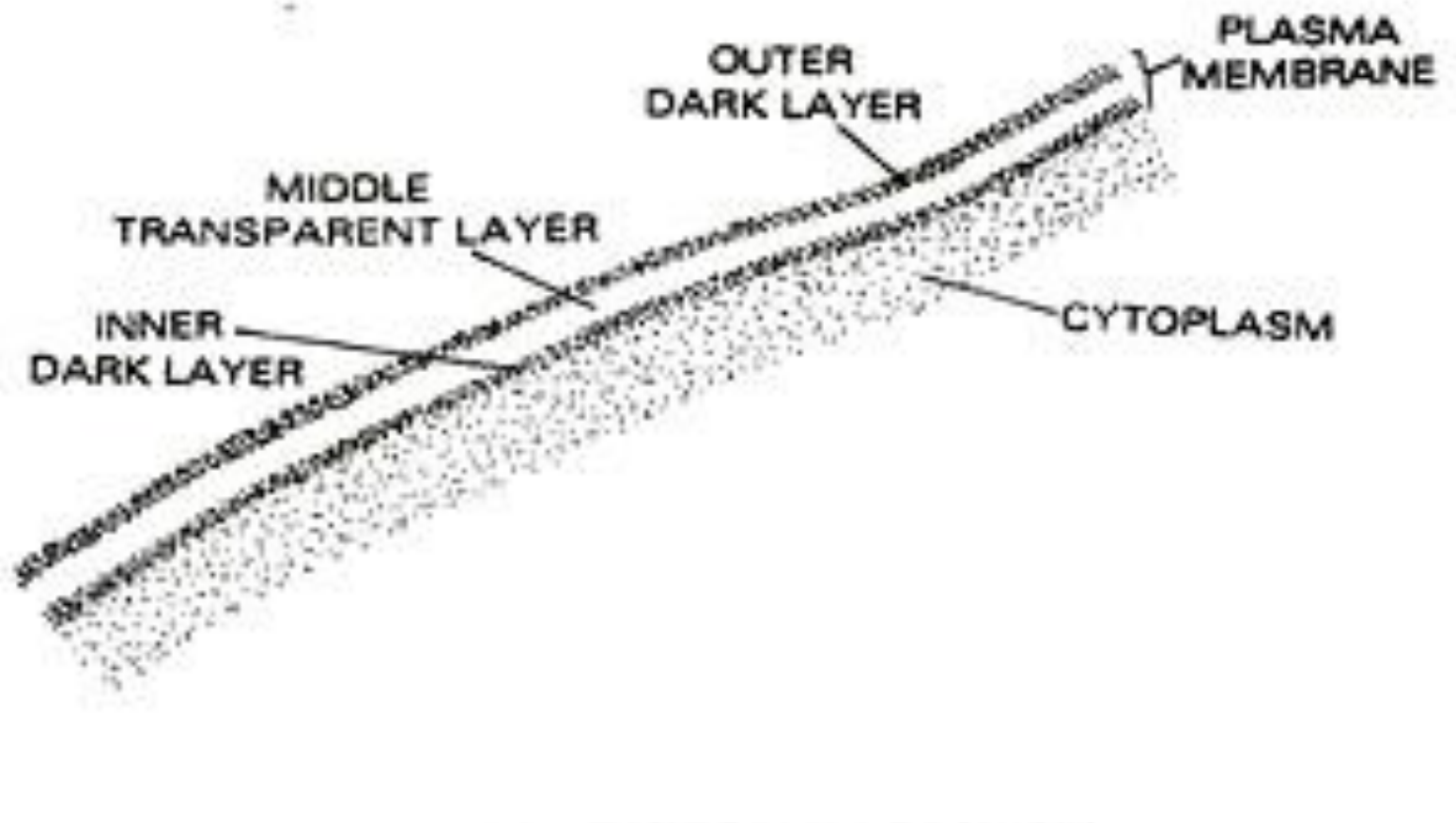

Sugar chain
of glycolipid
Sugar chain
of glycoprotein
Peripheral protein
Transmembrane protein
Lipid
a
1
2
E face
P face
b



Functions of Plasma Membrane

1. **Physical barrier:** Establishes a flexible boundary, protects cellular contents, and supports cell structure. Phospholipid bilayer separates substances inside and outside the cell
2. **Selective permeability:** Regulates entry and exit of ions, nutrients, and waste molecules through the plasma membrane
3. **Electrochemical gradients:** Establishes and maintains an electrical charge difference across the plasma membrane
4. **Communication:** Contains receptors that recognize and respond to molecular signals


Three-layered
(trilaminar)
Unit Membrane


PLASMA
MEMBRANE
OUTER
DARK LAYER
MIDDLE
TRANSPARENT LAYER
INNER
DARK LAYER
CYTOPLASM

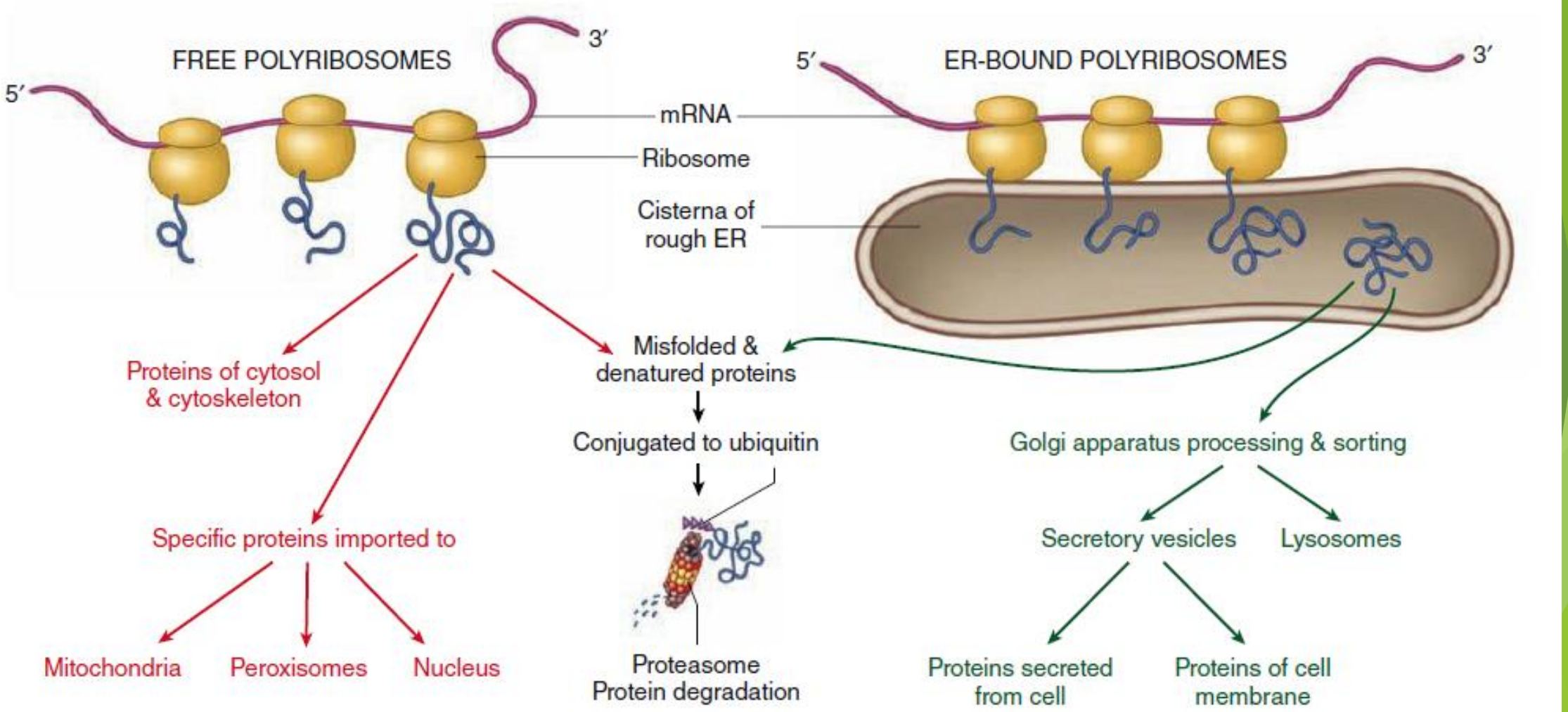
The Cytoplasm

Overview

- Inside the cell membrane, the fluid cytoplasm (or **cytosol**) bathes metabolically active structures called **organelles**, which may be membranous (such as mitochondria) or nonmembranous protein complexes (such as ribosomes).
- Most organelles are positioned in the cytoplasm by movements along the polymers of the **cytoskeleton**, which also determines a cell's shape and motility.

Ribosomes

- **Ribosomes** are macromolecular machines, about 20 × 30 nm in size, which assemble polypeptides (proteins) from amino acids in a sequence specified by mRNA.
- They can be free in the cytosol or bound to the rough endoplasmic reticulum
- During protein synthesis many ribosomes typically bind the same strand of mRNA to form larger complexes called **polyribosomes**, or **polysomes**

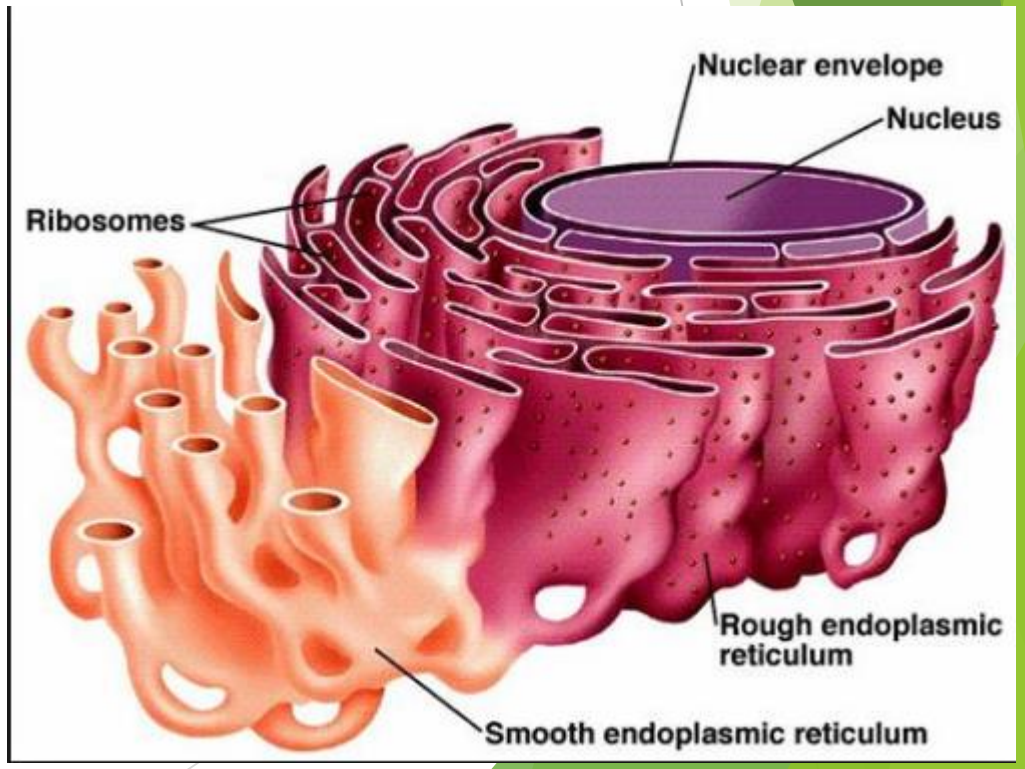

FREE POLYRIBOSOMES
5′
3′
mRNA
Ribosome
Cisterna of rough ER
ER-BOUND POLYRIBOSOMES
5′
3′
Proteins of cytosol & cytoskeleton
Misfolded & denatured proteins
Conjugated to ubiquitin
Golgi apparatus processing & sorting
Specific proteins imported to
Secretory vesicles
Lysosomes
Mitochondria
Peroxisomes
Nucleus
Proteasome
Protein degradation
Proteins secreted from cell
Proteins of cell membrane

Differences between free and bound ribosomes

- Free ribosomes synthesize cytosolic and cytoskeletal proteins and proteins for import into the nucleus, mitochondria, and peroxisomes.
- Bound ribosomes synthesize proteins that are to be incorporated into membranes, stored in lysosomes, or eventually secreted from the cell.
  - The proteins produced by these ribosomes are segregated during translation **into** the interior of the ER's membrane cisternae.

Endoplasmic Reticulum (ER)

- The **endoplasmic reticulum** is an anastomosing network of intercommunicating channels or **cisternae** formed by a continuous membrane network.
- Of two types:
  - Rough endoplasmic reticulum (rER)
  - Smooth endoplasmic reticulum (sER)

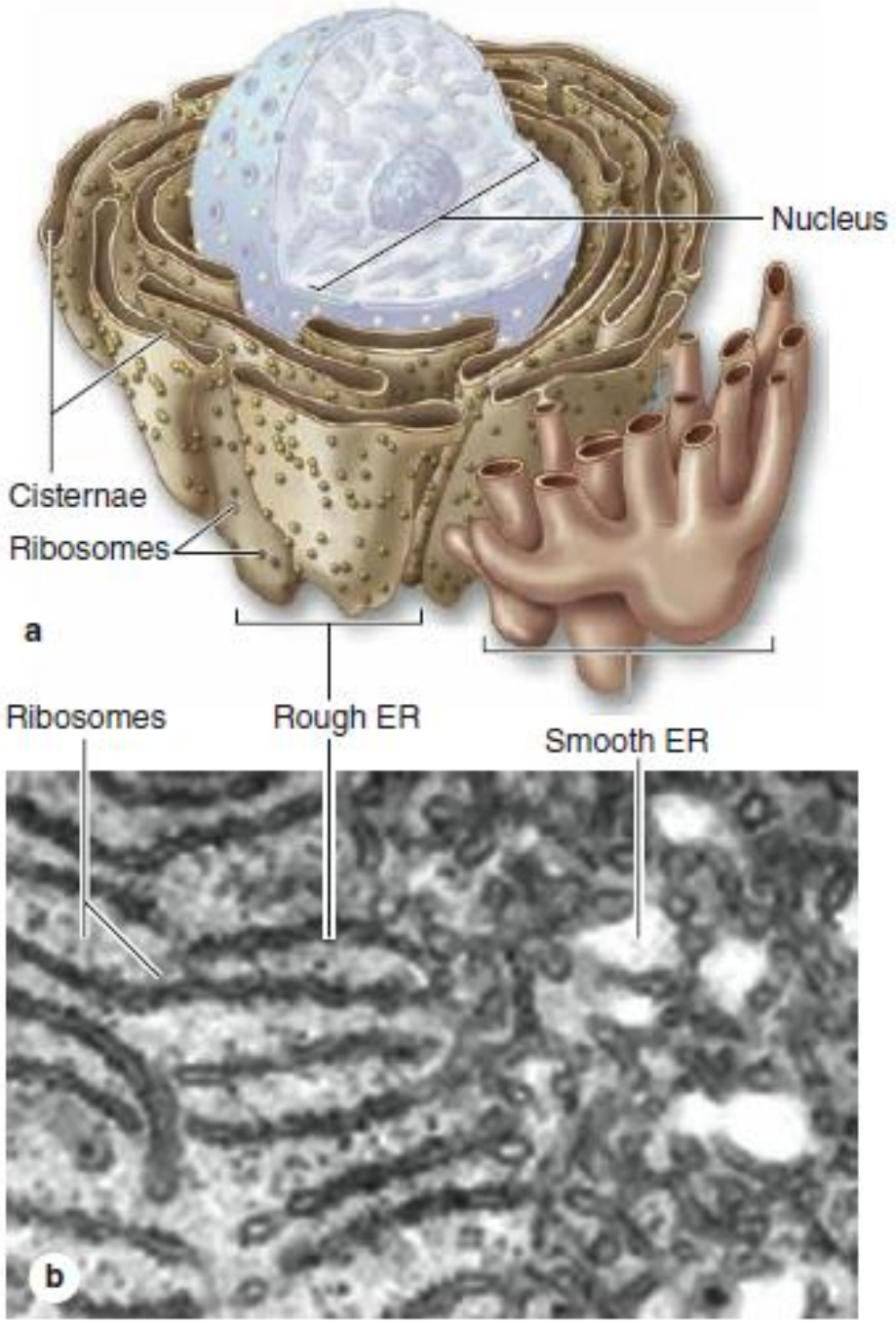


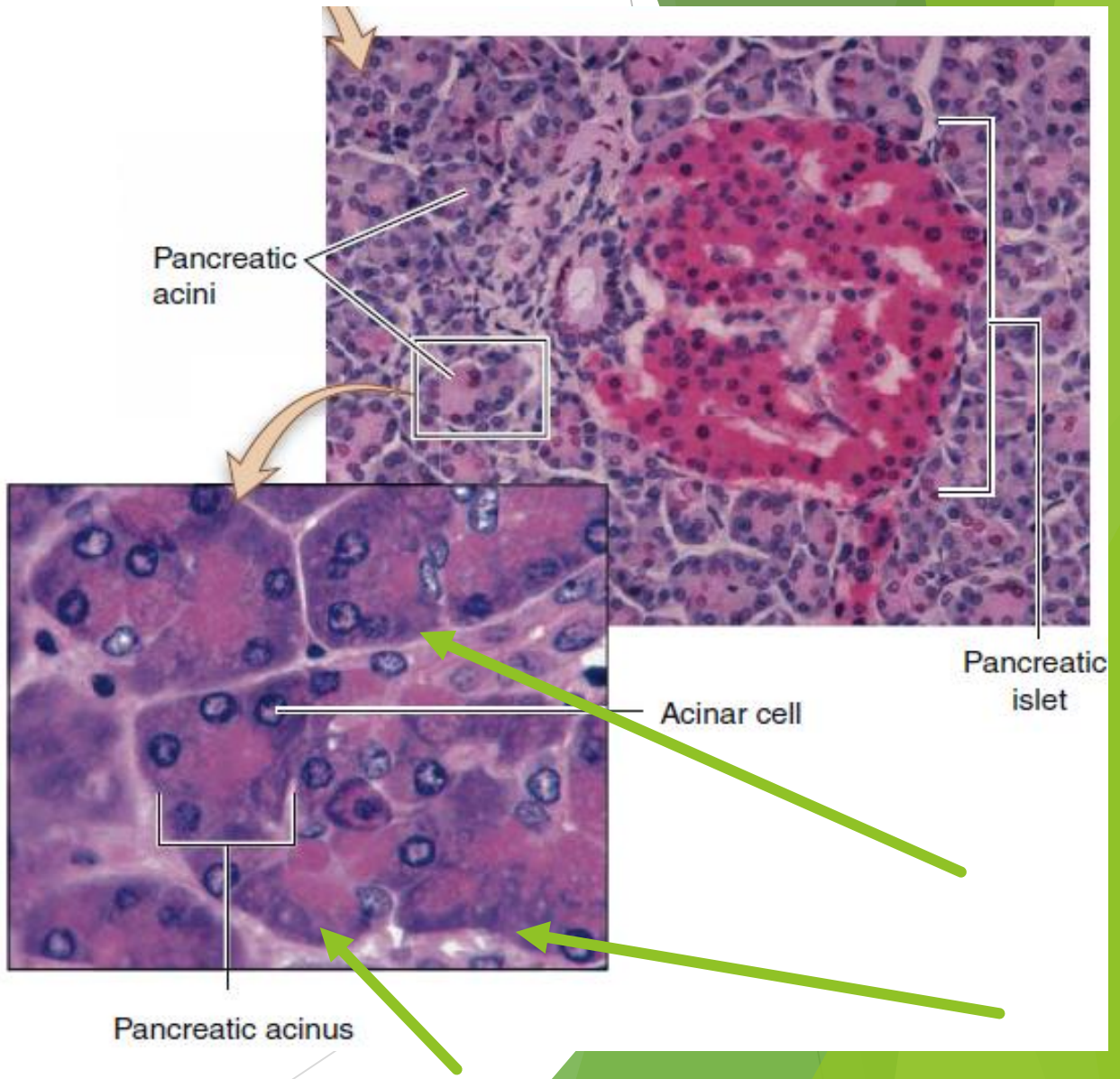
Functions of ER

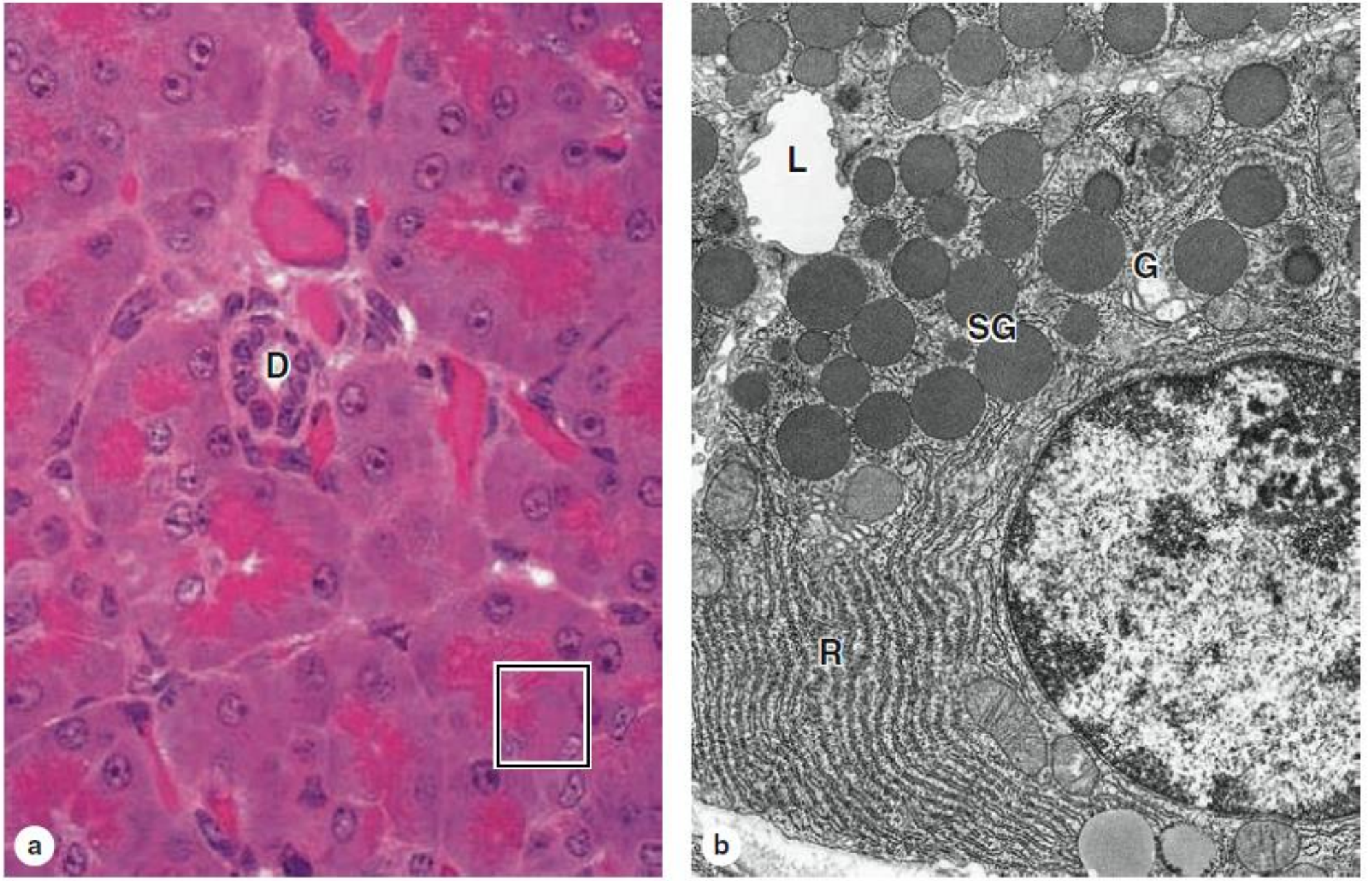
- **Synthesis:** Provides a place for chemical reactions
  - sER is the site of lipid synthesis and carbohydrate metabolism
  - rER synthesizes proteins for secretion, incorporation into the plasma, membrane, and as enzymes within lysosomes
- **Transport:** Moves molecules through cisternal space from one part of the cell to another, sequestered away from the cytoplasm
- **Storage:** Stores newly synthesized molecules, sER stores Ca^{++}
- **Detoxification:** sER detoxifies both drugs and alcohol

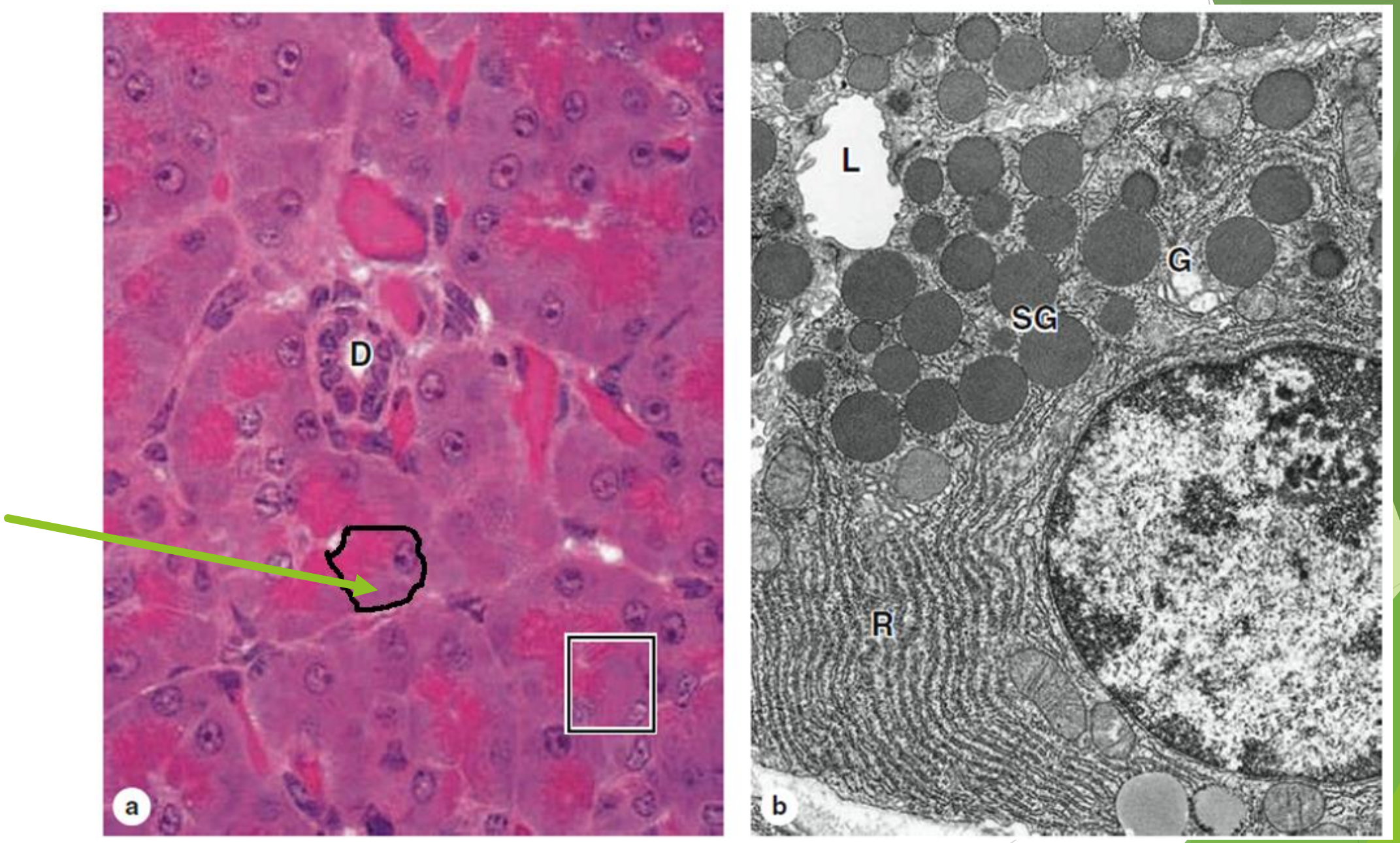
Histological appearance

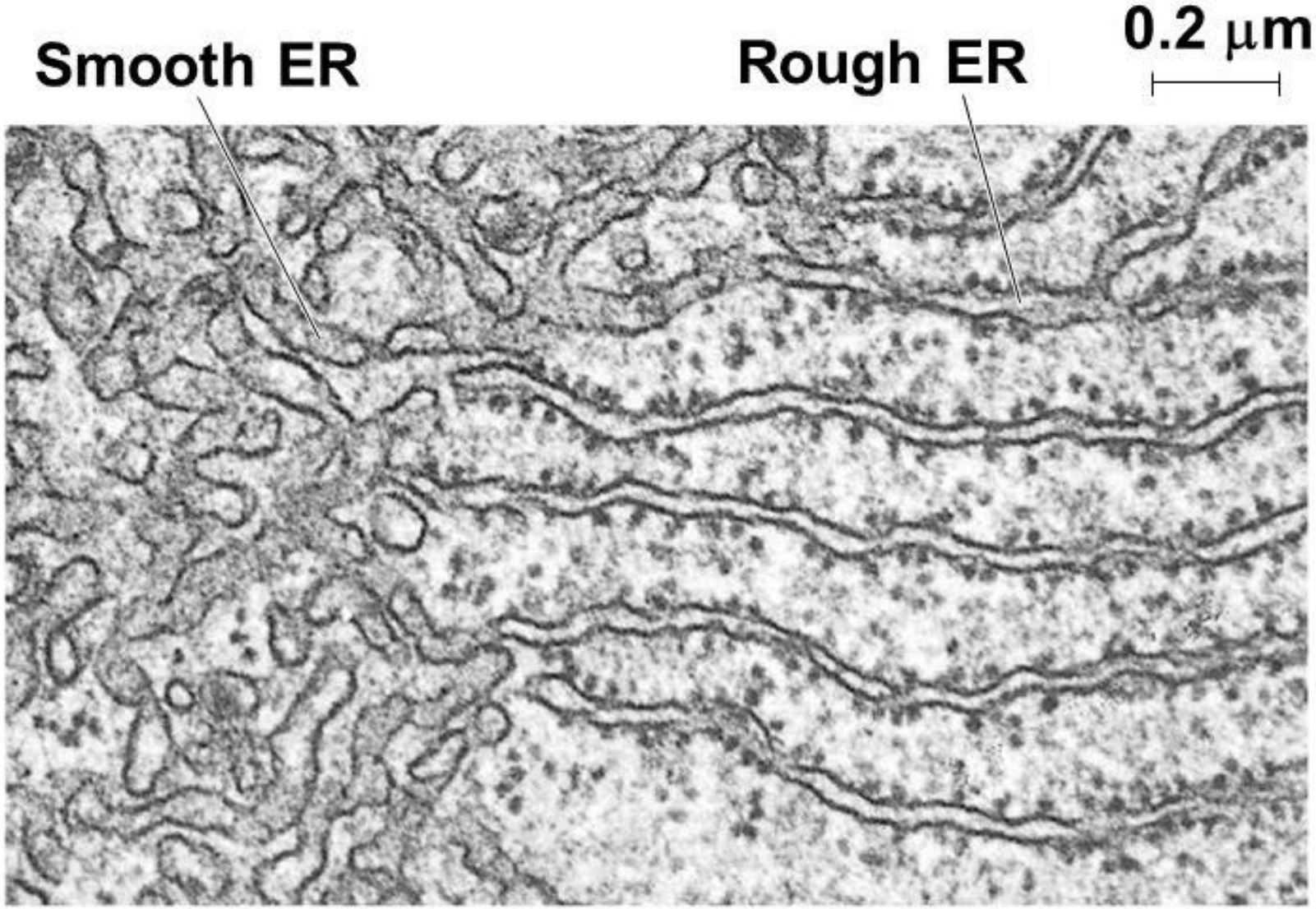
- rER:
  - Light microscopy: Intense basophilia (blue to purple on H & E)
  - Electron microscopy: Appears as interconnected flat cisternae and tubules associated with ribosomes
- sER:
  - Light microscopy: can not be seen under LM
  - Electron microscopy: Appears as interconnected tubules with various shapes and sizes and not stack of flattened cisternae not associated with ribosomes


Nucleus
Cisternae
Ribosomes
a
Ribosomes
Rough ER
Smooth ER
b


Pancreatic acini
Pancreatic islet
Acinar cell
Pancreatic acinus

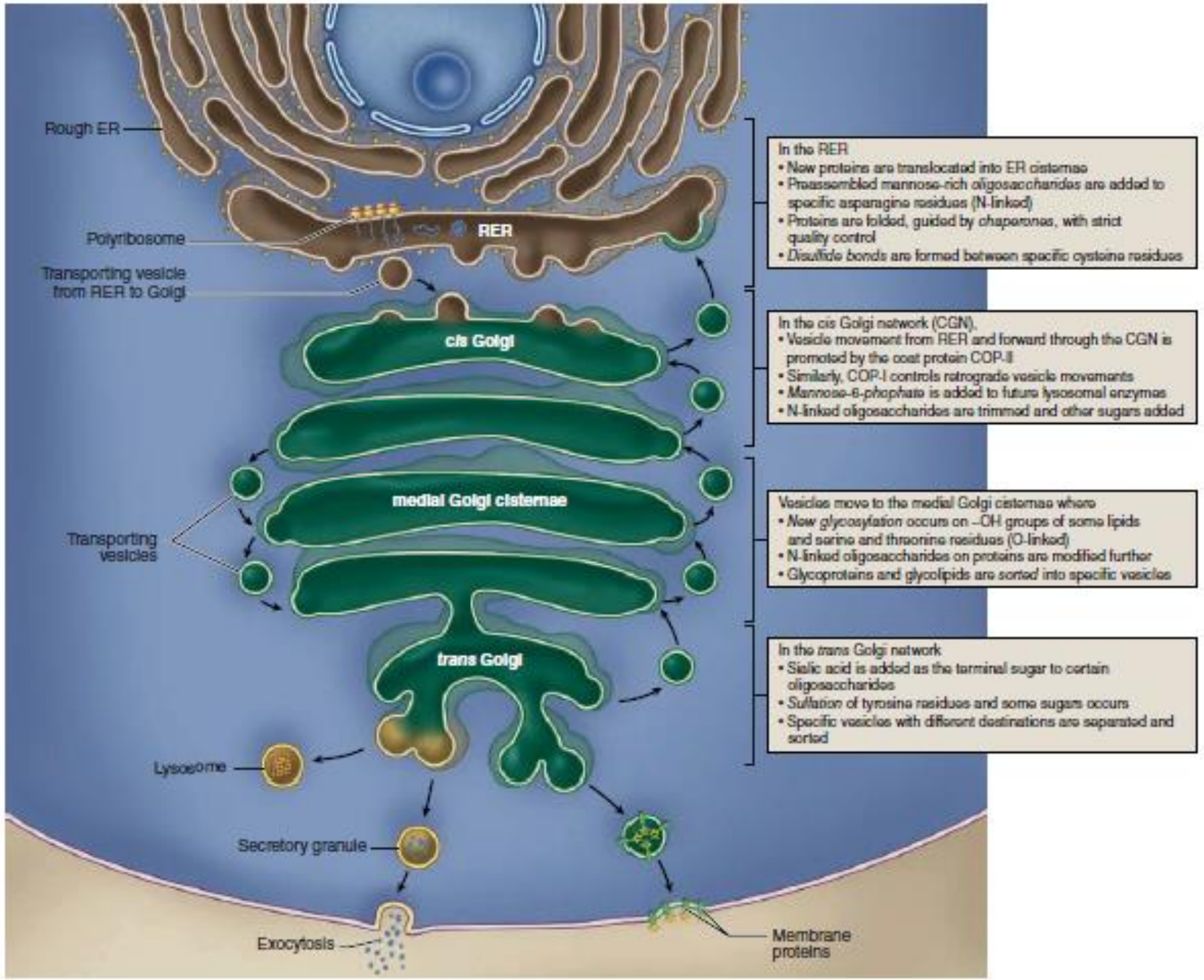

D
a
L
G
SG
R
b


D
a
L
G
SG
R
b


Smooth ER
Rough ER
0.2 μm

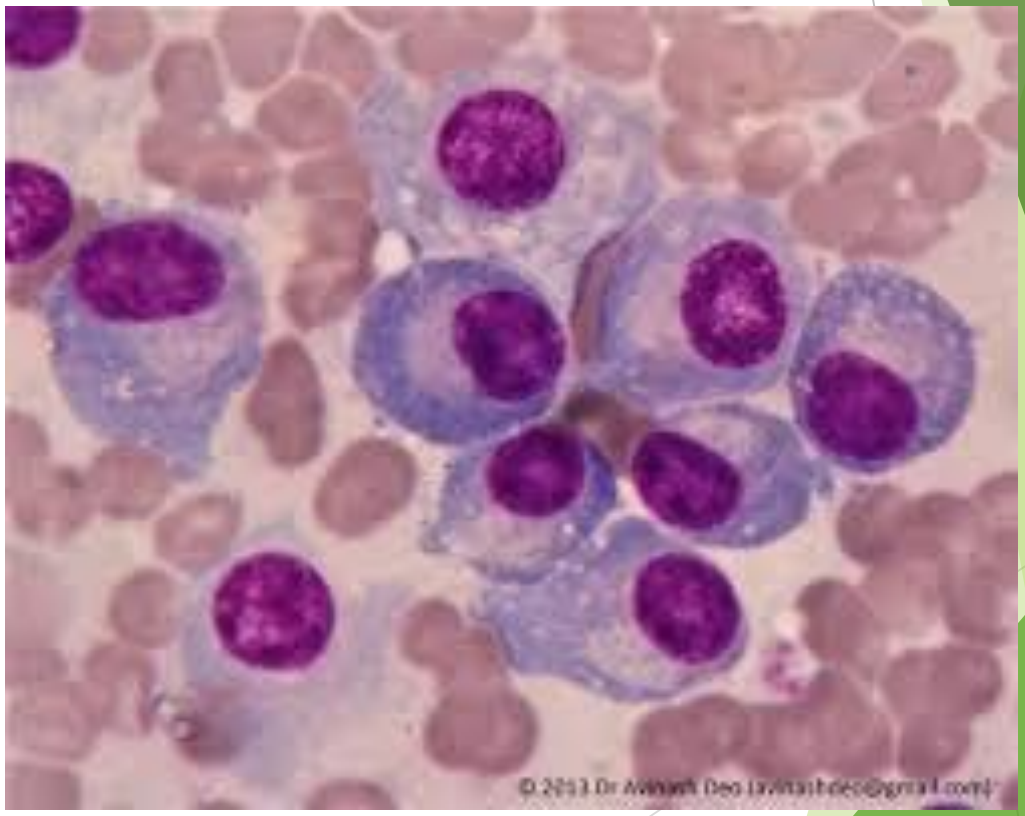
Golgi Apparatus

- **Golgi apparatus**, or Golgi complex, completes posttranslational modifications of proteins produced in the rER and then packages and addresses these proteins to their proper destinations.
- Material moves from the rER cisternae to the Golgi apparatus in small, membrane-enclosed carriers called **transport vesicles**
- Has two sides (ends):
  - Receiving end (cis): receives transport vesicles
  - Shipping end (tran): ships secretory vesicles


Rough ER
Polyribosome
RER
Transporting vesicle from RER to Golgi
cis Golgi
medial Golgi cisternae
Transporting vesicles
trans Golgi
Lysosome
Secretory granule
Exocytosis
Membrane proteins
In the RER
• New proteins are translocated into ER cisternae
• Preassembled mannose-rich oligosaccharides are added to specific asparagine residues (N-linked)
• Proteins are folded, guided by chaperones, with strict quality control
• Disulfide bonds are formed between specific cysteine residues
In the cis Golgi network (CGN),
• Vesicle movement from RER and forward through the CGN is promoted by the coat protein COP-II
• Similarly, COP-I controls retrograde vesicle movements
• Mannose-6-phophate is added to future lysosomal enzymes
• N-linked oligosaccharides are trimmed and other sugars added
Vesicles move to the medial Golgi cisternae where
• New glycosylation occurs on –OH groups of some lipids and serine and threonine residues (O-linked)
• N-linked oligosaccharides on proteins are modified further
• Glycoproteins and glycolipids are sorted into specific vesicles
In the trans Golgi network
• Sialic acid is added as the terminal sugar to certain oligosaccharides
• Sulfation of tyrosine residues and some sugars occurs
• Specific vesicles with different destinations are separated and sorted

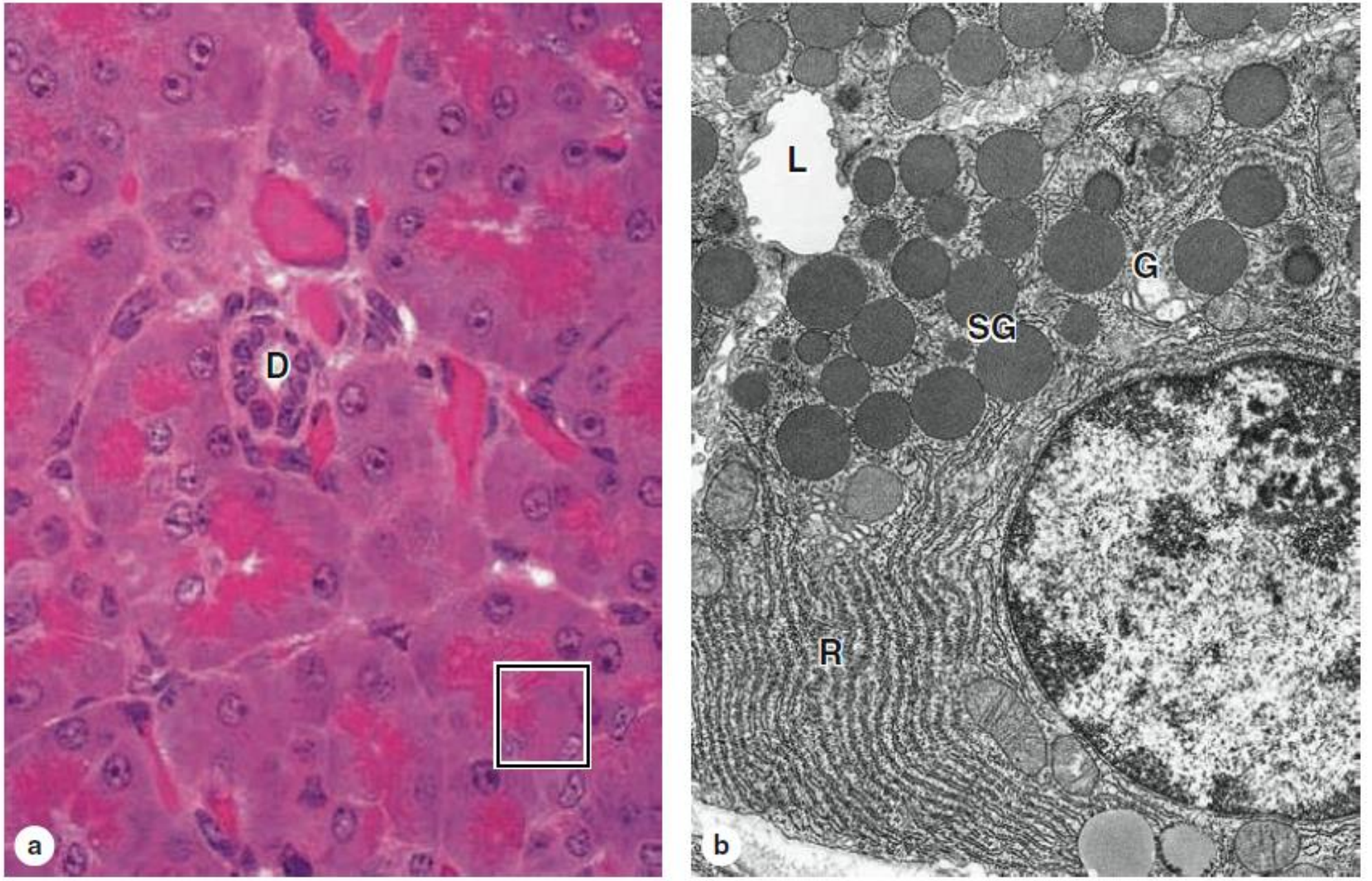
Histological appearance

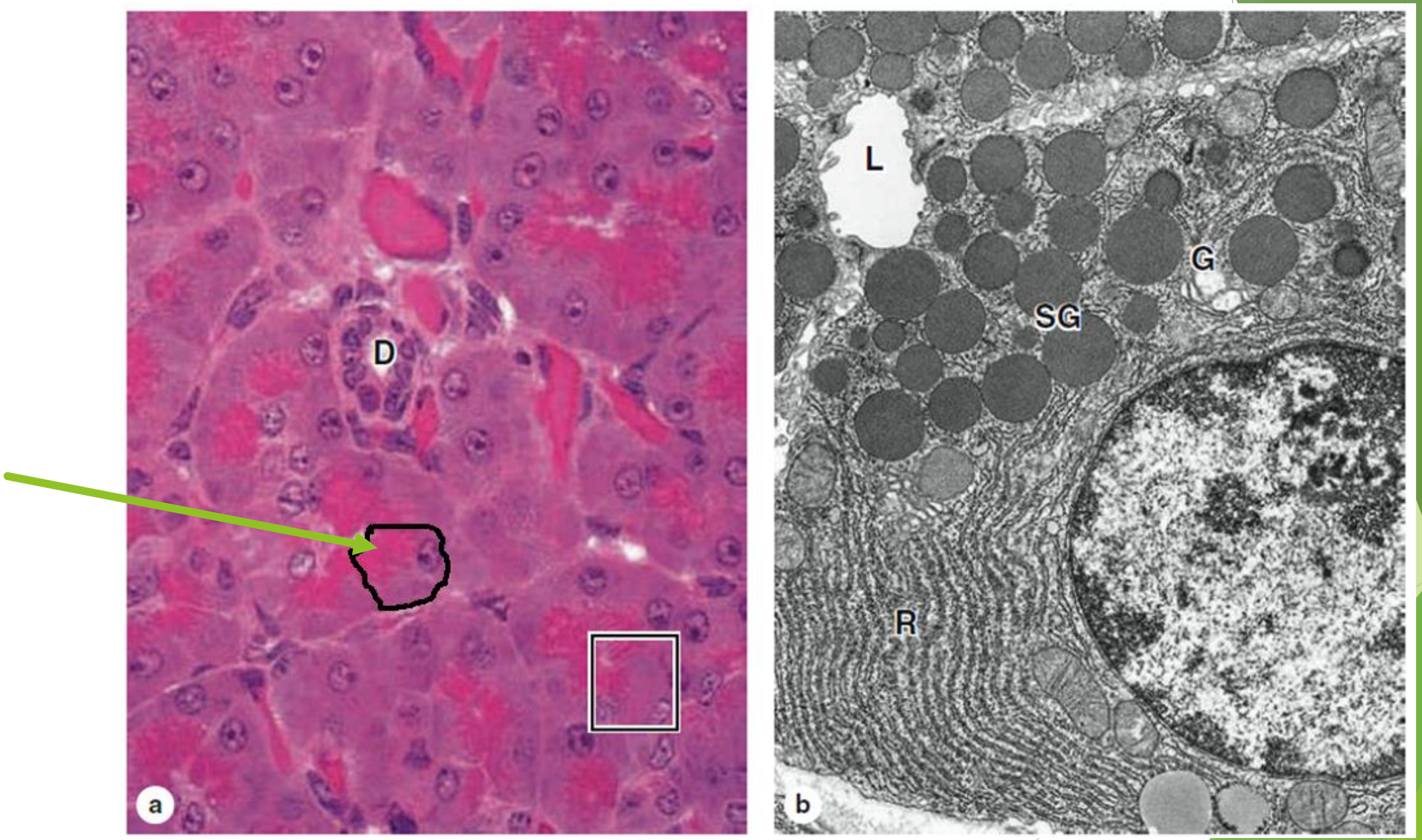
- Golgi cannot be seen in H & E staining.
- In highly active cells, with prominent golgi apparatus, it gives a negative image (as if an empty space)



Secretory Granules

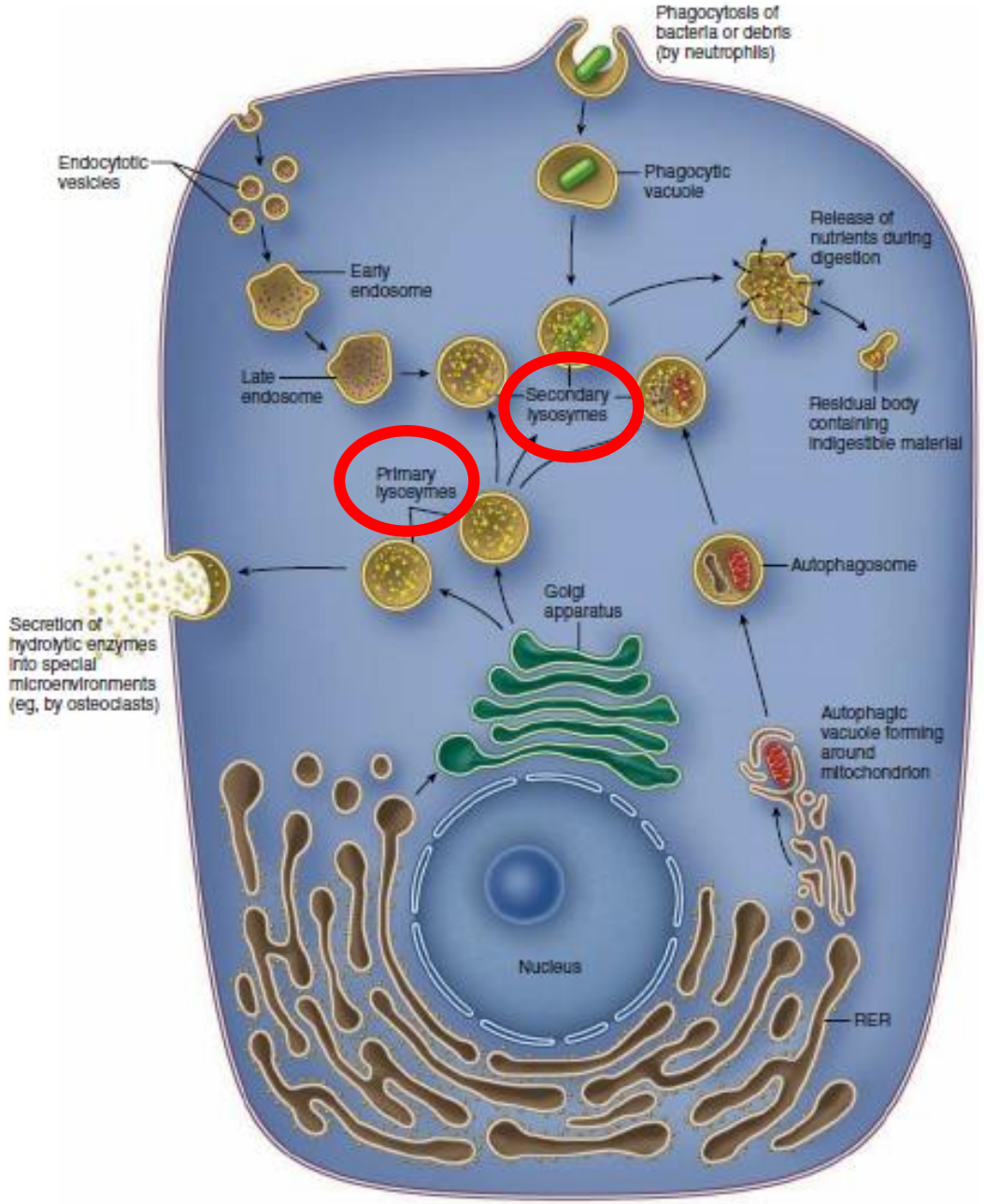
- The granules are surrounded by membrane and contain a concentrated form of the secretory product
- Histologically:
  - Light microscopy: they cannot be resolved, but in cells active in protein synthesis, they give apical cytoplasm intense eosinophilic appearance (pink)
  - Electron microscopy: homogenous electron dense structures near the apex of the cell

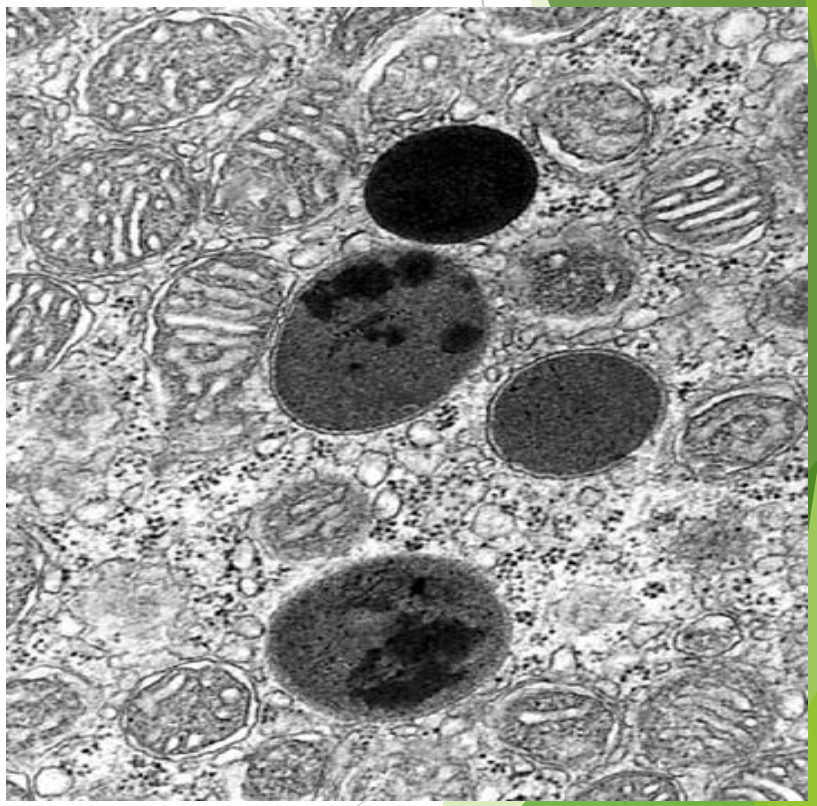

D
a
L
G
SG
R
b


D
a
L
G
SG
R
b

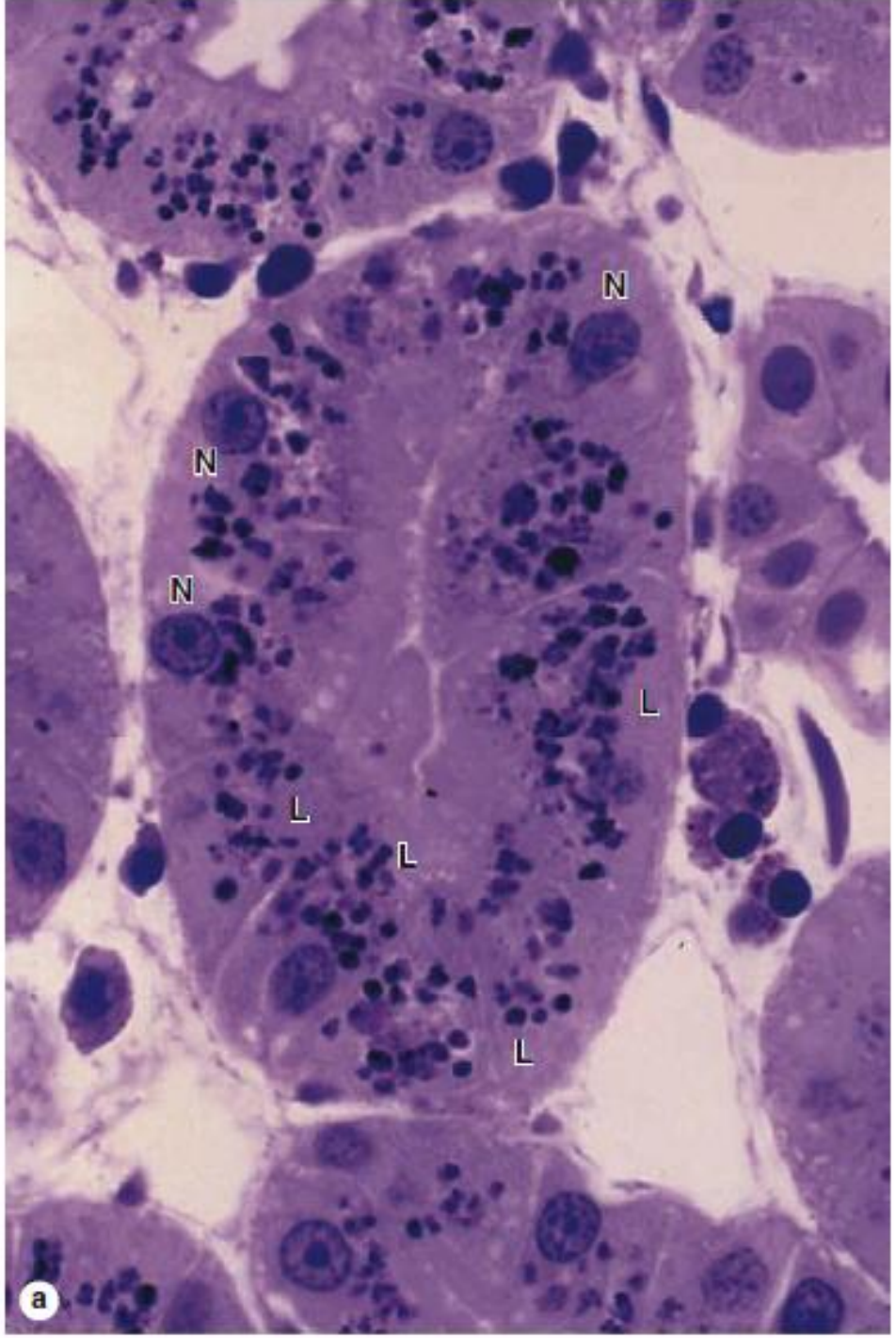
Lysosomes

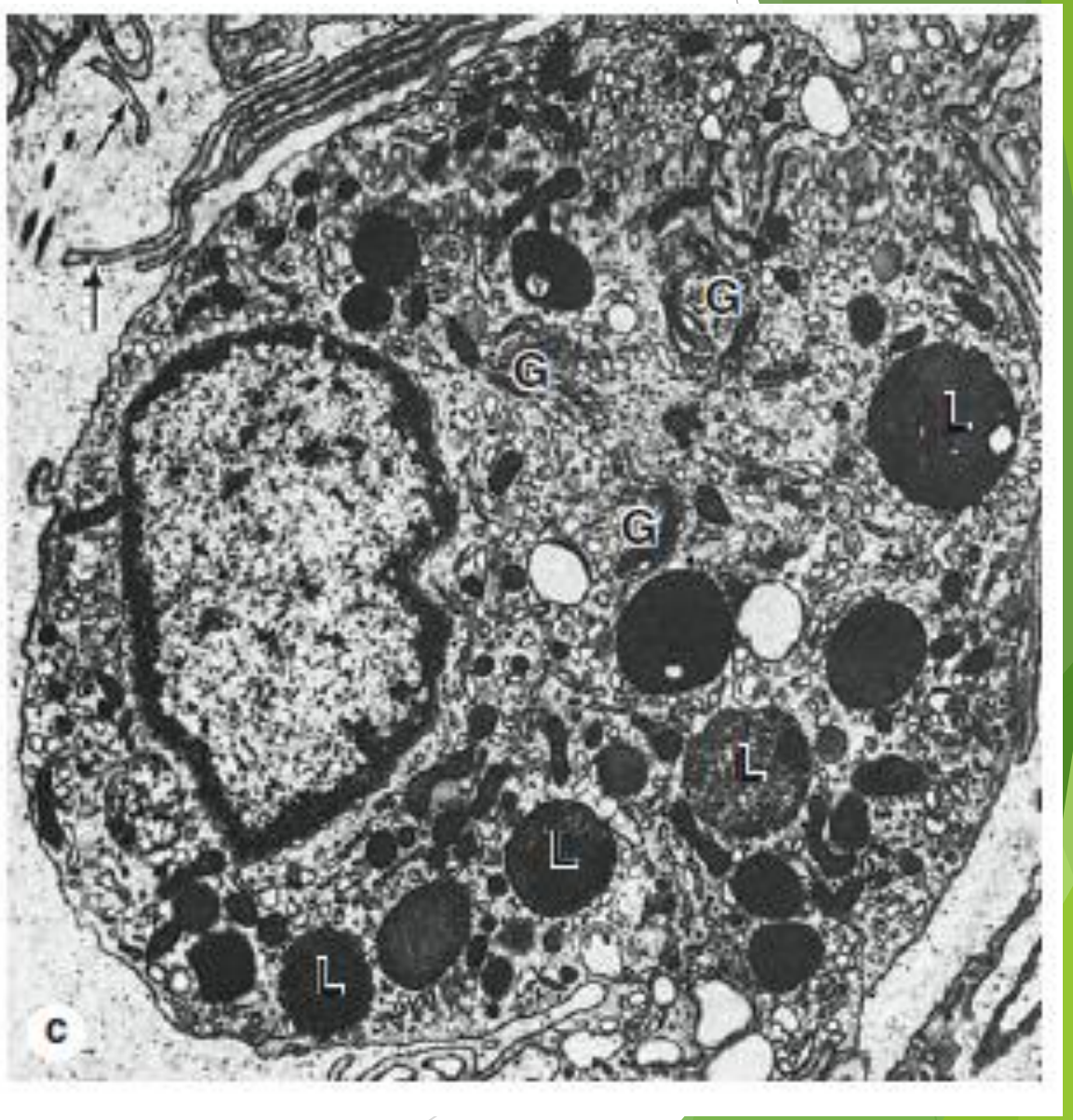
- **Lysosomes** are sites of intracellular digestion and turnover of cellular components.
- Under electron microscopy, we can distinguish between primary and secondary lysosomes:
  - *Primary*: Uniformly granular electron dense appearance
  - *Secondary*: Larger with heterogenous appearance (particulate content)
- Lysosomes are not well shown on H&E-stained cells but can be visualized by light microscopy after staining with toluidine blue.


Phagocytosis of bacteria or debris (by neutrophils)
Endocytotic vesicles
Phagocytic vacuole
Release of nutrients during digestion
Early endosome
Late endosome
Secondary lysosymes
Residual body containing indigestible material
Primary lysosymes
Autophagosome
Golgi apparatus
Secretion of hydrolytic enzymes into special microenvironments (eg, by osteoclasts)
Autophagic vacuole forming around mitochondrion
Nucleus
RER



- Synthesis of lysosomal enzymes occurs in the RER, with packaging in the Golgi apparatus. Endocytosis produces vesicles that fuse with **endosomes** before merging with **lysosomes**.
- Phagocytic vacuoles (or phagosomes) fuse with primary lysosomes to become **secondary lysosomes** (or heterolysosomes), in which ingested material is degraded.
- **Autophagosomes**, such as those depicted here with a mitochondrion in the process of digestion, are formed after nonfunctional or surplus organelles become enclosed with membrane and the resulting structure fuses with a lysosome.
- The products of lysosomal digestion are recycled to the cytoplasm, but indigestible molecules remain in a membrane-enclosed **residual body**, which may accumulate in long-lived cells as lipofuscin.
- In some cells, such as osteoclasts, the lysosomal enzymes are secreted into a restricted extracellular compartment.

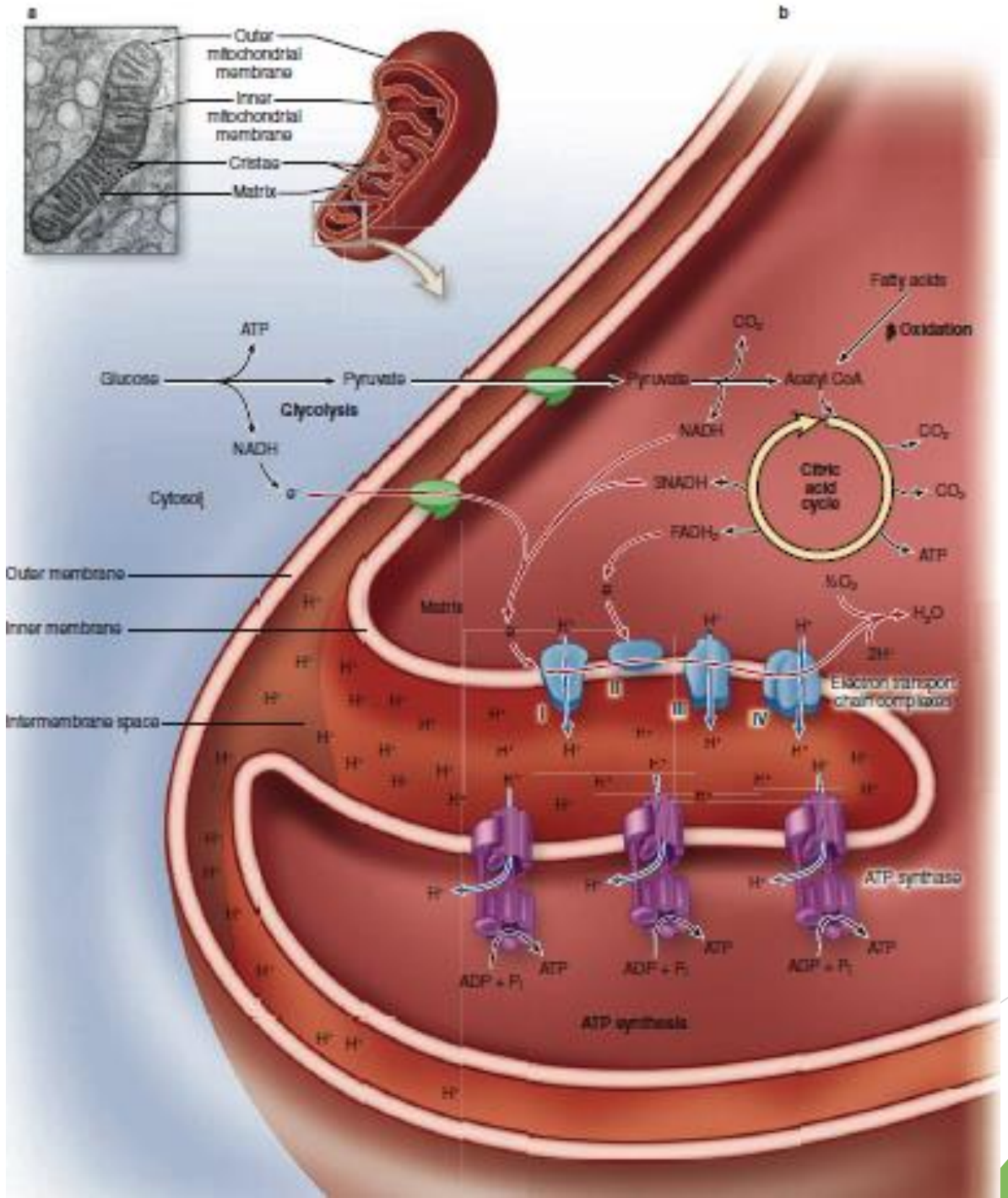

N
N
N
L
L
L
L
a


G
G
G
L
L
L
L
c

Mitochondria

- **Mitochondria** are membrane-enclosed organelles with arrays of enzymes specialized for aerobic respiration and production of **adenosine triphosphate (ATP)**, which supplies energy for most cellular activities.
- The number of mitochondria is related to the cell's energy needs: cells with a high-energy metabolism (eg, cardiac muscle, cells of some kidney tubules) have abundant mitochondria, whereas cells with a low-energy metabolism have few mitochondria.

- Under the TEM each mitochondrion is seen to have two separated and very different membranes that together create two compartments: the innermost **matrix** and a narrow **intermembrane space**
- The **outer membrane** contains many transmembrane proteins called **porins** that form channels through which small molecules such as pyruvate and other metabolites pass from the cytoplasm to the intermembrane space.
- The **inner membrane** has many long folds called **cristae**, which project into the matrix and greatly increase the membrane's surface area


a
b
Outer mitochondrial membrane
Inner mitochondrial membrane
Cristae
Matrix
Fatty acids
β Oxidation
ATP
Glucose
Pyruvate
Glycolysis
NADH
Cytosol
CO_2
Acetyl CoA
Citric acid cycle
3NADH
$FADH_2$
ATP
Outer membrane
Inner membrane
Intermembrane space
Matrix
H_2O
Electron transport chain complexes
ATP synthase
ADP + P_i
ATP synthesis

The cytoskeleton

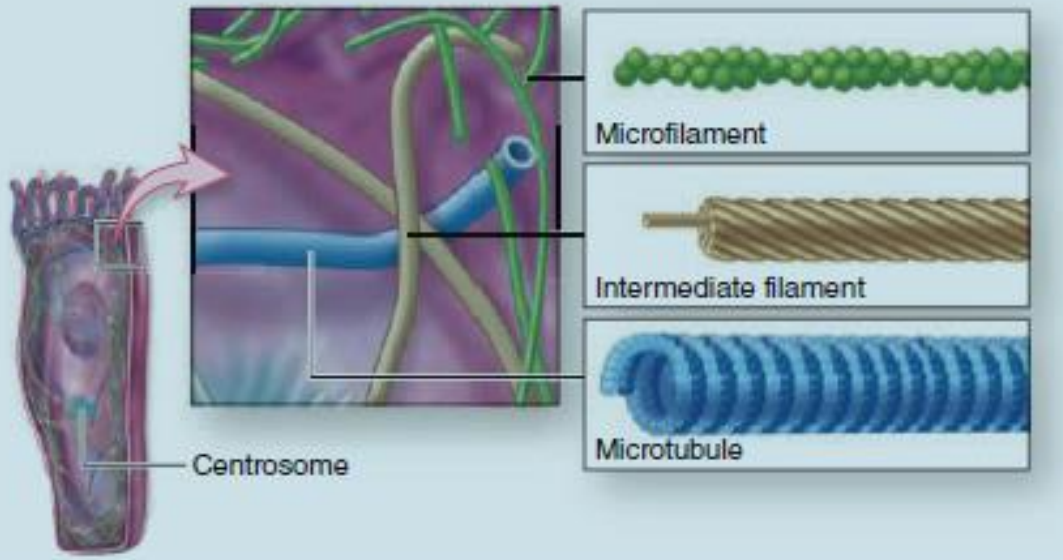
- The cytoplasmic **cytoskeleton** is a complex array of:

(1) microtubules,

(2) microfilaments (also called actin filaments)

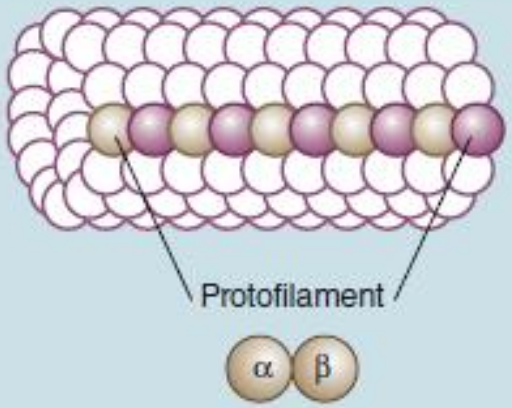
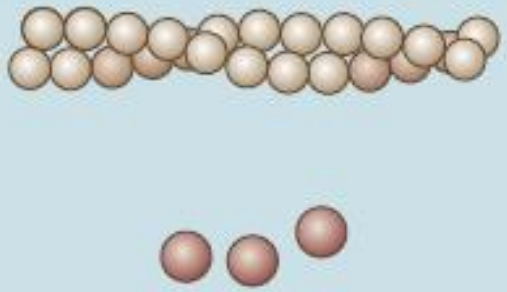
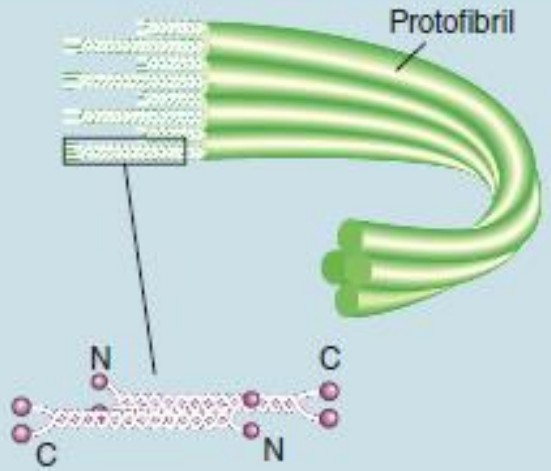
(3) intermediate filaments.

- These protein polymers determine the shapes of cells, play an important role in the movements of organelles and cytoplasmic vesicles, and also allow the movement of entire cells.



General Function of Cytoskeleton

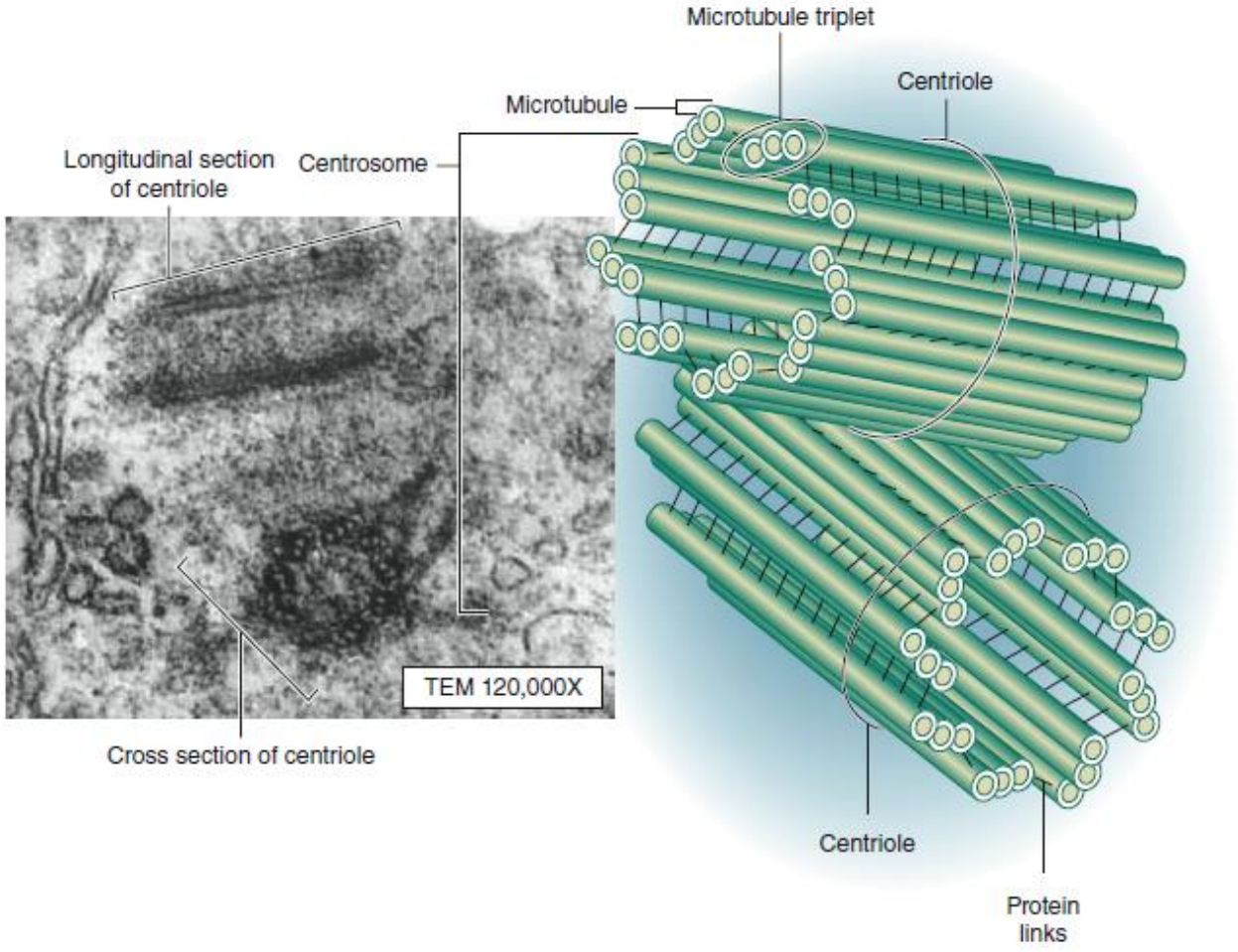
1. **Structural:** Provides structural support to cell; stabilizes junctions between cells
2. **Movement:** Assists with cytosol streaming and cell motility; helps move organelles and materials throughout cell; helps move chromosomes during cell division

	Microtubules	Microfilaments	Intermediate filaments
Polymer			

Centrosome

- The **centrosome** is the microtubule-organizing center for the mitotic spindle and consists of paired centrioles.
- The TEM reveals that the two centrioles in a centrosome exist at right angles to each other.
- Each centriole consists of **nine microtubular triplets** peripherally arranged, and no microtubules in the center (arrangement: 9+0)

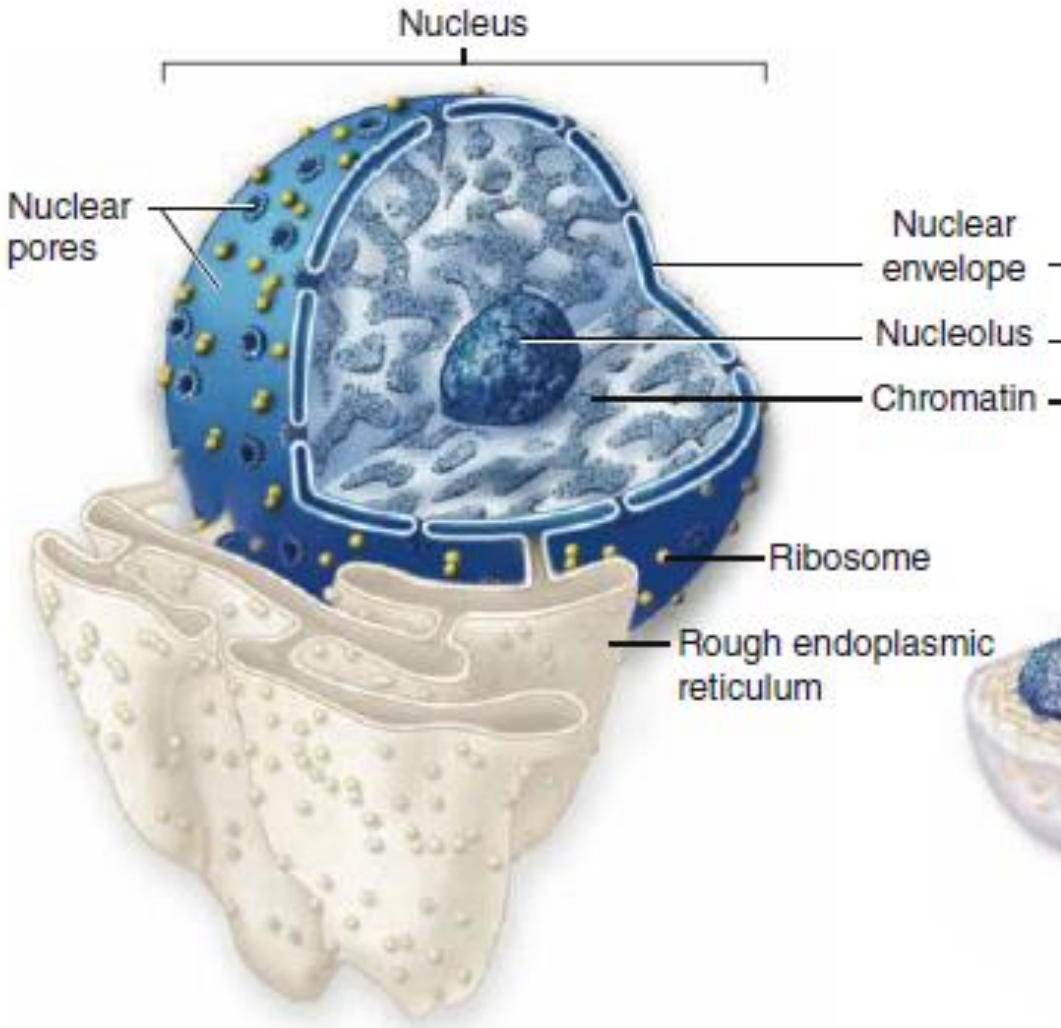
Centrosome

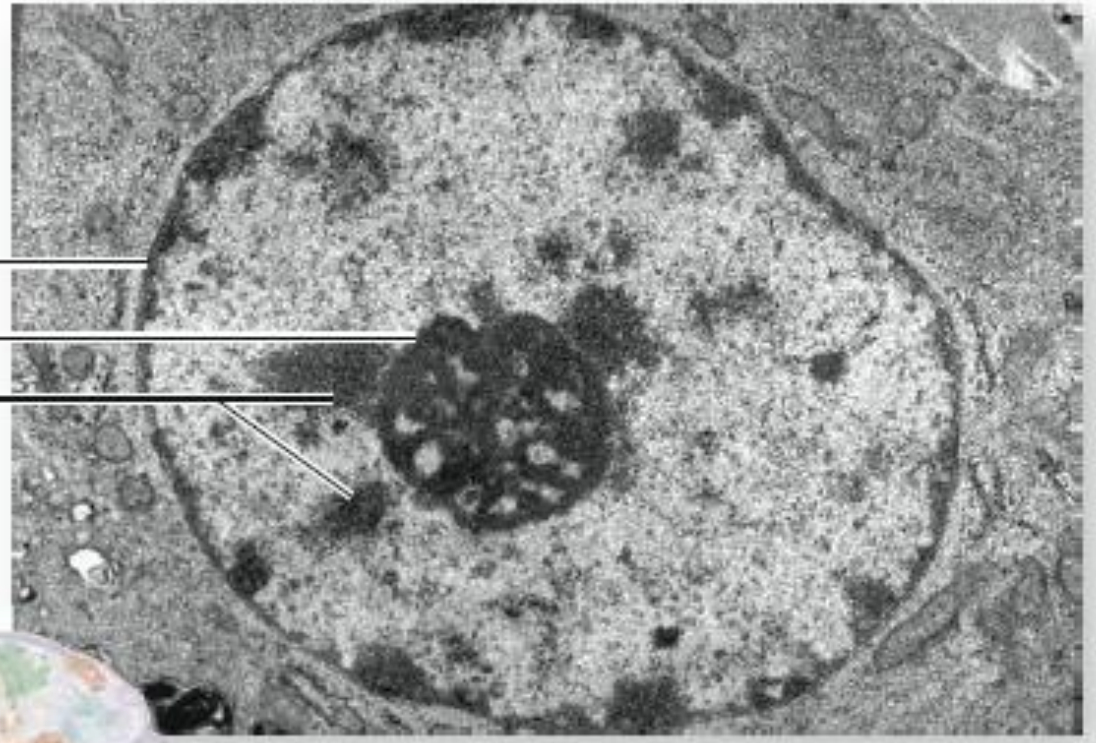

Microtubule triplet
Centriole
Microtubule
Longitudinal section of centriole
Centrosome
TEM 120,000X
Cross section of centriole
Centriole
Protein links

The Nucleus

The Nucleus

- The nucleus contains the code for all of a cell's enzymes and other proteins. It also contains the molecular machinery to replicate the DNA and to synthesize and process all types of RNA.
- The nucleus usually appears as a large rounded or oval structure, often near the cell's center.
- It consists of a **nuclear envelope** containing **chromatin**, with one or more specialized regions of chromatin called **nucleoli**.





Functions of the Nucleus

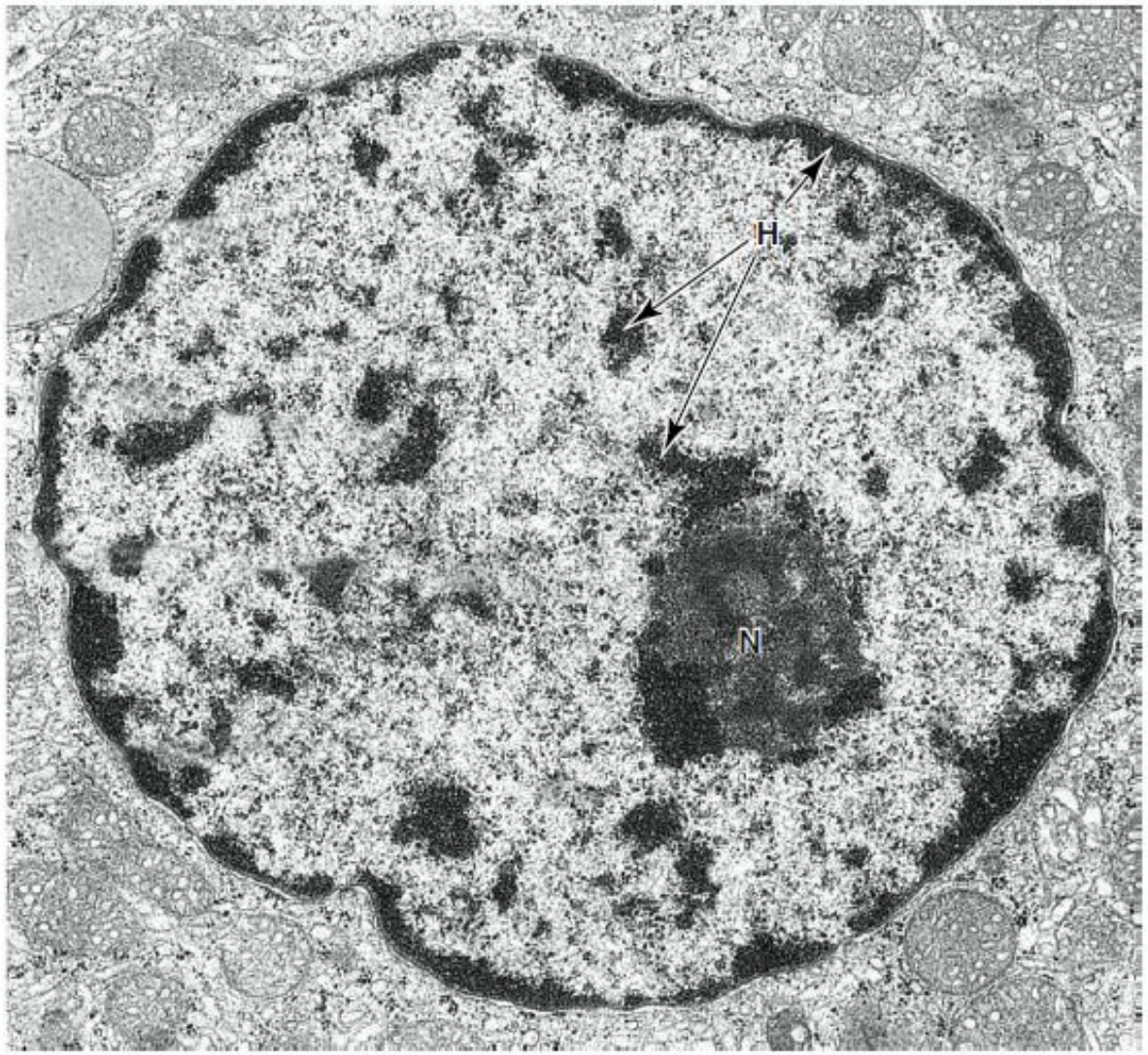
1. **Cellular regulation:** Houses genetic material, which directs all cellular activities and regulates cellular structure
2. **Production:** Produces ribosomal subunits in nucleolus and exports them into cytoplasm for assembly into ribosomes

Chromatin

- The mass of DNA and its associated proteins
- Microscopically two categories of chromatin can be distinguished:
  - **Euchromatin** is visible as finely dispersed granular material in the electron microscope and as lightly stained basophilic areas in the light microscope.

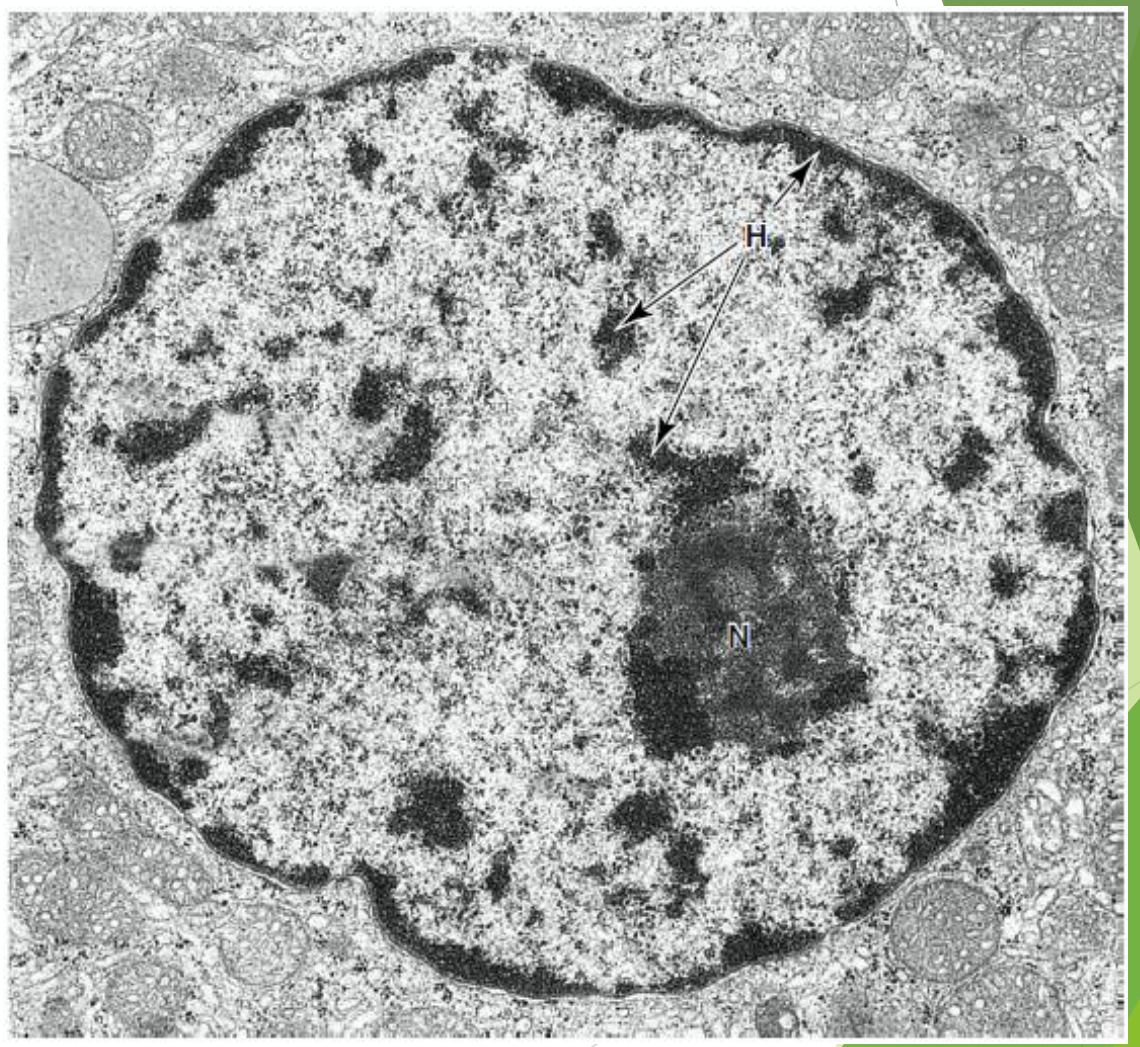
  → associated with **active** cells
  - **Heterochromatin** appears as coarse, electron-dense material in the electron microscope and as intensely basophilic clumps in the light microscope.

  → associated with **inactive** cells


H
N

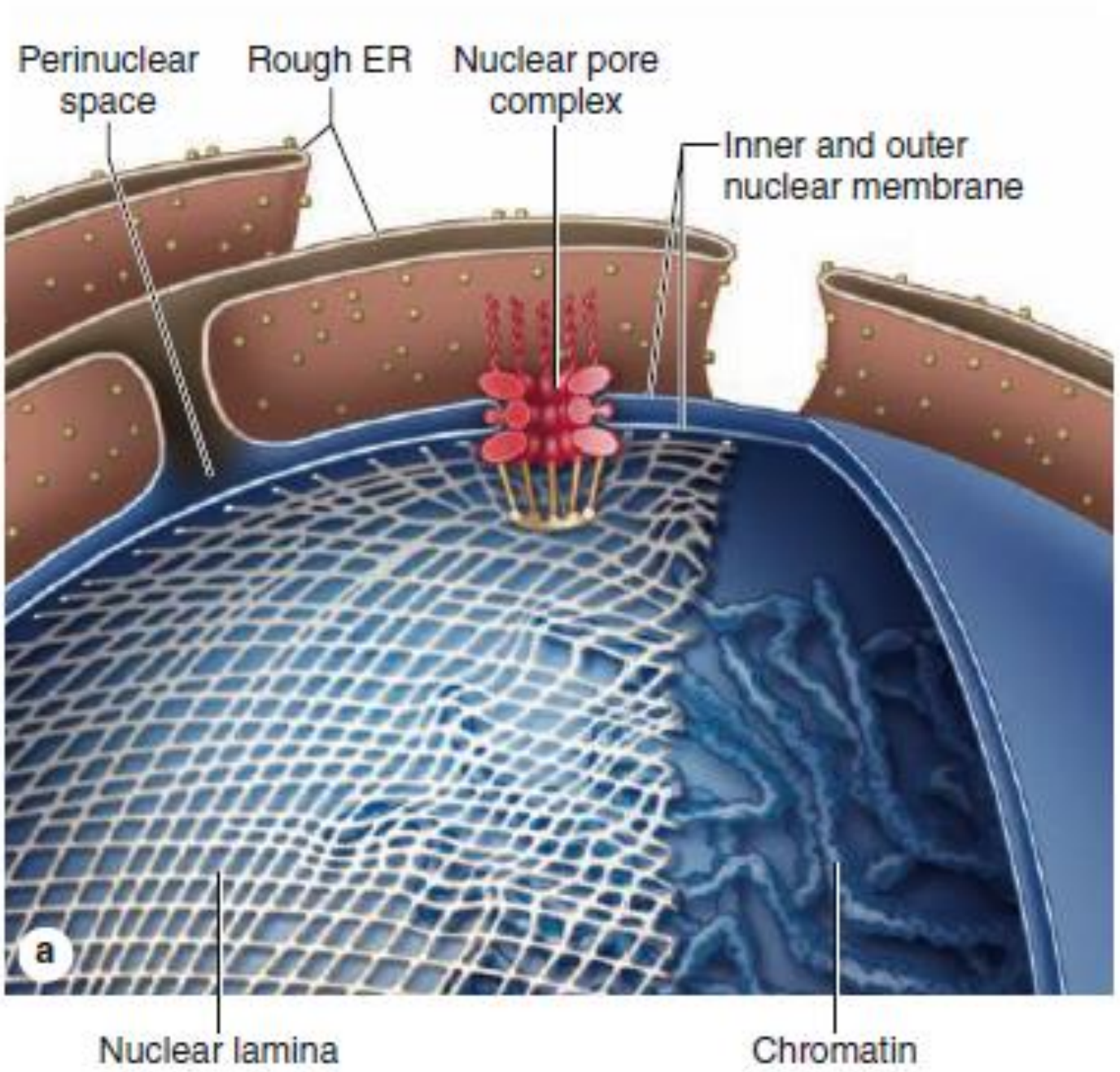
Nucleolus

- The **nucleolus** is a spherical, highly basophilic subdomain of nuclei in cells actively engaged in protein synthesis
- It is the location of ribosomal subunit assembly and transcription of ribosomal RNA (**rRNA**)
- The intense basophilia of nucleoli is due **not to** heterochromatin but to the presence of densely concentrated **rRNA**



The Nuclear Envelope

- The **nuclear envelope is** a double set of membranes with a narrow perinuclear space, which separates the cytoplasm from nucleoplasm
- The outer membrane binds ribosomes and is continuous with the RER.
- It is penetrated by **nuclear pore complexes**,
- It is supported internally by a meshwork, the nuclear lamina, composed of intermediate filament subunits called **lamins**.


Perinuclear space
Rough ER
Nuclear pore complex
Inner and outer nuclear membrane
a
Nuclear lamina
Chromatin

Nuclear pore complexes

- **Nuclear pore complexes (nuclear pores)** contain more than 30 core proteins (nucleoporins), span both membranes of the nuclear envelope, and regulate the bidirectional transfer of macromolecular complexes between the nucleus and cytoplasm