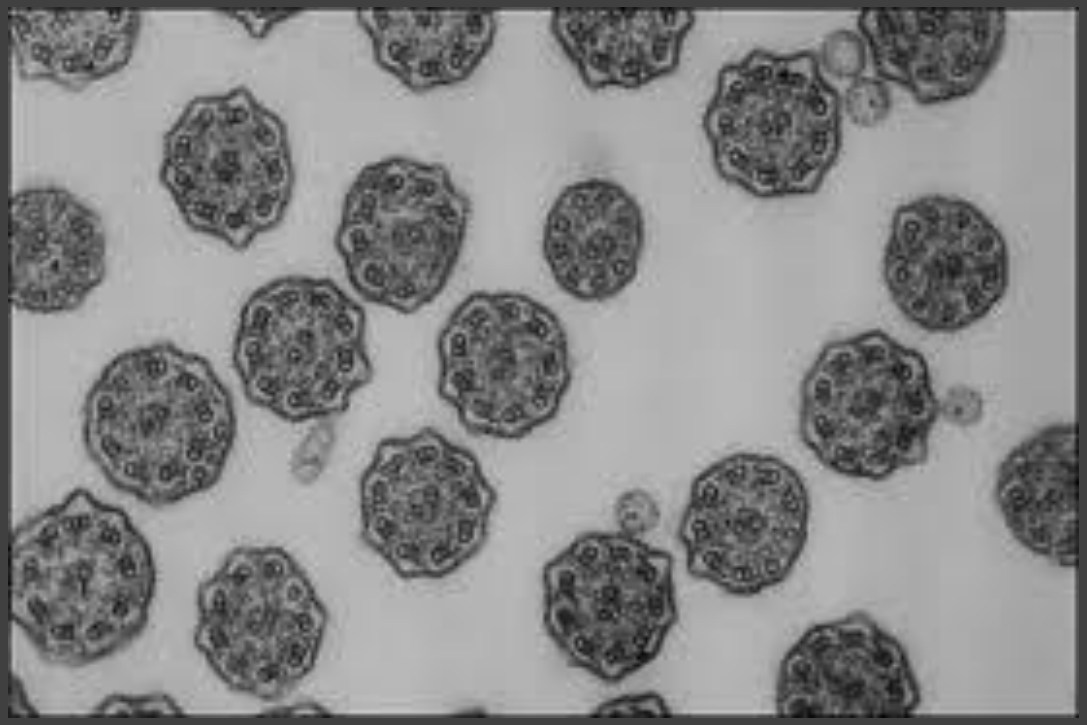
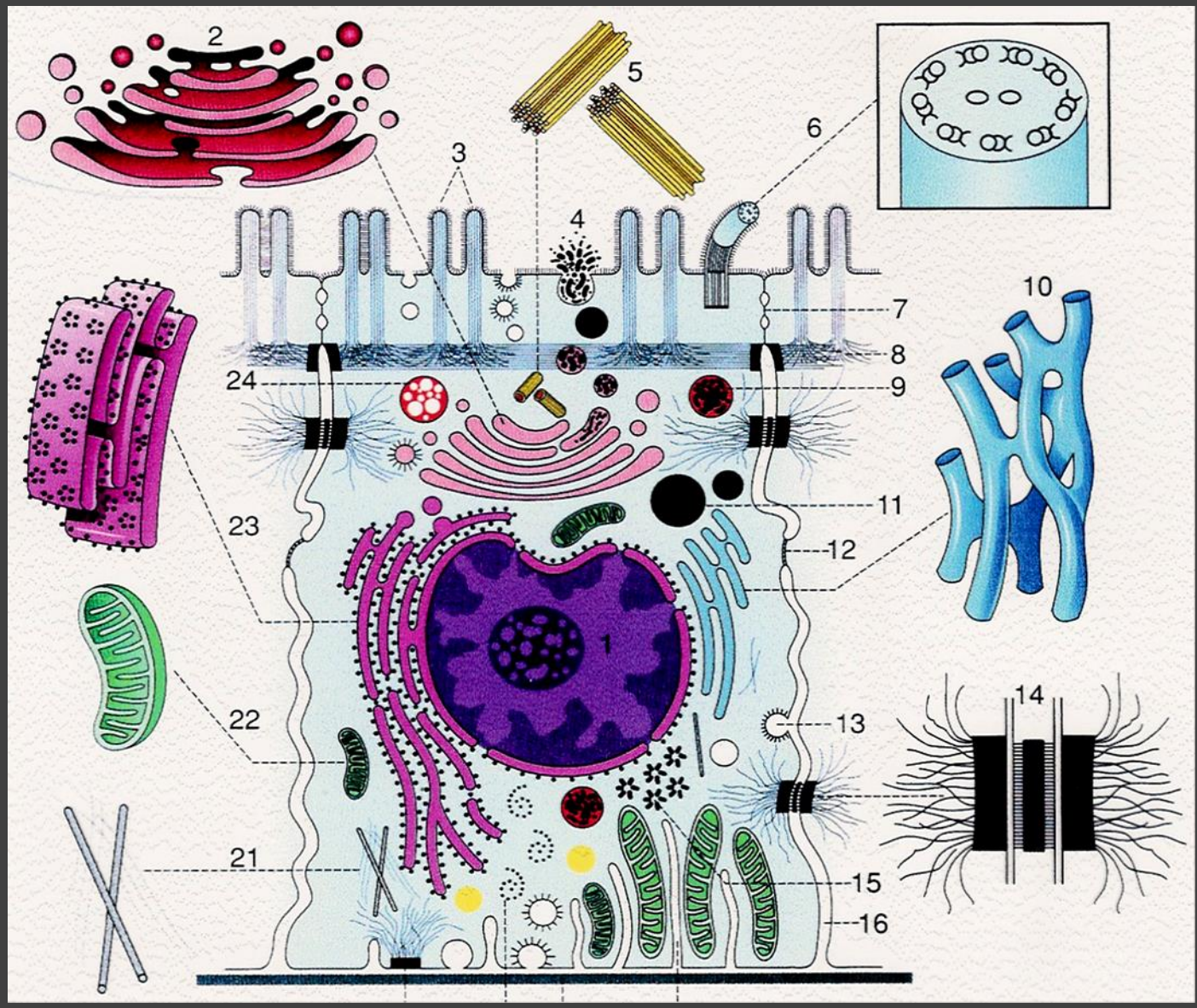
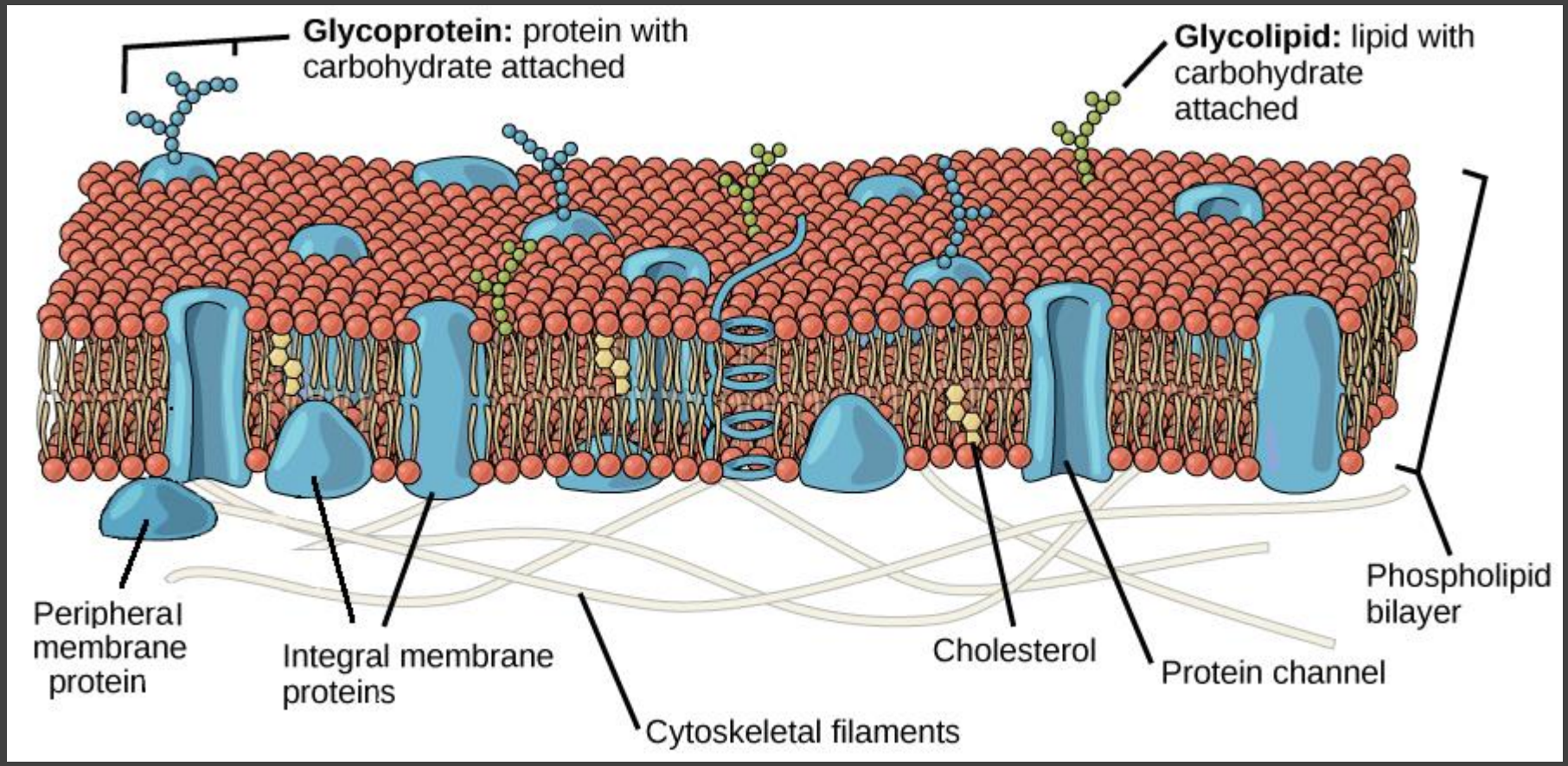


CELL ULTRASTRUCTURE

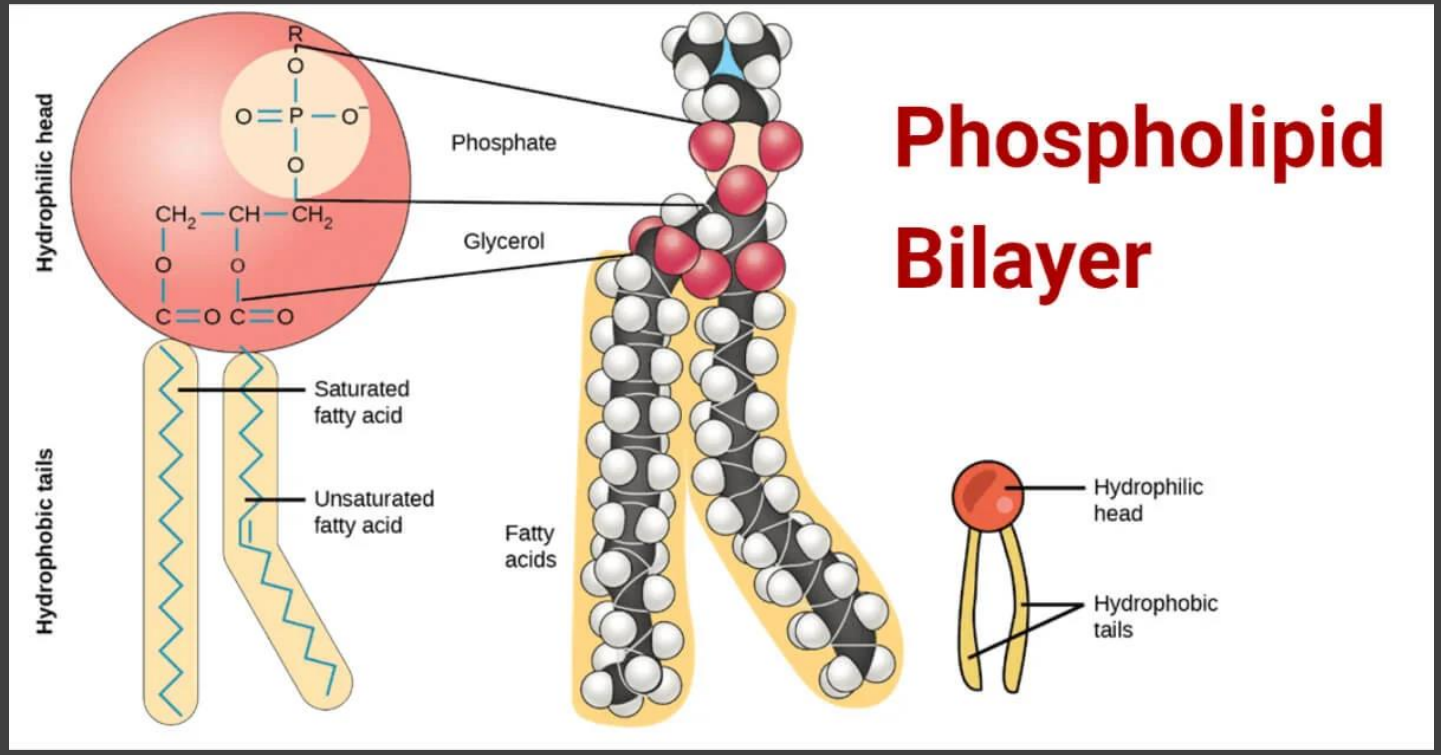

2
5
6
3
4
7
8
24
9
10
23
11
12
1
22
13
14
21
15
16

Functions of the cell membrane

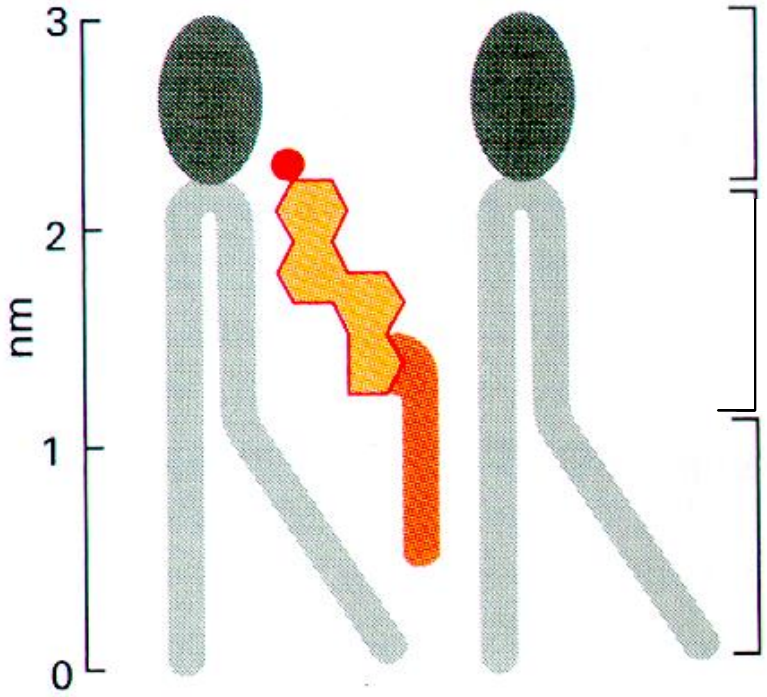
- Maintaining the integrity of the cell
- Controlling movements of substances in and out of the cell
- Regulating cell-cell interactions and recognizing of antigens
- Establishing transport system for specific molecules
- Transducing extracellular signals



Phospholipid Bilayer



Micelle

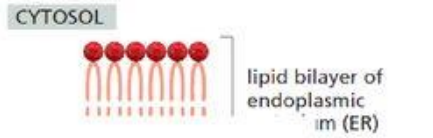


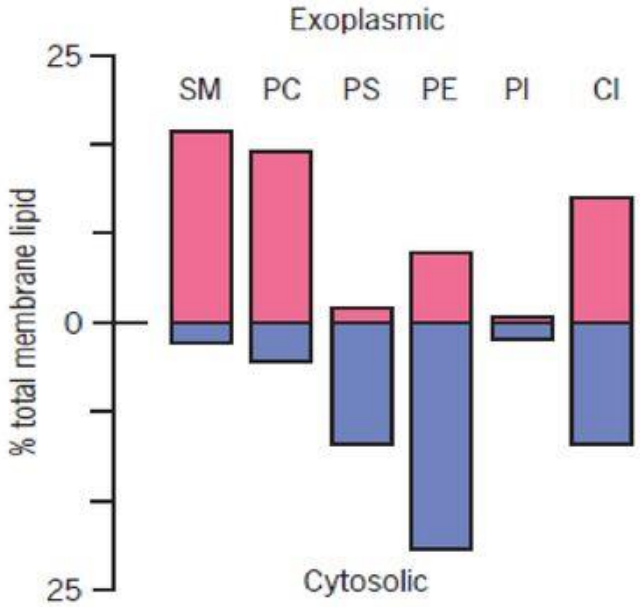
Cholesterol w dwuwarstwie lipidowej

Schemat pokazuje jak cząsteczka cholesterolu oddziaływuje z dwoma cząsteczkami fosfolipidów w jednej warstwie dwuwarstwy lipidowej

Asymmetry in membranes

- Cell membrane
- Phosphatidylch
  leaflet, while pl
  (PtdEtn) are res
- Scramblases no





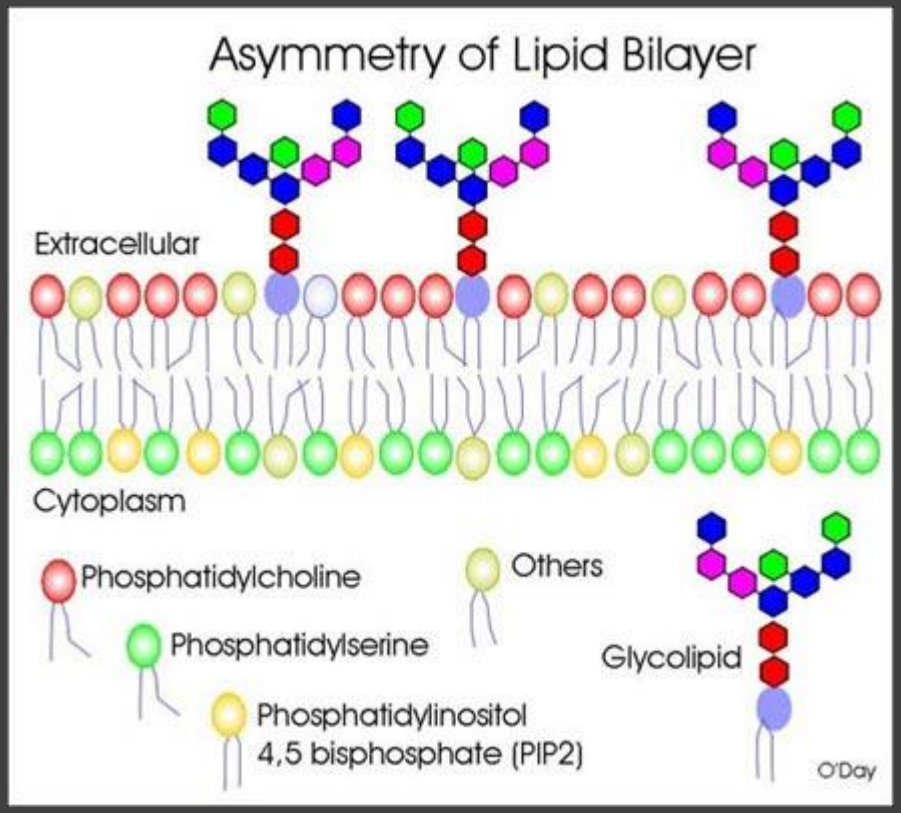
PIDS
SOLIC
AYER

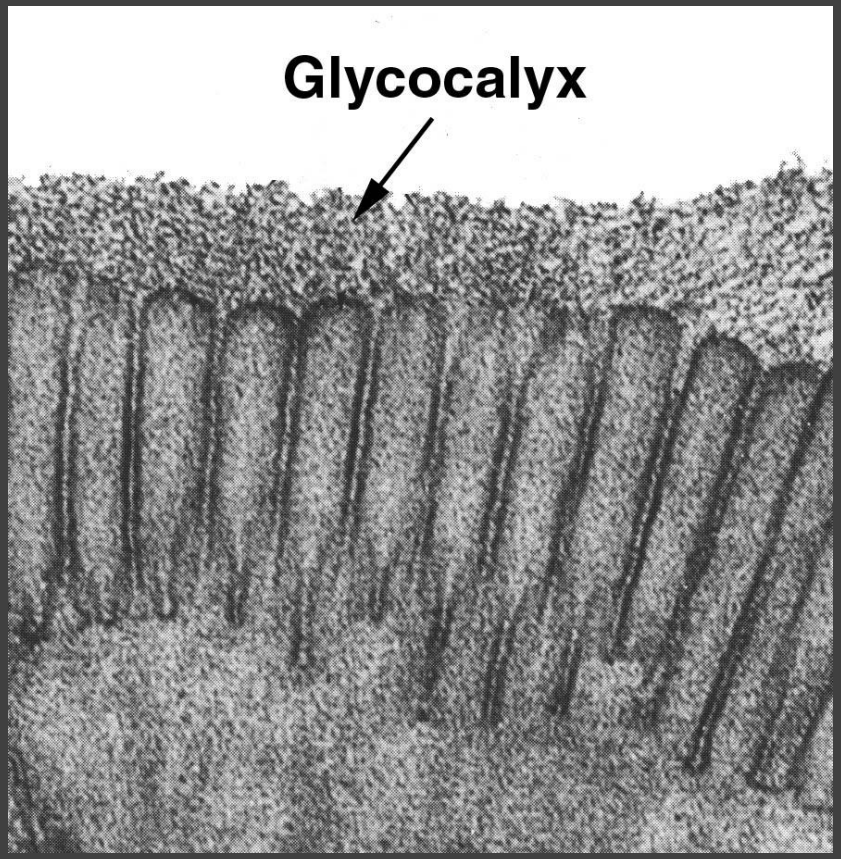
ERS

etric growth
h halves
yer

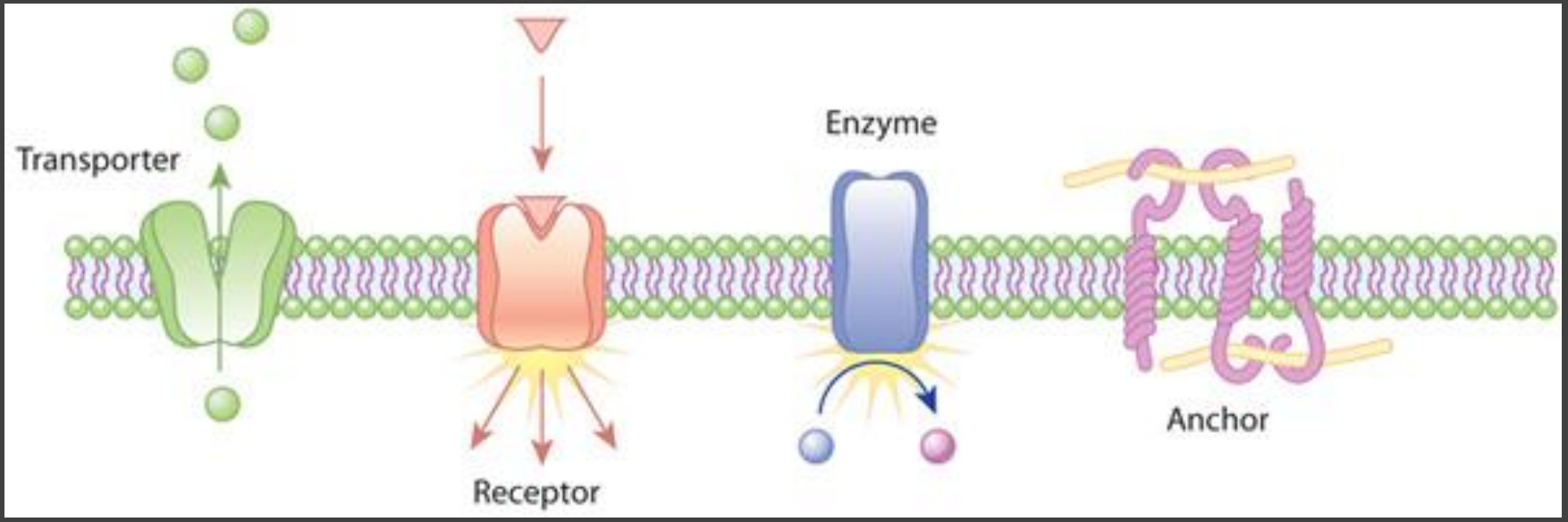
FIGURE 4.10 The asymmetric distribution of phospholipids (and cholesterol) in the plasma membrane of human erythrocytes. (SM, sphingomyelin; PC, phosphatidylcholine; PS, phosphatidylserine; PE,

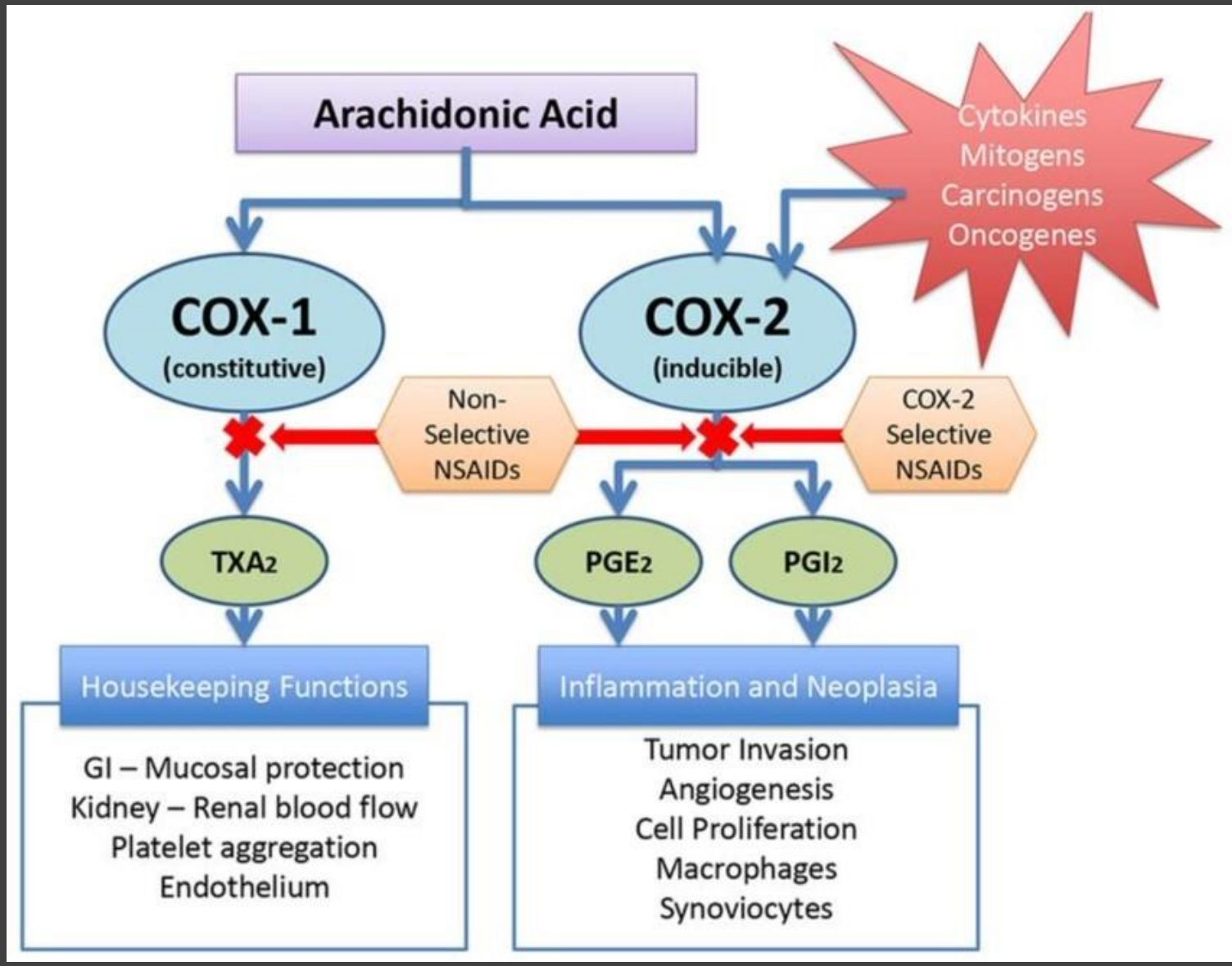
GLYCOLIPIDS



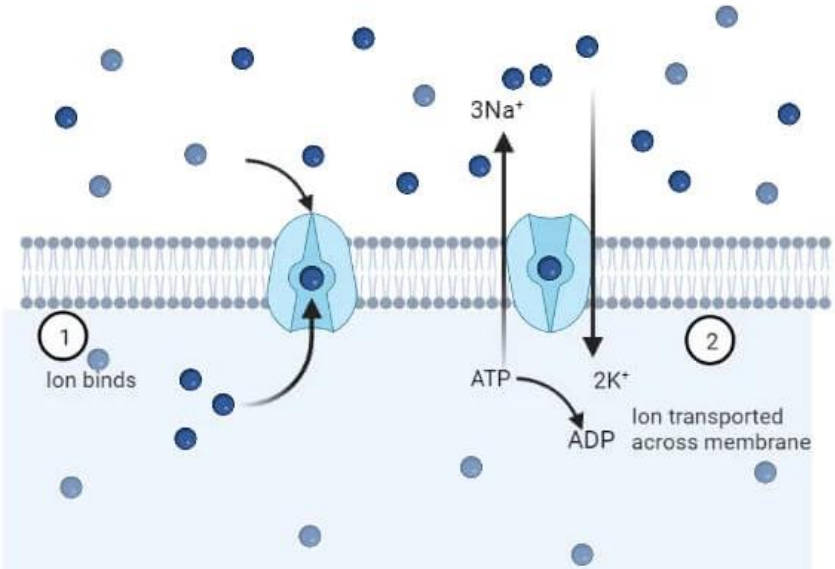


FUNCTION OF TRANSMEMBRANE PROTEINS

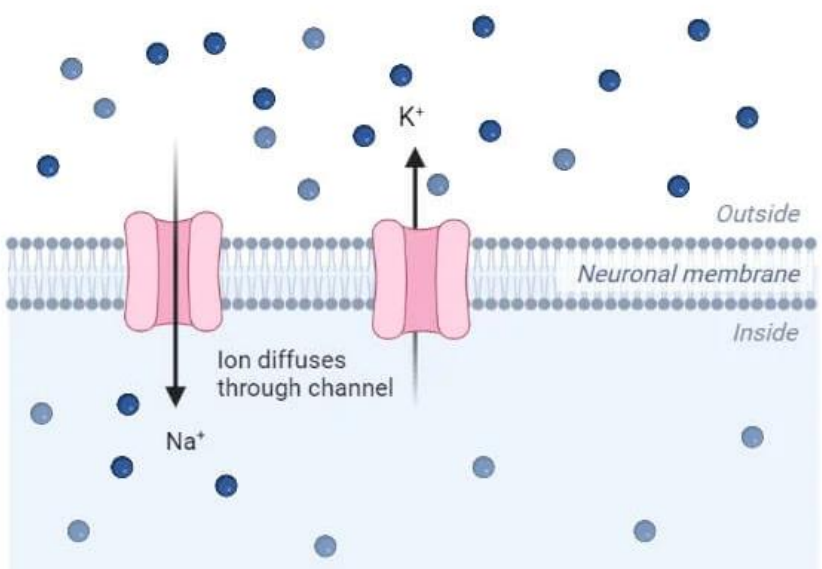



Arachidonic Acid
Cytokines
Mitogens
Carcinogens
Oncogenes
COX-1
(constitutive)
COX-2
(inducible)
Non-
Selective
NSAIDs
COX-2
Selective
NSAIDs
TXA2
PGE2
PGI2
Housekeeping Functions
GI – Mucosal protection
Kidney – Renal blood flow
Platelet aggregation
Endothelium
Inflammation and Neoplasia
Tumor Invasion
Angiogenesis
Cell Proliferation
Macrophages
Synoviocytes

MEMBRANE RESTING POTENTIAL



Na⁺-K⁺ pump
- Actively move ions **against** concentration gradient
- Create ion concentration gradients



Leak channel
- Allow ions to diffuse **down** concentration gradient
- Cause selective permeability to certain ions

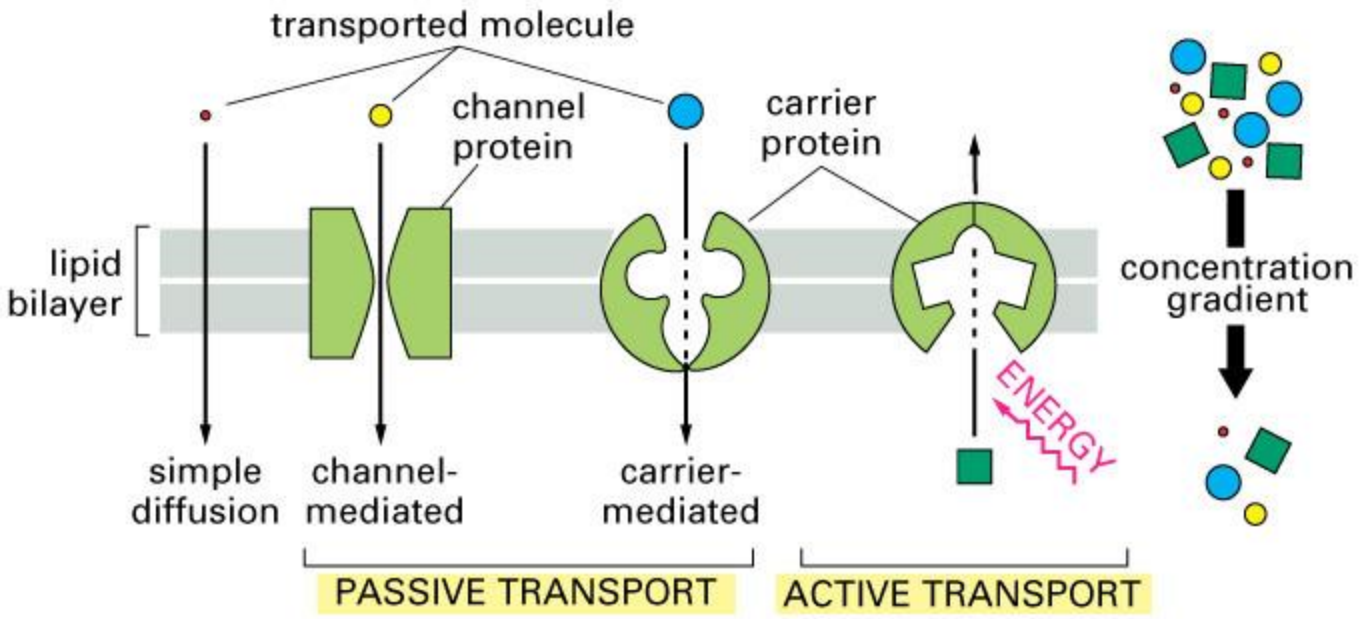


Figure 12-4 Essential Cell Biology, 2/e. (© 2004 Garland Science)

małe cząsteczki hydrofobowe

O_2
CO_2
N_2
benzen

małe cząsteczki polarne bez ładunku

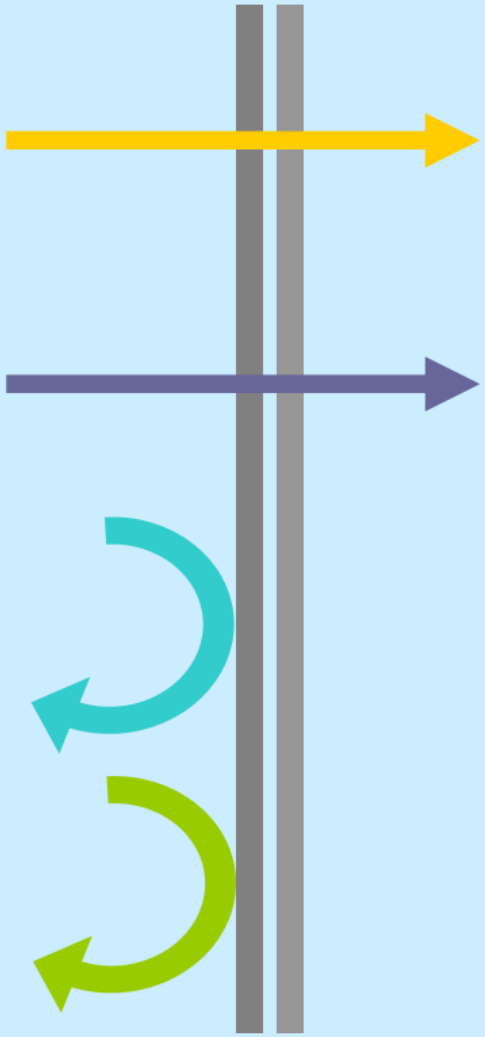
H_2O
glicerol
etanol

większe cząsteczki polarne bez ładunku

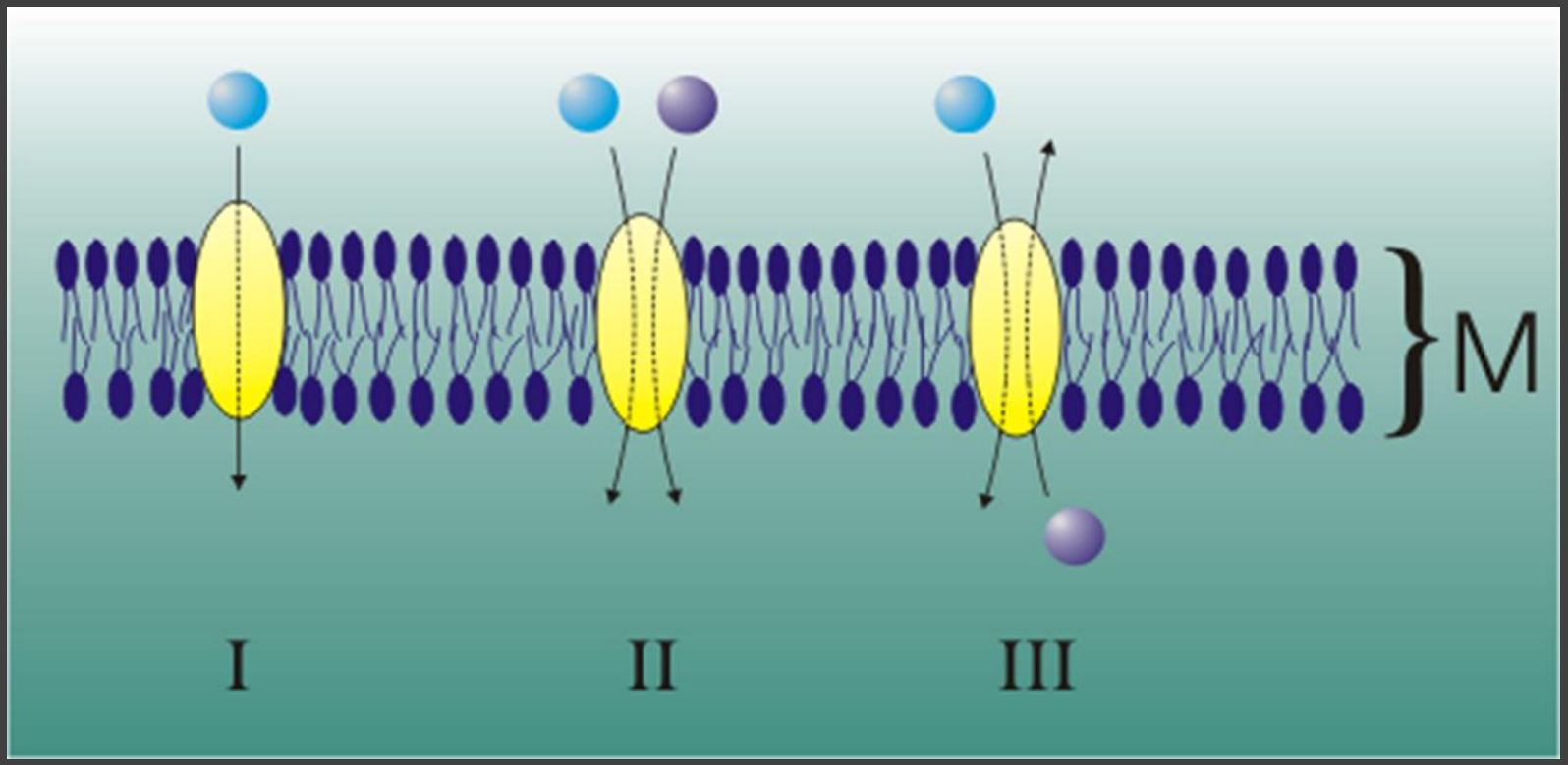
aminokwasy
glukoza
nukleotydy

jony

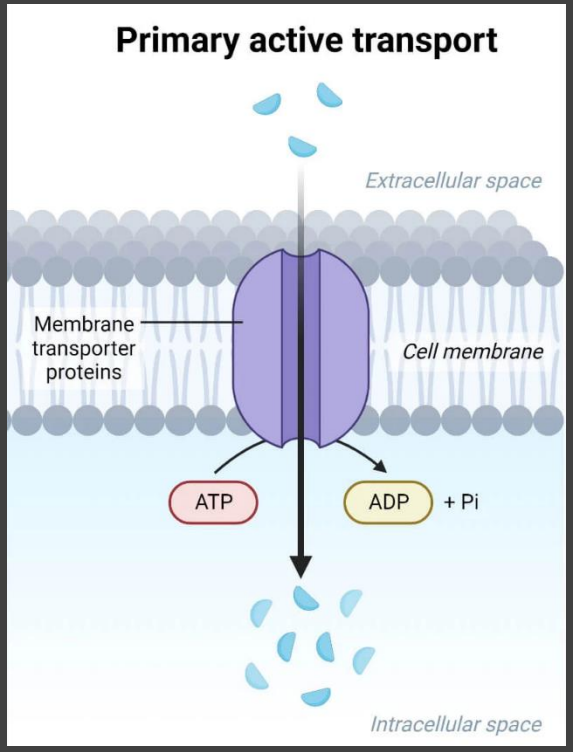
H^+, Na^+
HCO_3^-, K^+
Ca^{2+}, Cl^-
Mg^{2+}

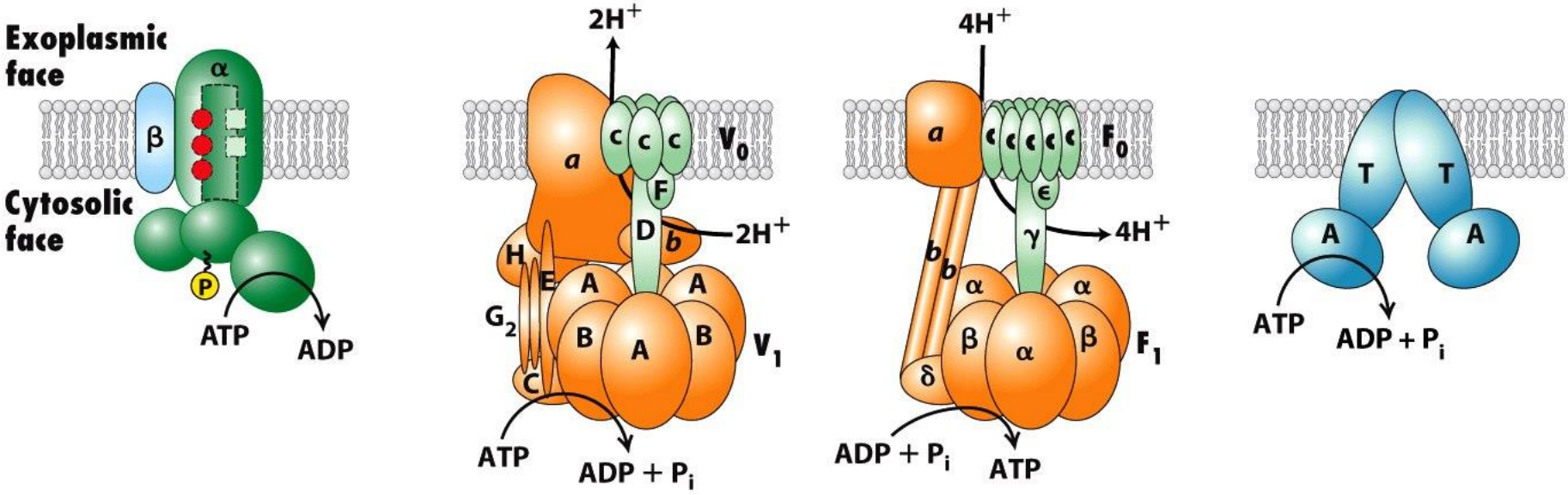


Uniport, symport, antiport



Uniport – primary active transport

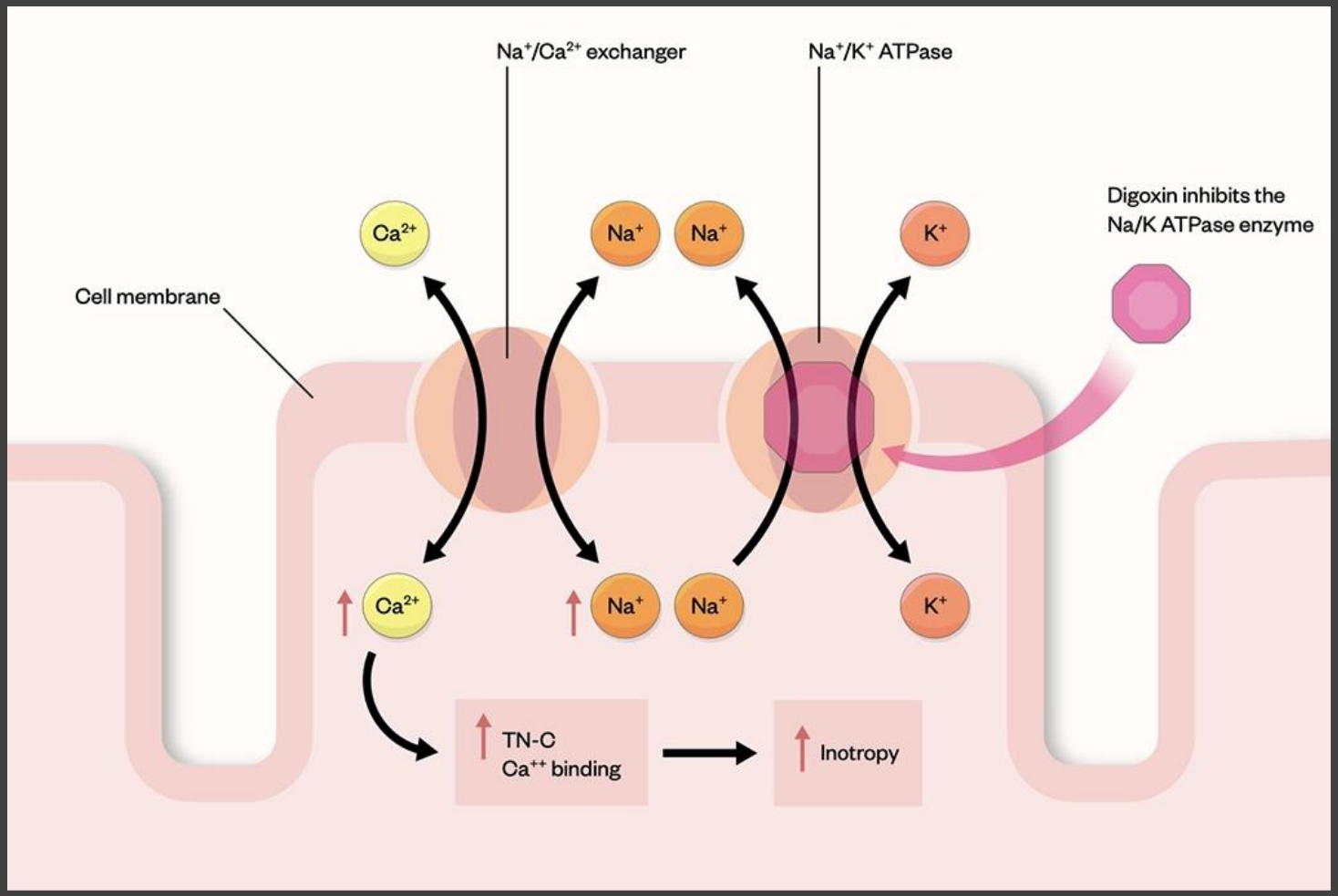




P-class pumps	V-class proton pumps	F-class proton pumps	ABC superfamily
Plasma membrane of plants, fungi, bacteria (H^+ pump)	Vacuolar membranes in plants, yeast, other fungi	Bacterial plasma membrane	Bacterial plasma membranes (amino acid, sugar, and peptide transporters)
Plasma membrane of higher eukaryotes (Na^+/K^+ pump)	Endosomal and lysosmal membranes in animal cells	Inner mitochondrial membrane	Mammalian plasma membranes (transporters of phospholipids, small lipophilic drugs, cholesterol, other small molecules)
Apical plasma membrane of mammalian stomach (H^+/K^+ pump)	Plasma membrane of osteoclasts and some kidney tubule cells	Thylakoid membrane of chloroplast	
Plasma membrane of all eukaryotic cells (Ca^{2+} pump)			
Sarcoplasmic reticulum membrane in muscle cells (Ca^{2+} pump)			

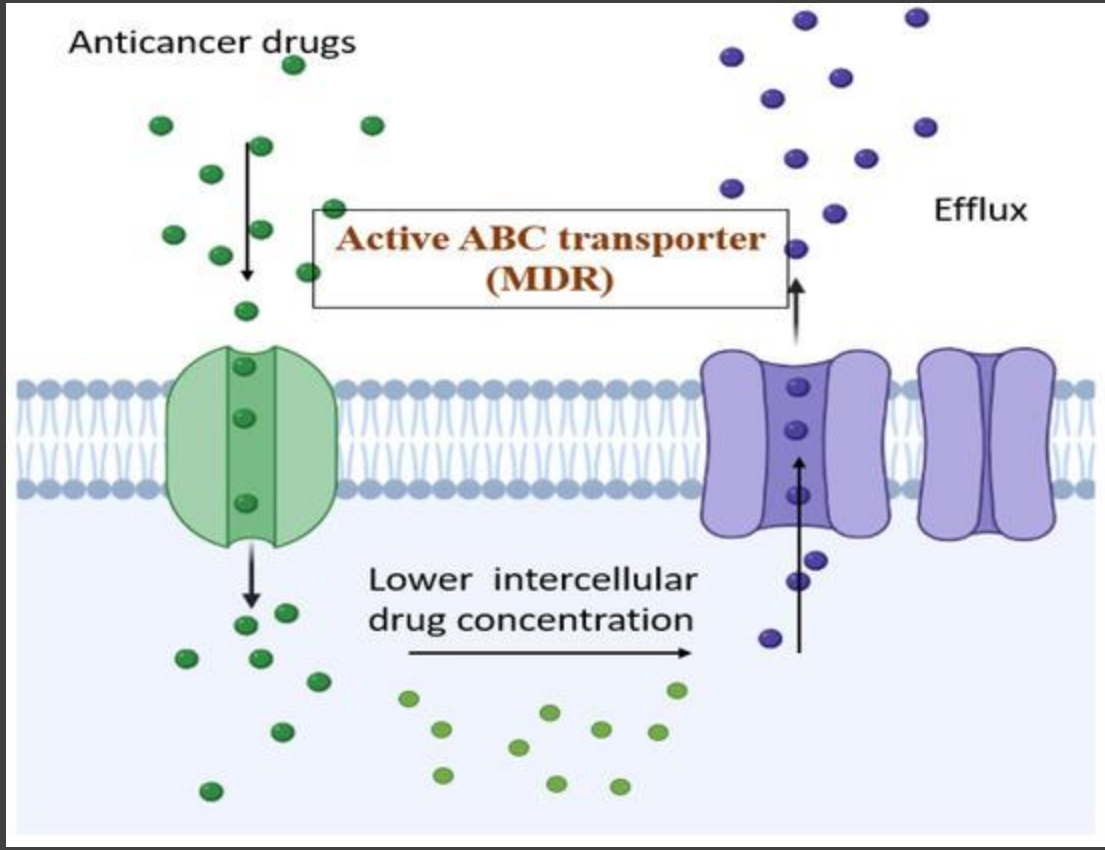
Figure 11-9
Molecular Cell Biology, Sixth Edition

Digoxin – selectine Na K pump inhibitor

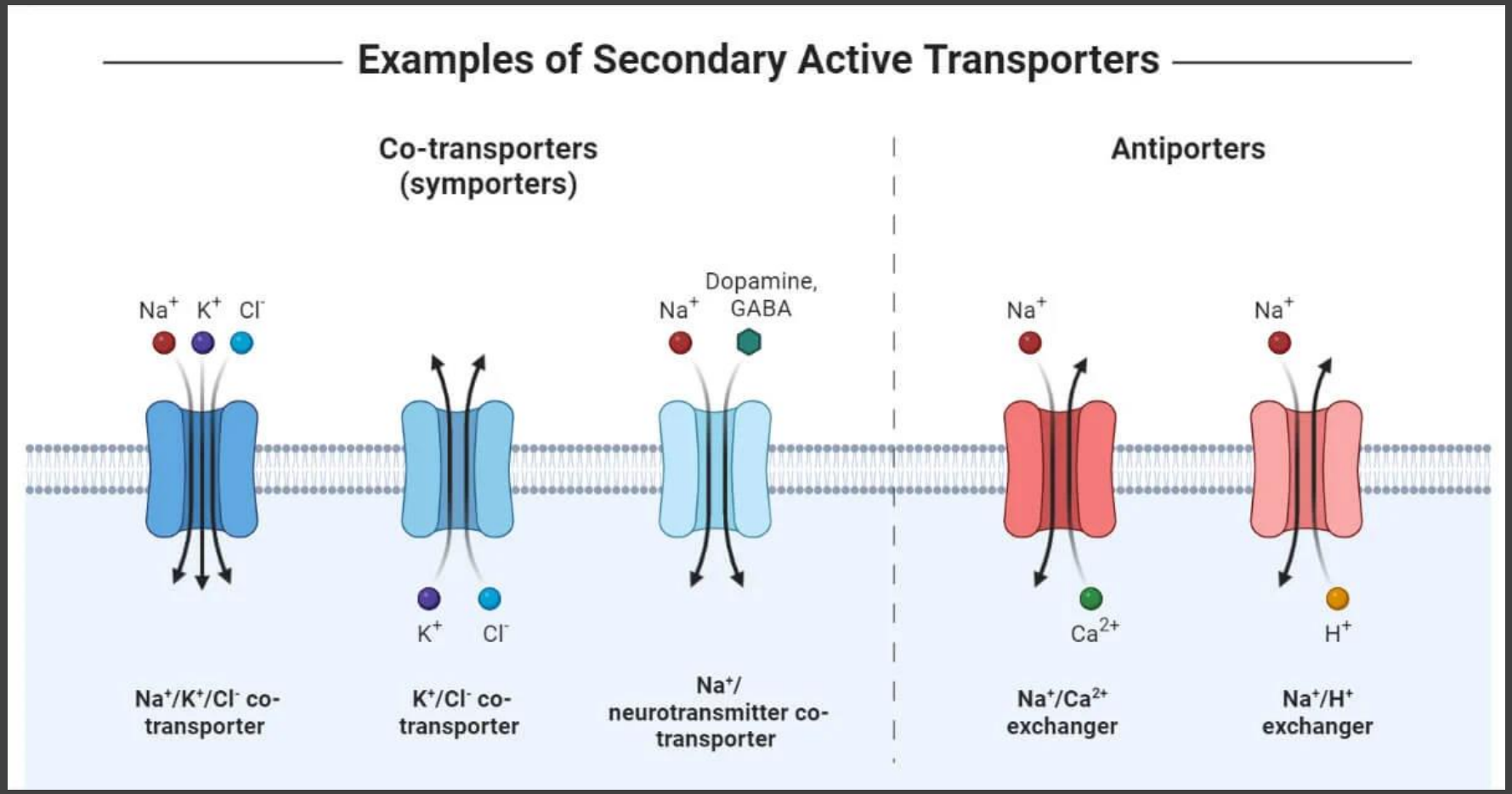


Inotropy is **the condition of contractility of the myocardium** and inotropes are substances that increase the force or energy of ventricular muscle contraction

Multidrug resistance



Symport and antiport – secondary active transport

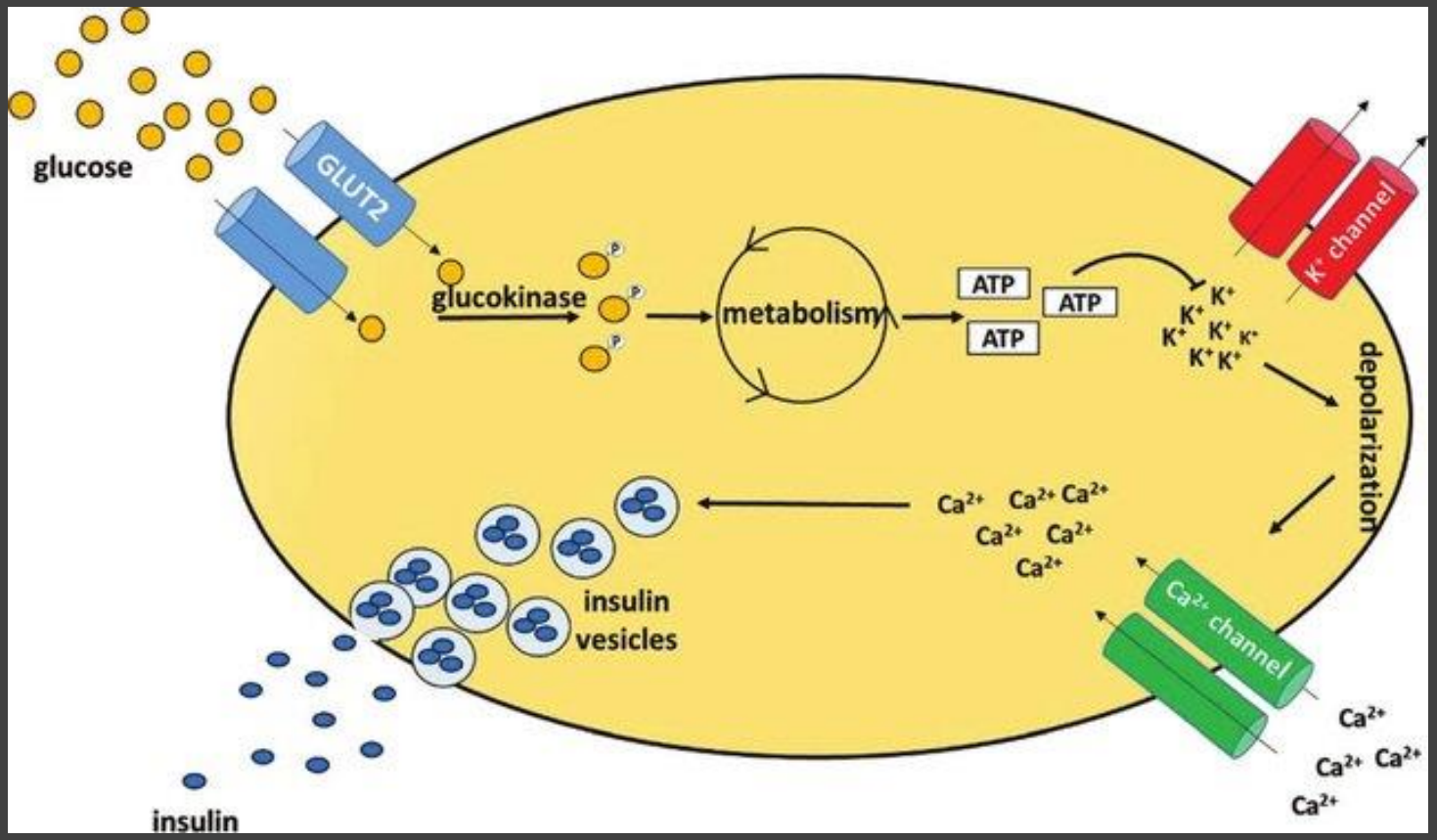


Glucose transporters

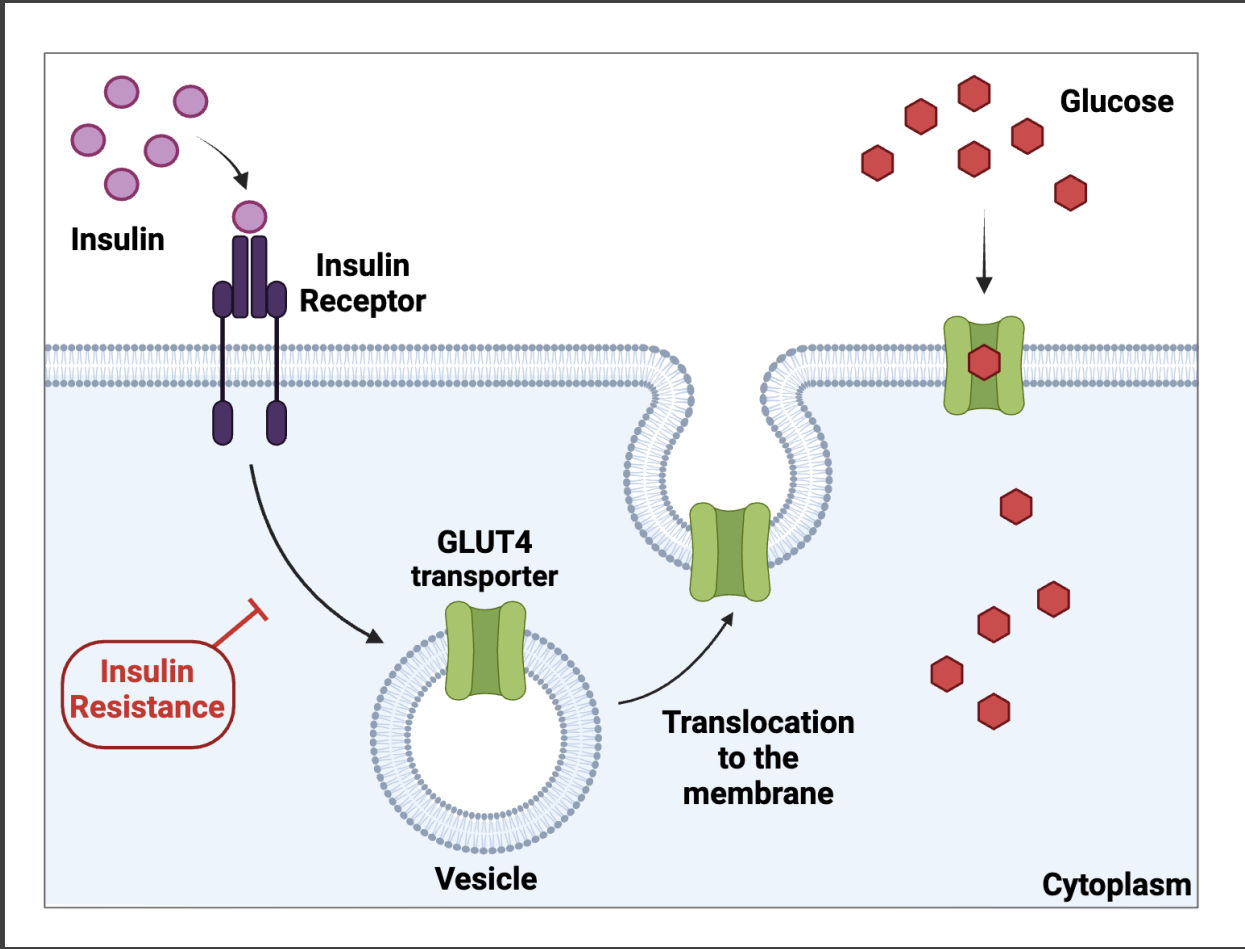
GLUT1	Brain, mammary gland, kidney, omental fat, skeletal muscle, bovine follicle, bovine ovary, and corpus luteum	Basal glucose transport across blood tissue barriers
GLUT2	Liver, islets, small intestine, kidney and jejunal region	Glucose (low affinity)
GLUT3	Brain, bovine ovary, follicles and corpus luteum	Glucose (high affinity)
GLUT4	Heart, muscle, brain and adipose tissue	Transport of glucose in all insulin-responsive tissues
SGLT1	Intestine and kidney	Glucose (high affinity)

transport aktywny wtórny

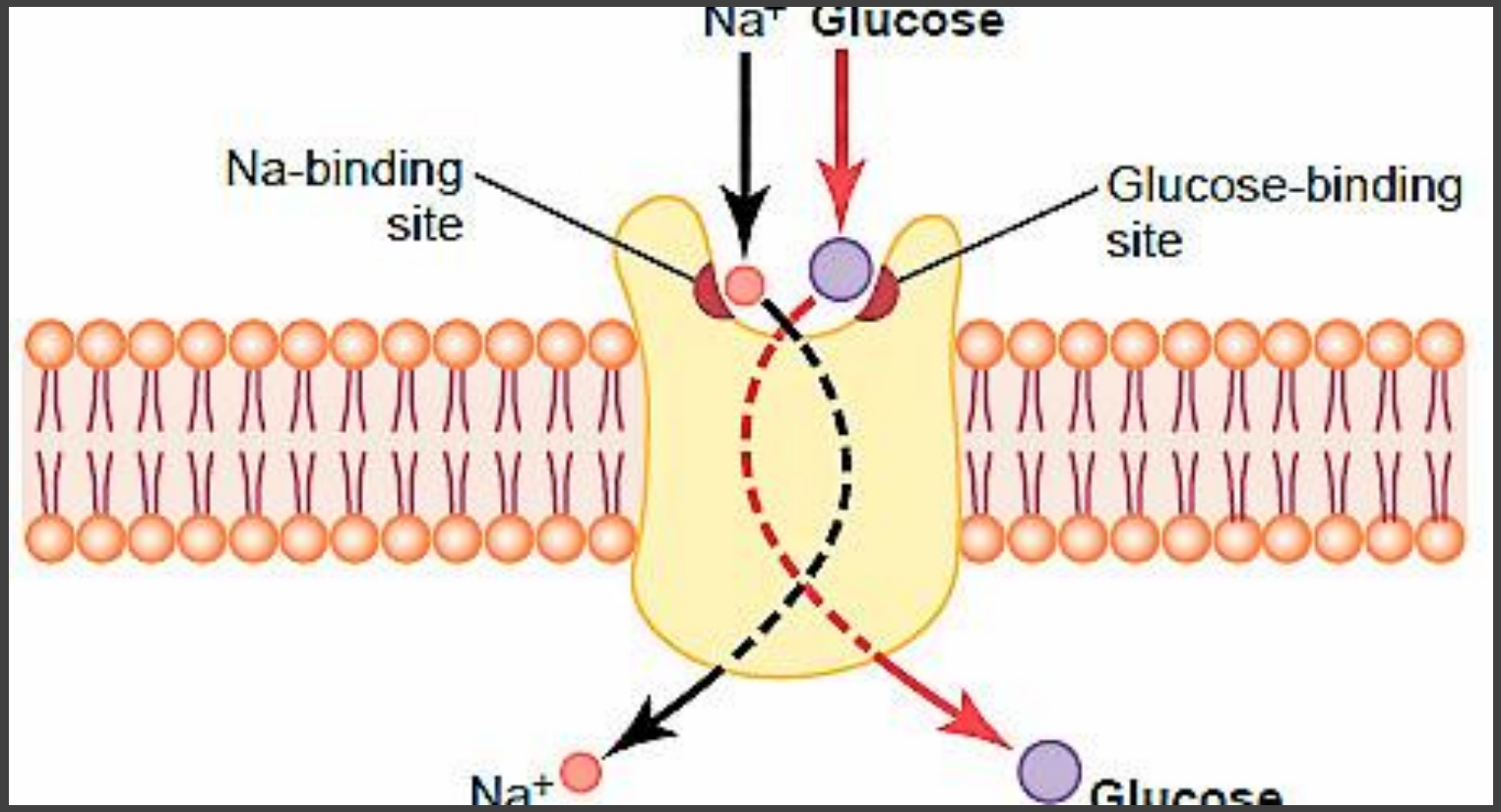
GLUT 2 and pancreatic islet beta-cells



GLUT 4 is insulin-sensitive

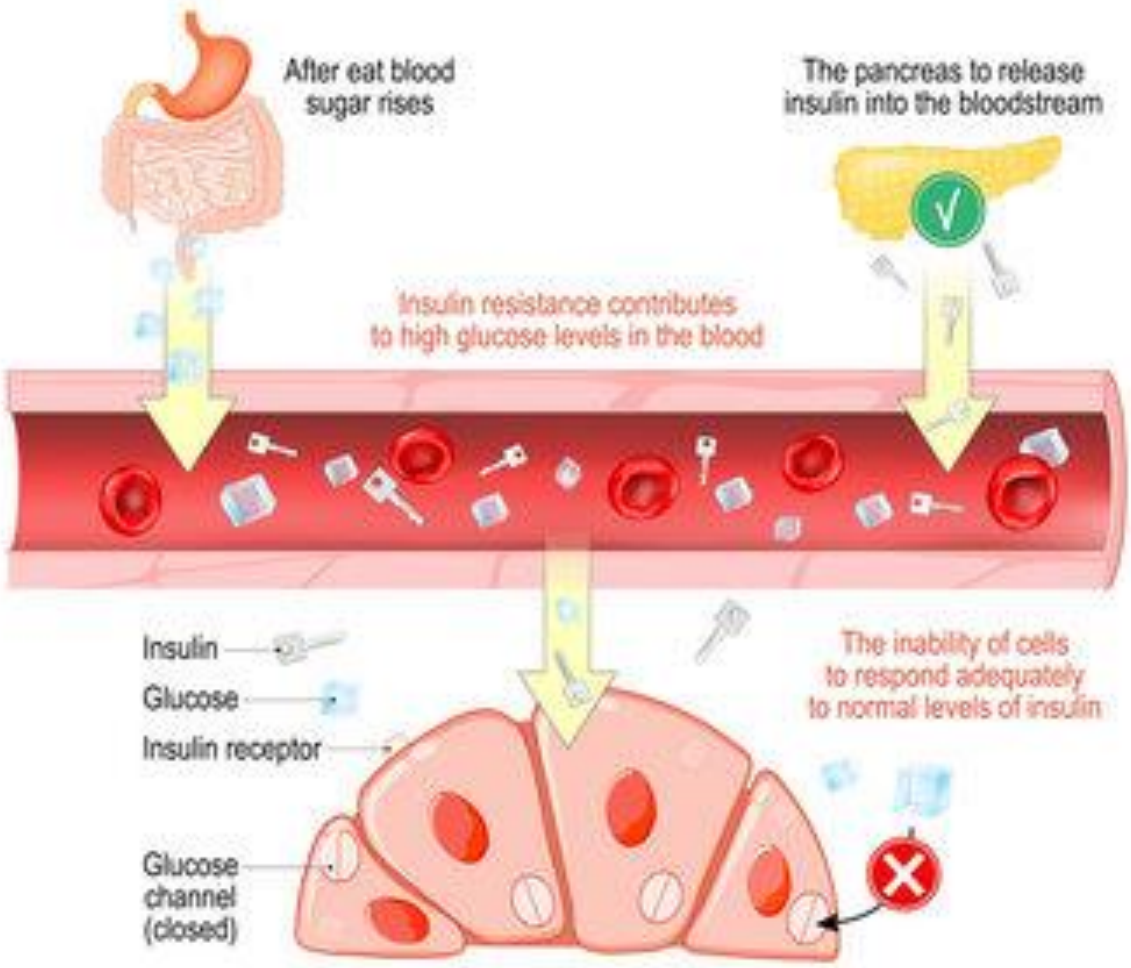


SGLT



Type 2 diabetes

(adult-onset diabetes)



What do we remember about plasma membrane?

Group 1

Phospholipids	
Cholesterol	
Resting potential	
Sodium-potassium pump	

Group 2

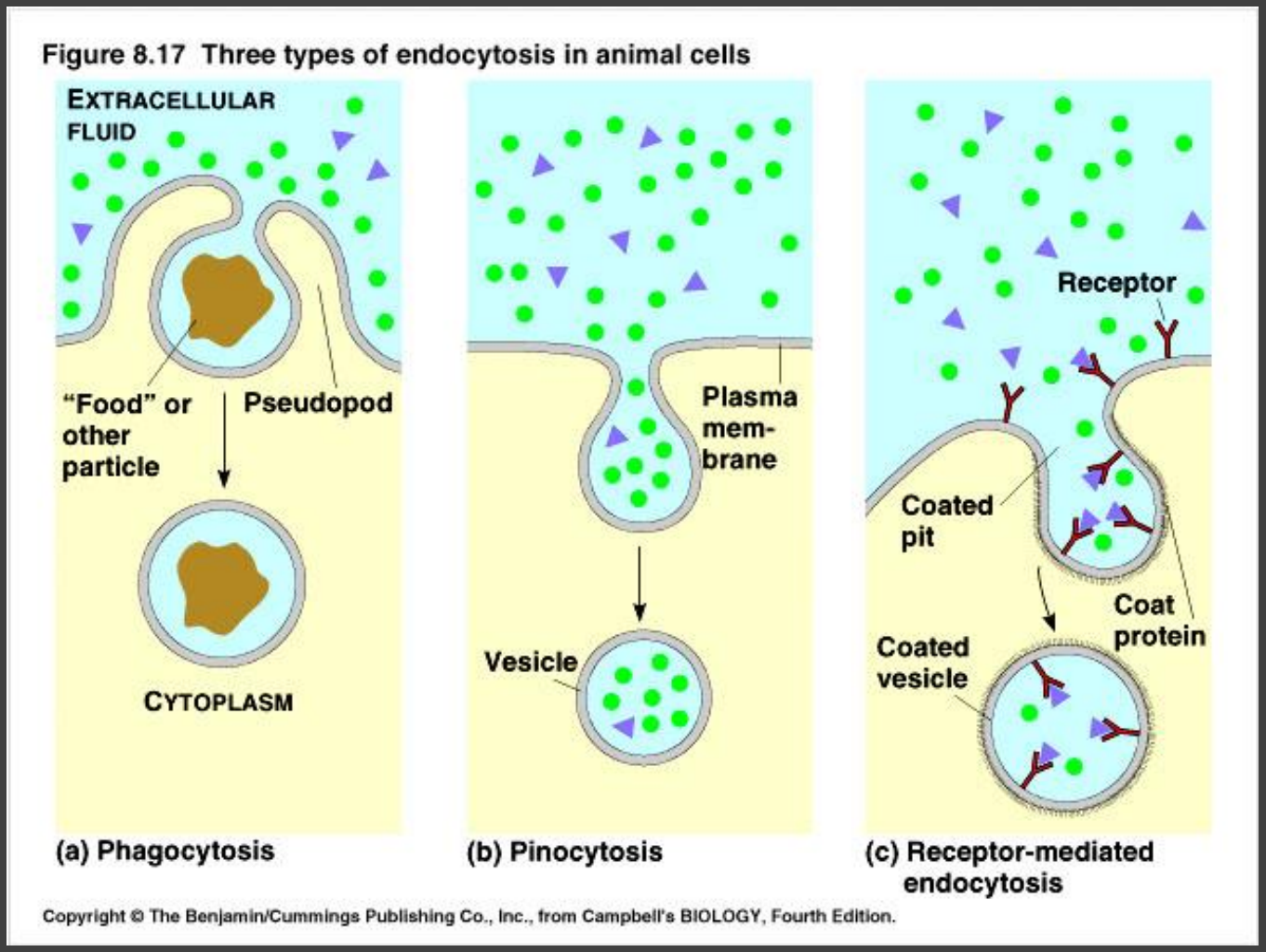
Glycocalyx	
Passive difussion	
Active primary transport	
Secondary active transport	

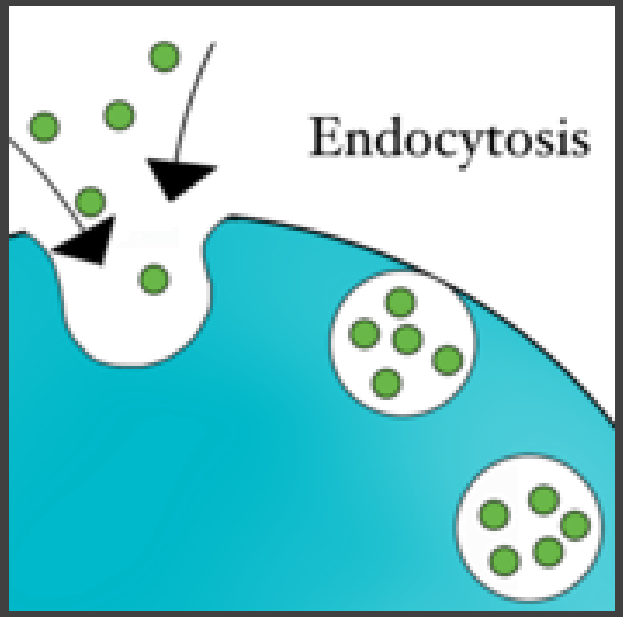
Glucose transporters

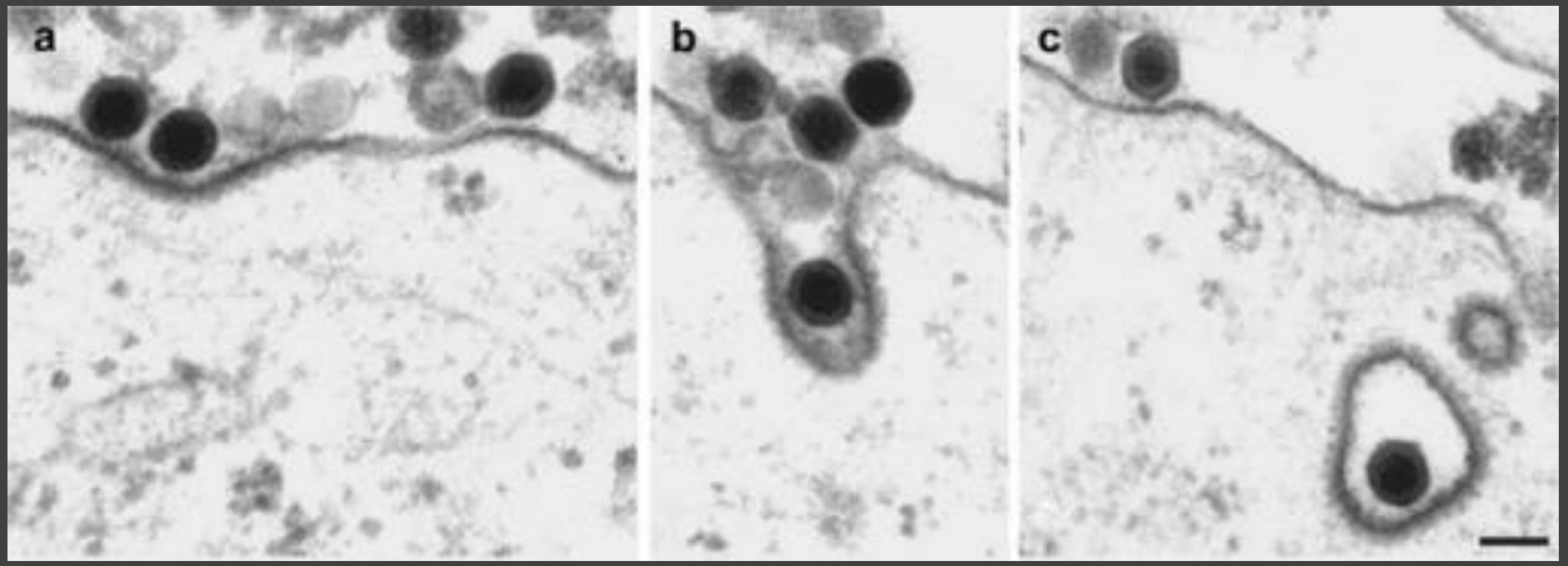
	Localisation	Function
GLUT1		
GLUT2		
GLUT3		
GLUT4		
SGT		

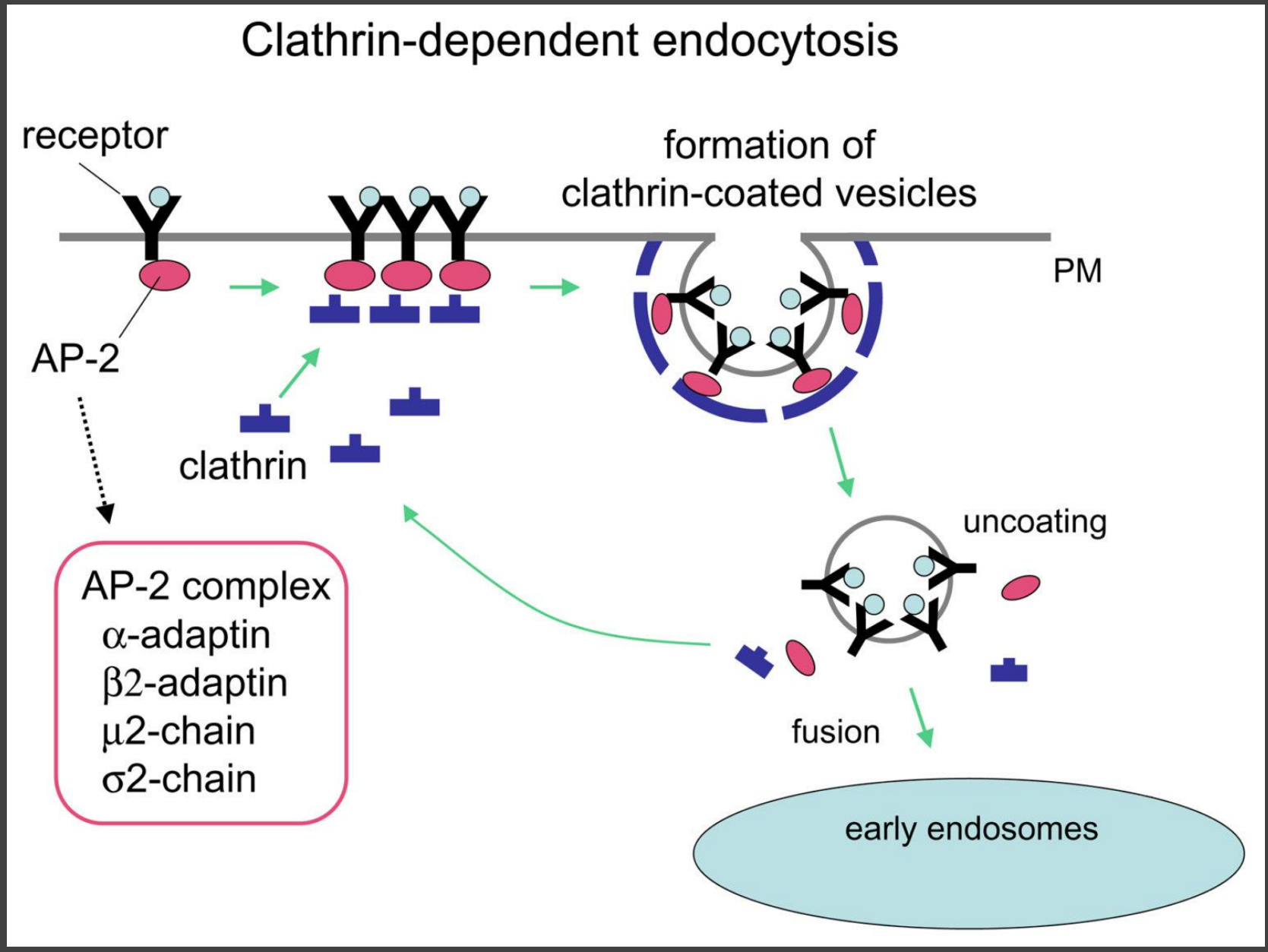
ENDOCYTOSIS - energy-using process by which cells absorb molecules

- Material is engulfed in the vesicle

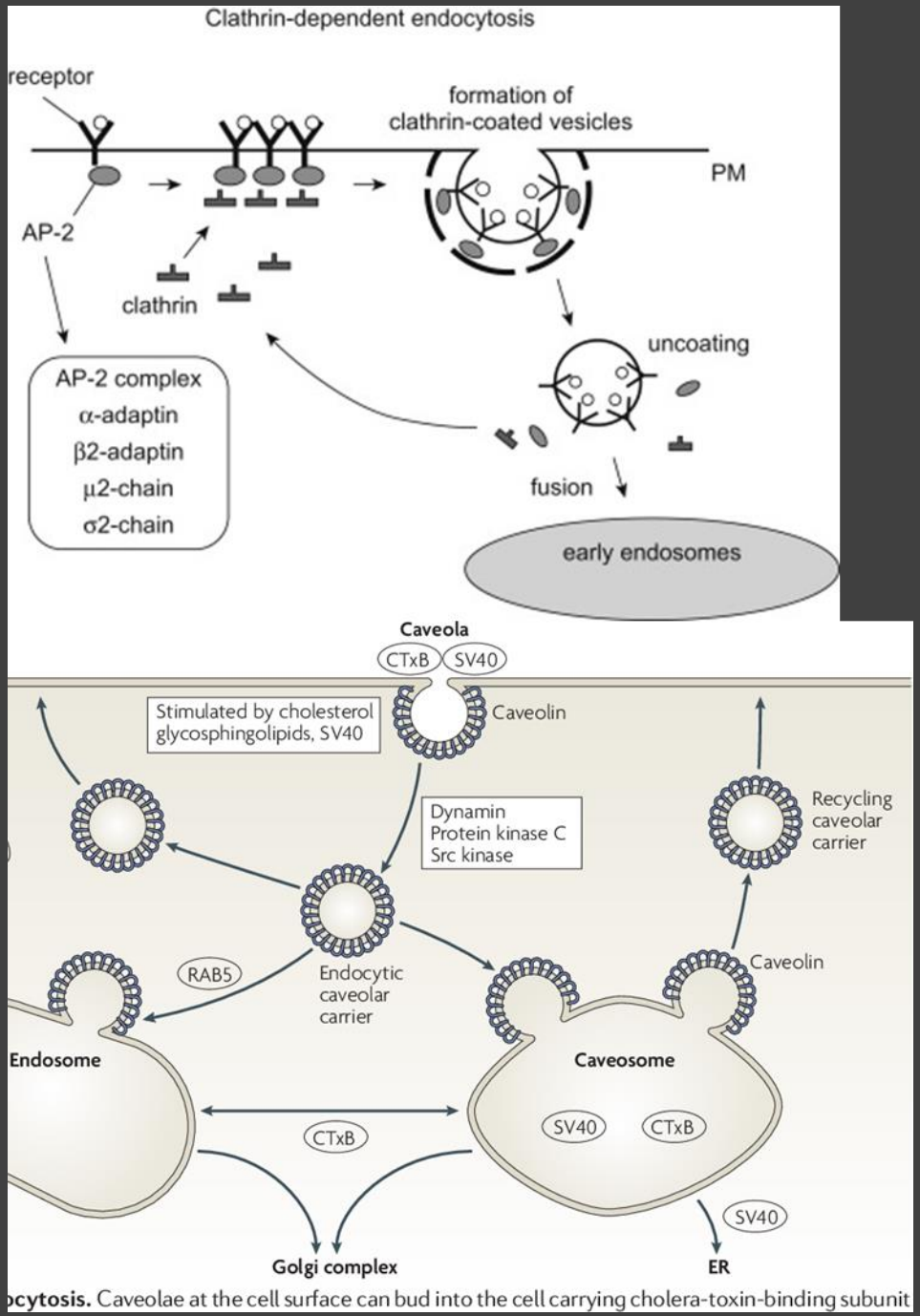



Endocytosis


a
b
c

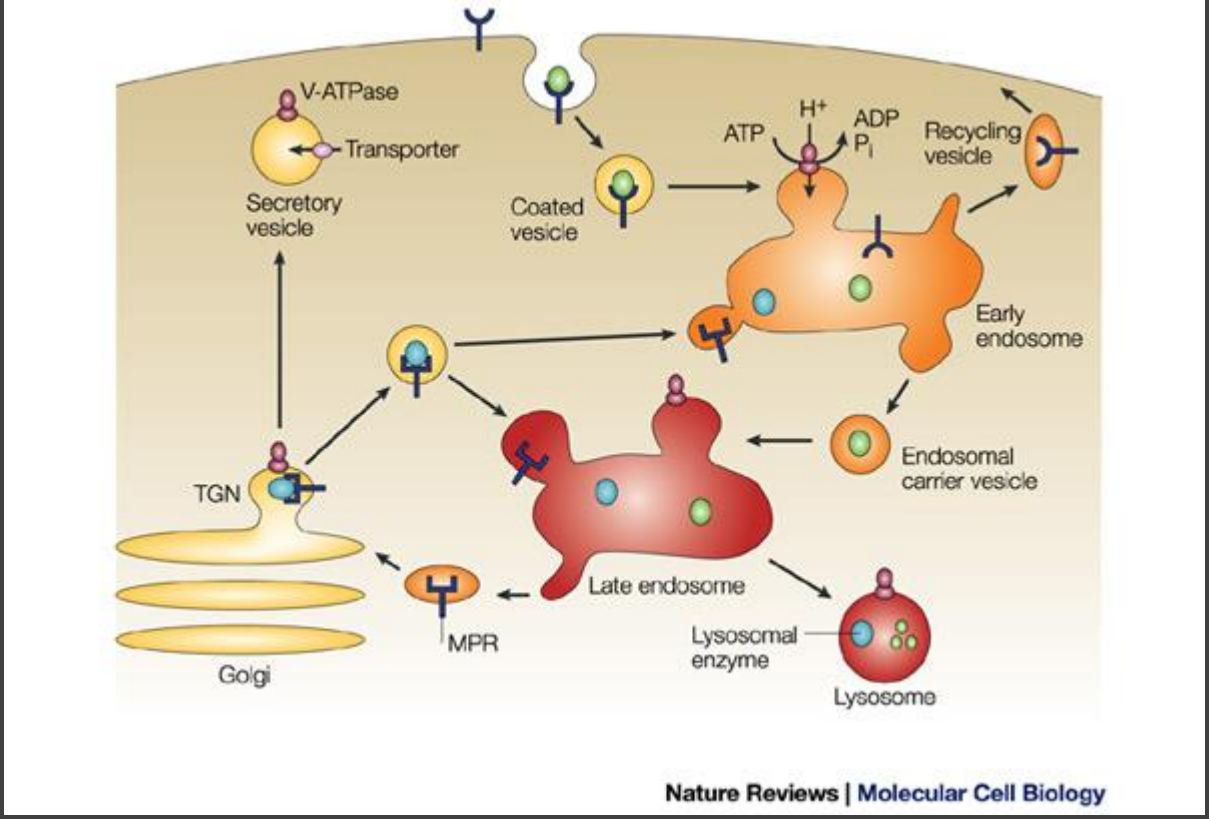

Clathrin-dependent endocytosis
receptor
formation of
clathrin-coated vesicles
PM
AP-2
clathrin
uncoating
AP-2 complex
α-adaptin
β2-adaptin
μ2-chain
σ2-chain
fusion
early endosomes

CLATHRIN vs CAVEOLIN



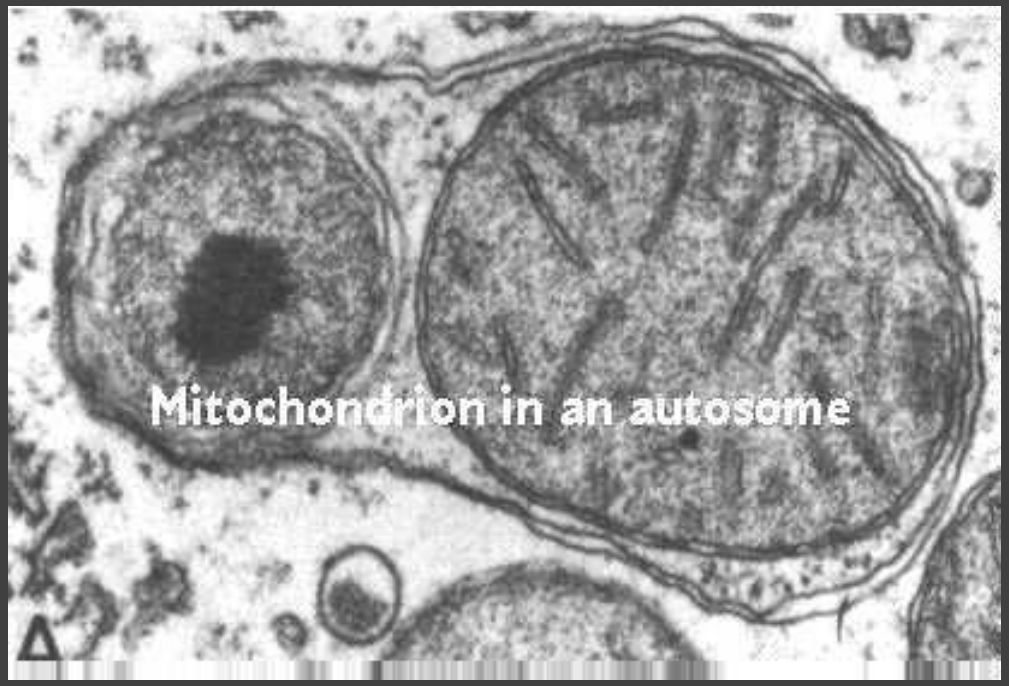
ENDOSOMES

- early endosomes – near the periphery of the cell – NEUTRAL pH
- late endosomes – deeper in the cytoplasm – LOW pH



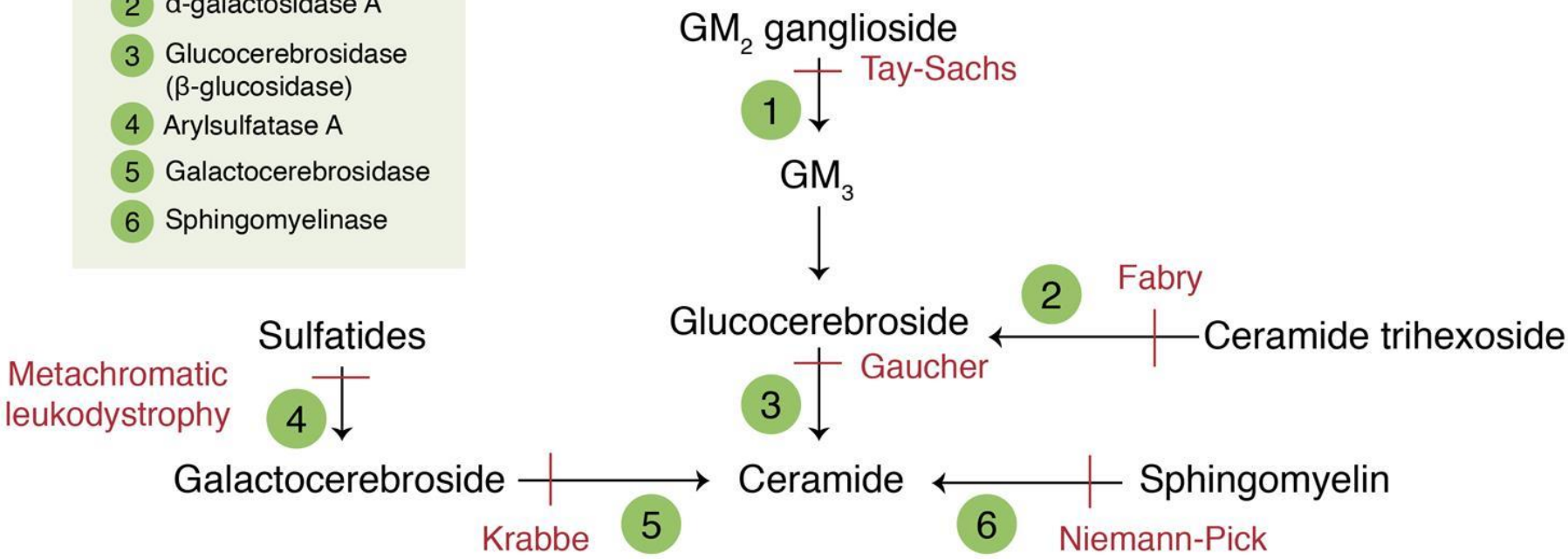
LYSOSOMES

- contain acid hydrolases (lipases, proteases, nucleases, sulfatases and glycosidases)
- pH 5.0
- digest excess or worn-out organelles (mitochondria), food particles,
and engulf viruses or bacteria



Lysosomal Storage Disorders

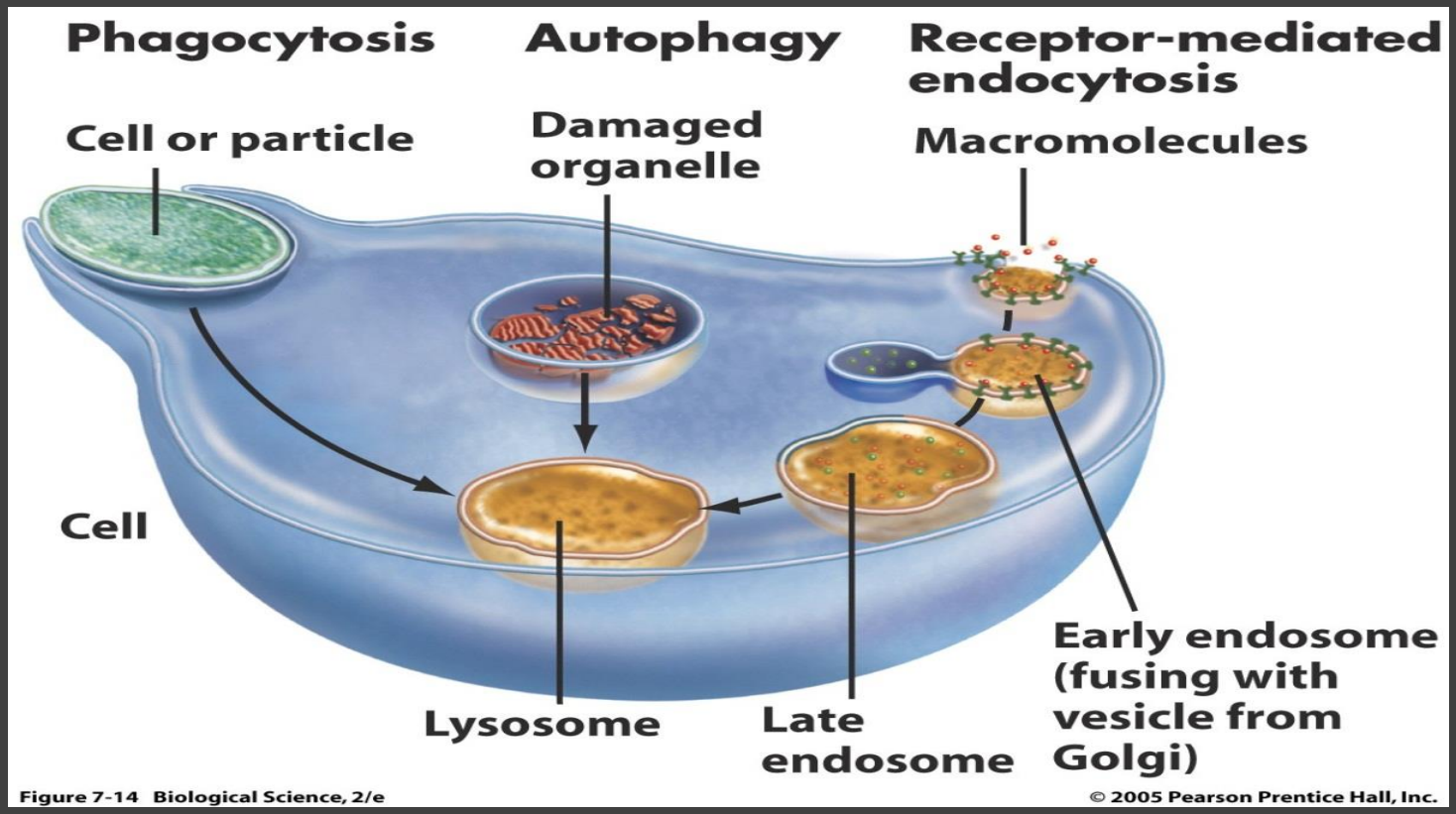
1. Hexosaminidase A
2. α-galactosidase A
3. Glucocerebrosidase (β-glucosidase)
4. Arylsulfatase A
5. Galactocerebrosidase
6. Sphingomyelinase



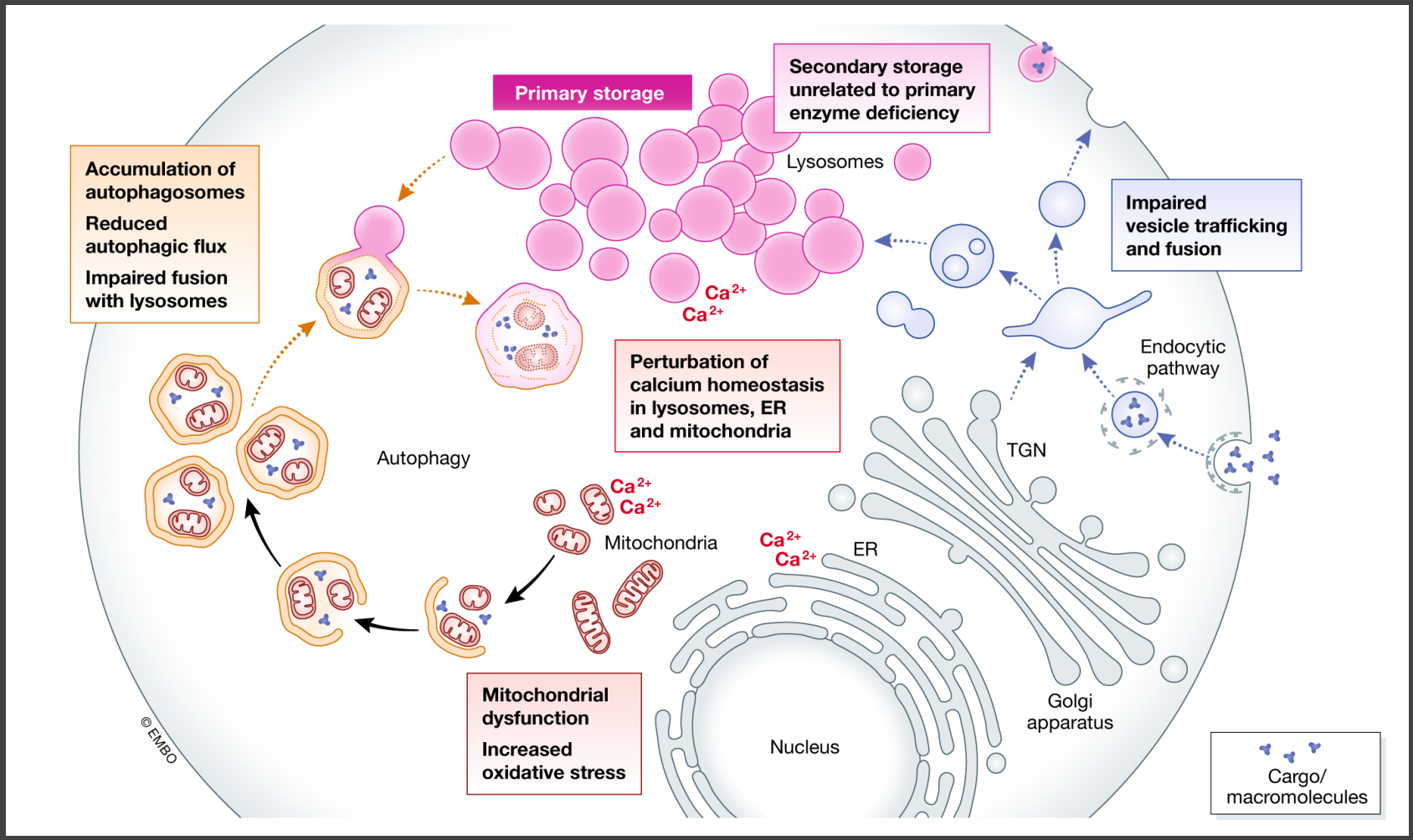
Lucy Liu

Transport of substances into lysosomes

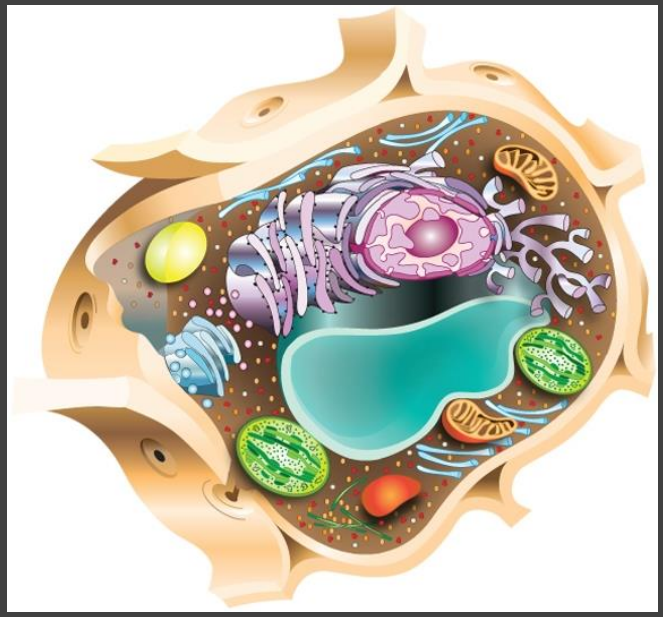
- **may be carried out by three ways**:
- Phagocytosis (viruses or bacteria)
- Autophagy (excess or senescent organells)
- Receptor-mediated endocytosis (macromolecules)

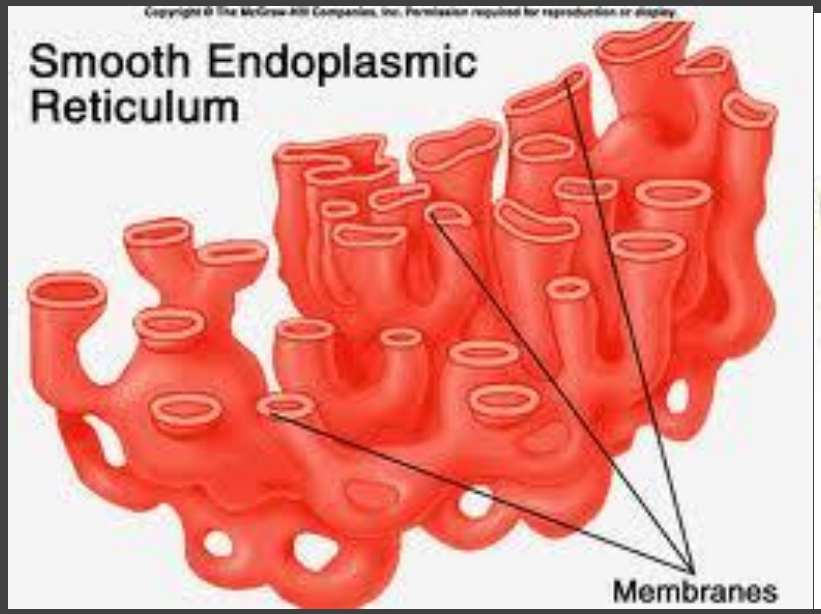


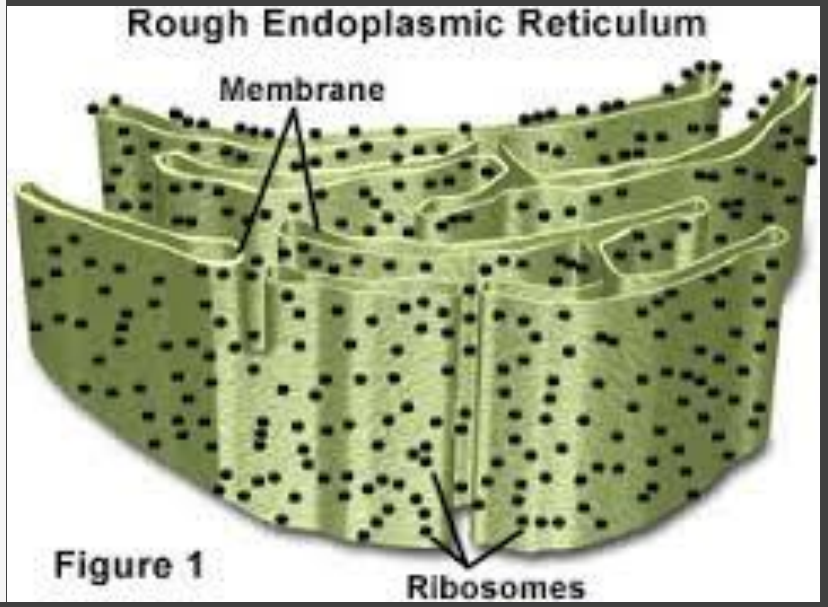
Autophagy


Primary storage
Secondary storage unrelated to primary enzyme deficiency
Lysosomes
Accumulation of autophagosomes
Reduced autophagic flux
Impaired fusion with lysosomes
Impaired vesicle trafficking and fusion
Endocytic pathway
Ca2+
Ca2+
Perturbation of calcium homeostasis in lysosomes, ER and mitochondria
TGN
Autophagy
Ca2+
Ca2+
Mitochondria
Ca2+
Ca2+
ER
Mitochondrial dysfunction
Increased oxidative stress
Nucleus
Golgi apparatus
Cargo/ macromolecules
© EMBO

ENDOPLASMIC RETICULUM







Smooth endoplasmic reticulum (SER)

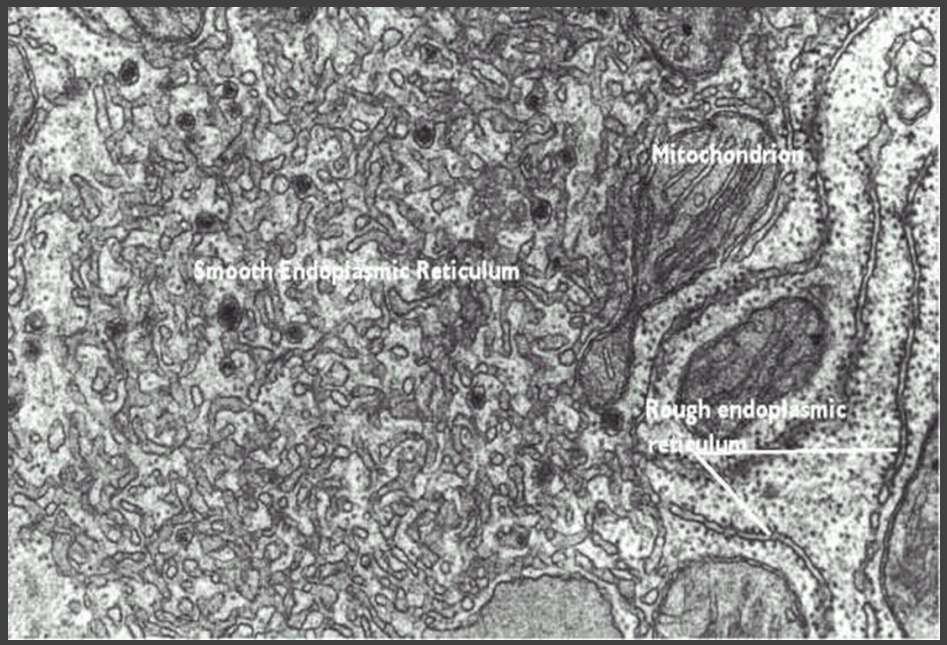
*Synthesis of lipids on the basis of cholesterol (components of cell membrane, steroid hormones)

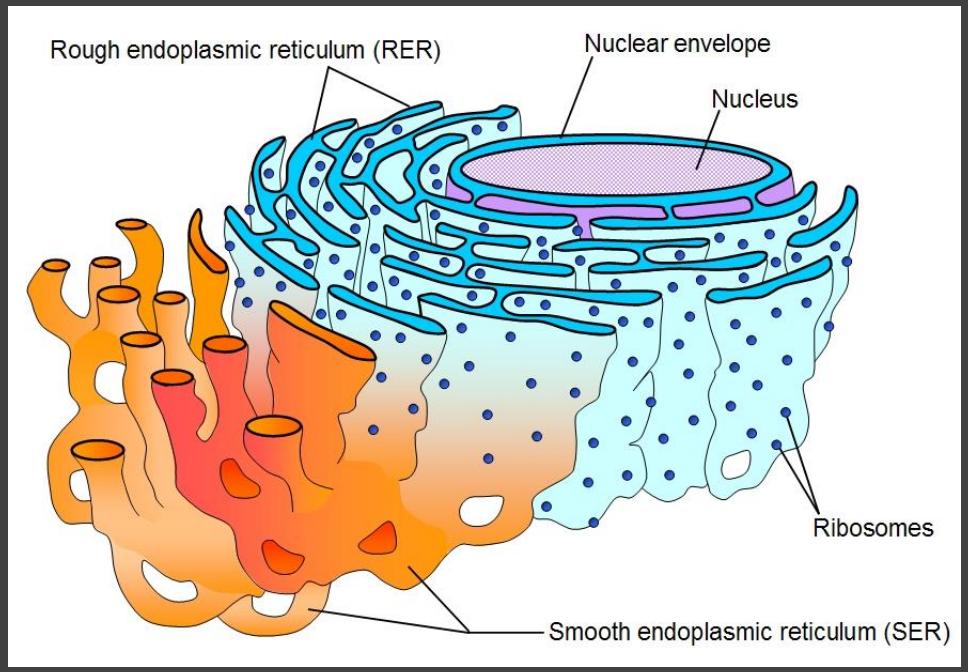
* Detoxification of harmful substances

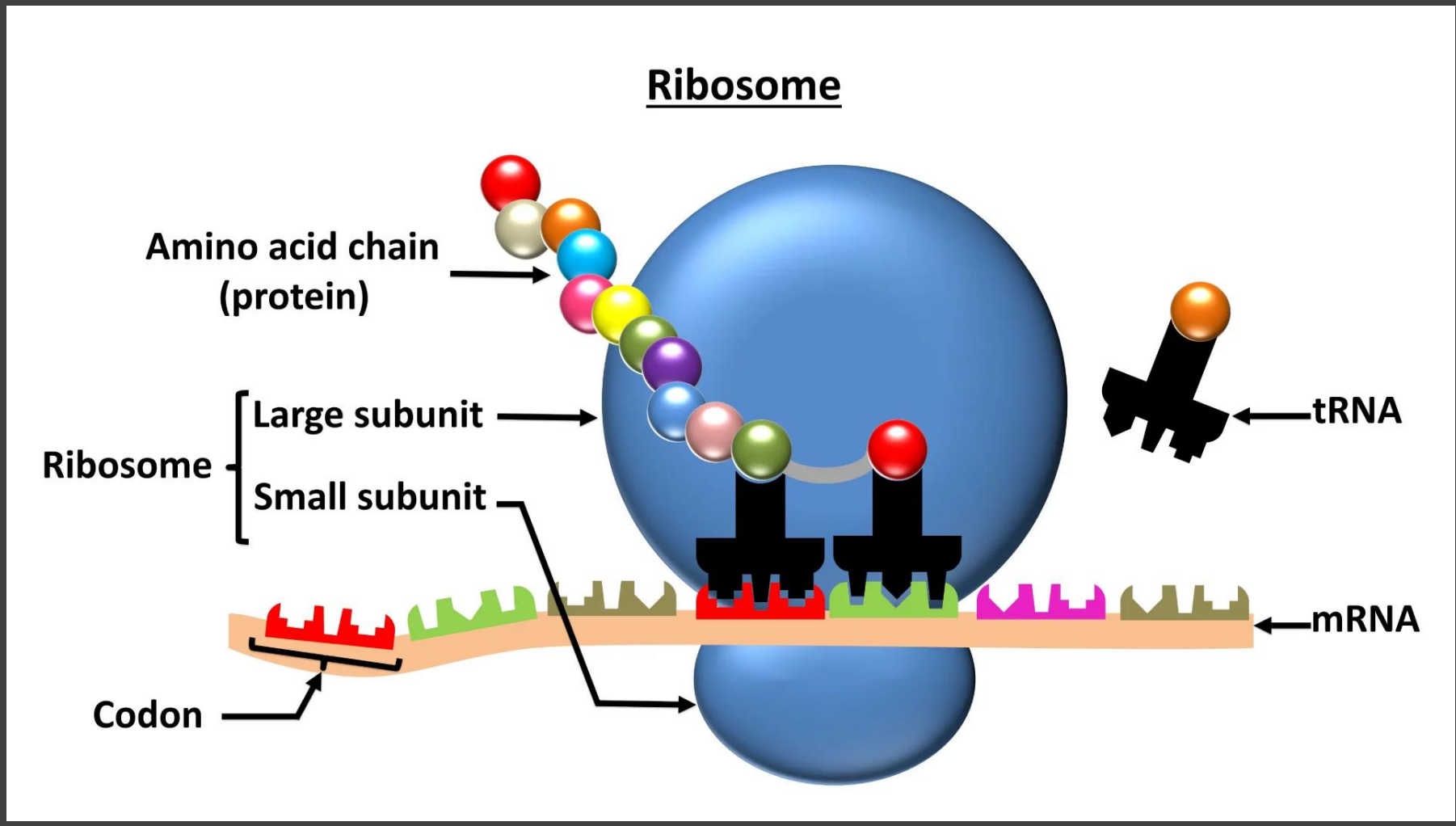
*Accumulation and storage of calcium

Rough endoplasmic reticulum (RER)

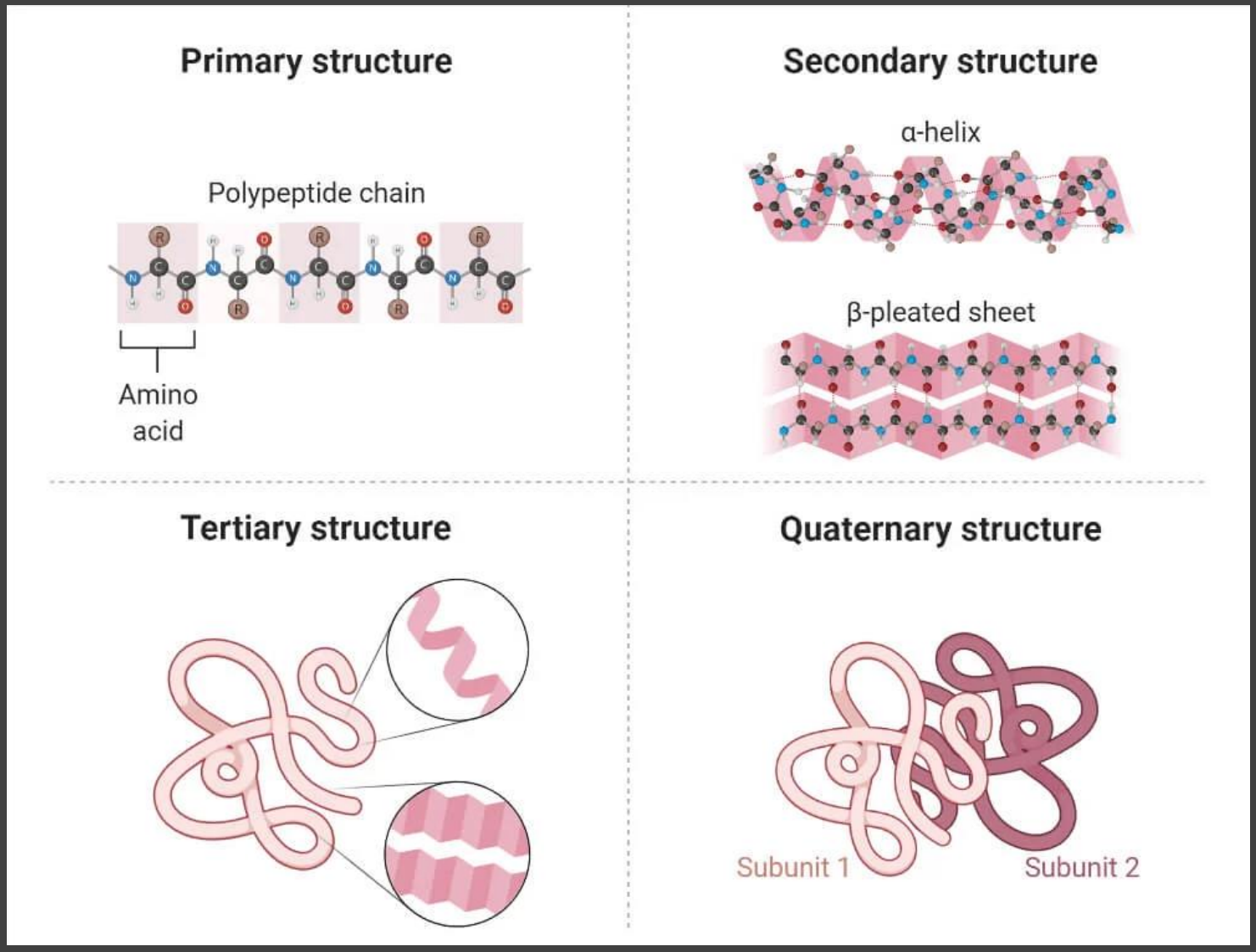
- contains **ribosomes** on the cytosolic face - the sites of protein synthesis
- is the site of synthesis of proteins
- post-translational modifications of proteins






Ribosome
Amino acid chain
(protein)
Large subunit
Ribosome
Small subunit
tRNA
mRNA
Codon

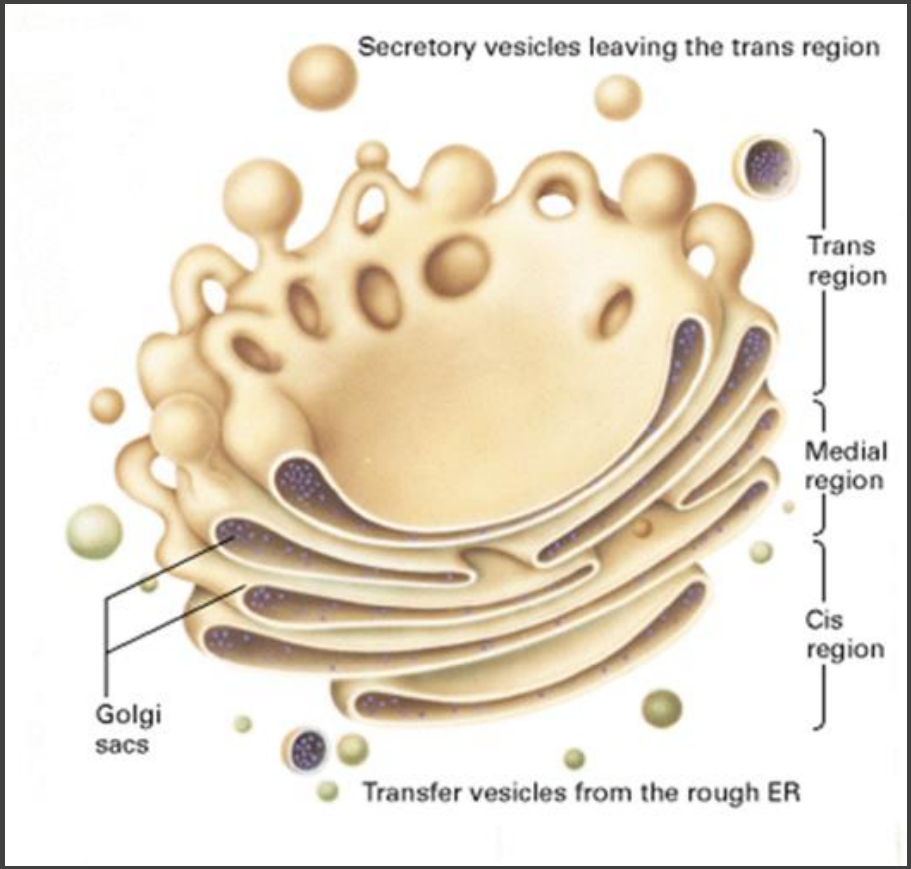
Protein synthesis

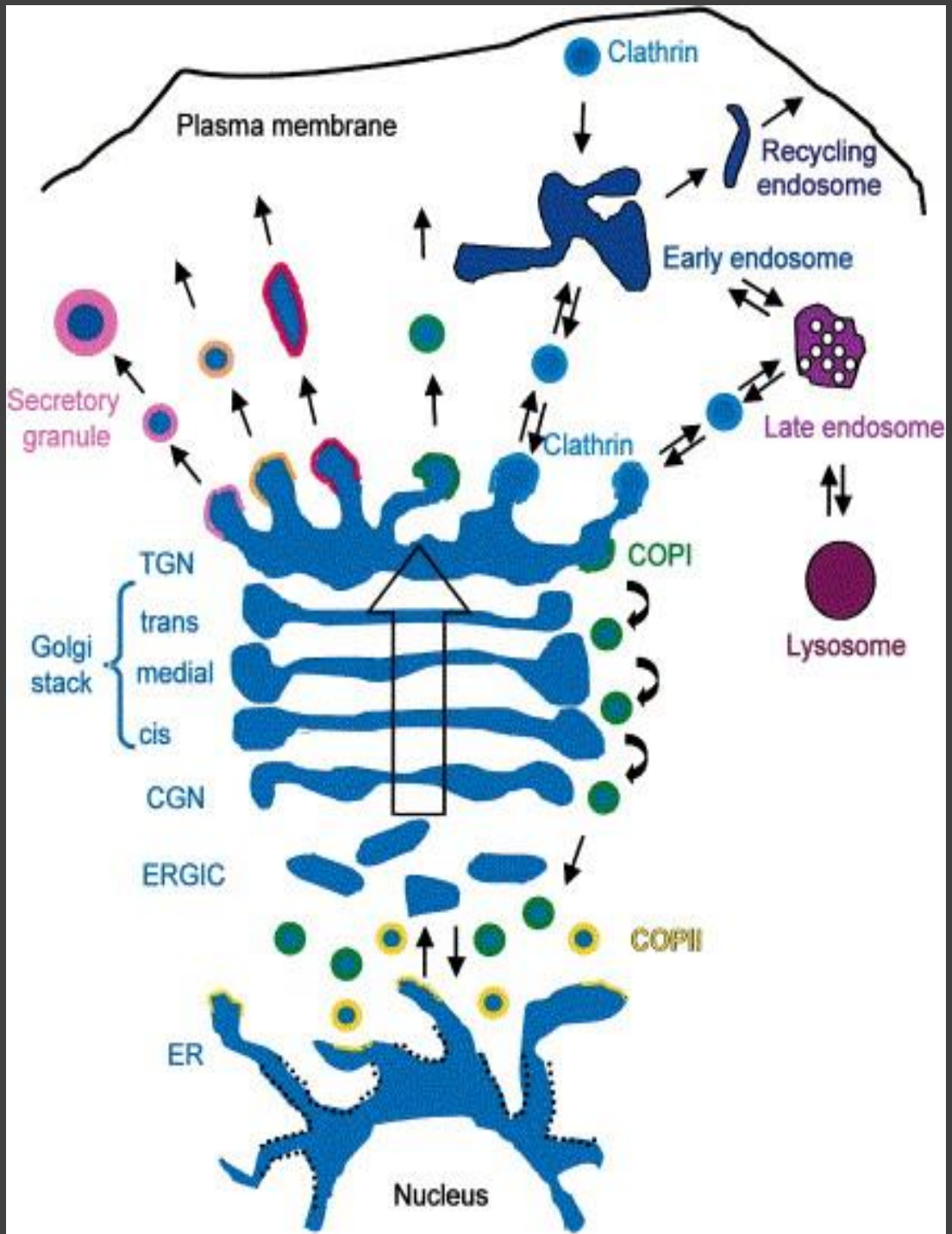


Golgi Apparatus

- flattened membrane-bounded cisternae – Golgi stack
- convex cis-face, closest to the RER (entry face)
- medial face
- concave trans-face (exit face)

Function:
posttranslational modification and packaging of proteins

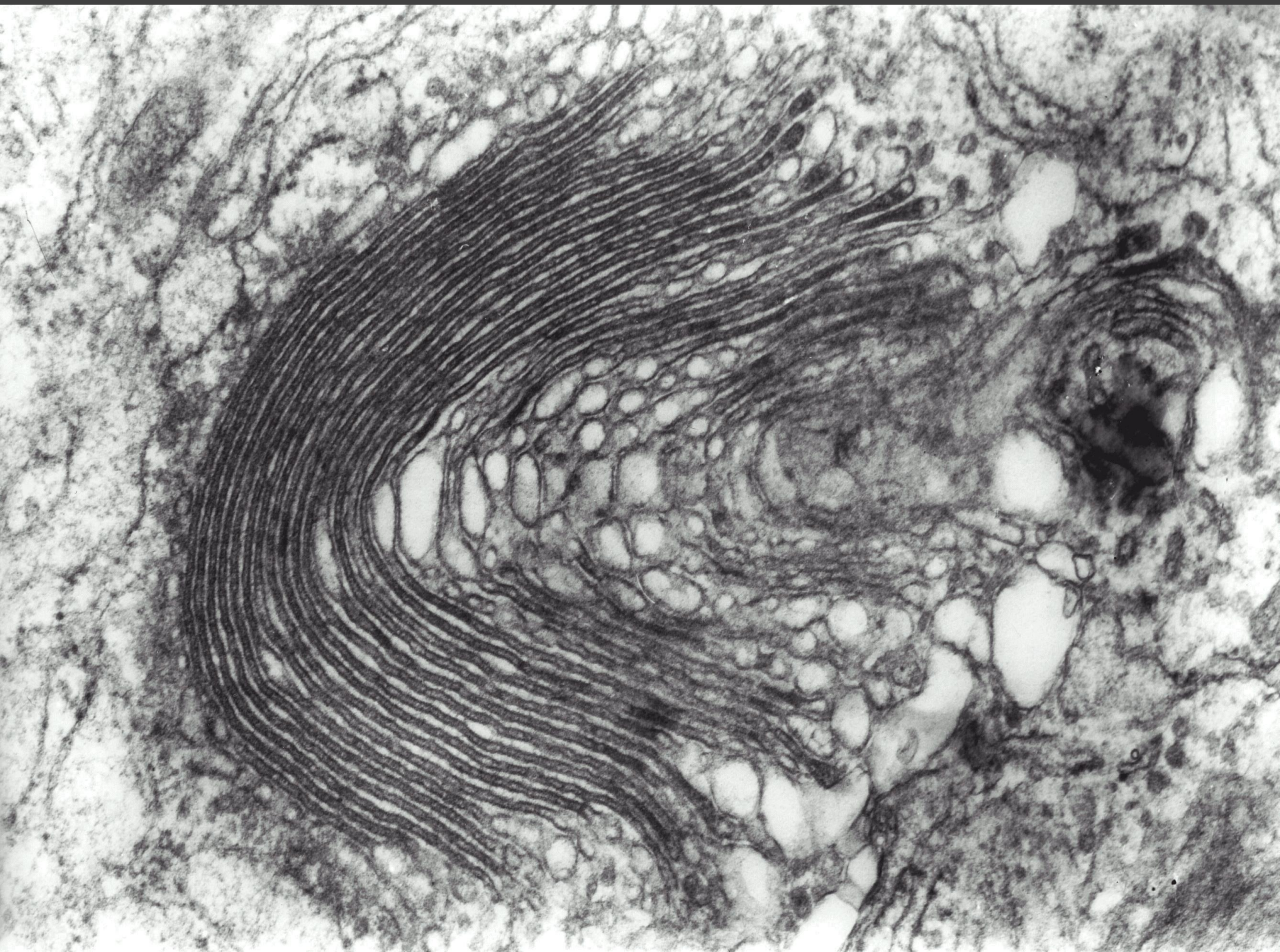




Vesicles that transport proteins are labeled by coat proteins (according to their destination)

Types of coat proteins

- **coatomer I (COP I)** – vesicles that are returned from trans-face
- **coatomer II (COPII)** – vesicles between RER and cis-face
- **clathrin –** vesicles which bud off the trans-face



What do we remember about endoplasmic membrane compartment?

Group 1

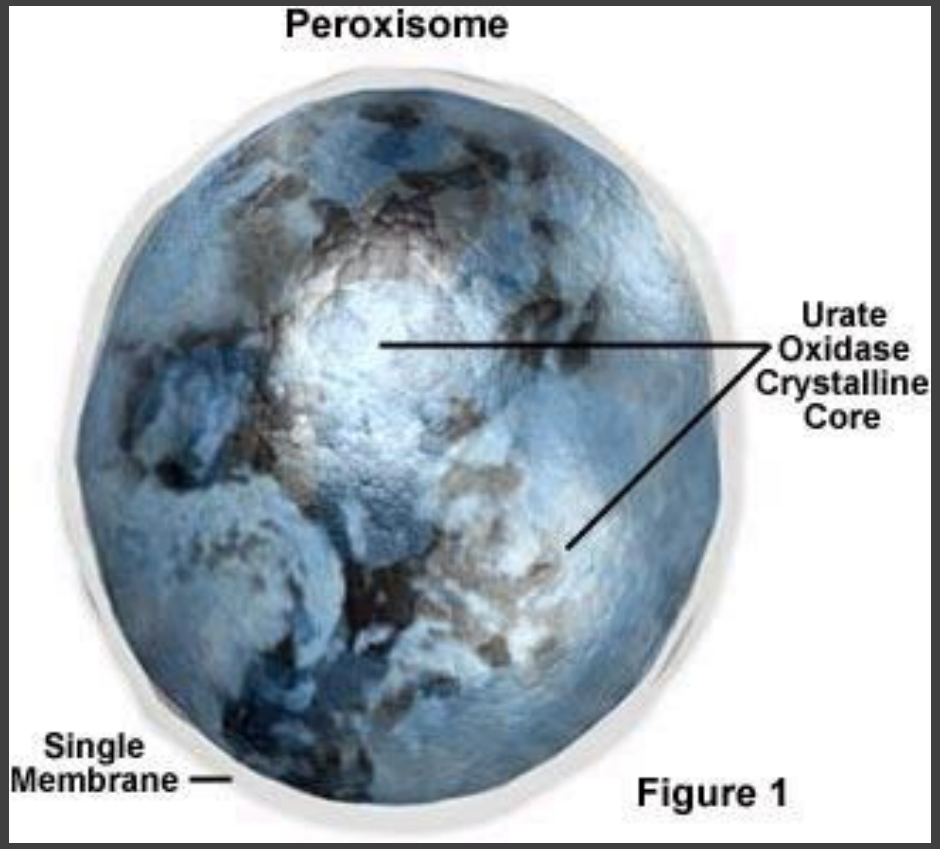
Rough endoplasmic reticulum	
Endosomes	
Lysosomes	

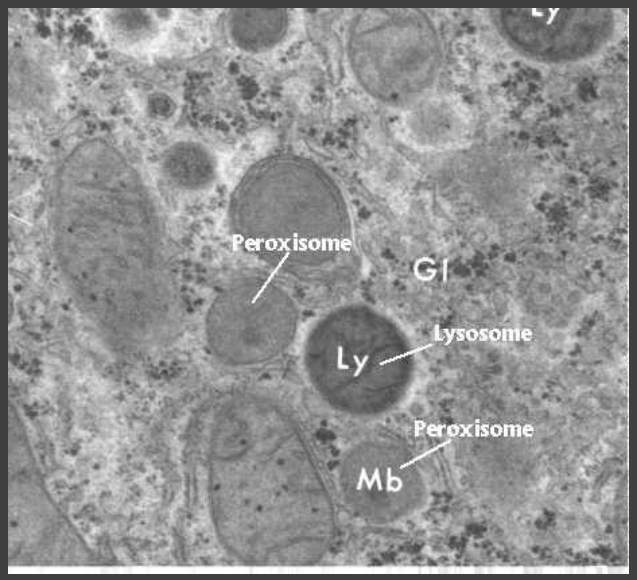
Group 2

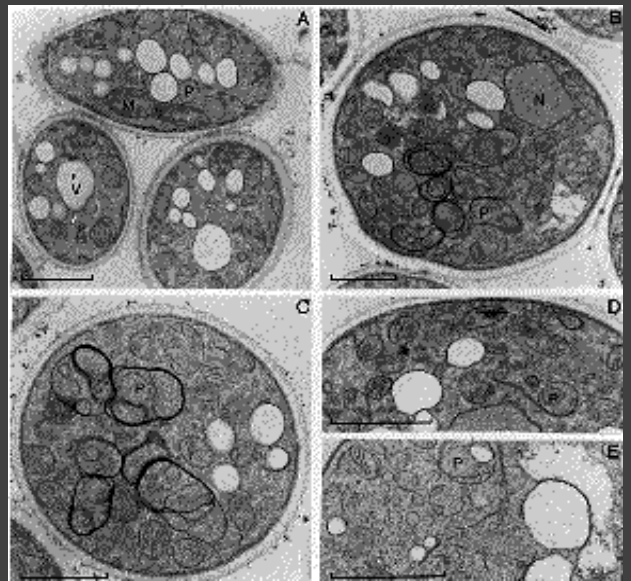
Smooth endoplasmic reticulum	
Golgi apparatus	
Exosomes	

PEROXISOMES

- Membrane-bound organelles.
- Present in all animal cells



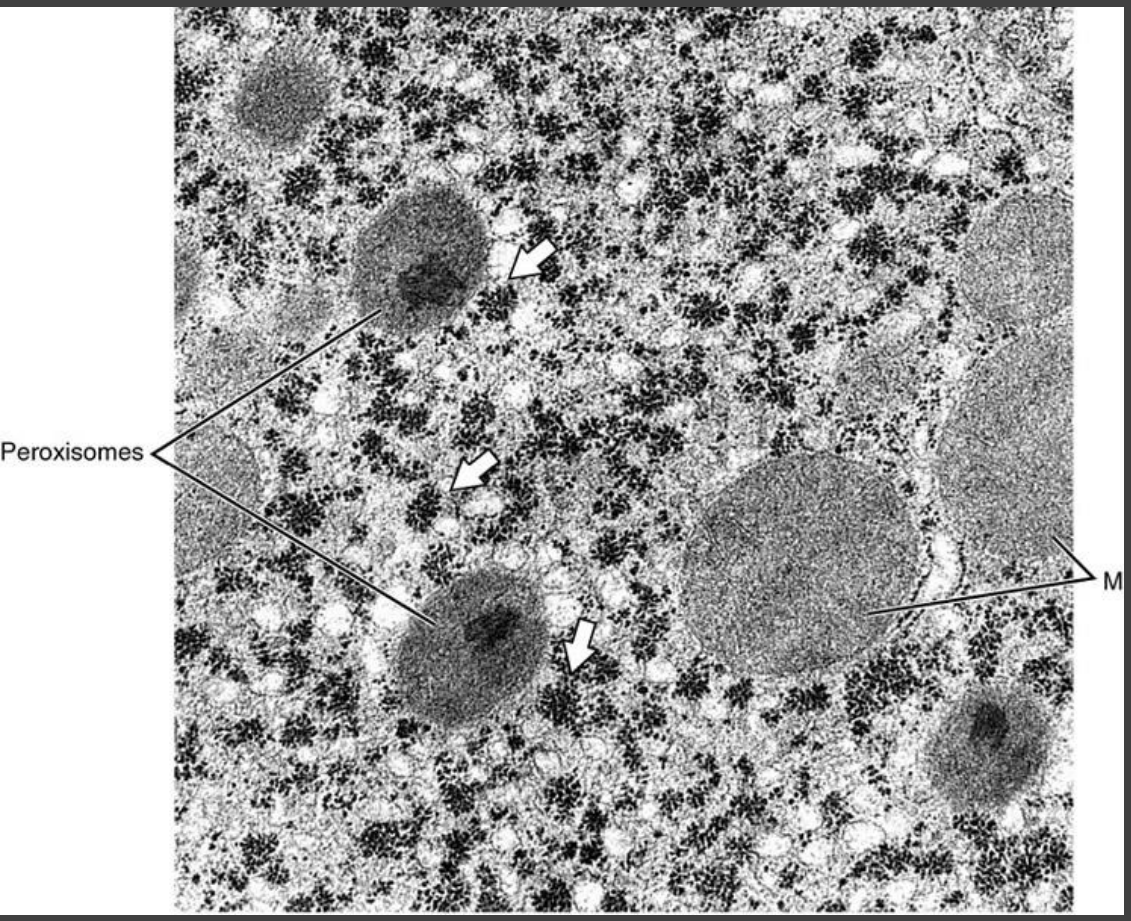




PEROXISOMES contain oxidative enzymes: catalase, D-amino acid oxidase and urate oxidase

Peroxisomes

(microbodies)

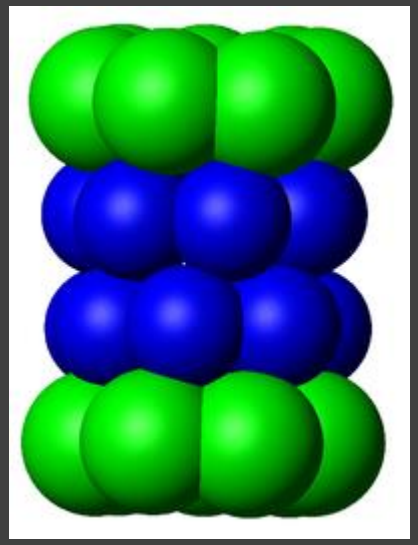


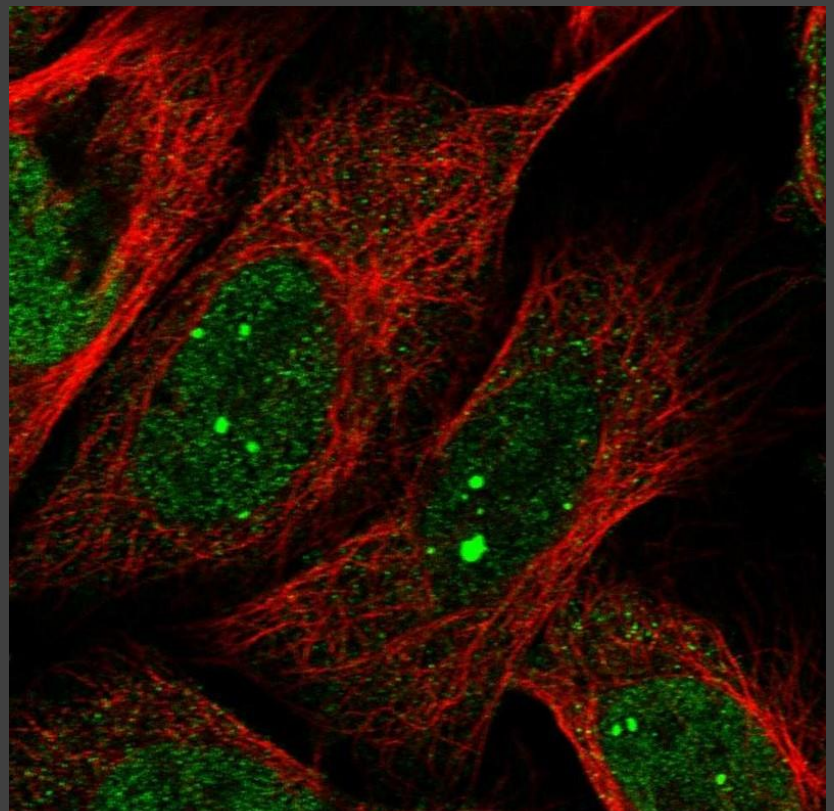
Urate oxidase
Catalase
D-amino acid oxidase

- Catabolism of long-chained fatty acids (beta oxidation)
- Forming acetyl coenzyme A (CoA)
- Forming hydrogen peroxide (H_2O_2) – detoxifies various noxious agents and kills microorganisms

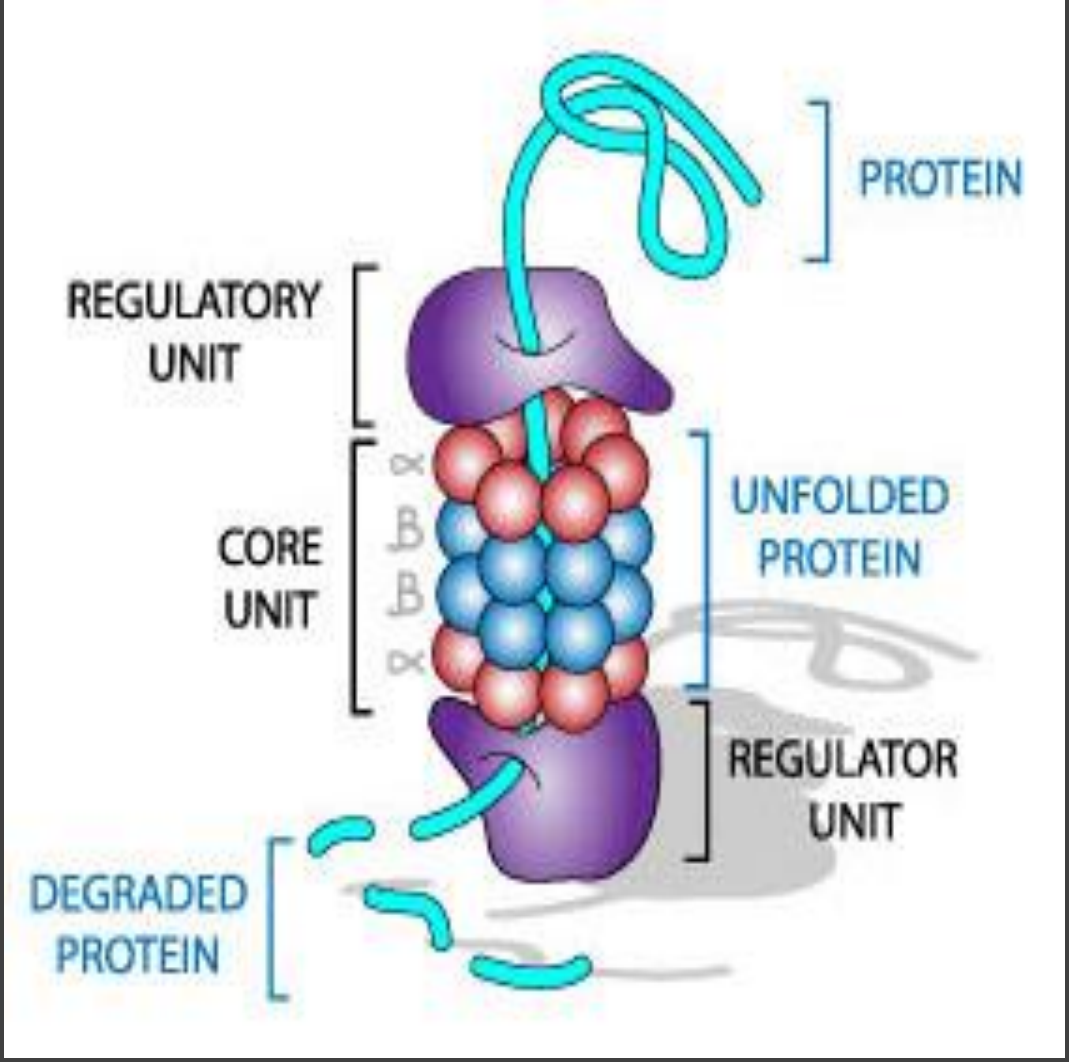
PROTEASOMES

- are protein complexes
- they are located in the nucleus and the cytoplasm
- the main function of the proteasome is to degrade unneeded or damaged proteins by proteolysis





PROTEASOME - STRUCTURE



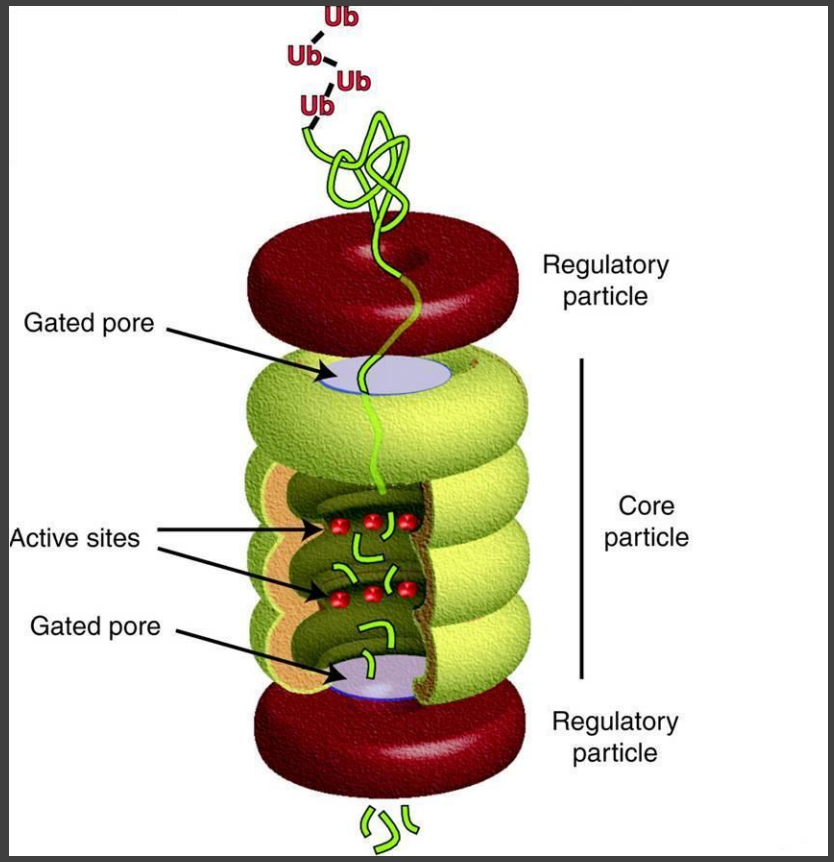
- cylindrical complex containing a „core” of four stacked rings forming a central pore

- each ring is composed of seven individual proteins

- the inner two rings are made of seven beta subunits that contain protease active sites

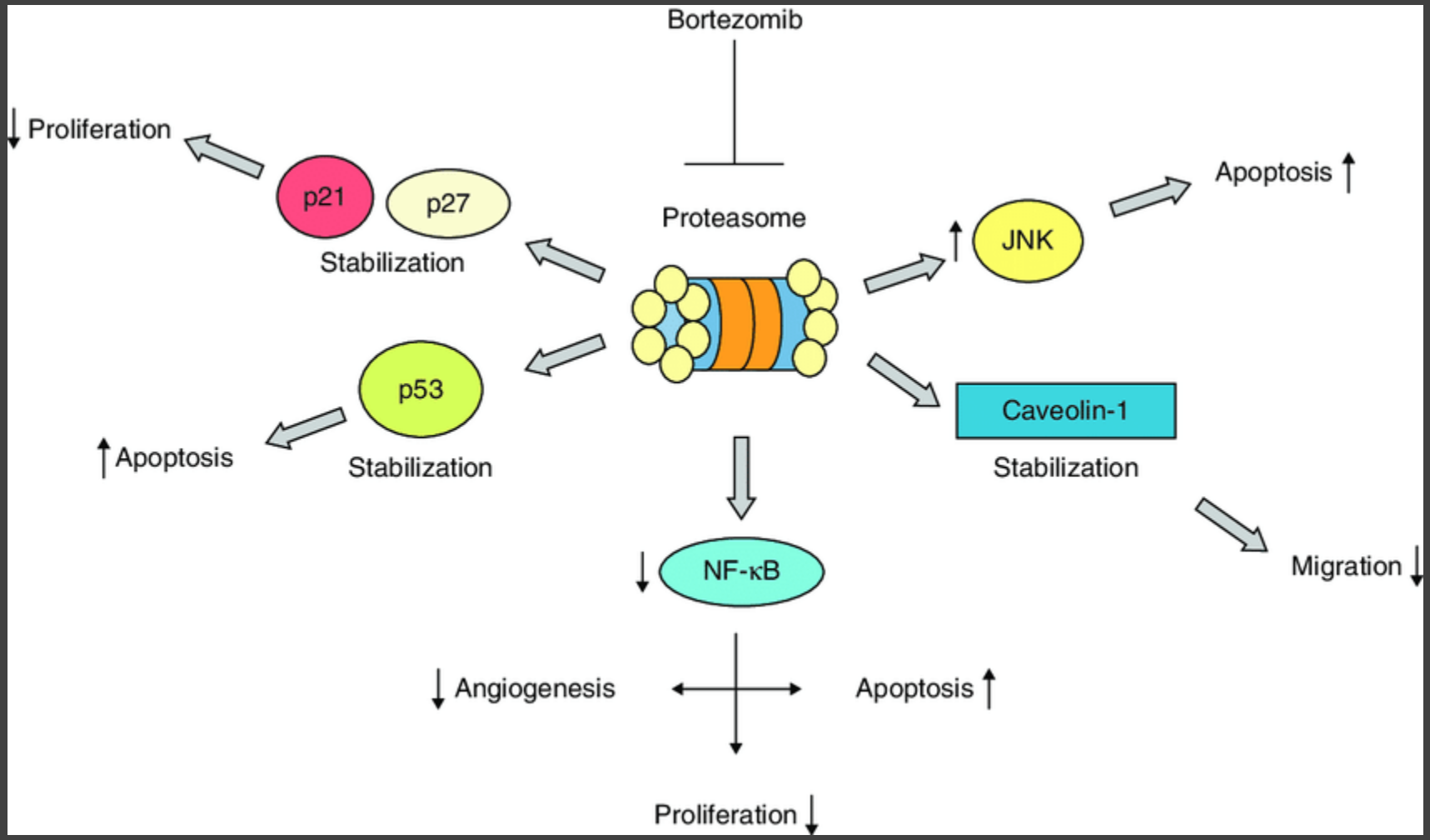
- the outer two rings contain a subunits whose function is to maintain a „gate”

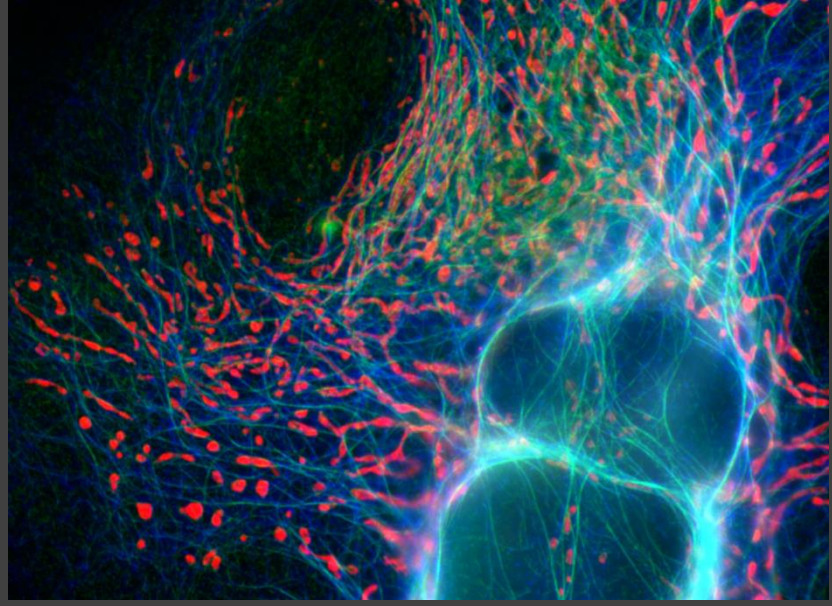
PROTEASOMES



- protein must be ubiquitinated before being degraded (several ubiquitin molecules are attached to a lysine residue of the protein to form polyubiquinated protein)
- protein must be at least partially unfolded before they enter the core

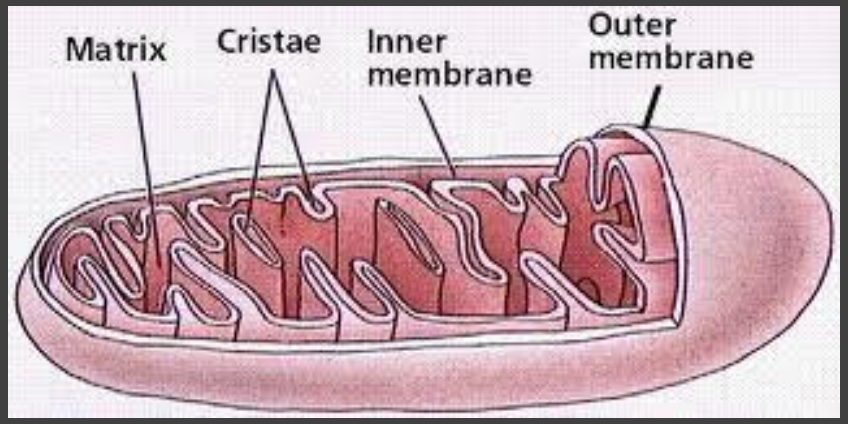
Proteasome inhibitors



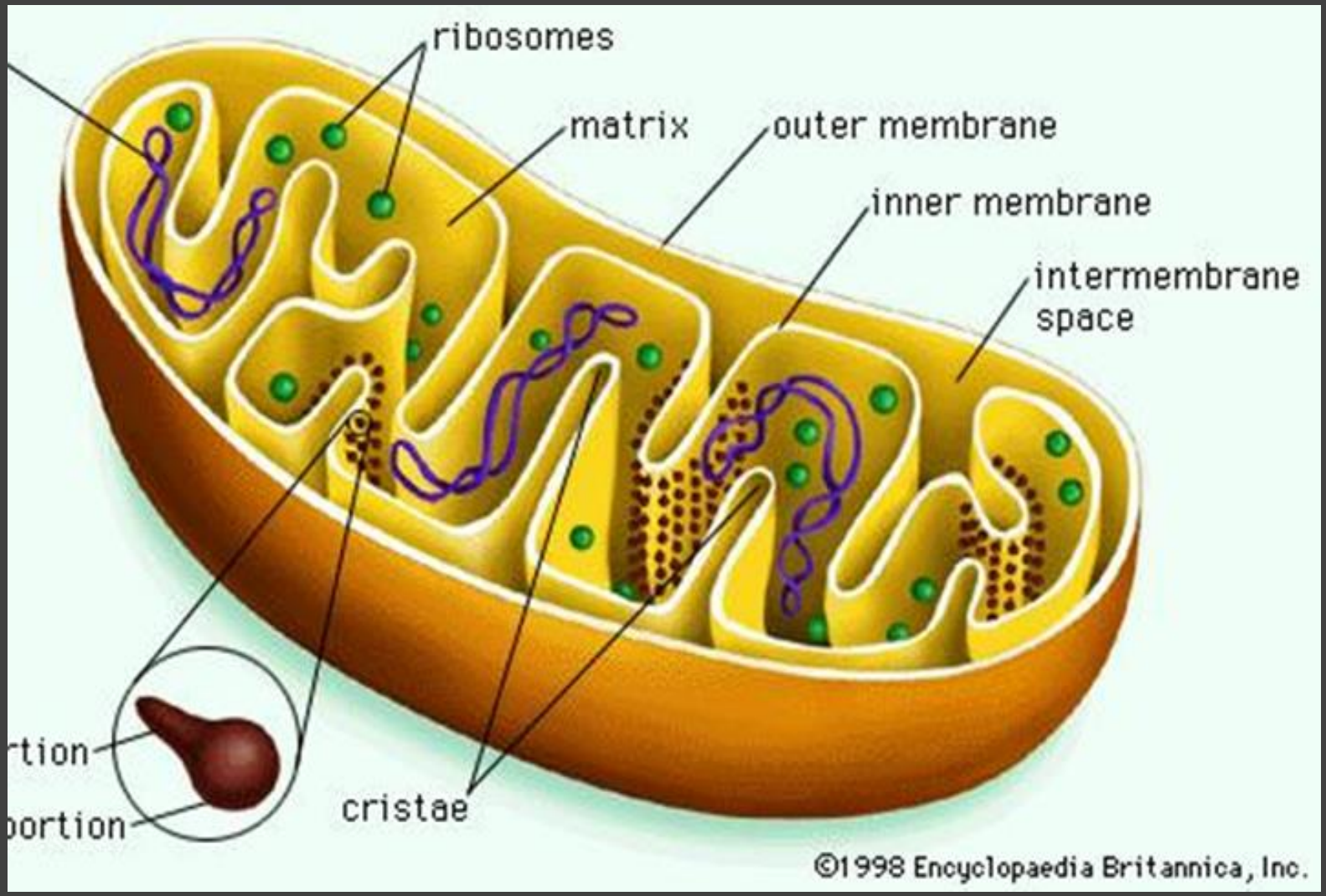


MITOCHONDRIA

- are membrane-bound structures
- they generate most of the cell's supply of adenosine triphosphate (ATP), used as a source of chemical energy
- the mitochondrion has its own independent genome

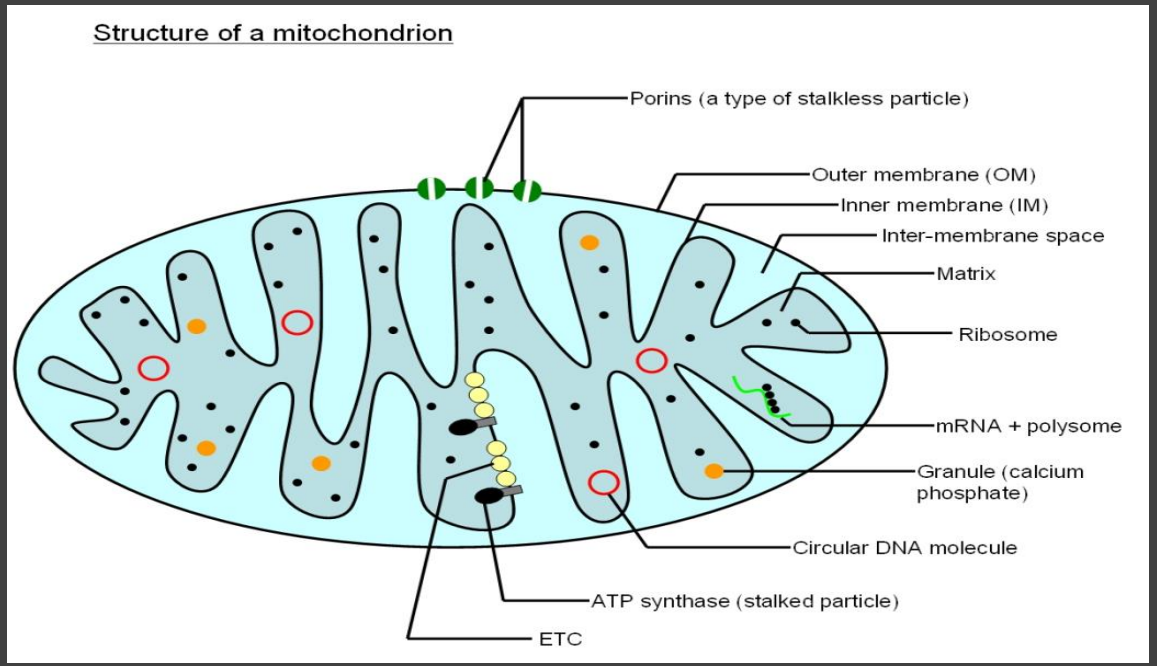


The structure of mitochondria



MITOCHONDRIA - FUNCTION

- **outer mitochondrial membrane**
  - porins - multipass transmembrane proteins – aqueous channels (water-soluble molecules may pass)-intramembrane space resemble cytosol
  - proteins responsible for the formation of mitochondrial lipids
- **inner mitochondrial membrane**
  - cardiolipin – phospholipid (with 4 fatty acyl chains) – impermeable to ions, electrons and protons
  - ATP synthase – protein complex responsible for the generation of ATP from ADP and inorganic phosphate
  - respiratory chains – protein complexes
- **contact sites** – regions in which outer and inner membranes contact each other



MITOCHONDRION - MATRIX

- enzymes responsible for the degradation of fatty acids to the acetyl CoA
- cytric acid cycle (Krebs cycle) – series of chemical reactions used by organisms to generate energy)
- DNA- double-stranded mitochondrial circular deoxyribonucleic acid

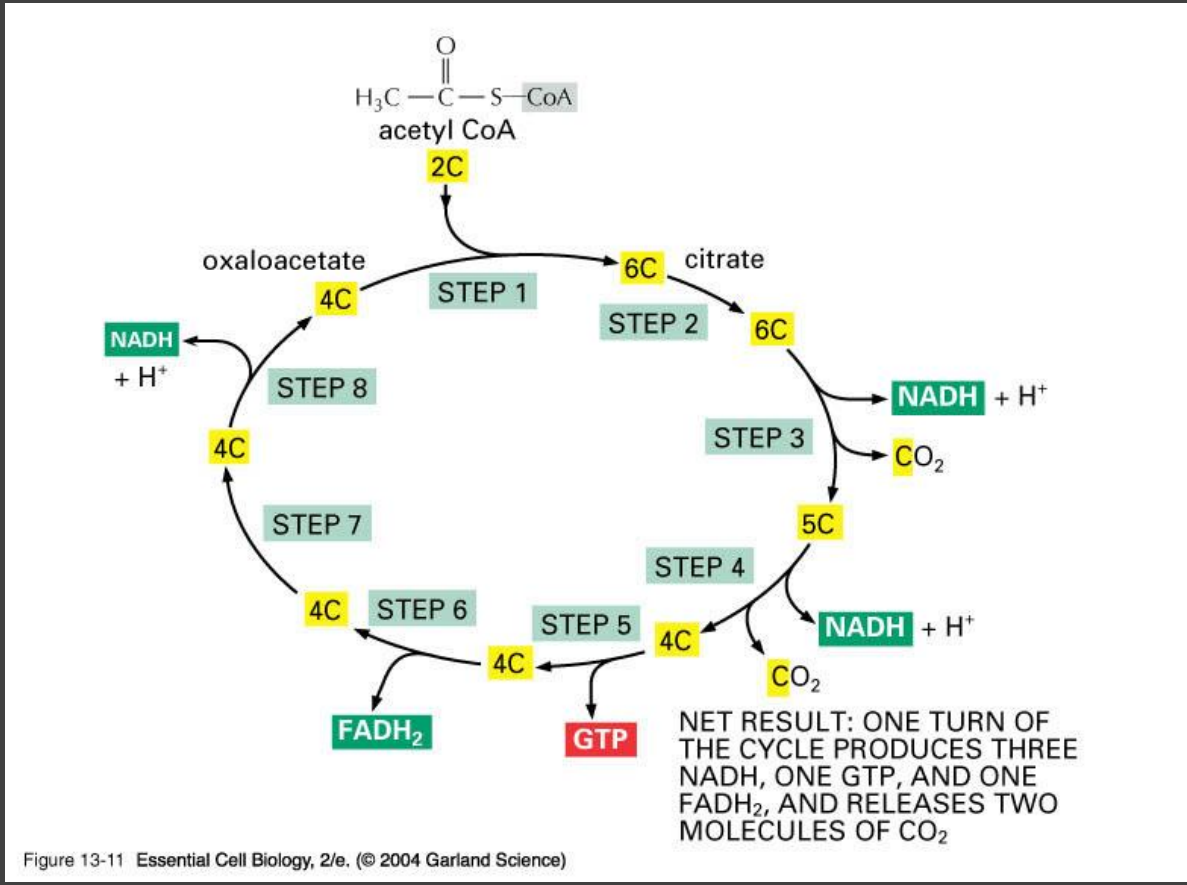
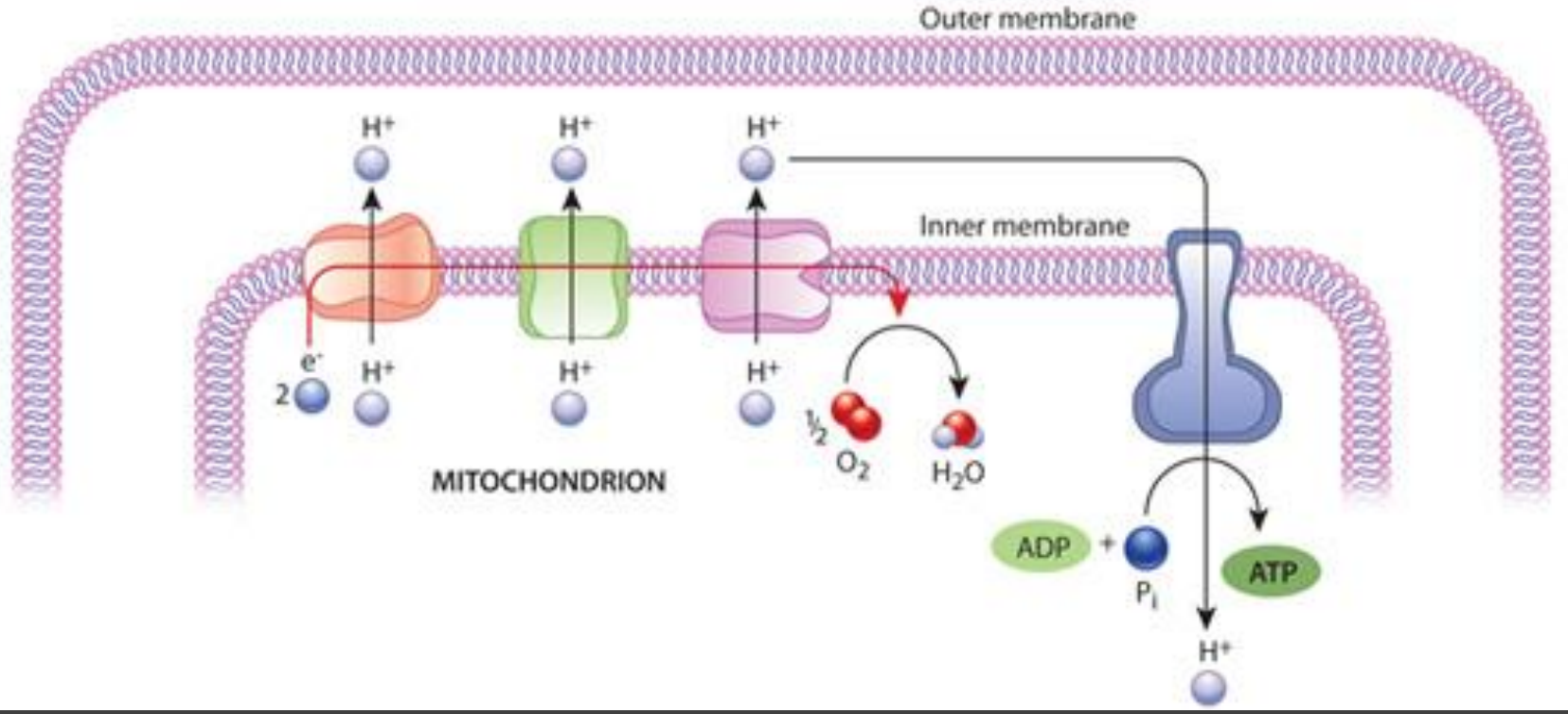


Figure 13-11 Essential Cell Biology, 2/e. (© 2004 Garland Science)


Outer membrane
Inner membrane
H+
H+
H+
H+
H+
H+
e-
2
½ O2
H2O
MITOCHONDRION
ADP
+
Pi
ATP
H+

What do we remember about mitochondria?

Group 1

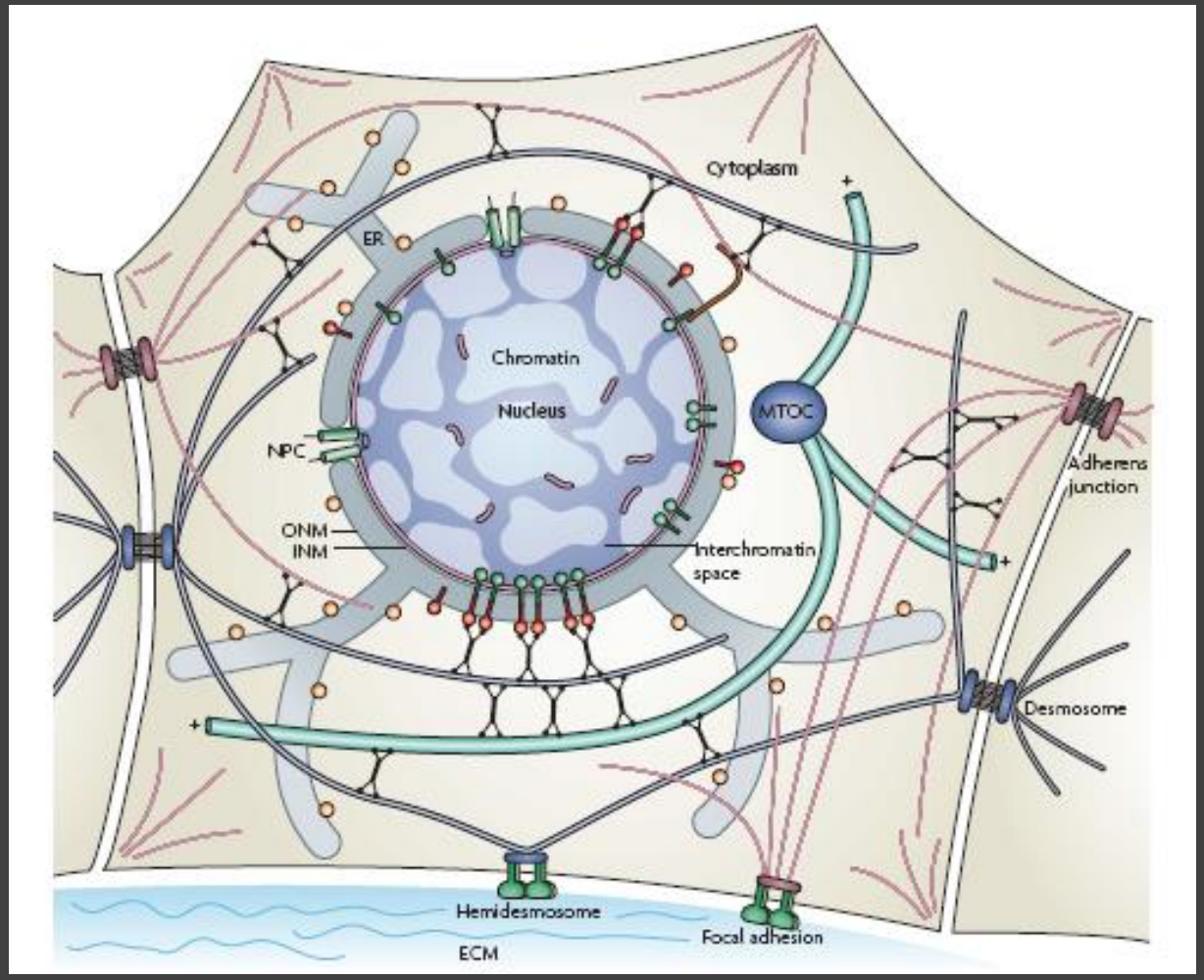
Mitochondrial functions	
Outer mitochondrial membrane	
Inner mitochondrial membrane	

Group 2

Intermembranous space	
Mitochondrial matrix	
ATP synthase	

CELL CYTOSKELETON

Cell cytoskeleton is a network made of biological polymers. They are three main types of polymer namely microtubules, actin (thin) filaments and intermediate filaments

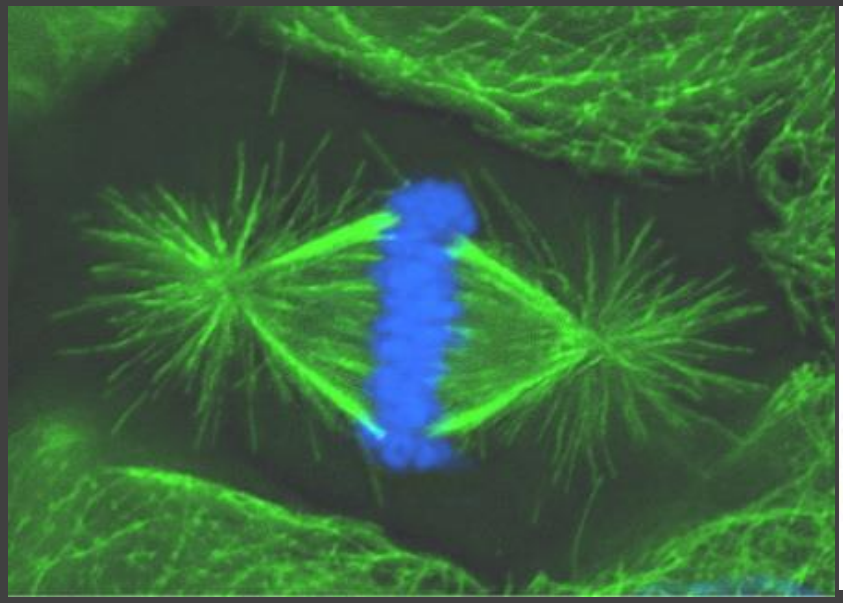


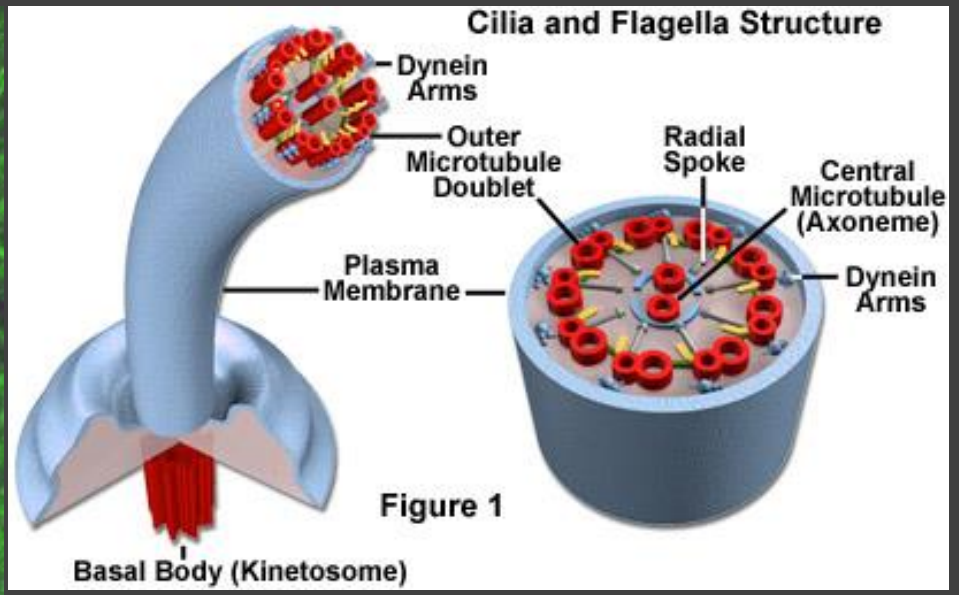
MICROTUBULES

- long, straight, cylindrical structures

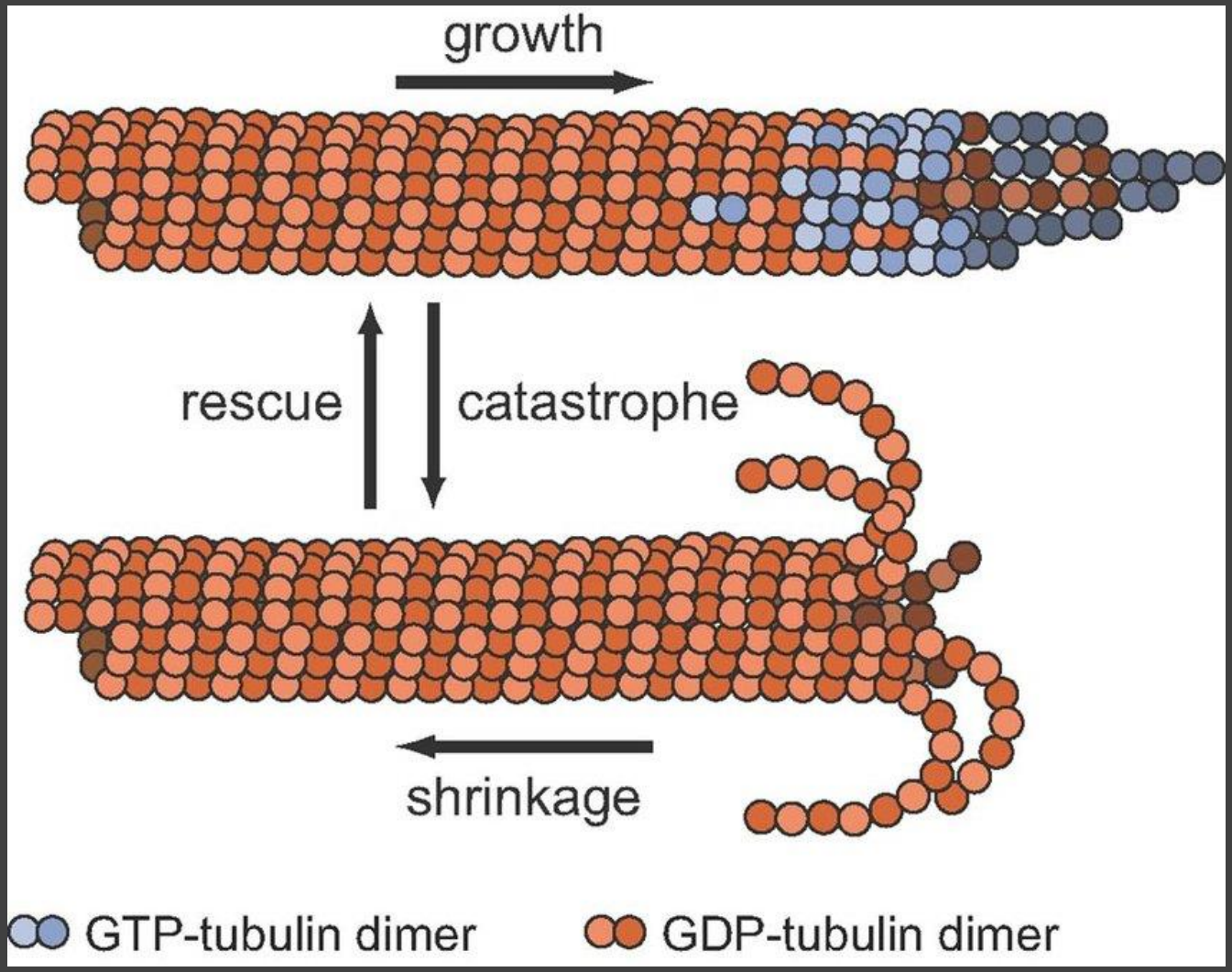
They play key roles in:

- intracellular transport of secretory vesicles and organelles
- cell division (mitosis and meiosis) including the formation of mitotic spindles
- They also form the internal structure of cilia and flagella



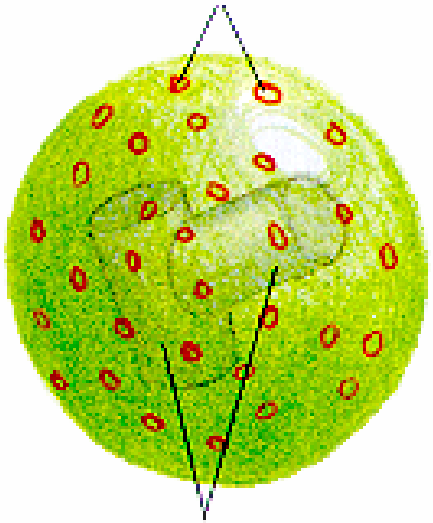


Microtubule instability

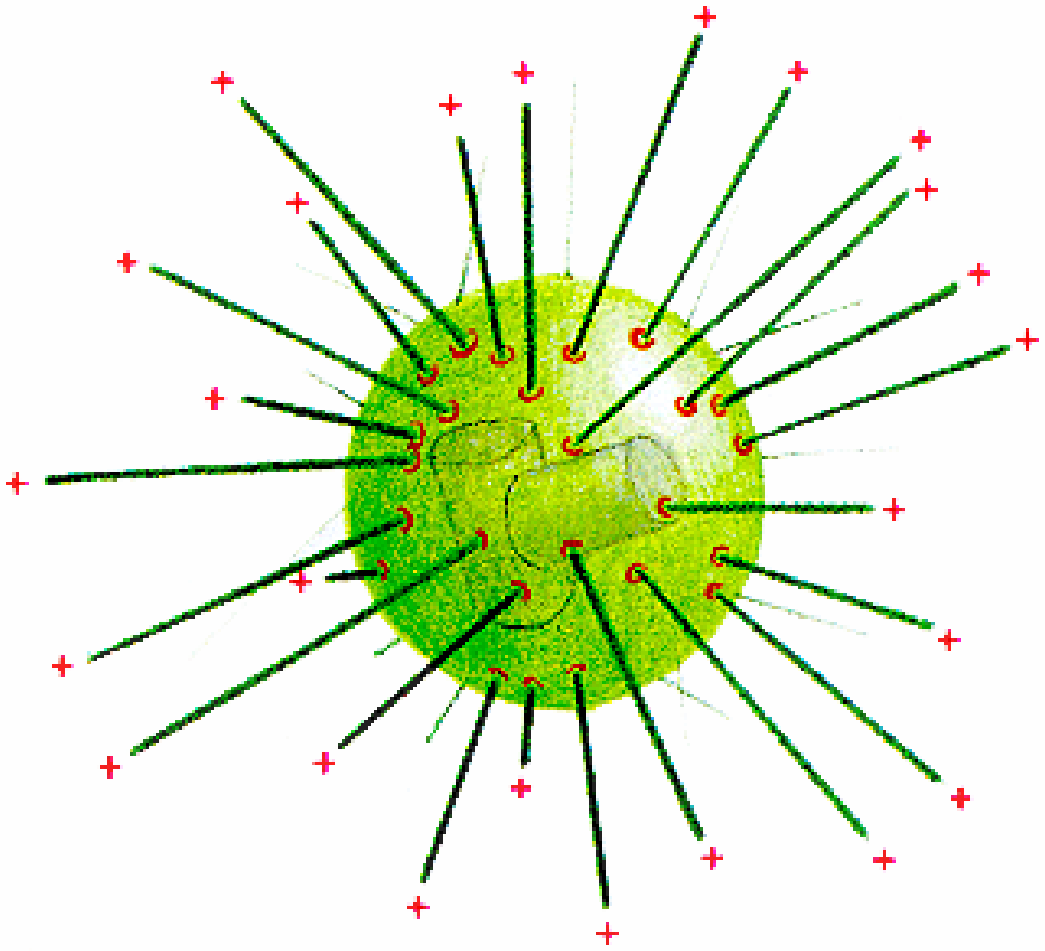


Centrosome

Nucleating sites
(γ tubulin ring complexes)



pair of centrioles



Microtubule-Associated Proteins (MAPs)

Motor proteins

- responsible for the intracellular movement of organelles and vesicles
- motor proteins which convert the chemical energy contained

in ATP into the mechanical energy of movement.

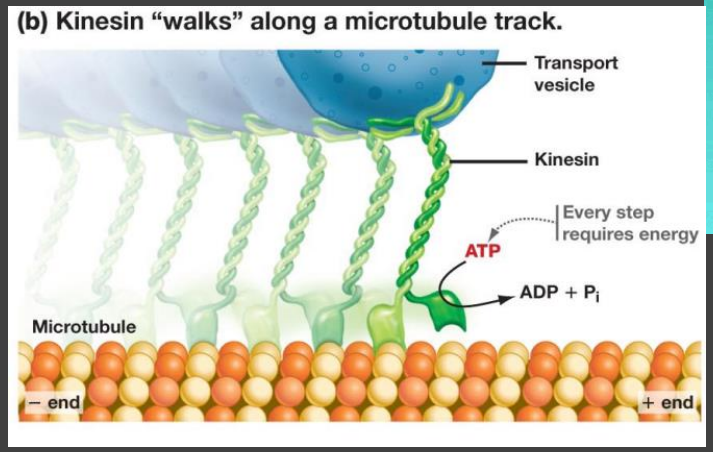
dynein - from plus to minus end

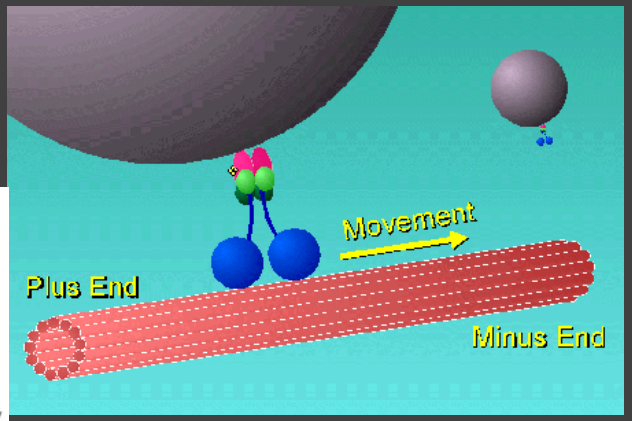
kinesin – from minus to plus end

Structural

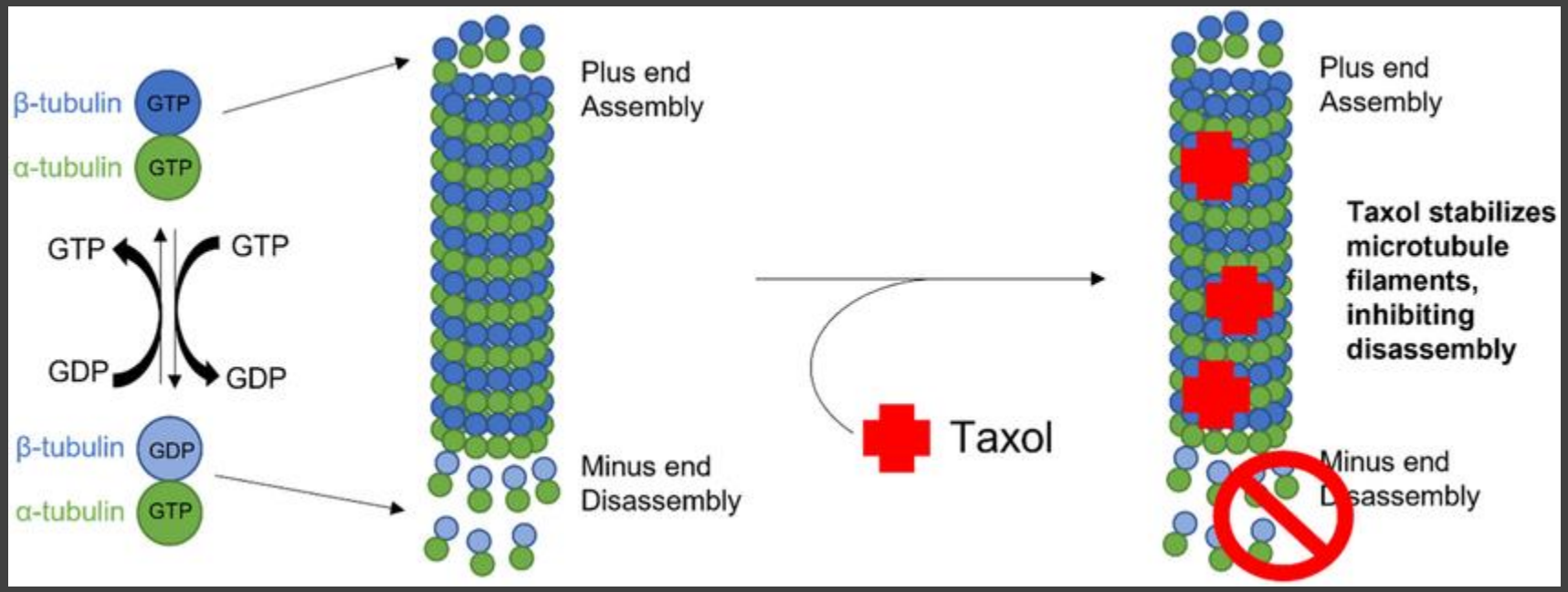
- Tau
- MAP2

Stabilizing

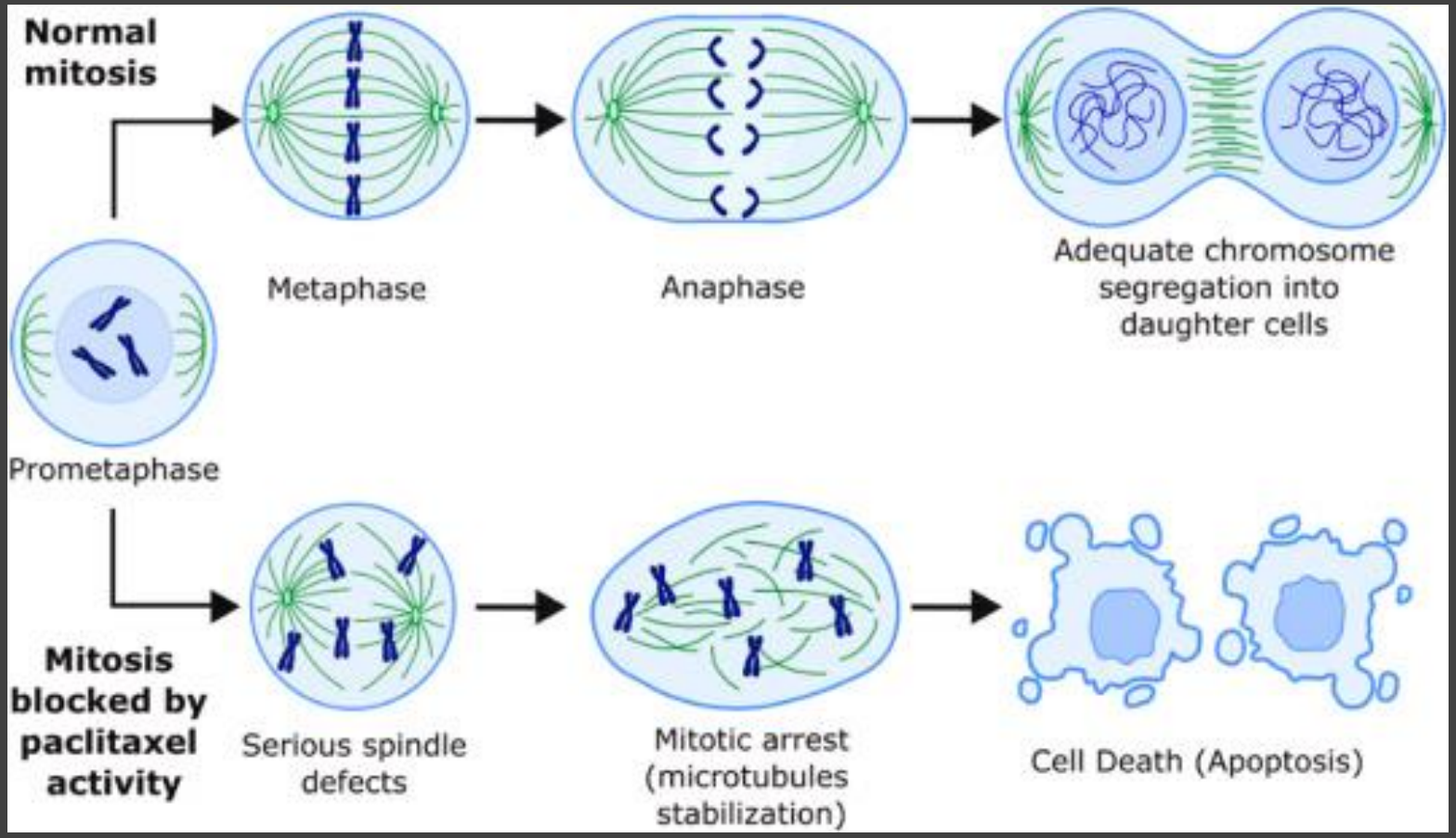




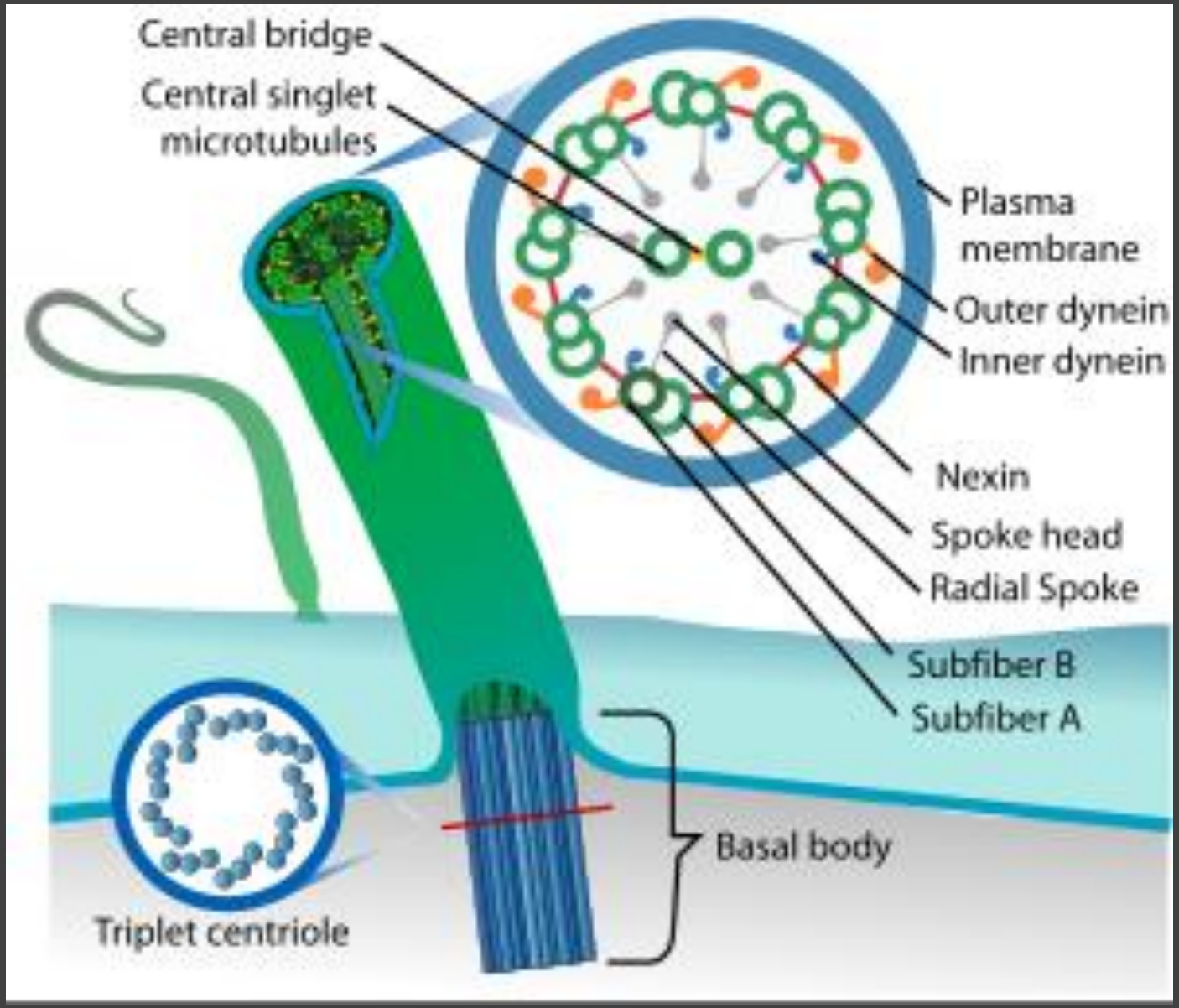
Taxol – microtubule stabiliser



Taxol – mitotic spindle poison

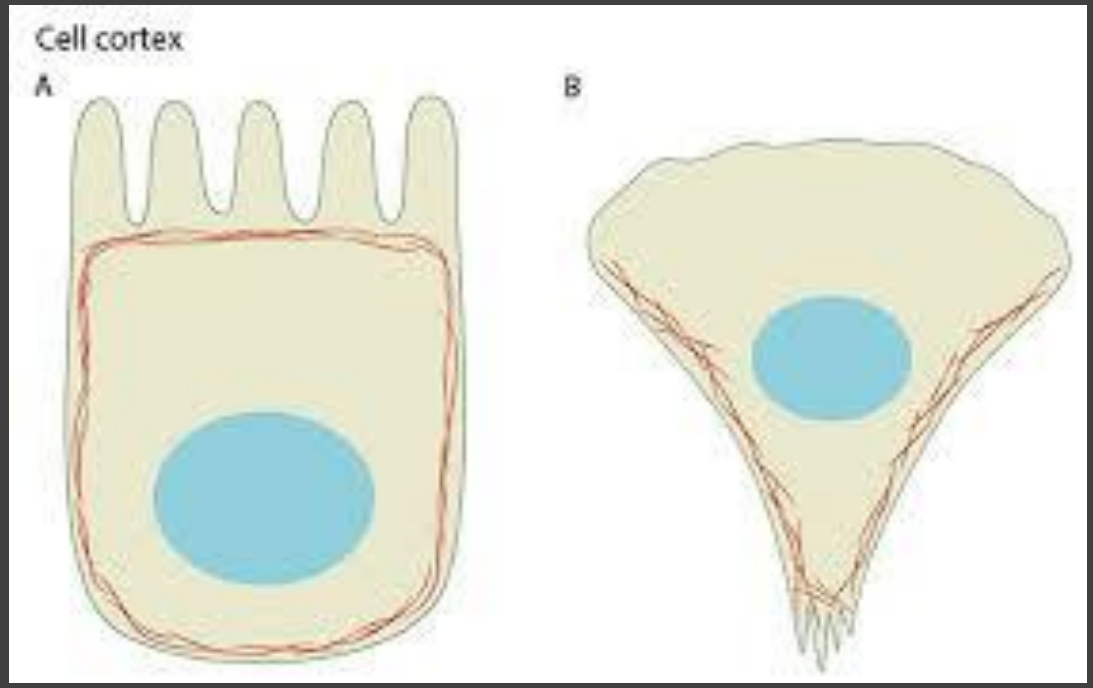


Cilium

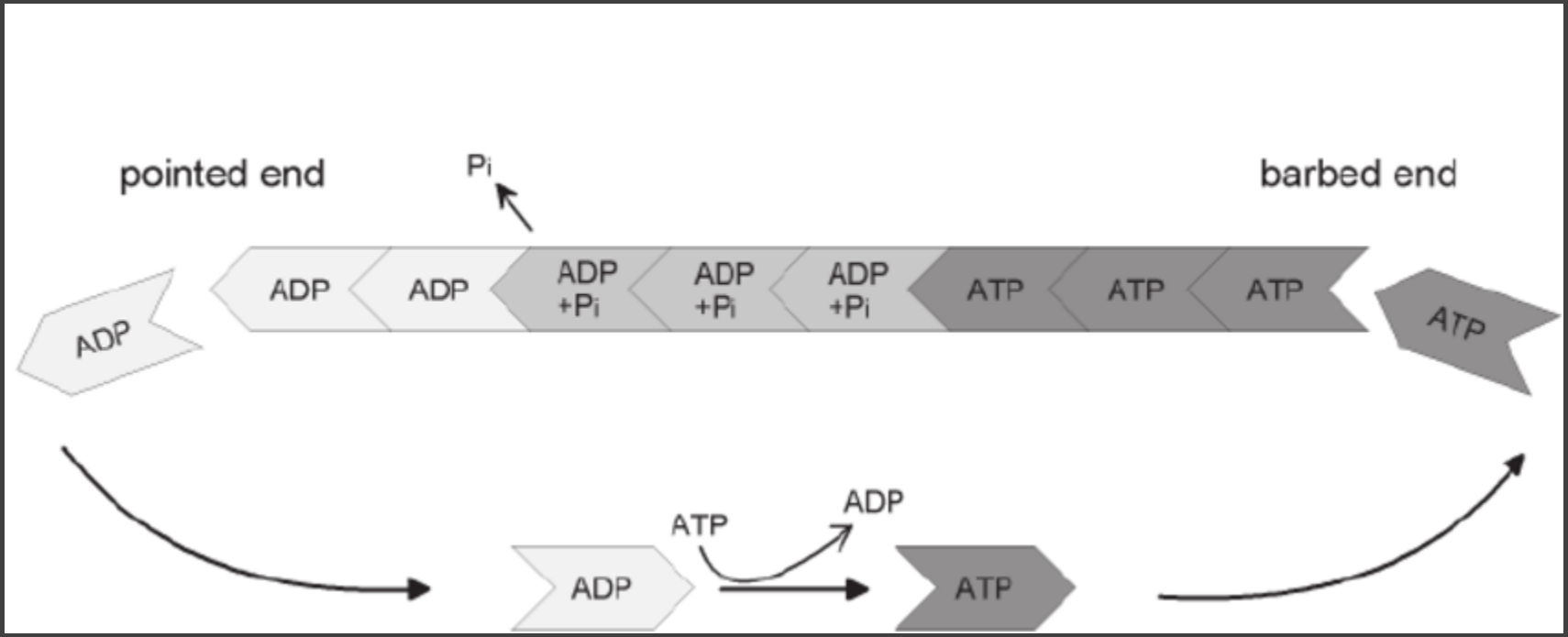

Central bridge
Central singlet microtubules
Plasma membrane
Outer dynein
Inner dynein
Nexin
Spoke head
Radial Spoke
Subfiber B
Subfiber A
Basal body
Triplet centriole

The actin (thin) filaments

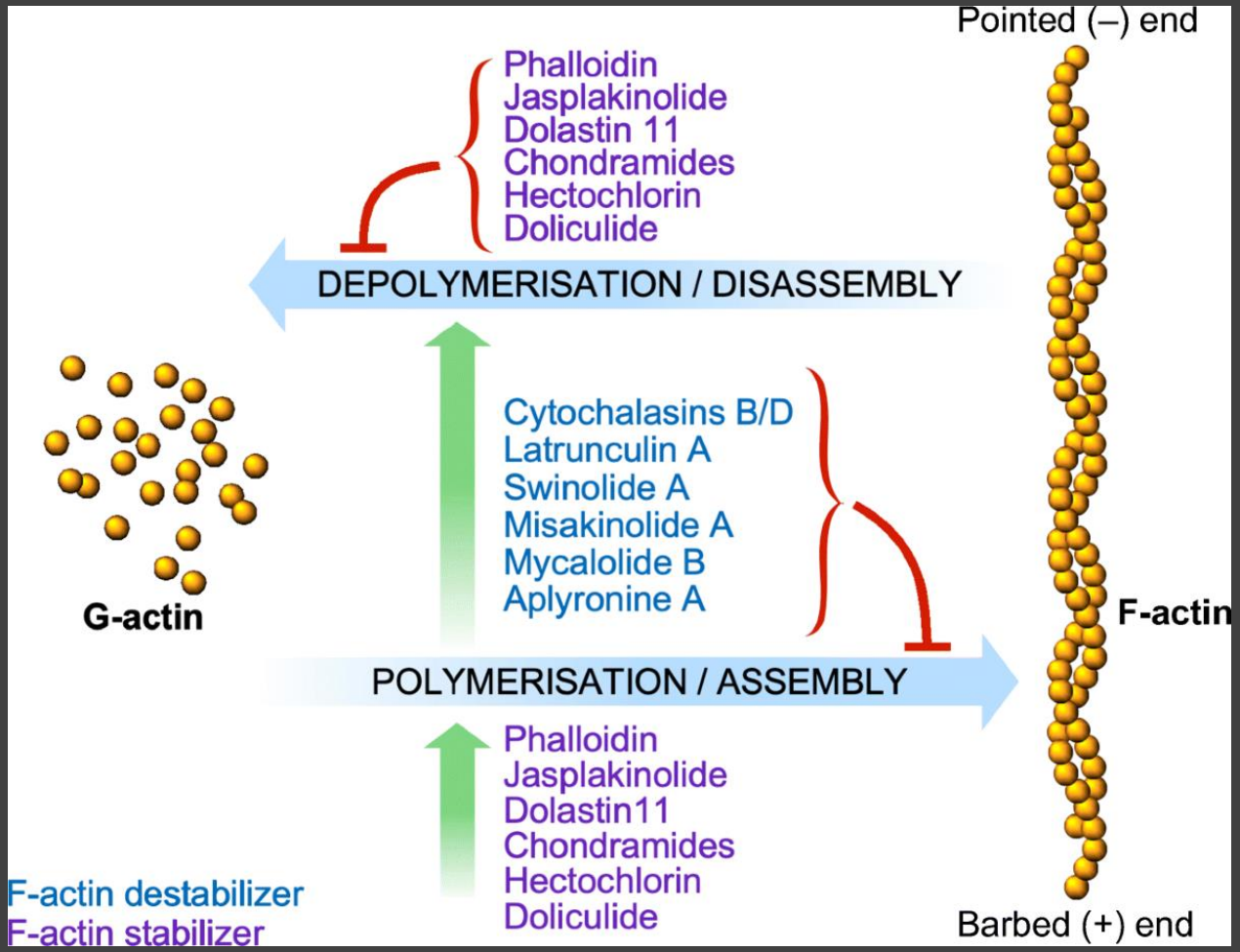
The actin cytoskeleton provides a structural framework for the mechanical stability of eukaryotic cells and is involved in functions including cell adhesion, motility, and division.

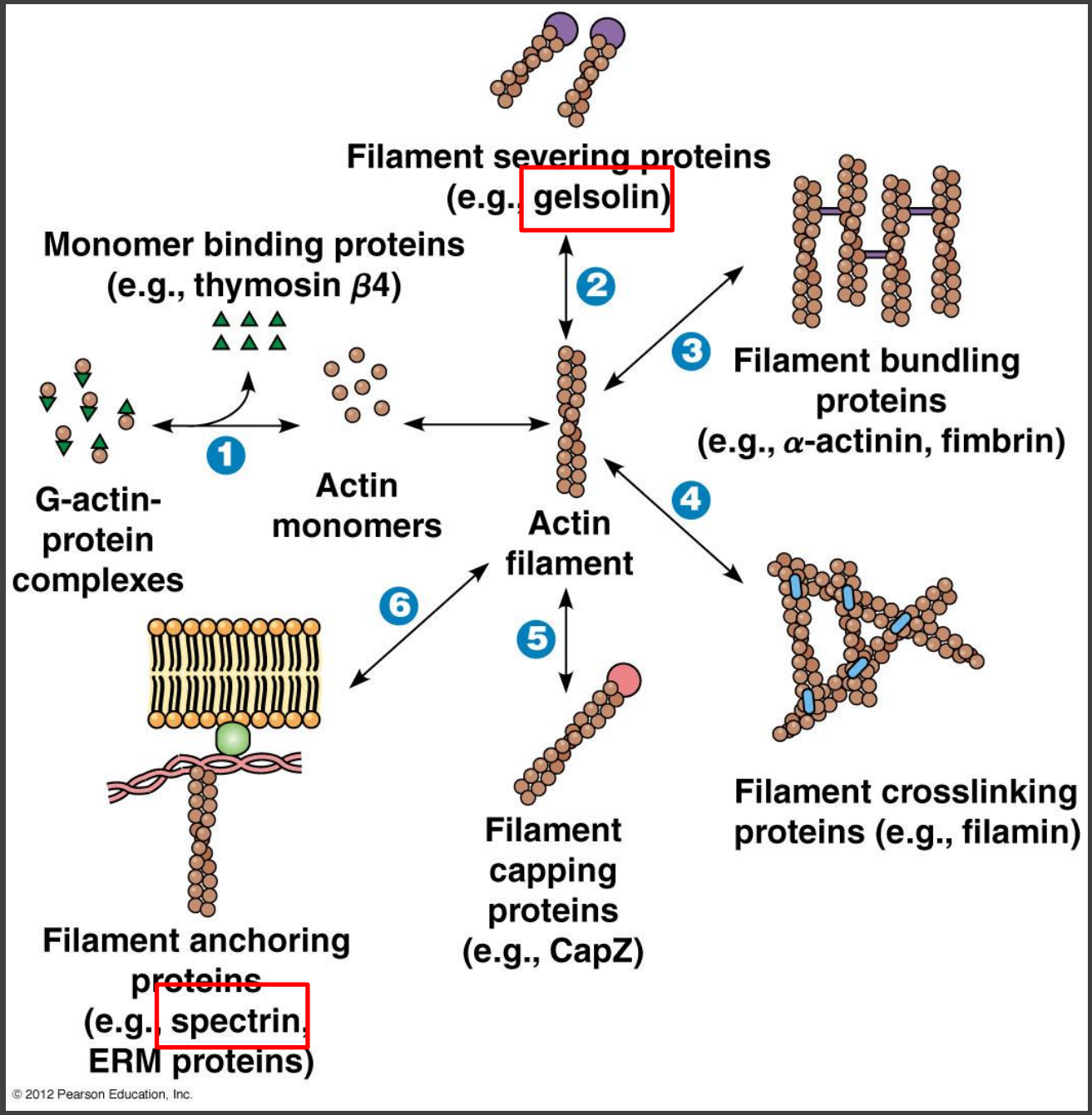


Actin treadmilling

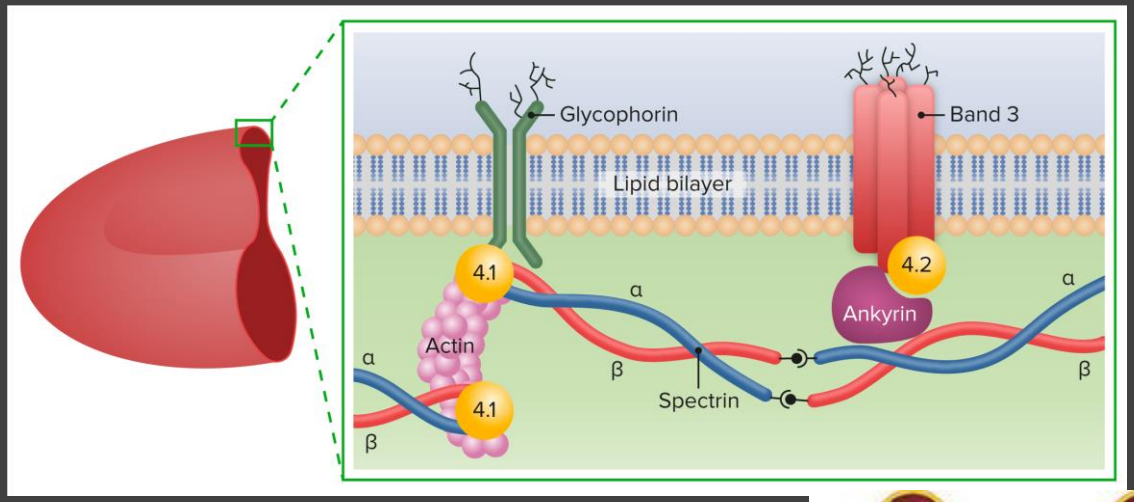


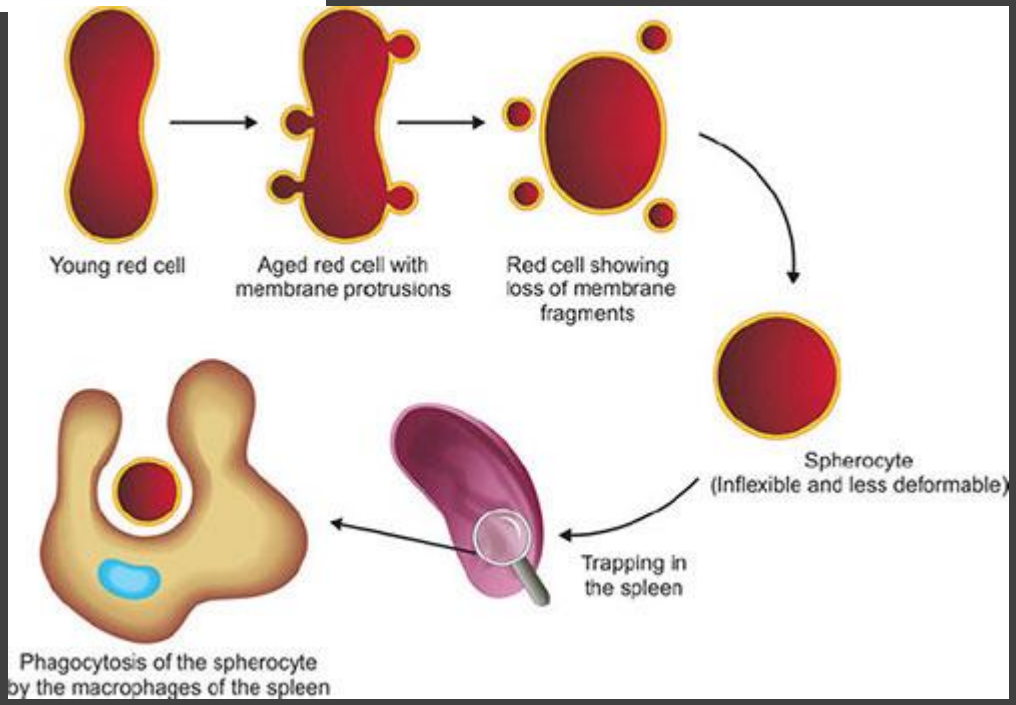
Phalloidin


Pointed (–) end
Phalloidin
Jasplakinolide
Dolastin 11
Chondramides
Hectochlorin
Doliculide
DEPOLYMERISATION / DISASSEMBLY
G-actin
Cytochalasins B/D
Latrunculin A
Swinolide A
Misakinolide A
Mycalolide B
Aplyronine A
F-actin
POLYMERISATION / ASSEMBLY
Phalloidin
Jasplakinolide
Dolastin11
Chondramides
Hectochlorin
Doliculide
F-actin destabilizer
F-actin stabilizer
Barbed (+) end

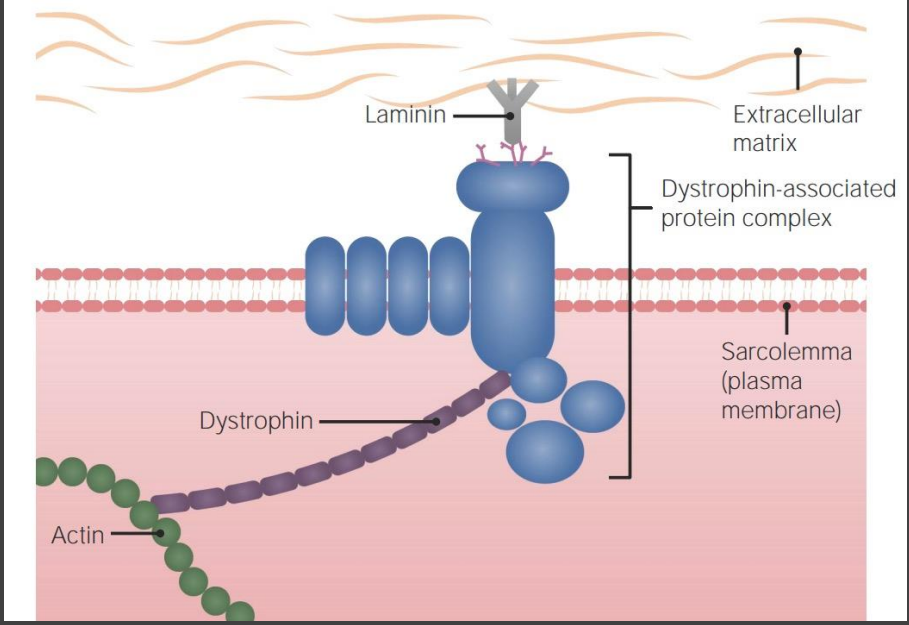

Filament severing proteins
(e.g., gelsolin)
Monomer binding proteins
(e.g., thymosin β4)
2
3
Filament bundling
proteins
(e.g., α-actinin, fimbrin)
1
G-actin-
protein
complexes
Actin
monomers
Actin
filament
4
6
5
Filament crosslinking
proteins (e.g., filamin)
Filament
capping
proteins
(e.g., CapZ)
Filament anchoring
proteins
(e.g., spectrin,
ERM proteins)
© 2012 Pearson Education, Inc.

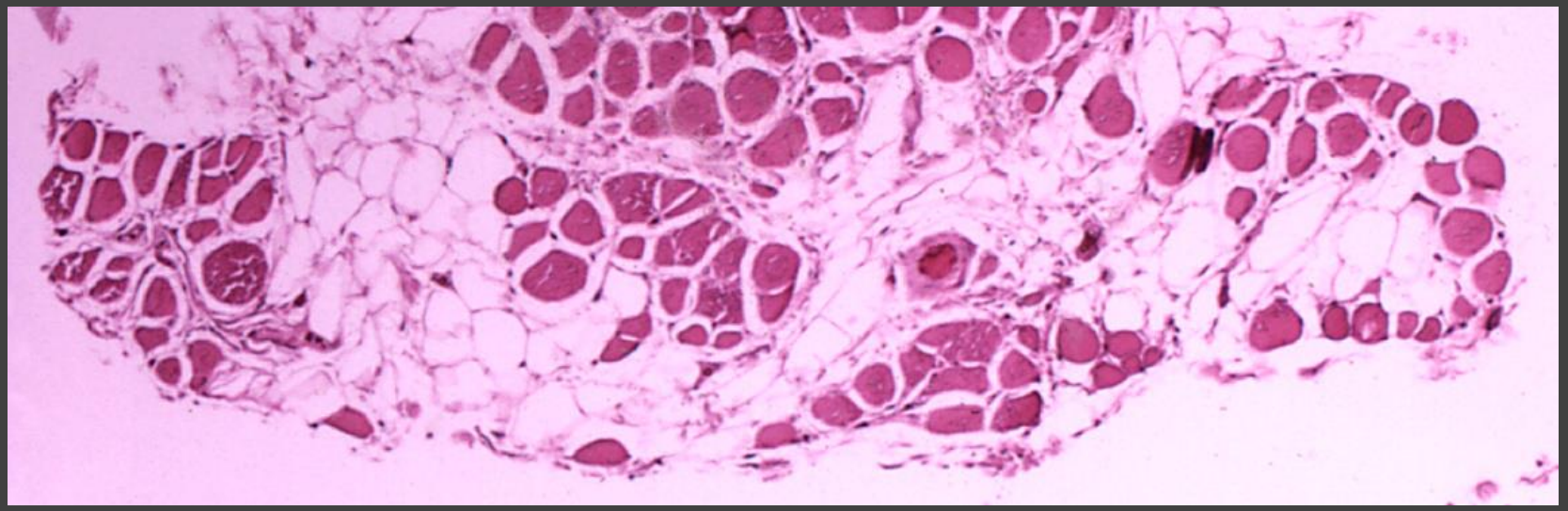
Spectrin – hereditary spherocytosis

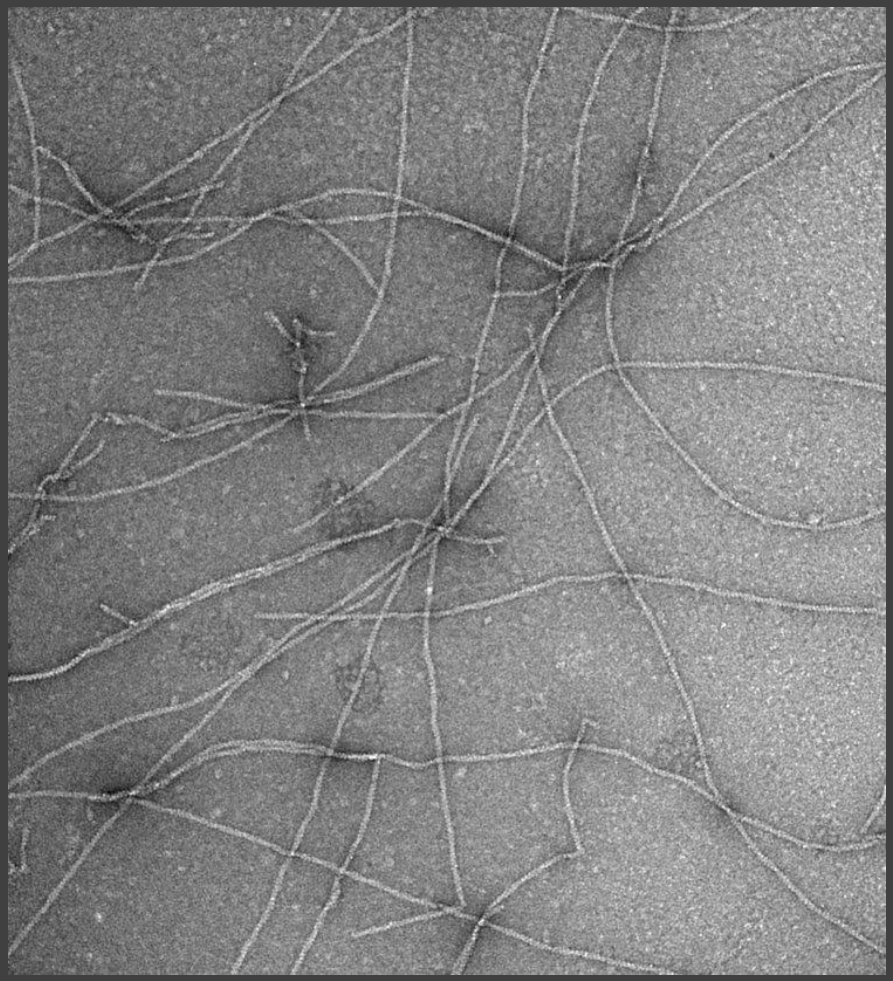


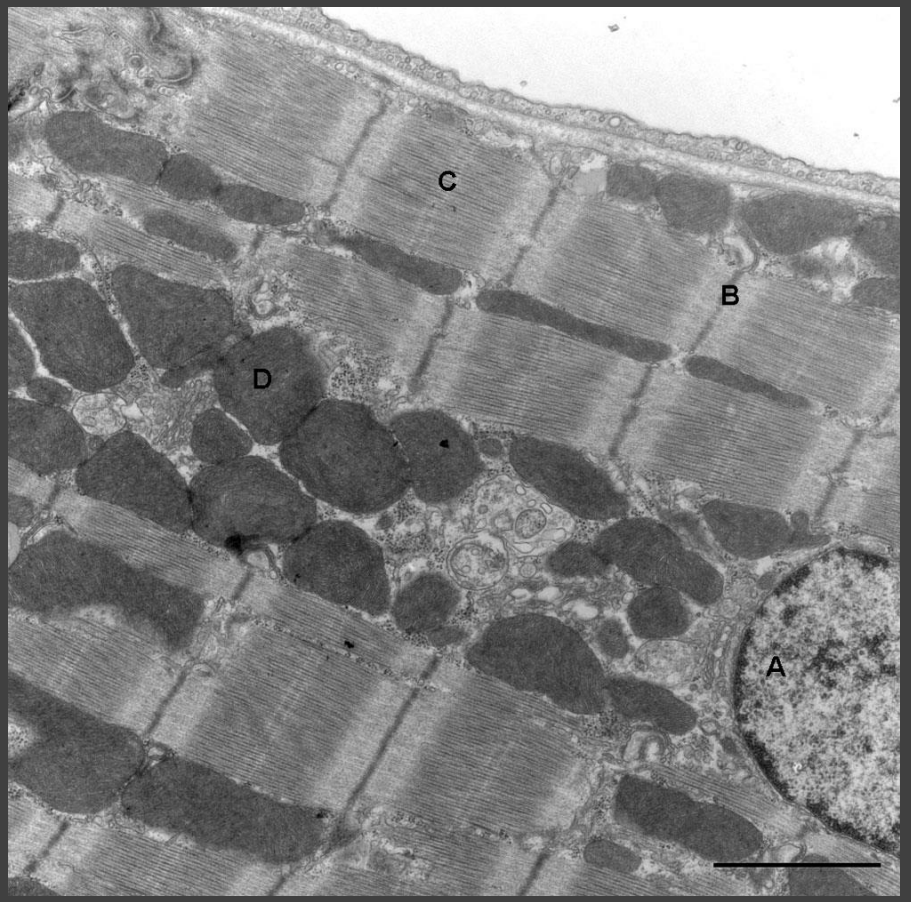


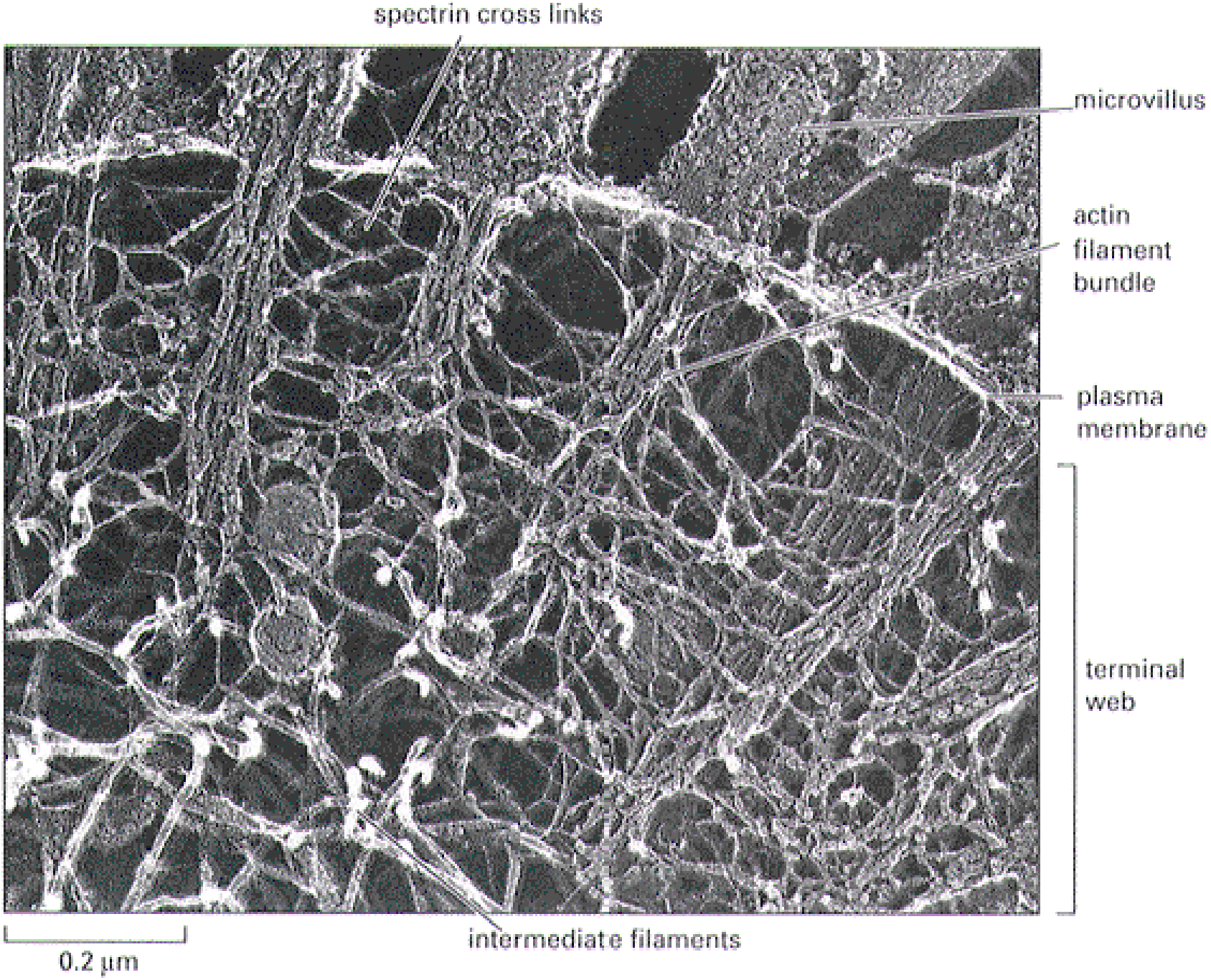
Dystrophin – muscular dystrophy



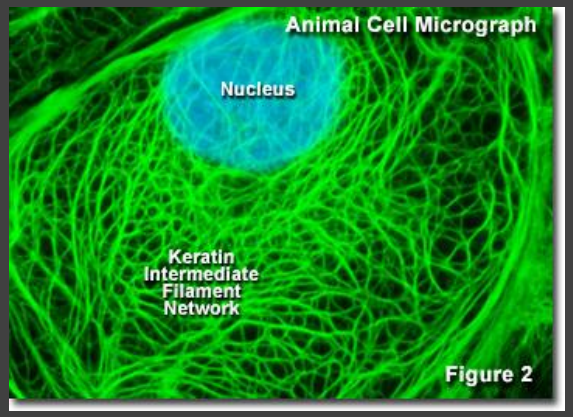





C
B
D
A

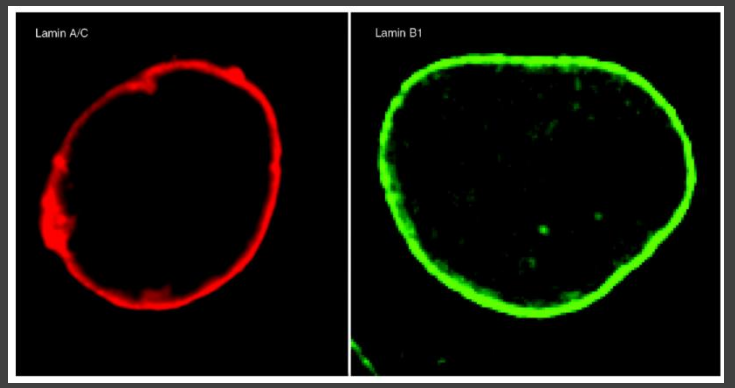


INTERMEDIATE FILAMENTS



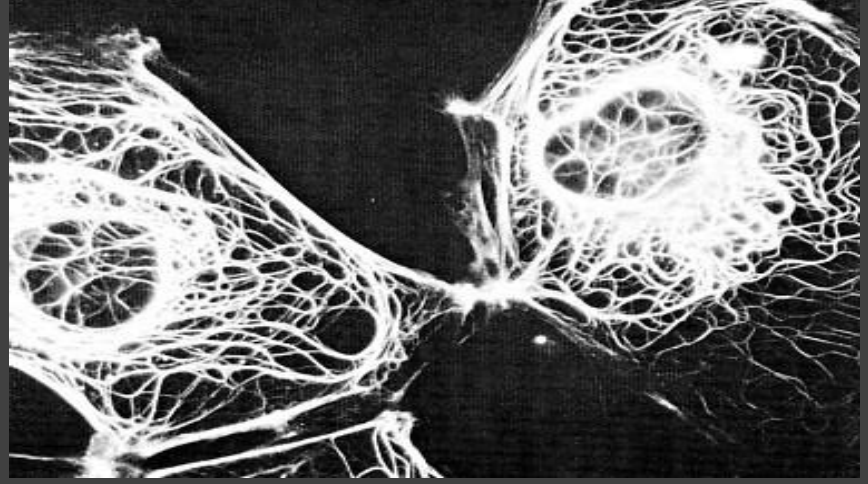
- have an average diameter of 10 nanometers, which is between that of 7 nm actin (microfilaments), and that of 25 nm microtubules

Most types of intermediate filaments are cytoplasmic, but one type, the lamins, are nuclear.



TYPES:

- **cytokeratins** in epithelial cells
- **desmin** in muscle cells
- **vimentin** in many mesodermal tissues
- **GFAP** (glial fibrillary acidic protein) in astrocytes and other glia
- **neurofilaments** in axons of vertebrate neurons
- **lamins** in the cell nucleus



FUNCTION OF INTERMEDIATE FILAMENTS

- provide structural support for the cell (form three-dimensional framework)
- anchor the nucleus in place
- they form the connection between the cell membrane and the cytoskeleton

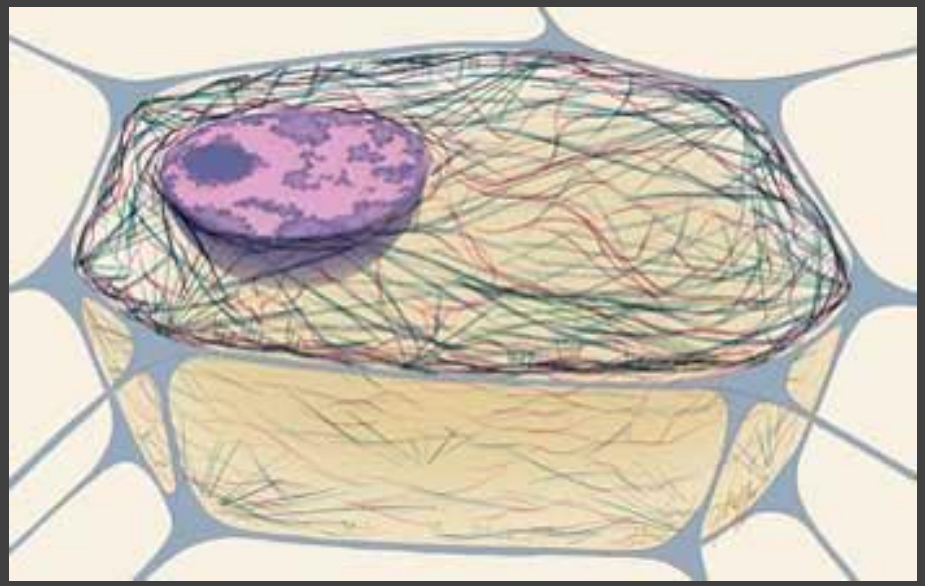
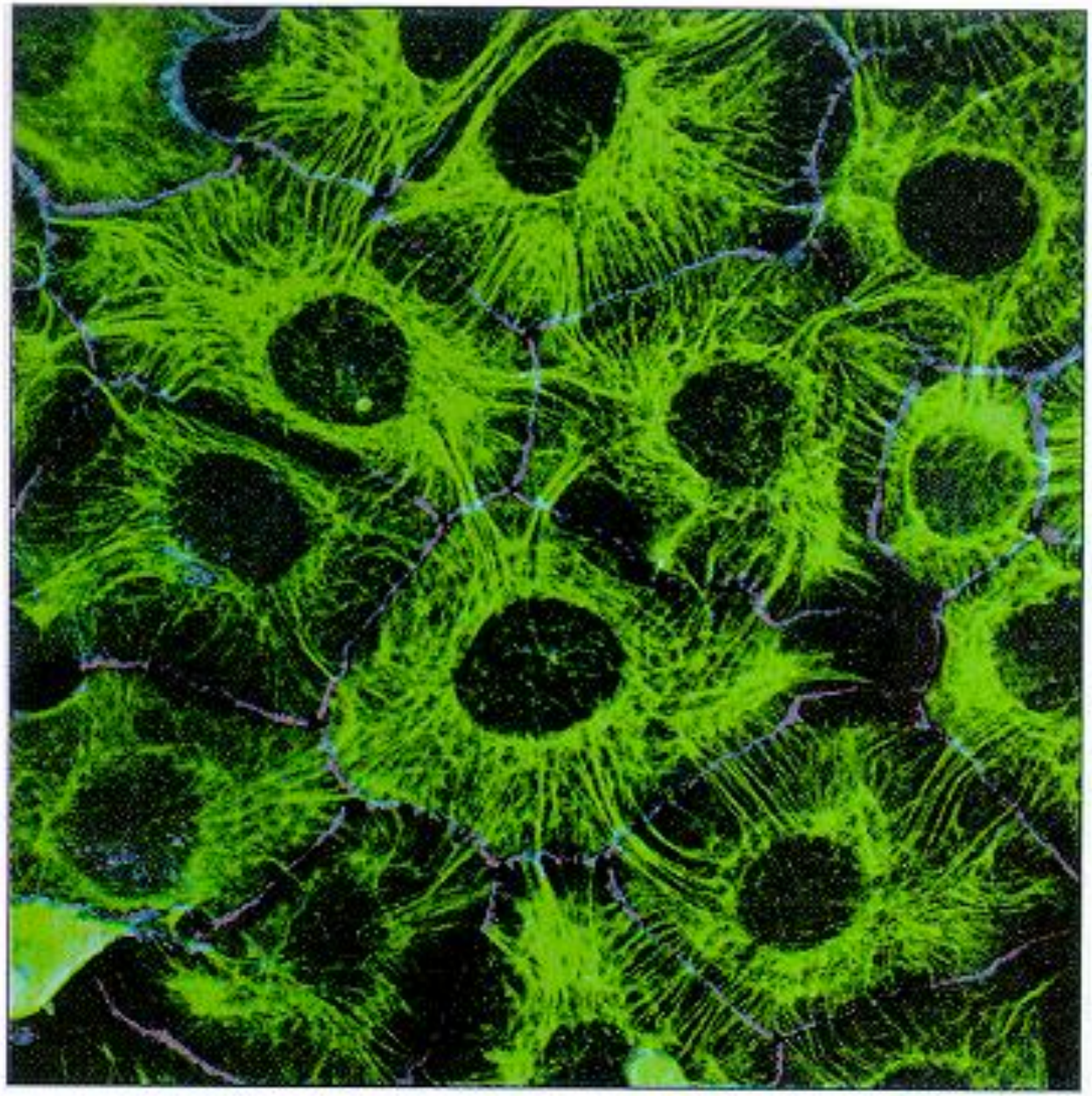


Table 4.1
TYPES OF INTERMEDIATE FILAMENTS

Type	Names	Functions
I and II	Acidic (I) and basic (II) keratins	Form complex network from nucleus to plasma membrane in epithelial cells
III	Desmin, vimentin	Support and structure
IV	Neurofilaments, synemin, syncoilin	Protect from mechanical stress and maintain structural integrity in various cell types
V	Nuclear lamina	Structural role in the nucleus of all cells
VI	Nestin	Expressed mainly in the nerve cells and is implicated in their growth



What do we remember about cytoskeleton?

Element	Description	Function
Actin filaments		
Actin binding proteins		
Intermediate filaments		

Element	Description	Function
Microtubules		
Microtubule associated proteins		
Kinesin and dynein		