Introduction on Biochemistry, Cell Biology, & TERM

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Current Life Science Topics

1. Fundamentals in Basic Biochemistry & Cell Biology
2. Introduction to Tissue Engineering & Regenerative Medicine
3. Developmental Tissue Reconstruction
4. Wound Healing & Regeneration
5. Natural Tissue Composition & Cell-ECM Interaction
6. Stem Cells & Cell-Based Therapy
7. Biomaterials
8. *Mid-Term Exam*
9. Mechano-transduction & Bioreactors
10. Discussions on Tissue Reconstruction
11. Regulation & Ethics
12. AI in Current Life Science
13. Machine Learning & Github
14. Deep Neural Network
15. Convolutional Neural Network
16. *Final Exam*

Study Materials & References

Lehninger Principles of Biochemistry (5^{th} Edition)

- David L Nelson & Michael M Cox

Molecular Biology of the Cells (6^{th} Edition)

- Bruce Alberts *et al.*

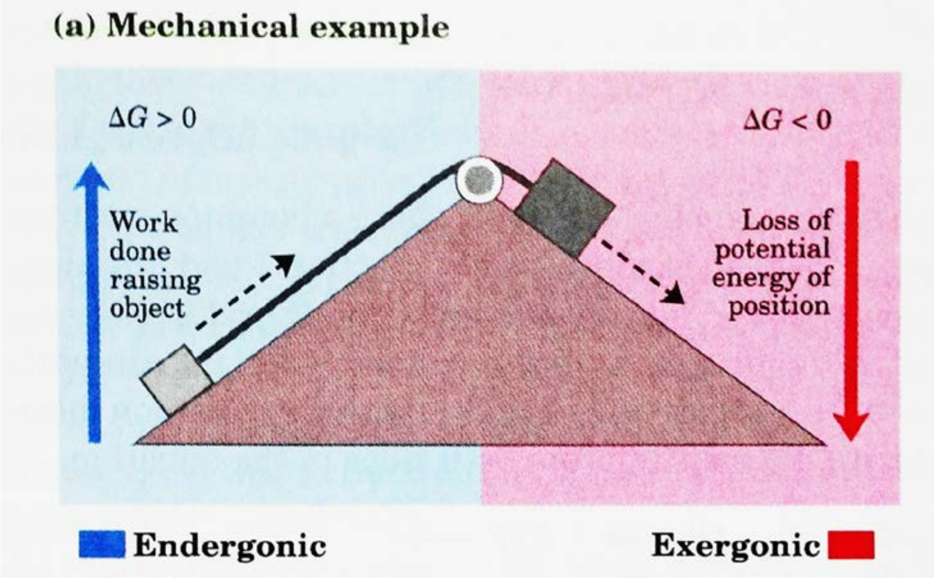
General Outline of Biochemistry

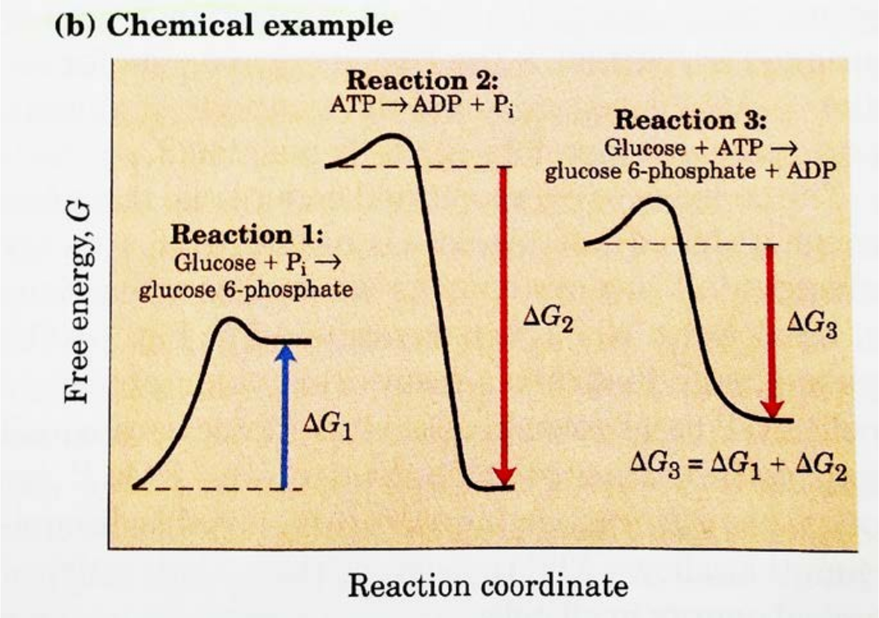
Physical Foundations of biochemistry

Entropy (S), Free-energy (G), & Enthalpy (H)

$$\Delta G = \Delta H - T\Delta S$$

- A process tends to occur spontaneously only if ΔG is negative (if free energy is released in the process).
- **Endergonic** reaction: energy-requiring
- **Exergonic** reaction: reaction that liberate free energy





Dynamic Steady State & Energy Transformation

A living organism are different in composition from their surroundings and maintain a more or less constant composition in the face of constantly changing surroundings

However, the population of molecules within the organism is far from static

- Biomolecules are continuously synthesized and broken down in chemical reactions
- This involves a constant flux of mass and energy through the system
  - Hemoglobin – synthesized within the past month
  - Glucose – ingested with most recent meal is not circulating!
- The amounts of hemoglobin and glucose in the blood remain nearly constant because the rate of synthesis or intake of each balances the rate of its breakdown
- This constancy of concentration is the result of a *dynamic steady state*

Dynamic steady state ≠ equilibrium

- It requires constant investment of energy
- When a cell can no longer generate energy, it dies and begins to decay

Pathways, Enzyme-Catalyzed Chemical Reactions

Metabolism

- Overall network of enzyme-catalyzed pathways

Catabolism

- Degenerative, free-energy-yielding reactions
- Degrade organic nutrients into simple end products
- Extract chemical energy and convert it into a form useful to the cell
- The energy release by catabolic reactions drives the synthesis of ATP

Anabolism

- Synthetic pathways that start with small precursor molecules and convert them to progressively larger and more complex molecules
- Require the input of energy

Enzymes, a Biocatalyst

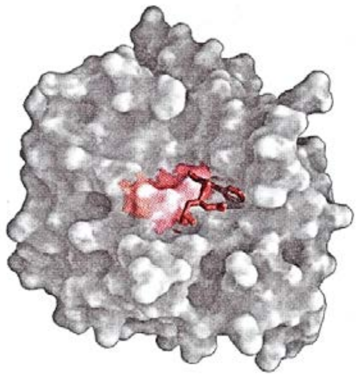
Virtually every chemical reaction in a cell occurs at a significant rate only because of the presence of enzymes.

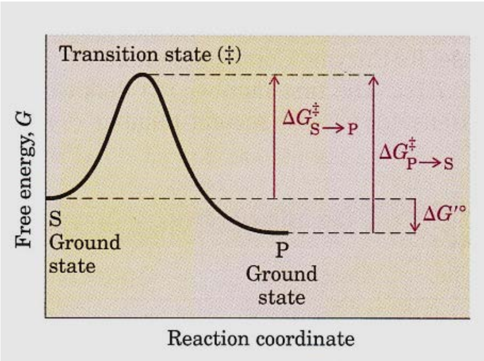
Transition state: created by distortion of the existing bonds

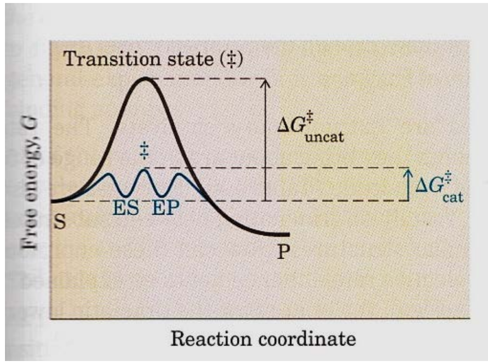
- **Higher free energy than either reactant or product**

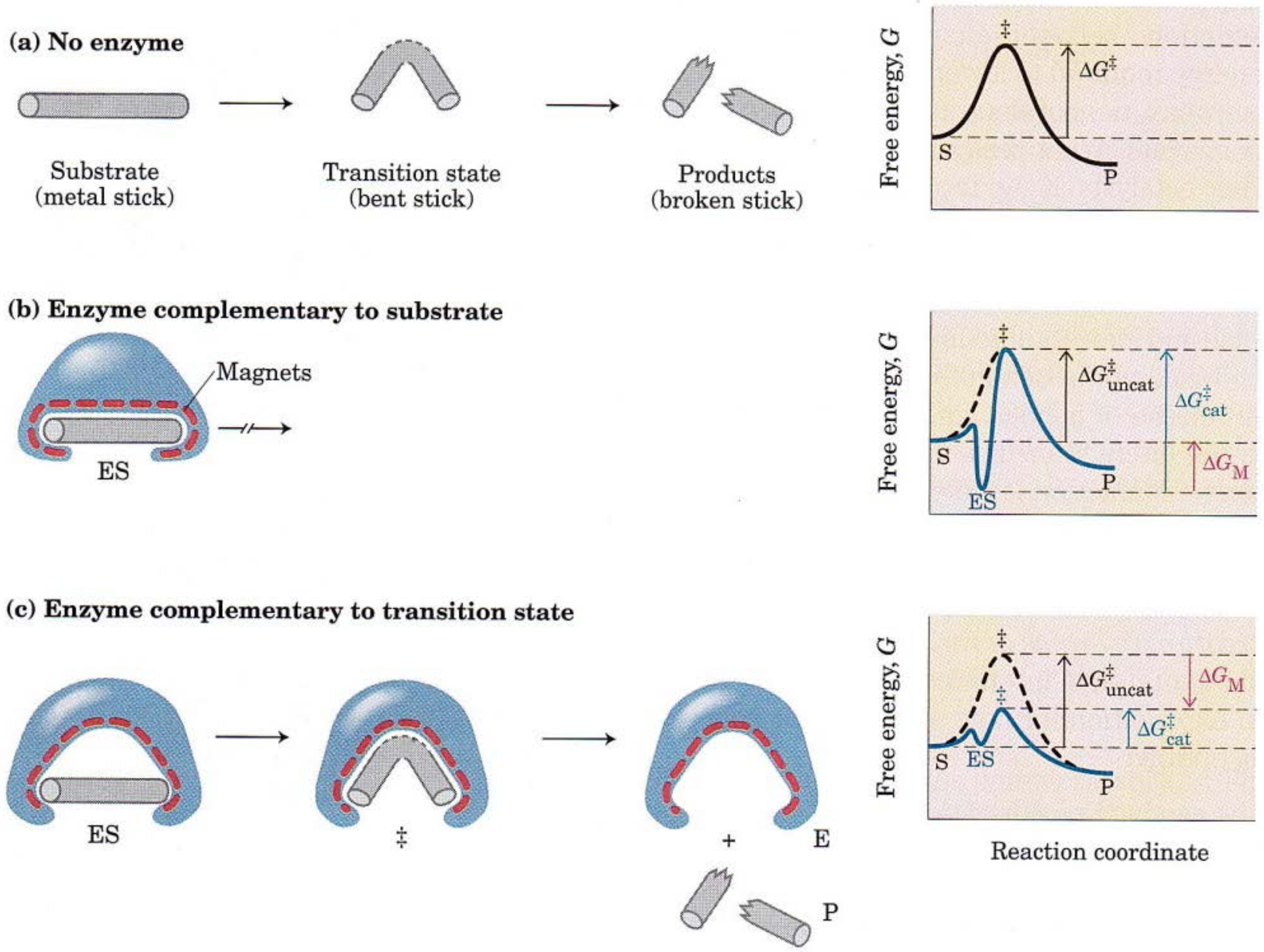
Enzymes provide more comfortable fit for the transition state

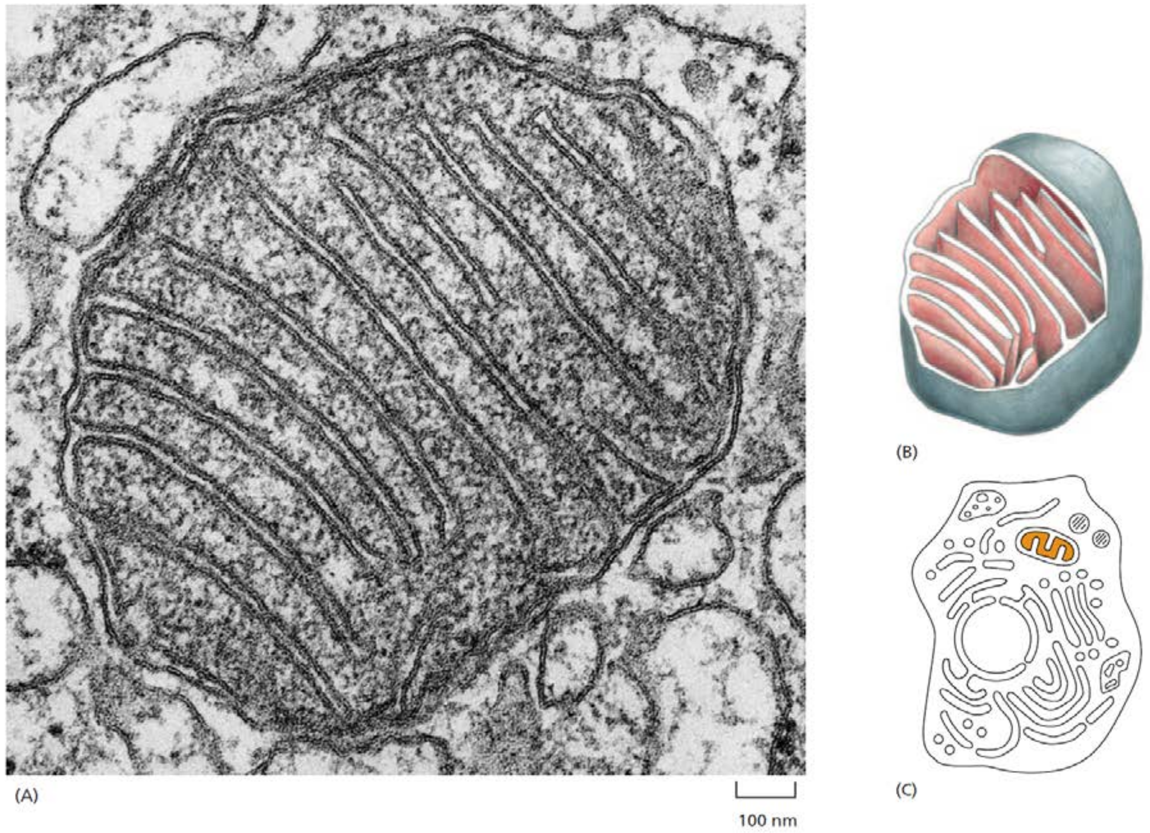
The binding of enzyme to the transition state is exergonic, and the energy released by this binding reduces the activation energy for the reaction and greatly in creases the reaction rate.

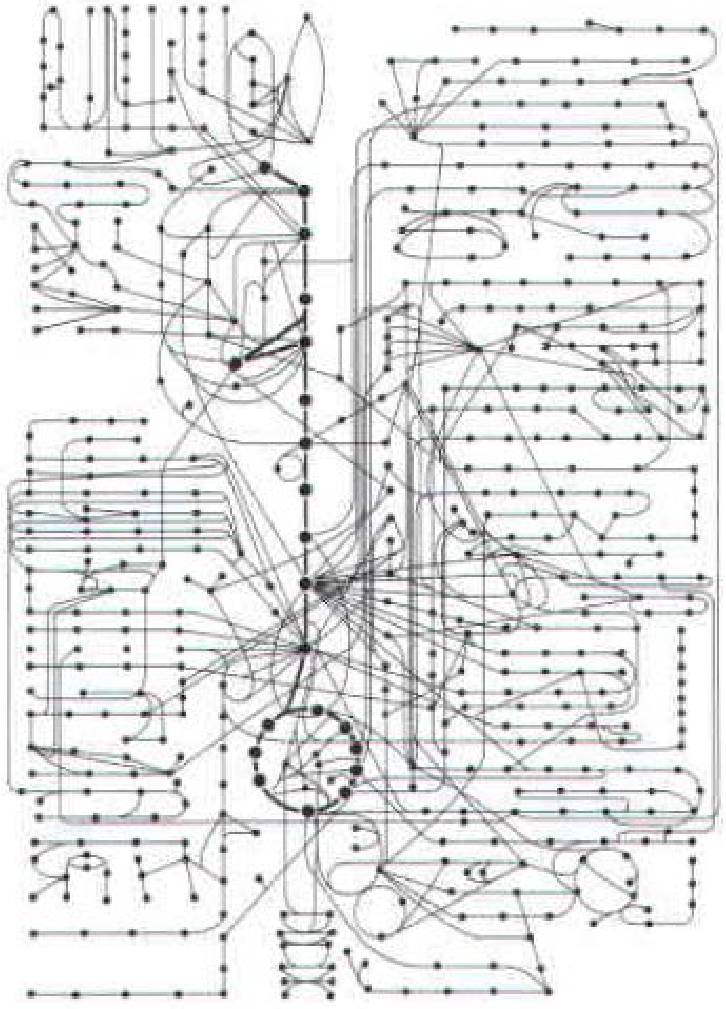



Transition state (‡)
$\Delta G^{\ddagger}_{S \to P}$
$\Delta G^{\ddagger}_{P \to S}$
$\Delta G'^{\circ}$
Free energy, G
S
Ground state
P
Ground state
Reaction coordinate


Transition state (‡)
$\Delta G^{\ddagger}_{uncat}$
‡
$\Delta G^{\ddagger}_{cat}$
Free energy, G
S
ES EP
P
Reaction coordinate


(a) No enzyme
Substrate
(metal stick)
Transition state
(bent stick)
Products
(broken stick)
Free energy, G
‡
$\Delta G^{\ddagger}$
S
P
(b) Enzyme complementary to substrate
Magnets
ES
Free energy, G
‡
$\Delta G^{\ddagger}_{uncat}$
$\Delta G^{\ddagger}_{cat}$
ΔG_M
S
ES
P
(c) Enzyme complementary to transition state
ES
‡
+
E
P
Free energy, G
‡
$\Delta G^{\ddagger}_{uncat}$
ΔG_M
‡
$\Delta G^{\ddagger}_{cat}$
S
ES
P
Reaction coordinate


(A)
100 nm
(B)
(C)



Distinguishing Features of Living Organisms

A high degree of chemical complexity and microscopic organization 화학적, 구조적 복잡성

Systems for extracting, transforming, and using energy from the environment 에너지 대사

Defined functions for each of an organism's components and regulated interactions among them 거시적 & 미시적 기능 분화 요소

Mechanisms for sensing and responding to alterations in their surroundings 환경 변화에 대한 반응(적응)

A capacity for precise self-replication and self-assembly 자기 복제 능력

A capacity to change over time by gradual evolution 진화 능력

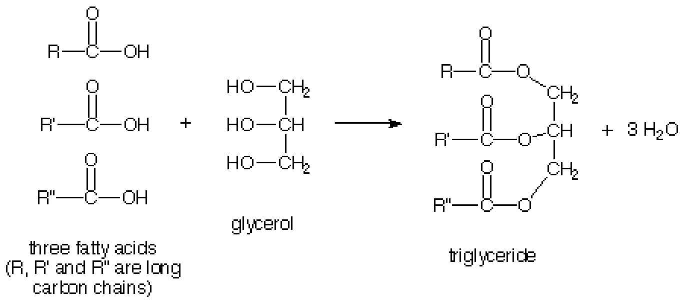
Biomacromolecules – building blocks of cells

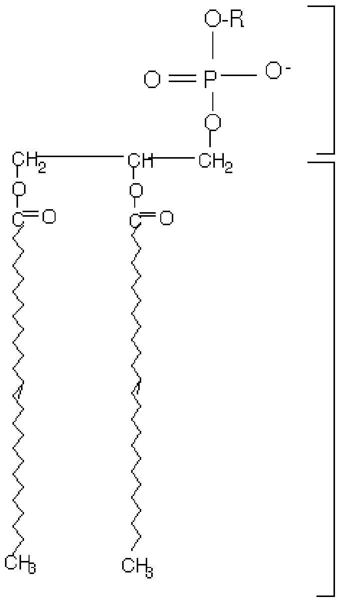
<u>4 Major Biomacromolecules (and their building blocks)</u>

- Lipids (phospholipids)
- Carbohydrate (monosaccharide)
- DNA or RNA (nucleotides)
- Protein (amino acids)

Lipid

Glycerol & Fatty acid



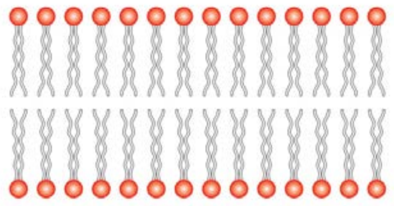


Polar head

Non-polar tails

Phosphoglyceride

Functions:
Energy storage
Components of cell membrane



Characteristics lipid

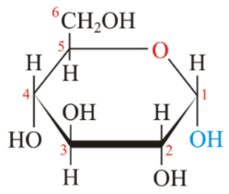
- Consists of hydrophilic head
  hydrophobic tail
- Amphiphilic molecule

Characteristics & function of lipid bilayer

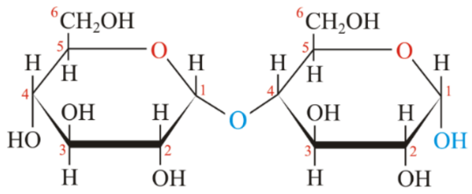
- Semi-permeable
- Protect cell
- Keep the cells compartmentalized
- Regulate the transport of molecules across the lipid bilayer

Sugar & Energy Metabolism

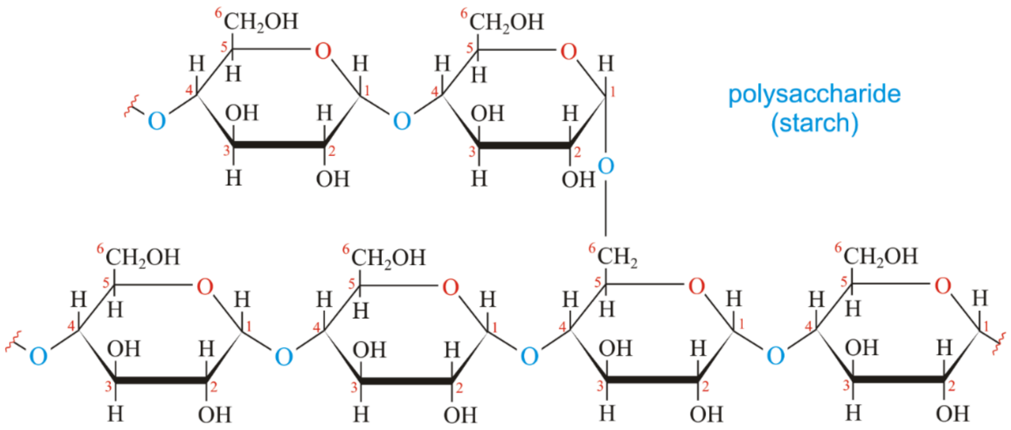
Carbohydrate - Sugar



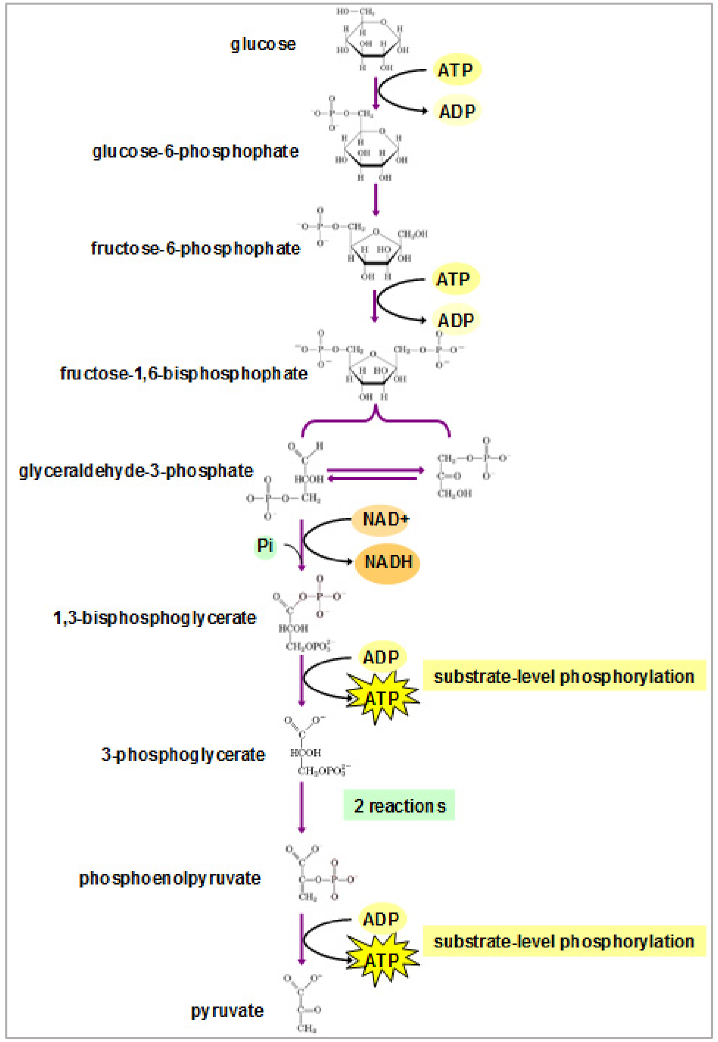
monosaccharide
(glucose)

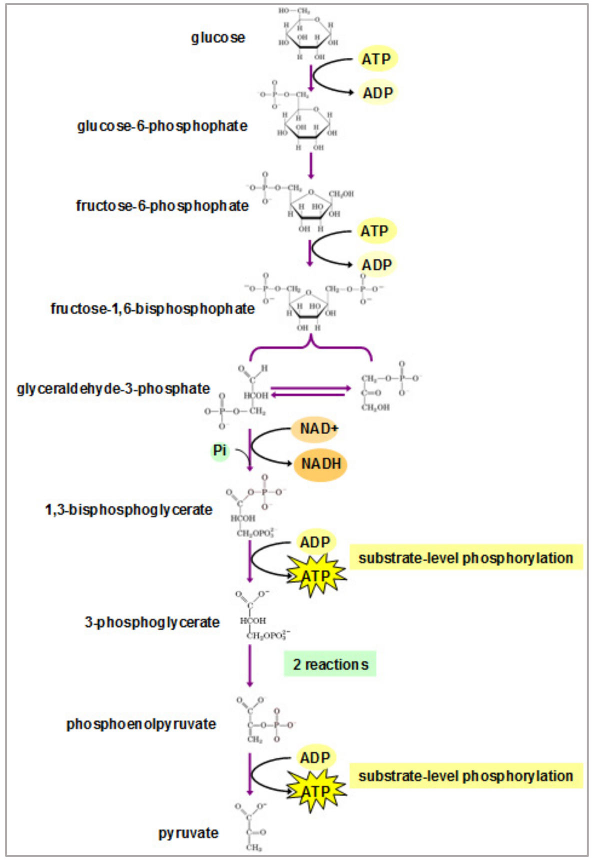


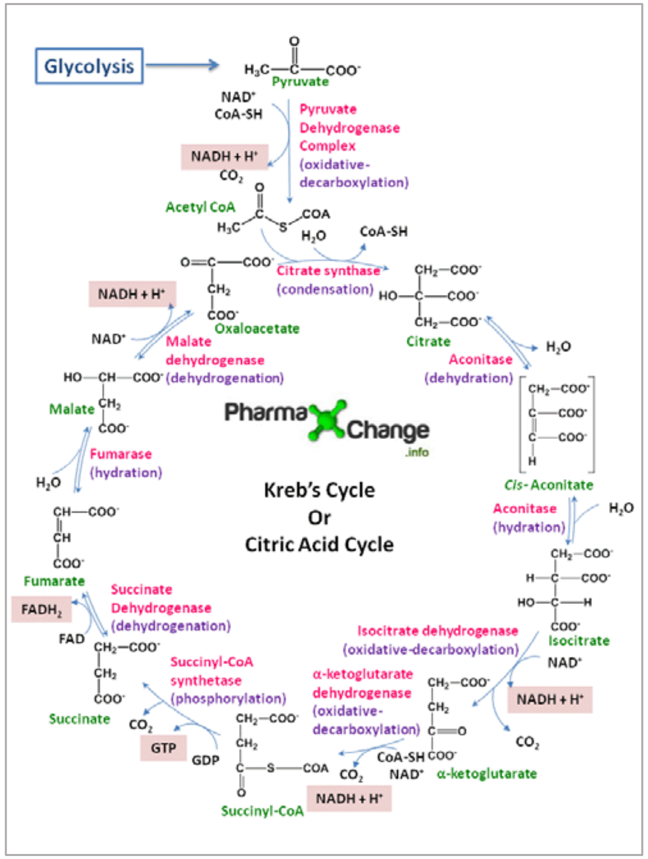
disaccharide
(maltose)

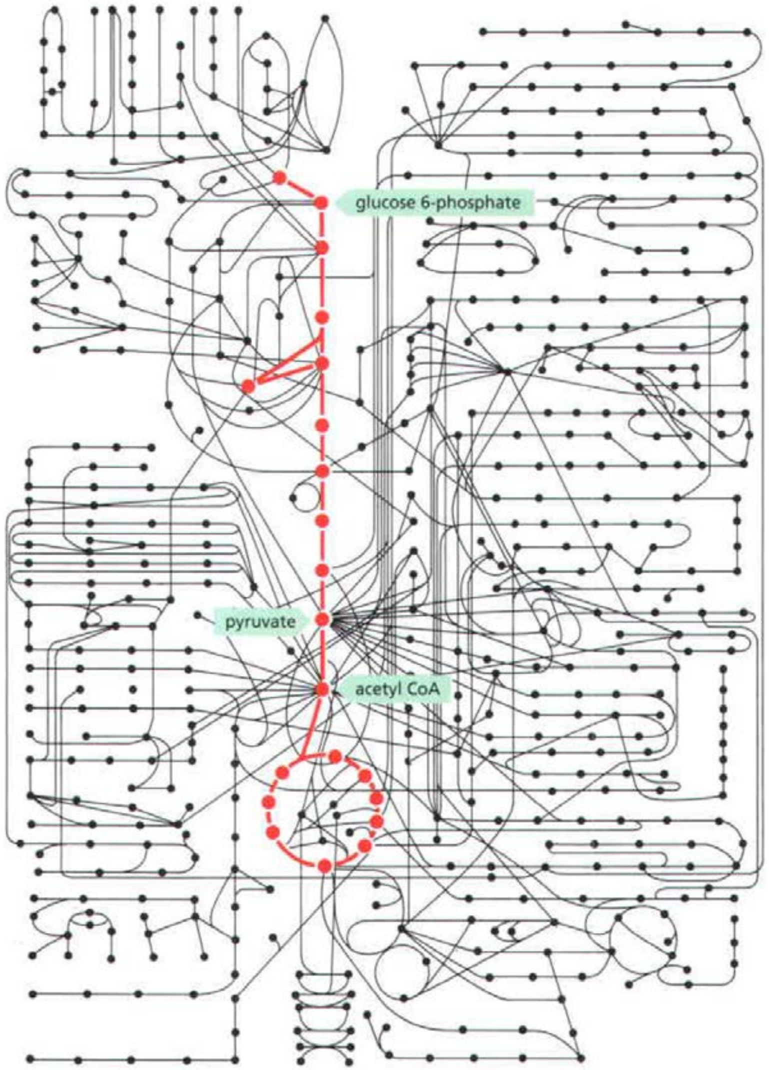


polysaccharide
(starch)

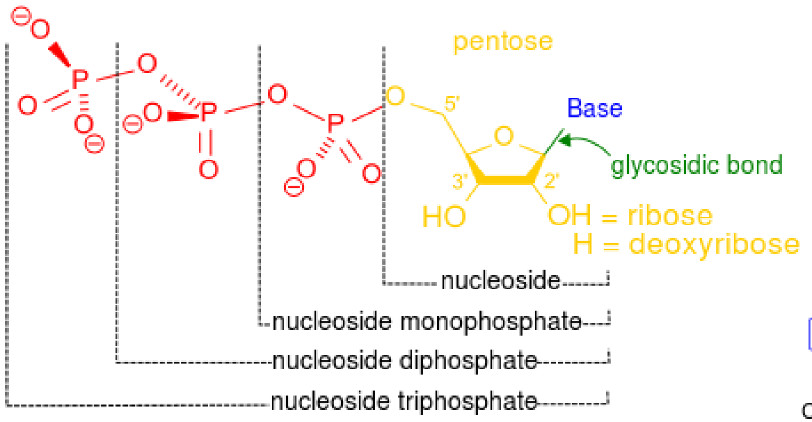


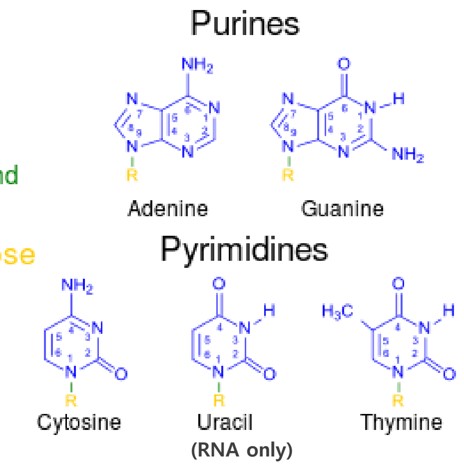

glucose
ATP
ADP
glucose-6-phosphophate
fructose-6-phosphophate
ATP
ADP
fructose-1,6-bisphosphophate
glyceraldehyde-3-phosphate
NAD+
Pi
NADH
1,3-bisphosphoglycerate
ADP
ATP
substrate-level phosphorylation
3-phosphoglycerate
2 reactions
phosphoenolpyruvate
ADP
ATP
substrate-level phosphorylation
pyruvate

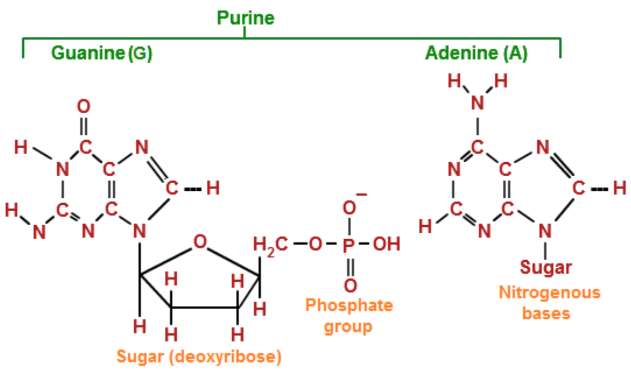

Glycolysis
Pyruvate
NAD+
CoA-SH
NADH + H+
CO2
Pyruvate Dehydrogenase Complex
(oxidative-decarboxylation)
Acetyl CoA
H2O
CoA-SH
Citrate synthase
(condensation)
Oxaloacetate
Citrate
NADH + H+
NAD+
Malate dehydrogenase
(dehydrogenation)
Aconitase
(dehydration)
H2O
Malate
PharmaXChange
.info
Kreb's Cycle
Or
Citric Acid Cycle
Cis-Aconitate
Fumarase
(hydration)
H2O
Aconitase
(hydration)
H2O
Fumarate
FADH2
FAD
Succinate Dehydrogenase
(dehydrogenation)
Isocitrate dehydrogenase
(oxidative-decarboxylation)
Isocitrate
NAD+
NADH + H+
CO2
Succinyl-CoA synthetase
(phosphorylation)
α-ketoglutarate dehydrogenase
(oxidative-decarboxylation)
Succinate
GTP
GDP
CoA-SH
CO2
NAD+
α-ketoglutarate
NADH + H+
Succinyl-CoA

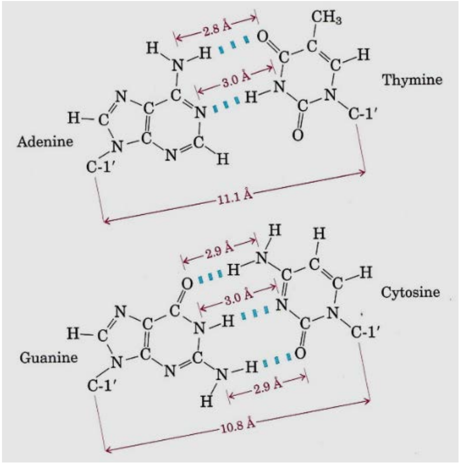

glucose 6-phosphate
pyruvate
acetyl CoA

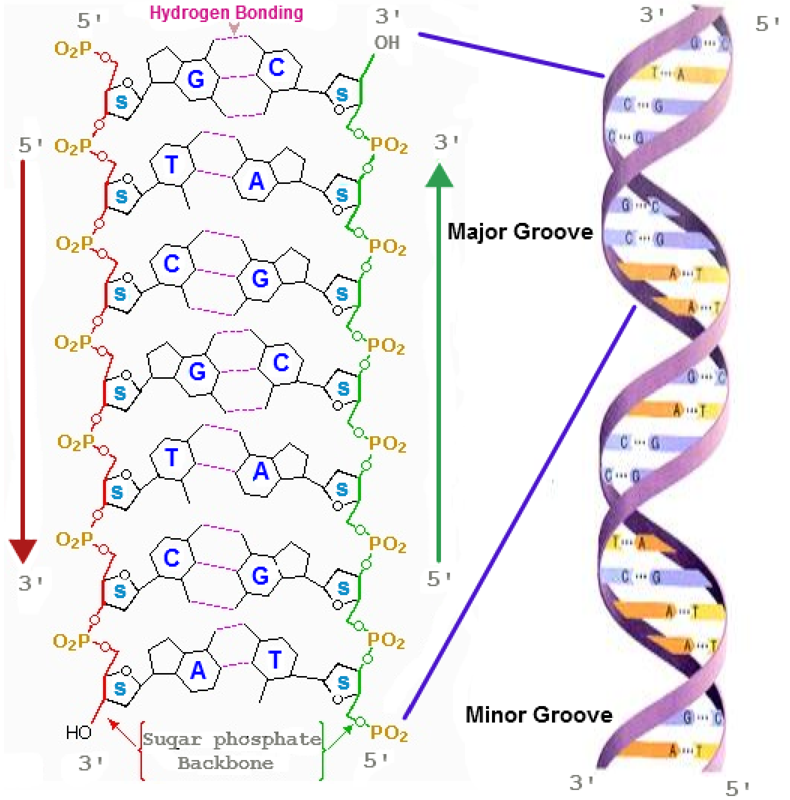
DNA & RNA Structure





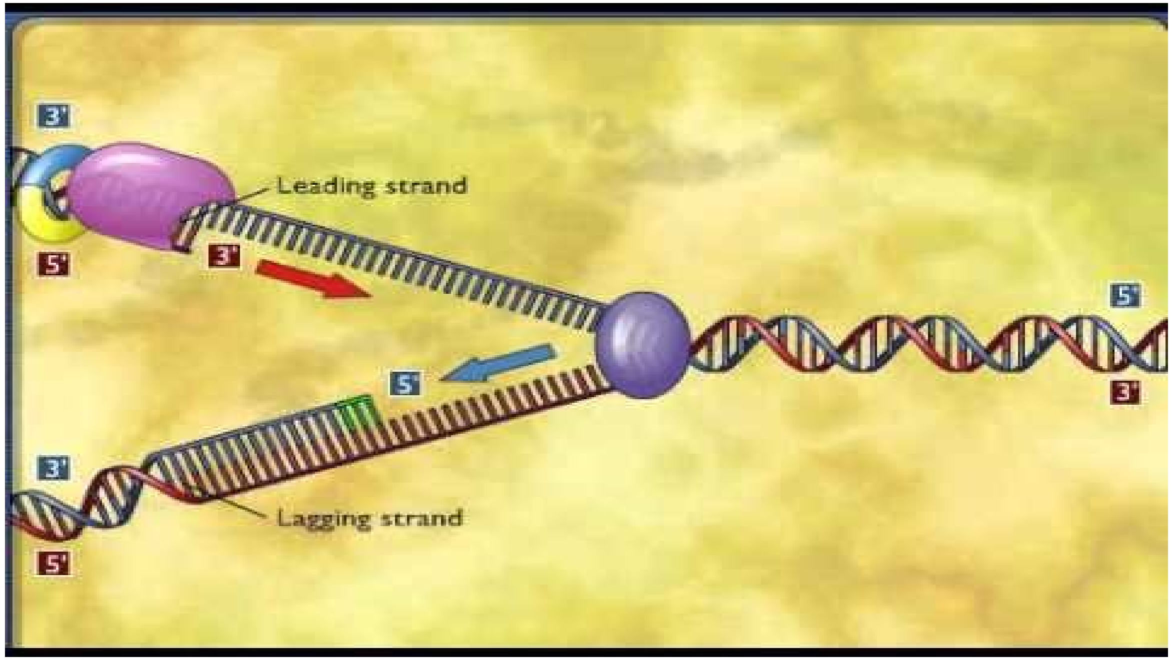




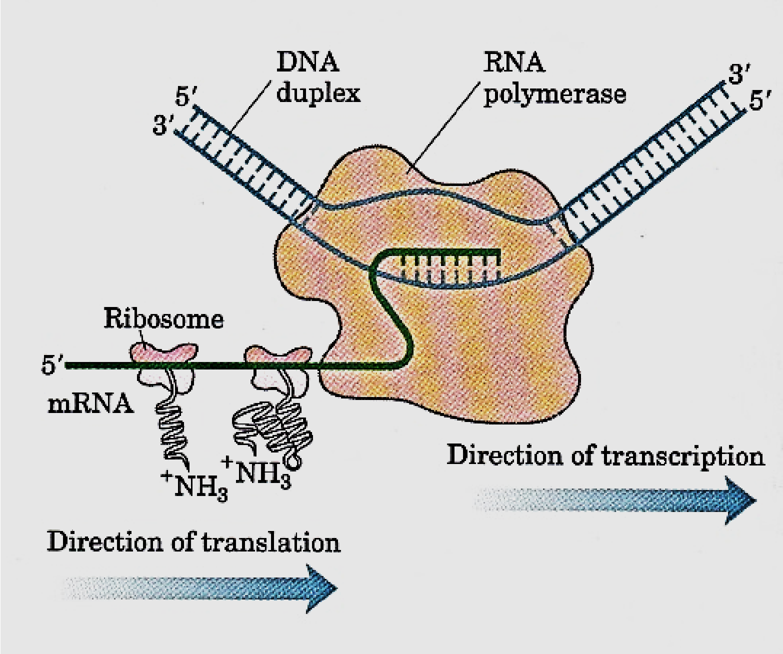


DNA Replication & Transcription

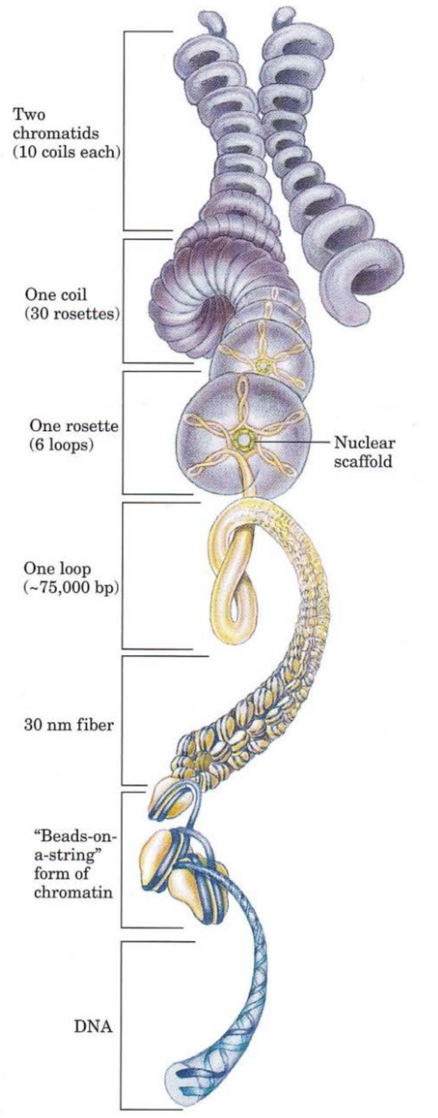
DNA Replication = DNA -> DNA^2

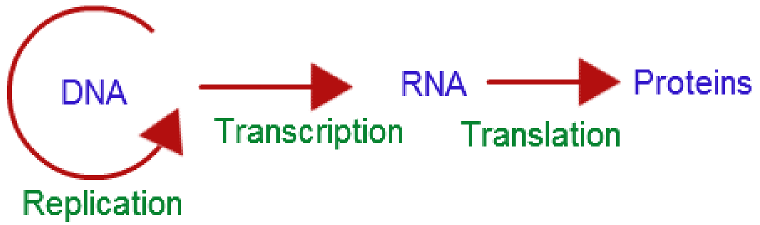


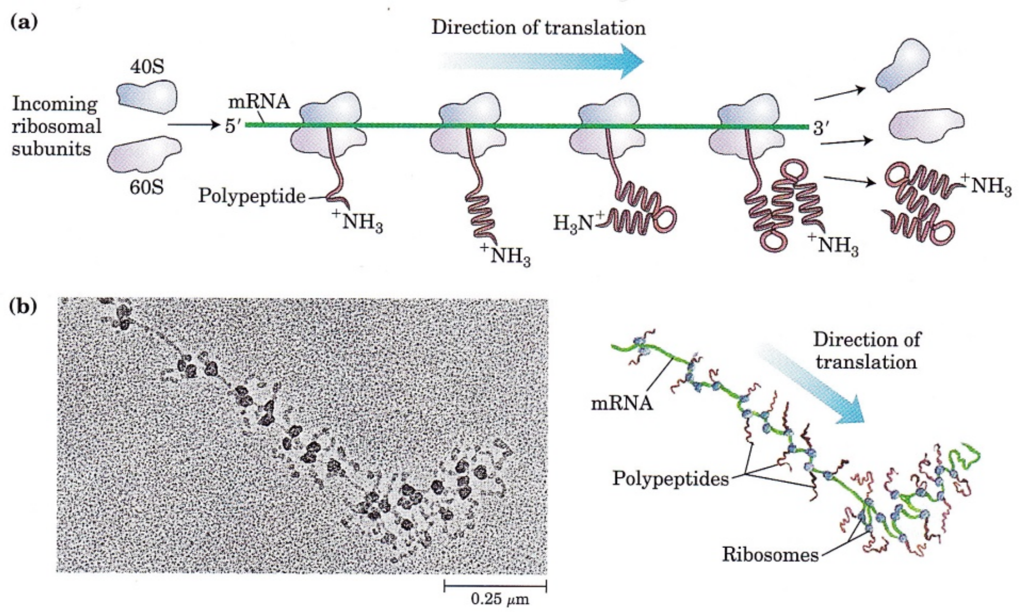
DNA Transcription = DNA -> RNA

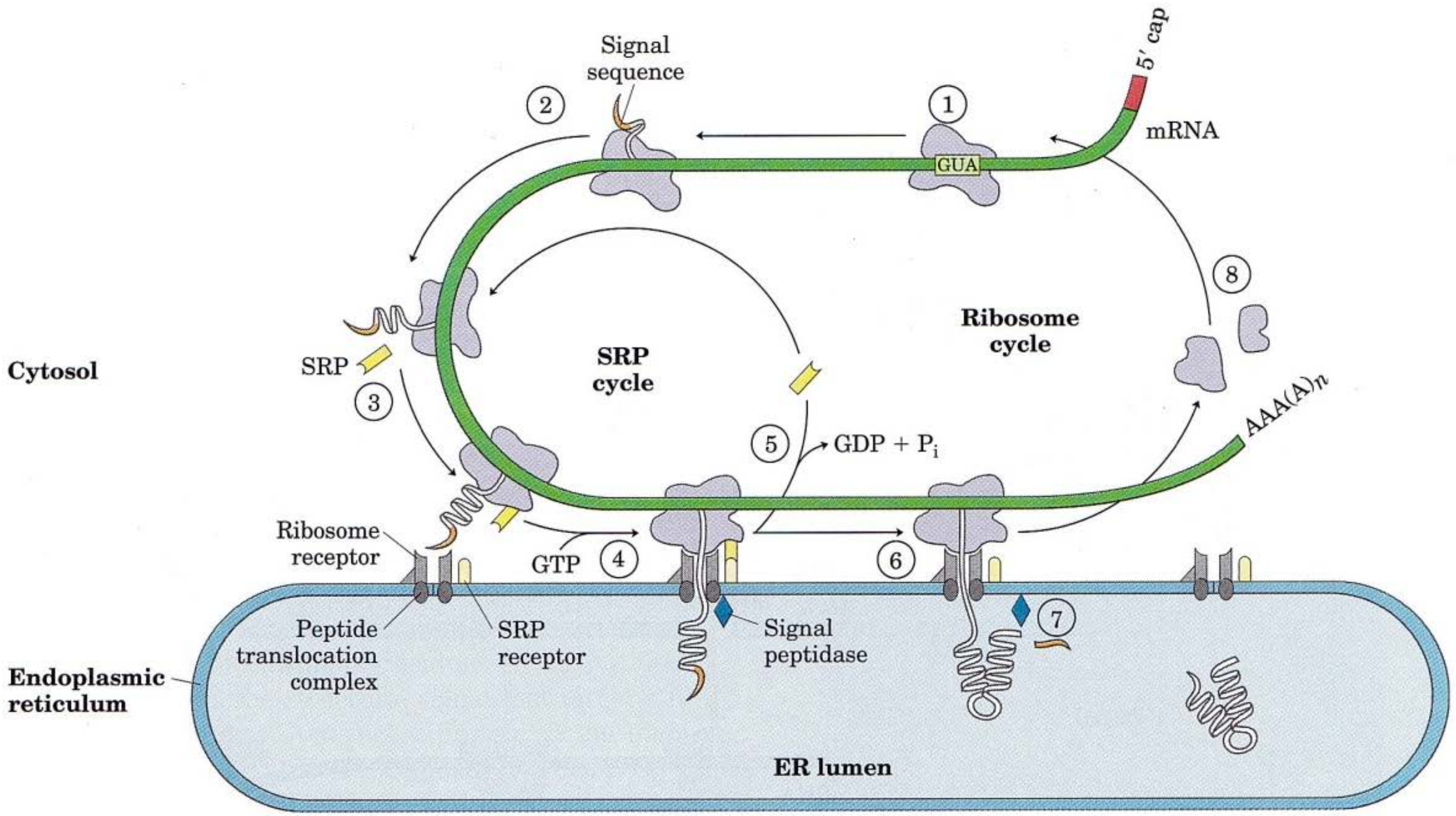


DNA to Proteins - An Information Pathways



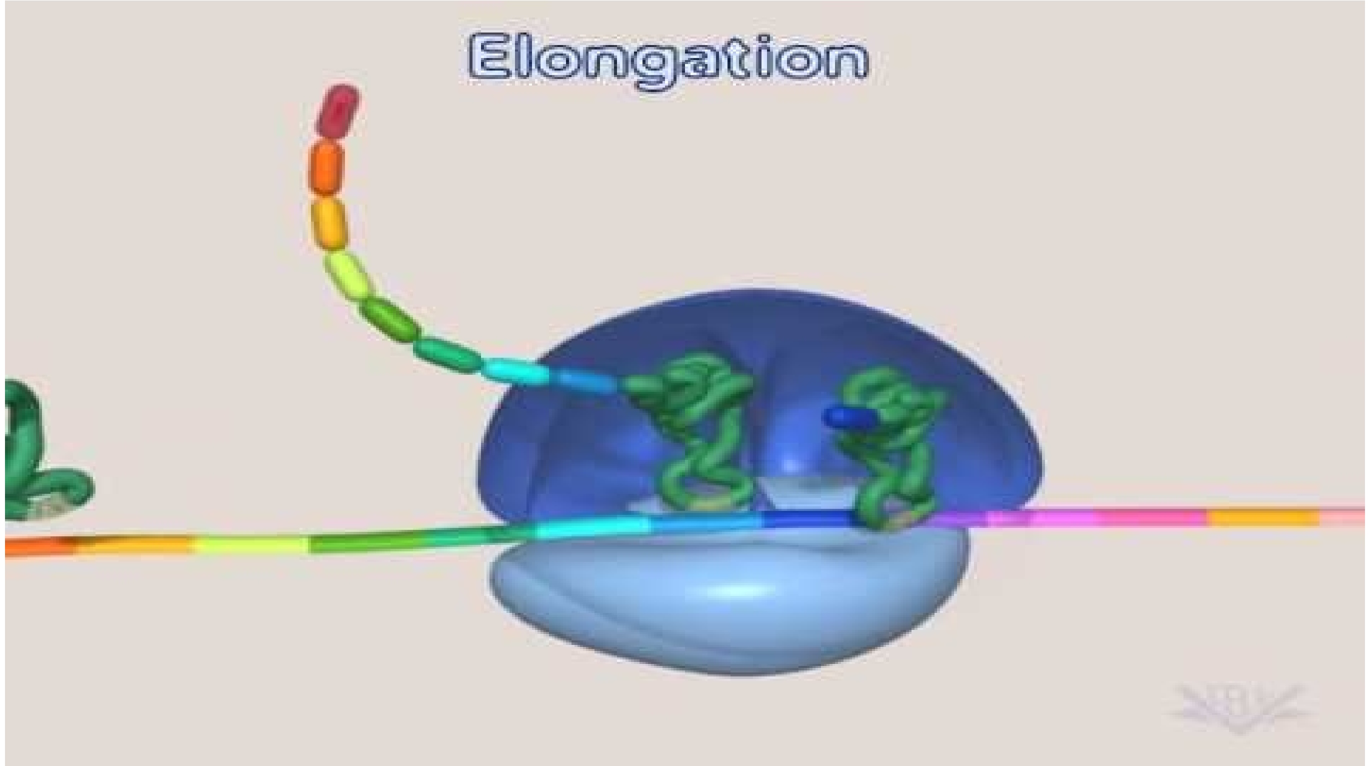






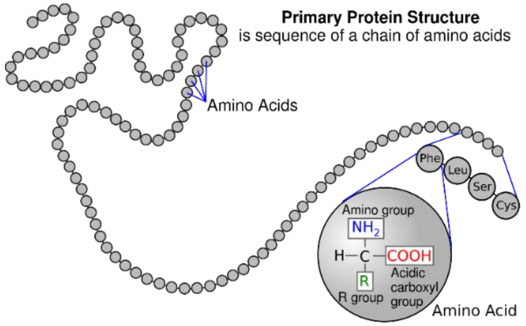
Signal sequence
1
2
3
4
5
6
7
8
5′ cap
mRNA
GUA
SRP
Cytosol
SRP cycle
Ribosome cycle
GDP + P_i
GTP
AAA(A)n
Ribosome receptor
Peptide translocation complex
SRP receptor
Signal peptidase
Endoplasmic reticulum
ER lumen

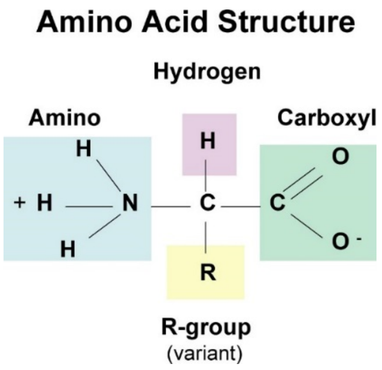
Protein Synthesis

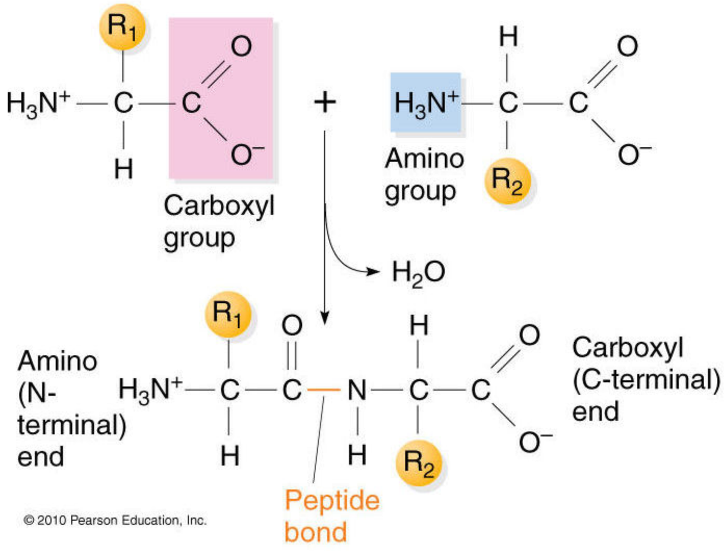


Amino Acid – Building Block of Protein

Proteins – Amino acids







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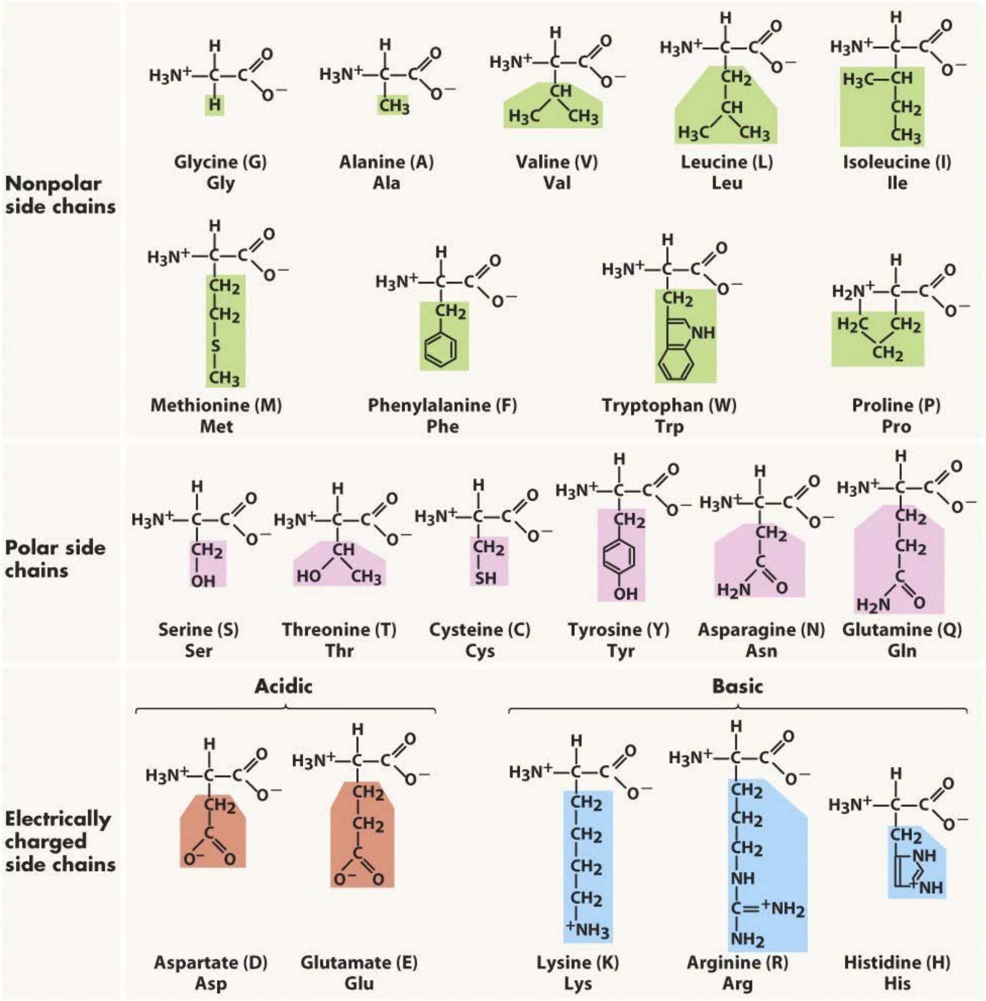
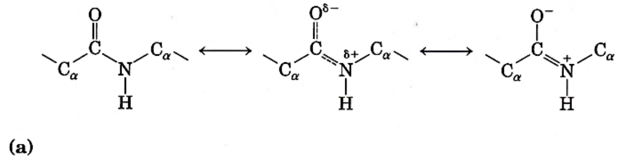
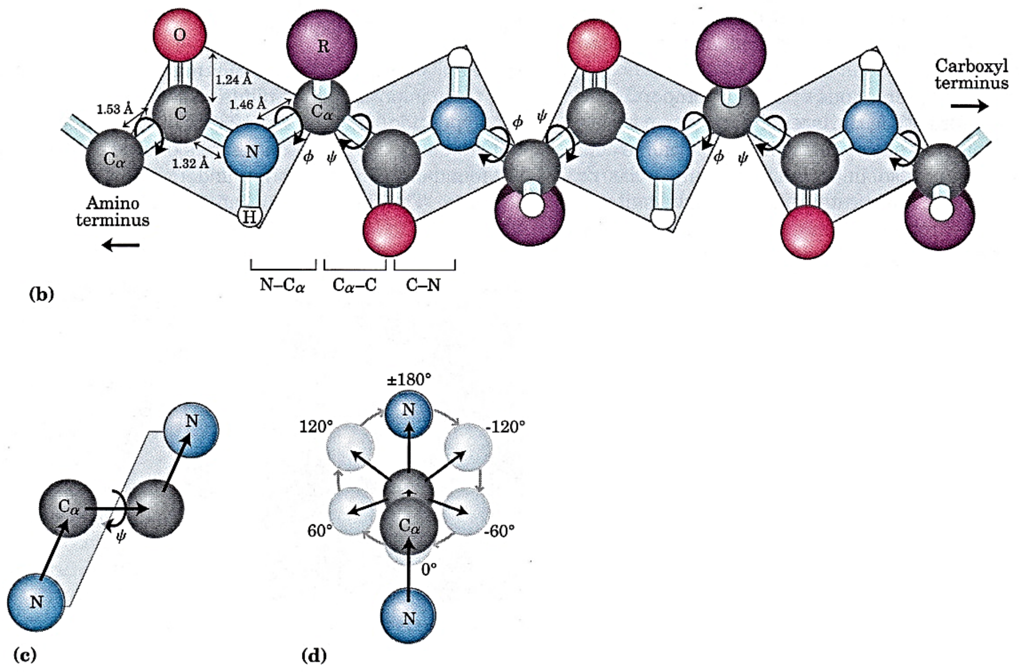
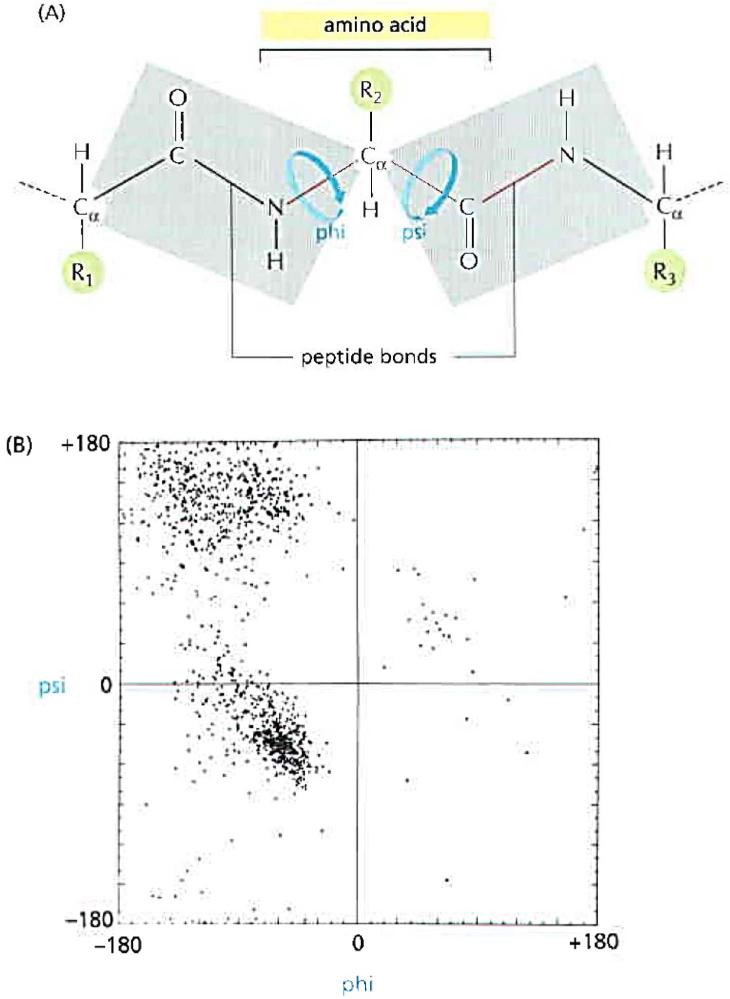


Determinant of Protein Conformation

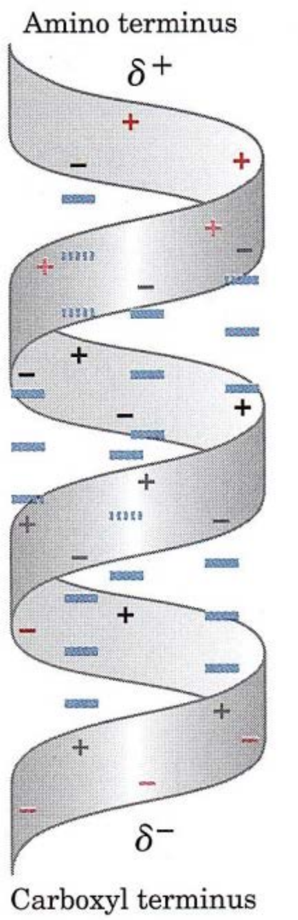


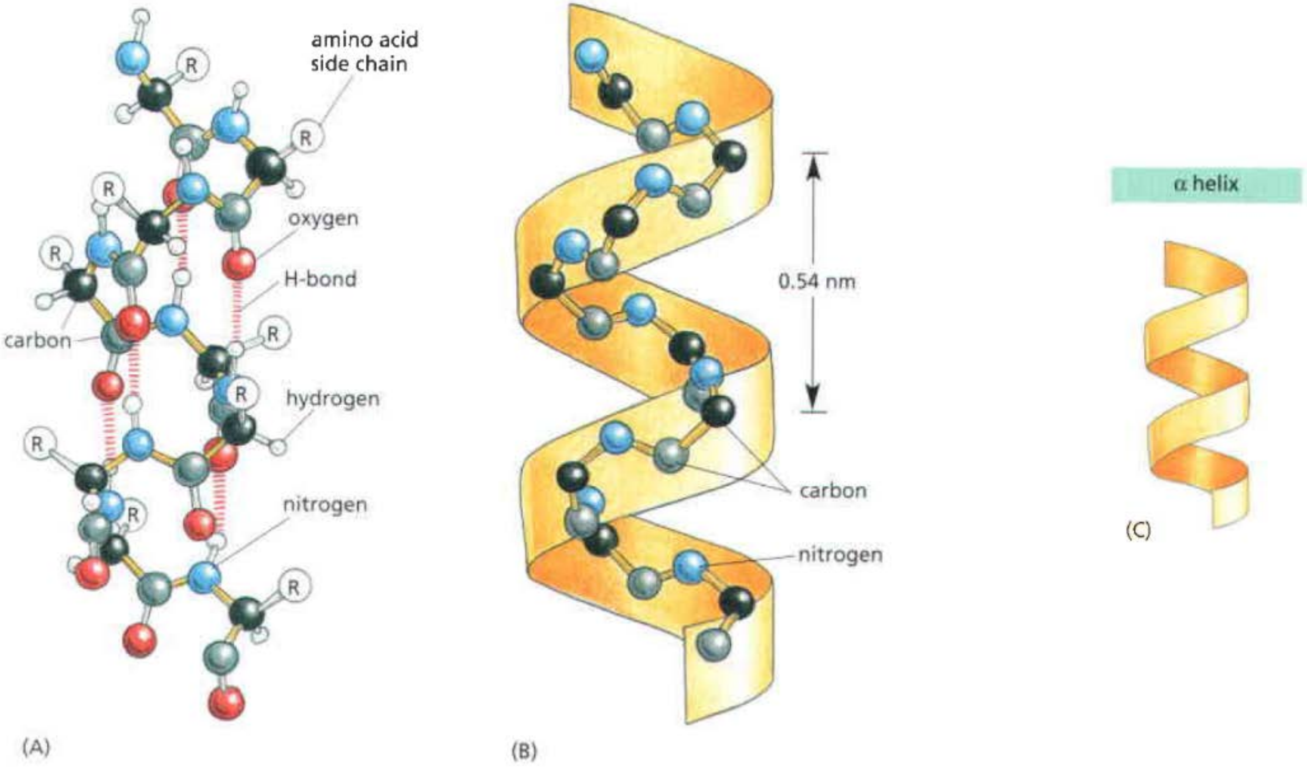
The carbonyl oxygen has a partial negative charge and the amide nitrogen a partial positive charge, setting up a small electric dipole. Virtually all peptide bonds in proteins occur in this trans configuration; an exception is noted in Figure 4–7b.



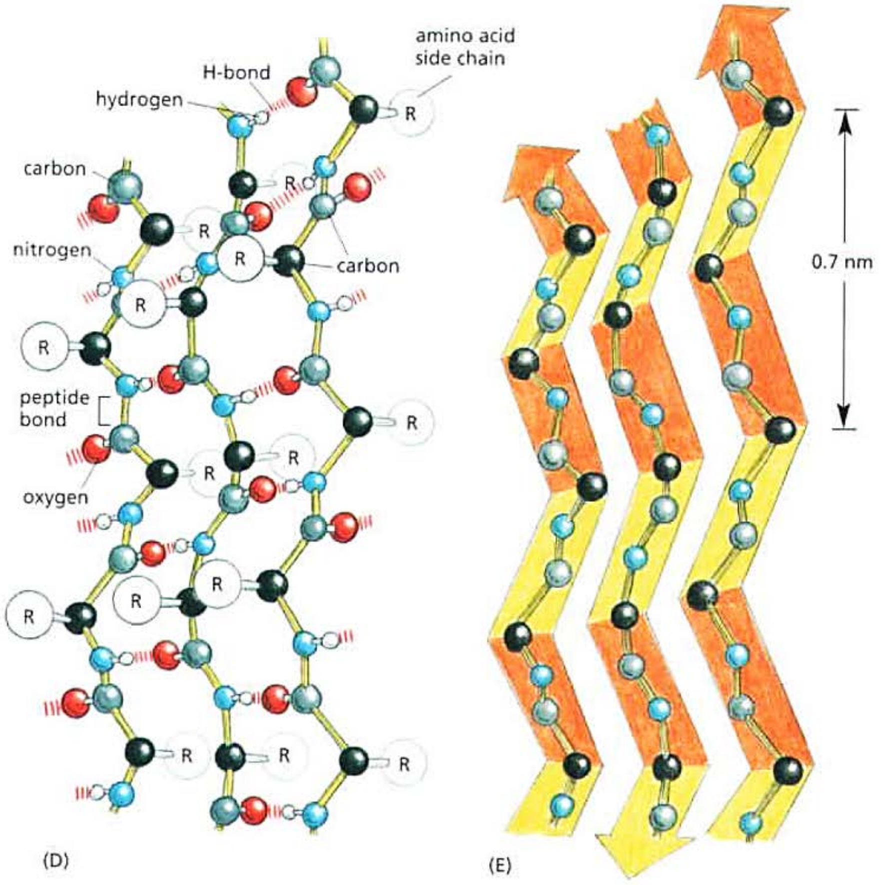


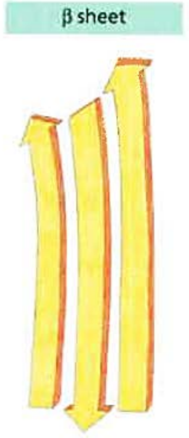
Protein Structure – α-Helix





Protein Structure – β-Pleated Sheet





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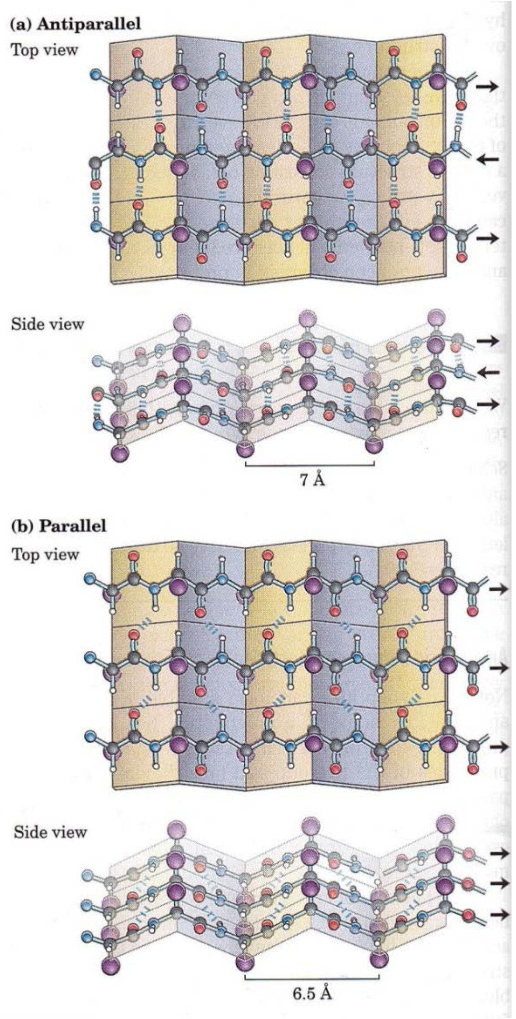
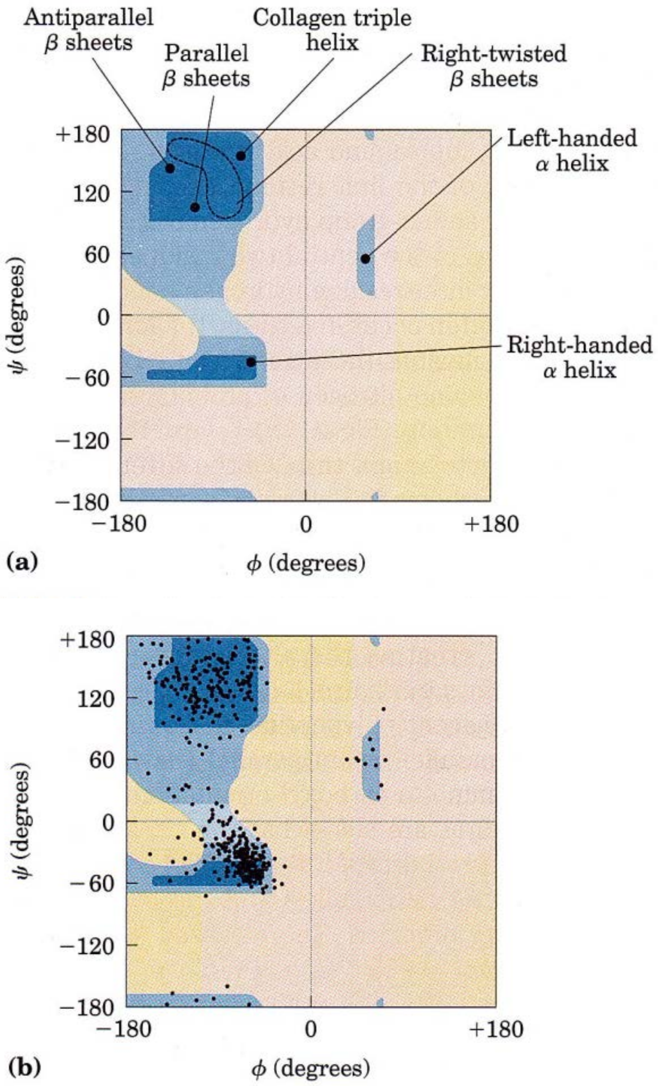




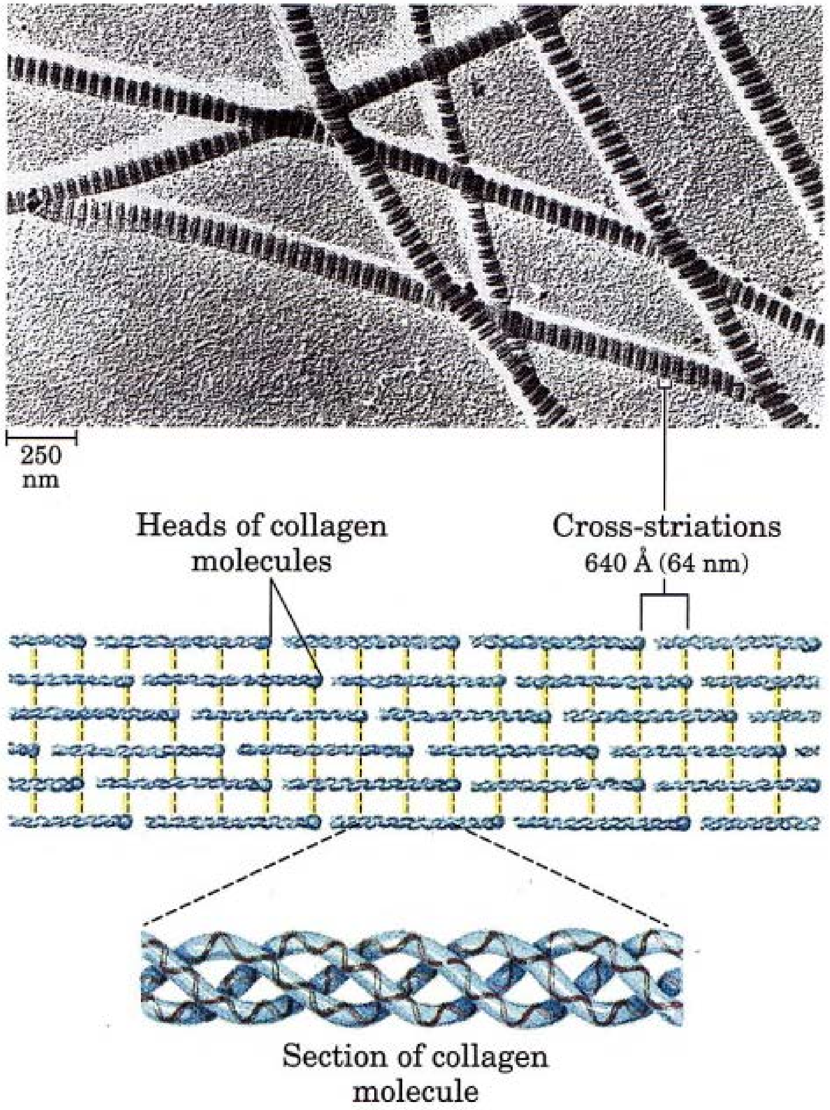
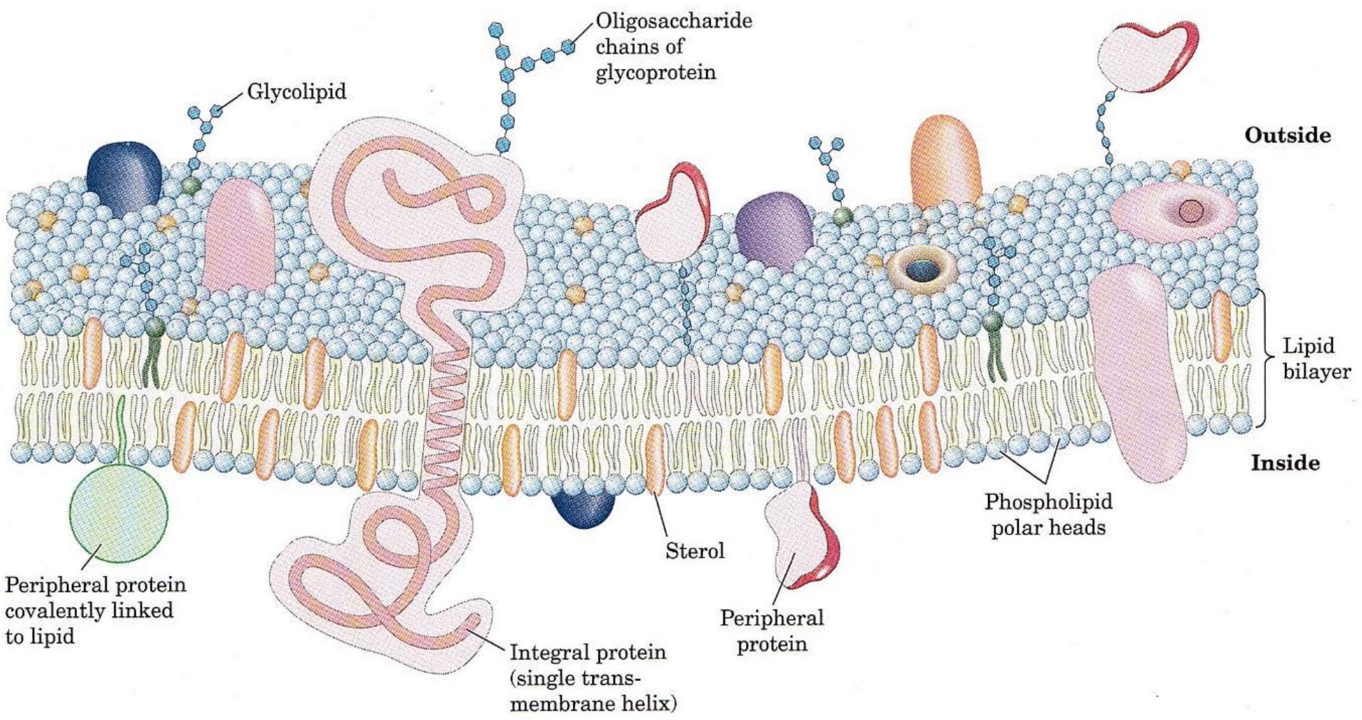
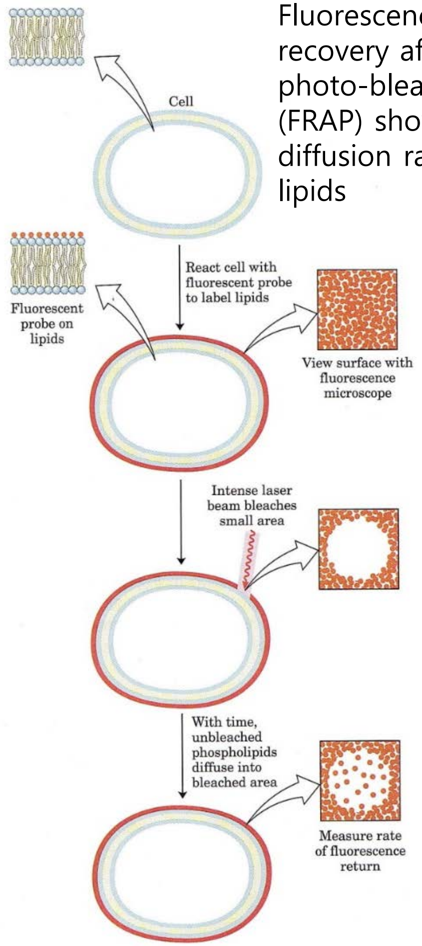


FIGURE 4–12 Structur
rod-shaped molecule, a
helically intertwined α
has about 1,000 amino
collagen molecules alig
strength. The specific a
the tissue and produce
crograph. In the examp
every fourth molecule p

Cell structure

Membrane Structure – Fluid Mosaic Model

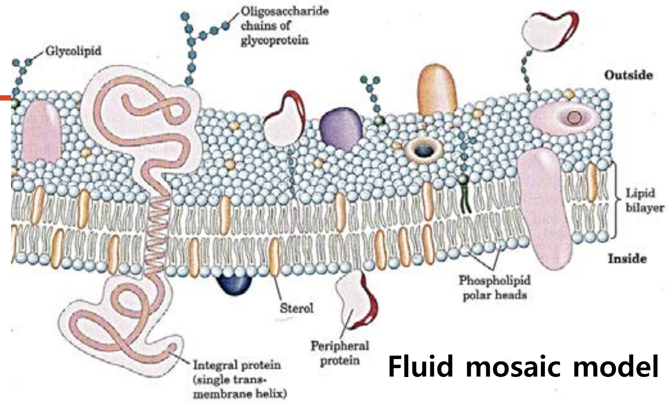




Fluorescence recovery after photo-bleaching (FRAP) shows lateral diffusion rate of lipids

The individual lipid and protein units in a membrane forma a fluid mosaic with a pattern that is free to change constantly

Osmolarity



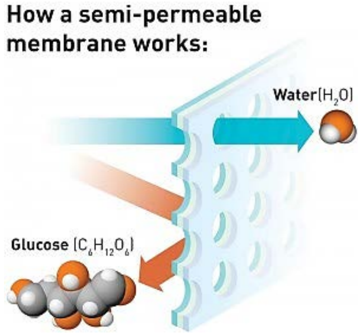
Fluid mosaic model

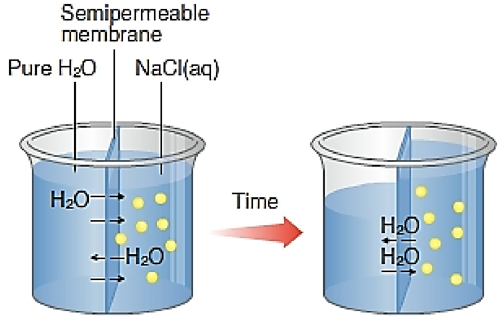
Semi-permeable membrane

- A membrane that allows some molecules to pass through but not others
(=selectively permeable membrane)

Osmosis

- Water movement across a semipermeable membrane driven by differences in osmotic pressure





Isotonic

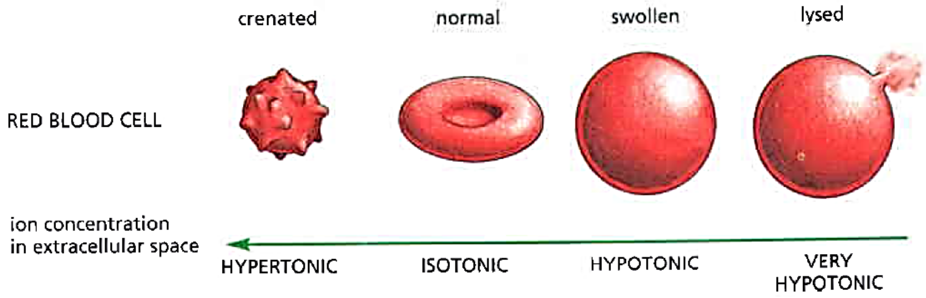
- Solutions of osmolarity equal to that of a cell′ s cytosol

Hypertonic

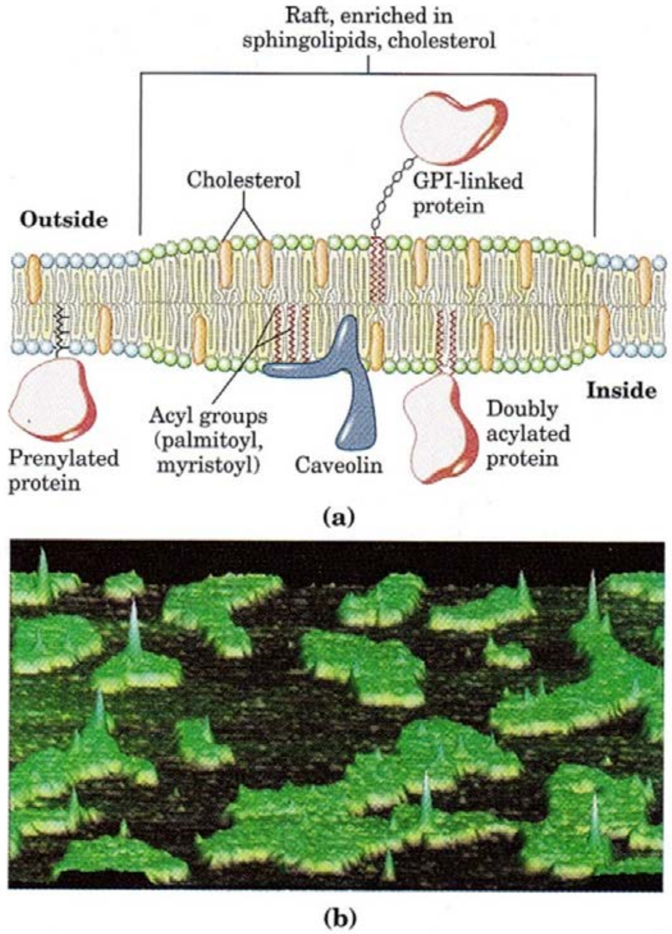
- Solution with higher osmolarity than that of the cytosol

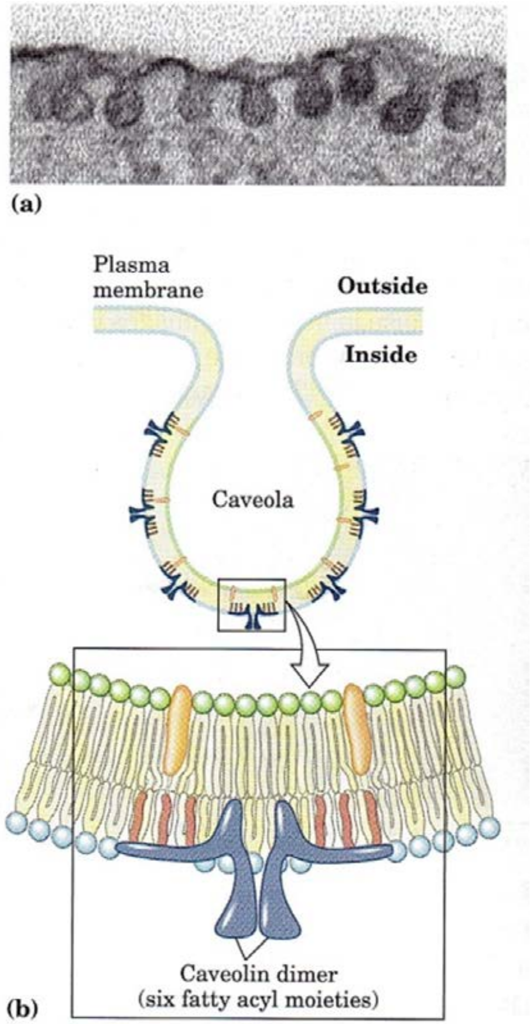
Hypotonic

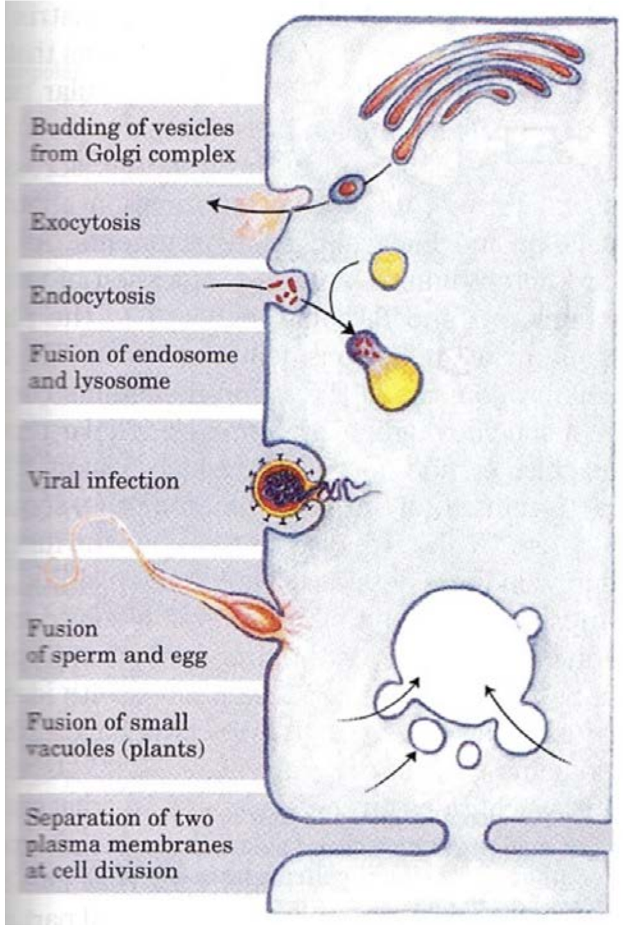
- Solution with lower osmolarity than the cytosol

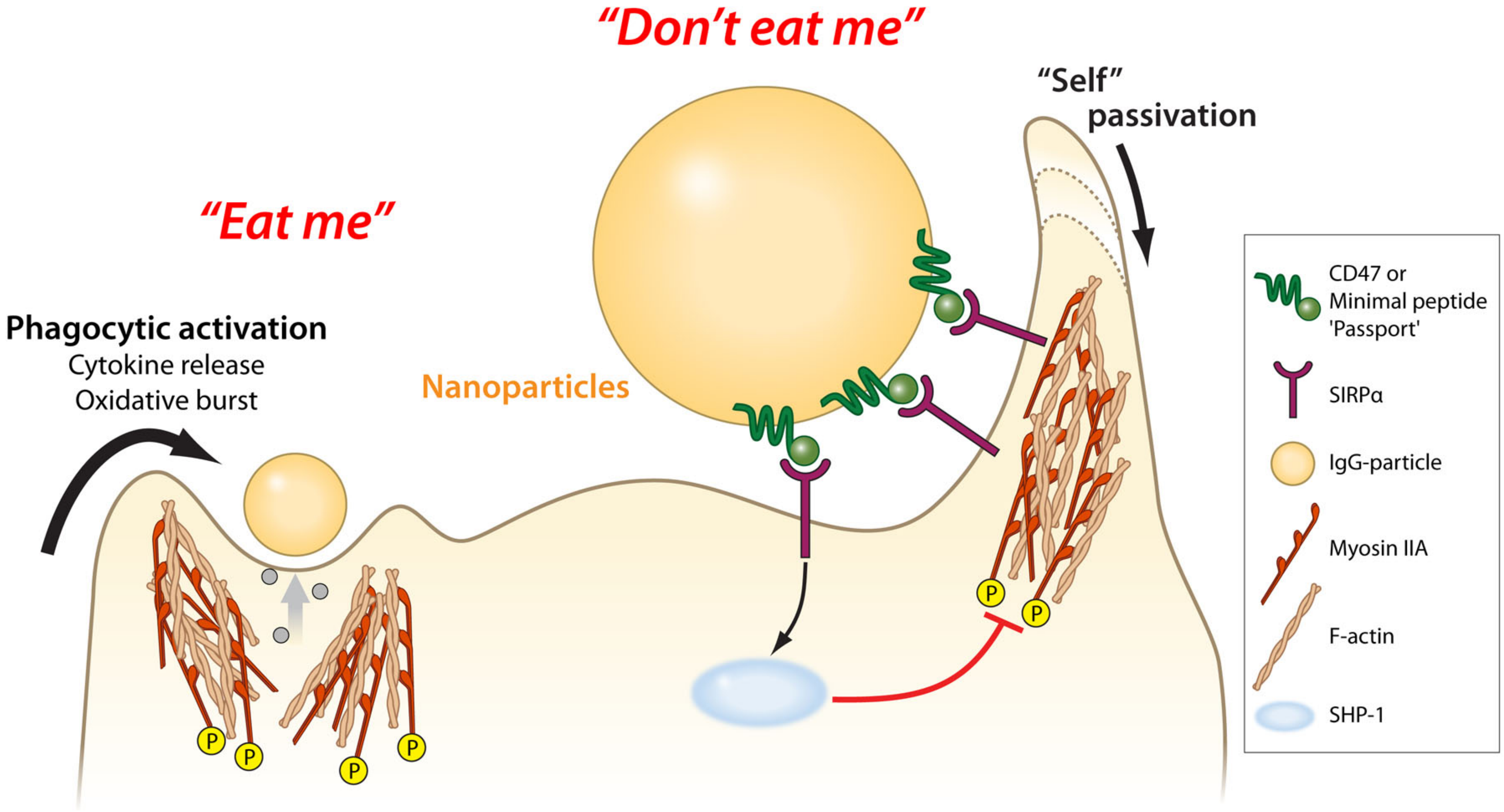


Membrane micro-domains (Rafts)

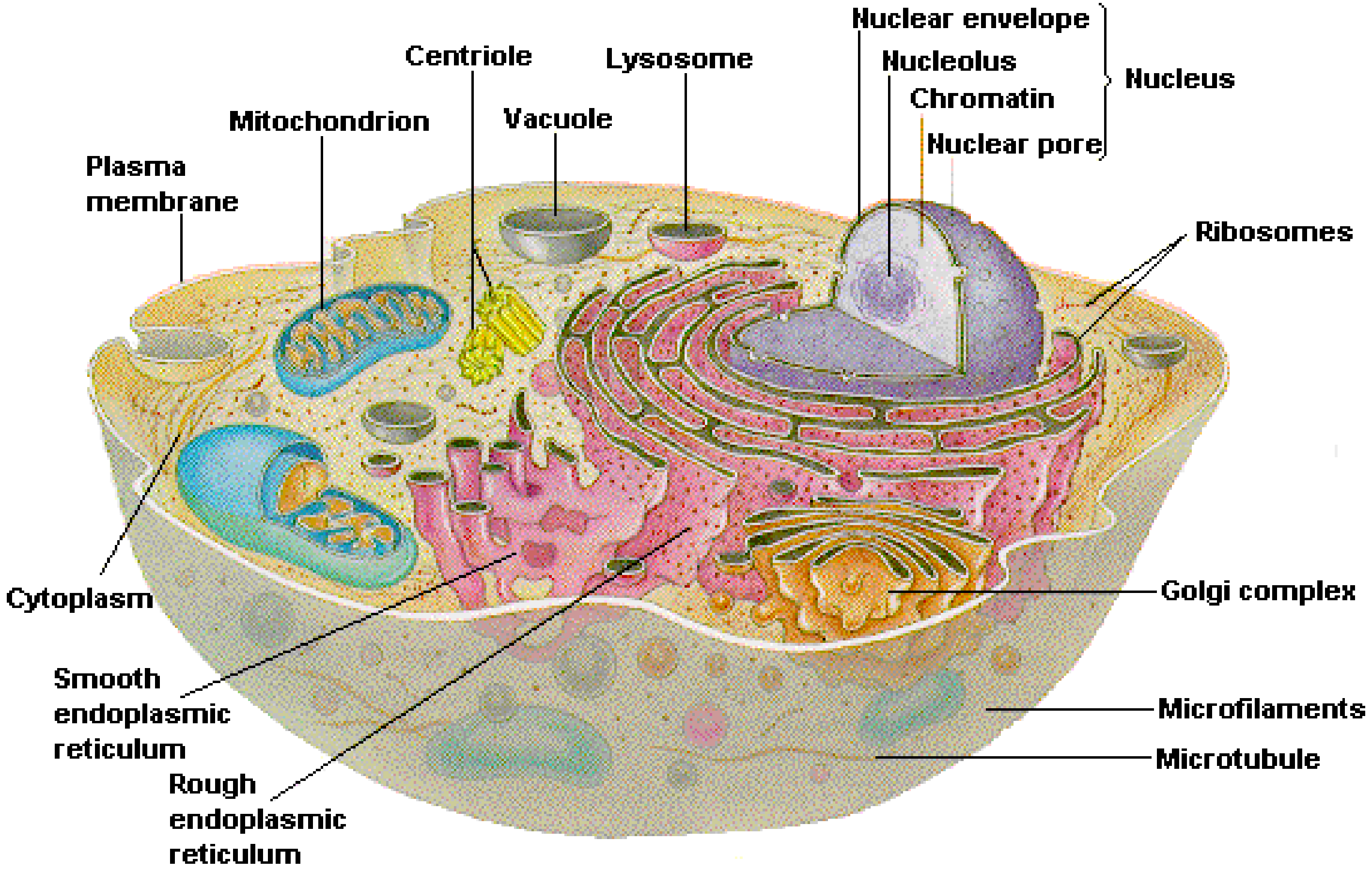







"Don't eat me"
"Self" passivation
"Eat me"
Phagocytic activation
Cytokine release
Oxidative burst
Nanoparticles
P
CD47 or
Minimal peptide
'Passport'
SIRPα
IgG-particle
Myosin IIA
F-actin
SHP-1

Cell Organelles



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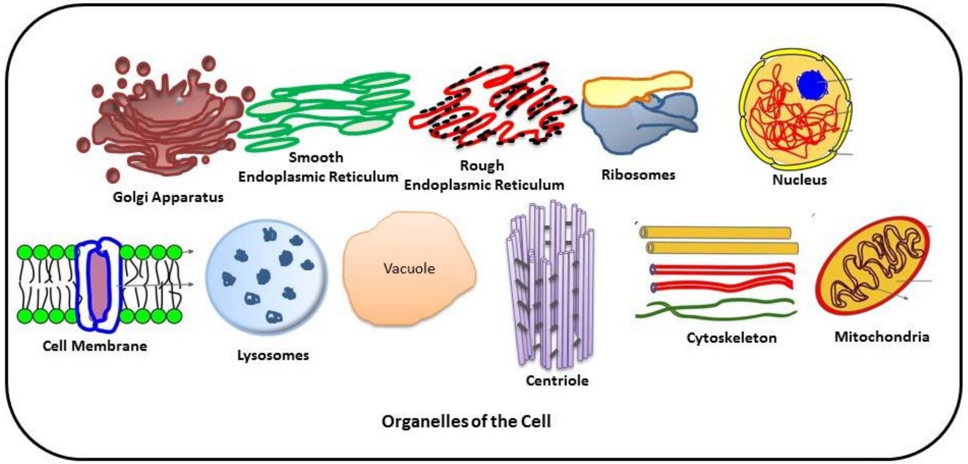

Namrata Heda

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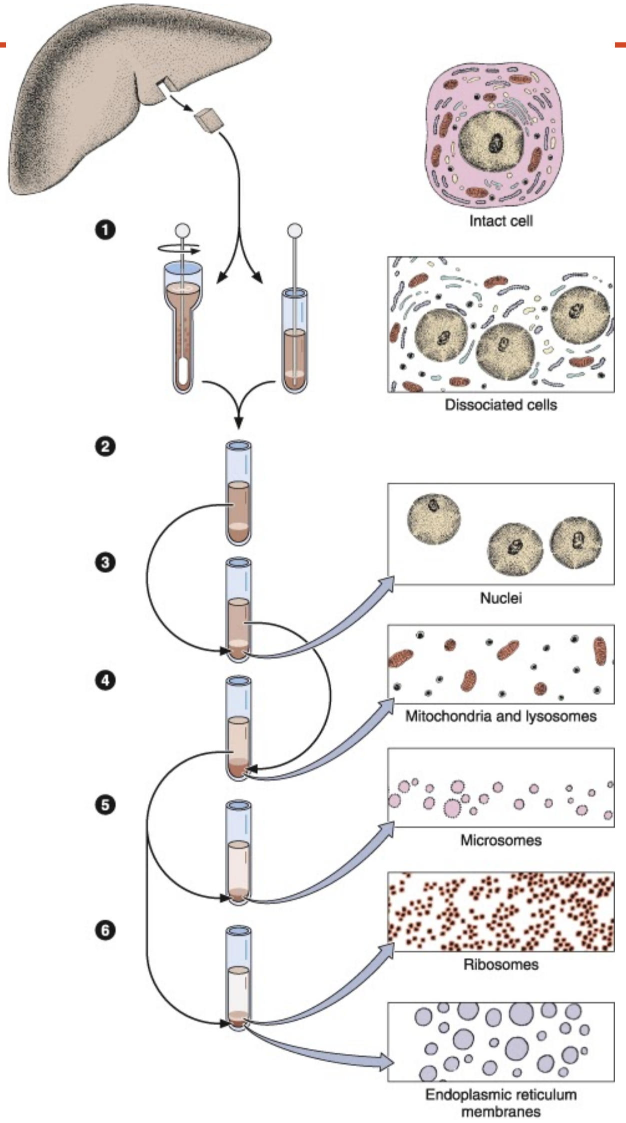
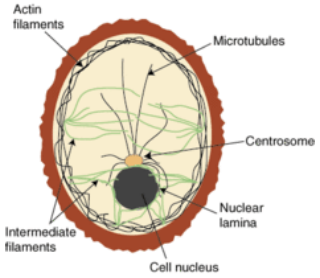
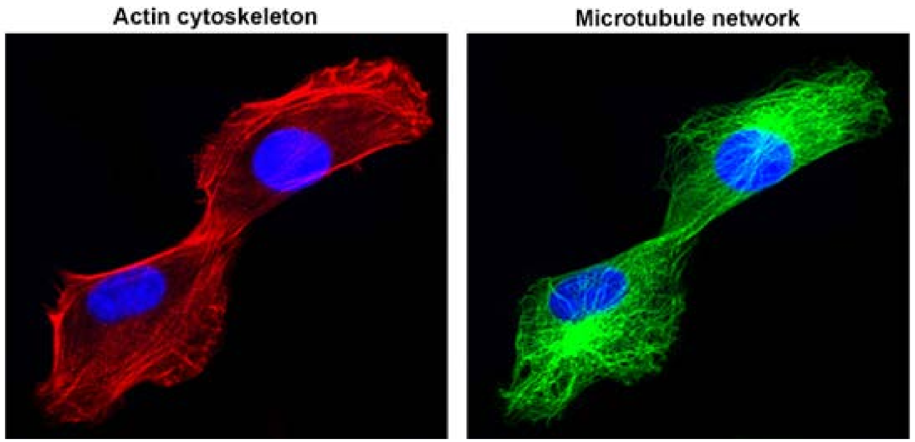
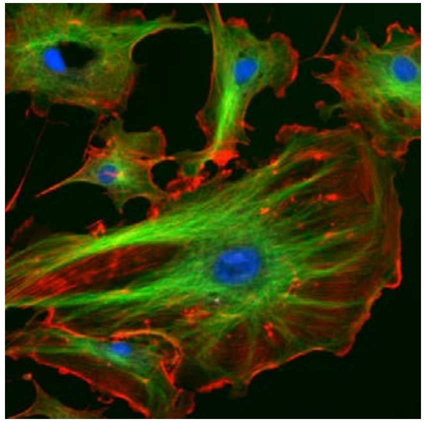
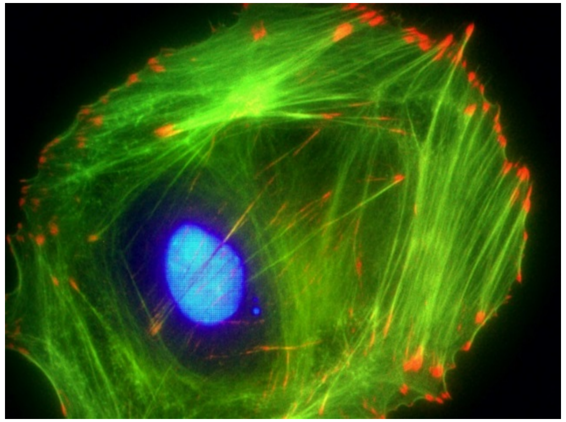


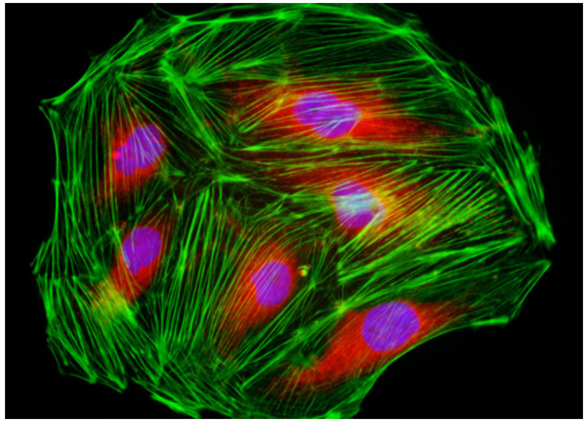
Cytoskeleton

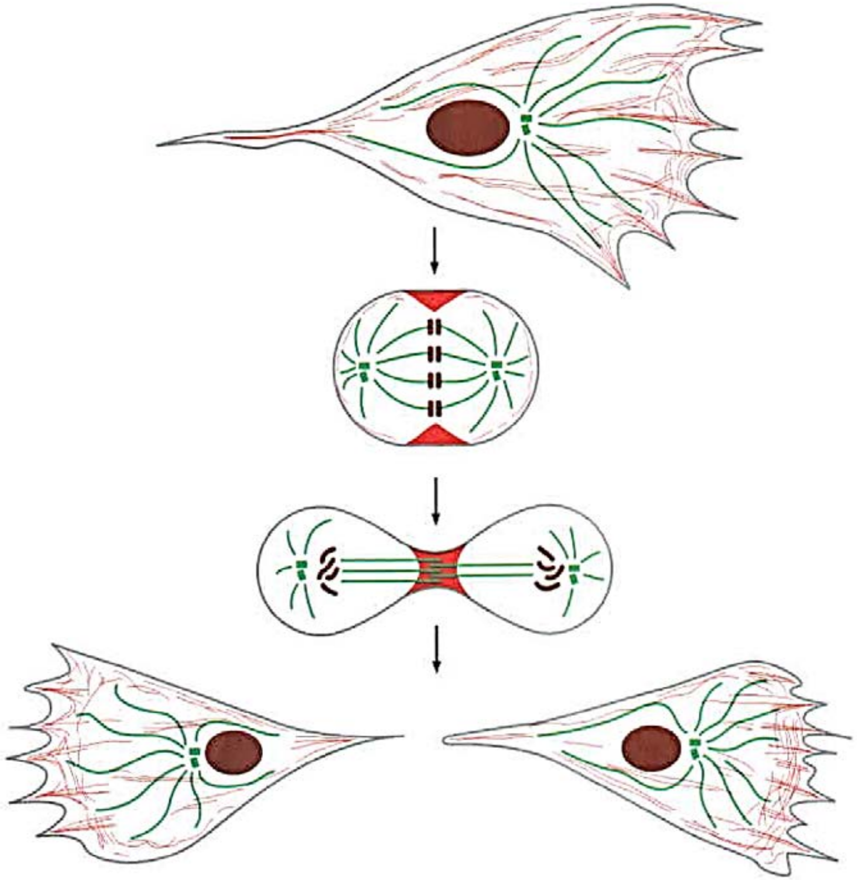


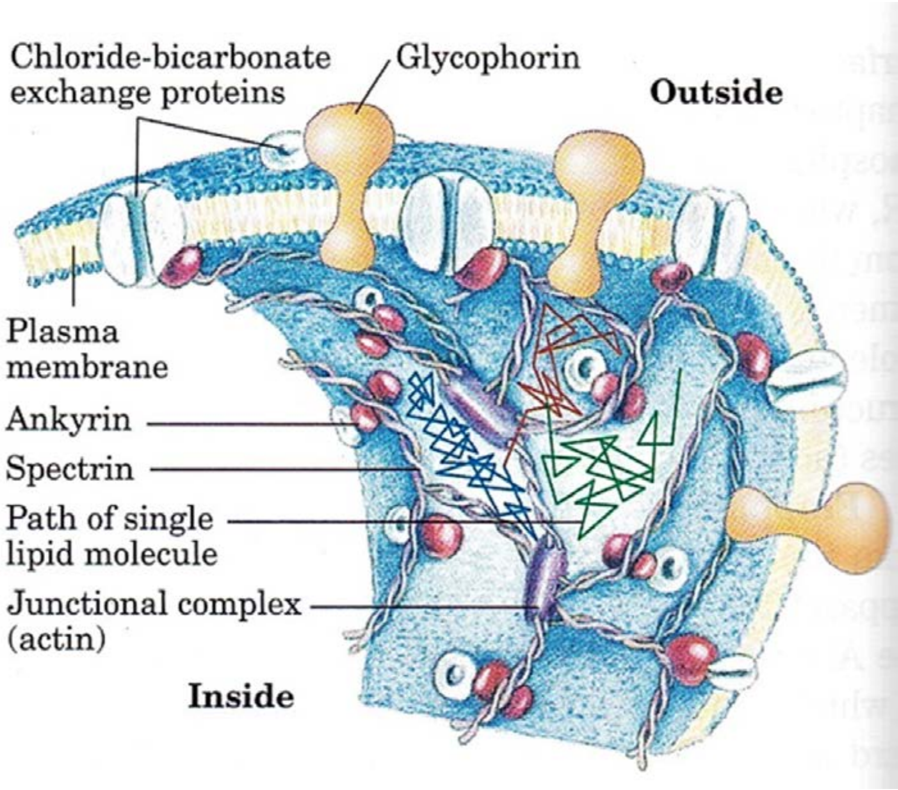











Chloride-bicarbonate exchange proteins
Glycophorin
Outside
Plasma membrane
Ankyrin
Spectrin
Path of single lipid molecule
Junctional complex (actin)
Inside

Introduction on Cell Biology

Distinguishing Features of Living Organisms

A high degree of chemical complexity and microscopic organization
화학적, 구조적 복잡성

Systems for extracting, transforming, and using energy from the environment
에너지 대사

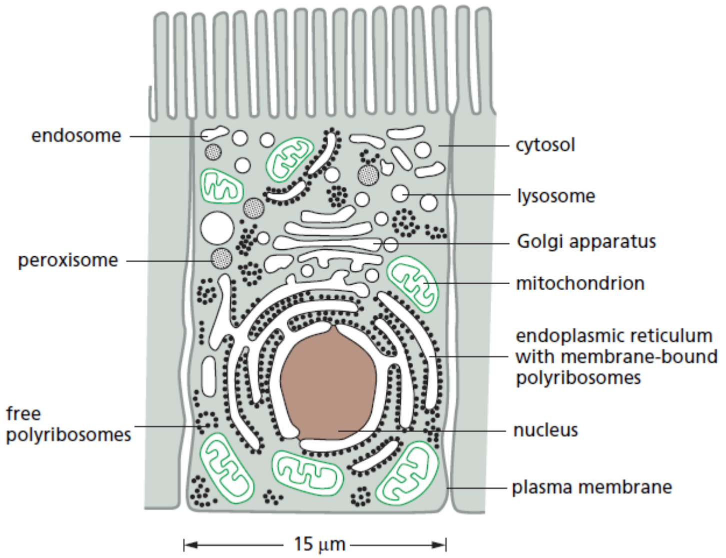
Defined functions for each of an organism′ s components and regulated interactions among them
거시적 & 미시적 기능 분화 요소

Mechanisms for sensing and responding to alterations in their surroundings
환경 변화에 대한 반응(적응)

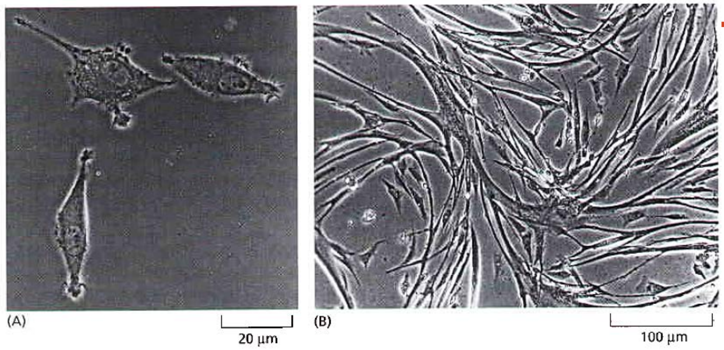
A capacity for precise self-replication and self-assembly
자기 복제 능력

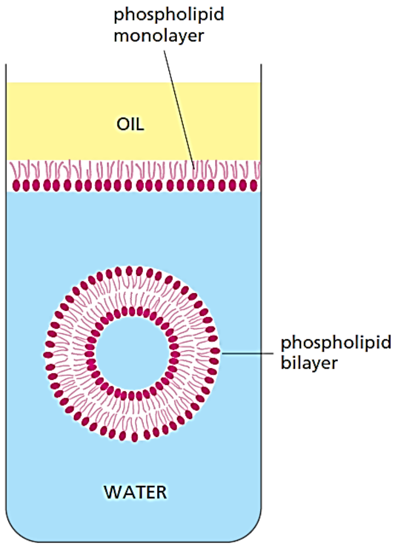
A capacity to change over time by gradual evolution
진화 능력

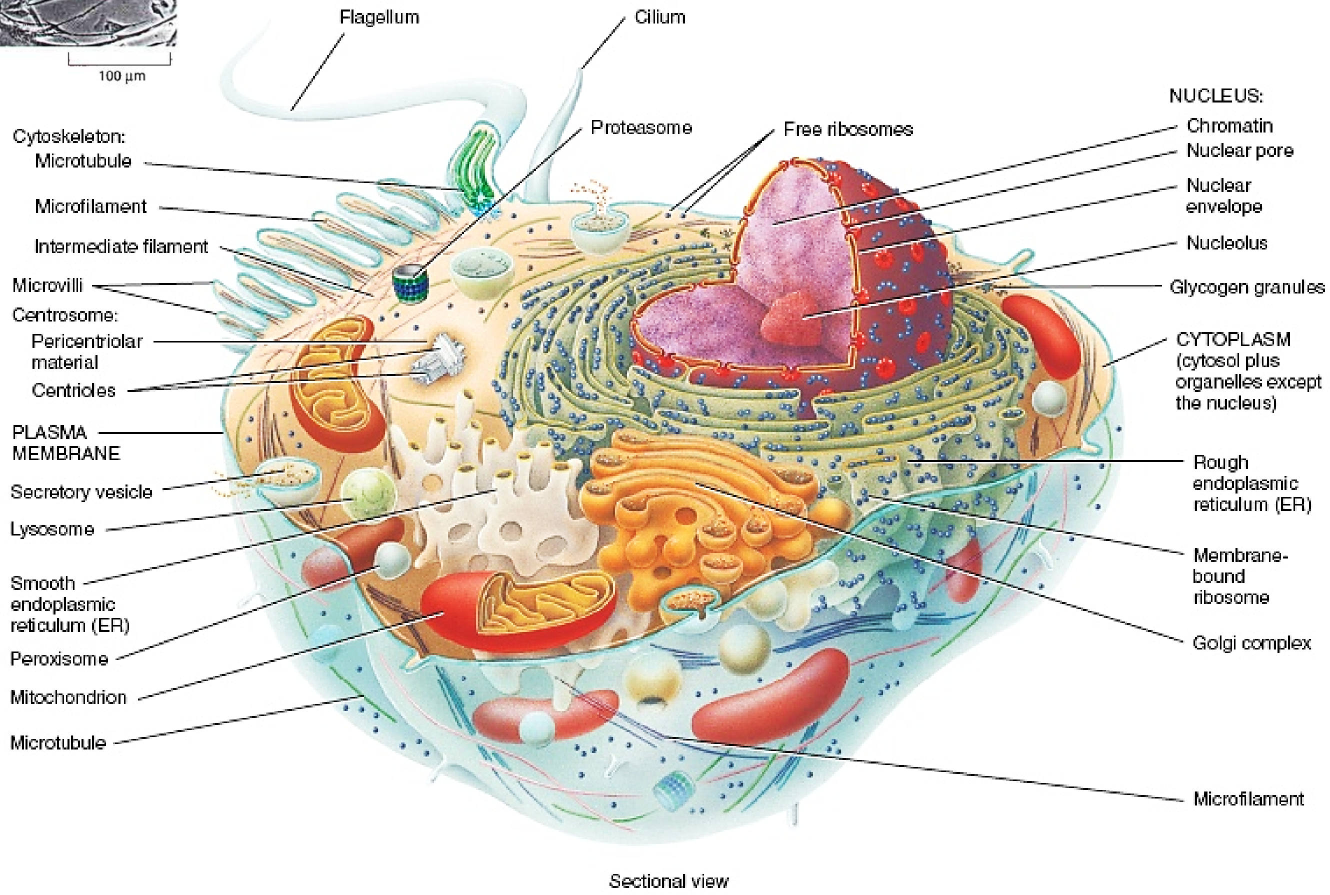
Internal organization of the cell



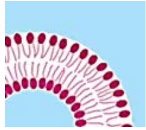
Universal Features of Living Cells







Cell Organelles



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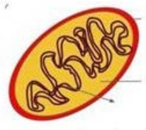
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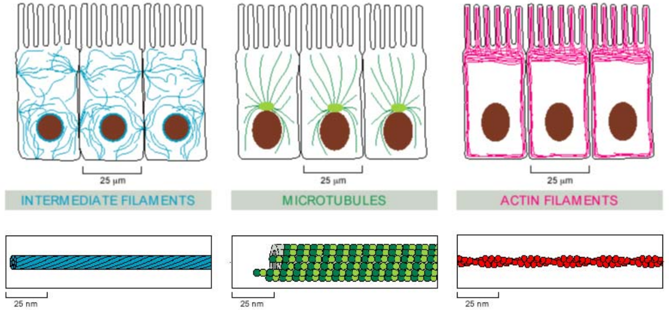

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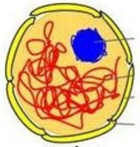
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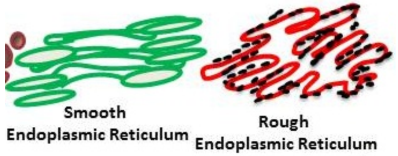

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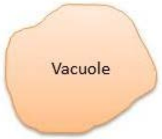

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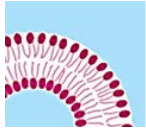
Cell Organelles

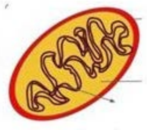


Cell Membrane
Composed of lipid bilayer
Compartmentalize (special, functional separation)

Cytosol Intracellular field composed of cytosolic fluid where the biochemical reactions are occurring

Centriole

Centriole A cylindrical cell structure composed mainly of a protein called tubulin
Centrioles are involved in the organization of the mitotic spindle and in the completion of cytokinesis. The centrioles can self replicate during cell division.

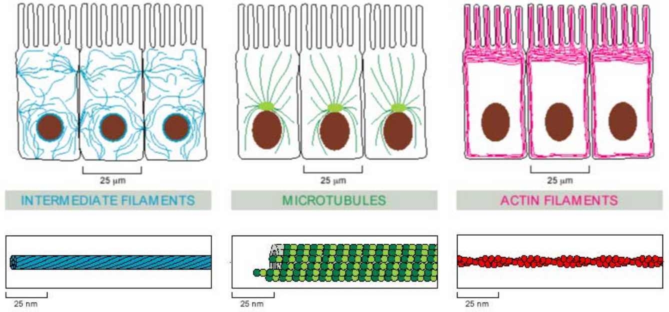


Mitochondria

Mitochondria described as "the powerhouse of the cell" because they generate most of the cell's supply of adenosine triphosphate (ATP), used as a source of chemical energy.

Golgi Apparatus

Golgi Apparatus Major site of carbohydrate synthesis as well as a sorting and dispatching station for products of ER – Proteins and Lipids

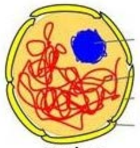


Cytoskeleton Systme of protein filaments in the cytoplasm of a eukaryotic cell that gives the cell shape and the capacity for directed movement. Its most abundant components are actin filaments, microtubules, and intermediate filaments

i. **Microtubules** Long hollow cylindrical structure composed of the protein tubulin
ii. **Microfilament/Actin Filaments** Helical protein filament formed by polymerization of globular actin molecules. A major constituent of the cytoskeleton of all eukaryotic cells and part of the contractile apparatus of skeletal muscle.
iii. **Intermediate Filaments** Fibrous protein filament that forms rope-like networks in animal cells. One of the three most prominent types of cytoskeletal filaments.

Lysosomes

Lysosomes Membrane-bound organelle in eukaryotic cells containing digestive enzymes, which are typically most active at the acid pH found in the lumen of lysosomes.



Nucleus

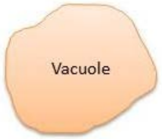
Nucleus Prominent membrane-bound organelle in eukaryotic cells, containing DNA organized into chromosomes

Ribosomes

Ribosomes Particle composed of rRNA and ribosomal proteins that catalyzes the synthesis of protein using information provided by mRNA

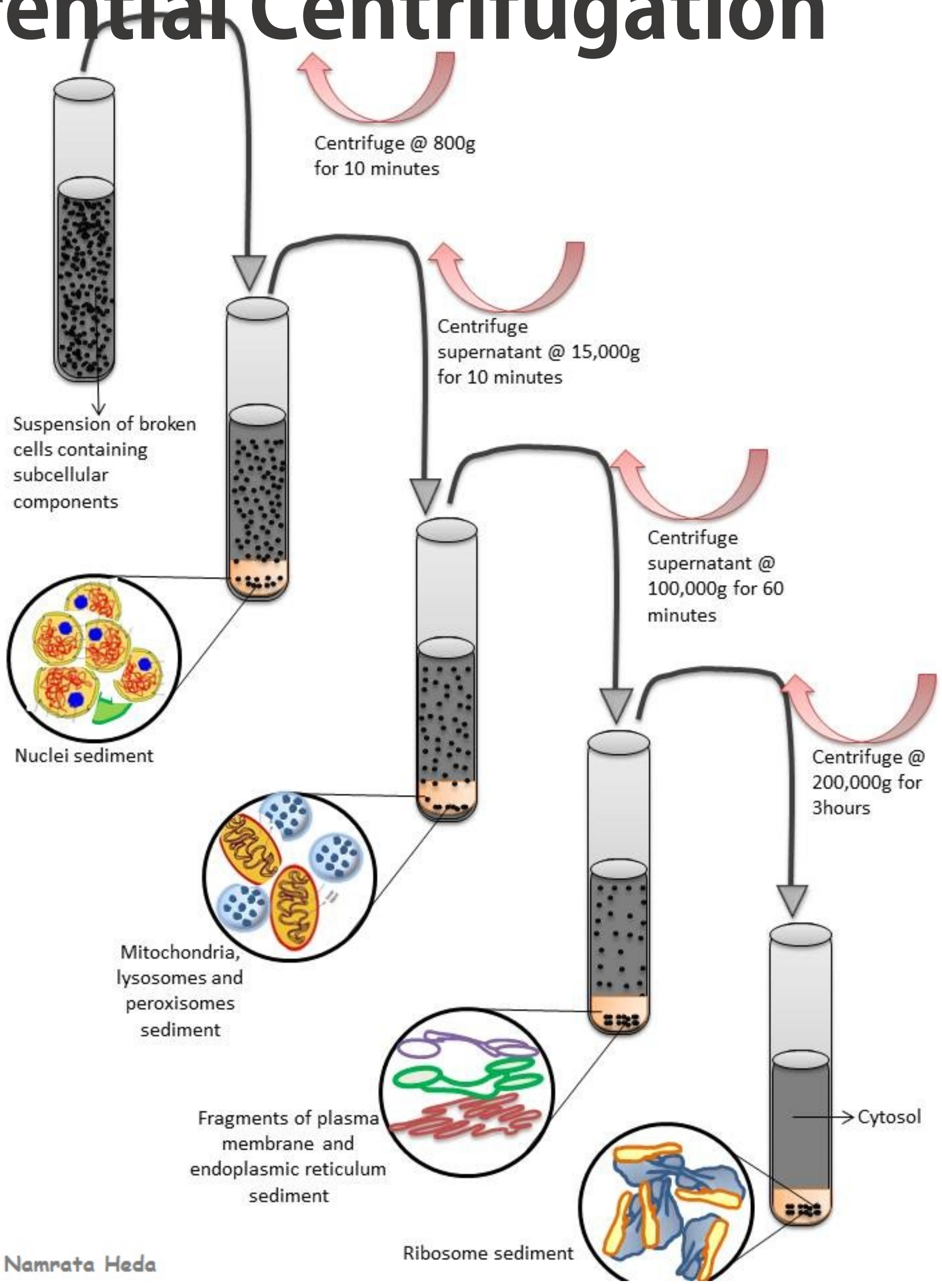
Smooth Endoplasmic Reticulum
Rough Endoplasmic Reticulum

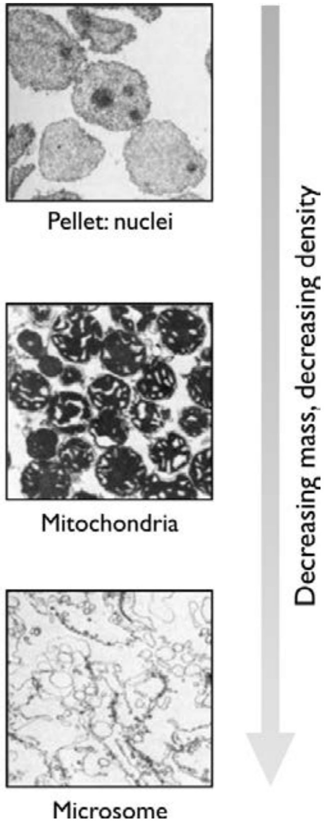
Endoplasmic Reticulum Labyrinthine membrane-bound compartment in the cytoplasm of eukaryotic cells, where lipids and proteins are synthesized.

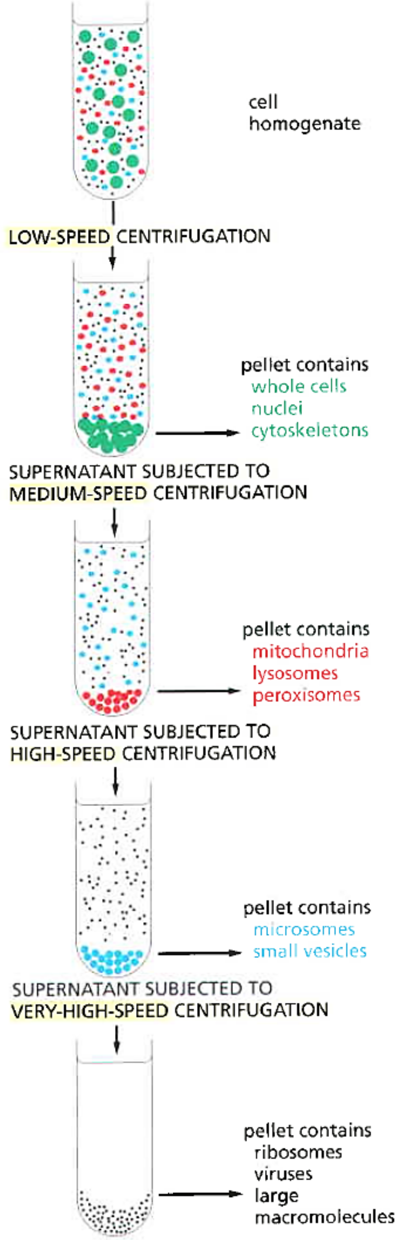


Vacuole Very large fluid-filled vesicle found in most plant and fungal cells, typically occupying more than a third of the cells volume

Differential Centrifugation

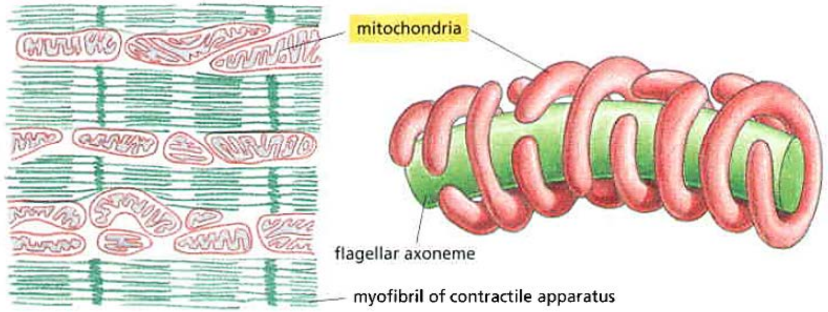




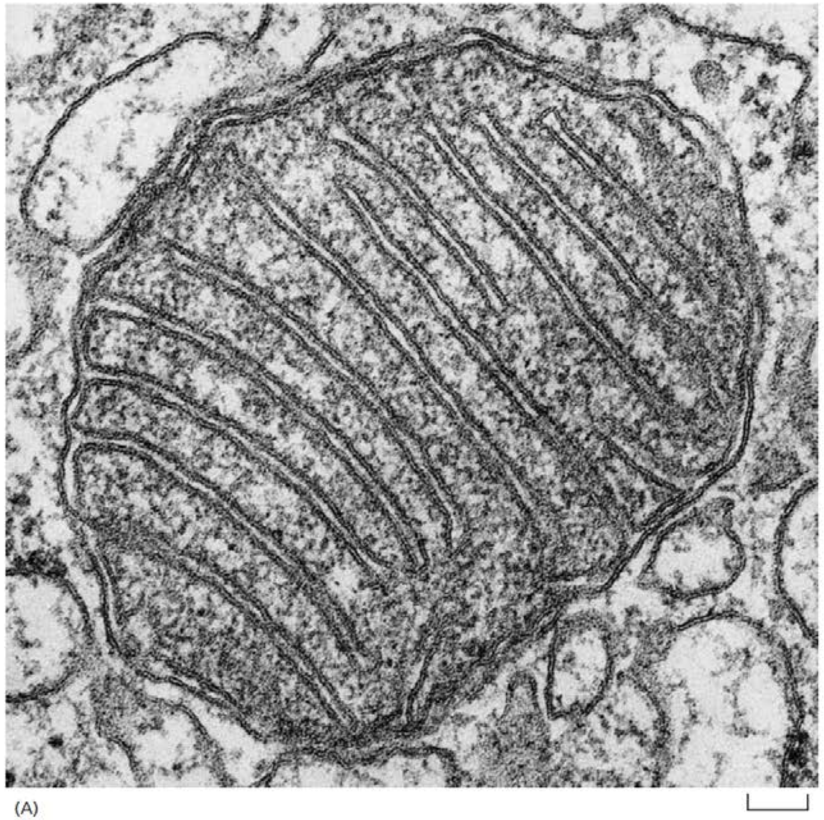


Functional Aspect of Cell Organelles

Mitochondria



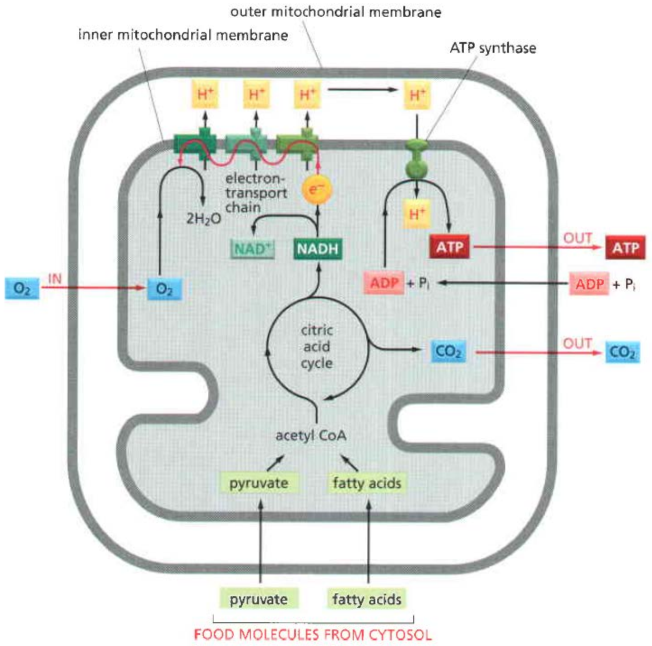
(A) CARDIAC MUSCLE (B) SPERM TAIL

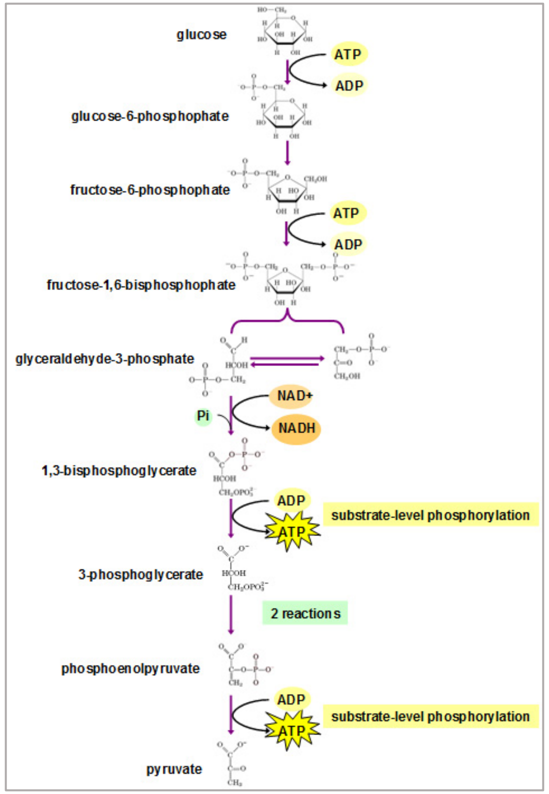


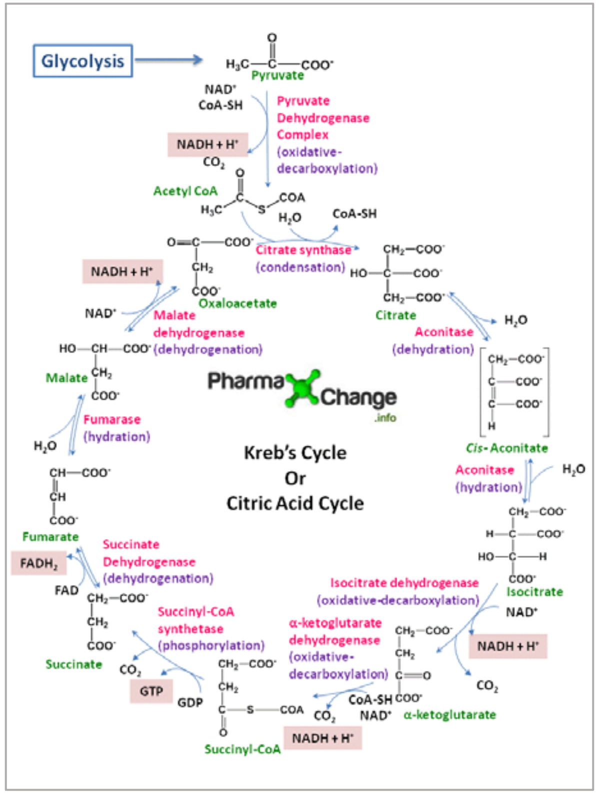
(A)

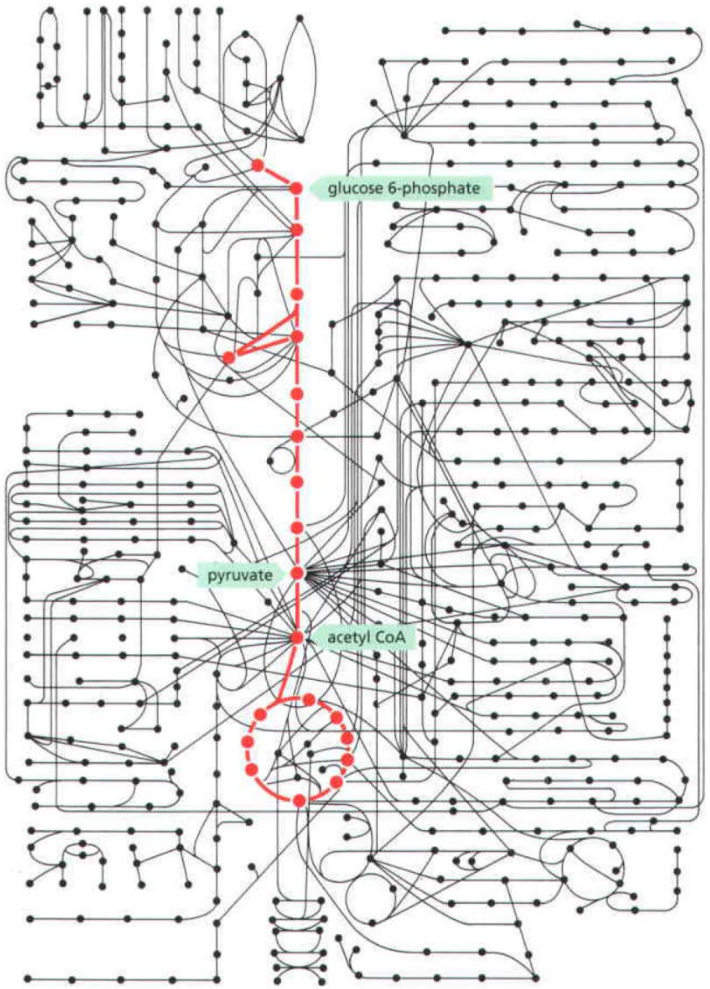

(B)


(C)




glucose
ATP
ADP
glucose-6-phosphate
fructose-6-phosphate
ATP
ADP
fructose-1,6-bisphosphate
glyceraldehyde-3-phosphate
NAD+
Pi
NADH
1,3-bisphosphoglycerate
ADP
ATP
substrate-level phosphorylation
3-phosphoglycerate
2 reactions
phosphoenolpyruvate
ADP
ATP
substrate-level phosphorylation
pyruvate

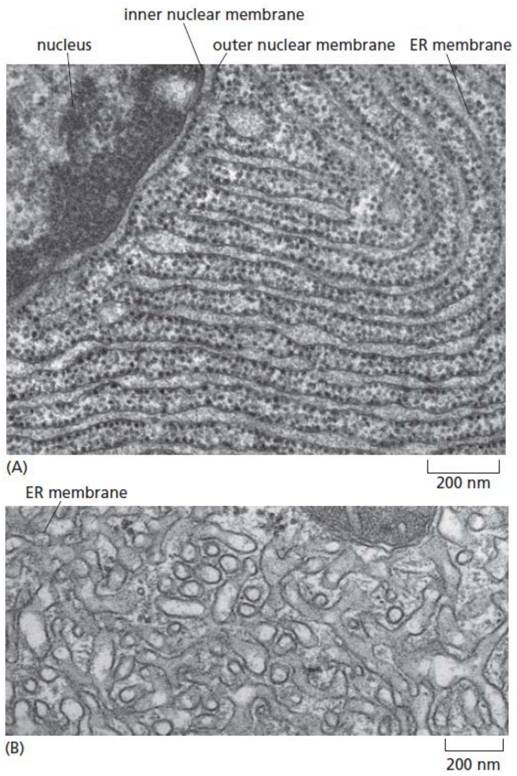

Glycolysis
Pyruvate
Pyruvate Dehydrogenase Complex (oxidative-decarboxylation)
NADH + H+
Acetyl CoA
Citrate synthase (condensation)
Oxaloacetate
Citrate
Malate dehydrogenase (dehydrogenation)
Aconitase (dehydration)
Malate
Cis-Aconitate
PharmaChange .info
Kreb's Cycle
Or
Citric Acid Cycle
Fumarase (hydration)
Aconitase (hydration)
Fumarate
Isocitrate
FADH2
Succinate Dehydrogenase (dehydrogenation)
Isocitrate dehydrogenase (oxidative-decarboxylation)
Succinyl-CoA synthetase (phosphorylation)
α-ketoglutarate dehydrogenase (oxidative-decarboxylation)
Succinate
GTP
GDP
Succinyl-CoA
α-ketoglutarate

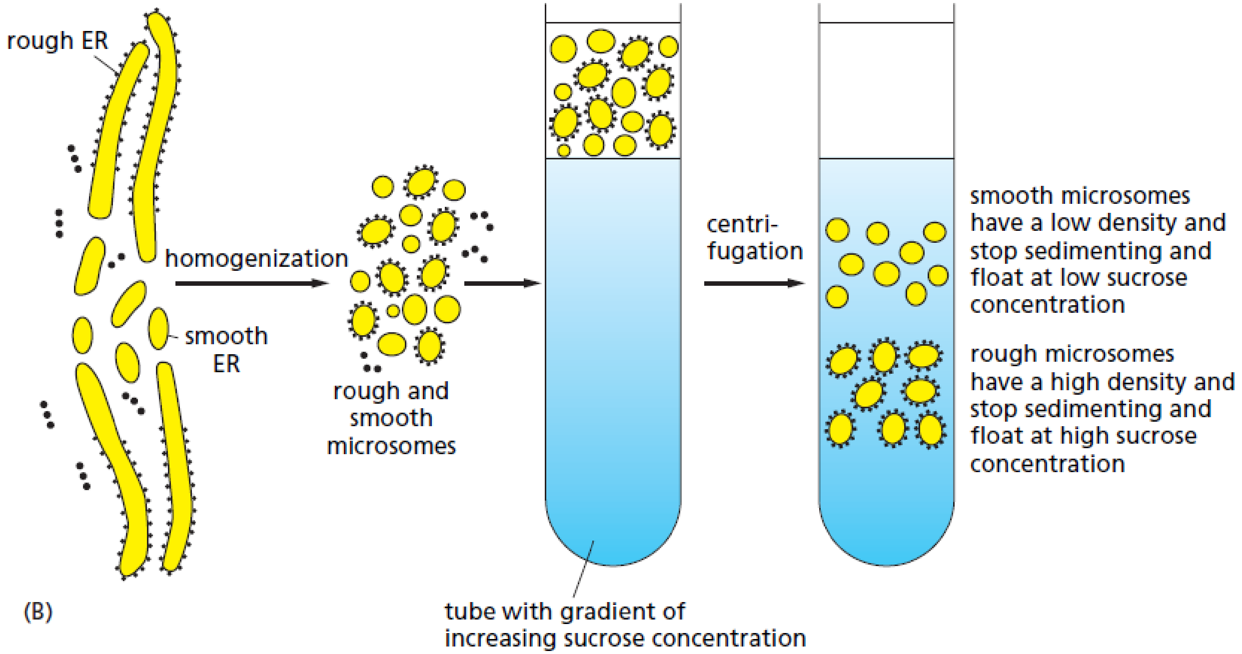

glucose 6-phosphate
pyruvate
acetyl CoA

Endoplasmic Reticulum – RER & SER

Smooth ER Regions of ER that lack bound ribosomes

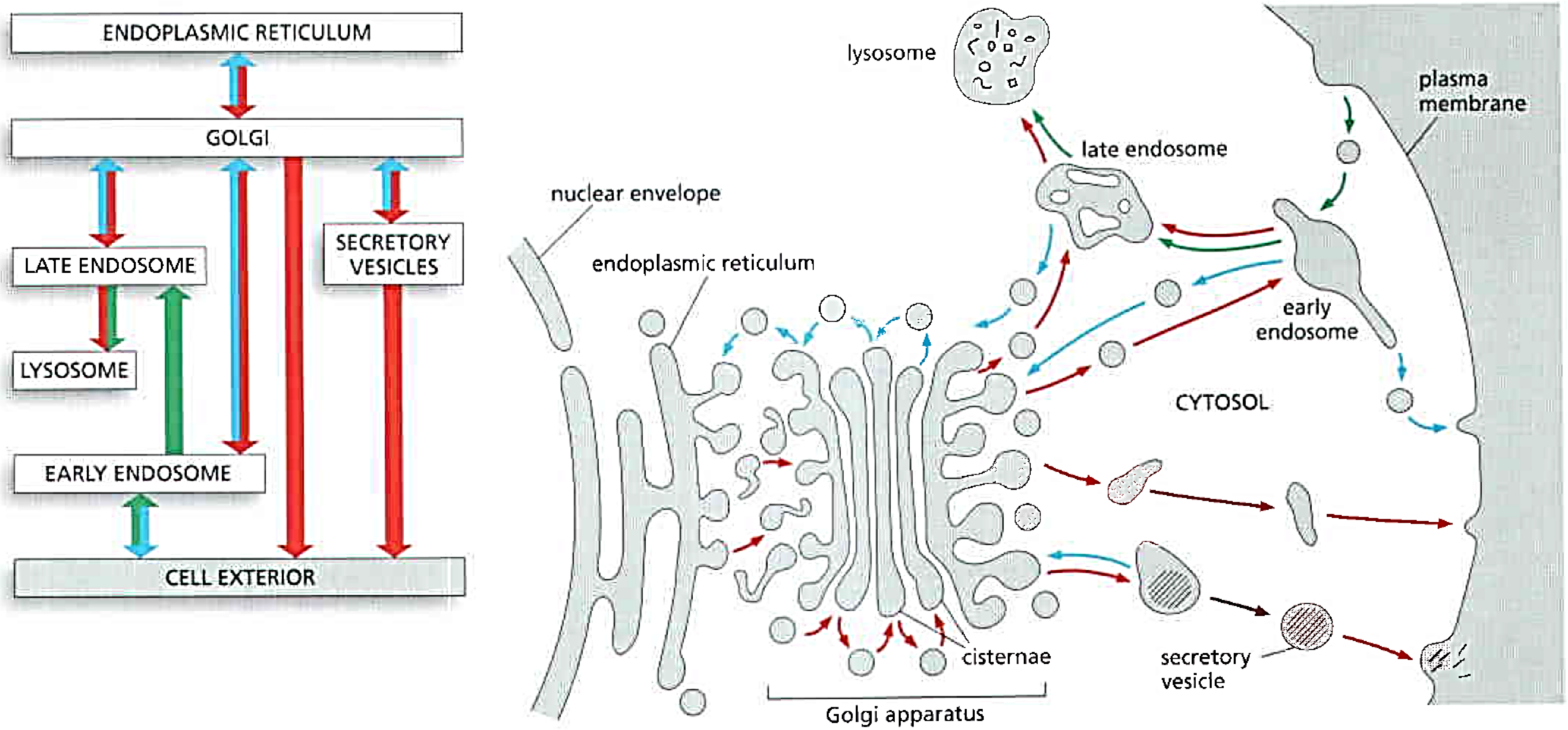
Hepatocytes has abundant *smooth ER*, which is the principal site of production of lipoprotein particles that carry lipids via the blood stream to other parts of the body.
The enzymes that synthesize the lipid components of the particles are located in the membrane of the smooth ER.



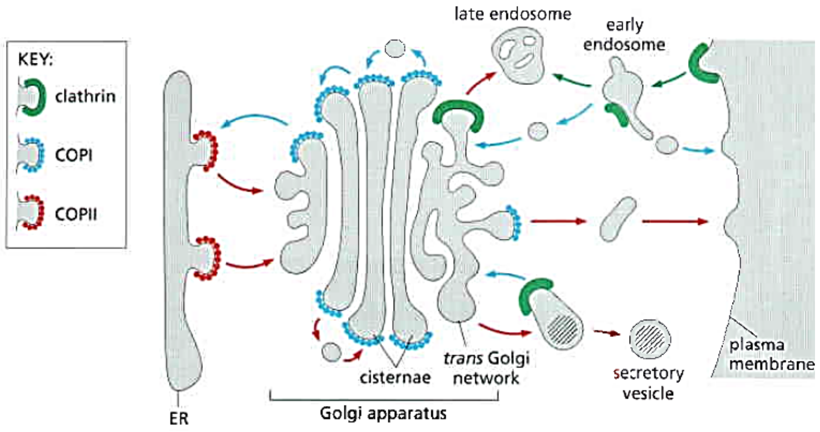


ER to Golgi Apparatus – Vesicular Traffic

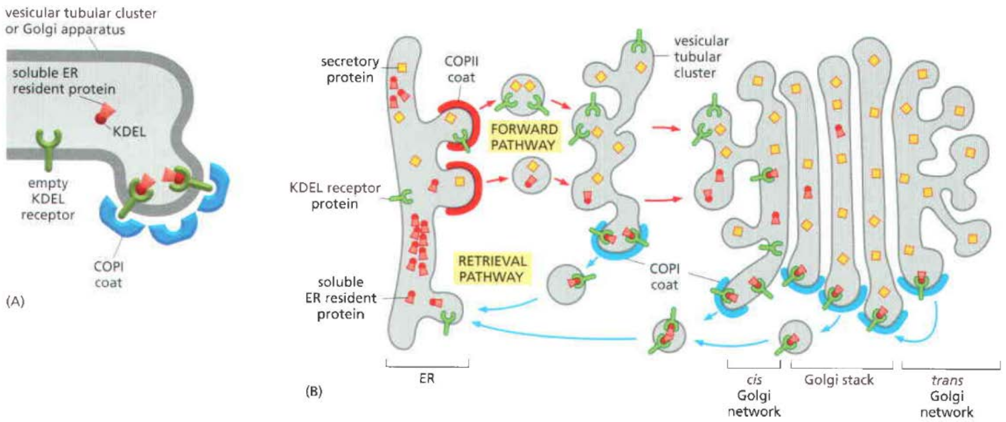
A road map of the biosynthetic-secretory and endocytic pathways



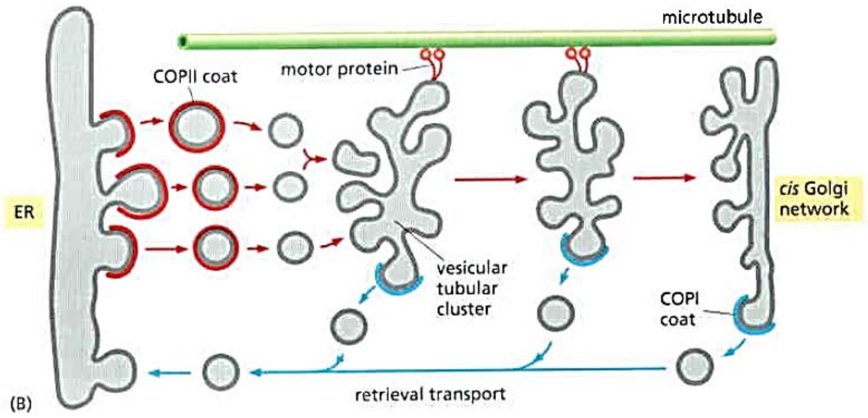
Use of different coats in vesicular traffic



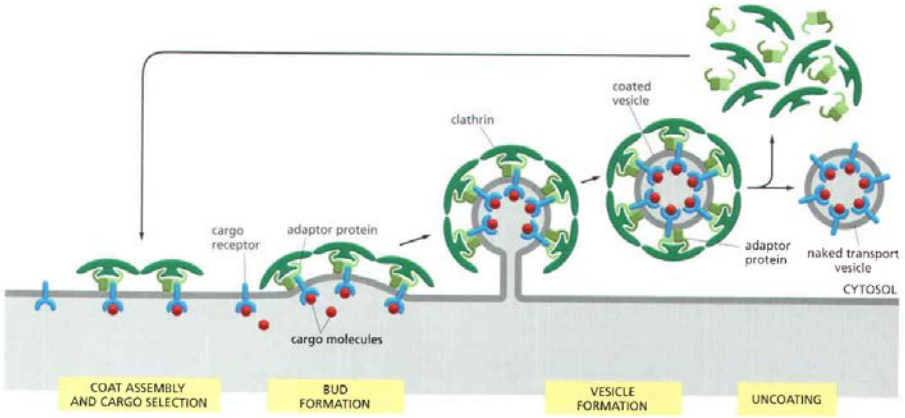
A model for the retrieval of soluble ER resident proteins



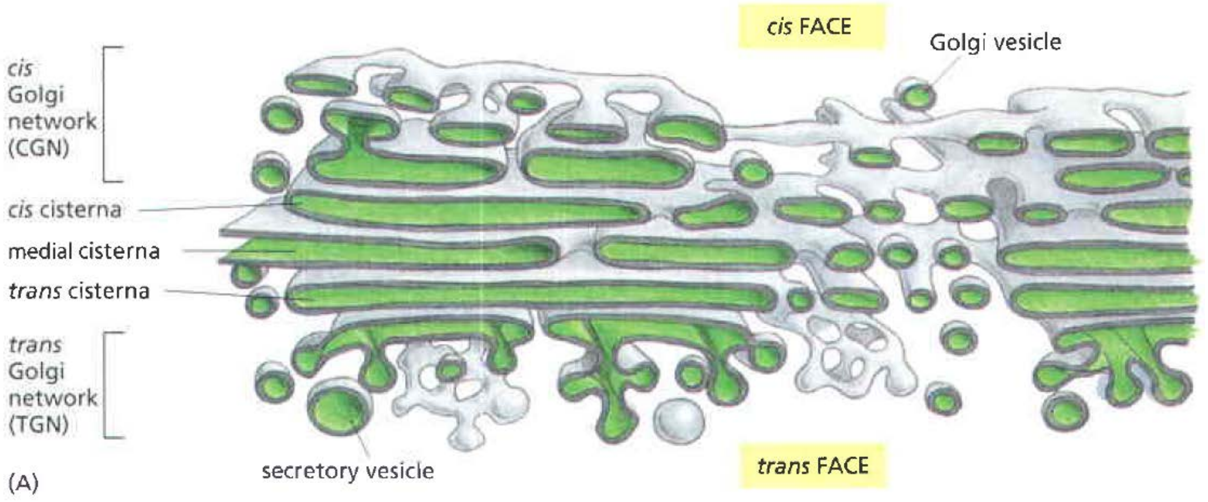
Vesicular tubular clusters



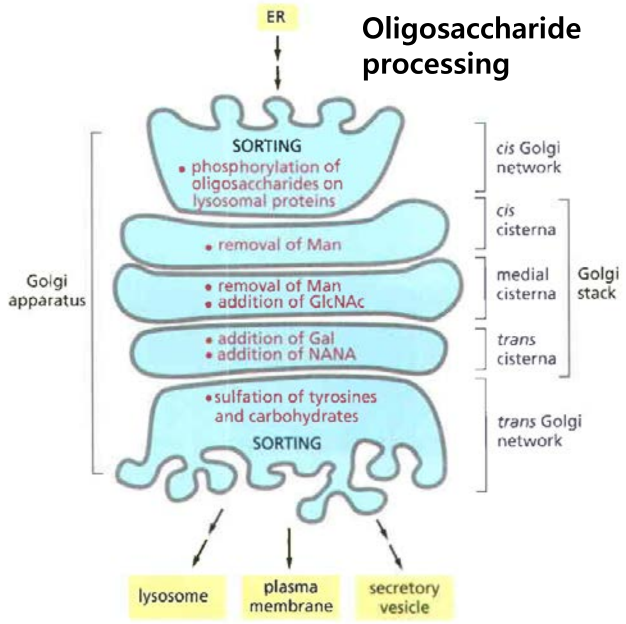
Assembly and disassembly of a clathrin coat



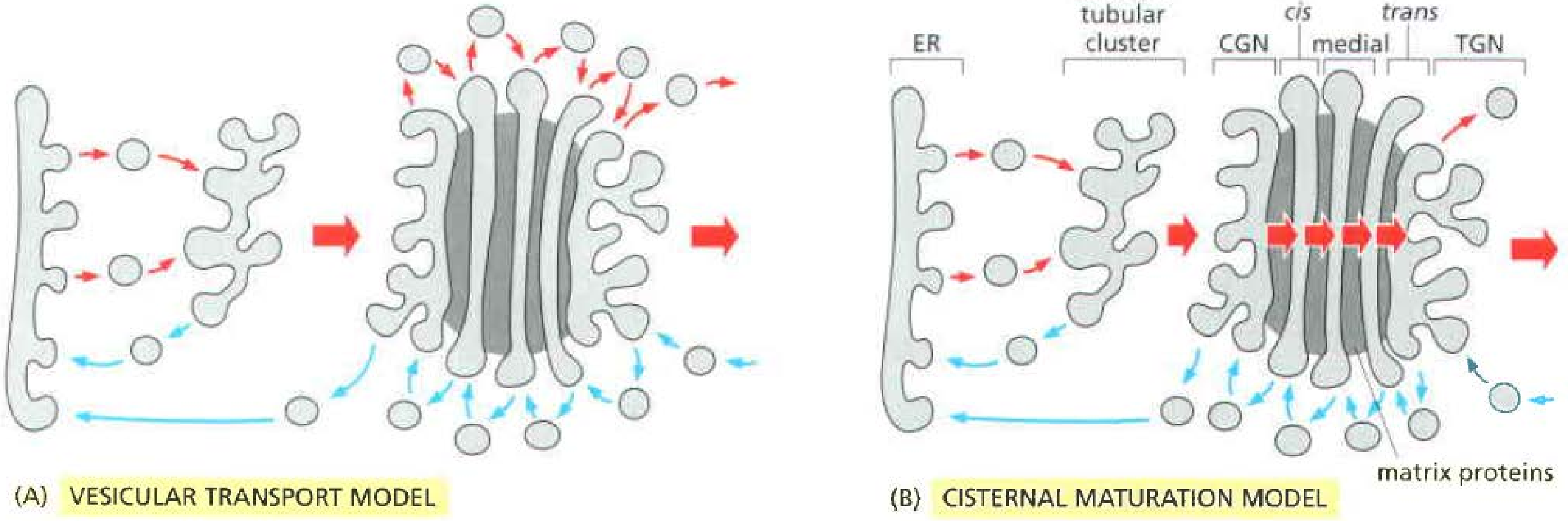
The Golgi Apparatus



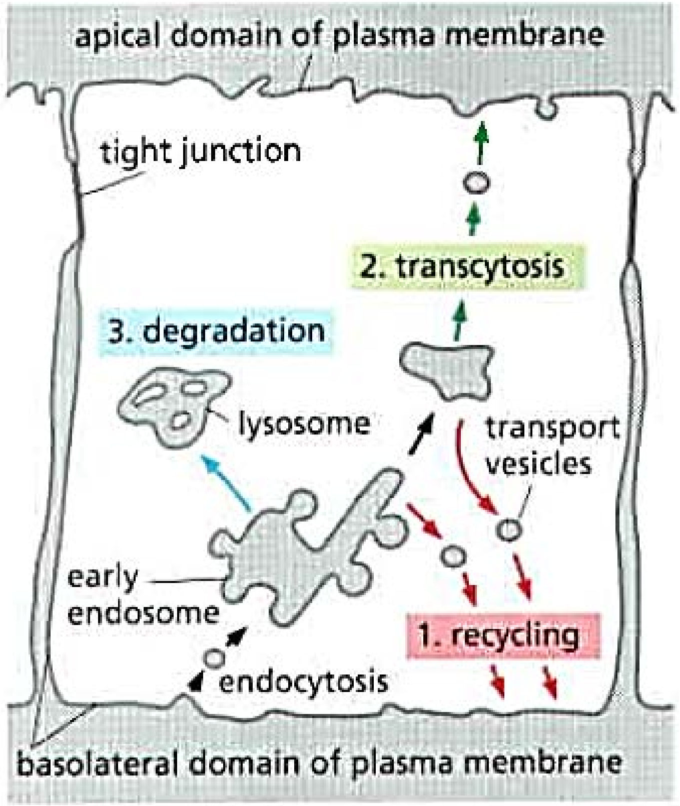
Oligosaccharide processing



Two possible models explaining the organization of the Golgi apparatus and the transport of proteins



The receptor-mediated endocytosis of LDL



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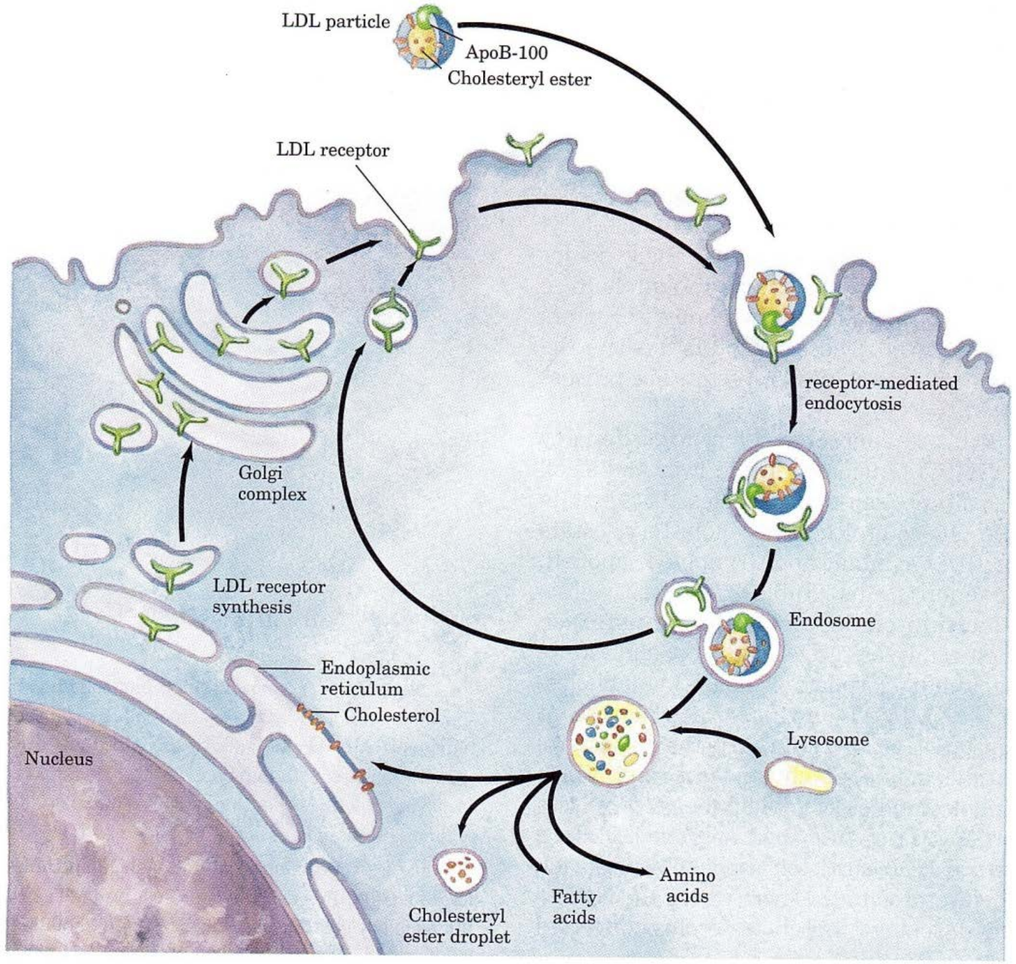
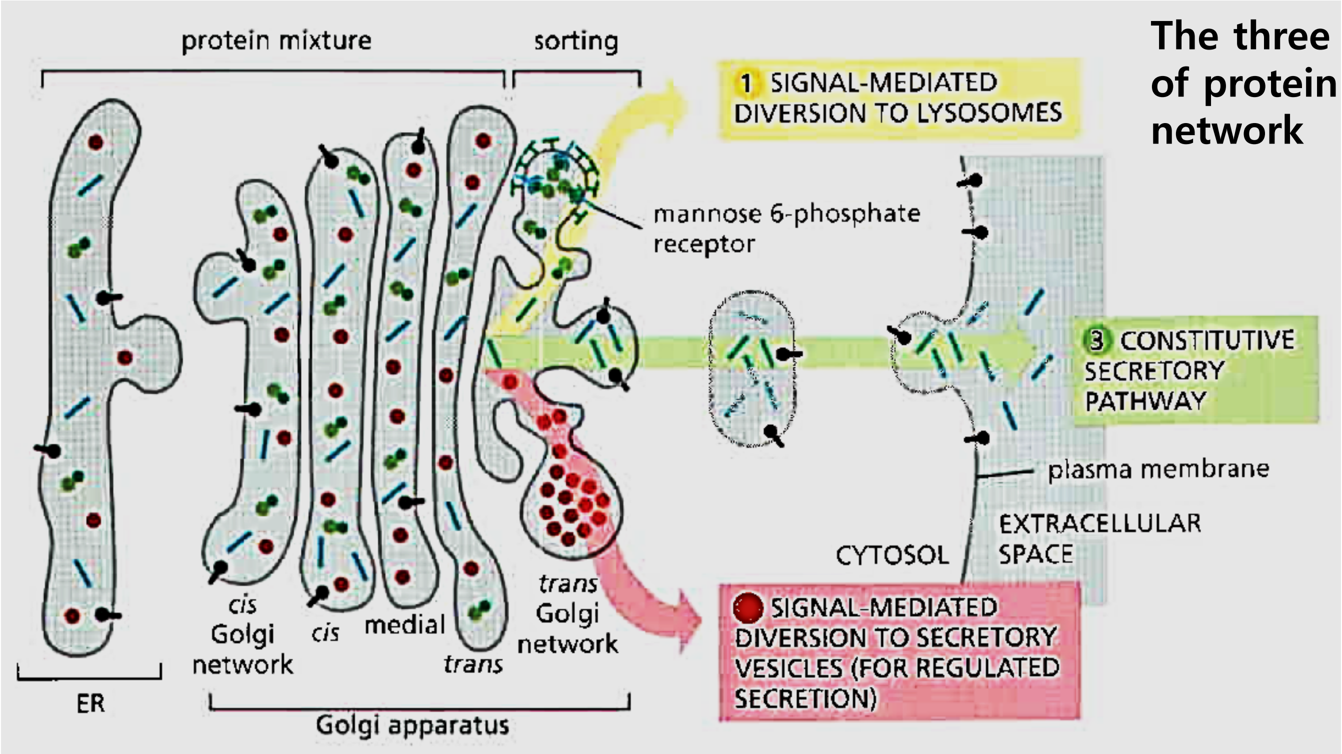
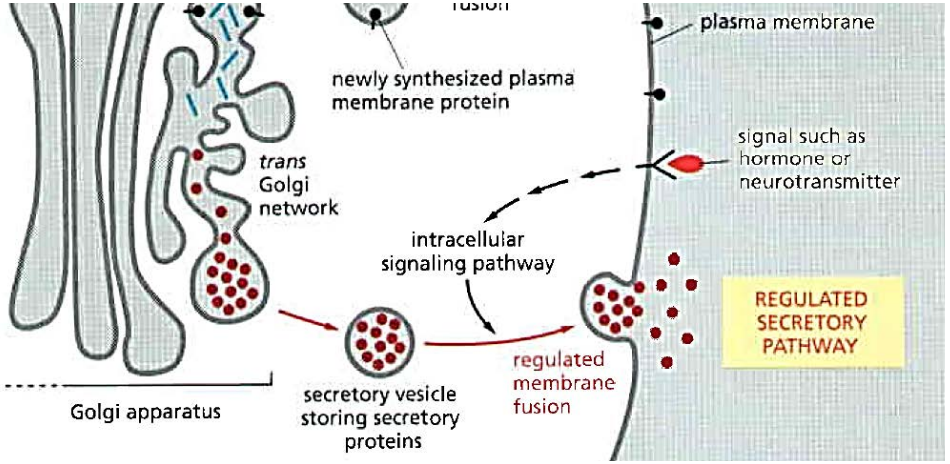


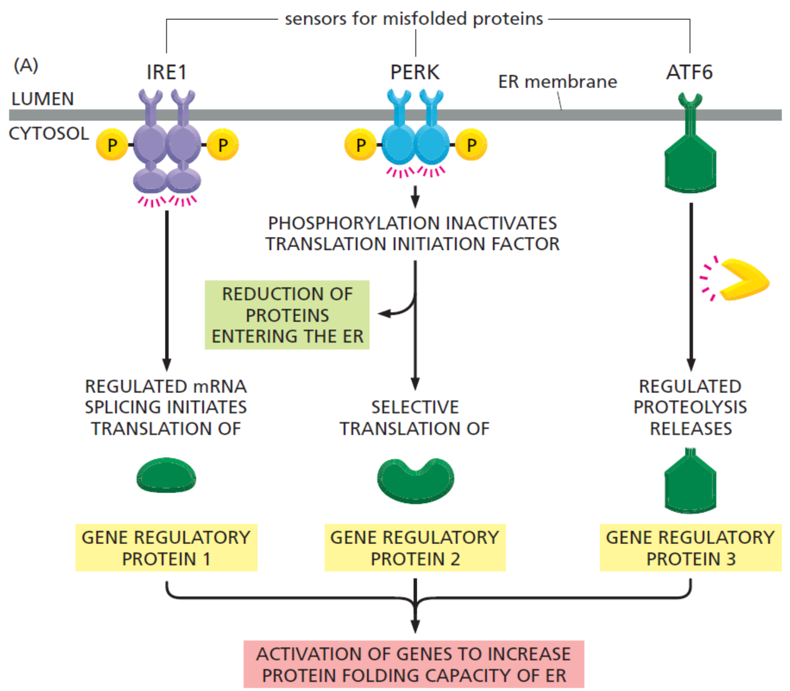


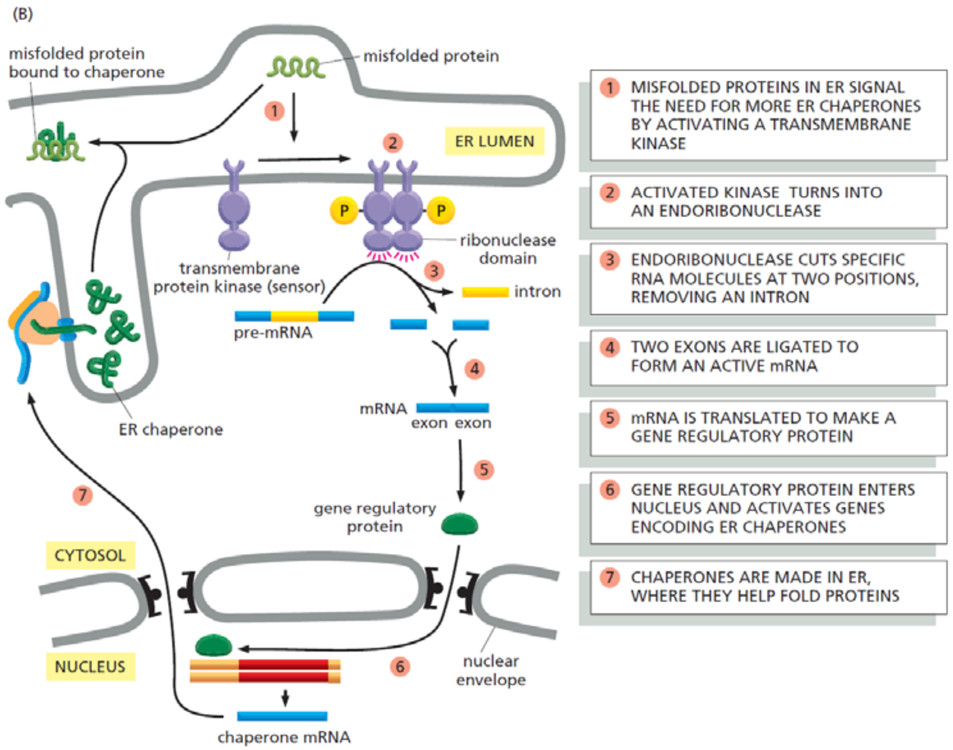
The three best-understood pathways of protein sorting in the *trans* Golgi network

Regulated secretory pathway

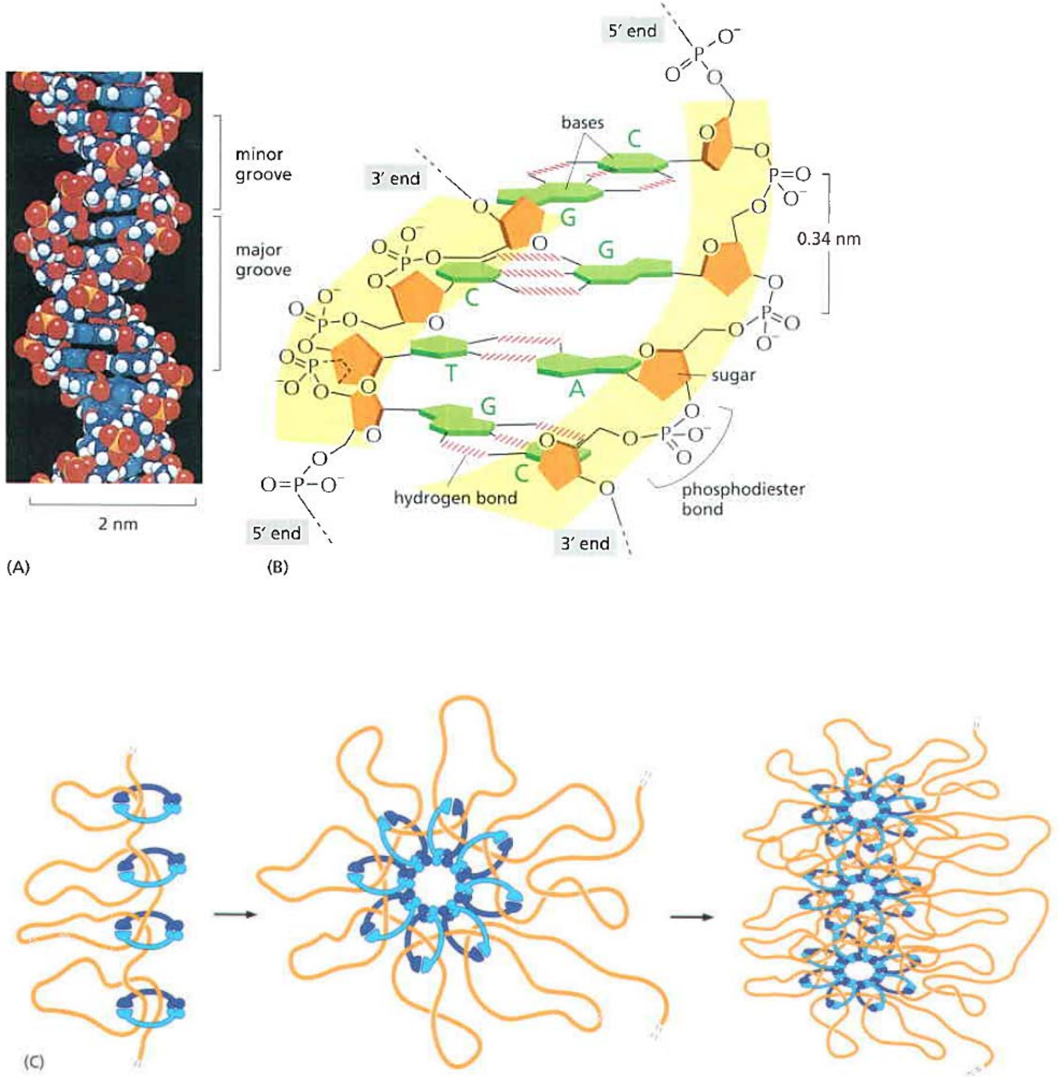


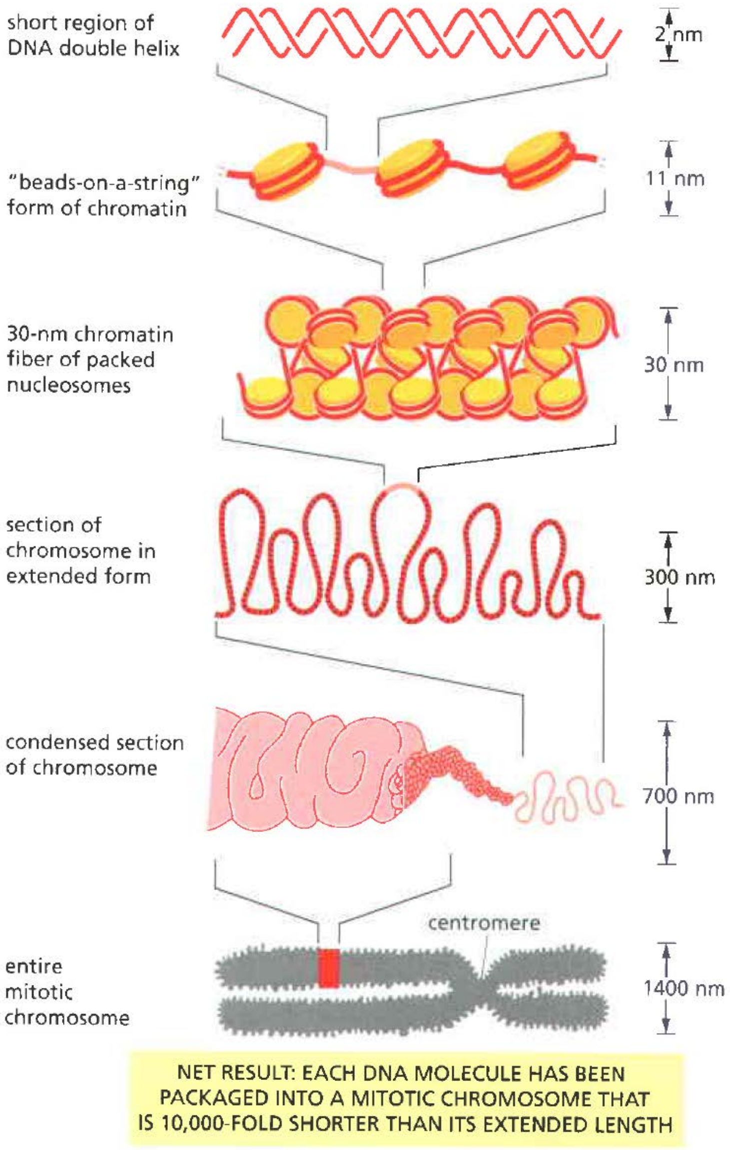
ER stress – a stress caused by misfolded proteins



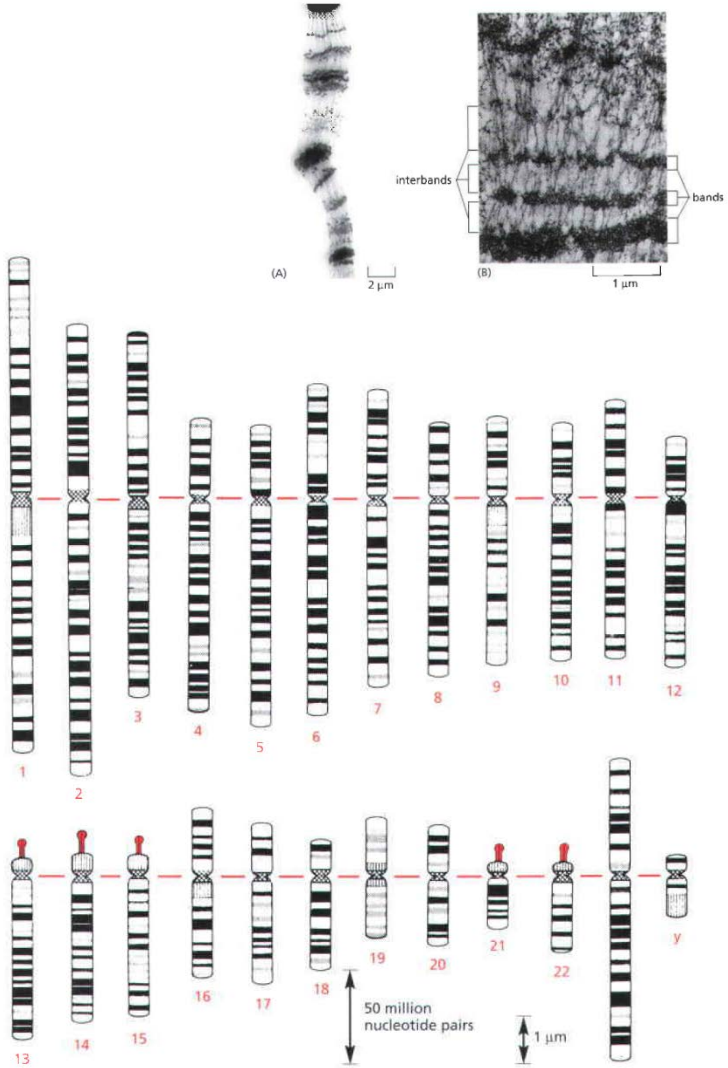


DNA Structure

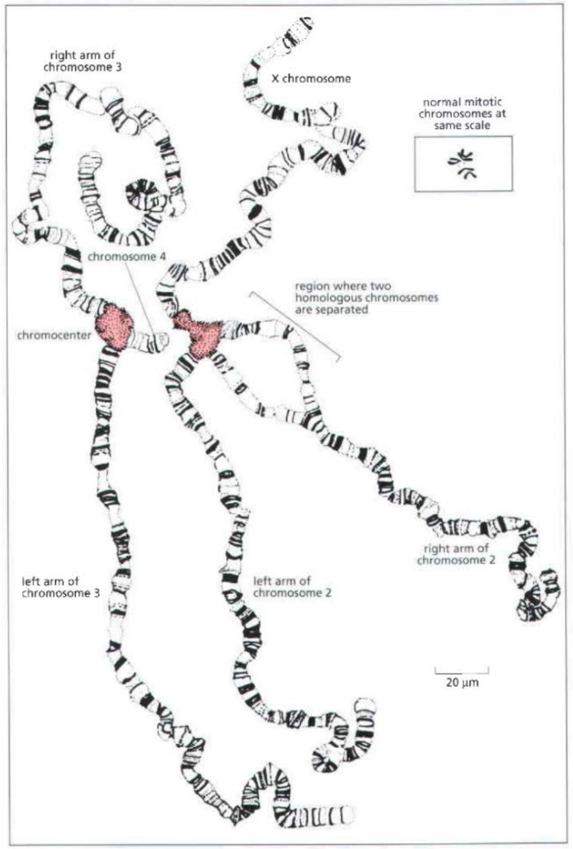


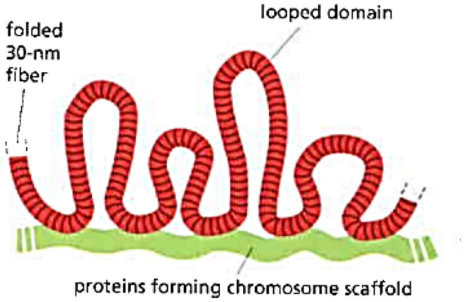


A distinct pattern of bands and inter-bands

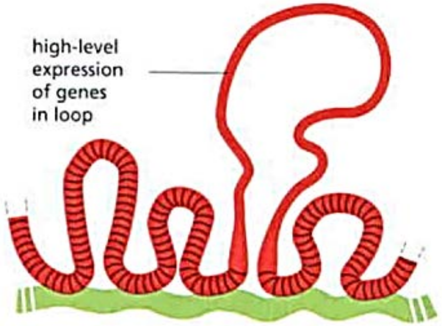


Polytene chromosomes in *Drosophila* salivary gland cell

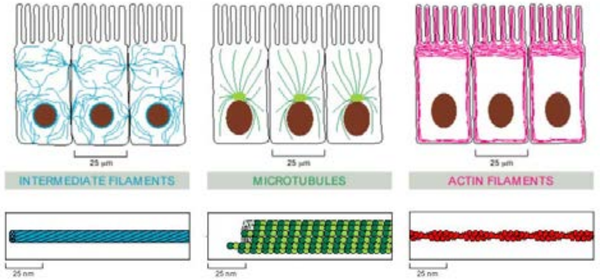




Histone modifying enzymes
Chromatin remodeling complexes
RNA polymerase

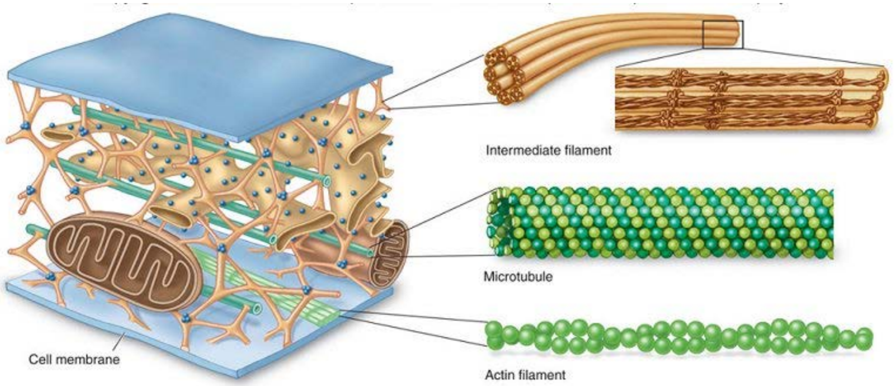


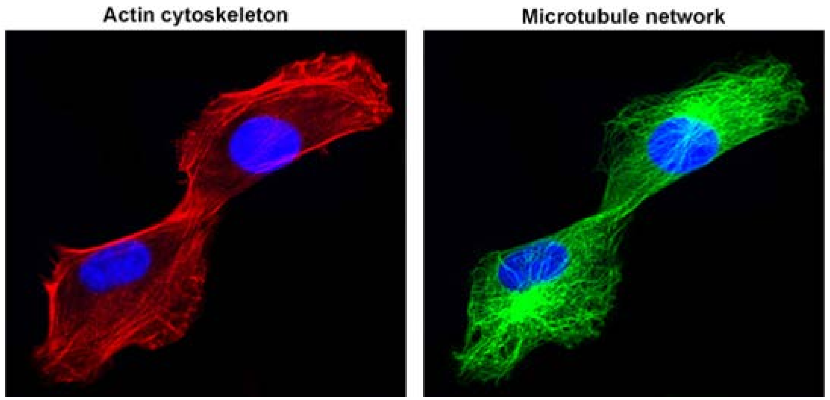
Cytoskeleton

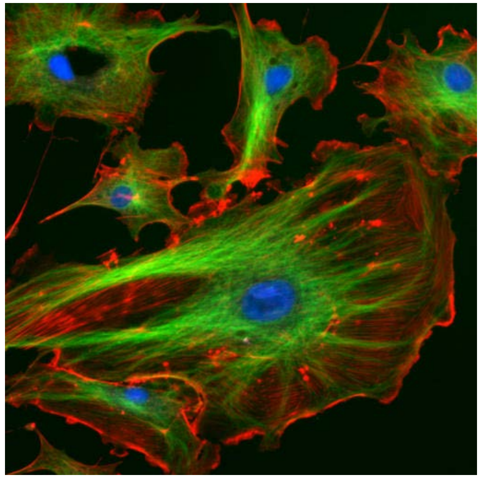


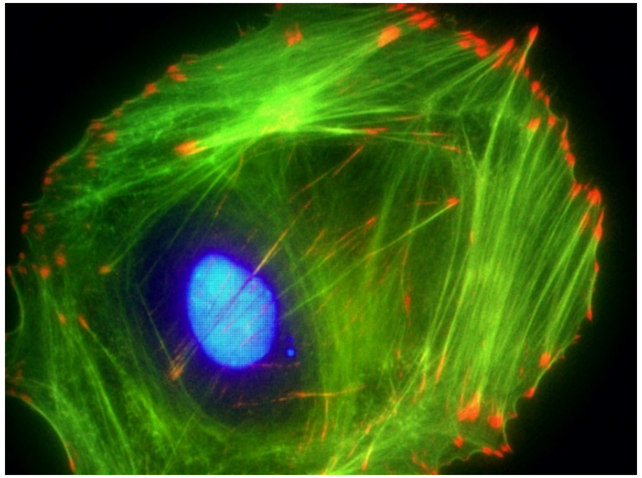
Cytoskeletal Functions

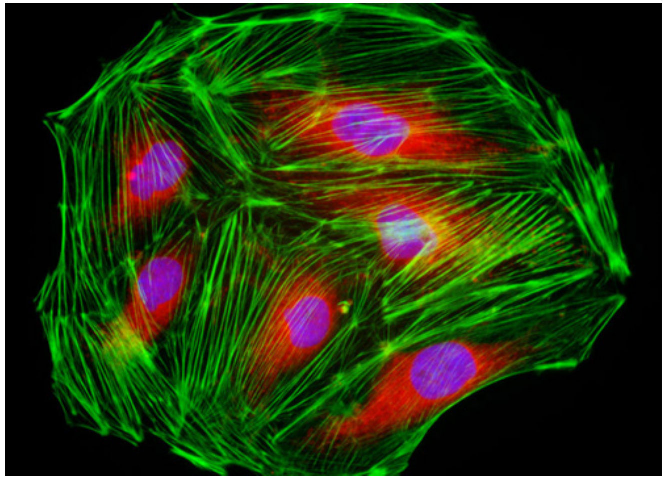
1. Structure and support
2. Intracellular transport
3. Contractility and motility
4. Spatial organization



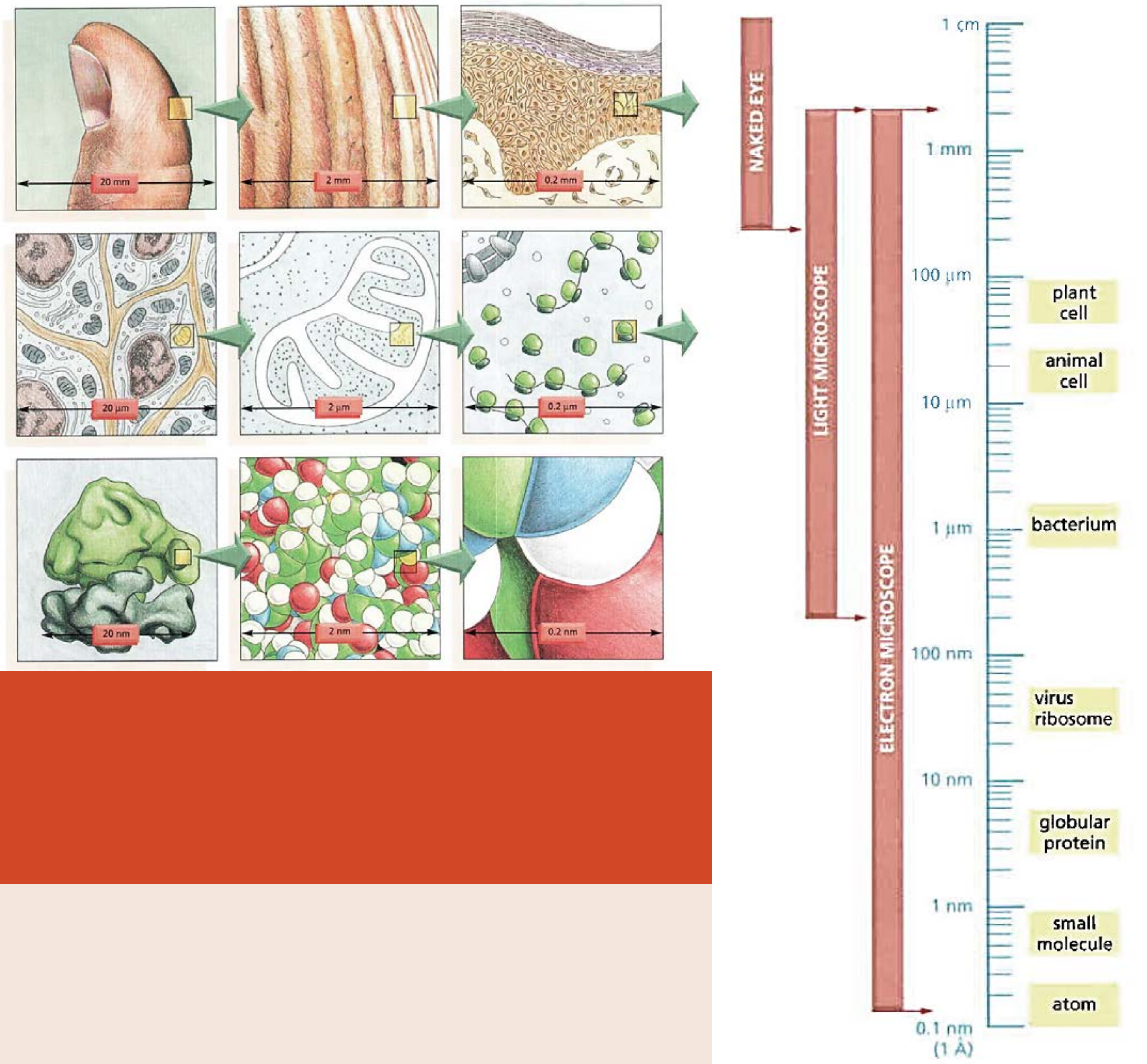






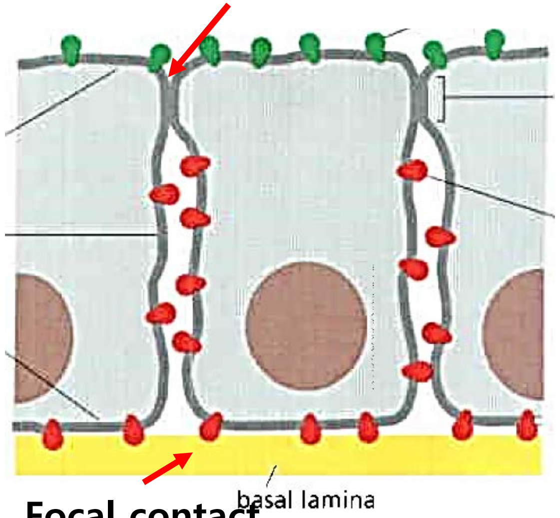


Cells in tissue context

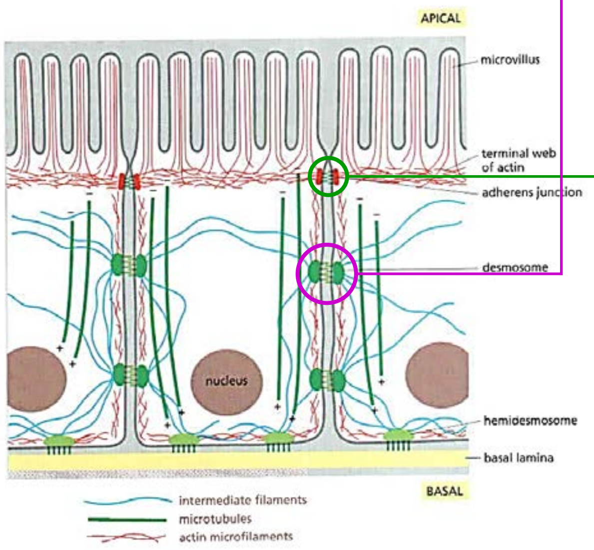


Cell Adhesion

Cell-cell contact

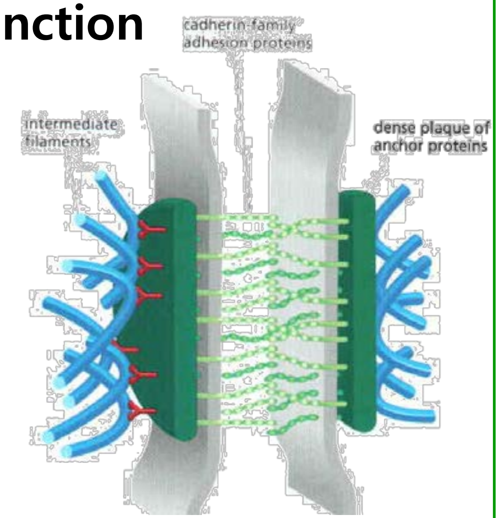


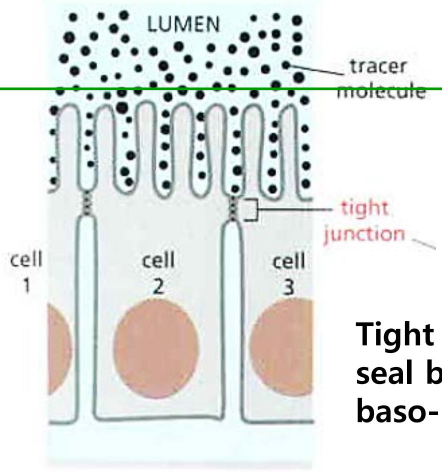
Focal contact



Desmosome

Cell-cell anchoring junction

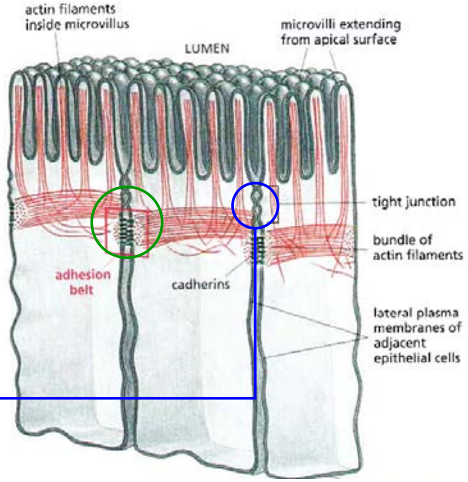




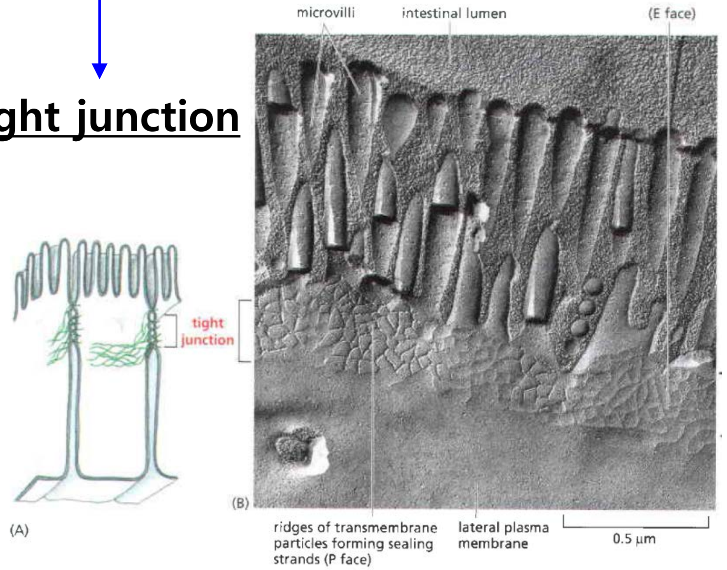
Tight junction constitutes seal between apical and baso-lateral domain

Adherens junction

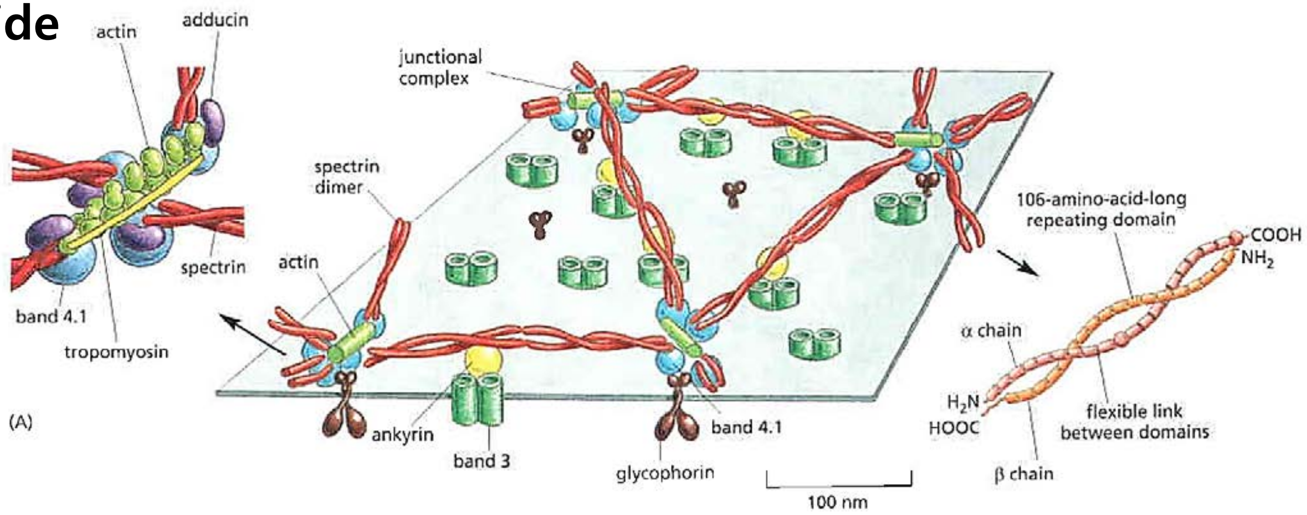
Adherens junction connects actin filament bundle



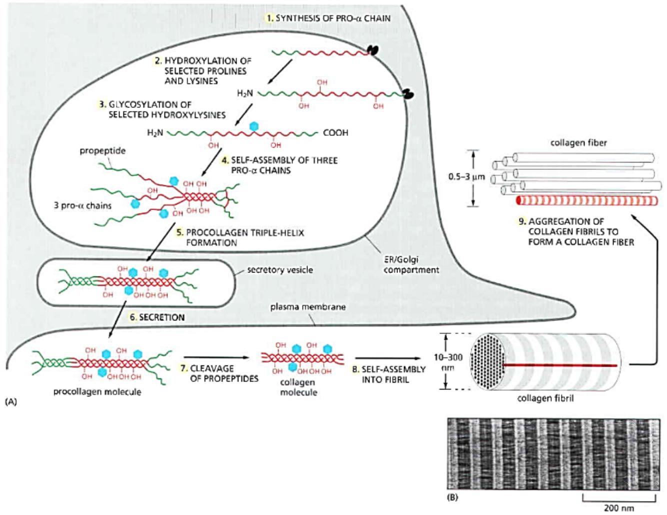
Tight junction

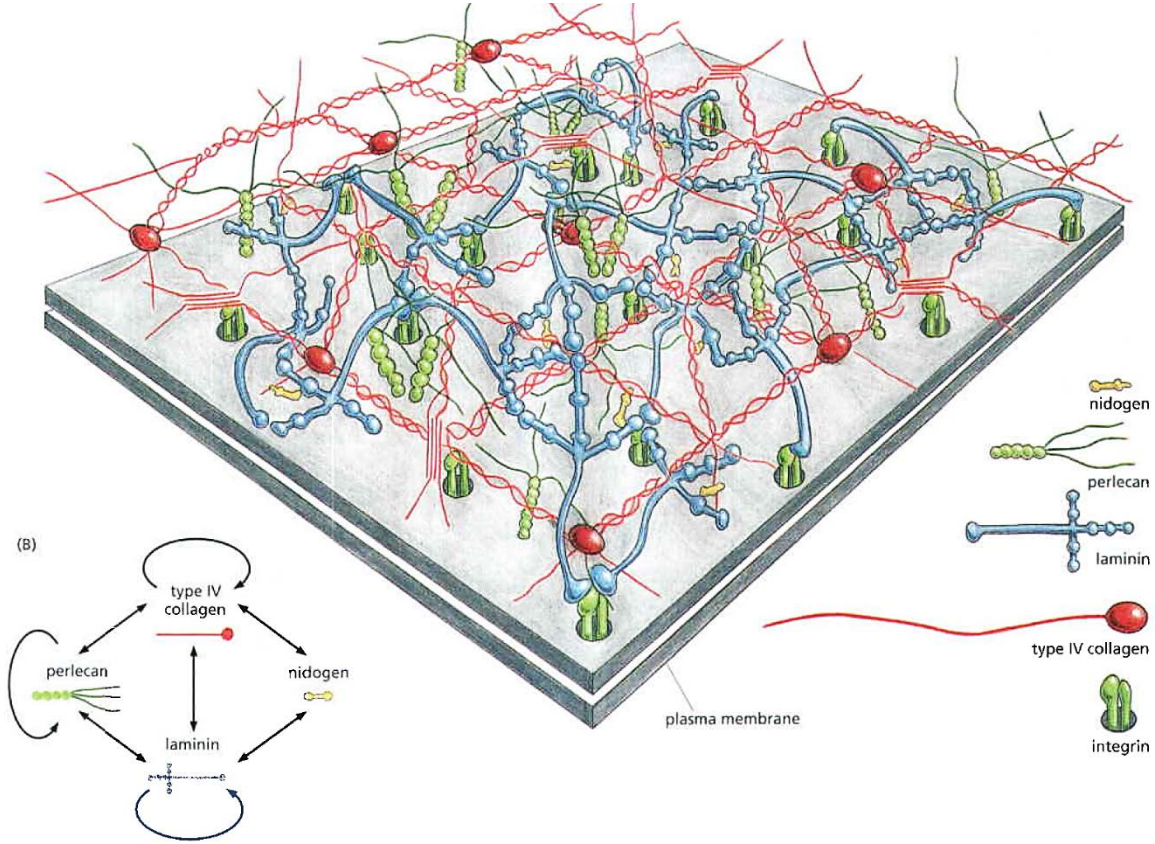


Cytoskeleton on the cytosolic side

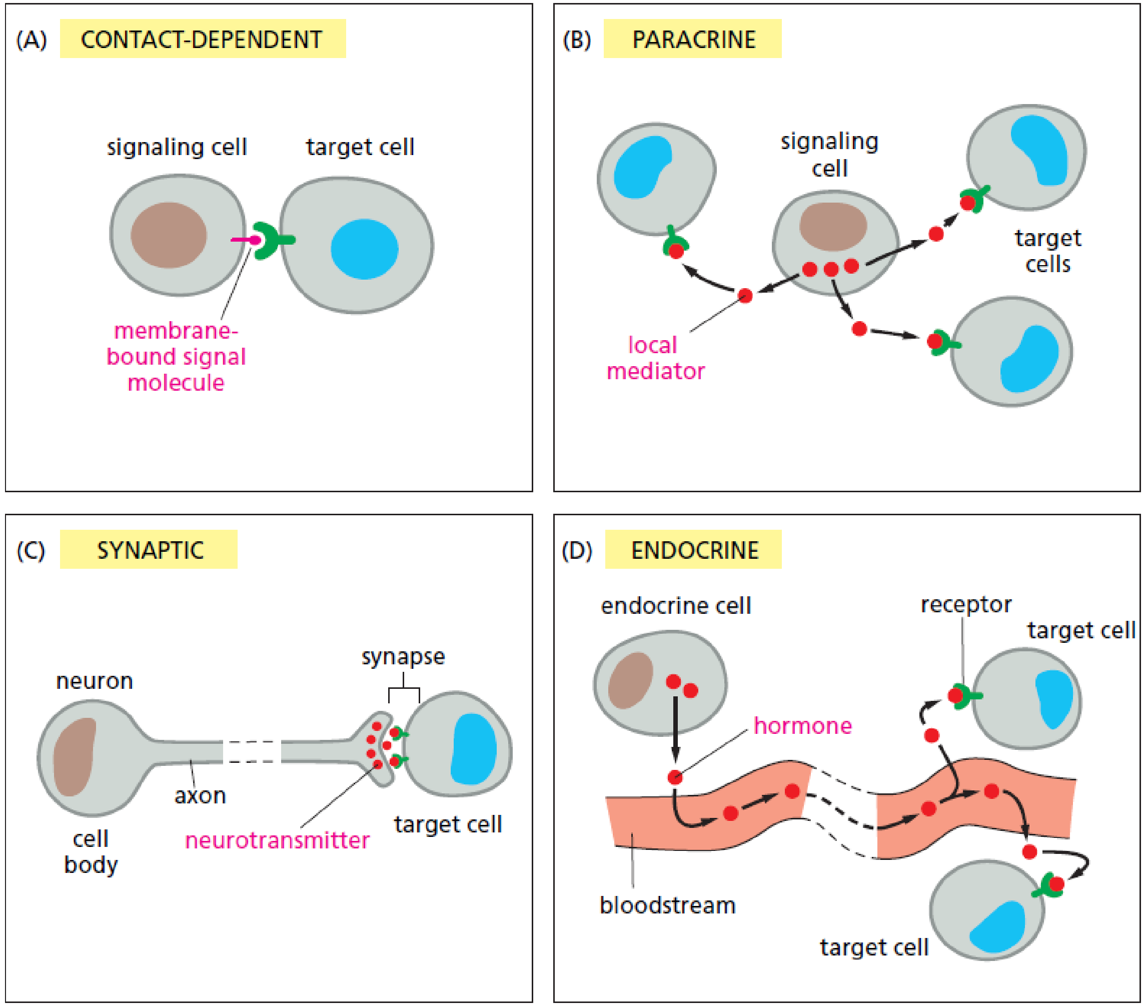


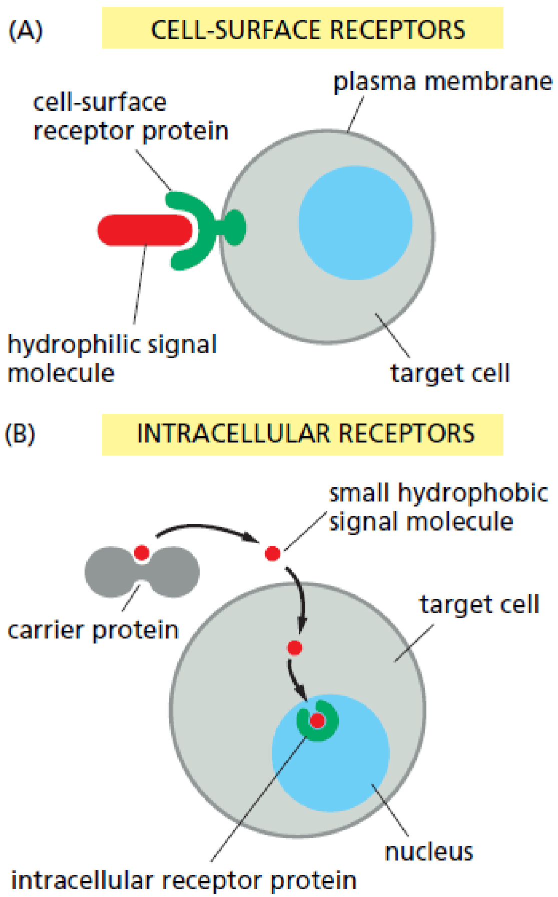
Molecular structure of basal lamina on the extracellular side





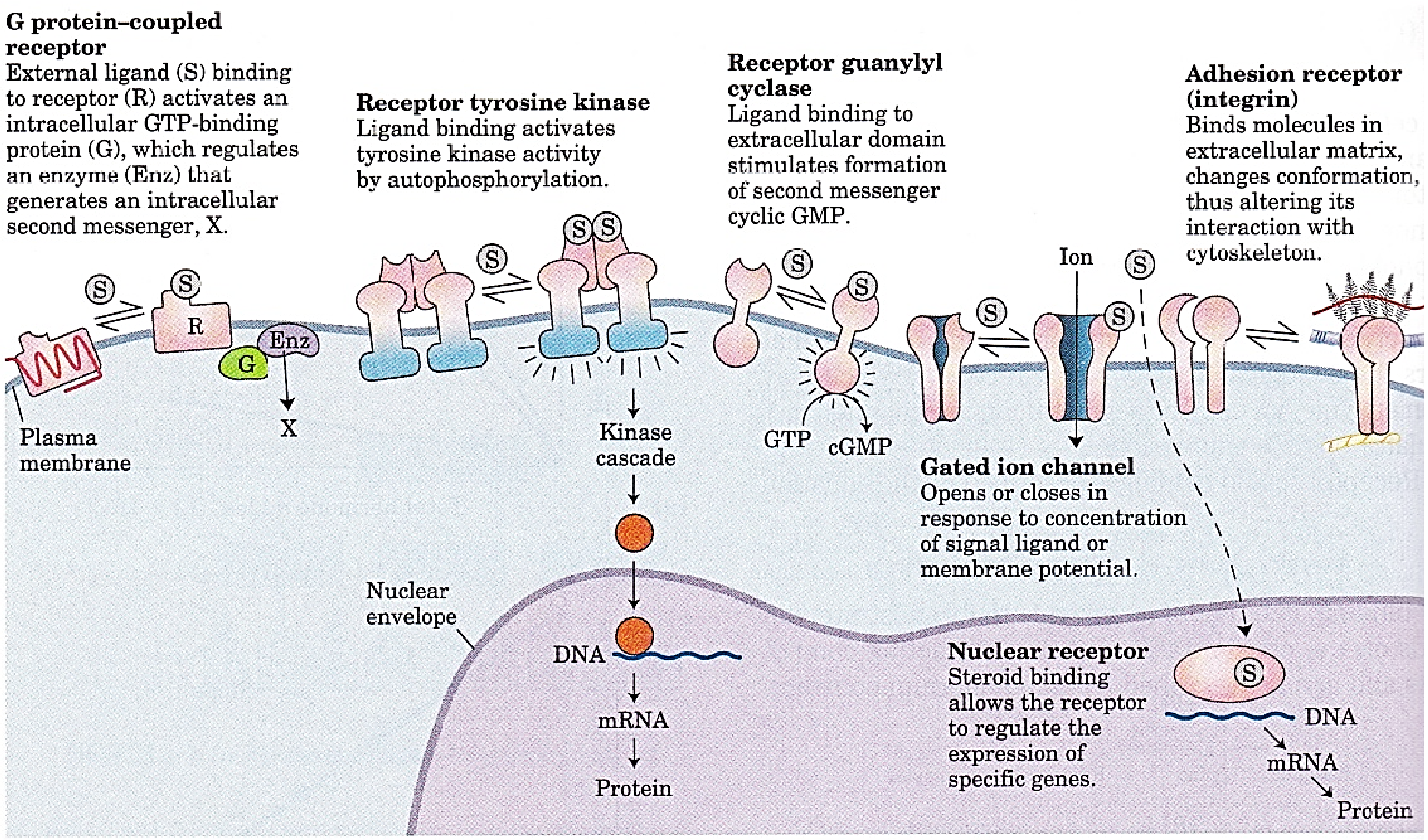
Endocrine, Paracrine, & Autocrine Signaling



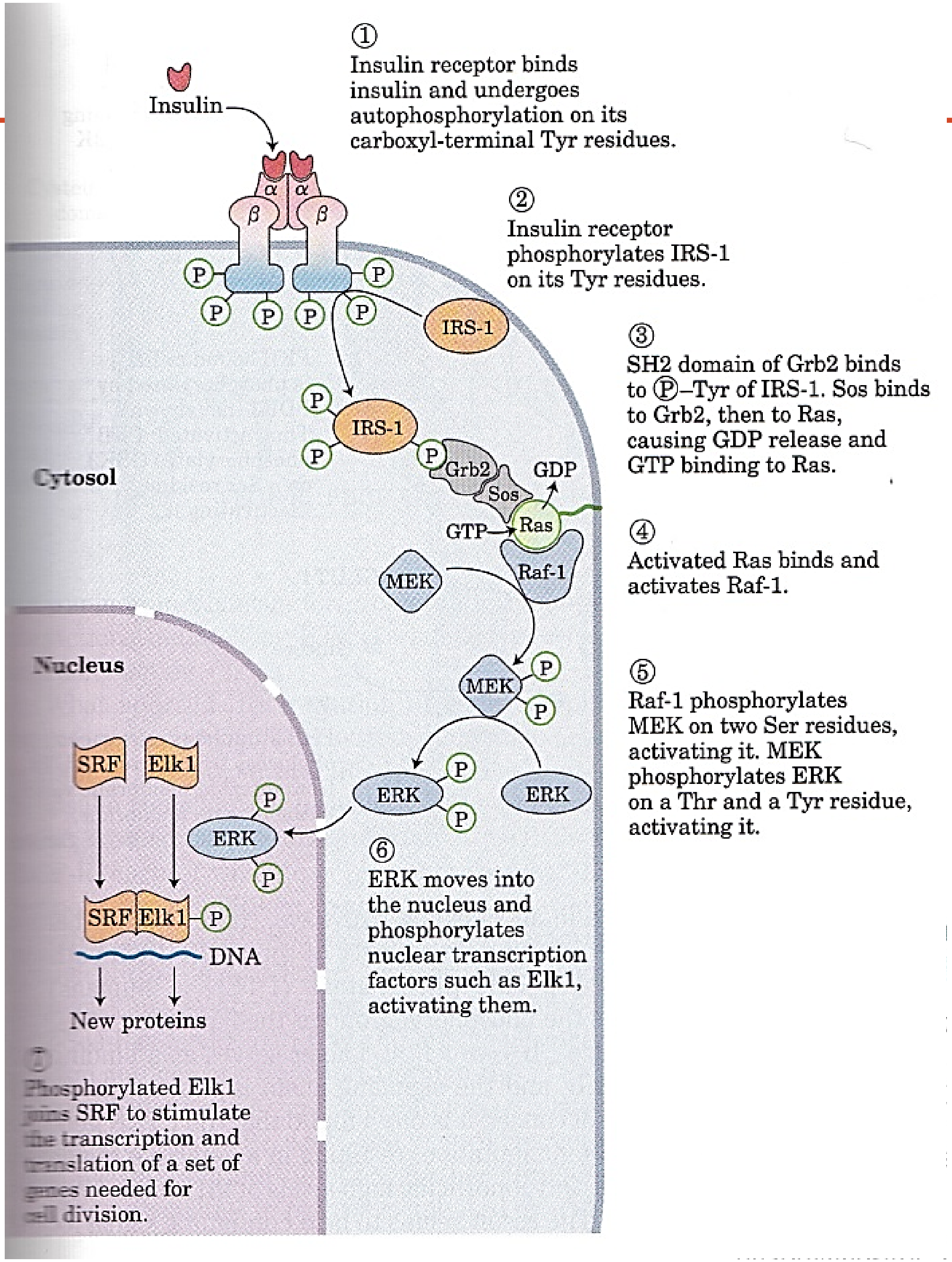


Cell Signaling

Types of signal transducers



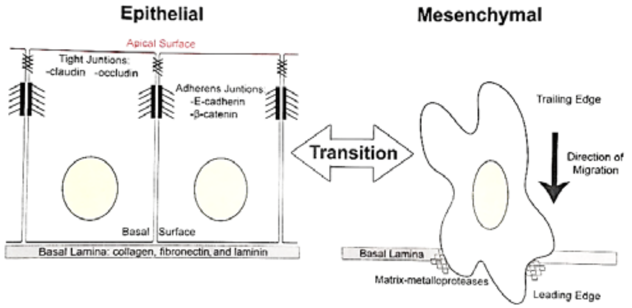
Intracellular Signal Transduction

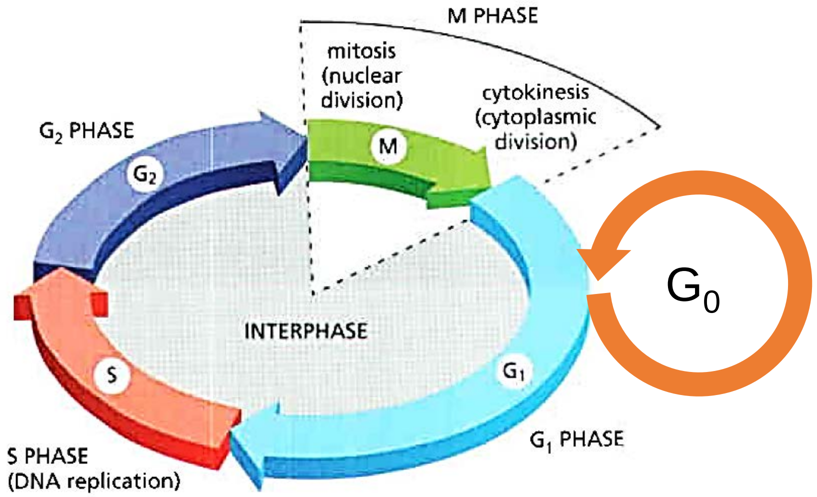


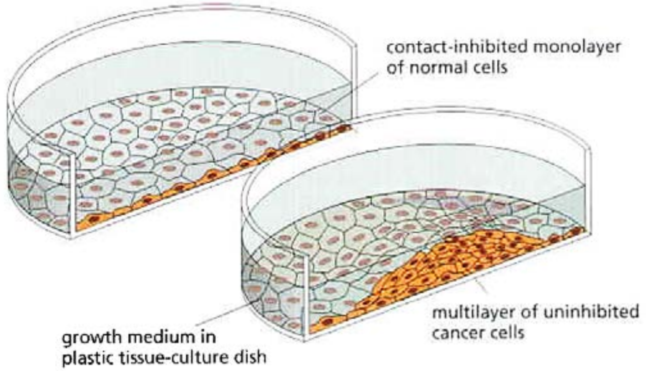
1. Ligand-receptor binding
2. Activation of receptor (phosphorylation)
3. Activation of adaptor proteins
4. Activation of MAPK
5. Activation of transcription factors
6. Induction of gene expression

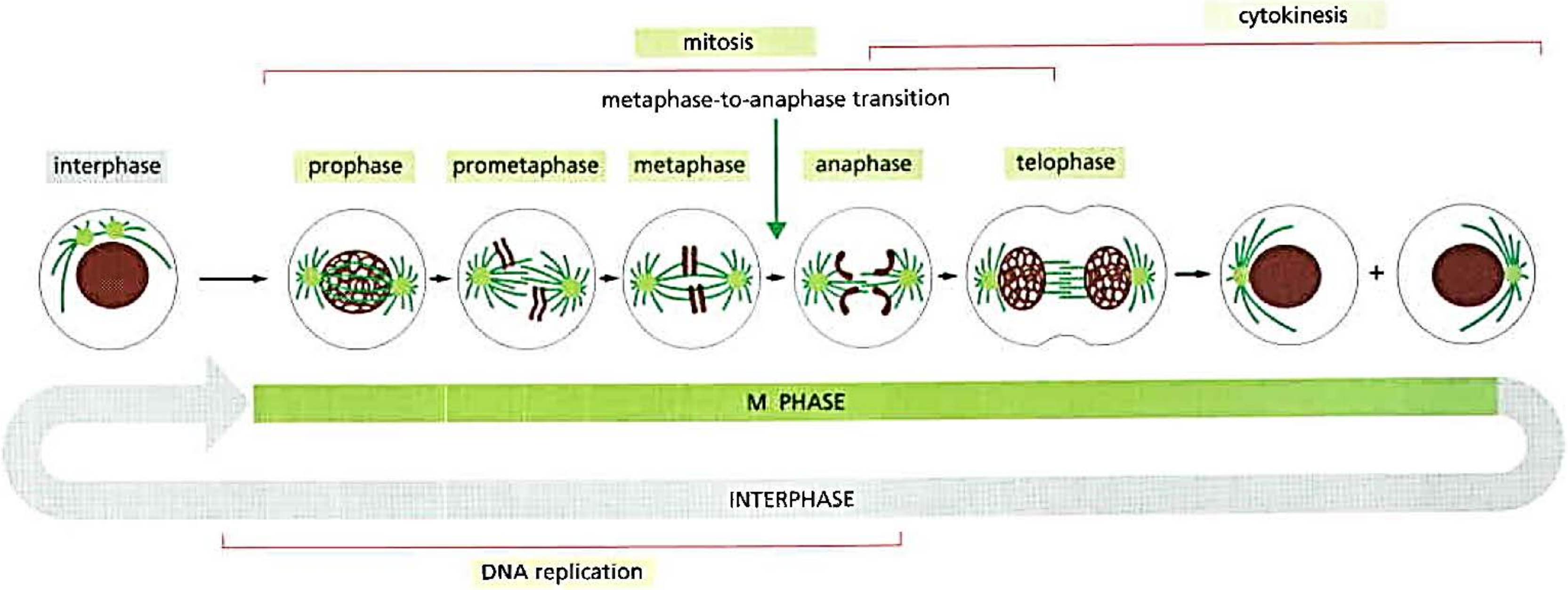
Cell physiology

Cell Cycle – Cell Proliferation



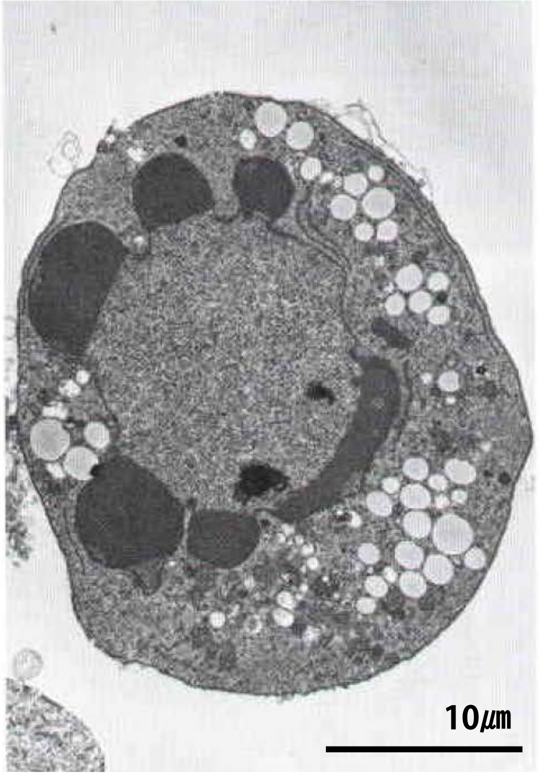




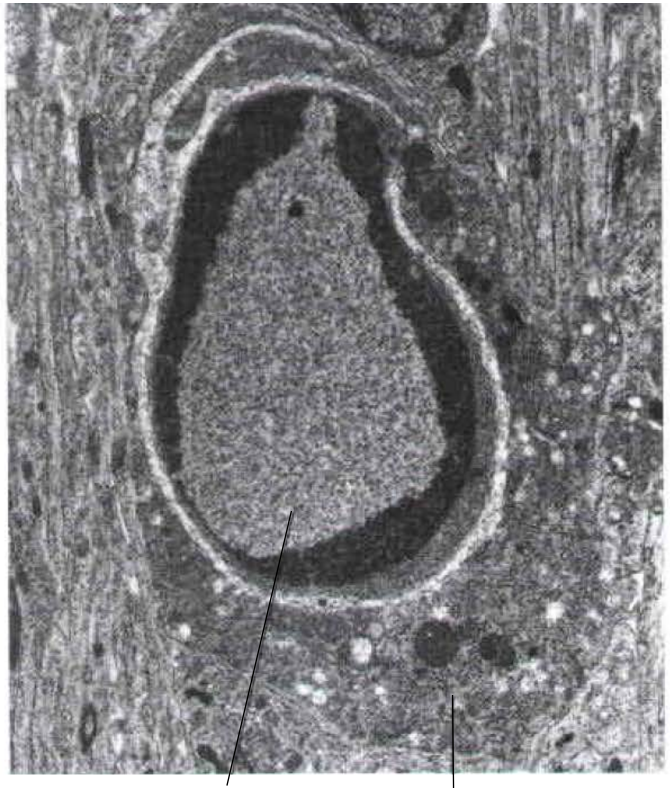


Cell Death – Apoptosis vs Necrosis

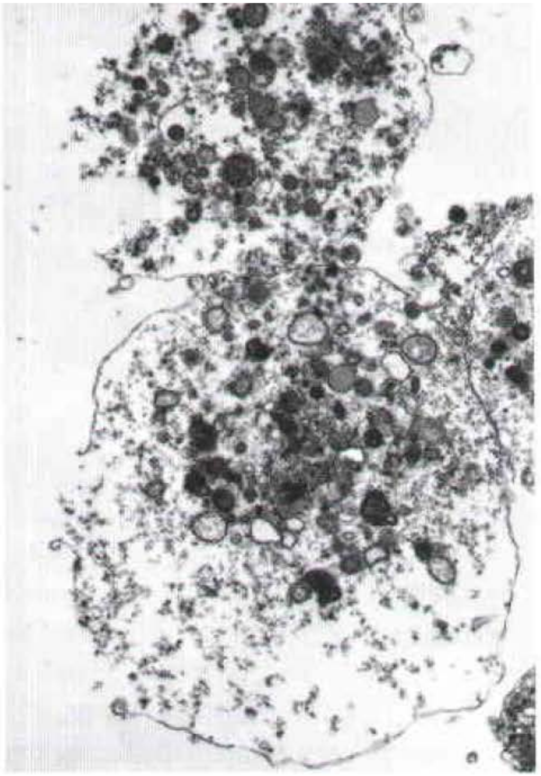
Apoptosis
– the altruistic cell death



Dead cell engulfed by phagocytic cell



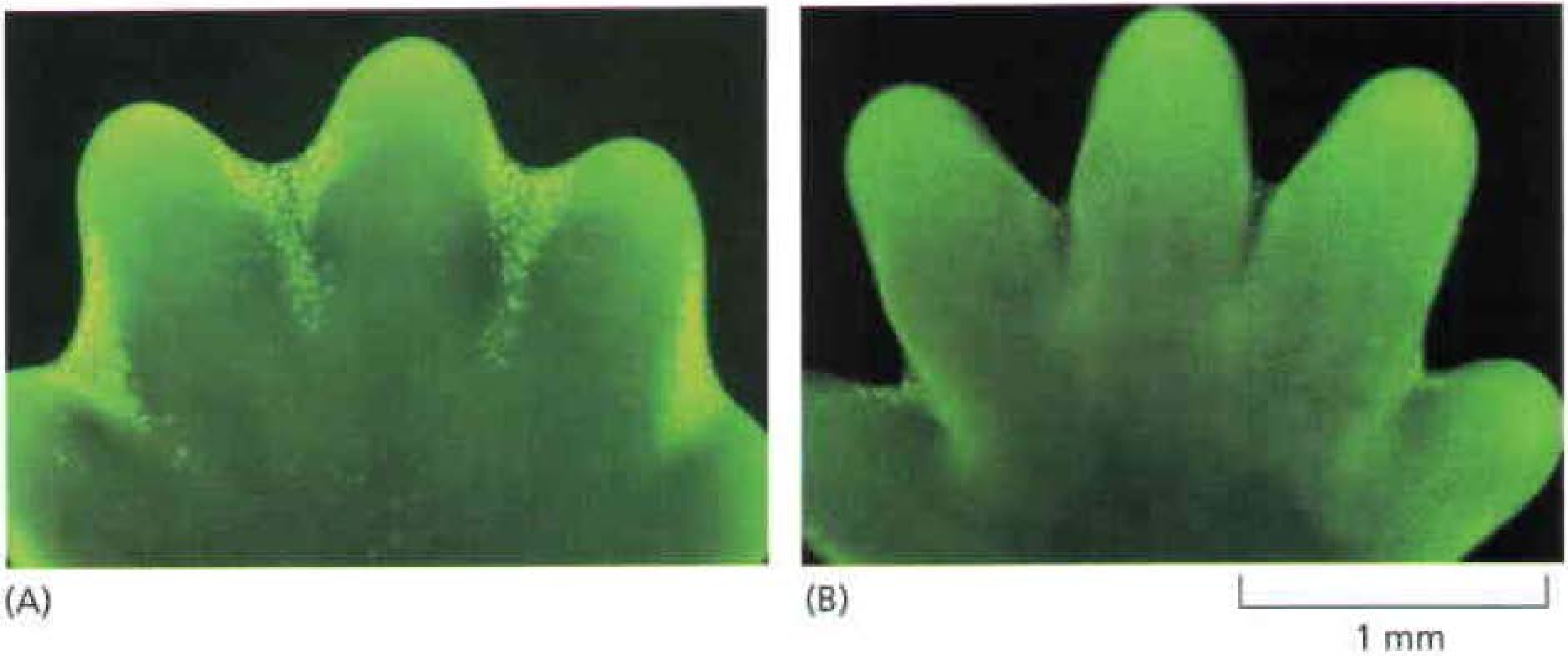
Necrosis
– uncontrolled cell death



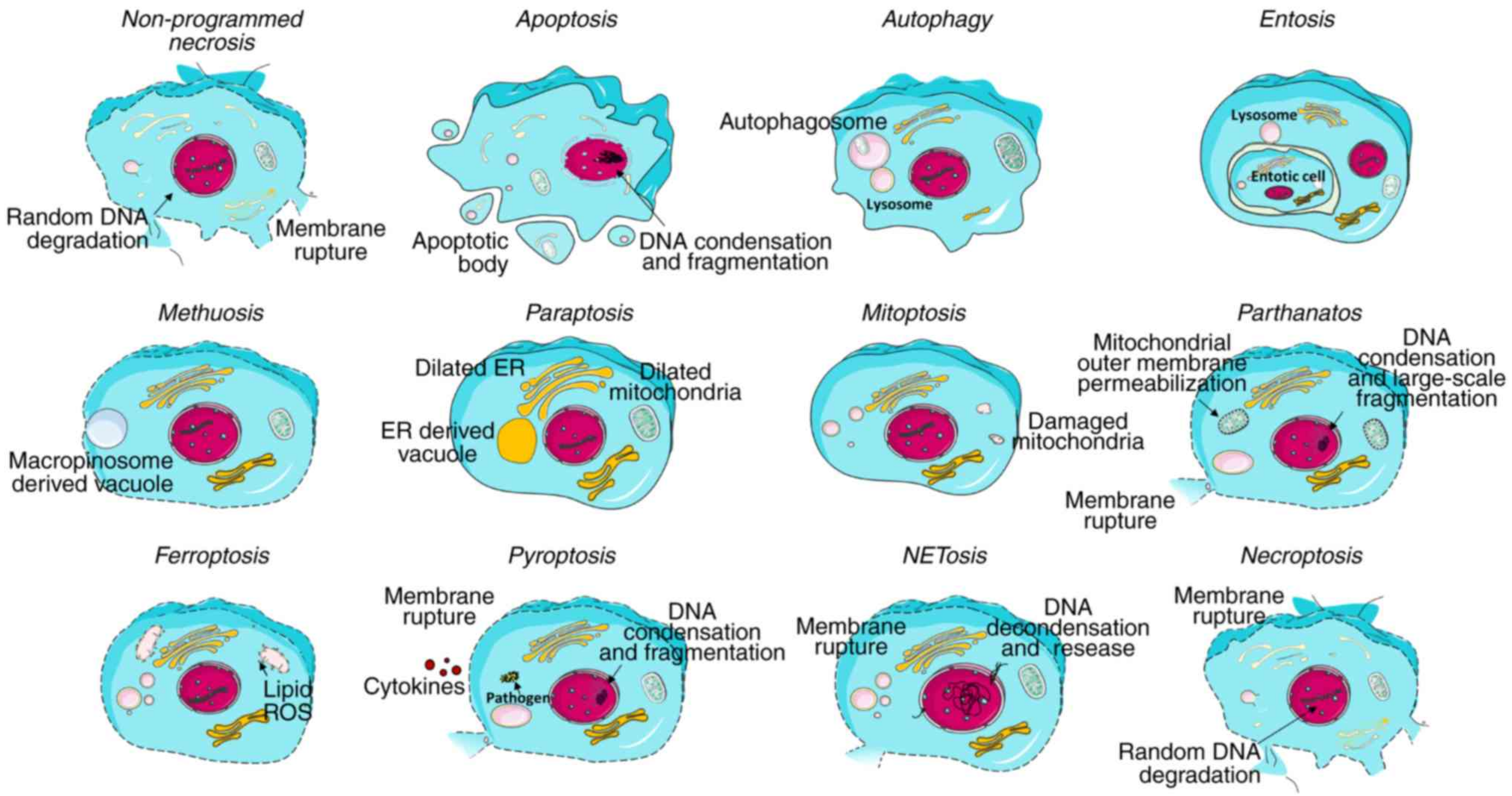
Condensed, intact morphology

Exploded morphology

Apoptosis during embryonic development



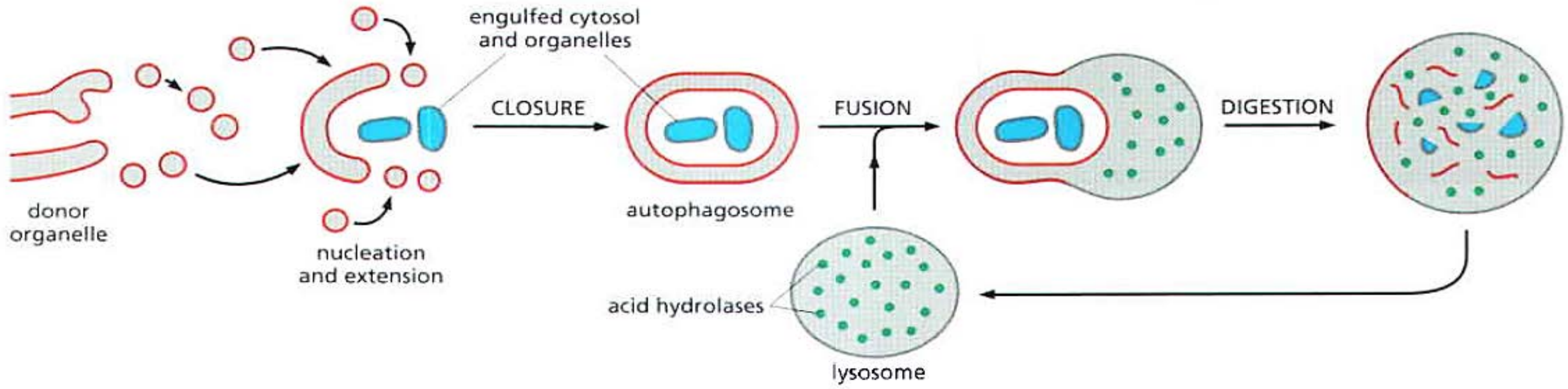
Various Types of Programmed Cell Death

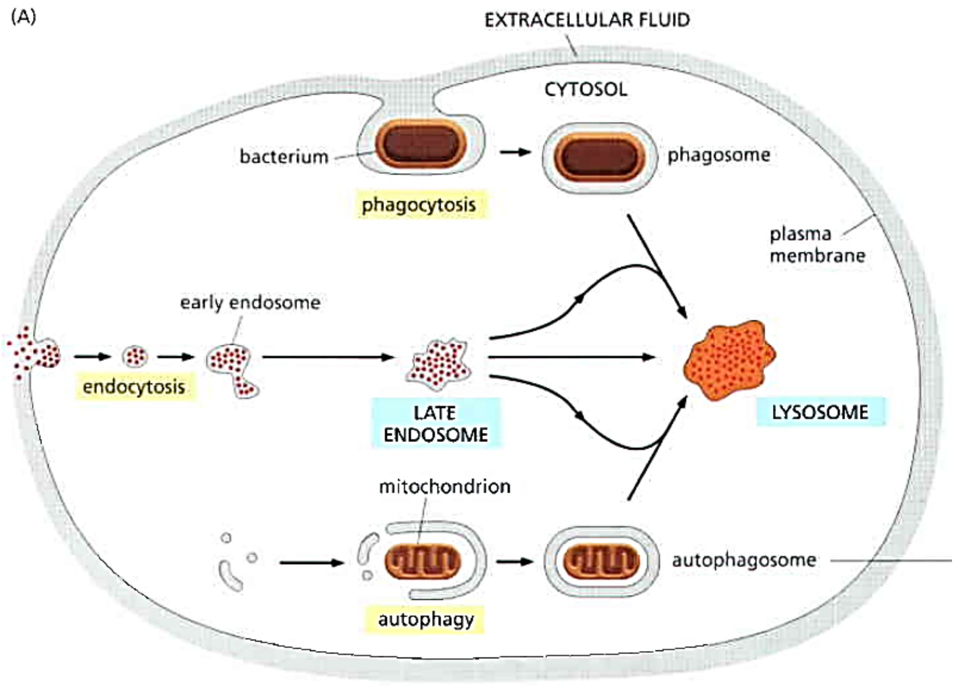


Yan G 2020 World Academy of Sciences Journal (https://doi.org/10.3892/wasj.2020.40)

Autophage

A model of autophagy

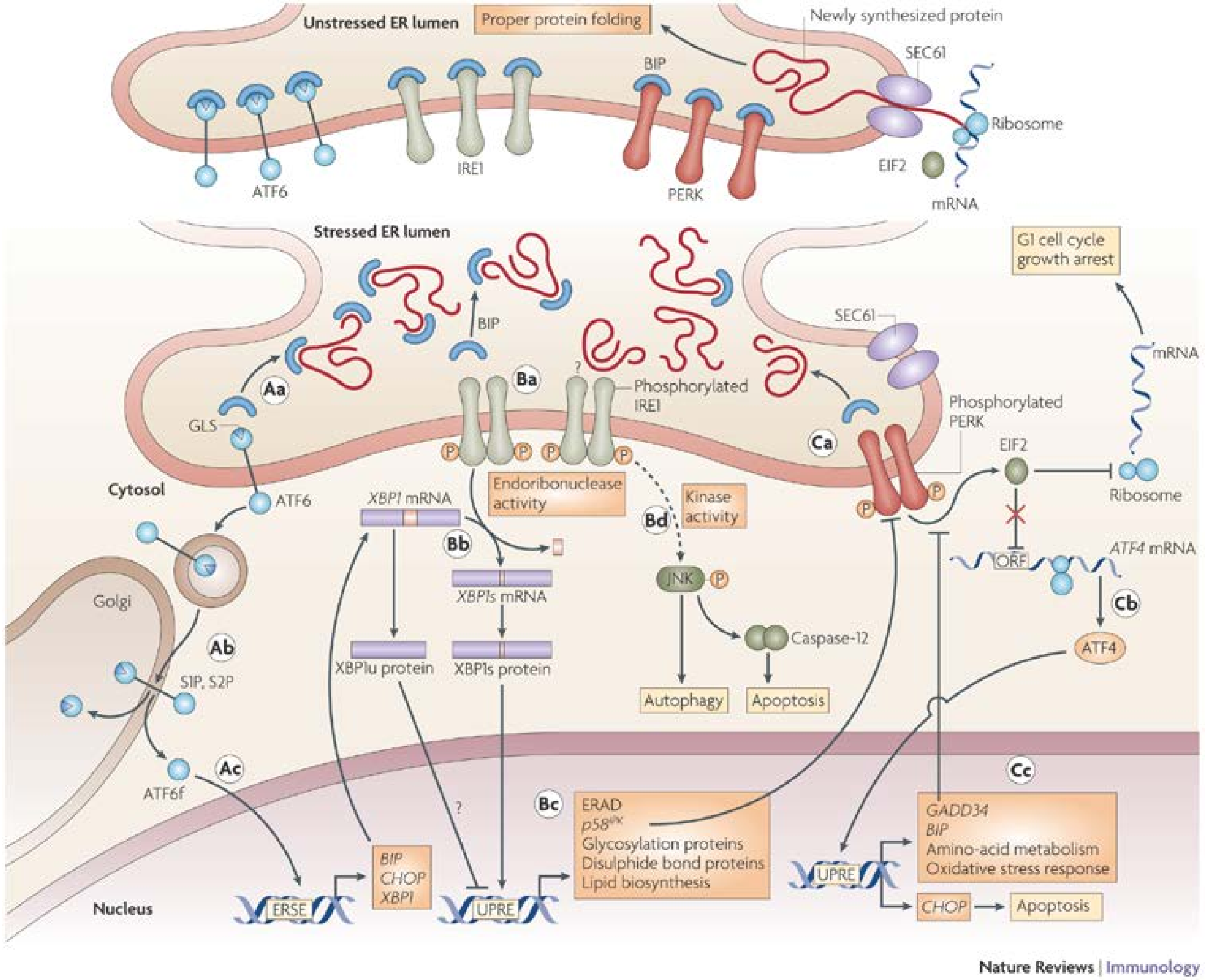




In the absence of survival factors, the cells cannot efficiently import nutrients. Such cells fuel their metabolic needs through *autophagy*, in which the cell sequesters organelles and bits of its cytoplasm within autophagosomes, which then fuse with lysosomes. The cells eventually die from starvation, but not by apoptosis.

ER Stress

- **ER stress** (unfolded protein response**,** UPR) is a cellular stress response caused by unfolded or misfolded proteins accumulating in ER.
- The ER stress response three aims:
  - initially to restore normal function of the cell by halting protein translation, degrading misfolded proteins, and activating the signaling pathways that lead to increasing the production of molecular chaperones involved in protein folding.
  - If these objectives are not achieved within a certain time span or the disruption is prolonged, the UPR aims towards apoptosis.
- Sustained over-activation of the UPR has been implicated in prion diseases as well as several other neurodegenerative diseases, and inhibiting the UPR could become a treatment for those diseases.
- Diseases amenable to UPR inhibition include Creutzfeldt-Jakob disease, Alzheimer's disease, Parkinson's disease, and Huntington's disease.



Todd DJ 2008 Nature Reviews Immunology

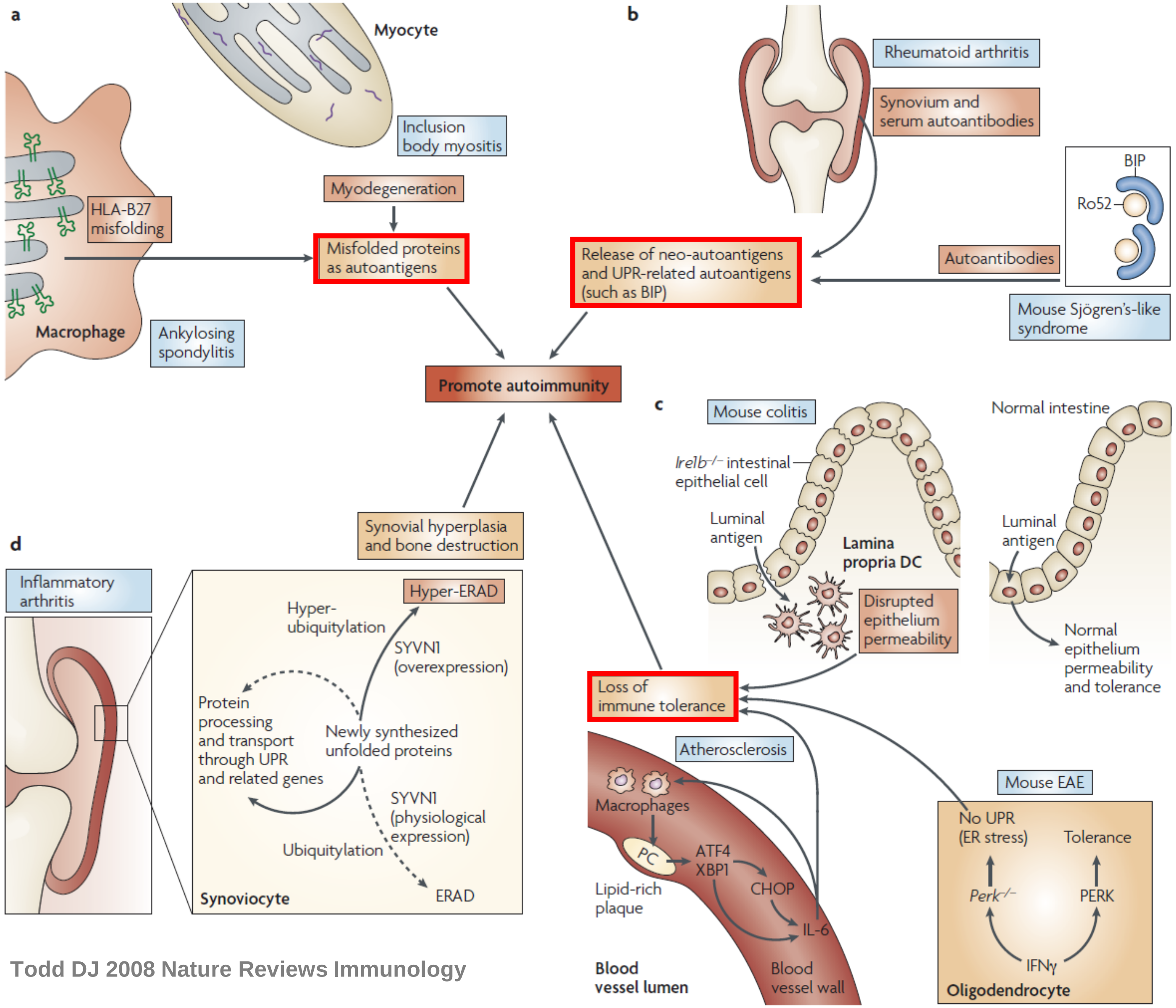
Potential Mechanisms Whereby the Unfolded-Protein Response Might Allow Autoimmunity

Myodegeneration

Synovial hyperplasia

Bone destruction

Rheumatoid arthritis



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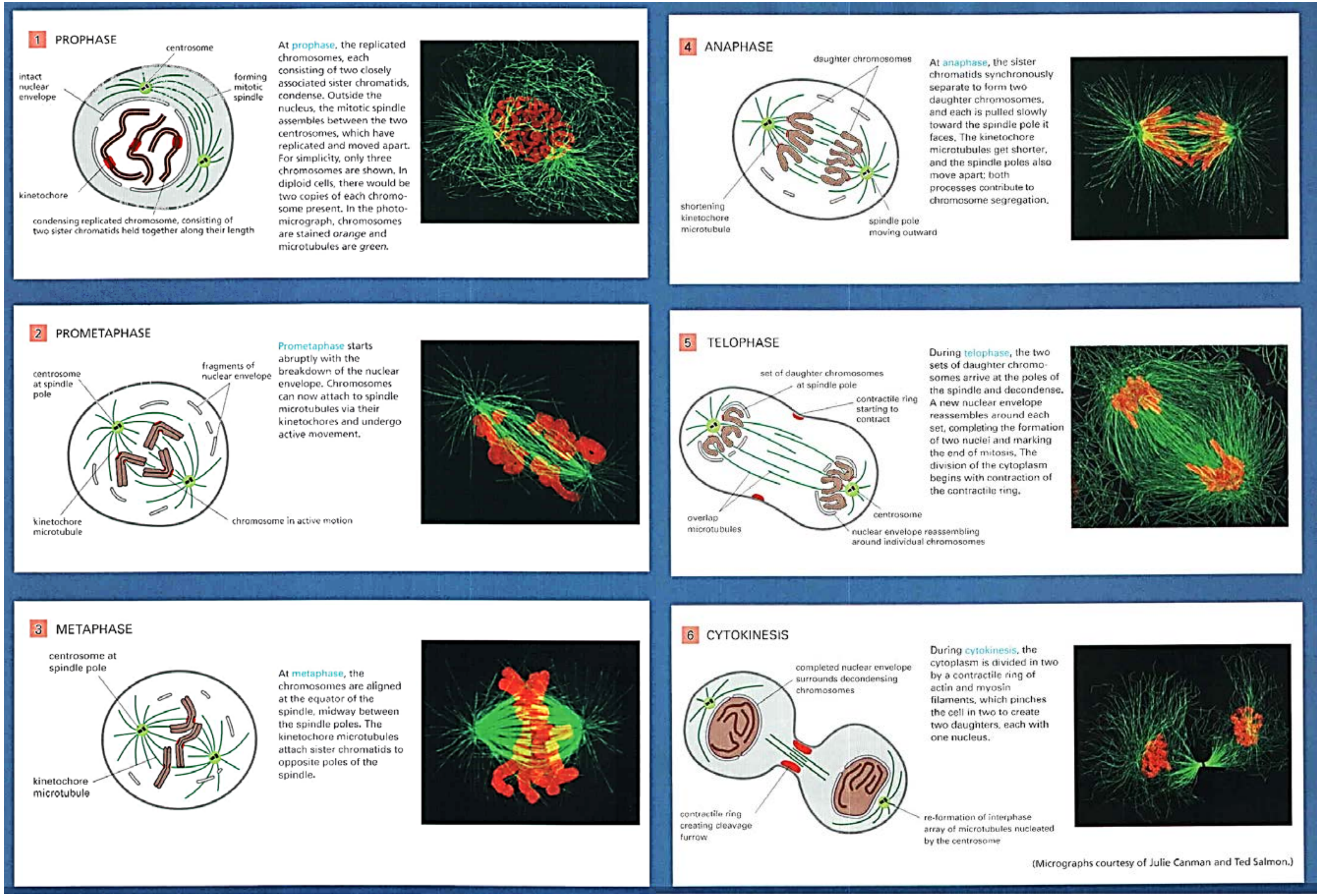
EOD

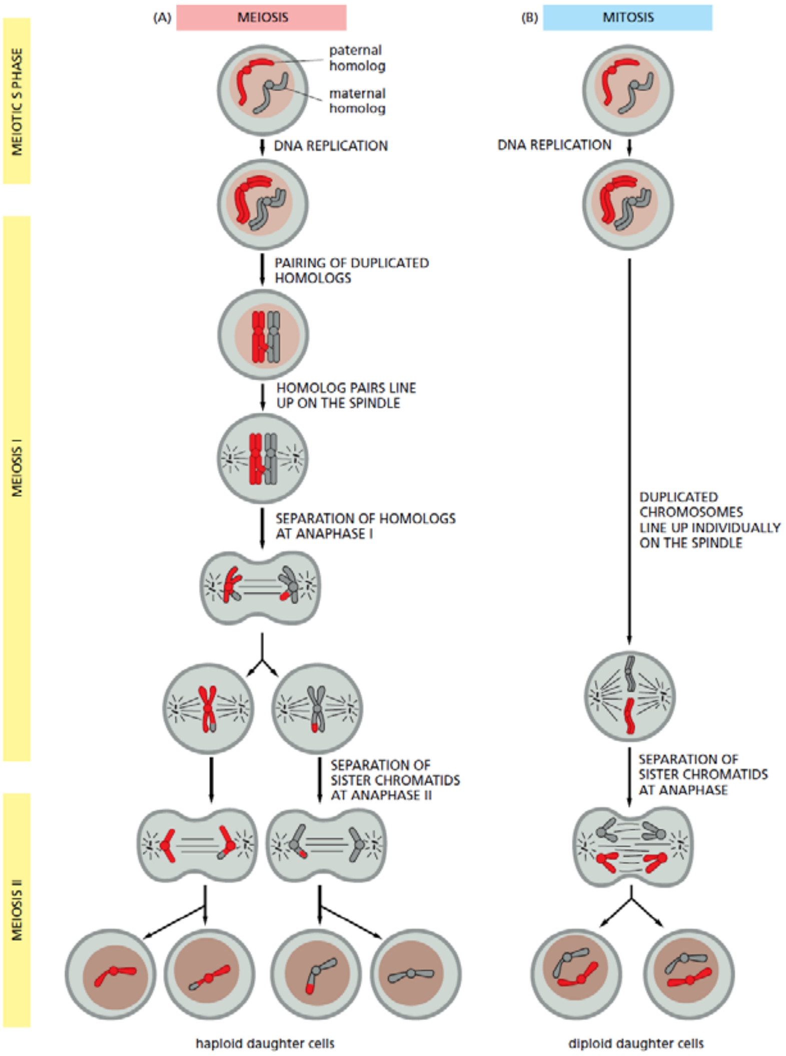
Development of multi-cellular organisms

Cell Division - Mitosis

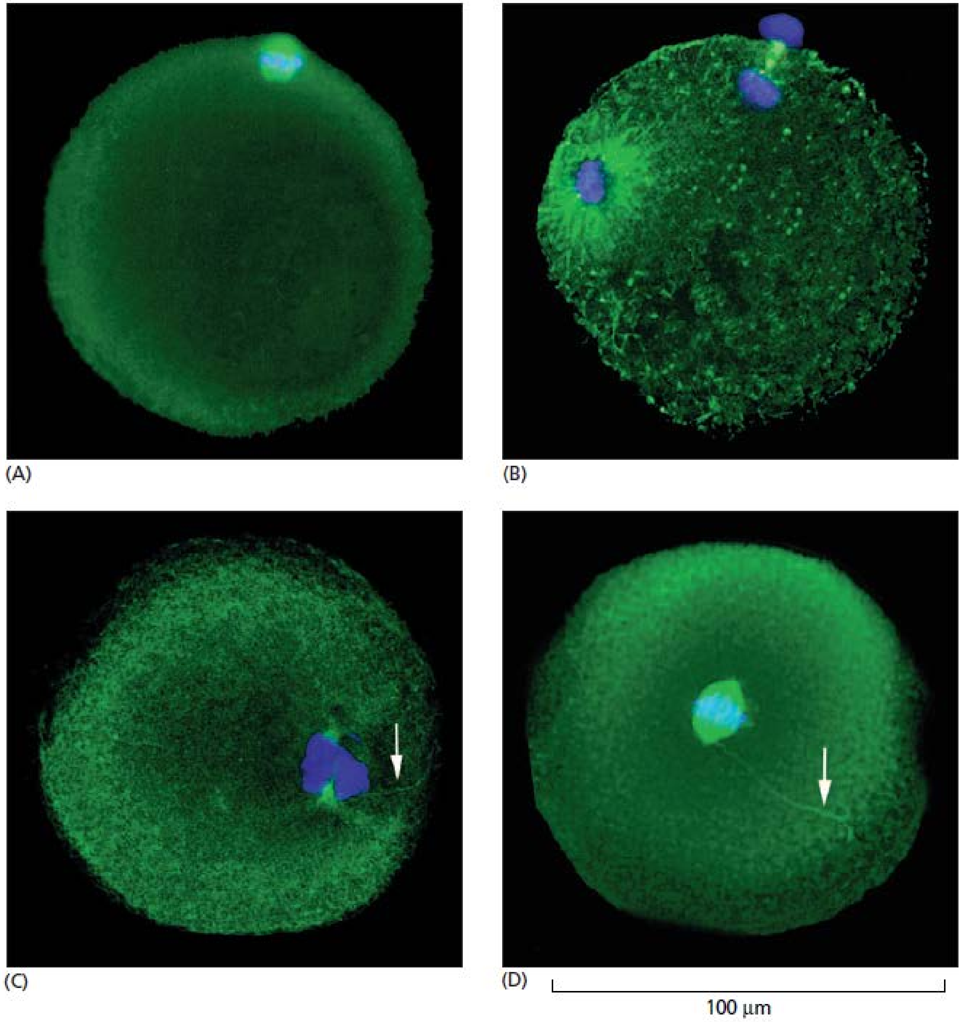


Germ Cells & Fertilization

Germ cell formation by meiosis

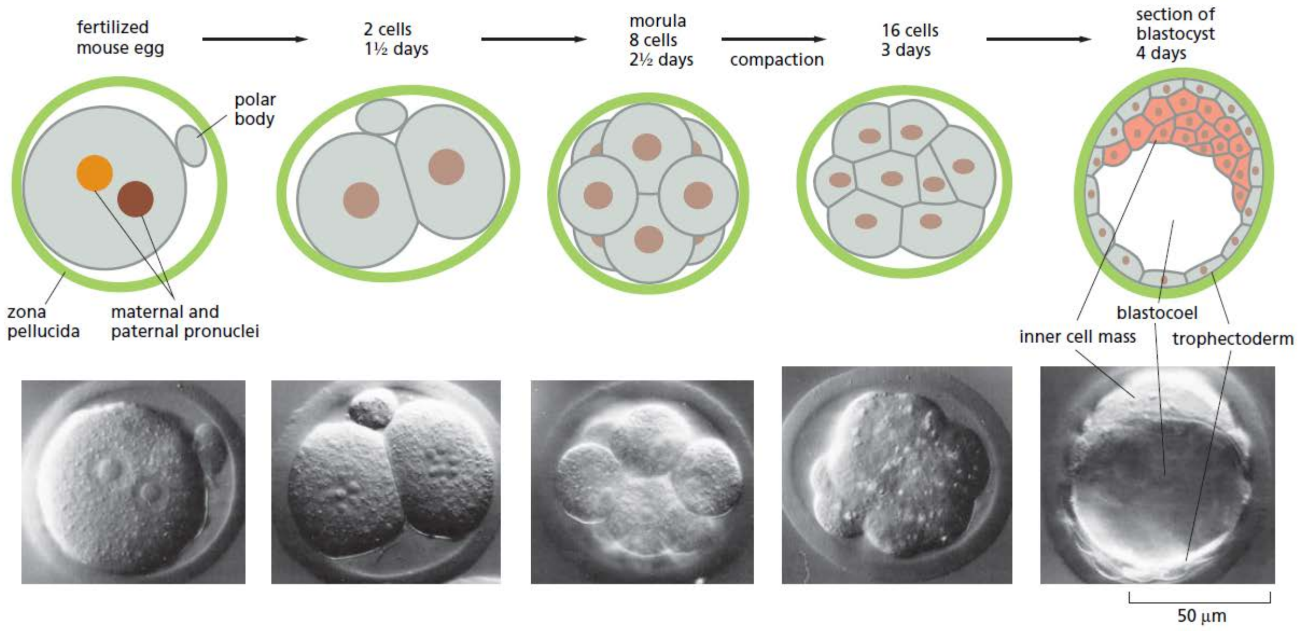


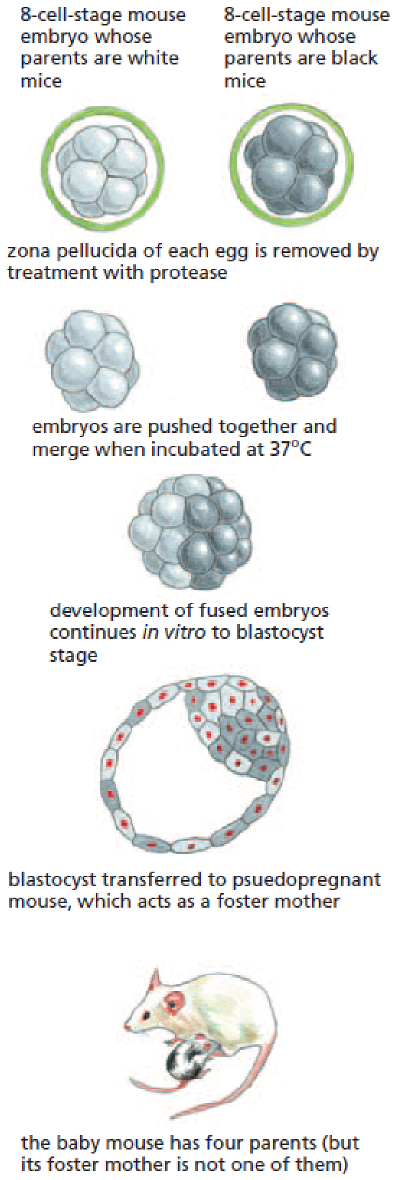
Fertilization



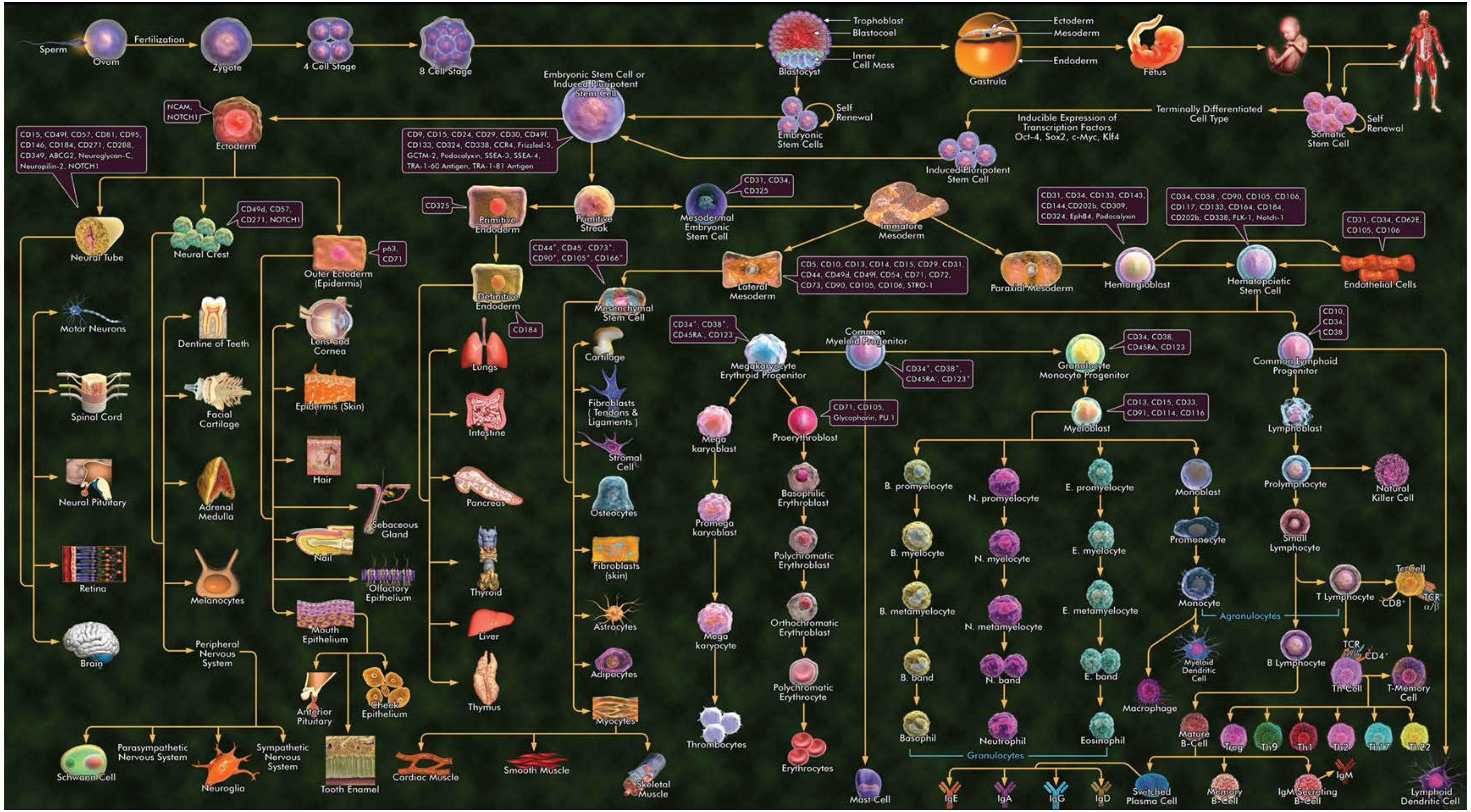
Early Development

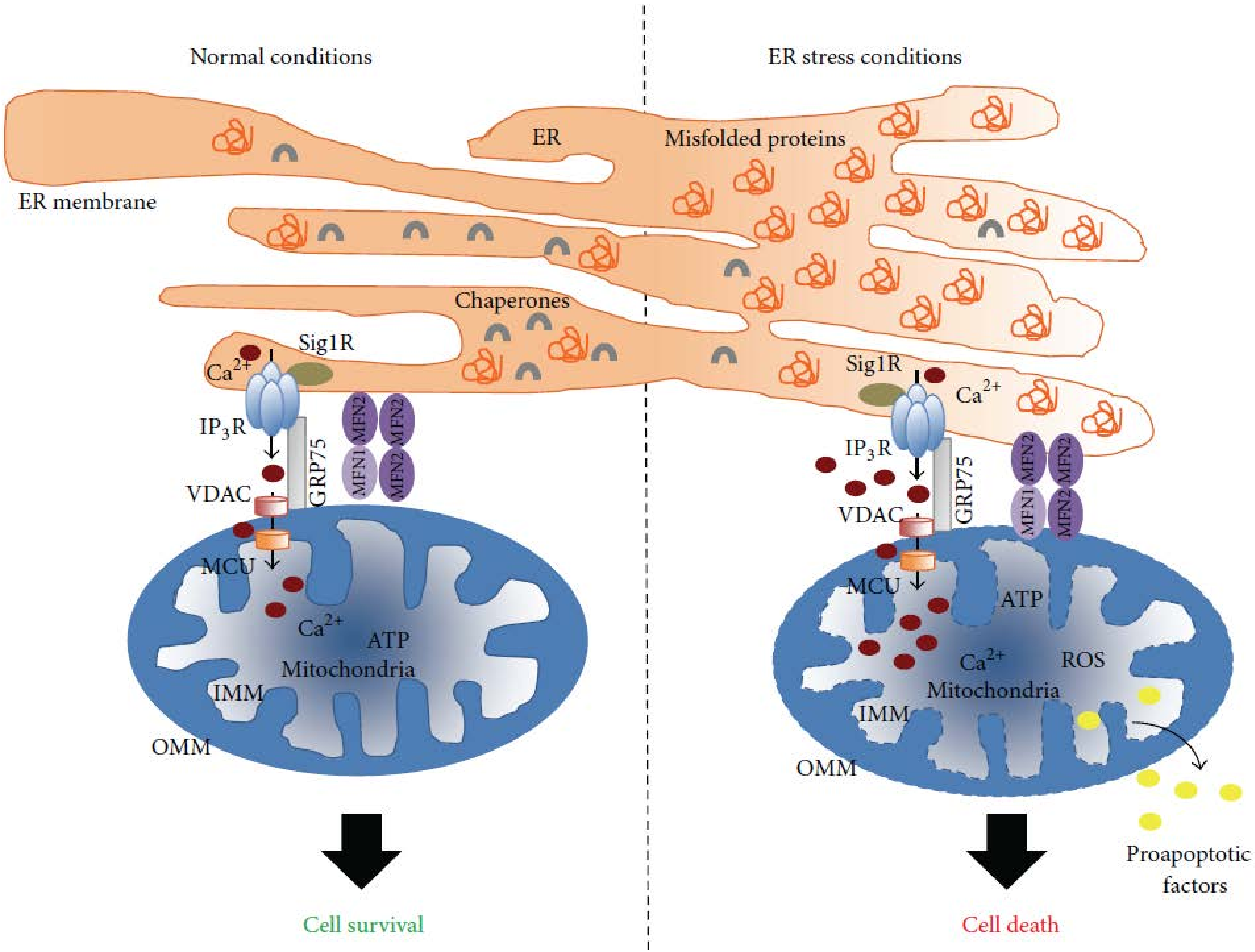
The early stages of mouse embryonic development





Tissue Formation




Normal conditions
ER stress conditions
ER
Misfolded proteins
ER membrane
Chaperones
Sig1R
Ca2+
IP3R
GRP75
MFN2
MFN1
VDAC
MCU
Ca2+
ATP
Mitochondria
IMM
OMM
Cell survival
Sig1R
Ca2+
IP3R
GRP75
MFN2
MFN1
VDAC
MCU
ATP
Ca2+
ROS
Mitochondria
IMM
OMM
Proapoptotic factors
Cell death