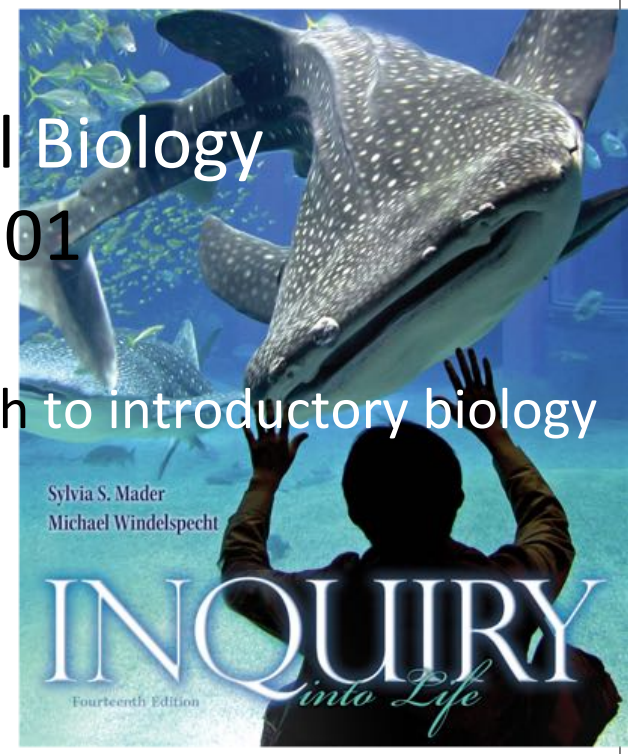
Fundamental Biology
BI 1101

an interdisciplinary approach to introductory biology



Anggraini Barlian
SITH-ITB

Five Levels of Organization

Molecular

Cellular

Organismal

Population

Ecological System

Ch 03: CELL (2)

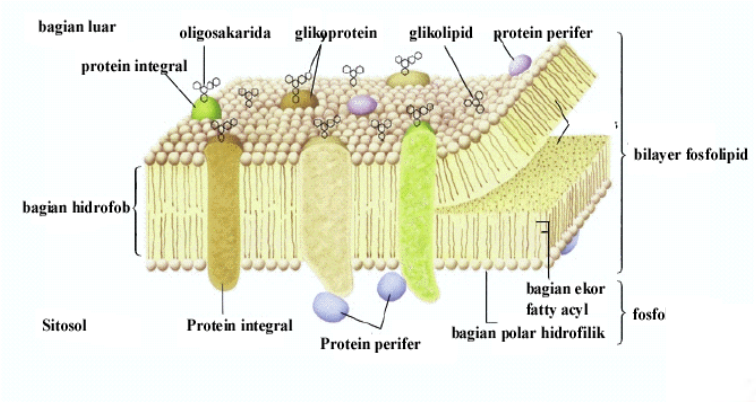
Cell Membrane, Communication and
Cell Cycle

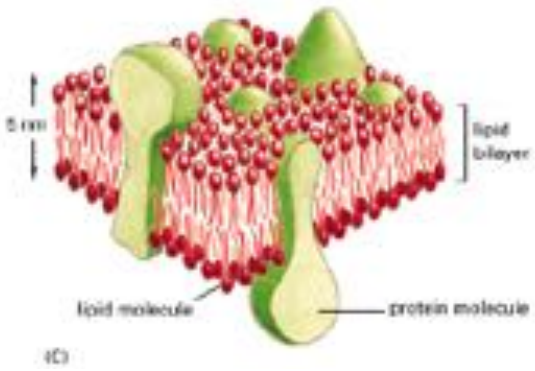
Learning Outcomes

After this chapter, students are able to:

- Explain the structure and function of cell membrane
- Explain the basic concept of cell communication and the importance of cell communication
- Explain the regulation in cell cycle

CELL MEMBRANE





Function of cell membrane:

- **Boundary**

Continuous, encloses the cell, nucleus, organelles

- **Selective permeable barrier**

Avoid molecules exchange from one side to the other side.
Avoid the entrance of certain molecules to the cytoplasm

- **Movement of soluble molecules**

Make the entrance of certain substances to cytoplasm from outside cell possible

- **Responding to extracellular stimuli**

→ Signal Transduction → receptor + ligand.
Different type of cell, different receptor molecule

- **Inter-celullar interaction**

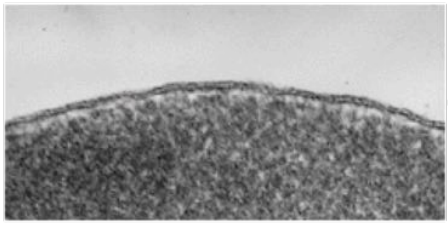
Plasma membrane mediates cell interaction in multicellular organism → cell communication

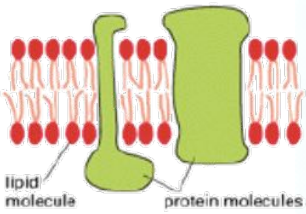
- **Place for biochemical activities**

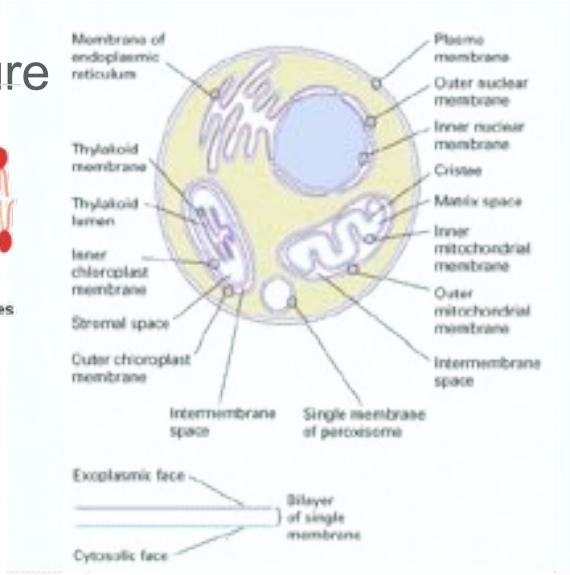
- **Energy transduction**

Involved in the process of energy transformation

Membrane structure







lipid bilayer :

•Polar molecules (hydrophilic) face to the outer part

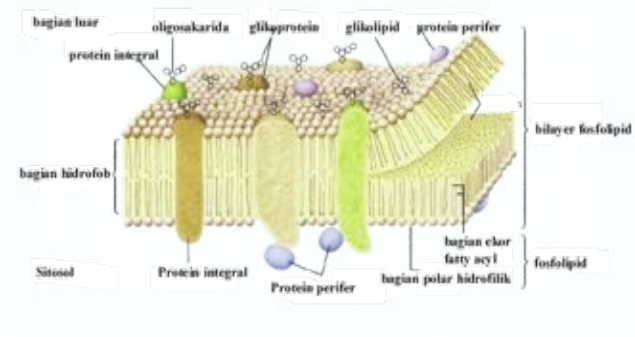
•hydrophobic part (fatty acyl chain) protected from water environment → amphipathic .

Protein

•Trans-membrane Molecules or attached in lipid layer

Carbohydrate

•biomarker in the cell surface



Fluid mosaic model
(Jonathan Singer & Garth Nicolson, 1960)

The Lipid Bilayer

Amphipathic molecules → spontaneously forms bilayer

- **hydrophilic/ polar end & hydrophobic/ non polar end**
- **most abundant membrane lipids → phospholipids: polar head group & 2 hydrophobic hydrocarbon tails**

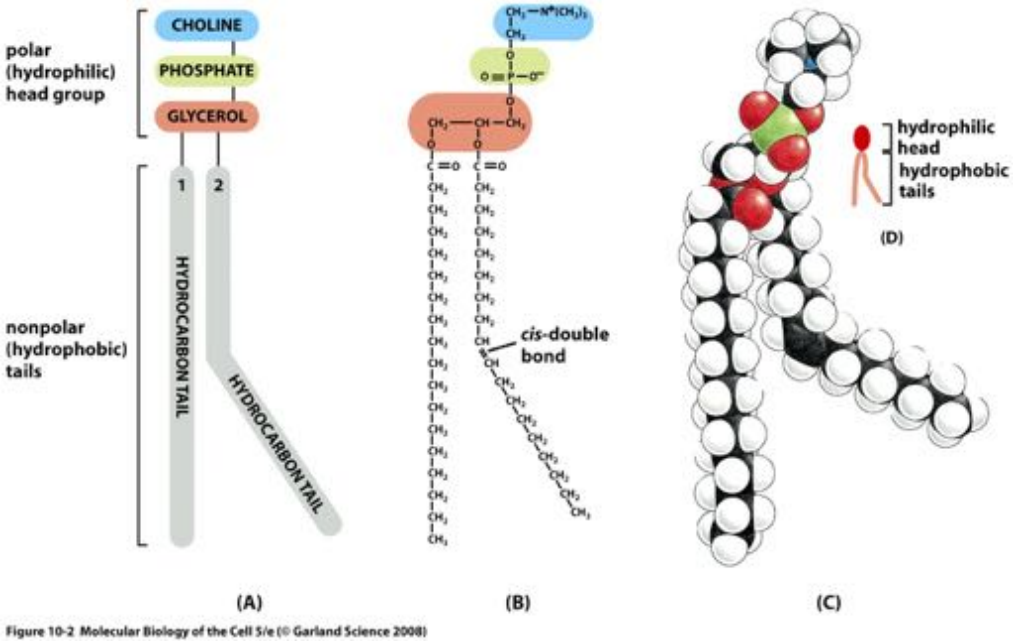


Figure 10-2 Molecular Biology of the Cell 5/e (© Garland Science 2008)

4 types of phospholipids in the mammalian plasma membranes

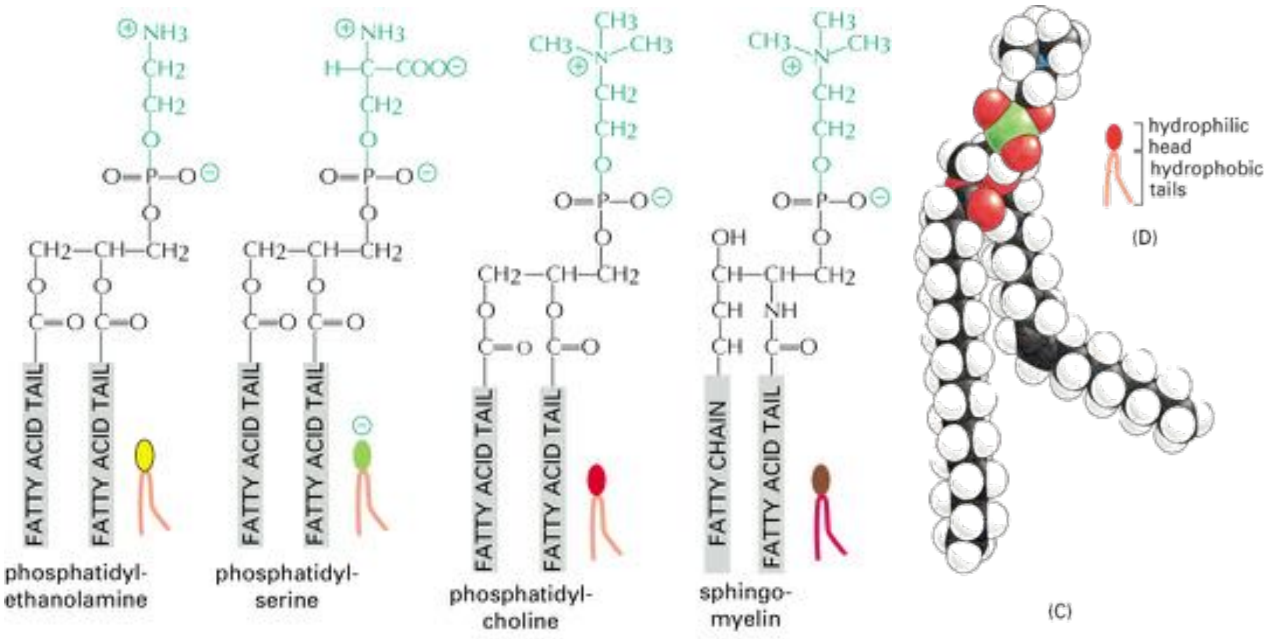


Figure 10–12. Molecular Biology of the Cell, 4th Edition.

Figure 10–2 part 3 of 3. Molecular Biology of the

Four major phospholipids in mammalian plasma membrane (different head group). All lipid molecules are derived from phosphoglycerides, except for sphingomyelin, which is derived from sphingosine

Membrane Proteins

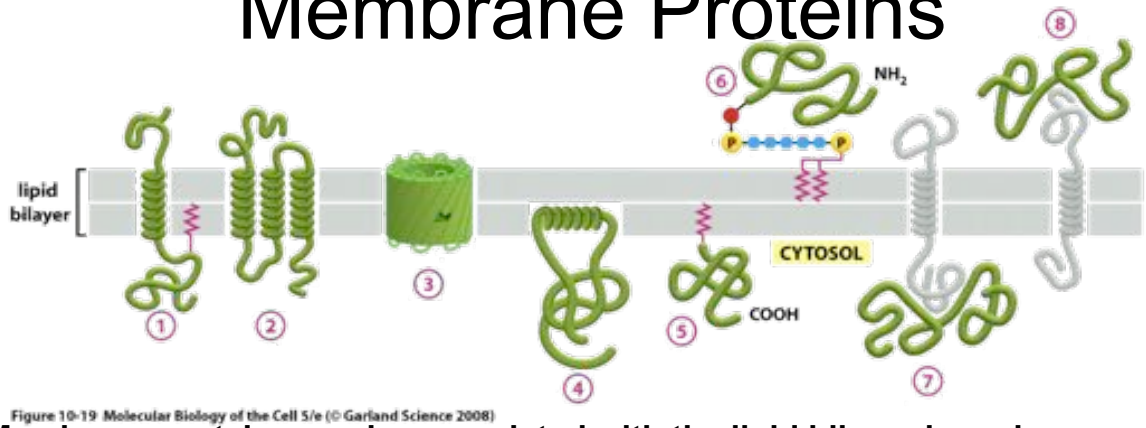


Figure 10-19 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Membrane proteins can be associated with the lipid bilayer in various ways:

1.trans-membrane proteins are thought to extend across the bilayer as a single α helix

2.As multiple α helices

3.As a rolled-up β sheet (a β barrel)

4.Anchored to the cytosolic surface by an amphipatic α helix that partitions into the cytosolic monolayer of the lipid bilayer through the hydrophobic face of the helix

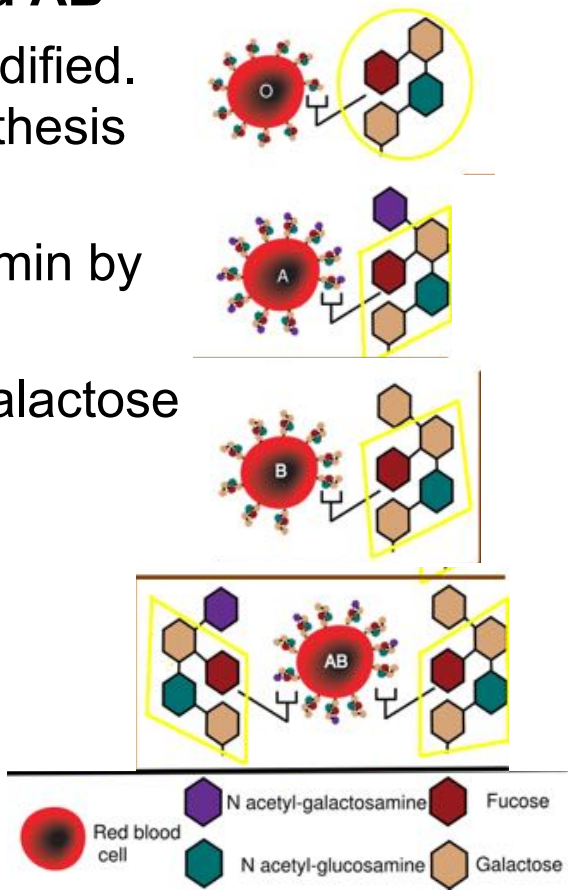
5.Attached to the bilayer solely by a covalently attached lipid chain (fatty acid / prenyl group) in the cytosolic monolayer

6.Via an oligosaccharide linker to phosphatidylinositol in noncytosolic monolayer

7 & 8. Attached to the membrane by noncovalent interactions with other proteins

The difference between blood type: O, A, B, and AB

- O → H-determinant is not modified. Everyone has enzyme to synthesis antigen.
- A → plus N-acethylgalactosamin by GalNAc transferase.
- B → H-determinant plus D-Galactose by Gal transferase.
- AB → has 2 transferase and synthesize antigen A and B



Relative Permeability of phospholipid bilayer

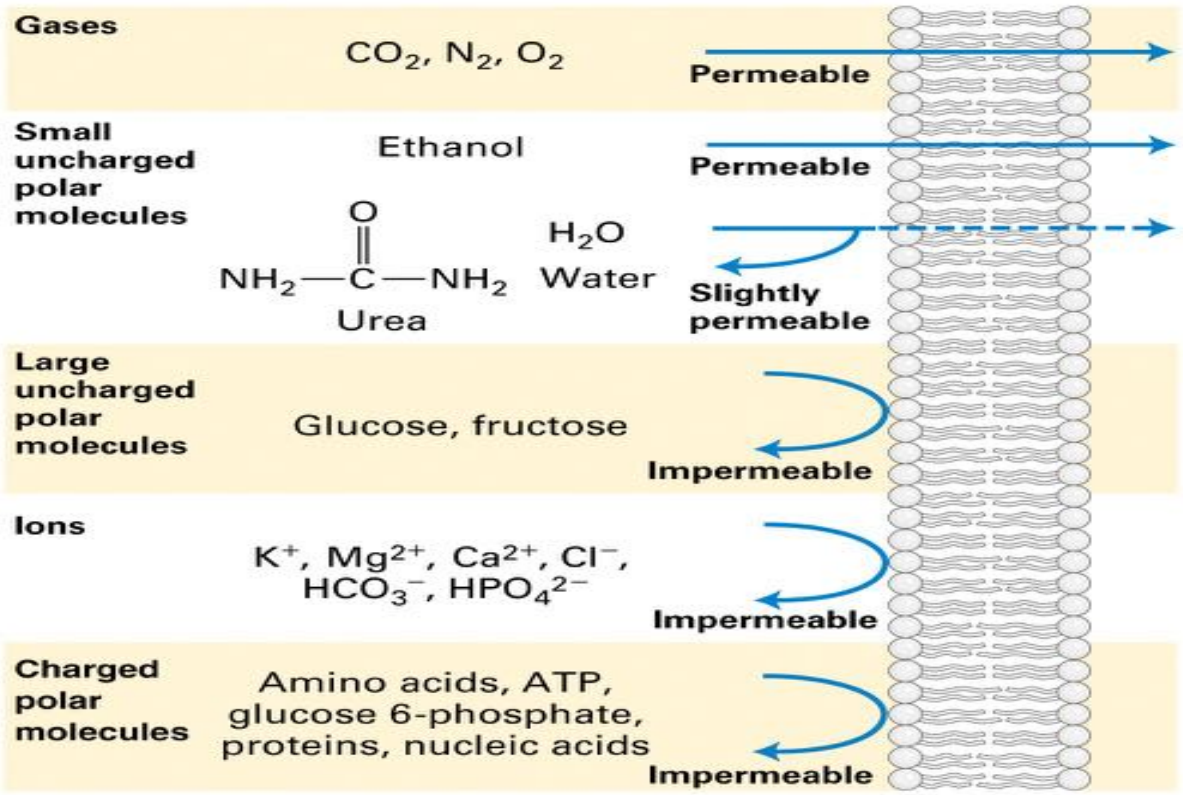


TABLE 7-1 Mechanisms for Transporting Ions and Small Molecules Across Cell Membranes

	Transport Mechanism			
Property	**Passive Diffusion**	**Facilitated Diffusion**	**Active Transport**	**Cotransport***
Requires specific protein	–	+	+	+
Solute transported against its gradient	–	–	+	+
Coupled to ATP hydrolysis	–	–	+	–
Driven by movement of a cotransported ion down its gradient	–	–	–	+
Examples of molecules transported	O_2, CO_2, steroid hormones, many drugs	Glucose and amino acids (uniporters); ions and water (channels)	Ions, small hydrophilic molecules, lipids (ATP-powered pumps)	Glucose and amino acids (symporters); various ions and sucrose (antiporters)

*Also called *secondary active transport*.

***Facilitated* difussion**

diffusion of compound from high concentration to low concentration. The compound binds to facilitative transporter

(integral protein) → as a diffusion fasilitator on cell membrane

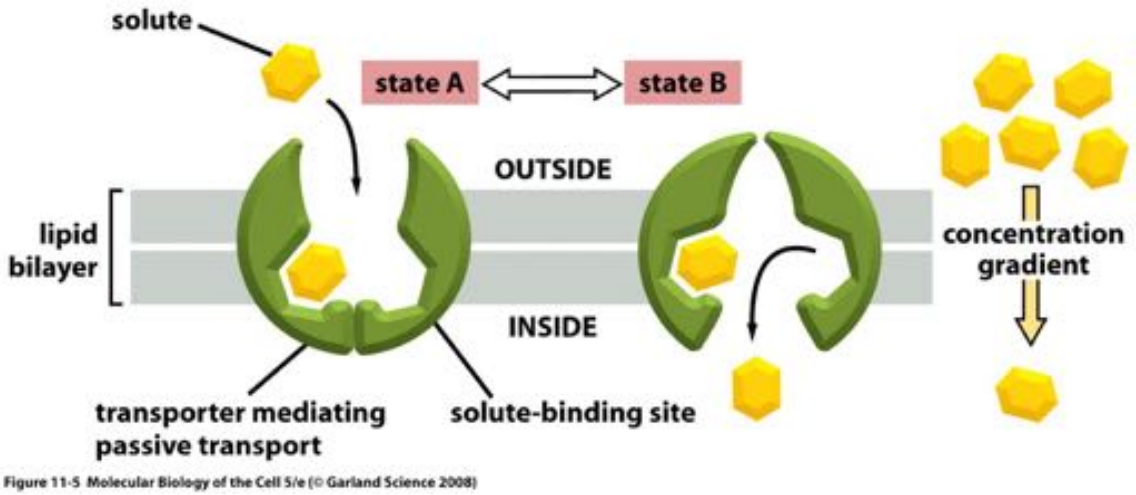


Figure 11-5 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Active Transport : **against concentration gradient**

a) needs energy

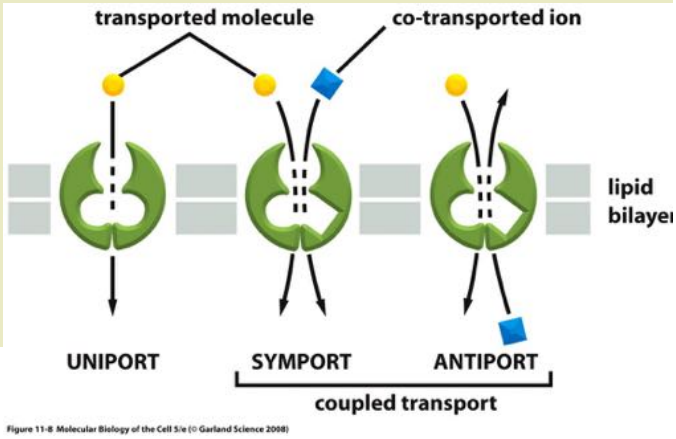
b) involve integral protein →pump

1. Binds to hydrolize ATP : Na+/K+-ATP-ase (natrium-kalium pump)→ type-P pump
   - Ca2+-ATP-ase Ca transport from ER to extracellular part or inside ER
   - H+/K+-ATP-ase in epithelial cell in digestive system

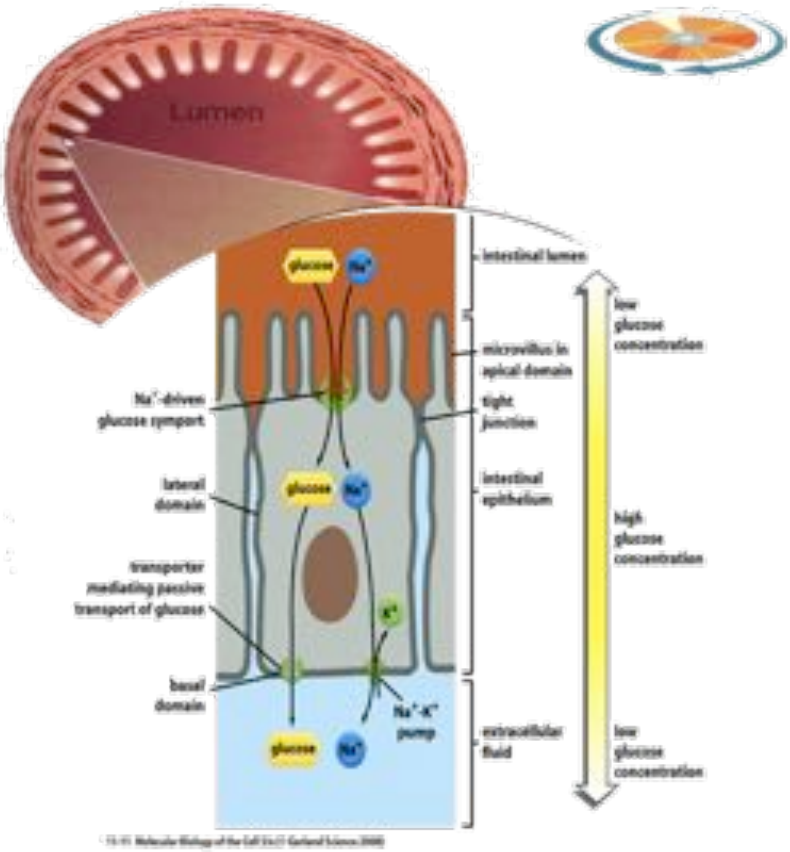
2. Co-transport : bind to ion gradient
   - Transfer of glucosa : Na ion – epithelial
   - Sucrosa – H+ ion (in plants)

→ simport

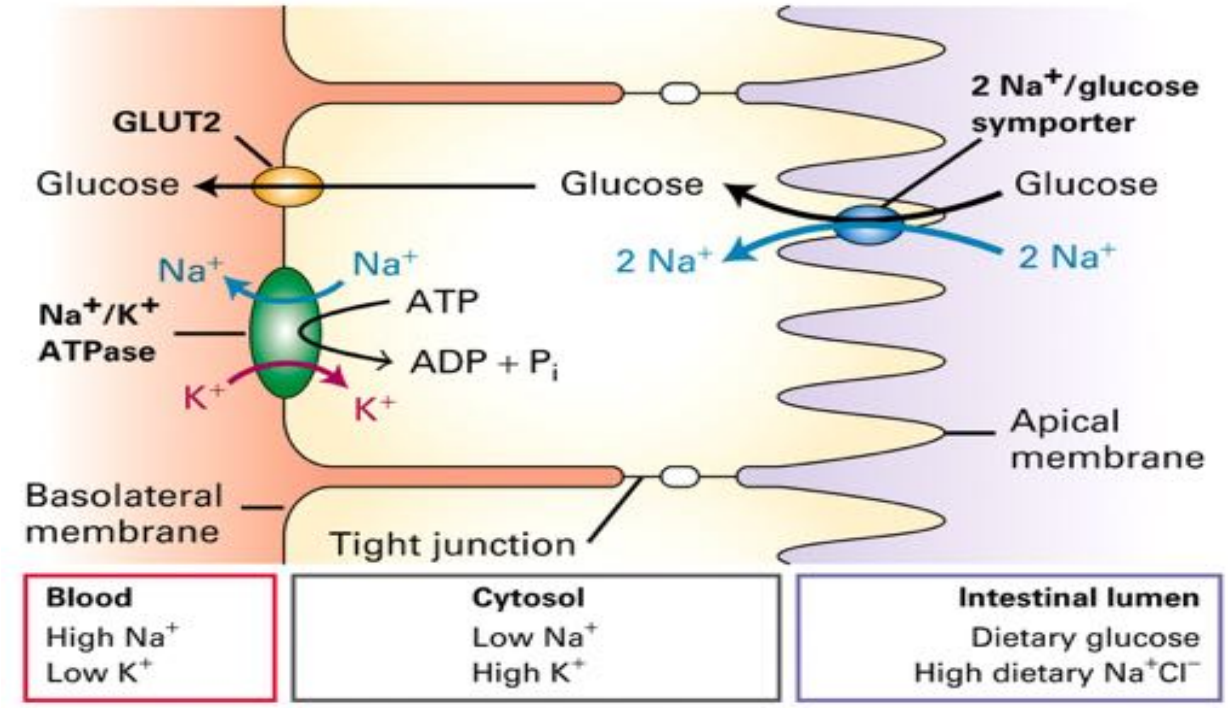
→ antiport



Co-transport : animation



example : Oralit - Pocari

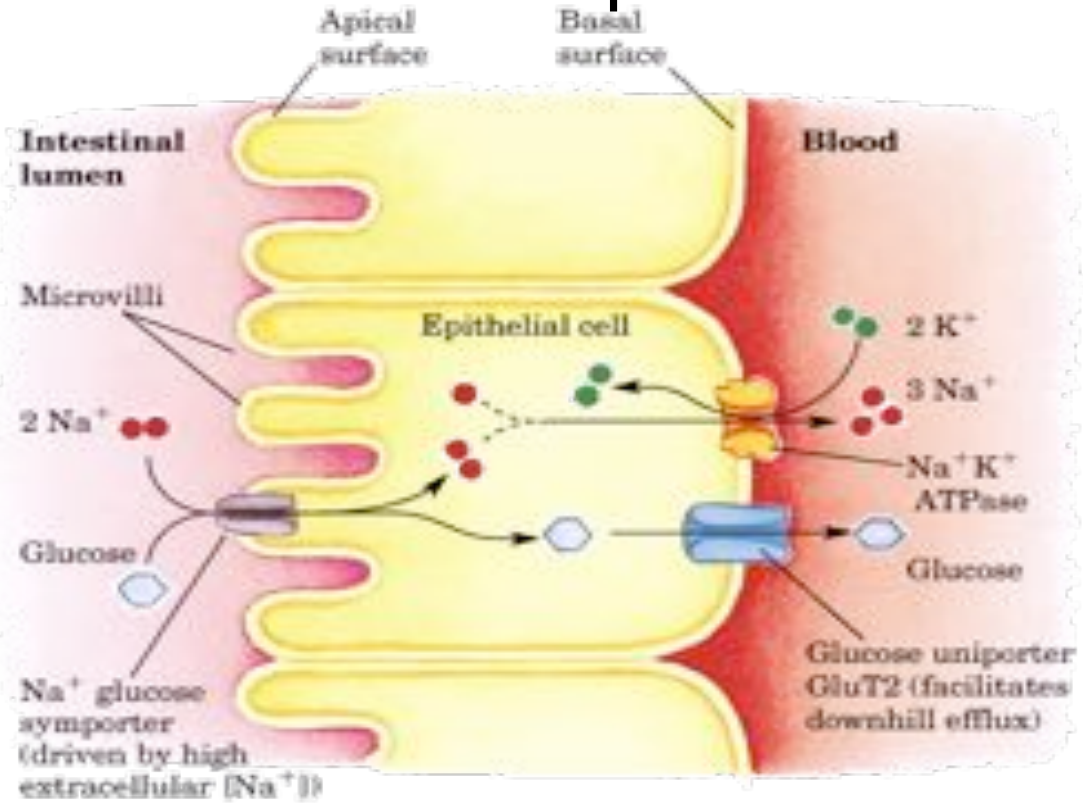


Oralit & pocari contains sugar and Na+ that can avoid the body from dehydration → because always induce water uptake

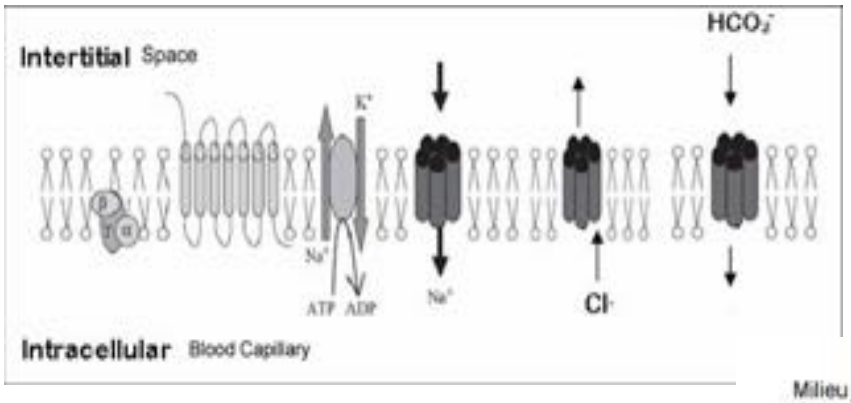
Oral Rehydration Salts and Ionic Drinks

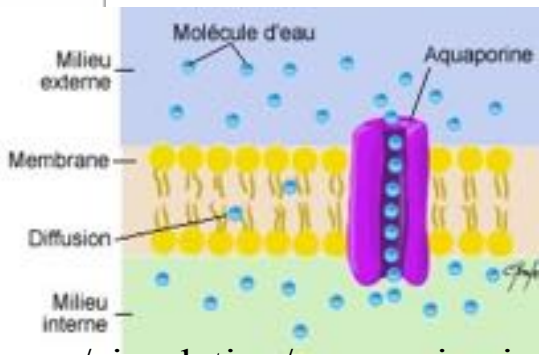
- General composition of ionic drinks: water, sugar, Sodium chloride (Na^+ dan Cl^-) , Kalium (K^+)
- Our body needs ions: (Na^+), (K^+), (Ca^{2+}), (Mg^{2+}), (Cl^-), (HPO_4^{2-}), dan (HCO_3^-)
- Ions cannot be produced by our body

Glucose uptake



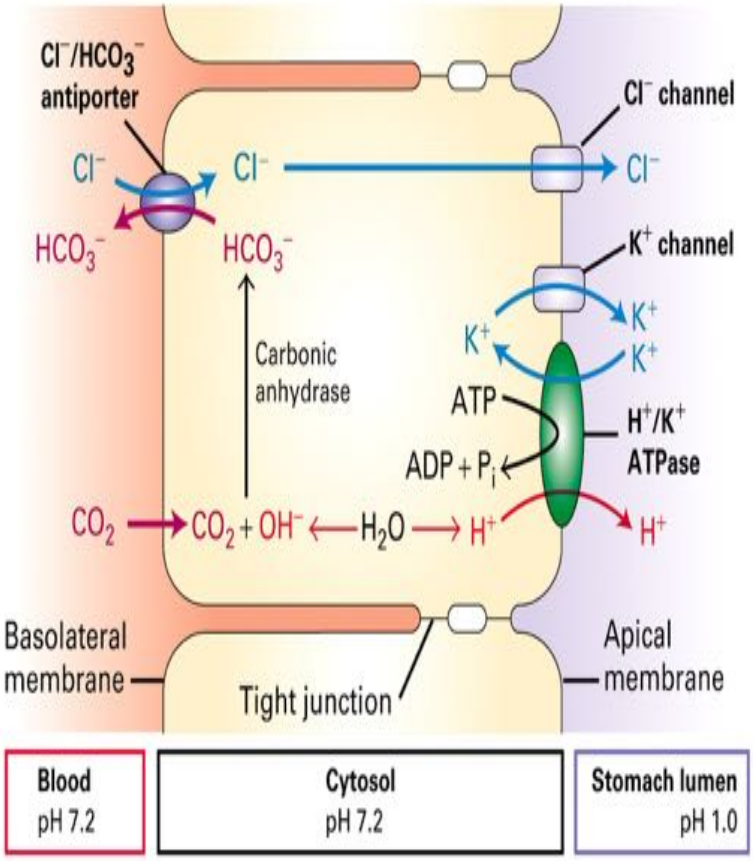
Mechanism in membrane Transport: intravenous





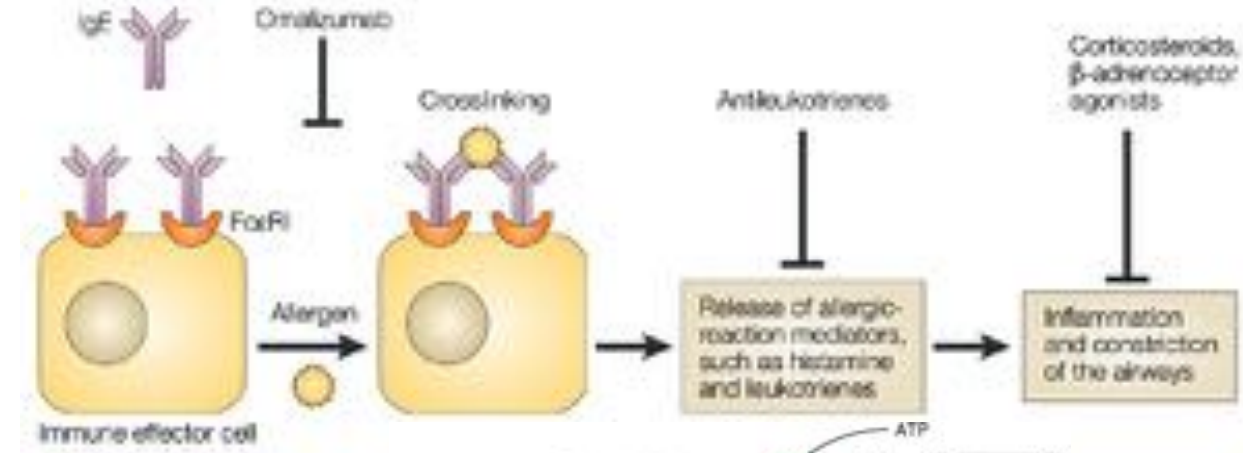
http://www.colfir.net/rof/chantal.proulx/images/circulation/aquaporine.jpg

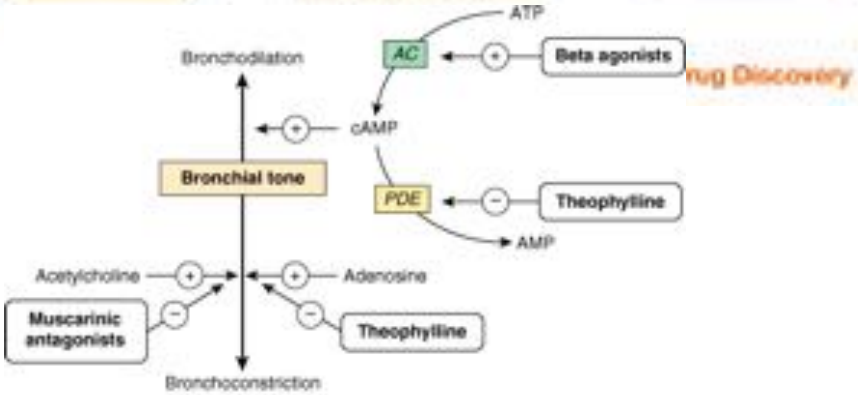
Mechanism HCl Secretion



- Hydrogen ions are formed from the dissociation of water molecules.
- Carbonic anhydrase converts CO_2 and water to HCO_3^- and H^+.
- HCO_3^- is exchanged for Cl^- on the basal side of the cell and HCO_3^- diffuses into the blood.
- K^+ and Cl^- ions diffuse into the canaliculi.
- Hydrogen ions are pumped out of the cell into the canaliculi in exchange for K^+, via the H+/K+ ATPase

Mechanism action of asthmatic drugs



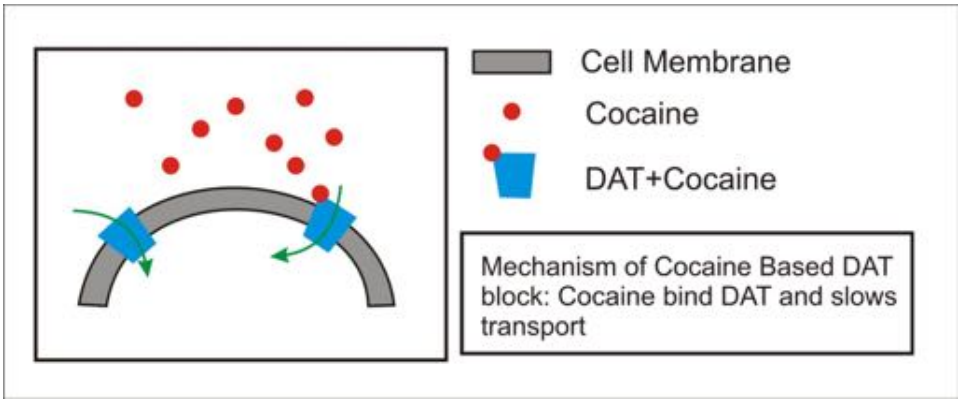


Various Anesthetic Drugs (and its mechanism)

Example: Cocaine

A stimulant of a central nervous system and appetite suppressant.

This drug binds to dopamine transporter protein → pre-synaptic neuron can't reuptake the dopamine from post-synaptic neuron → pre-synaptic neuron will in polarization state.



Example: gas across the membrane: Viagra →NO → plasma membrane of blood vessel → relaxation of blood vessel

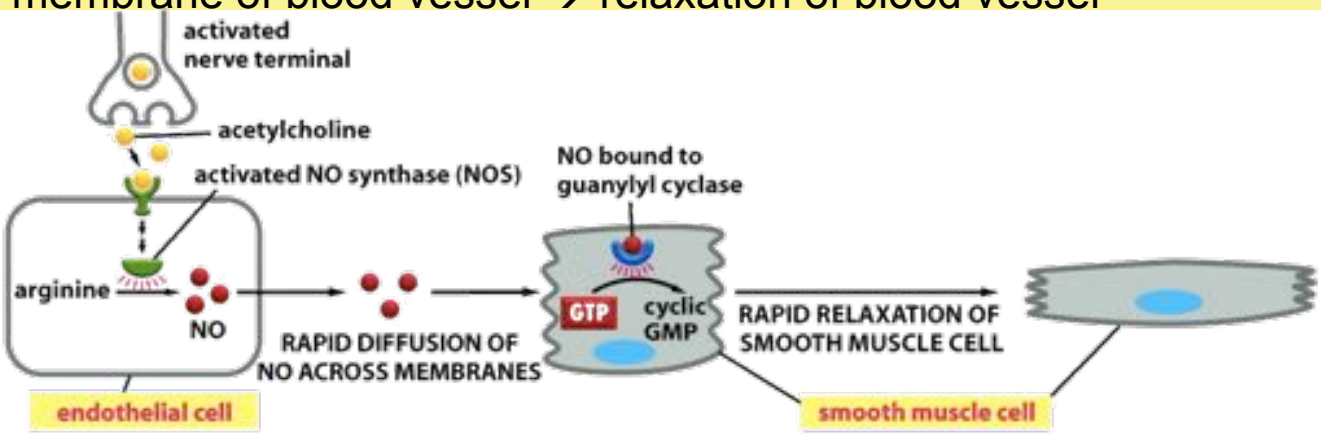


Figure 15-12b Molecular Biology of the Cell 5/e (© Garland Science 2008)

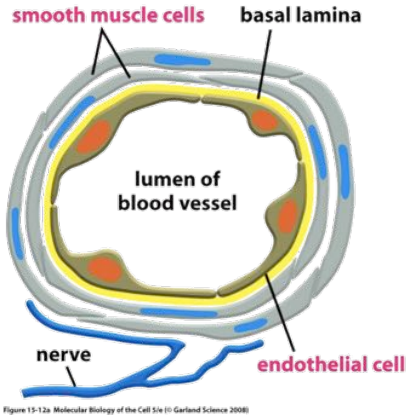
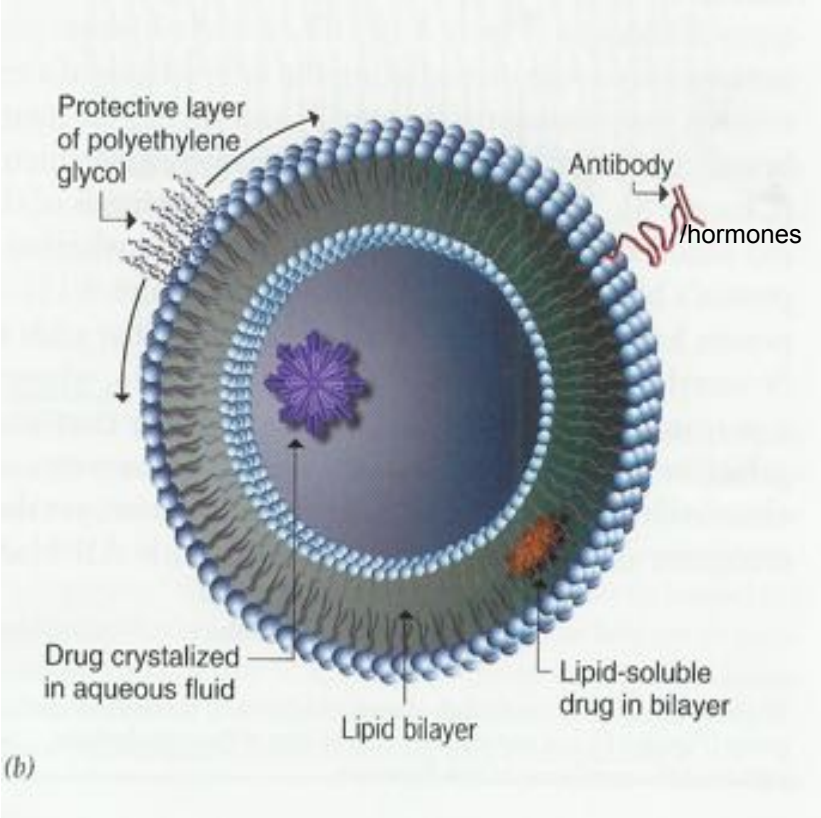


Figure 15-12a Molecular Biology of the Cell 5/e (© Garland Science 2008)

Application of Lipid membrane : liposome vesicle with diameter 40 – 100 nm, contains i.e. : anti-cancer drug(doxorubicin-sulfat), DNA



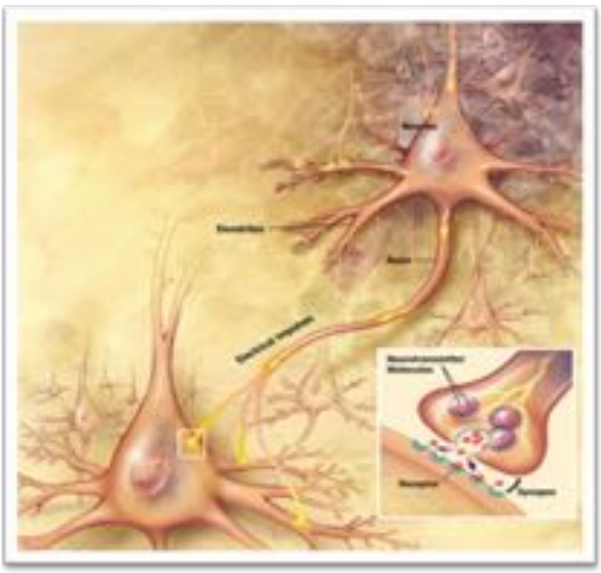
Liposomes can be formulated and processed to differ in size, composition, charge, and lamellarity and accordingly, a wide range of compounds may be incorporated into either the lipid or trapped aqueous space

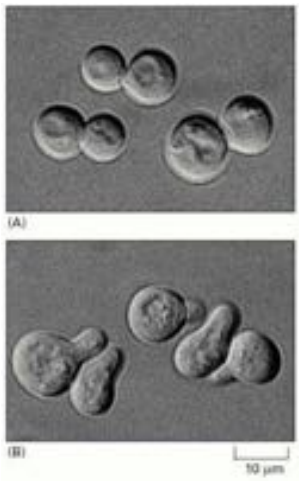
The biodegradable and non-toxic nature of phospholipid vesicles proposes that these formulations are amenable to administration without serious side effects

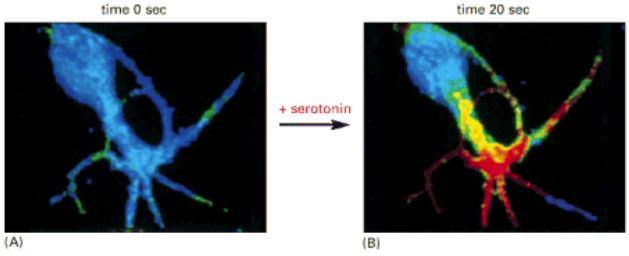
Liposomes can alter the biodistribution of entrapped substances and protect the enclosed materials from inactivation by the host defense mechanisms.11 Therefore, liposomes can be used as vehicles to achieve specific delivery of therapeutic drugs to target organs. In addition, liposomes can reduce toxicity of antimicrobial, antiviral, and chemotherapeutic agents, and they have demonstrated the ability to modulate or potentiate the immunogenicity of antigenic substances

To enhance tissue targeting, liposome surface has been modified with antibodies or ligands recognized by specific cell types. To enhance the efficiency of gene delivery by the introduction of molecules directly into cells, virosomes have been developed by combining liposomes with fusiogenic viral envelope proteins. Liposomes are now being used in the treatment of intractable human diseases such as cancer and monogenic disorders

Cell Communication







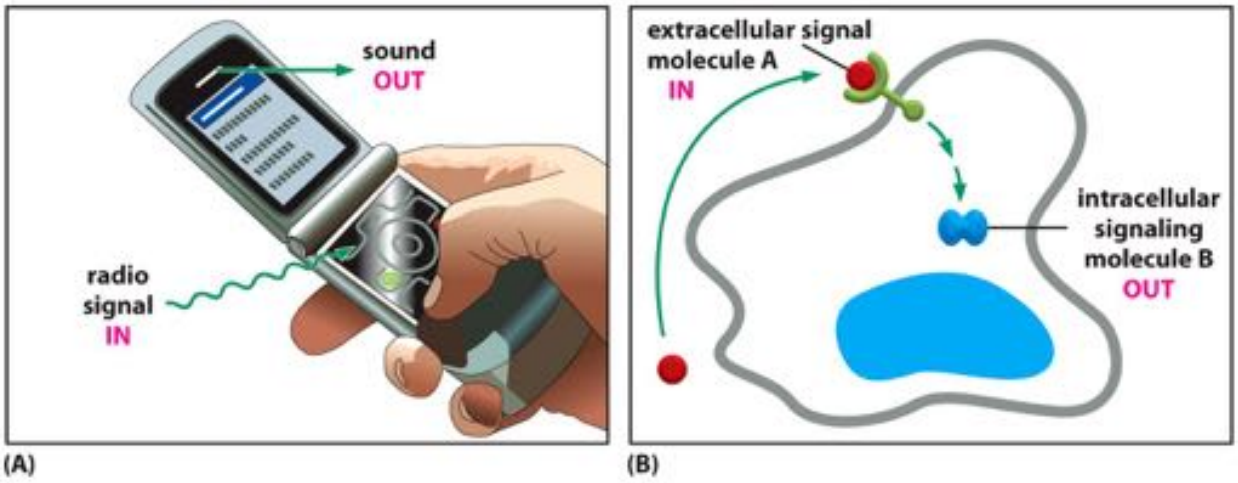


Figure 16-2 *Essential Cell Biology* (© Garland Science 2010)

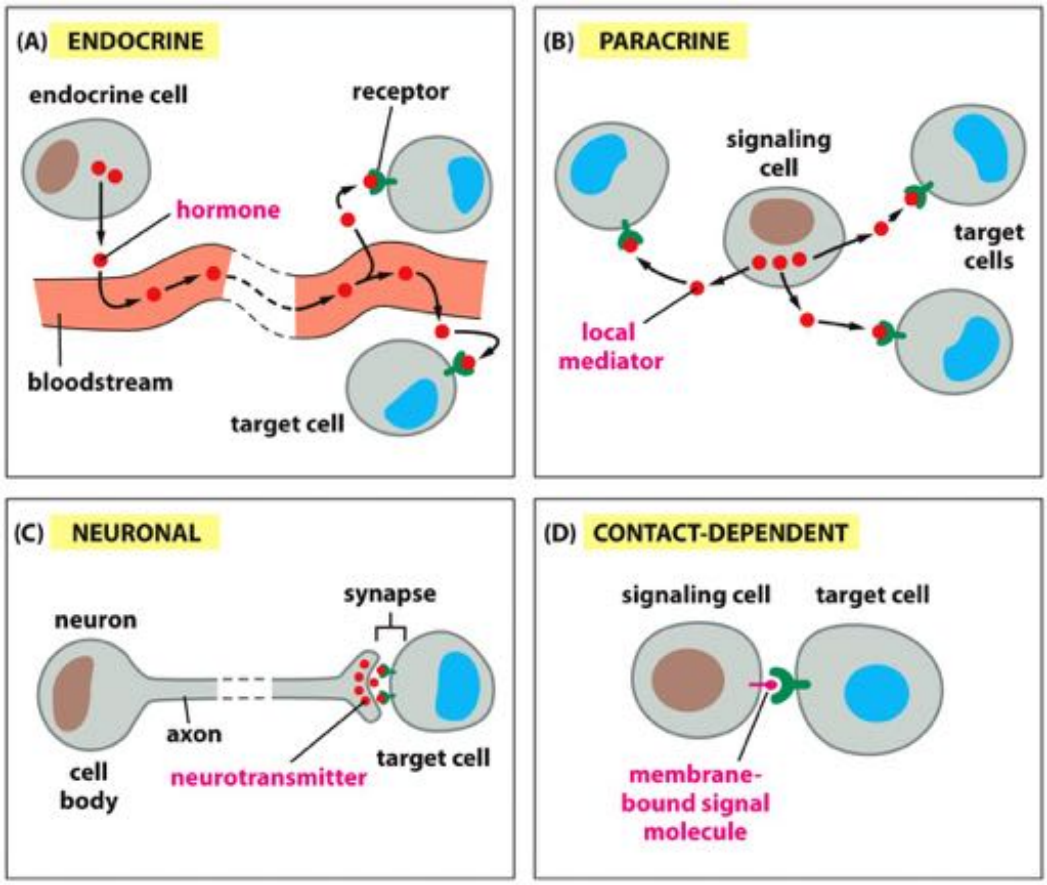


Figure 16-3 *Essential Cell Biology* (© Garland Science 2010)

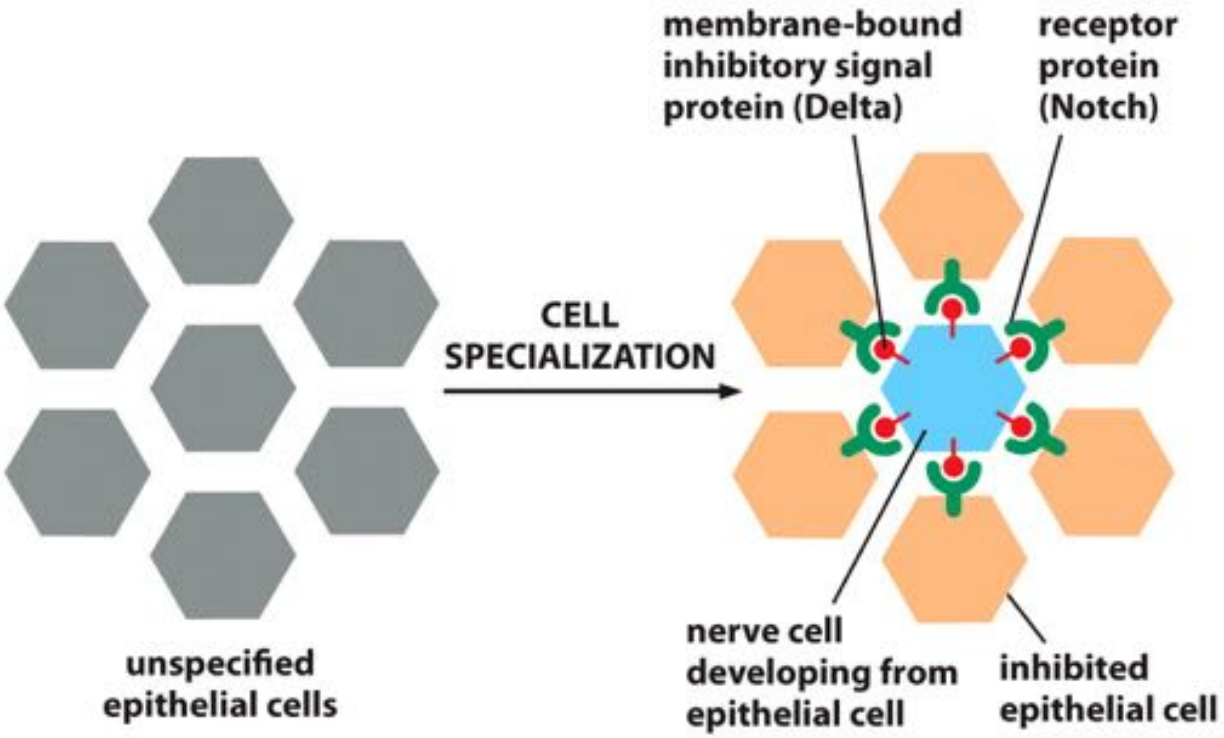


Figure 16-4 *Essential Cell Biology* (© Garland Science 2010)

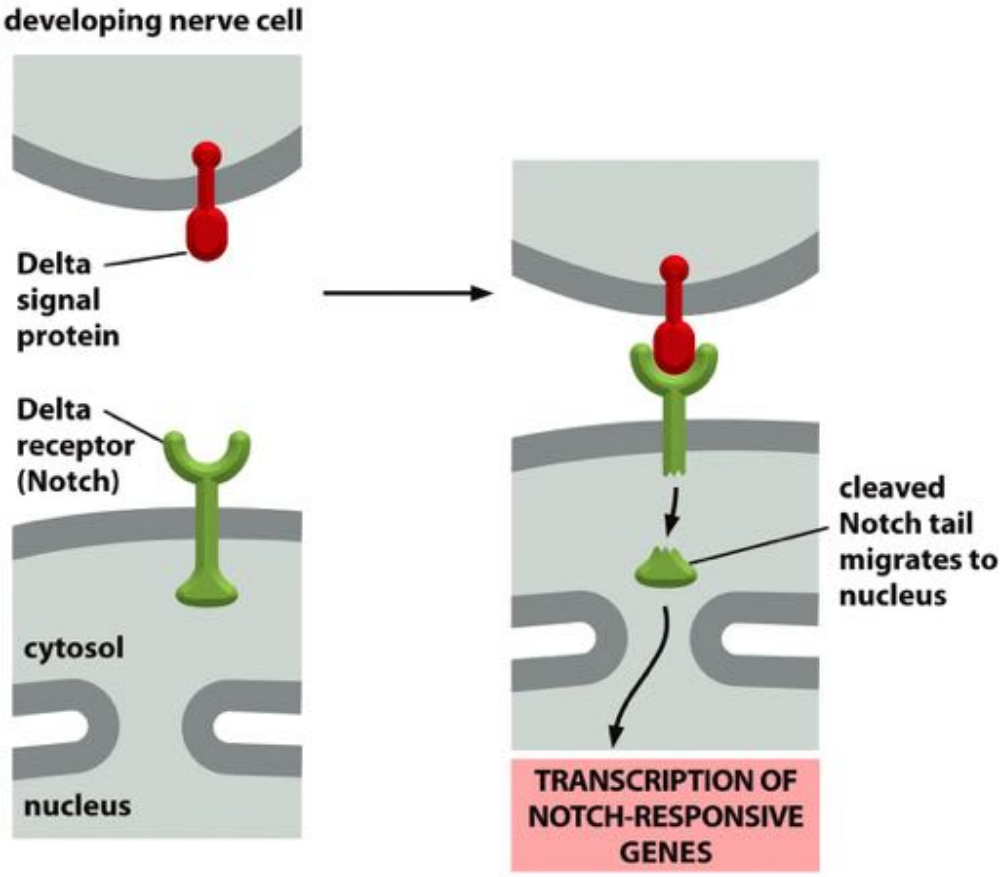


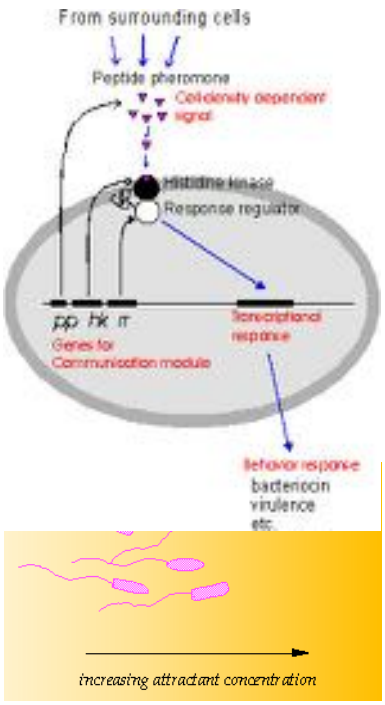
Figure 16-40 *Essential Cell Biology* (© Garland Science 2010)

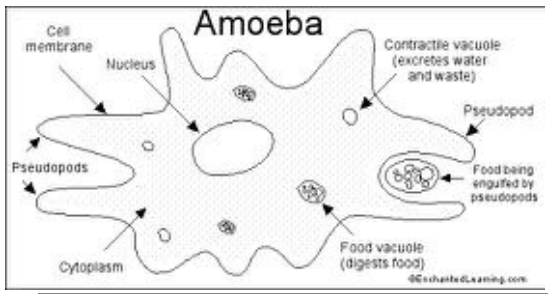
Cellular Signaling

- an organism does involves communication (signaling) among cells
  - e.g., Sensing the environment, moving, digesting food
- Cell-to-cell communication ~ cellular internet
  - Is essential for multicellular organisms
  - Cells must signal, receive, interpret and respond to chemical signals secreted by other cells
  - Ex: Embryonic development & hormone action rely on Cell-Cell communication.
- *Cell signaling* – communication between cells
  - Signaling cell: sends a signal (usually chemical)
  - Target cell: receives the signal

Cell Signaling

- Signaling in bacteria
  - •Bacteria can respond to their environment
  - •Chemotaxis, phototaxis etc.
- Other single cells - receptor

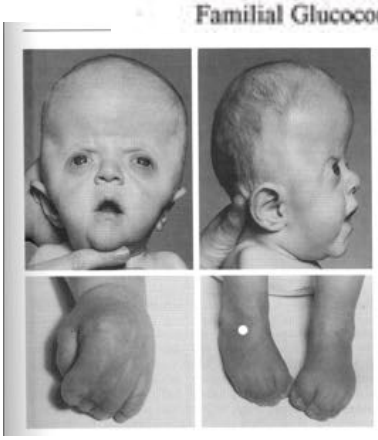




Without the cell surface receptors, the amoeba will not find where the food is

RECEPTOR DISEASES

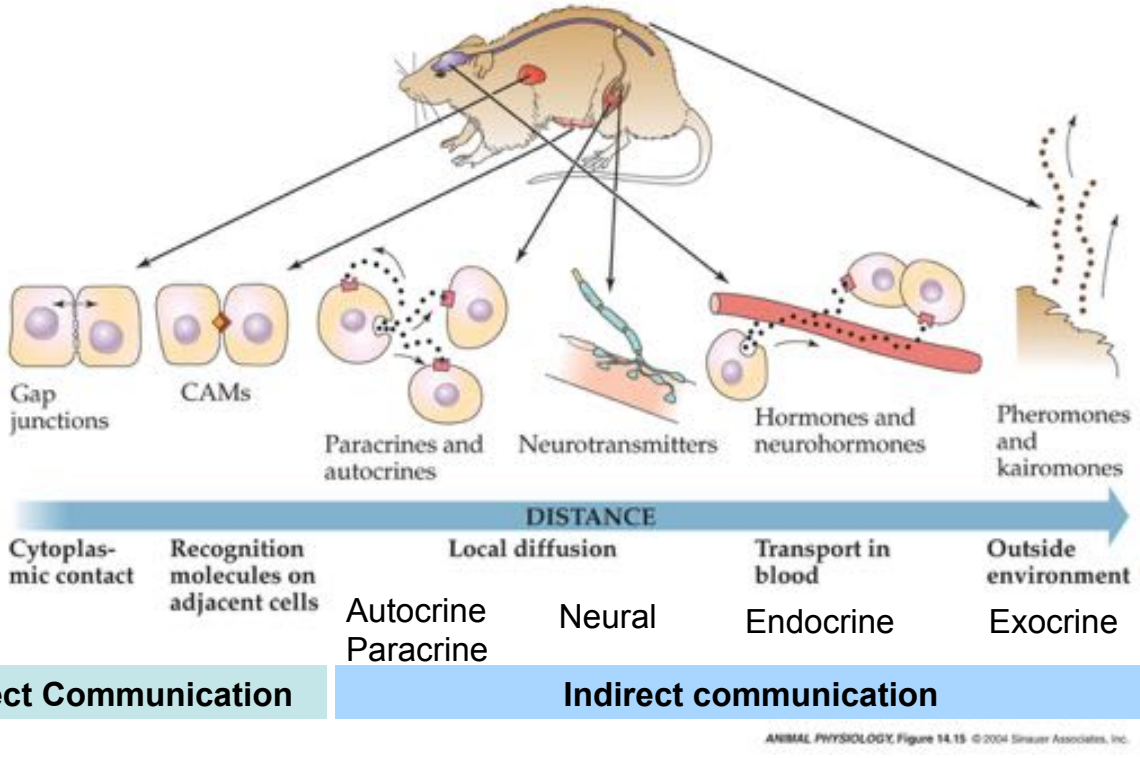
DISEASE	RECEPTOR DYSFUNCTION
Testicular feminization, pseudohermaphoditism	Testosterone Receptor
Graves Disease	Thyroid Receptor
Leprechaunism, Insulin-resistant Diabetes, Rabson-Mendenhall Syndrome	Insulin Receptor
Familial Hypercholesterolemia, Coronary Heart Disease	LDL-Receptor
Myasthenia Gravis	Acetylcholine Receptor
Cystic Fibrosis	GABA Receptor/Chloride Channel
Dysautonomia, Asthma?	Adrenergic Receptor
Schizophrenia, Parkinson's Disease	Dopamine Receptor
Color Blindness	Red/Green Cone Opsins
Retinitis Pigmentosa	Rhodopsin
Nephrogenic Diabetes Insipidus	V2 Vasopressin Receptor
Familial Glucocorticoid Deficiency	ACTH Receptor



Apert Syndrome

- D2-D3 FGFR2 linker mutations responsible for AS
- ~67% Ser252Trp
  32% Pro253Arg
- Severe limb phenotype

Signaling in multicellular organisms



Direct communication

- In local signaling, animal cells
  - May communicate via direct contact

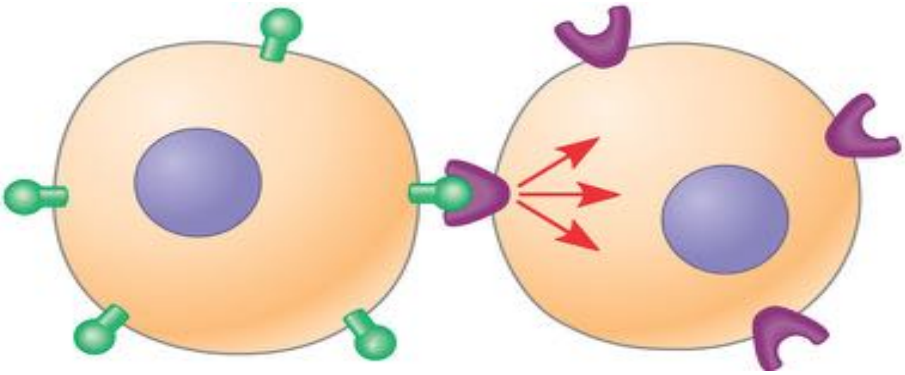
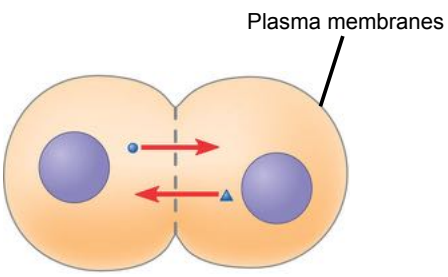


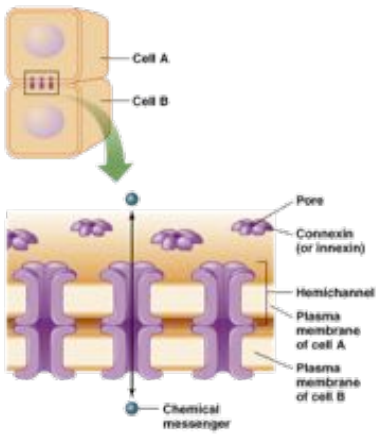
Figure 11.3(b) Cell-cell recognition. Two cells in an animal may communicate by interaction between molecules protruding from their surfaces.

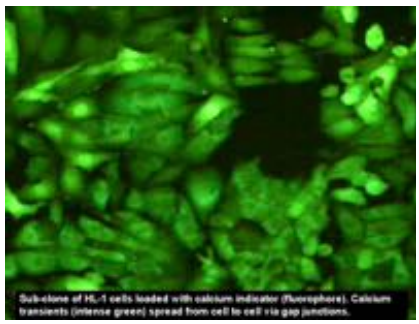
Direct Contact – Cell Junctions

- Animal cells
  - Have cell junctions that directly connect the cytoplasm of adjacent cells (Diffusion)
  - Gap junctions allow signaling information to be shared by neighboring cells : Ca2+, cAMP etc. but not for proteins or nucleic acids, Intracellular electrodes, small water-soluble dyes



(a) Cell junctions. animals cells have cell junctions that allow molecules to pass readily between adjacent cells without crossing plasma membranes.

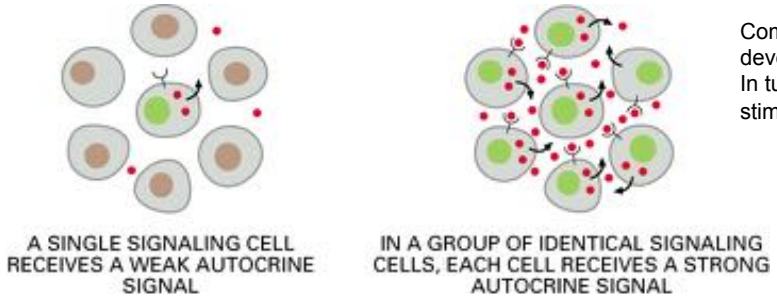




- Allows *Hydrophilic* chemical messengers to travel across the hydrophobic lipid membrane
- Signaling molecules are often ions

Indirect communication-Local regulation

- Autocrine
  - Cellular self-signaling
  - Autocrine signaling can coordinate decision by groups of identical cells

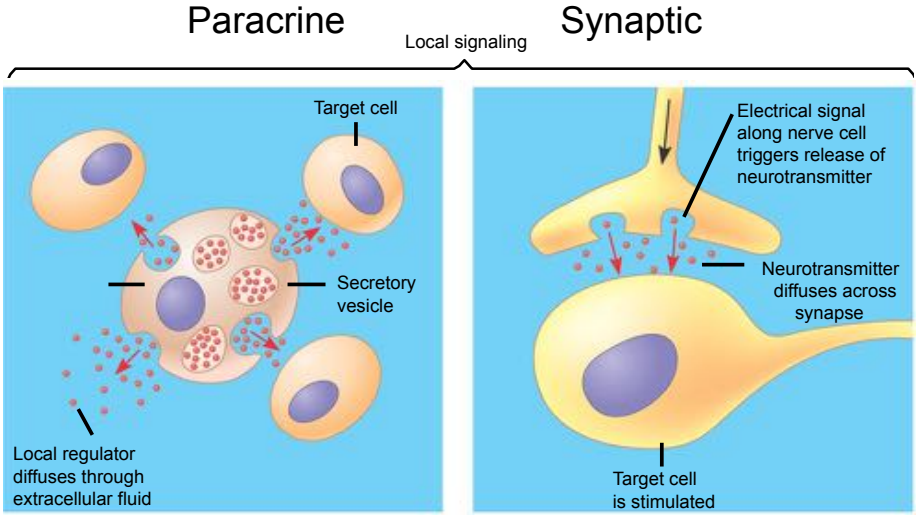


Community effect" in early development
In tumor biology---cancer cells stimulate their own proliferation

- Paracrine
  - Features most similar to endocrine signaling
  - Major difference
    - Target cell found in the same tissue
    - Messenger molecules carried across extra-cellular matrix or through extra-cellular fluid
    - Many growth factors are associated with the matrix

Local Regulation

- In other cases, animal cells communicate using local regulators.

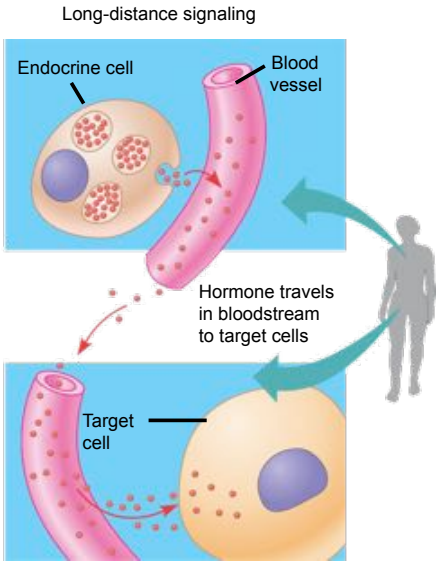


(a) Paracrine signaling. A secreting cell acts on nearby target cells by discharging molecules of a local regulator (a growth factor, for example) into the extracellular fluid.

(b) Synaptic signaling. A nerve cell releases neurotransmitter molecules into a synapse, stimulating the target cell.

Long Distance Signaling

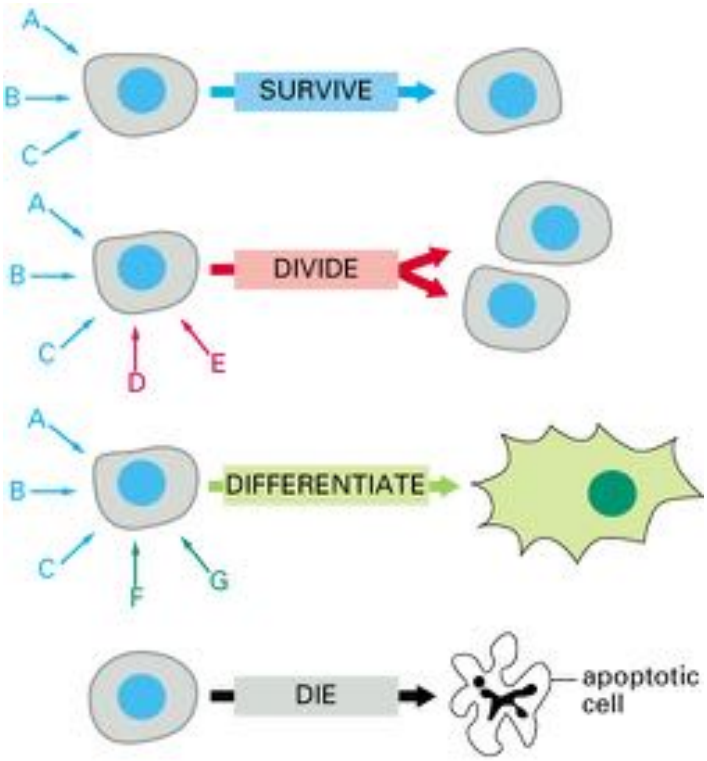
- Endocrine
  - Cells producing signaling factors are physically separated
  - Messenger molecules are secreted
  - Carried in blood or extra-cellular fluid
  - Target Cells
    - Membrane receptors
      - Intracellular actions via signal cascade
    - Cytoplasmic receptors
      - Usually a specific transport system to move signal molecule-receptor complex to nucleus – *response element*
    - Ex: Insulin



(c) Hormonal signaling. Specialized endocrine cells secrete hormones into body fluids, often the blood. Hormones may reach virtually all body cells.

Figure 11.4 C

Each cell is programmed to respond to specific combinations of extracellular signal molecules



Different cells can respond differently to the same extracellular signal molecules

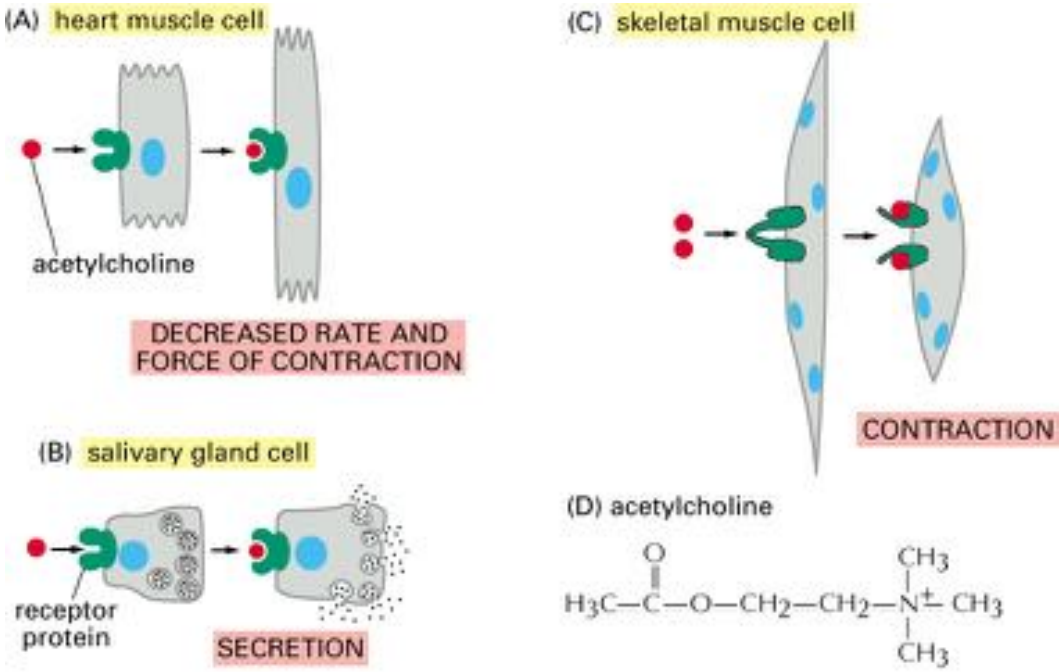


TABLE 16–1 SOME EXAMPLES OF SIGNAL MOLECULES

SIGNAL MOLECULE	SITE OF ORIGIN	CHEMICAL NATURE	SOME ACTIONS
Hormones			
Adrenaline (epinephrine)	adrenal gland	derivative of the amino acid tyrosine	increases blood pressure, heart rate, and metabolism
Cortisol	adrenal gland	steroid (derivative of cholesterol)	affects metabolism of proteins, carbohydrates, and lipids in most tissues
Estradiol	ovary	steroid (derivative of cholesterol)	induces and maintains secondary female sexual characteristics
Glucagon	α cells of pancreas	peptide	stimulates glucose synthesis, glycogen breakdown, and lipid breakdown, e.g., in liver and fat cells
Insulin	β cells of pancreas	protein	stimulates glucose uptake, protein synthesis, and lipid synthesis, e.g., in liver cells
Testosterone	testis	steroid (derivative of cholesterol)	induces and maintains secondary male sexual characteristics
Thyroid hormone (thyroxine)	thyroid gland	derivative of the amino acid tyrosine	stimulates metabolism of many cell types

Table 16-1 (part 1 of 2) *Essential Cell Biology* (© Garland Science 2010)

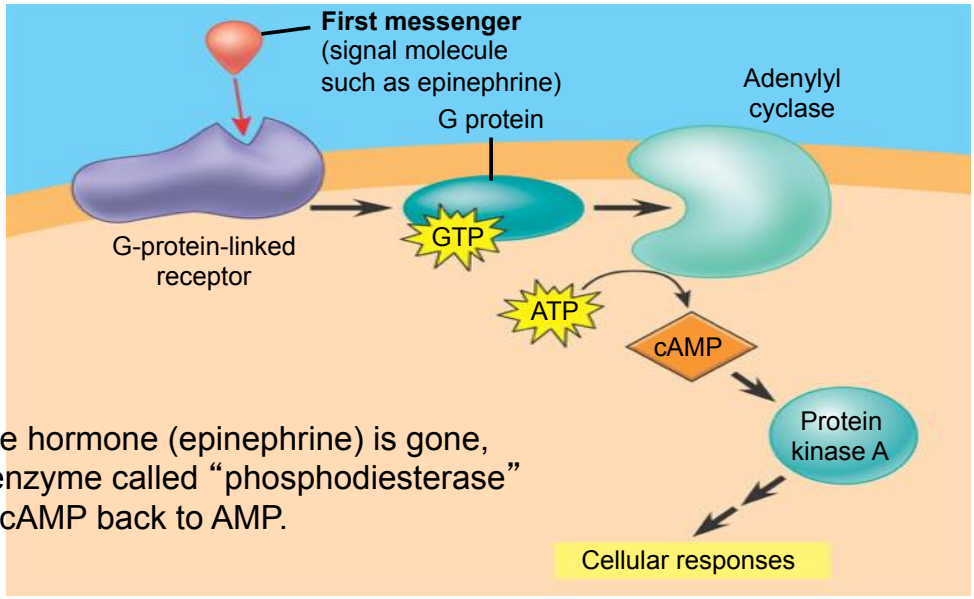
TABLE 16–1 SOME EXAMPLES OF SIGNAL MOLECULES

SIGNAL MOLECULE	SITE OF ORIGIN	CHEMICAL NATURE	SOME ACTIONS
Local Mediators			
Epidermal growth factor (EGF)	various cells	protein	stimulates epidermal and many other cell types to proliferate
Platelet-derived growth factor (PDGF)	various cells, including blood platelets	protein	stimulates many cell types to proliferate
Nerve growth factor (NGF)	various innervated tissues	protein	promotes survival of certain classes of neurons; promotes growth of their axons
Transforming growth factor-β (TGF-β)	many cell types	protein	inhibits cell proliferation; stimulates extracellular matrix production
Histamine	mast cells	derivative of the amino acid histidine	causes blood vessels to dilate and become leaky, helping to cause inflammation
Nitric oxide (NO)	nerve cells; endothelial cells lining blood vessels	dissolved gas	causes smooth muscle cells to relax; regulates nerve cell activity
Neurotransmitters			
Acetylcholine	nerve terminals	derivative of choline	excitatory neurotransmitter at many nerve–muscle synapses and in central nervous system
γ-Aminobutyric acid (GABA)	nerve terminals	derivative of the amino acid glutamic acid	inhibitory neurotransmitter in central nervous system
Contact-dependent Signal Molecules			
Delta	prospective neurons; various other developing cell types	transmembrane protein	inhibits neighboring cells from becoming specialized in same way as the signaling cell

Table 16-1 (part 2 of 2) *Essential Cell Biology* (© Garland Science 2010)

Epinephrine (Adrenaline) stimulates G-Proteins

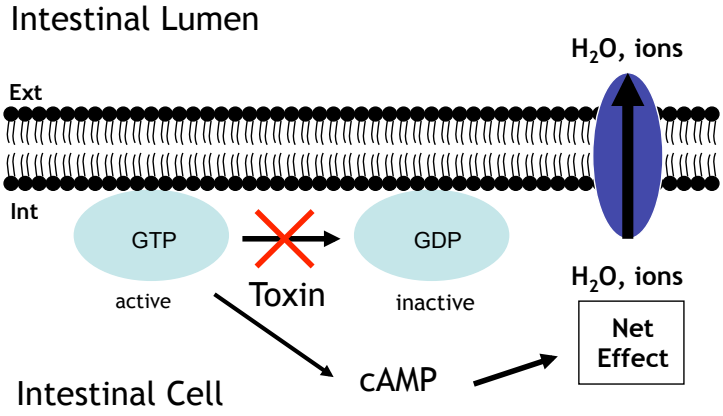
- Many G-proteins stimulate Adenylyl cyclase, which triggers the formation of cAMP, which then acts as a second messenger in cellular pathways

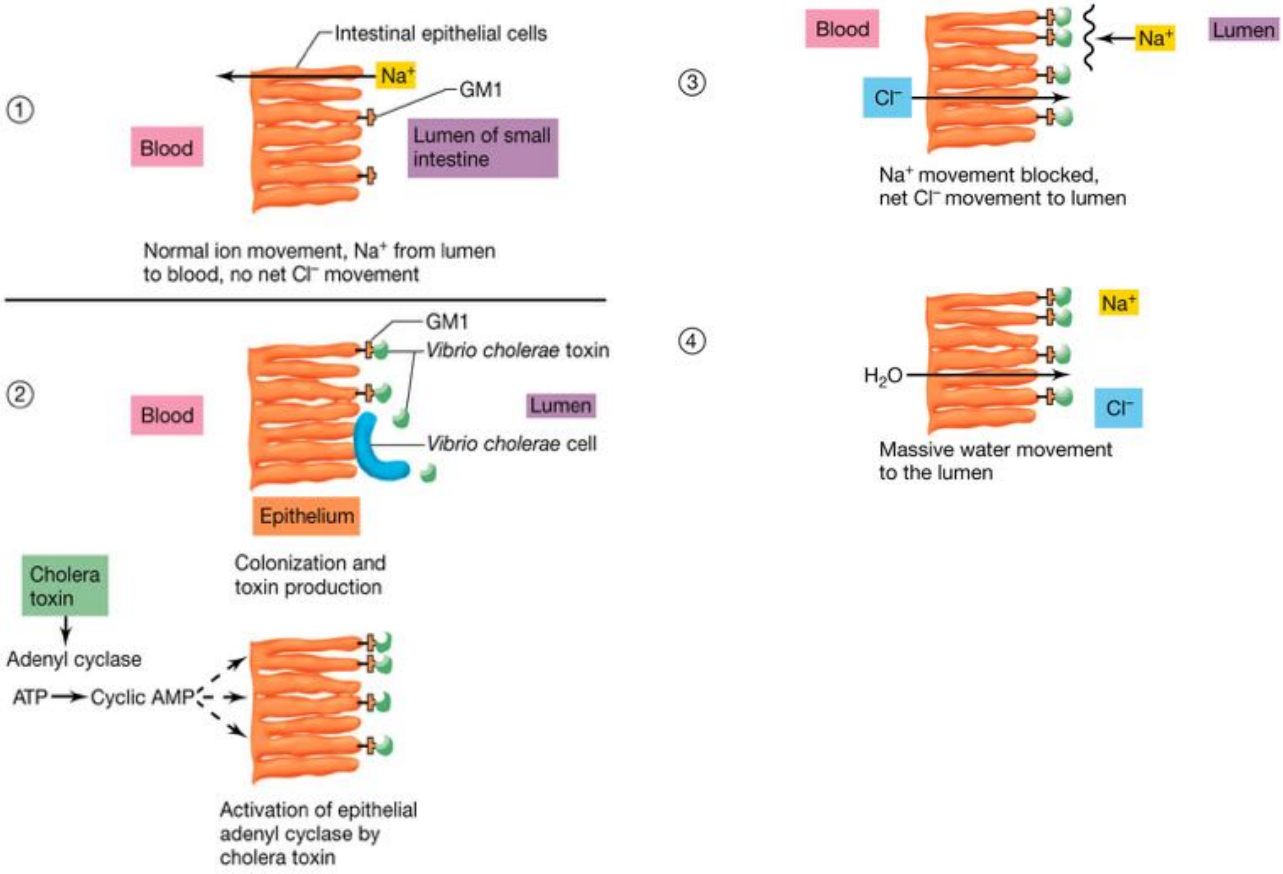


•When the hormone (epinephrine) is gone, another enzyme called “phosphodiesterase” converts cAMP back to AMP.

Microbial Diseases and Cell Signaling

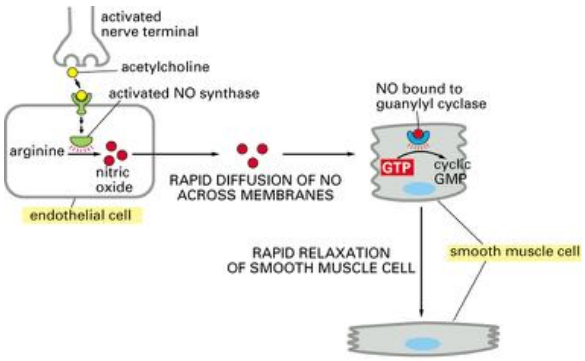
- Cholera bacterium (from contaminated water) gets into intestinal lining.
- Produces a toxin which is an enzyme that modifies a G-protein involved in salt and water secretion.
- The G-protein stays stuck inactivated from & cAMP concentration stays high, causing the cell to secrete large amounts of water & salts into the intestines (diarrhea)



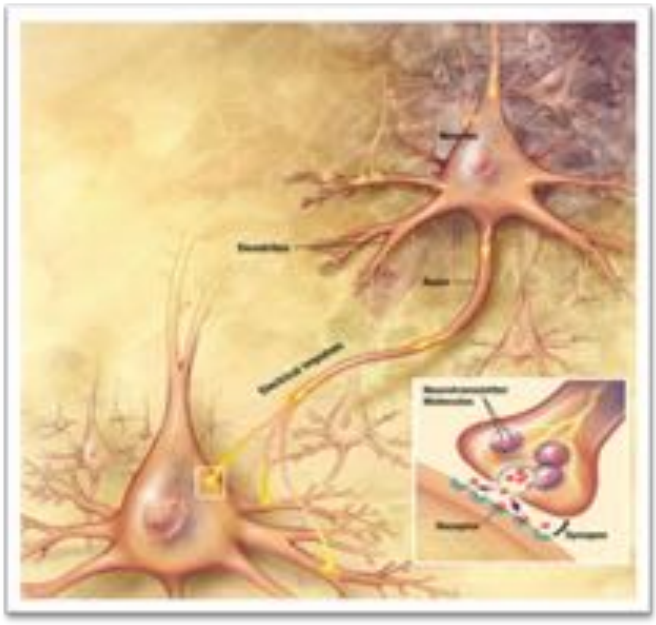


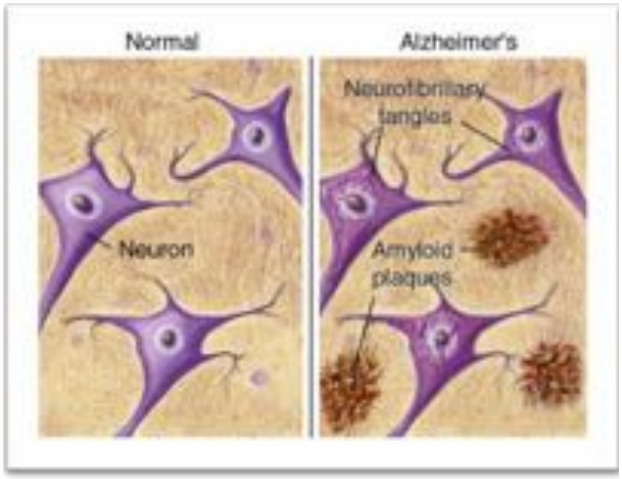
Another example of drugs affecting cell signaling

- cGMP is a compound that relaxes smooth muscles in arterial walls.
- A drug that inhibits the hydrolysis of cGMP to GMP (doesn't let cGMP get back to GMP) was found to prolongs the signal of relaxation of arteries, which increases blood flow to the heart.
- This drug was prescribed for chest pain.
- Now…used for E.D. (Viagra) *Think about it.
  - Ex: Viagra is an external signal from a chemical (drug) which leads to dilation of blood vessels (a response). Originally intended for heart patients.

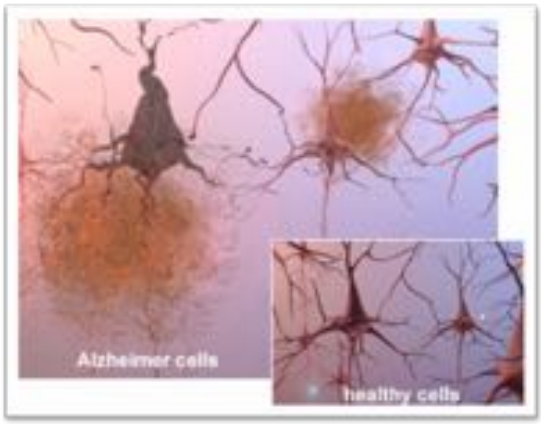


Normal Vs Alzheimer's

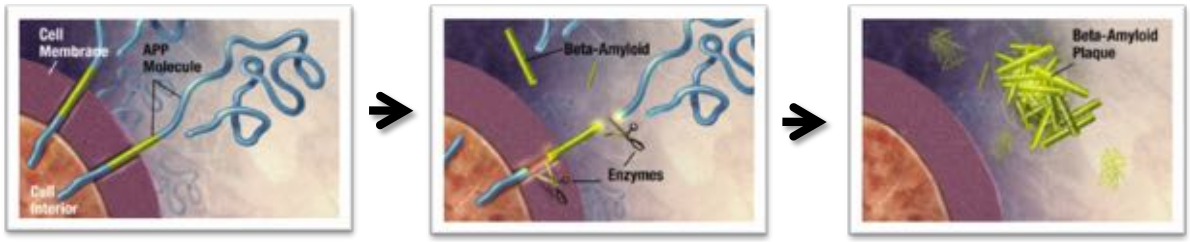


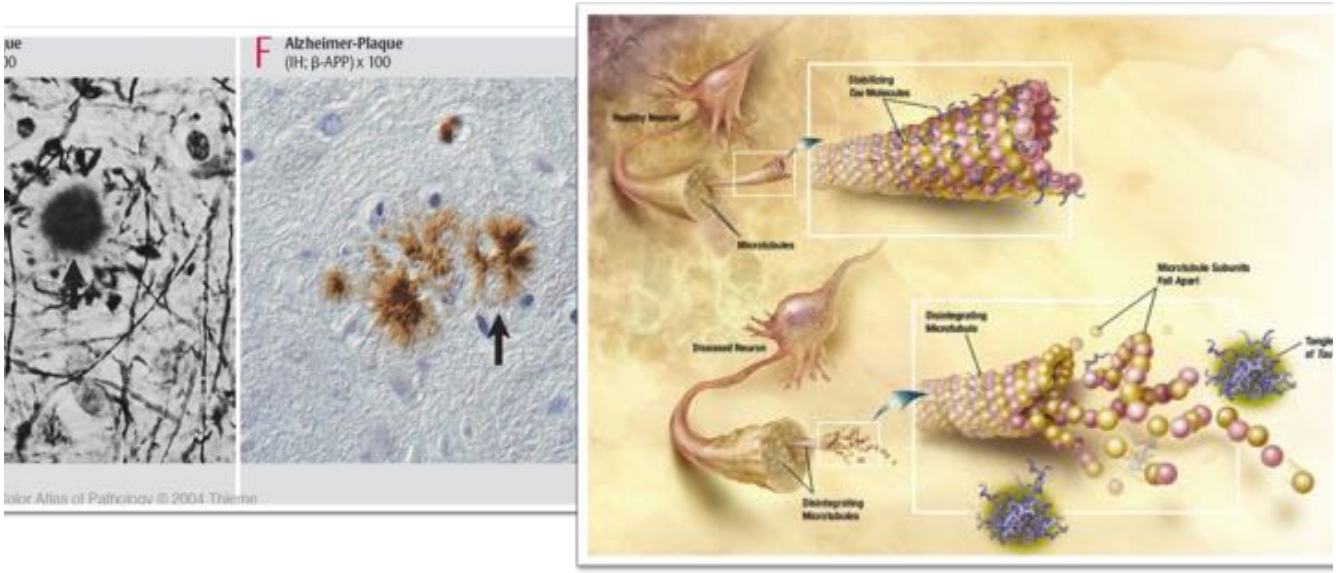


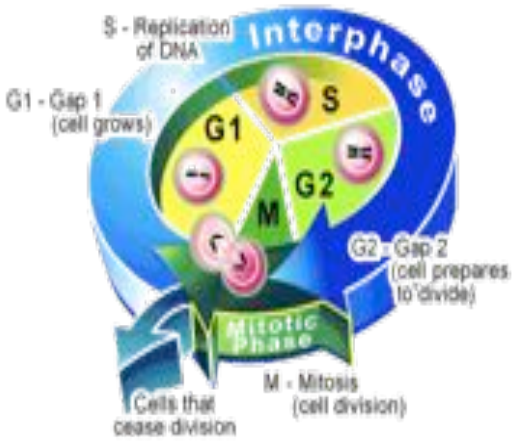
- To stay healthy, neurons (brain cells) must communicate with each other, carry out metabolism, and repair themselves.
- AD disrupts all three of these essential jobs.

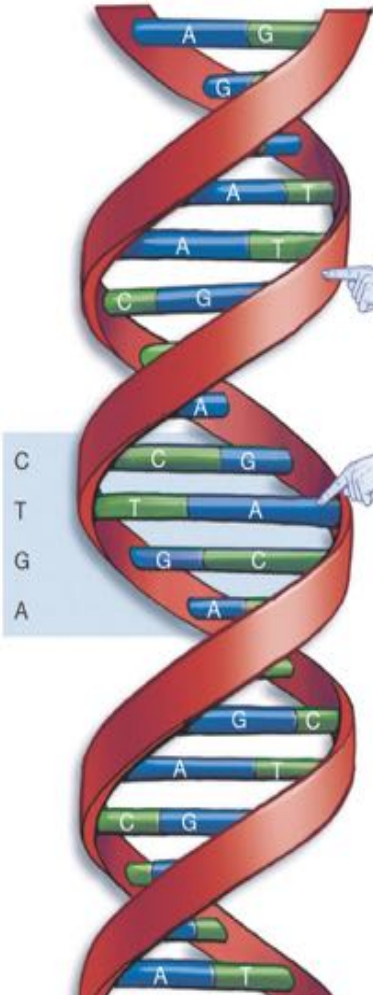


Beta Amyloid (Aβ) a protein fragment snipped from an amyloid precursor protein (APP).





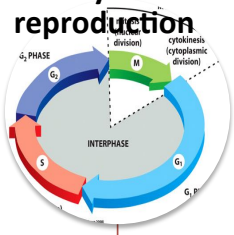




Cell reproduction and Cell cycle

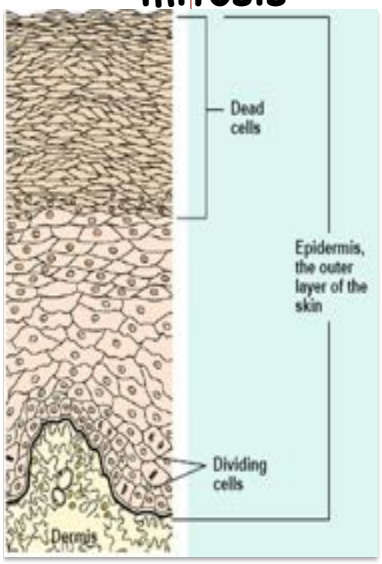
Eukaryotic cells divide in one of two ways

Eukaryotic cell reproduction



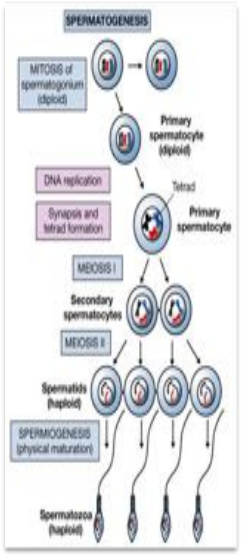
In eukaryotes, nuclei divide by either: mitosis or meiosis.

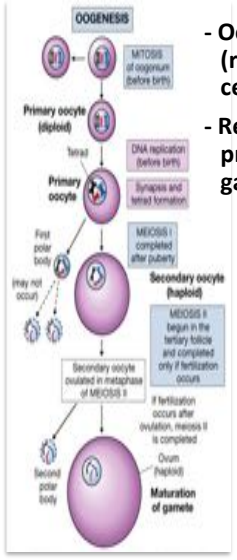
mitosis



- Occurs in somatic (nonreproductive) cells
- Asexual reproduction, development, growth and cell replacement are mitotic divisions

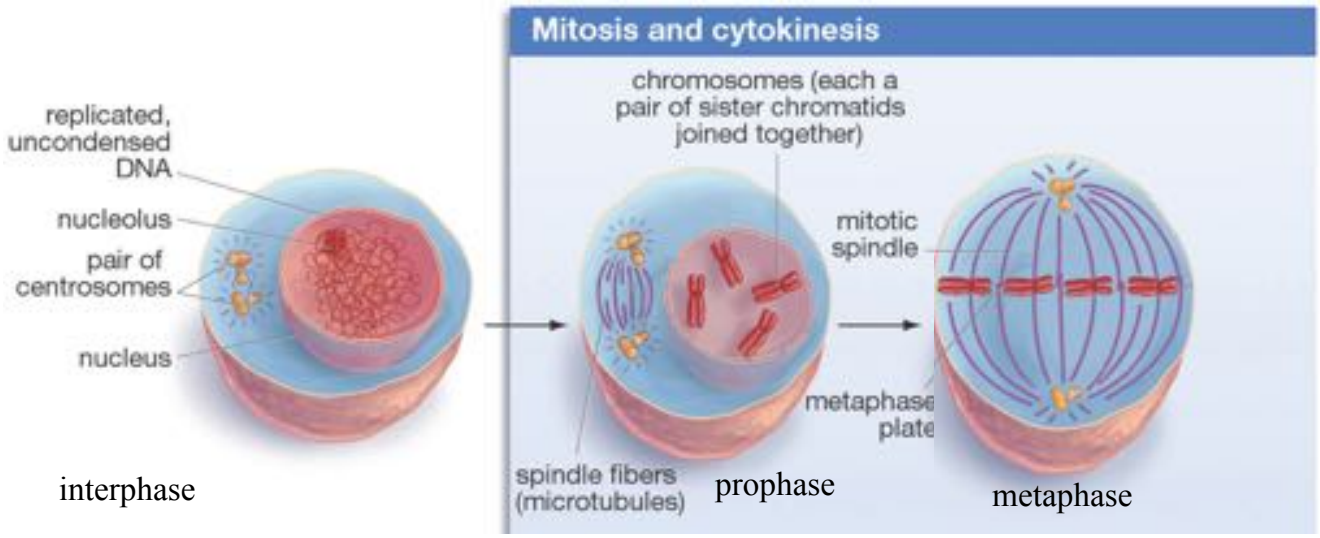
meiosis





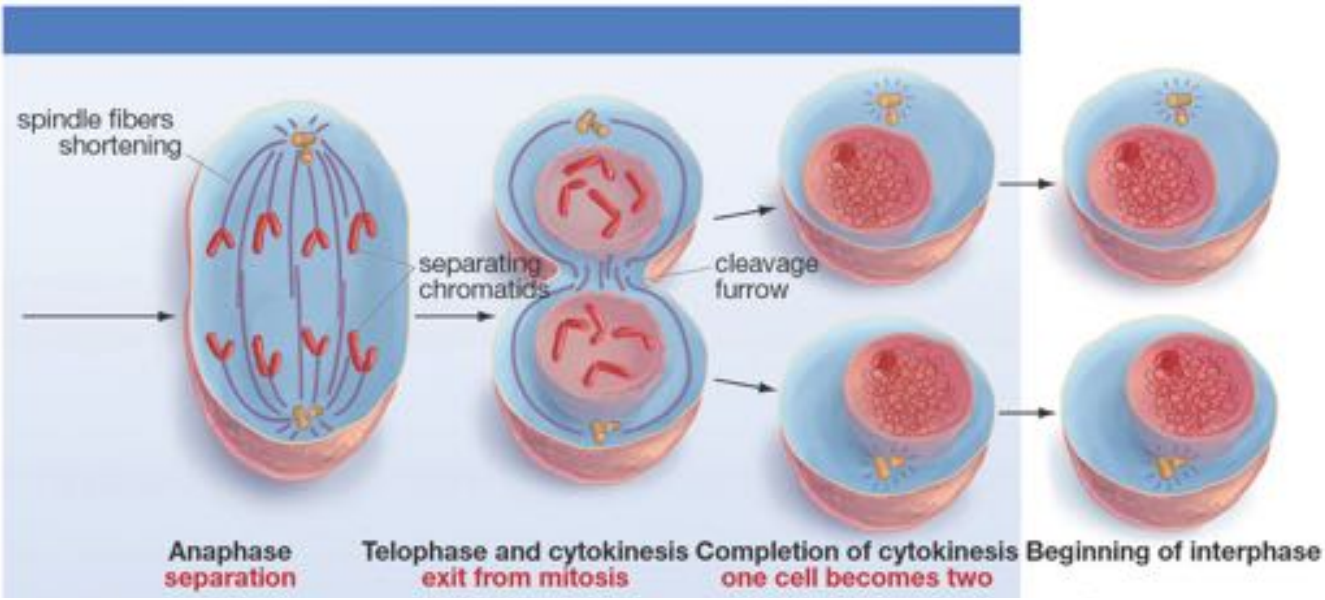
- Occurs in germ (reproductive) cells
- Results in the production of gametes

The Knit of Identity - Mitosis Precisely and Evenly Divides Duplicated Chromosomes

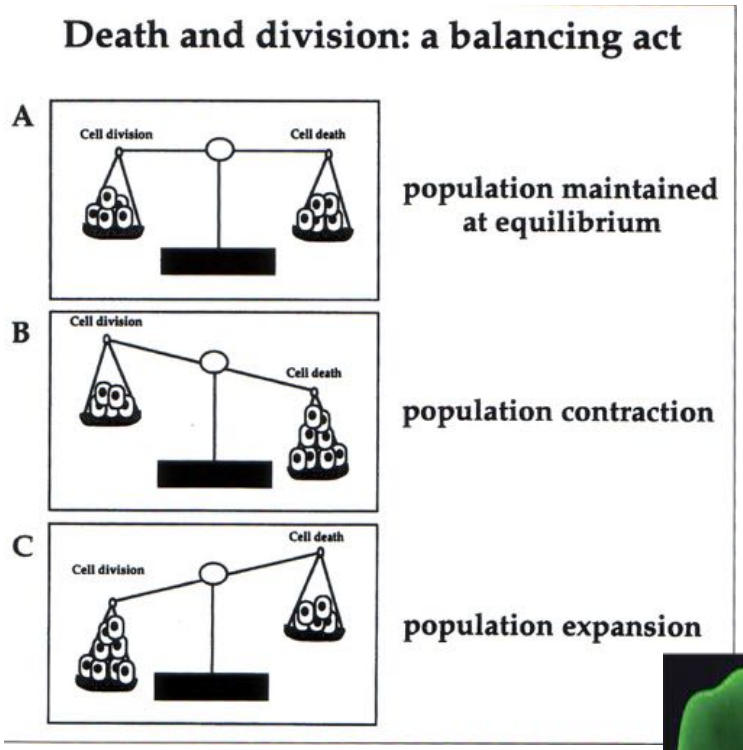


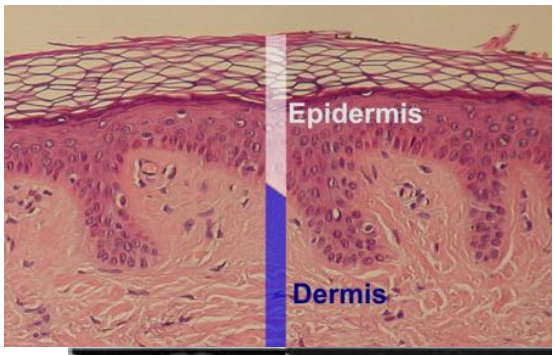
Precisely dividing the duplicated chromosomes has the consequence of providing each new cell with an identical and complete set of genetic instructions.

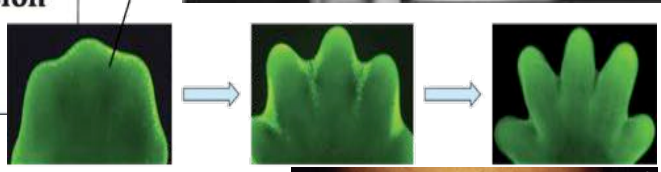
Mitosis Precisely and Evenly Divides Duplicated Chromosomes



Cytokinesis is the process of cell division and it is distinct and separable from mitosis. Cell division is necessary for reproduction, growth, and repair of an organism.

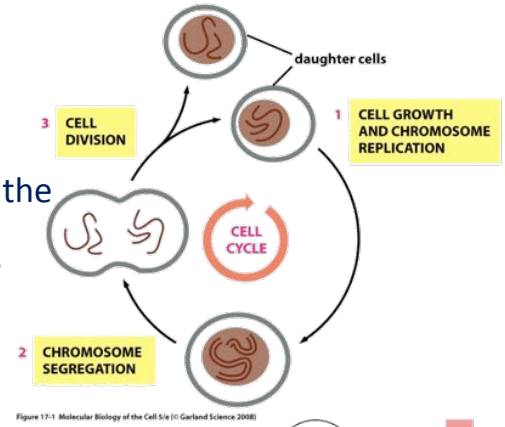






Programmed Cell death – apoptosis

Cell cycle



- The most basic function of the cell cycle is to **duplicate** accurately the vast amount of DNA in the chromosomes and then **segregate** the copies precisely into two genetically identical daughter cells.
- The eucaryotic cell cycle is divided into four sequential phases: G_1, **S**, G_2, and **M**.
- During most of the cell cycle, the cell is in interphase, which is divided into three subphases : S, G1, and G2.
- **two major** *phases* of the cell cycle: S and M
  1) **DNA duplication occurs during *S phase*** (S for synthesis)→ 10–12 hours (about half of the cell-cycle time in a typical mammalian cell).
  2) After S phase, **chromosome segregation and cell division occur in *M phase*** (M for *m*itosis)→less time (less than an hour in a mammalian cell). M phase involves a series of dramatic events that begin with nuclear division, or mitosis.

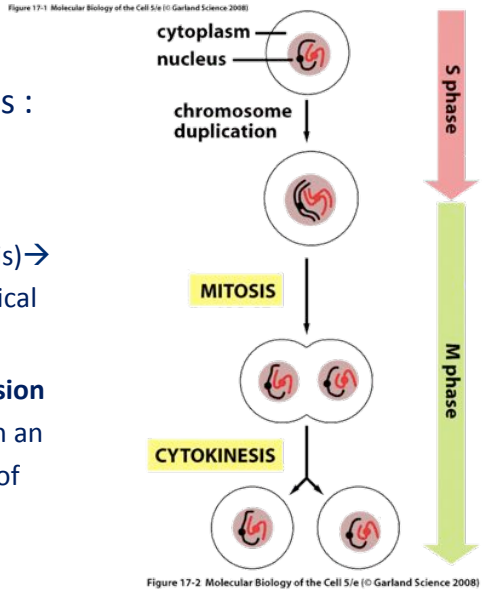


Figure 17-2 Molecular Biology of the Cell 5/e (© Garland Science 2008)

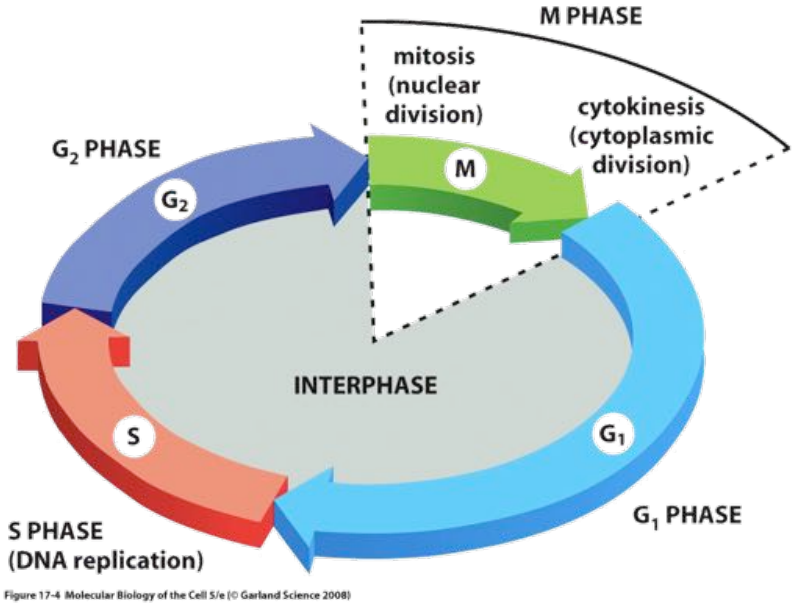
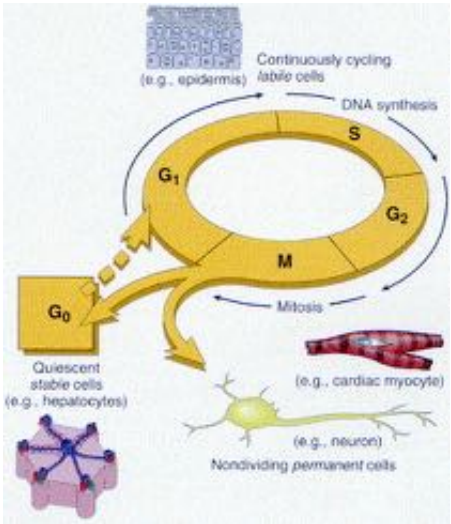


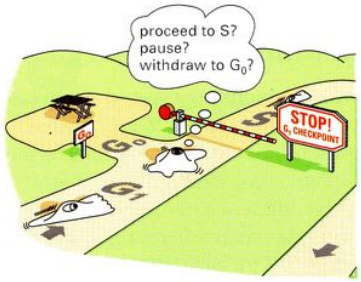
Figure 17-4 Molecular Biology of the Cell 5/e (© Garland Science 2008)

- Most cells require much more time to grow and double their mass of proteins and organelles than they require to replicate their DNA and divide.
- More time for growth → extra *gap phases* are inserted in cell cycles →a **G_1 phase** between M phase and S phase →a **G_2 phase** between S phase and mitosis.

Regulation of Cell Cycle

- Check points or switches control the rate of the cell cycle
- Intracellular and extracellular control
- G0 state is the resting state
- G1 checkpoint or the start checkpoint is said to be the beginning of the cell cycle.





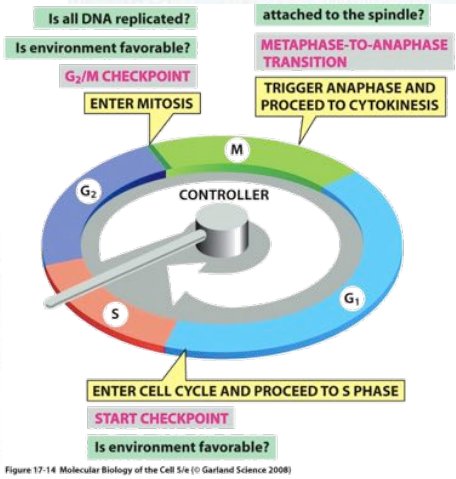
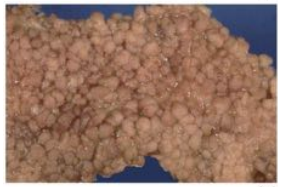


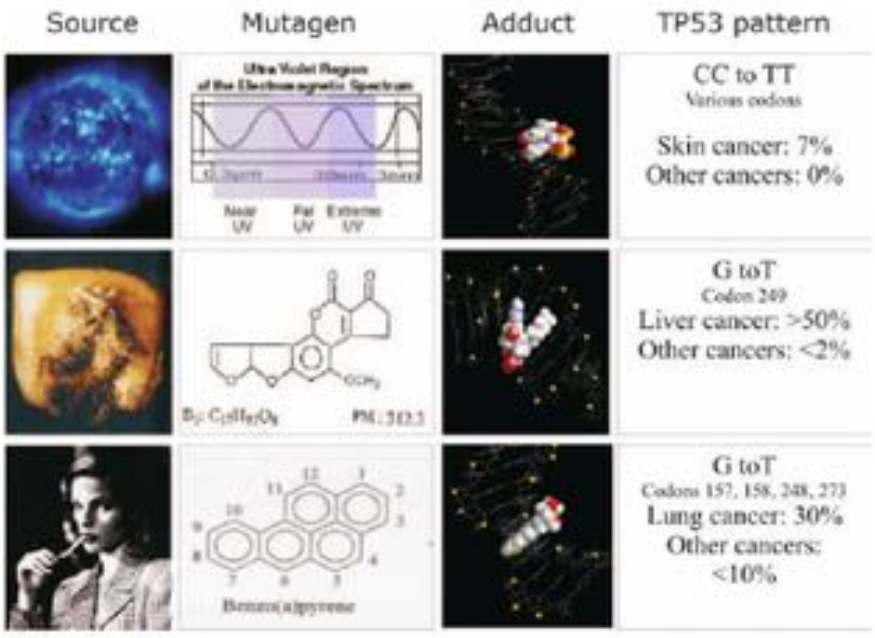
Figure 17-14 Molecular Biology of the Cell 5/e (© Garland Science 2008)

Tumor suppressor mutation and cancer


(A)

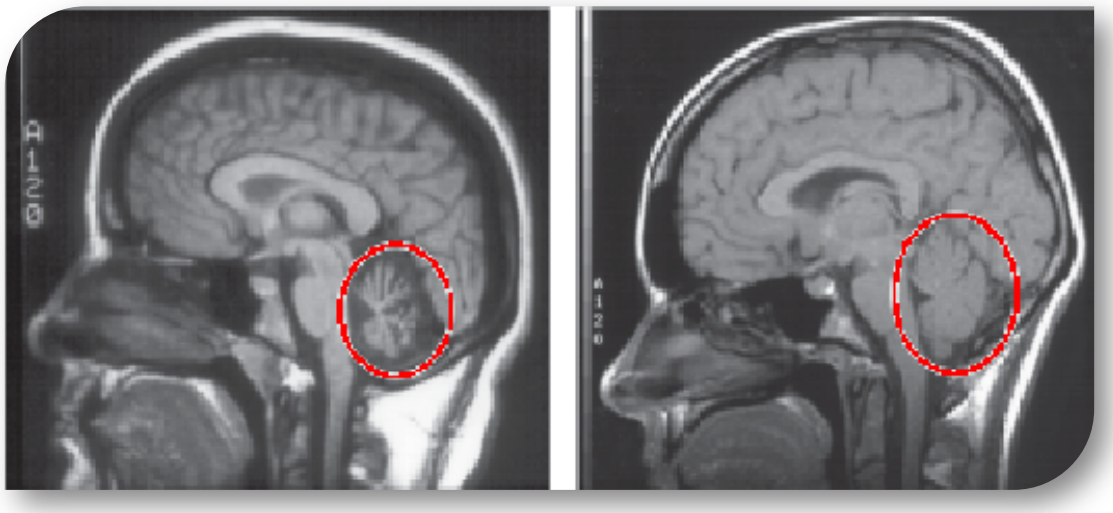

(B)

- ATM/ATR (Ataxia telangiectasia)
- P53 (tumor suppressor gene) regulate cell cycle

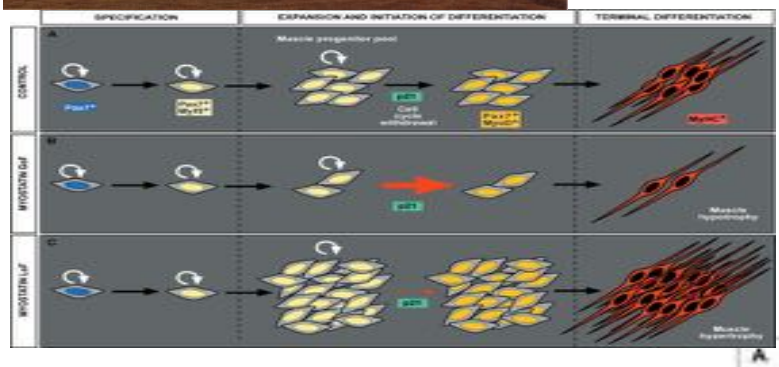


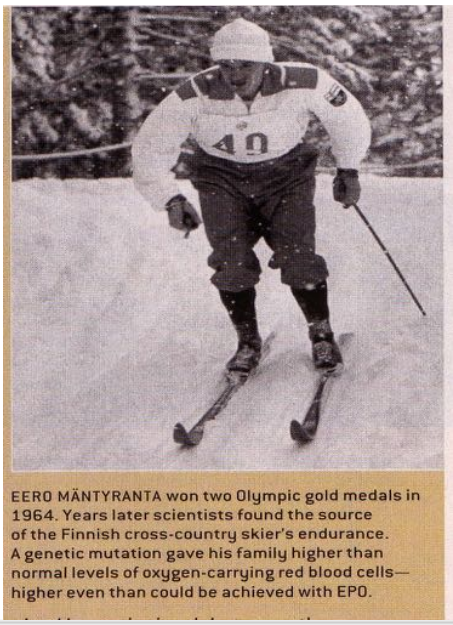
Ataxia: disease → progressive damage in nervous system, Fe toxicity, free radical

Diagram scanning results from Ataxia brain and normal brain
FXN mutation: frataxin (Chr9), mitochondrial nerve and muscle



Atrophy cerebellum (shrink) Normal cerebellum





EERO MÄNTYRANTA won two Olympic gold medals in 1964. Years later scientists found the source of the Finnish cross-country skier's endurance. A genetic mutation gave his family higher than normal levels of oxygen-carrying red blood cells—higher even than could be achieved with EPO.

Myostatin acts by inhibiting the growth of muscles, It prevents muscles from growing too large i.e. **inhibits proliferation of myoblasts** that fuse to form skeletal muscle cells.

- Mutation in myostatin → proliferation & growth >>>
- Inactivated myostatin → German Superboy