Ch11: Cell Communication

Cell Communication

- Cell-to-cell communication is critical to the development and functioning of multicellular organisms and communication between unicellular organisms
  - Cellular interactions provide evidence of evolution

Video

- Cell Communication Overview
  - http://learn.genetics.utah.edu

I. External Signaling

- Evolution of Signaling
  - 2 mating types of yeast release chemical factors that bind to the other type of initiate the fusion of the 2 types
  - The signal will trigger the mating gene's expression and sexual reproduction will occur

- Signal transduction pathway = steps involved in the conversion of a surface signal to a cellular response

Local and Long-Distance Signaling

- Direct contact:
  - cell to cell junctions in plant and animal cells
  - macrophage cells activating Helper T cells in the immune system

- Contact to surface molecules
  - Paracrine signaling – (local) messenger released into extracellular fluid and influence nearby cells
    - Ex: mast cells in nose that bind to pollen release histamine that stimulates other cells nearby
  - Synaptic signaling – (local) neurotransmitters released from nerve cells into synaptic cleft (space between cells)
  - Hormones – (long-distance) chemical signals that travel through the circulatory system to distant cells

3 Stages of Cell Signaling:

- Developed by E. W. Sutherland studies of epinephrine's effect on the hydrolysis of glycogen in the liver

1. Reception – chemical signal binds to a receptor protein either on the inside or surface of the cell
2. Transduction – sequence that moves the signal along a pathway
3. Response – cell responds to the signal

II. Reception

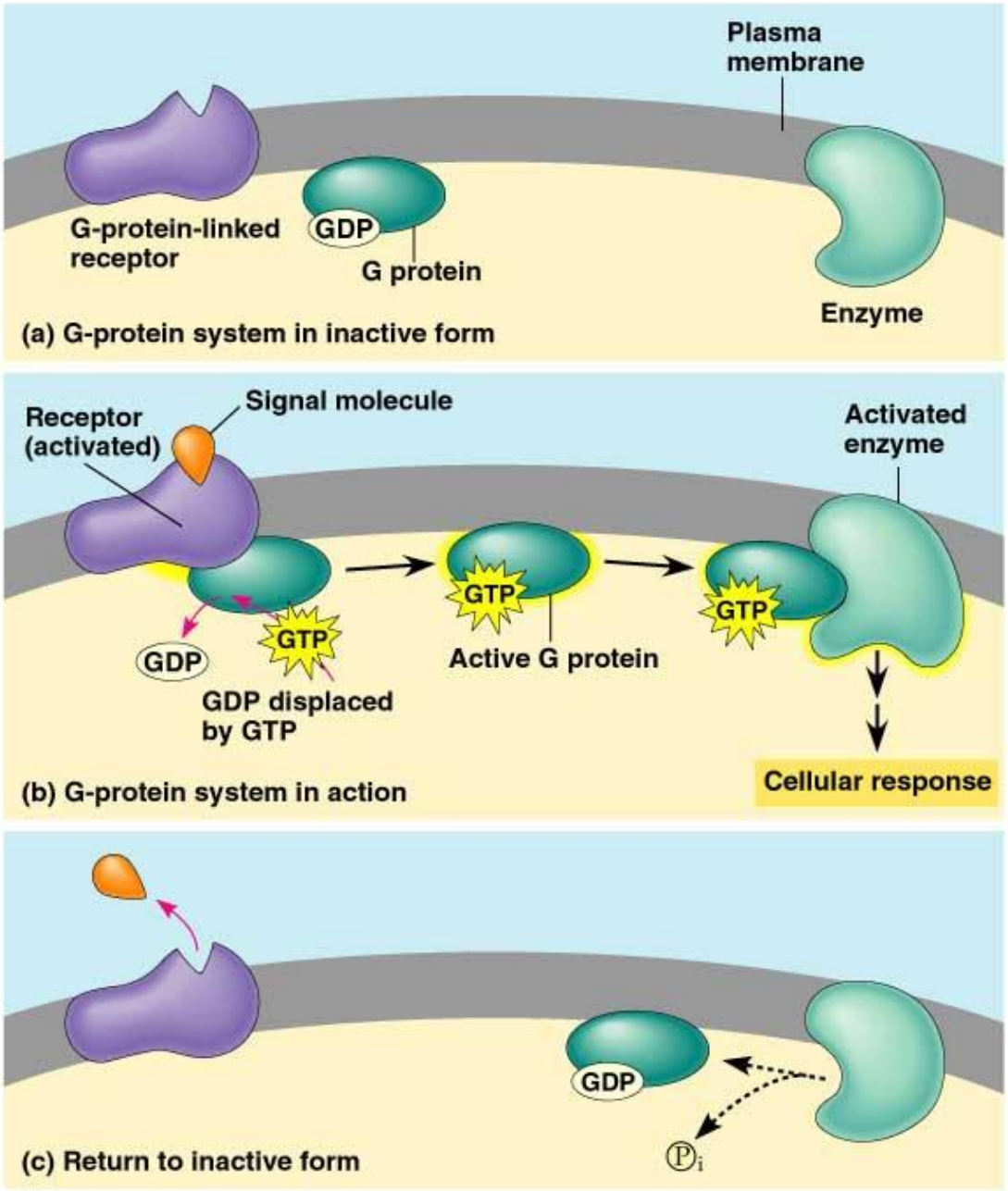
- Ligand = signal molecule that binds to a receptor protein and usually induces a change in the protein

- Intracellular Receptors
  - Found inside the plasma membrane in the cytoplasm or nucleus where they bind to proteins
  - Must cross through the plasma membrane
    - Hydrophobic chemical messengers
  - Ex) steroids (lipid) – regulate gene expression

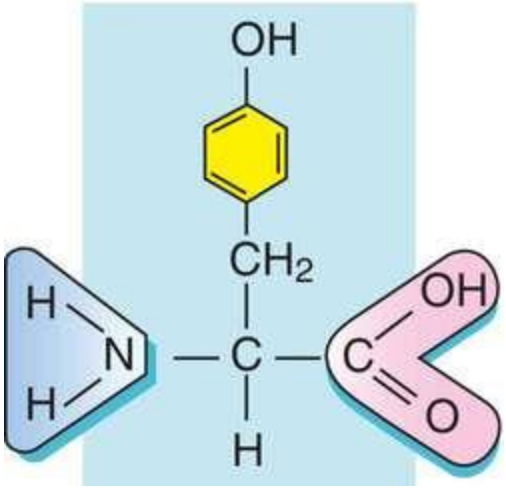
Receptors in Plasma Membrane: water-soluble ligands

- G-protein linked receptors
  - Signal molecule binds to receptor, which can now bound to an inactive G-protein
  - Activation occurs when GDP is replaced by a GTP on the G-protein
  - G-protein binds to a specific enzyme and activates it
  - Activated enzyme can now cause a cellular response
  - Change from GTP back to GDP, shuts off the G-protein until another messenger binds to the membrane

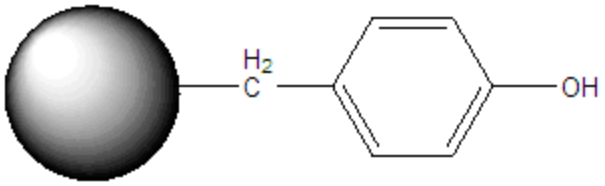
- Stimulated by hormones and neurotransmitters
- Involved in embryological development and sensory reception
- 60% of all medicines influence G-protein pathways



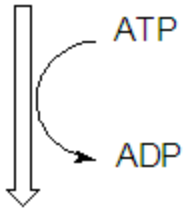
- Receptor tyrosine kinase
  - Signal molecules binds to a receptor protein and forms a dimer
    - Receptor proteins trigger several pathways at once
  - Dimer transfers phosphate group from ATP to amino acid tyrosine (part of the membrane protein)
  - Complex binds to other proteins in the cell – can cause multiple cellular responses
  - Helps with cell growth, cell reproduction, and immune system activation (cytokine storm)

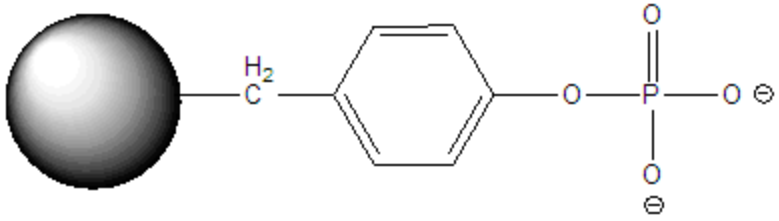


Tyr side chain

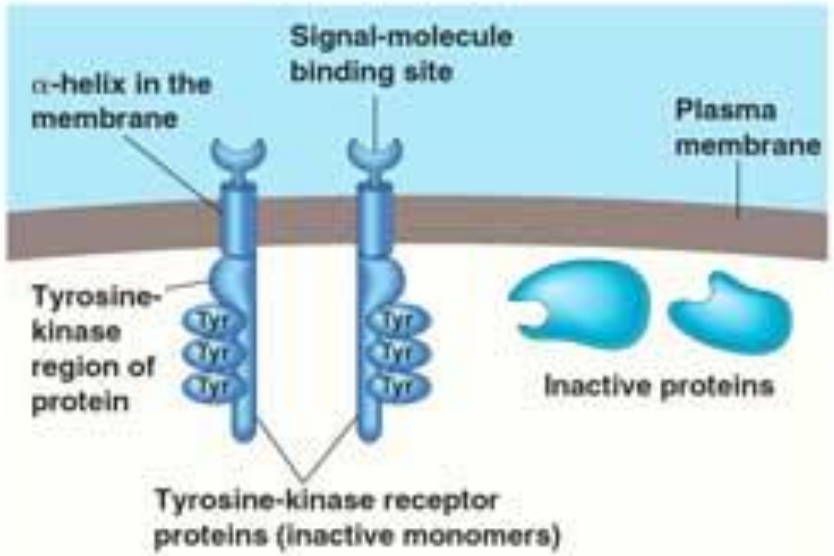


protein

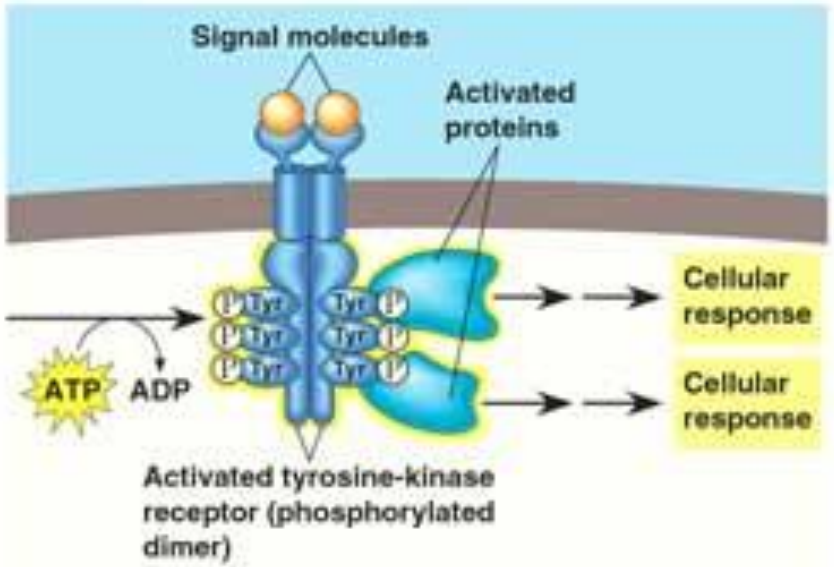




phosphorylated protein

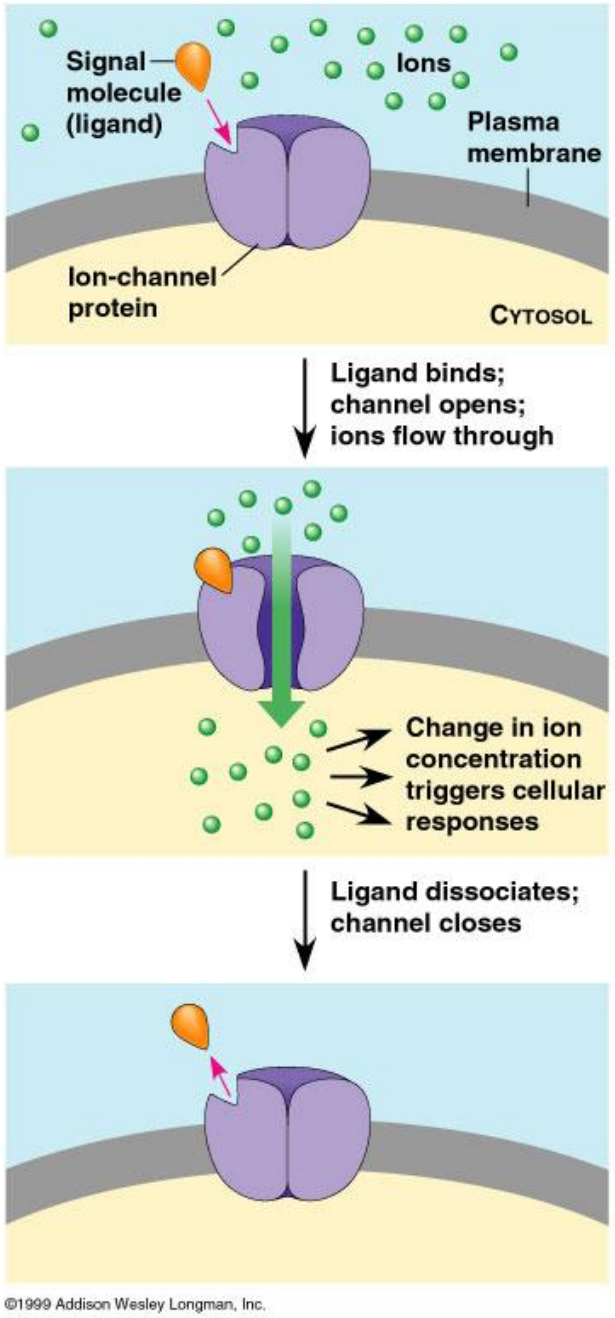


(a) Inactive tyrosine-kinase receptor system



(b) Activated system

- Ligand-gated ion channels
  - Allows or blocks the flow of specific ions
  - Helps with transmission of nervous signals



Video

- G-protein
- Tyrosine kinase
- Ligand gated channel
- cAMP

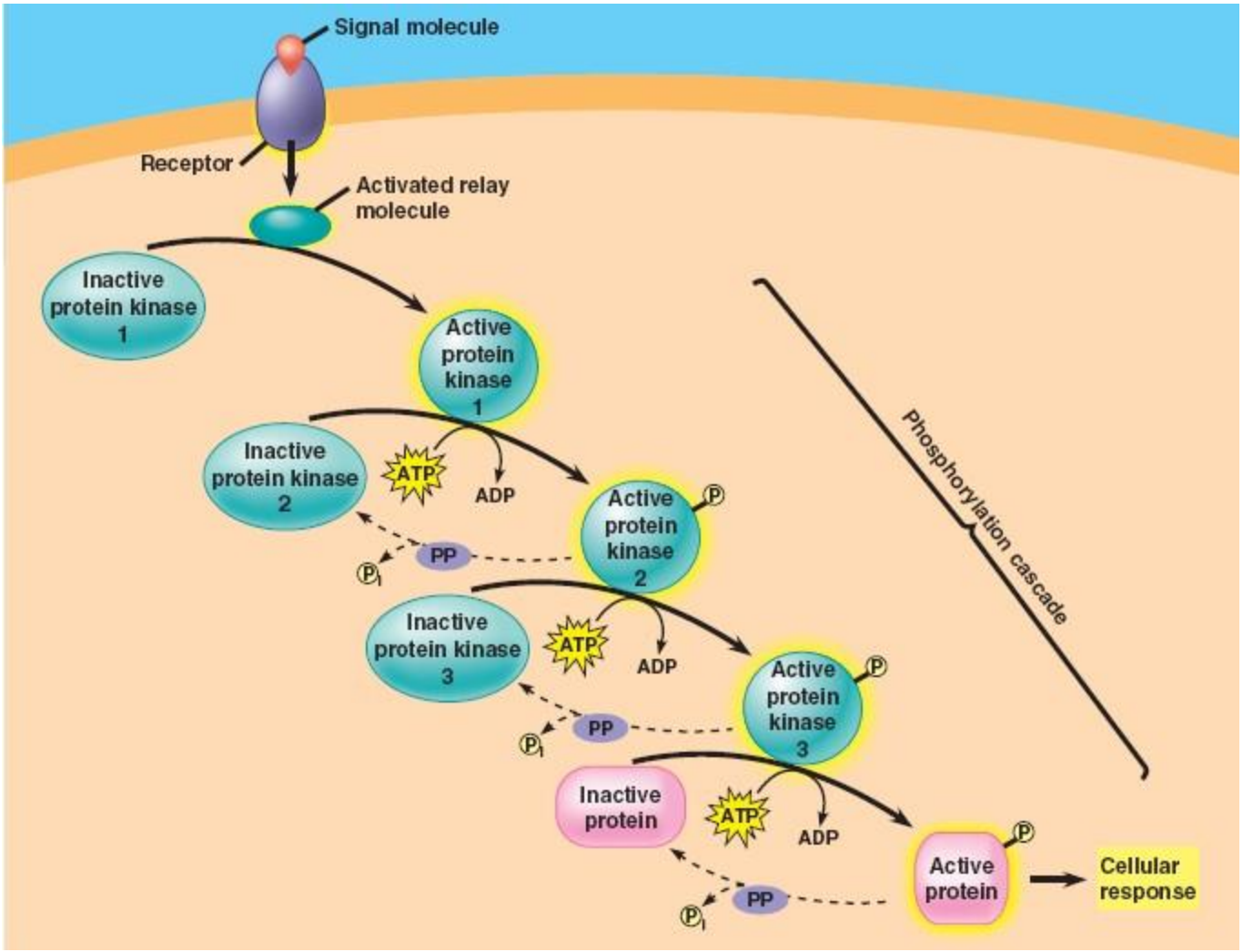
Transduction

- Signal transduction pathways
  - Signaling cascades relay signals from receptors to cell targets
  - Pathways often amplify the signal to create the desired cell response
  - Relay molecules are usually proteins

1. Protein phosphorylation cascade and dephosphorylation

- Series of protein kinases in order to greatly amplify the signal

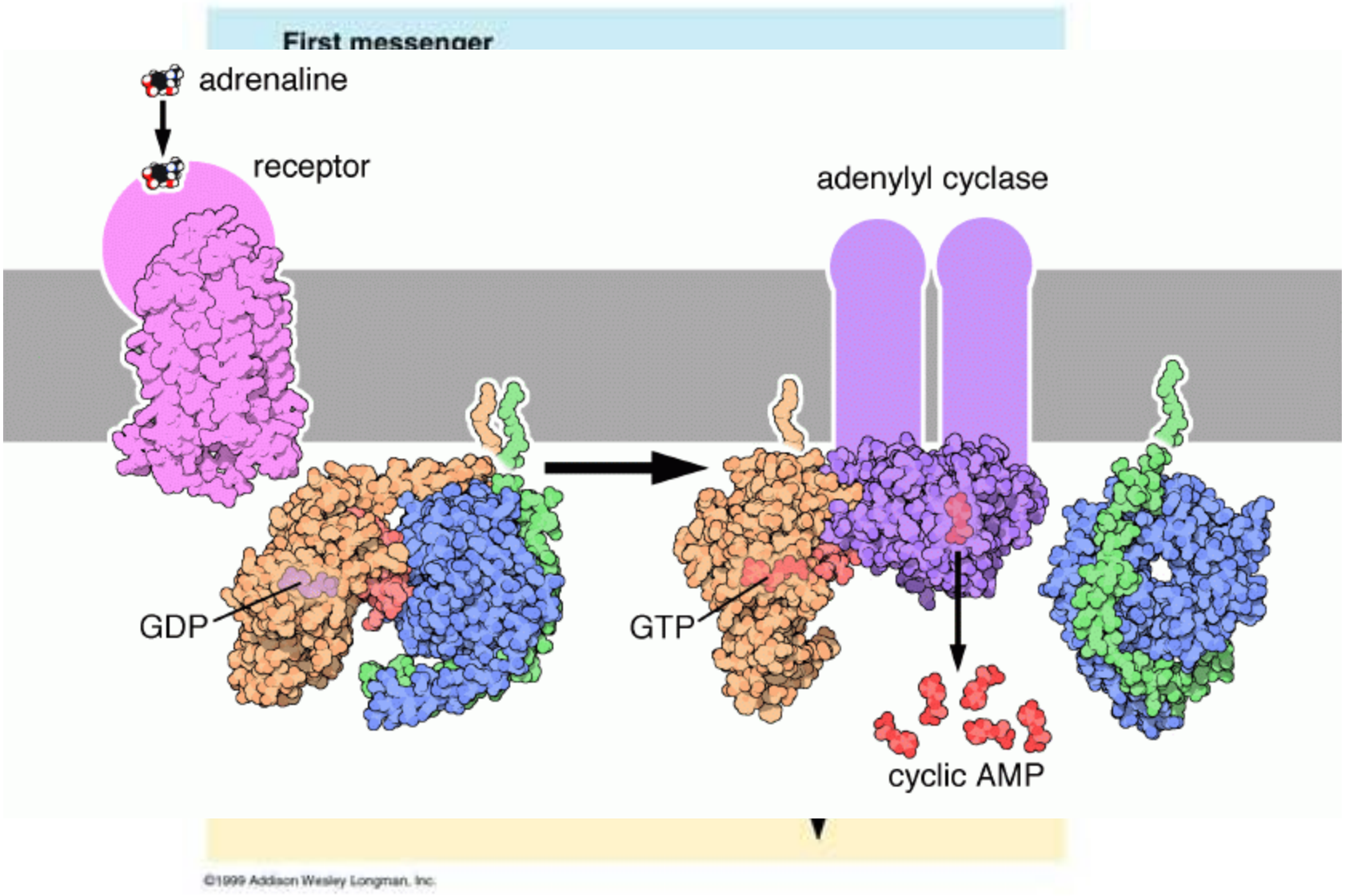
- Protein kinases – transfer phosphate groups from ATP to proteins
- Protein phosphatases – remove phosphate groups from proteins to shut down signaling pathways

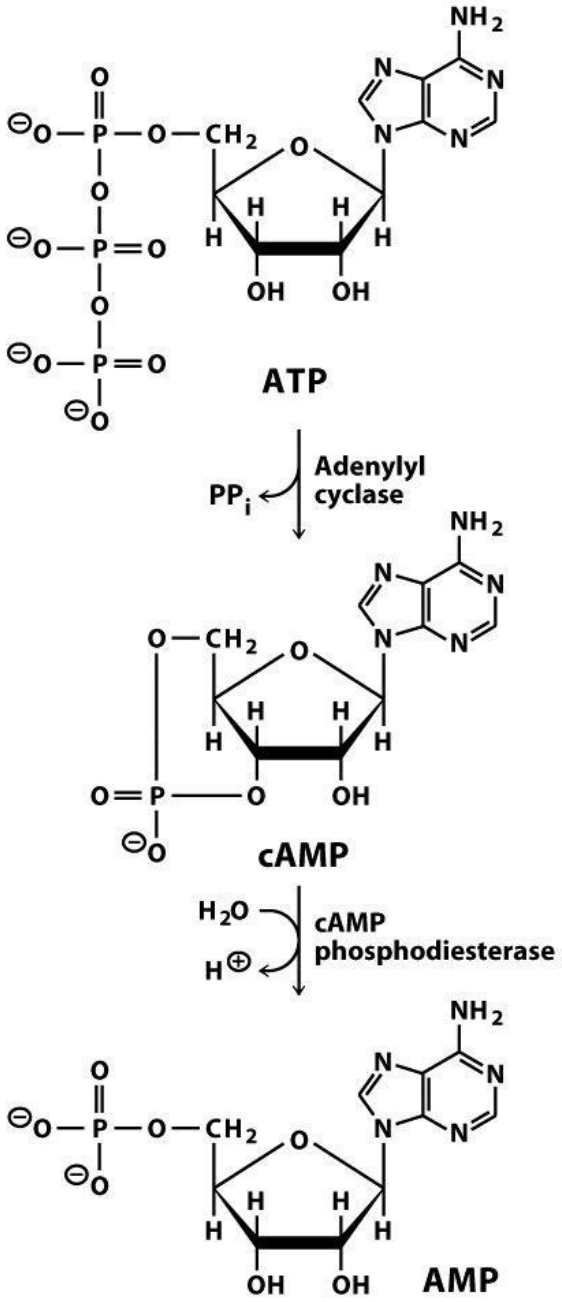

Signal molecule
Receptor
Activated relay molecule
Inactive protein kinase 1
Active protein kinase 1
Inactive protein kinase 2
ATP
ADP
Active protein kinase 2
P
PP
Pi
Inactive protein kinase 3
ATP
ADP
Active protein kinase 3
P
PP
Pi
Inactive protein
ATP
ADP
Active protein
P
PP
Pi
Cellular response
Phosphorylation cascade

Transduction

- Second messengers
  - Works with the signal cascade
    - Some are small, water-soluble molecules or ions
  - Rapidly relay signals from receptors into cell's interior
  - Examples: cyclic AMP, cyclic GMP, calcium ions (Ca^{2+}), and inositol triphospate (IP_3)

- Adenylyl cyclase – membrane protein that is activated by a G-protein and used to convert ATP to cyclic adenosine monophosphate (cyclic AMP or cAMP)
  - cAMP – activates protein kinase
    - When it is converted into AMP second messengers stop
    - Helps with cell growth and cell differentiation
- Ca^{2+} ions
  - Used in G-protein and receptor tyrosine kinase pathways
  - Release or uptake of Ca^{2+} can induce cellular responses





Principles of Biochemistry, 4/e

Responses

- Cytoplasmic and nuclear responses
  - May activate or deactivate enzymes and other proteins
  - Change the membrane permeability
  - Trigger cell division
  - Synthesis of proteins
  - Apoptosis – programmed cell death

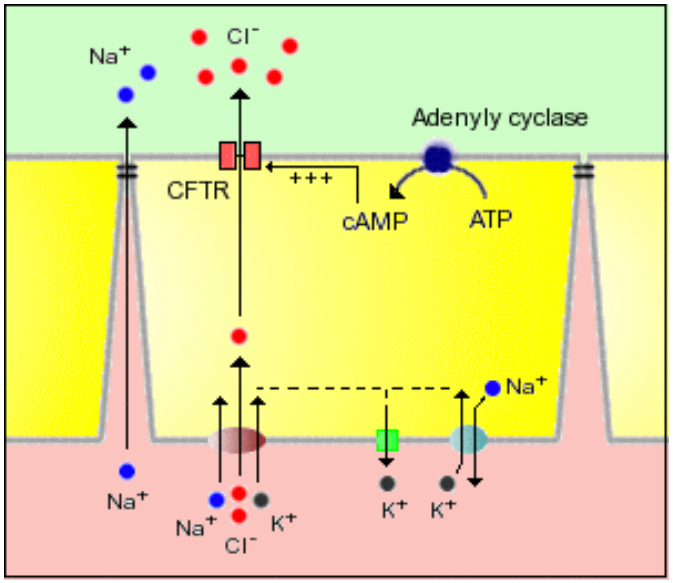
- Fine tuning the response – not a simple “on” or “off”
  - Pathway can amplify a response or shut down a response
  - Signals have specific reactions for different cells
    - Ex: liver cells and hear cells can respond to different signaling molecules or respond to the same one but have different cellular responses
  - Pathways can produce multiple responses or 2 responses can “cross-talk” to create 1 response
  - Cells must have inactivation mechanisms to stop the cellular response

Evolution

- Signaling mechanisms are thought to have first evolved in prokaryotes
- Bacteria secrete small molecules that can be detected by other bacteria which is called quorum sensing
  - This signal allows bacteria to monitor local cell density so they don't overproduce cells. They only need what is necessary to carry out activities for survival and no more

Small Intestine Secretion

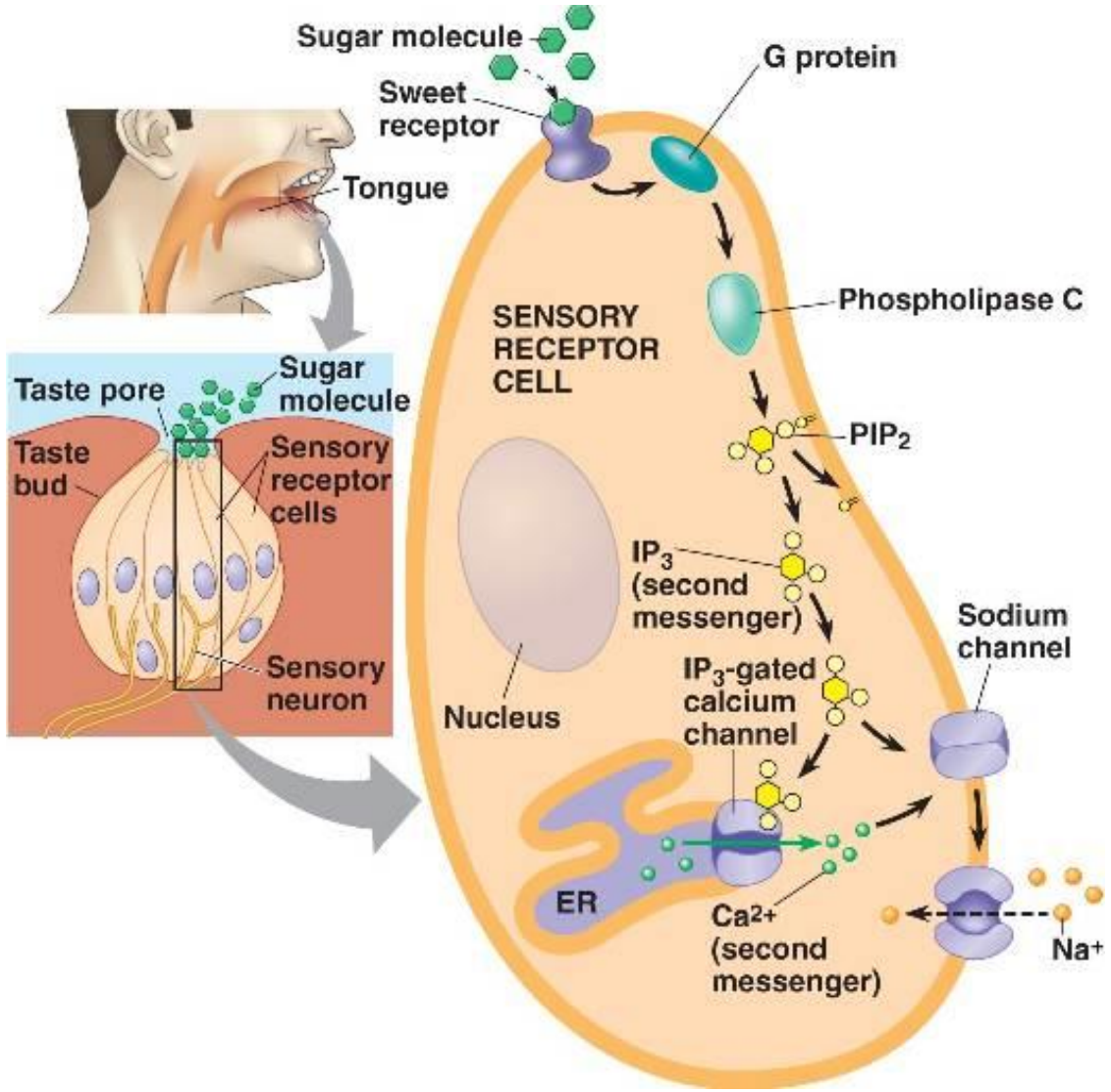
- Through the action of G protein and adenylyl cyclase, chloride ions and the eventually sodium ions (through tight junctions) are moved into the small intestines
  - Salt is added to the intestines (NaCl)
- Also digested food from the stomach adds to the osmolarity inside the intestines
- Water will then flow into the intestines
- As absorption of nutrients occurs, osmolarity goes down and water can be reabsorbed back to the blood through the rest of the intestines



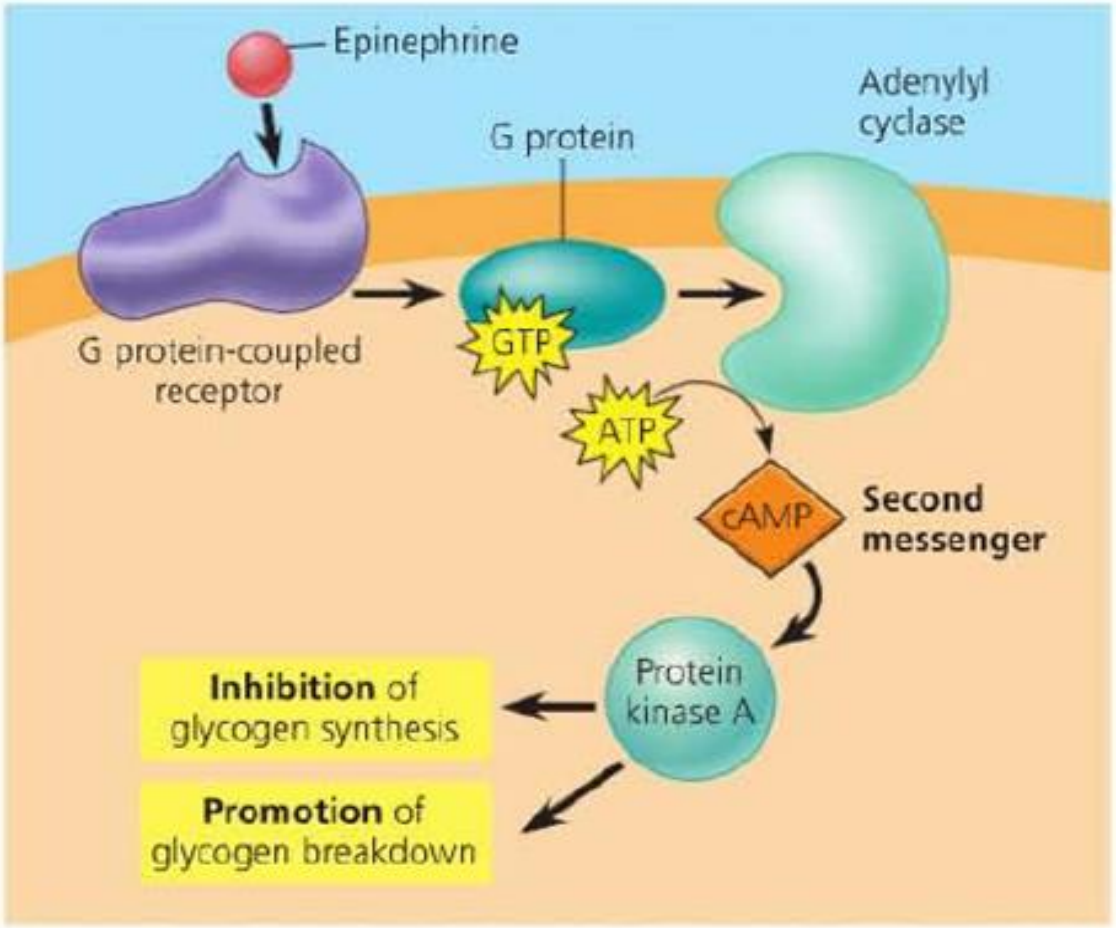
Disease Example

- Vibrio cholerae bacterium causes the disease Cholera when you consume water that is contaminated with human feces
- The bacteria create a biofilm in the intestines and releases a toxin
- This toxin is an enzyme that chemically modifies the G protein regulating salt and water secretion
- This causes the G protein to be stuck in its active form because it is unable to hydrolyze GTP to GDP and the cell continually makes cAMP
- High levels of cAMP cause more salt to be secreted into the intestines and water follows by osmosis
- The infected person will have profuse diarrhea and could die from loss of water and salt if left untreated

Taste Buds


Sugar molecule
Sweet receptor
G protein
Tongue
Phospholipase C
SENSORY RECEPTOR CELL
Taste pore
Sugar molecule
Taste bud
Sensory receptor cells
PIP2
IP3 (second messenger)
Sodium channel
Sensory neuron
Nucleus
IP3-gated calcium channel
ER
Ca2+ (second messenger)
Na+

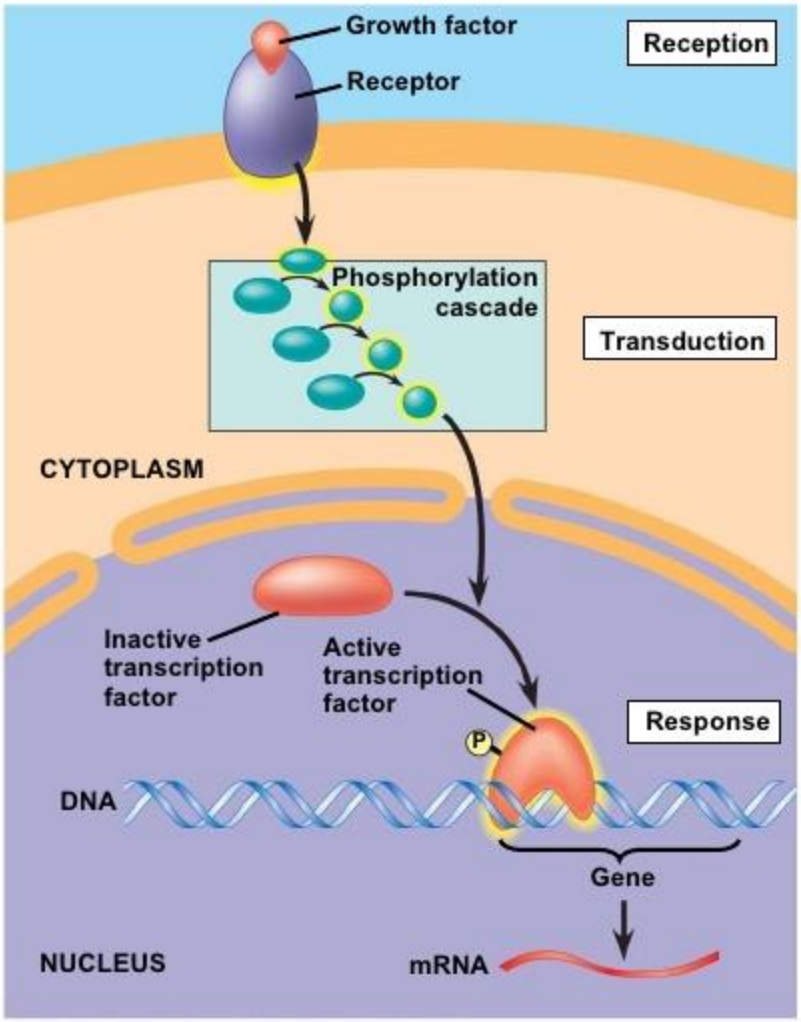
Epinephrine Hormone



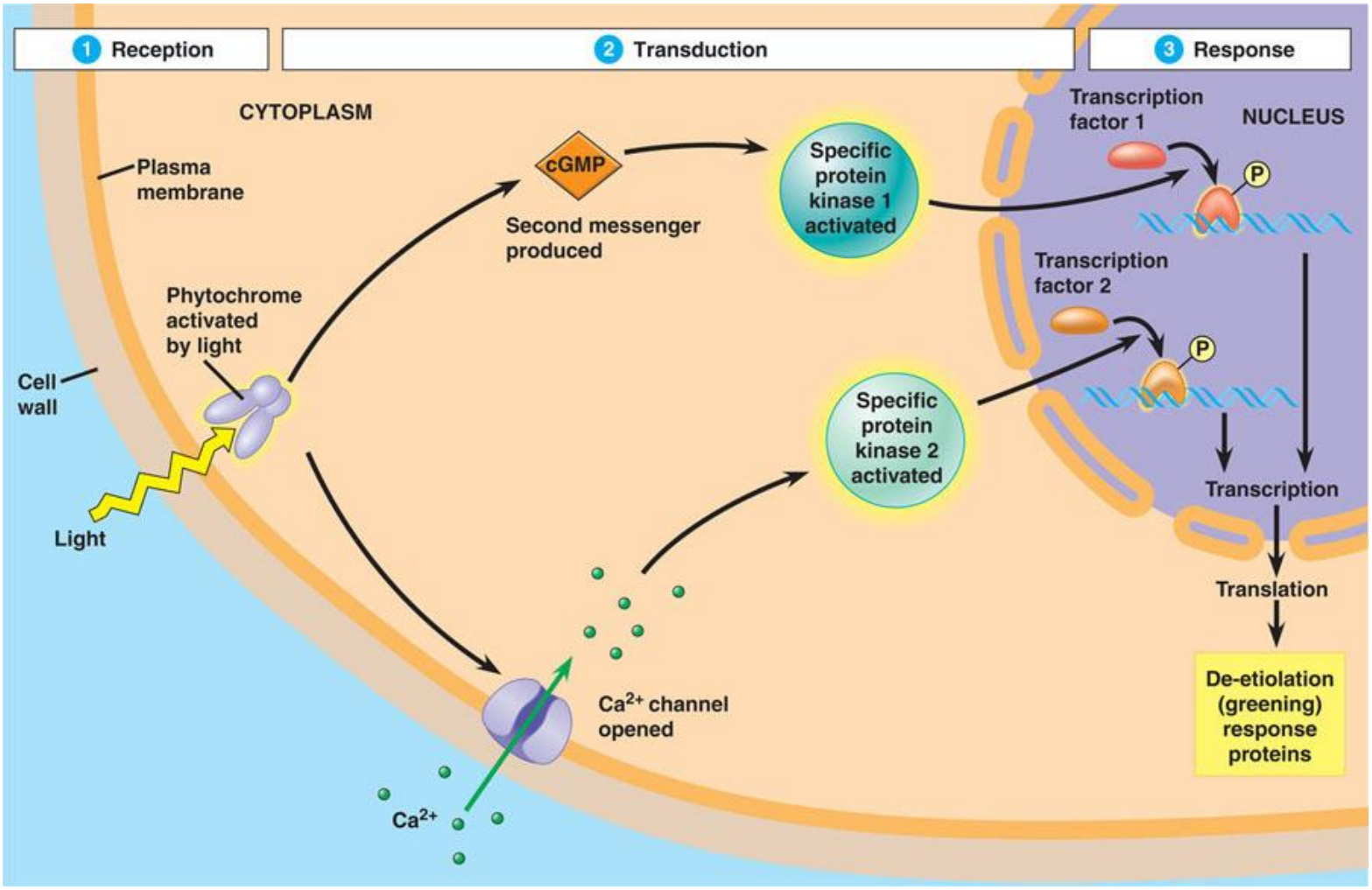
▲ **Figure 45.6** **Cell-surface hormone receptors trigger signal transduction.**

Growth Factor

Fig. 11-14



Phytochrome Proteins in Plants



Vision in Humans