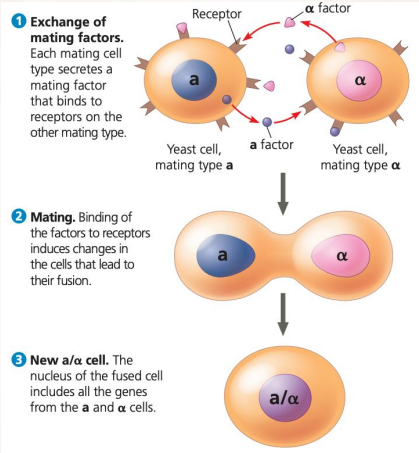
# Cell Communication

Presentation by Laurie, Slides by Slidesgo

# Sensing between organisms

Yeast (Saccharomyces cerevisiae)

- 2 mating types, a and α
  - Type a cells secrete a factor, which binds to specific receptor proteins on α cells, and vice versa → fusion of two opposite type cells

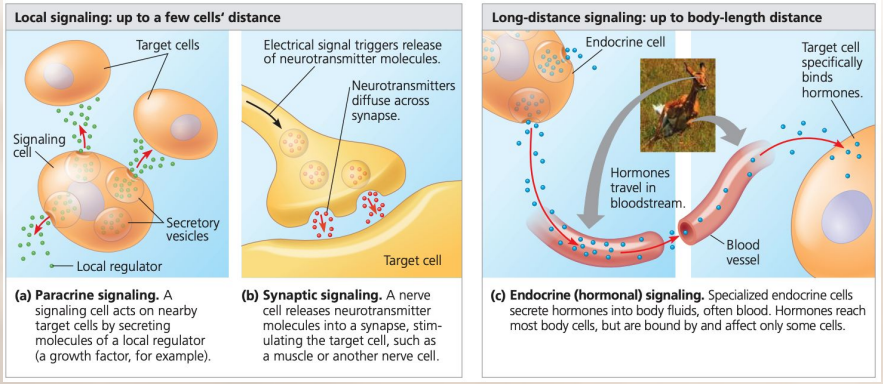



Bacteria

- Quorum sensing – using concentration of signaling molecules to coordinate density and behavior
  - Biofilms
  - Secreting toxins

# Local + Long Distance Signaling

- Eukaryotic cells may use direct contact
  - Cell junctions
  - Cell surface molecules
- Autocrine signaling
- Paracrine signaling – signaling cell secretes molecules that travel short distances
  - Growth factors
- Synaptic signaling – neurotransmitters diffuse across synapses
- Endocrine signaling – hormones



# Stages of Signal Transduction

1. Reception – target cell detects signaling molecule when it binds to a cell receptor protein
2. Transduction – cell receptor changes shape and leads to a cellular response; may involve multiple steps
3. Response
    a. Enzyme catalysis
    b. Rearrangement of cytoskeleton
    c. Activation of certain genes in nucleus

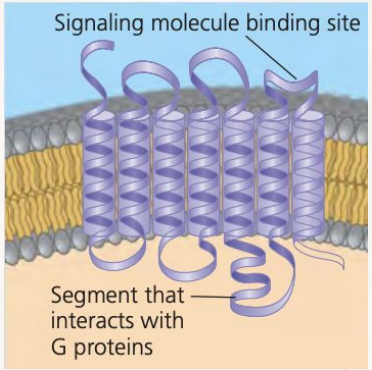
# Reception

The signaling molecule matches the shape of the receptor's binding site – in this case, we call the signaling molecule the "ligand"

- Binding usually causes receptor to change shape
- Binding commonly activates the receptor
- May cause 2+ receptors to aggregate

Most receptors are on the plasma membrane because ligands are usually big and water soluble

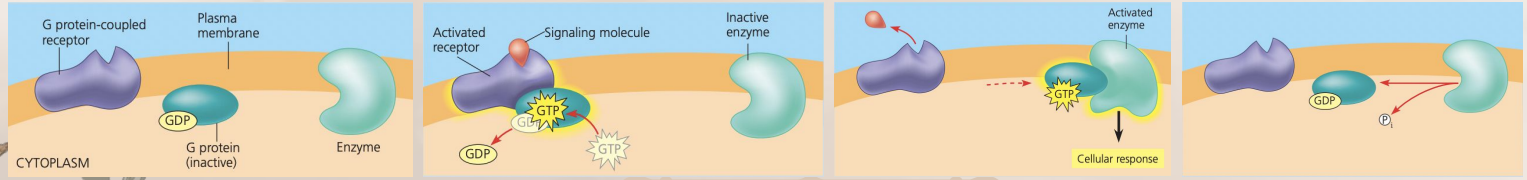
# Reception: Plasma Membrane Receptors




## GPCR family

- Involves a GTP-binding G protein
- Wide diversity of GPCRs – bind to yeast mating factors, epinephrine, neurotransmitters
- Structure
  - Single polypeptide with 7 transmembrane α-helices
  - Loops for signaling molecule binding site and segment that interacts with G protein
- Evolved very early on
- Involved in many diseases

1. G protein is attached loosely to membrane, on/off based on whether it's bound to GDP or GTP
2. Signaling molecule binds, receptor changes shape, cytoplasmic side of receptor binds to inactive G protein to replace GDP with GTP
3. Activated G protein binds to an enzyme → transduction
4. G protein hydrolyzes its bound GTP to GDP

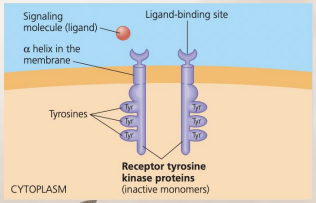


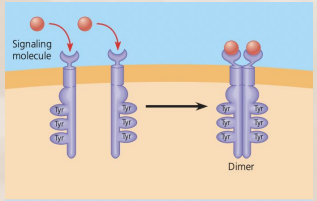
# Reception: Plasma Membrane Receptors

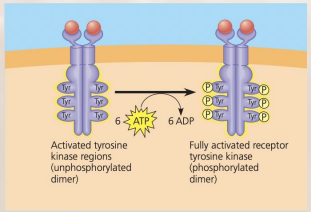
## Receptor Tyrosine Kinases (RTKs)

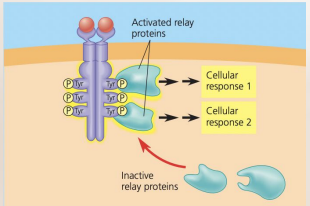
- Kinase – catalyzes transfer of phosphate groups
  - RTK's have kinases sticking into the cytoplasmic side
- Phosphates are attached to tyrosines
- One complex may activate 10+ transduction pathways and cellular responses
- Cancer
  - Herceptin (a protein) can bind to HER2 (type of RTK) to inhibit cellular growth

1. Individual monomers
2. Signaling molecule binds → monomers form dimer (dimerization)
3. Tyrosine kinases add phosphates from ATP to the other monomer
4. Activated receptor leads to transduction



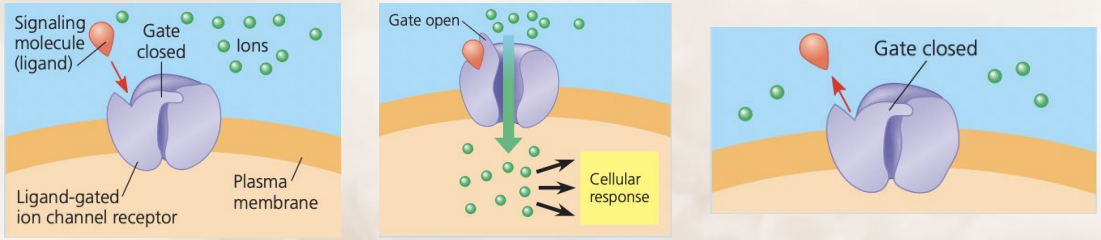



# Reception: Plasma Membrane Receptors

## Ion Channel Receptors

- Ligand-gated ion channel – membrane receptor with a “gate” to a channel that opens/closes based on receptor shape

1. Gate closed
2. Ligand binds → gate opens, ions flow in
3. Ligand dissociates, gate closes




- Important in the nervous system – neurotransmitters bind to ion channels of receiving cell at synapse, causing channels to open

# Intracellular Receptors

- Cytoplasm or nucleus
- Signaling molecule must pass through plasma membrane
- Hydrophobic or small molecules
  - Steroid and thyroid hormones
  - Nitric acid (NO), which is a gas
- Testosterone
  - Secreted by cells of testes
  - Travels through blood and enters all sorts of cells; only cells with testosterone receptors respond
  - Receptor protein activated and enters nucleus to activate certain genes
- May act as a transcription factor

# Transduction

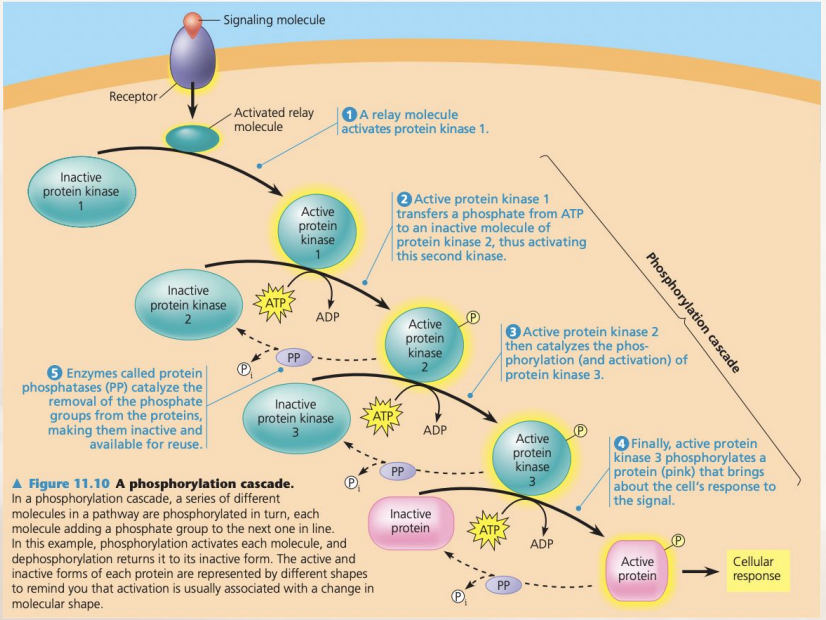
Usually multistep – allows for more amplification and coordination

Signal transduction pathway

- Signal-activated receptor, which activates a molecule, which activates another molecule, etc.
- Relay molecules – proteins that relay signal from receptor to response

Protein phosphorylation and dephosphorylation

- Protein kinase – enzyme that transfers phosphates from ATP to proteins
- STY
- May decrease activity
- Protein phosphatase




▲ **Figure 11.10 A phosphorylation cascade.** In a phosphorylation cascade, a series of different molecules in a pathway are phosphorylated in turn, each molecule adding a phosphate group to the next one in line. In this example, phosphorylation activates each molecule, and dephosphorylation returns it to its inactive form. The active and inactive forms of each protein are represented by different shapes to remind you that activation is usually associated with a change in molecular shape.

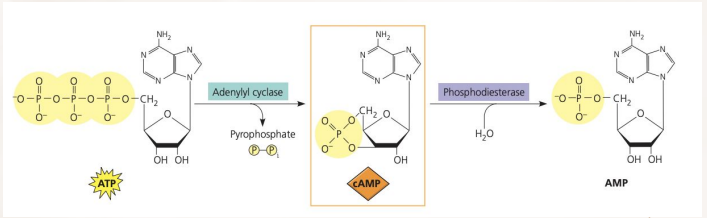
# Transduction – Second Messengers

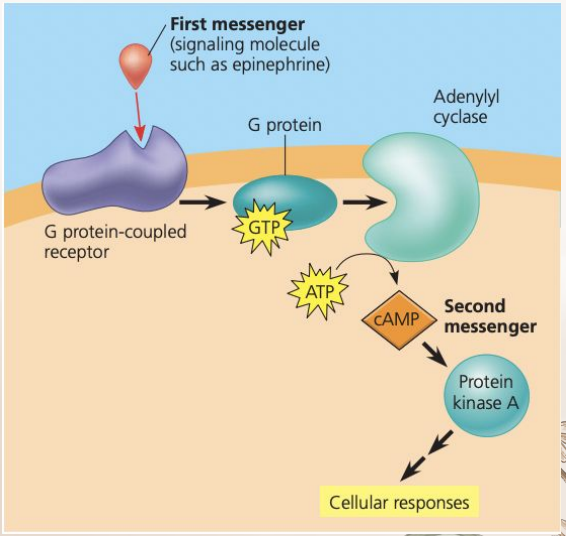
- Small, non-protein, water-soluble/ions
- Participate in GPCR and RTK-initiated pathways
- cAMP, Ca2+

# Cyclic AMP (cAMP)

Epinephrine

- Binds to liver cell surface GPCR
- G protein activates adenylyl cyclase, which converts ATP to cAMP
  - Concentration of cAMP can increase 20-fold in seconds
- cAMP broadcasts signal
  - Usually activates protein kinase A (serine/threonine kinase)
- Phosphodiesterase converts cAMP to AMP



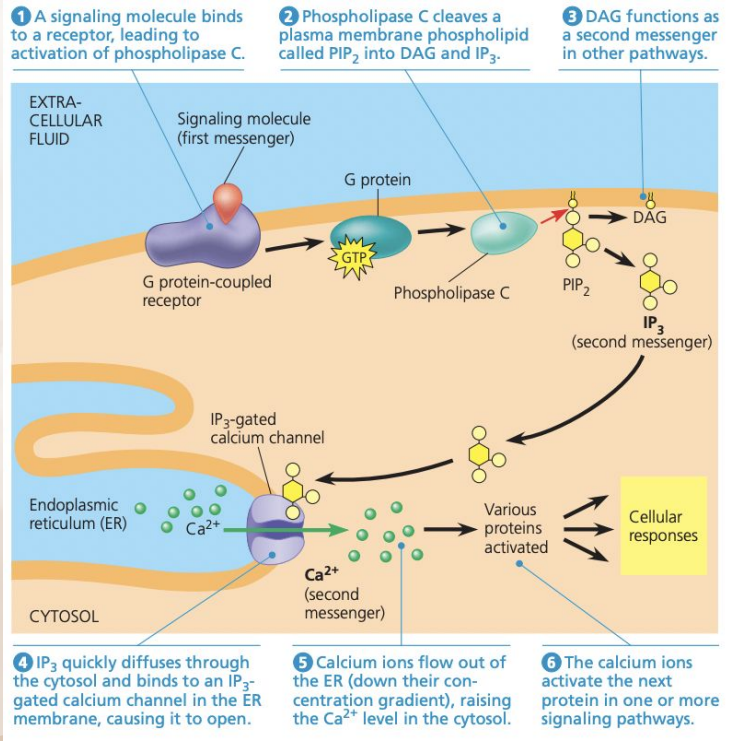




Cholera (from Vibrio cholerae)

- Forms biofilm on small intestine lining, which produces cholera toxin (modifies G proteins)
- G proteins unable to hydrolyze GTP → GDP, thus stay active and cause adenylyl cyclase to make lots of cAMP
- High cAMP concentration causes salts to go into intestinal lumen, water follows

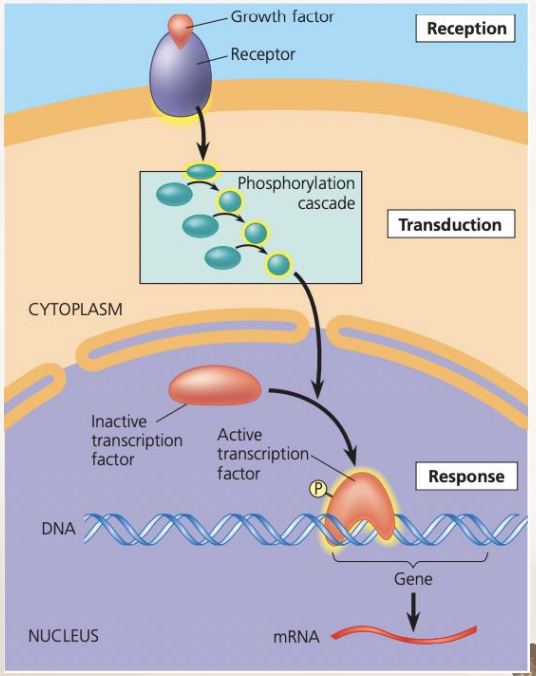
# Calcium Ions + Inositol Triphosphate ($IP_3$)

- More common than cAMP
  - Muscle cell contraction, secretion, cell division, plant responses
- Very low cytosolic concentration compared to extracellular concentration
  - Actively pumped out of cell and into ER
  - A little change makes a big difference
- PIP3 in membrane



# Response

- Regulate protein synthesis (nucleus)
- Regulate protein activity (cytoplasm)
  - Open/close of ion channel
  - Change in metabolism
    - Liver cells + epinephrine → break down glycogen



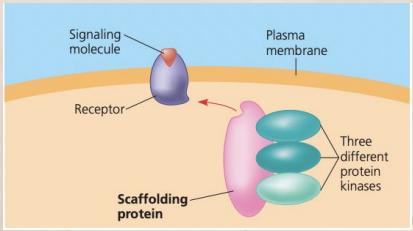
# Response

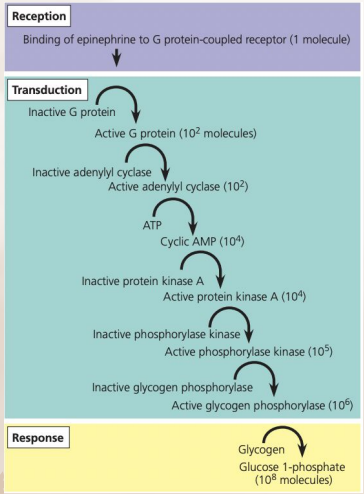
Signal amplification

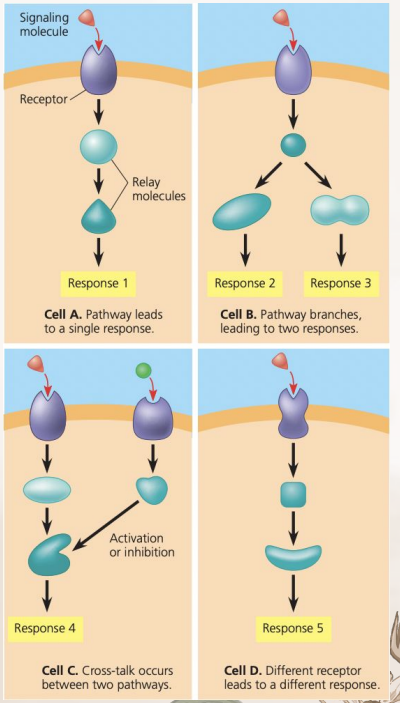
- Because proteins are active for long enough to process multiple substrates before becoming inactive

Pathways may interact with each other

Scaffolding proteins carry relay proteins together, which enhances speed and accuracy



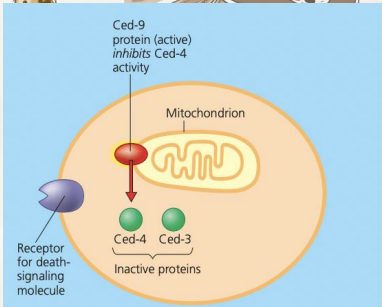



# Apoptosis

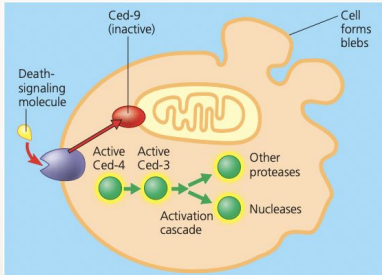
Programmed cell death in infected, damaged, or old cells
- DNA chopped up, organelles fragmented
- Blebbing – cell shrinks, develops lobes
- Cell parts put in vesicles, digested by scavenging cells

Apoptosis in C. elegans
- ~1000 cells, apoptosis occurs exactly 131 times
- ced-3 and ced-4 genes make Ced-3 and Ced-4 proteins
  - Ced-9 on mitochondria inhibits Ced-4
- Death signal results in Ced-9 being inactivated and apoptotic pathway begins
  - Proteases and nucleases chop up proteins and DNA
    - Caspases are main protease

Apoptosis in humans/other mammals
- 15 different caspases, multiple pathways
- Mitochondrial proteins make pores in outer mitochondrial membrane → releases more apoptosis-promoting proteins
  - Cytochrome c
- Signal can come from within cell – DNA suffers bad damage, bad protein misfolding



**(a) No death signal.** As long as Ced-9, located in the outer mitochondrial membrane, is active, apoptosis is inhibited, and the cell remains alive.



**(b) Death signal.** When a cell receives a death signal, Ced-9 is inactivated, relieving its inhibition of Ced-3 and Ced-4. Active Ced-3, a protease, triggers a cascade of reactions leading to activation of nucleases and other proteases. The action of these enzymes causes the changes seen in apoptotic cells and eventual cell death.

# Apoptosis

- Important for development of hands and feet and paws
  - Less apoptosis in webbed feet
- Involved in Parkinson's disease and Alzheimer's disease
- Faulty apoptosis can cause cancer

# Thanks!