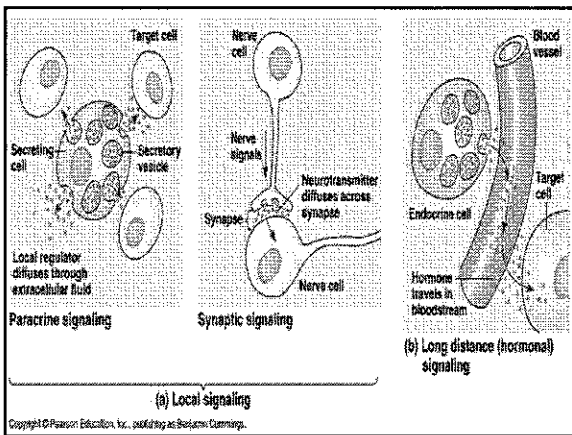


Signal-Transduction Pathway

- Signal on a cell's surface is converted into a specific cellular response
- _____ (short distance) - *Paracrine* (growth factors); *Synaptic* (neurotransmitters)
- _____ - hormones



Stages of Cell Signaling

- Earl Sutherland (Nobel Prize in '71)
- Glycogen depolymerization by epinephrine
- Found epinephrine stimulates glycogen breakdown by activating an enzyme.
- When epinephrine was added to test tube with enzyme and glycogen (substrate) - Nothing happened.
- Epinephrine could ONLY activate the enzyme when in solution with intact cells.

What did Sutherland Learn?

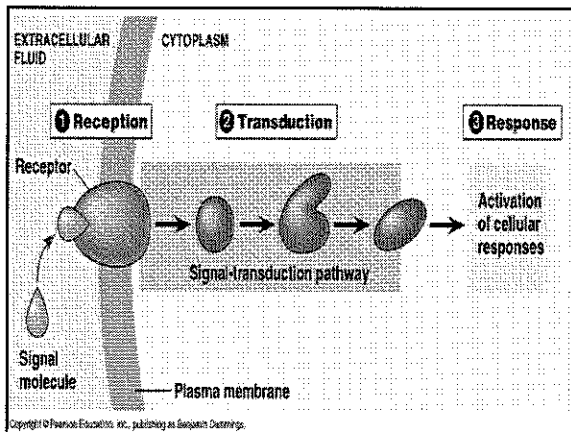
1) Epinephrine does not interact directly with the enzyme responsible for glycogen breakdown and intermediate step or series of steps must occur in cell.

2) The _____ is involved in transmitting the signal. Very Important

STAGES OF CELL SIGNALING

- 1) _____, a chemical signal binds to a cellular protein, typically at the cell's surface.
- 2) _____, binding leads to a change in the receptor that triggers a series of changes along a signal-transduction *pathway*.
- 3) _____, the transduced signal triggers a specific cellular activity.

Fig. 11.5



Plasma membrane Receptors

- 1) G- Protein Linked Receptors
- 2) Tyrosine-Kinase Receptors
- 3) Ligand-Gated Ion Receptors

G-Protein Linked Receptors

Plasma membrane receptor - works with a G protein.

G Proteins are like _____ switches.

The diagram shows a G-protein linked receptor embedded in the plasma membrane. It has an extracellular domain with a signal-binding site, a transmembrane domain with NH₂ and COO⁻ ends, and a cytosolic domain that interacts with G proteins. Labels include 'EXTRACELLULAR FLUID', 'Plasma membrane', 'CYTOSOL', 'Signal-binding site', 'NH₂', 'COO⁻', and 'Segment that interacts with G proteins'.

G Protein linked Receptor

- No extracellular signal = _____

This diagram shows the inactive state of a G-protein system. A G-protein-linked receptor is embedded in the plasma membrane, and a G protein is bound to it. The G protein is bound to GDP. An enzyme is also shown nearby. Label: 'Plasma membrane', 'G-protein-linked receptor', 'GDP', 'G protein', 'Enzyme'. (a) G-protein system in inactive form.

The diagram shows the activation process: 1) A signal molecule binds to the activated receptor. 2) GTP binds to the G protein, displacing GDP. 3) The activated G protein moves along the membrane and activates an enzyme. 4) This triggers the next step in the pathway, leading to a cellular response. Labels include 'Activated receptor', 'Signal molecule', 'Activated enzyme', 'GDP displaced by GTP', 'GTP', 'Activated G protein', and 'Cellular response'.

- 1) Signal molecule binds to receptor protein - changes shape and binds to G protein.
- 2) GTP molecule displaces GDP on G protein - activating the protein.
- 3) Active G protein moves along membrane and activates an enzyme.
- 4) Triggers next step in pathway - leads to cell response.

G protein catalyzes hydrolysis of GTP back to GDP - Inactive

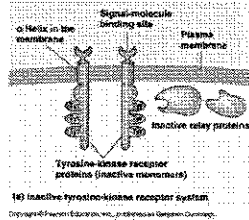
This diagram shows the G protein returning to its inactive state. The G protein has catalyzed the hydrolysis of GTP back to GDP. Labels include 'GDP'. (c) Return to inactive form.

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- All three proteins remain ATTACHED to the cell membrane.

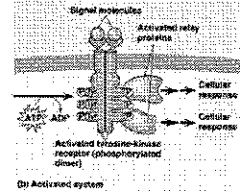
Tyrosine-Kinase Receptors

- When _____ ligand signal molecules are bound to the receptors - receptor is _____.
- Tyrosine receptors that extend into the cytoplasm are _____ and inactive.



Tyrosine-Kinase Receptors

- 1) Signal molecules attach to binding sites - to monomers join and form _____.
- 2) ATP _____ the tyrosine - ACTIVE
- 3) Receptor protein binds to relay proteins which activates the relay proteins
- 4) Relay proteins initiate a signal transduction pathway causing a cellular response.



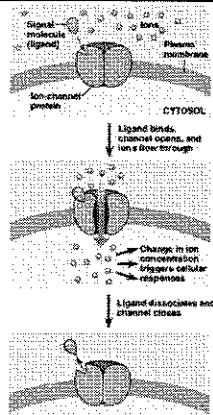
Hint:
Kinase =
Phosphorylation

Remember Action Potentials!!!

Ion-Channel Receptors

Bound ligand opens ion-channel.

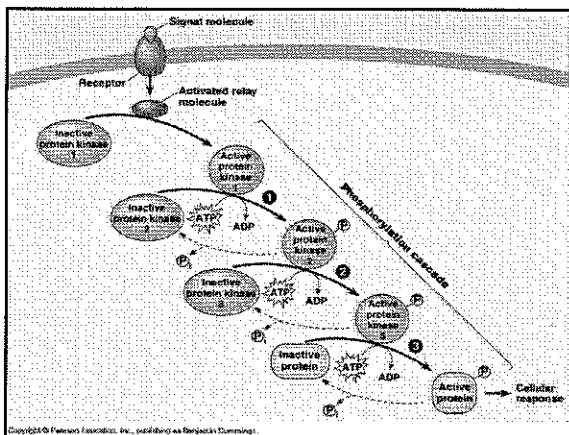
Remove of ligand closes the channel



Signal Transduction Pathways

Protein Phosphorylation

- Protein activity regulation
- Adding phosphate from ATP to a protein (activates proteins)
- Enzyme: protein kinases (1% of all our genes)
- Example: cell reproduction
- Reversal enzyme: protein phosphatases

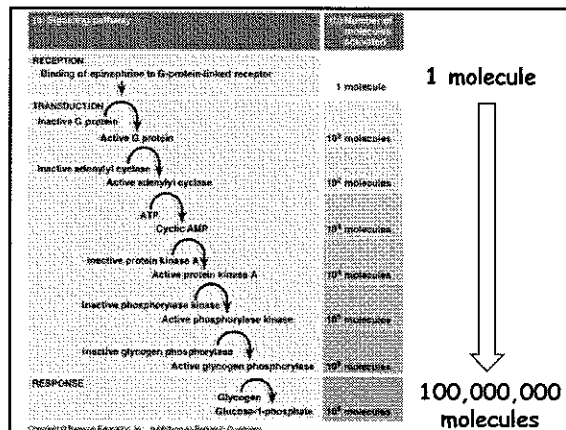


Phosphorylation Cascade

- A series of different molecules in a pathway are phosphorylated.
- The phosphorylated proteins are now active and can catalyze the phosphorylation of another protein in the pathway.
- The cascade continues until a cellular response is produced.
- The removal of phosphate groups then deactivates the proteins.

Purpose of Signal Transduction pathways

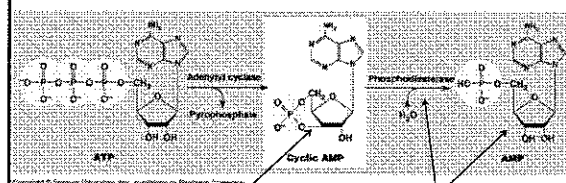
- Series of chain reactions
- Each reaction in the series _____ the signal being sent.
- The molecules that are activated in each step, activate many molecules that in turn activate many molecules.
- So one molecule at the beginning creates a huge cellular response due to the signal transduction pathways.



Second Messengers

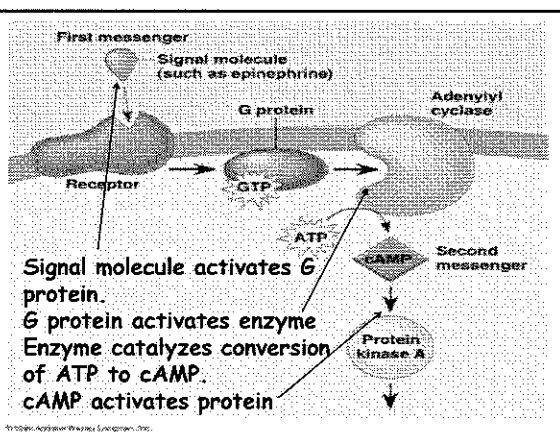
- Non-protein signaling pathway
- Example: _____ (cAMP)
- Ex: Glycogen breakdown with epinephrine
- Enzyme: *adenylyl cyclase*
- *G-protein-linked receptor* in membrane (guanosine di- or tri- phosphate)

cAMP



Notice the bond and the removal of 2 phosphates

Hydrolysis occurs, now bond is broken



Cellular Responses to Signals

- Cytoplasmic activity regulation
- Cell metabolism regulation
- Nuclear transcription regulation

