AP Biology Reading Guide — *Julia Keller 12d*

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Chapter 11: Cell Communication

1. What is a signal transduction pathway?

A signal transduction pathway is the series of steps by which a signal from outside the cell is converted (transduced) into a functional change within the cell.

2. How does yeast mating serve as an example of a signal transduction pathway?

Yeast cells use chemical signaling to identify cells of opposite mating type (**a** and **α**) and initiate the mating process.

3. Complete the chart of local chemical signaling in cell communication in animals.

Local Signaling Types	*Specific Example*
paracrine	numerous cells can simultaneously receive and respond to molecules of growth factor (consisting of compounds that stimulate nearby target cells to grow and divide) produced by a single cell in their vicinity
synaptic	an electrical signal along a nerve cell triggers the secretion of neurotransmitter molecules carrying a chemical signal that diffuse across the synapse, triggering a response in a target cell

4. How does a hormone qualify as a long-distance signaling example?

In endocrine signaling (hormonal signaling in animals), hormone molecules are released by specialized cells, which travel to other parts of the body through the circulatory system to reach target cells that recognize and respond to the hormones. Plant hormones (plant growth regulators) sometimes travel in vessels but more often reach their targets by moving through cells or by diffusing through the air as a gas.

5. A signal transduction pathway has three stages. Explain each step.

During reception, the target cell's detection of a signaling molecule coming from outside the cell, a chemical signal is "detected" when the signaling molecule binds to a receptor protein located at the cell's surface or inside the cell.

During transduction, the signal is converted to a form that can bring about a specific cellular response. The binding of the signaling molecule changes the receptor protein in some way, initiating the second stage.

The specific cellular response triggered by the transduced signal may be almost any imaginable cellular activity.

6. What is a ligand?

A ligand is a molecule that specifically binds to another molecule, often a larger one. Ligand binding generally causes the receptor protein to undergo a chance in shape.

7. What is a G protein-lined receptor? Describe the role of the three components in the first stage.

A G protein-coupled receptor (GPCR) is a cell-surface transmembrane receptor that works with the help of a G protein, a protein that binds the energy-rich molecule GTP. GPCRs vary in the binding sites for their signaling molecules (ligands) and also for different types of G proteins inside the cell. In the first stage, the G protein is loosely attached to the cytoplasmic side of the membrane, where it functions as a molecular switch that is either on or off, depending on which of two guanine nucleotides is attached, GDP or GTP. When GDP is bound to the G protein, the G protein is inactive. The receptor and G protein work together with another protein, usually an enzyme.

8. Describe what happens in the second stage.

When the appropriate signaling molecule binds to the extracellular side of the receptor, the receptor is activated and changes shape. Its cytoplasmic side then binds an inactive G protein, causing a GTP to displace the GDP. This activates the G protein.

9. Describe what happens in the third stage.

The activated G protein dissociates from the receptor, diffuses along the membrane, and then binds to an enzyme, altering the enzyme's shape and activity. Once activated, the enzyme can trigger the next step leading to a cellular response. Binding of signaling molecules is reversible.

10. Describe how the signal is halted.

The G protein also functions as a GTPase enzyme: it hydrolyzes its bound GTP to GDP. Now inactive again, the G protein leaves the enzyme, which returns to its original state. The G protein is now available for reuse.

11. What activates a G protein?

A G protein is activated when the cytoplasmic side of the GPCR binds an inactive G protein, causing a GTP to displace the GDP.

12. A G protein is also a GTPase enzyme. Why is this important?

The GTPase function of the G protein allows the pathway to shut down rapidly when the signaling molecule is no longer present.

13. The second type of receptor described is receptor tyrosine kinase. Explain what a kinase enzyme does.

A kinase is an enzyme that catalyzes the transfer of phosphate groups. The part of the receptor protein extending into the cytoplasm functions as a tyrosine kinase, an enzyme that catalyzes the transfer of a phosphate group from ATP to the amino acid tyrosine on a substrate protein.

14. How does tyrosine kinase function in the membrane receptor?

Tyrosine kinases are membrane receptors that attach phosphates to tyrosines.

15. What is a key difference between receptor tyrosine kinases and G protein-coupled receptors?

One receptor tyrosine kinase complex may activate ten or more different transduction pathways and cellular responses. Often, more than one signal transduction pathway can be triggered at once. The ability of a single ligand-binding event to trigger so many pathways is a key difference between receptor tyrosine kinases and G protein-coupled receptors.

16. Explain what happens in the first step.

Before the signaling molecule binds, the receptors exist as individual units referred to as monomers. Each has an extracellular ligand-binding site, an **α** helix spanning the membrane, and an intracellular tail containing multiple tyrosines.

17. Describe what happens to receptors tyrosine kinases when signaling molecules have attached.

The binding of a signaling molecule causes two receptor monomers to associate closely with each other, forming a complex known as a dimer (dimerization).

18. Explain how the receptors are activated in the third step.

Dimerization activates the tyrosine kinase region of each monomer; each tyrosine kinase adds a phosphate from an ATP molecule to a tyrosine on the tail of the other monomer.

19. Explain how the activated receptor can stimulate multiple cellular response pathways.

Once the receptor is fully activated, it is recognized by specific relay proteins inside the cell. Each such protein binds to a specific phosphorylated tyrosine, undergoing a resulting structural change that activates the bound protein. Each activated protein triggers a transduction pathway, leading to a cellular response.

21. What are ion channel receptors?

Ligand-gated ion channels are a type of membrane receptor containing a region that can act as a "gate" when the receptor changes shape. When a signaling molecule binds as a ligand to the receptor protein, the gate opens or closes, allowing or blocking the flow of specific ions through a channel in the receptor.

22. Explain what has happened with the binding of the ligand to the receptor. ✎

When the ligand binds to the receptor and the gate opens, specific ions can flow through the channel and rapidly change the concentration of that particular ion inside the cell. This change may directly affect the activity of the cell.

23. The ligand attachment to the receptor is brief. Explain what happens as the ligand dissociates. ✎

When the ligand dissociates from the ligand-gated ion channel, the gate closes and the ions no longer enter the cell.

24. In what body system are ligand-gated ion channels and voltage-gated ion channels of particular importance?

Ligand-gated ion channels and voltage-gated ion channels (gated ion channels controlled by electrical signals instead of ligands) are crucial to the functioning of the nervous system.

26. This diagram uses testosterone, a hydrophobic hormone, to detail how intracellular receptors work. ✎

Intracellular receptors are found in either the cytoplasm or nucleus of target cells, where they bond to chemical messengers that are either hydrophobic enough (steroids, thyroid hormones) or small enough (nitric acid) to cross the hydrophobic interior of the membrane. [1] The steroid hormone testosterone passes through the plasma membrane. [2] Testosterone binds to a receptor protein in the cytoplasm, activating it. [3] The hormone-receptor complex enters the nucleus and binds to specific genes. [4] The bound protein acts as a transcription factor, stimulating the transcription of the gene into mRNA. [5] The mRNA is translated into a specific protein.

27. Explain the function of transcription factors in the cell.

Special proteins called transcription factors control which genes are turned on (and thus transcribed into mRNA) in a particular cell at a particular time.

28. What are two benefits of multistep pathways?

Firstly, multiple steps may greatly amplify a signal. If some of the molecules in a pathway transmit the signal to numerous molecules at the next step in the series, the result can be a large number of activated molecules at the end of the pathway. Secondly, multi-step pathways provide more opportunities for coordination and regulation than do simpler systems, allowing for greater fine-tuning of the response.

29. Explain the role of two categories of enzymes, protein kinase and protein phosphatases, in transduction.

Protein kinases transfer phosphate groups from ATP to a protein. Many of the relay molecules in signal transduction pathways are protein kinases, and they often act on other protein kinases in the pathway. A single cell may have hundreds of different kinds, each specific for a different protein. Together, they probably regulate a large proportion of the thousands of proteins in a cell. Protein phosphatases can rapidly remove phosphate groups from proteins, a process called dephosphorylation. By dephosphorylating and thus inactivating protein kinases, phosphatases provide the mechanism for turning off the signal transduction pathway when the initial signal is no longer present. Phosphatases also make the protein kinases available for reuse. At any given moment, the activity of a protein regulated by phosphorylation depends on the balance in the cell between active kinase molecules and active phosphatase molecules.

30. Explain what is occurring in the cell at each arrow. ✎

[1] A relay molecule activates protein kinase 1. [2] Active protein kinase 1 transfers a phosphate from ATP to an inactive molecule of protein kinase 2, thus activating this second kinase. [3] Active protein kinase 2 ten catalyzes the phosphorylation and activation of protein kinase 3. [4] Finally, active protein kinase 3 phosphorylates a protein that brings about the cell's response to the signal. [5] Enzymes called protein phosphatases (PP) catalyze the removal of the phosphate groups from the proteins, making them inactive and available for reuse.

31. What is the difference between a first messenger and a second messenger?

The first messenger is the extracellular signaling molecule, the ligand, that binds to the membrane receptor. Many signaling pathways involve small, non-protein, water-soluble ions or molecules called second messengers, which can rapidly spread through the cell by diffusion.

32. Two common second messengers are cyclic AMP (cAMP) and Ca^{2+} ions. Explain the role of the second messenger cAMP.

The second messenger cAMP is made from ATP by adenylyl cyclase, an enzyme embedded in the plasma membrane. Cyclic AMP is inactivated by phosphodiesterase, an enzyme that converts it to AMP.

33. What is the important relationship between the second messenger and protein kinase A?

The immediate effect of cAMP is usually the activation of a serine/threonine kinase called protein kinase A. The activated protein kinase A then phosphorylates various other proteins, depending on the cell type.

34. How might a cellular response be inhibited?

In G protein systems that inhibit adenylyl cyclase, a different signaling molecule activates a different receptor, which in turn activates an inhibitory G protein.

35. Using your knowledge of cell signaling, explain the mechanism of disease in cholera.

People acquire the cholera bacterium by drinking contaminated water. The bacteria form a biofilm on the lining of the small intestine and produce a toxin, specifically an enzyme that chemically modifies a G protein involved in regulating salt and water secretion. Because the modified protein is unable to hydrolyze GTP to GDP, it remains stuck in its active form, continuously simulating adenylyl cyclase to make cAMP. Consequently, the high concentration of cAMP causes intestinal cells to secrete large amounts of salts into the intestines, with water following by osmosis. An infected person quickly develops profuse diarrhea and if left untreated can soon die from loss of water and essential salts.

36. List three types of pathways often induced by calcium ions.

Increasing the cytosolic concentration of Ca^{2+} causes many responses in animal cells, including muscle cell contraction, secretion of certain substances, and cell division. In plant cells, a wide range of hormonal and environmental stimuli can cause brief increases in cytosolic Ca^{2+} concentration, triggering various signaling pathways, such as the pathway for greening in response to light. Ca^{2+} are actively transported out of the cell and are actively imported from the cytosol into the endoplasmic reticulum (and, under some conditions, into mitochondria and chloroplasts) by various protein pumps.

37. What happens to the cytoplasmic concentration of calcium when it is used as a second messenger?

Although cells always contain some Ca^{2+}, this ion can function as a second messenger because its concentration in the cytosol is normally much lower than the concentration outside the cell. As a result of using Ca^{2+} as a second messenger, the calcium concentration in the ER is usually much higher than that in the cytosol. Because the cytosolic calcium level is low, a small change in absolute numbers of ions represents a relatively large percentage change in calcium concentration.

38. When cell signaling causes a response in the nucleus, what normally happens?

Signaling pathways may ultimately regulate protein synthesis by turning specific genes on or off in the nucleus. The final activated molecule in a signaling pathway may function as a transcription factor, which often regulates several different genes.

39. When cell signaling causes a response in the cytoplasm, what normally happens?

Signaling pathways may regulate the activity of proteins, directly affecting proteins that function outside of the nucleus. A signal may cause the opening or closing of an ion channel or a change in cell metabolism.

40. Fig. 11.16 shows a single molecule of epinephrine resulting in the formation of 10^8 molecules of glucose-1-phosphate!

This pathway amplifies the hormonal signal: one receptor protein can activate about 100 molecules of G protein, and each enzyme in the pathway, once activated, can act on many molecules of its substrate, the next molecule in the cascade.

41. Fig. 11.18 shows four different cellular results from a single signaling molecule. Briefly describe each response.

In Cell A, the pathway leads to a single response. In Cell B, the pathway branches, leading to two responses. In Cell C, cross-talk occurs between two pathways. In Cell D, a different receptor leads to a different response.

42. How do scaffolding proteins enhance a cellular response?

In many cases, the presence of scaffolding proteins, large relay proteins to which several other relay proteins are simultaneously attached, apparently increases the efficiency of signal transduction. Some scaffolding proteins in brain cells permanently hold together networks of signaling-pathway proteins at synapses.