STUDY GUIDE - *Ch.11.3 - Signal Transduction: Cascades of Molecular Interactions Transmit Signals from Receptors to Relay Molecules in the Cell* **NAME:** _____

- **PHYSICALLY PRINT OUT this PDF and HANDWRITE (with a black or blue pen) your answers directly on this PDF.** *Typed or digitally-written work is **not** accepted. Do **not** answer questions on separate paper.*
- **Importantly, study guides are NOT GROUP PROJECTS!!!** *You, and you alone, are to answer the questions as you **read** your assigned textbook. You are **not** to share answers with other students. You are **not** to copy any answers from any other source, including the internet.*
- **Get in the habit of writing LEGIBLY, neatly, and in a medium-sized font.** *AP essay readers and I will skip grading anything that cannot be easily read so start perfecting your handwriting, and don't write so large you can't add all the relevant details and key elaborations in the space provided.*
- **SCAN physical documents in color and with good resolution. Then, upload your final work as PDFs to Archie.** *Avoid uploading dark, shaded, washed-out, sideways, or upside-down scans of homework. Keep completed physical study guides organized in your biology binder to use as future study and review tools.*
- **READ FOR UNDERSTANDING and not merely to complete an assignment.** ***First**, read a section quickly to get an overview of the topic covered. Then, read it a **second** time slowly, paraphrasing each paragraph **out loud** and analyzing every figure. Finally, read it a **third** time as you answer the study guide questions if assigned and start building your memory. Try to write answers out in your own words, when possible, and try to purposefully and accurately use all new terminology introduced.*

1. In this section, we will look more carefully at the process of **transduction**, in which an external message, brought to a cell by a primary signaling molecule, the ligand, is translated into an internal message within the cell.

   Fill in the missing words in the following sentence:

   When receptors are _____ _____ proteins, the transduction stage of cell signaling is often a multi-step pathway with steps that often include activation of proteins by the addition or removal of _____ groups or the formation or release into the cytoplasm of other small _____ or _____ that act as secondary, internal, signaling molecules.

2. What are **two benefits of using multi-step pathways to relay an external message to the inside of a cell in order to induce a cellular response**?

   1.

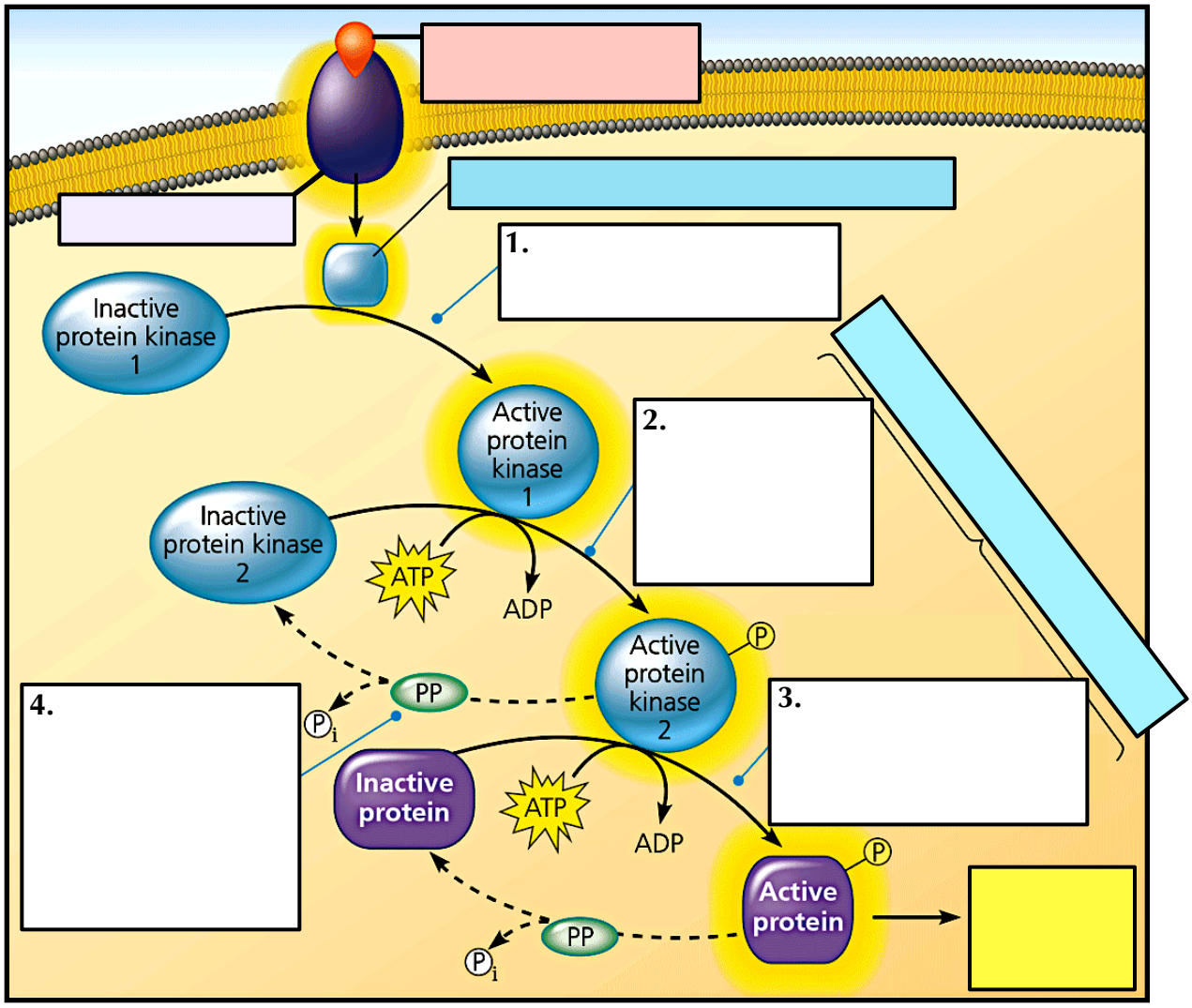
   2.

3. Most often, like **when the ligand is hydrophilic**, the initial signaling molecule **(the primary messenger)** does **NOT enter the target cell**. Instead the binding of this ligand to a cell receptor, activates the receptor, which then activates another molecule inside the cell, which activates yet another molecule, and so forth, until a final response is triggered inside the cell. These **molecules, which relay the message are often what type of macromolecule**?

4. Relaying a signal on the inside of the cell is often accomplished by a series of protein-to-protein interactions, the **proteins often changing shape**, and, as a consequence, **changing their behavior**. Often these proteins **become activated (or sometimes deactivated), by getting phosphorylated**. What was the name of the category of **enzymes that transfer organic phosphate groups from ATP to their substrate molecules, which often are other proteins themselves**?

5. What do enzymes known as protein **phosphatases** do?

6. Interestingly, **many cytoplasmic protein kinases** activated by a ligand binding to a receptor, **phosphorylate other cytoplasmic protein kinases, until a final target protein inside the cell is activated as a result.** Study carefully Figure 11.10. You should not only understand the steps involved in phosphorylation cascades, but also be able to describe them in writing and draw them too! After studying the figure, fill in the missing information below as a self-quiz to see if you have it all memorized.



Now that you know the information well, fill in the following summary paragraph as a final review.

A _____ cascades is similar to a row of dominoes falling down. A phosphate being added (or sometimes removed) activates other molecules, often a protein _____ as well, which activate yet other protein _____, eventually a target protein being activated (or deactivated) by phosphorylation. For example, in the figure above, an inactive protein kinase 1 gets a _____ added by a relay molecule, activated by the activated receptor. Inactive protein kinase 1 becomes an _____ protein kinase 1. This protein kinase 1 then transfers a _____ from _____ to the next molecule in the pathway, in this case, a protein kinase 2. Now _____ protein kinase 2 is made _____ too. This sequential activation of kinase enzymes continues until the desired protein is activated causing a cellular _____. Ligands reversibly bind receptors, their concentrations dropping in the extracellular fluid in time. Inside the cell, protein _____ remove phosphates from recently phosphorylated proteins.

7. What are two reason why **phosphatase activity** (**the dephosphorylation of proteins that were phosphorylated as part of an activated phosphorylation cascade**) is so important to cells?

   1.

   2.

8. Refer back to the illustration in question #6 above. A DNA mutation results in the making of Protein Kinase 2 that can no longer get phosphorylated by Protein Kinase 1. A researcher wonders how the signal transduction pathway **(reception, transduction, response)** would be affected should ligand be present in the extracellular fluid.

   a. Which part(s) of the signal transduction pathway would still occur normally in the presence of the ligand?

   b. Which part(s) of the signal transduction pathway would no longer occur even in the presence of the ligand?
   *(Check your answer to question #8.b by going to the **Figure Questions Figure 11.10** answer in Appendix A)*

9. **NOT all components of the signal transduction stage of a signal transduction pathway**, the stage in which a signal is transmitted from the plasma membrane to the metabolic machinery of the cytoplasm, **are always proteins.**

   a. What are **second messengers**?

   b. If second messengers are made inside the cell as part of the signal transduction process, what then is considered the **first messenger**?

   c. What is the **benefit of producing second messengers inside the cell** (after a ligand has bound to a receptor)?

   d. Name the two **most common second messengers**?

   _____ & _____

   (Note: These are not the only second Messengers. For example, cGMP, made from the nucleoside triphosphate GTP (Guanosine triphosphate), instead of ATP, is also a second messenger in some cells)

   e. What are the target molecules second messengers interact with that change the behavior inside the cell?

10. Earl Sutherland established that epinephrine caused glycogen breakdown without the epinephrine passing through the plasma membrane. He found that the second messenger used to transmit the signal from the plasma membrane to the cytoplasm was a **cyclic adenosine monophosphate, known as cyclic AMP or cAMP**.

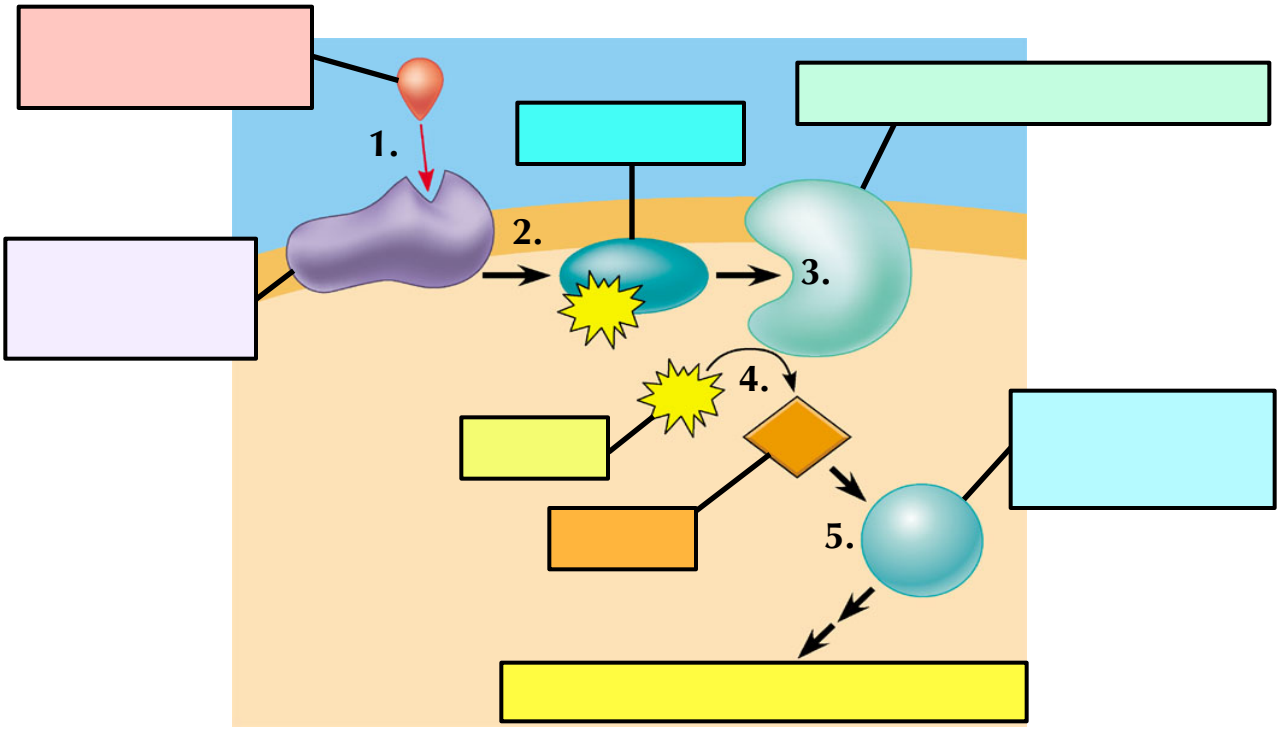
    a. What is **adenylyl cyclase**?

    b. Where is **adenylyl cyclase found** in the cell?

c. How does **adenylyl cyclase get activated**?

d. What are the **immediate effects of cyclic AMP inside the cell**? So, what does cAMP do **and** what is the consequence of that activity.

11. Complete the diagram below showing the functioning of **cAMP as second messenger** in the presence of a G-Protein-Coupled Receptor (Note: Tyrosine Kinase receptors can activate the production of second messengers also)



Step 1:
Step 2:
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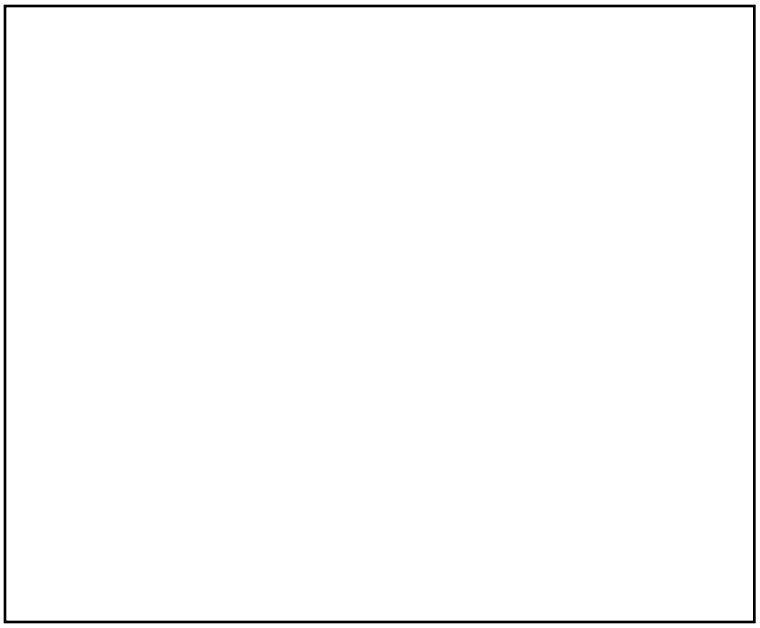
12. a. How is **cAMP deactivated** (turned "off")?

b. *Think:* What would happen if an inhibitor molecule that inactivated the enzyme phosphodiesterase were introduced into a cell? *Think about what effect that would have on a cell after ligands are bound to receptors as well as once ligands are no longer present anymore in the extracellular fluid of a cell.*
*(Check your answer by going to the **Figure Questions Figure 11.11** answer in Appendix A)*

13. The bacterium, *Vibrio cholera,* causes the often deadly infectious disease cholera. It produces a toxin that locks the G Protein in its active state, unable to hydrolyze GTP back into GDP, causing illness. This G protein is an allosteric **activator** of adenylyl cyclase. Redraw a fully labeled signal transduction pathway, like the one in question #11, in the space below, this time showing what would be the case if **cholera toxin was present**, even after the ligand that initially activated the signal transduction pathway was **NO LONGER** around. Be sure to think of where the **G protein** would be found at almost all times under this altered circumstance and what the consequence of that would be.
*(Once you gave it a good try, check your answer by going to the **Figure Questions Figure 11.12** answer in Appendix A)*



14. Many different types of G proteins exist, each activated by a different G-Protein-Coupled Receptor. What are the two **possible effects different categories of G proteins have on** the cAMP-producing enzyme **adenylyl cyclase**?

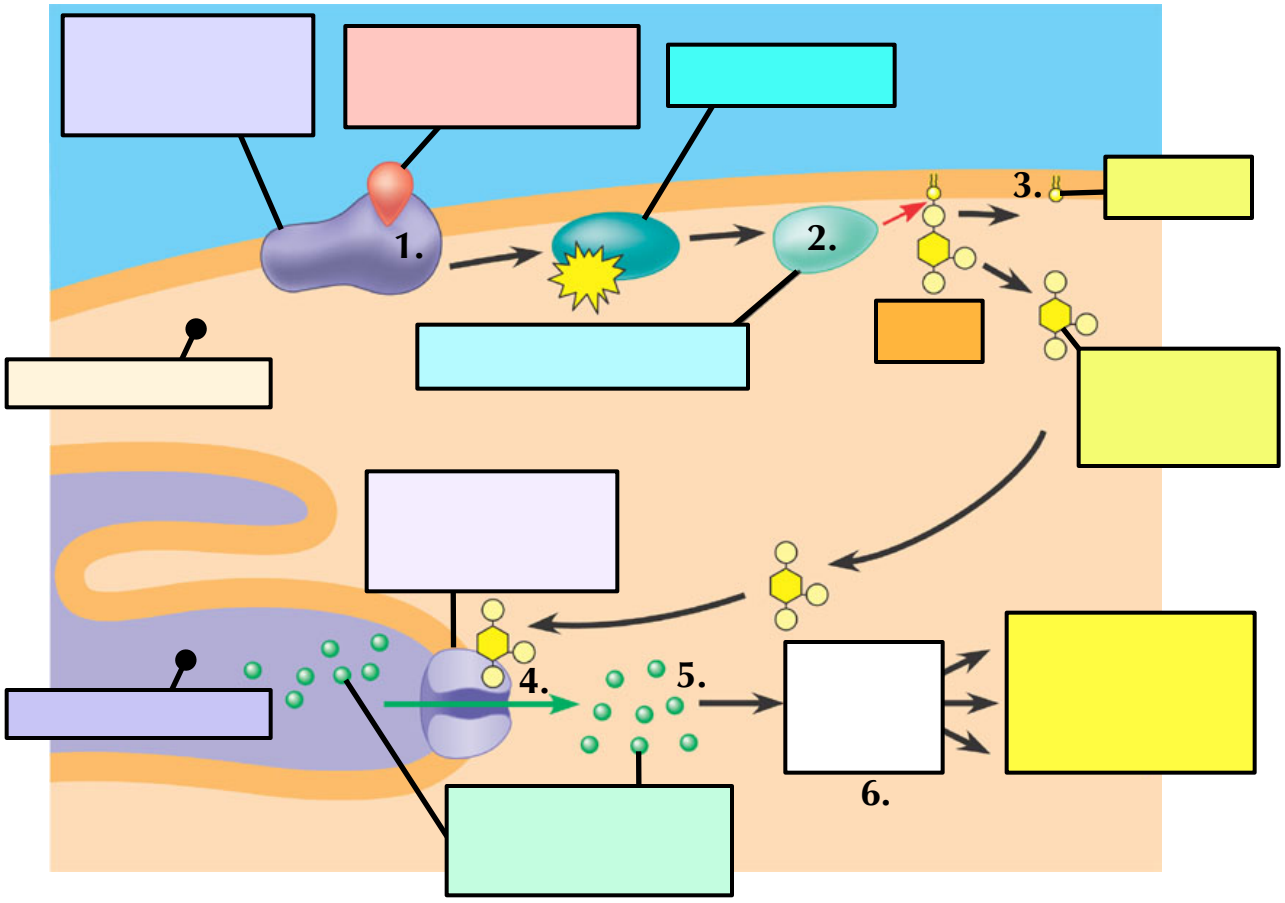
1.

2.

15. Calcium, even more so than cAMP, is widely used as a second messenger. In animals, increasing cytosolic Ca^{+} levels can trigger responses such as muscle cell contraction, secretion of certain substances, and cell division. In plants it plays a role in greening in response to light. Calcium uses both G-protein and receptor tyrosine kinase pathways. **Calcium concentrations are kept different, comparatively, in the endoplasmic reticulum, mitochondria cytoplasm, and/or extracellular fluid, the cytoplasmic calcium levels usually being much lower than the rest.**

a. How do cells keep cytoplasmic calcium concentrations so much lower inside the cytoplasm compared to outside the cell or inside the endoplasmic reticulum?

b. The calcium is unable to exit the endoplasmic reticulum because of its positive charge unless IP_3-gated calcium channels open, allowing calcium ions to diffuse down their concentration gradients and into the cytoplasm, where the Ca^{2+} ions acts as a second messenger inside the cell, helping trigger other cell responses. First, study carefully Figure 11.14, highlighting another signal transduction pathway in cells that leads often to calcium release. Once you feel you have the steps and information mastered, see if you can label the following diagram and explain the 6 steps of the **Calcium and IP3 signaling pathway**.



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