QUESTIONS, Cell signaling part 1

1: TRUE OR FALSE? Explain why. There is no fundamental distinction between signaling molecules that bind to cell surface receptors and those that bind to intracellular receptors.

2 If we draw an analogy between modes of cellular communication and human communication, which corresponds best to which?

1. A) paracrine signaling
2. B) autocrine signaling
3. C) hormonal communication
4. D) synaptic signaling

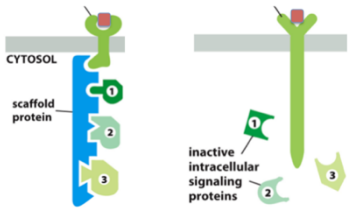
1. a) telephone communication
2. b) talking to yourself
3. c) announcement at the radio
4. d) talking to people at a cocktail reception

3 A ligand called LIG-AT, which binds and activates its receptor REC-AT in melanoma cells, activates a signaling pathway that stimulates melanoma cell proliferation. In pancreatic cancer cells, it is observed that LIG-AT also stimulates cell proliferation but that these cells have a complete deletion of the gene coding for REC-AT. How is this possible?

4 Imagine a signaling pathway involving two kinases, K1 and K2, acting sequentially (but we do not know the order of sequence). When they are inactive, cells do not respond to an external signal called X. However, when X is present, this leads to activation of this signaling pathway.
If cells contain a mutant form of K1 that is always active, called K1+, they activate this signaling pathway even in the absence of X. Double mutant cells that contain a mutant of K2 that is always inactive, called K2-, and a mutant always active K1+, also activate this signaling pathway even in the absence of X.

4A) In this kinase cascade, do you deduct that K1 activates K2, or the reverse, that K2 activates K1? Why?
4B) If there was, in other cells, mutant forms like that: K1- (always inactive) and K2+ (always active), what would happen to this signaling pathway?

5: Compare the two situations below, on the left the kinases are held in close proximity by a scaffold. On the right the Kinases are free and will be free once activated. Additionally, the kinases can interact transiently, for example two kinases A and B can interact and then stop interacting and interact with another kinase A or B also when phosphorylated. Each case signaling pathway consists of three kinases. Each time the signaling cascade is as follows: Kinase (1) activates Kinase (2) and Kinase (2) activates Kinase (3). As they are kinases, activation of a downstream target is caused by phosphorylation.

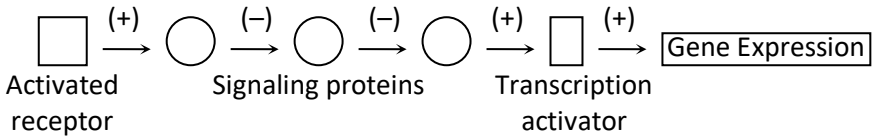


What are your predictions for differences between the receptor types in A) speed of signal transduction, B) signal amplification, and C) cross-talk with other signaling pathways.

6: What do you answer to this statement: A receptor that is bound by its ligand will stimulate a signaling cascade ultimately leading to the activation of a transcription factor; a receptor is therefore never a transcription factor by itself.

7: In which one(s) of the following schematic drawings of signaling pathways does the activation of the receptor lead to gene expression? Activating and inhibitory steps are indicated with (+) and (–), respectively.

A.



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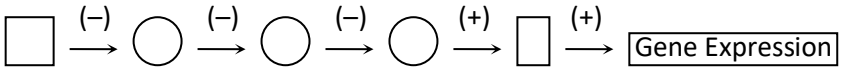

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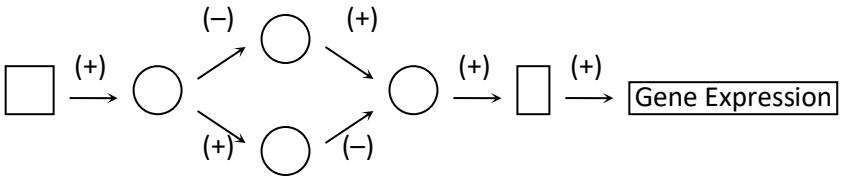

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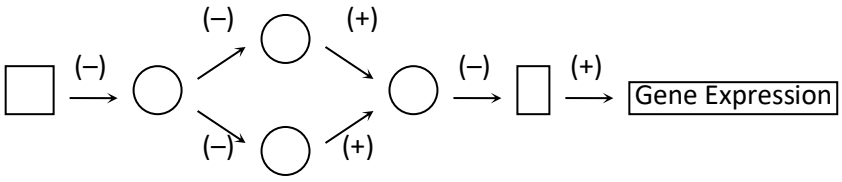
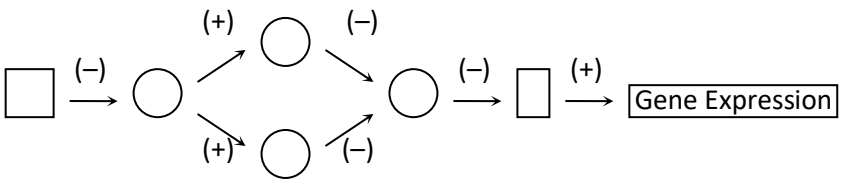


E.



8 How is it that diferent cells can respond in diferent ways to exactly the same signaling molecule even when they have identical receptors?

9 Why do you suppose that phosphorylation/dephosphorylation, as opposed to allosteric binding of small molecules, for example, has evolved to play such a prominent role in switching proteins on and of in signaling pathways?

10 Two intracellular molecules, A and B, are normally synthesized at a constant rate of 1000 molecules per second per cell. Each molecule of A survives an average of 100 seconds, while each molecule of B survives an average of 10 seconds.

1. How many molecules of A and B will a cell contain?
2. If the rates of synthesis of both A and B were suddenly increased 10-fold to 10,000 molecules per second—without any change in their average lifetimes—how many molecules of A and B would be present after 1 sec- ond?
3. Which molecule would be preferred for rapid signaling? Explain your answer.

11 Describe three ways in which a gradual increase in an extracellular signal can be sharpened by the target cell to produce an abrupt or nearly all-or- none response.