**Guide Questions for Topic: Cell Signaling**

1. Which of the following are cell behaviors that are regulated by extracellular signaling molecules?

2. Which of the following statements best describes the term “extracellular signaling molecule”?

3. During development of mammals (included humans), the extracellular signaling molecule BDNF (brain-derived neurotrophic factor) is secreted by cells within the developing brain, which then triggers the differentiation of nearby cells into neurons. This represents an example of _____ signaling.

4. Adrenaline (aka, epinephrine) is an extracellular signaling molecule secreted from the adrenal medulla into the blood circulation in response to stress. Upon reaching muscle cells, it triggers them to rapidly catabolize (i.e., breakdown) glycogen to glucose. This represents an example of _____ signaling.

5. Testosterone, progesterone, and cortisol are all examples of steroid hormones. Based on this information, what would you predict they have in common with each other?

6. What are nuclear receptors?

7. TRUE or FALSE: All transcription factors are nuclear receptors.

8. All nuclear receptors have the following three domains: _____.

9. How does glucocorticoid affect gene expression in cells?

10. Which of the following mutations would you predict to cause constitutive expression of genes that are activated by the glucocorticoid receptor?

11. How does thyroid hormone affect gene expression in cells?

12. Which of the following mutations would you predict to cause constitutive repression of genes that are activated by the thyroid hormone receptor?

13. Peptide growth factors are composed of _____ and affect cell behavior through binding and activation of _____.

14. In the absence of ligand, G-protein coupled receptors (GPCRs) form protein-protein interactions with _____ through their _____ domain.

15. Binding of a ligand to the _____ domain of a GPCR activates its _____ activity within its _____ domain.

16. How do GPCRs activate G proteins?

17. Once activated, G proteins regulate target proteins mostly through _____.

18. Most ligands for receptor protein-tyrosine kinases (RTKs) are growth factors that exist and function as dimers. Why is their dimeric form critical to the activation of RTKs?

19. The extracellular domain of RTKs contains its _____ domain, whereas its intracellular domain contains _____ activity.

20. Dimerization of RTKs causes _____.

21. Grb2 and PIK3R1 are two proteins that contain SH2 domains. Based on this information, what would you predict that Grb2 and PIK3R1 have in common?

22. Which of the following statements accurately distinguishes molecules that would be classified as "extracellular signaling molecules" versus "intracellular signaling proteins"?

**GQs for the cAMP pathway:**

23. cAMP is a _____ and is synthesized by _____.

24. How does cAMP activate protein kinase A (aka, cAMP-dependent protein kinase)?

25. How does epinephrine activate the cAMP pathway in cells?

26. What does the acronym "CRE" refer to?

27. c-fos, BDNF, VGF, and PER1 are four examples of genes that are activated by CREB. Based on this information, what would you predict those genes have in common with each other?

28. Which of the following is/are required for CREB to activate its target genes?

29. What class of proteins does CBP (CREB-binding protein) belong to? What does that indicate about how CBP contributes to gene expression in cells?

**GQs for second messengers:**

30. What does the term "second messenger" refer to within the context of cell signaling?

31. Why are cAMP and calcium both examples of second messengers, whereas protein kinase A (PKA) and adenylyl cyclase are not?

**GQs for part 2b video on the ERK MAP kinase pathway:**

32. Ras is an example of a _____ and is thus activated by a _____.

33. How does the covalent modification of Ras with a prenyl group affect it?

34. How does activation of an RTK cause Ras activation?

35. Upon activation, Ras activates _____ via _____.

36. What do Raf, MEK, and ERK have in common with each other?

37. The genes encoding Mcl-1, cyclin D, and Egr1 are all activated by the Elk-1/SRF transcription factor complex in response to growth factors. Based on this information, what do you predict those genes would have in common with each other?

38. How do growth factors activate Elk-1/SRF target genes?

**<u>GQs for the PI 3-kinase/Akt pathway</u>:**

39. $PIP_3$ is another example of a _____ and is generated by _____.

40. Where are $PIP_2$ and $PIP_3$ localized within cells?

41. Why does activation of RTKs cause PI 3-kinase to phosphorylate $PIP_2$?

42. The major target activated by production of $PIP_3$ is _____, which belongs to what class of proteins?

43. Upon binding to $PIP_3$, Akt must be _____ by mTORC2 and PDK1 for its activation.

44. Which of the following mutations in Akt would you predict to prevent Akt activation following activation of PI 3-kinase?

45. How does PI 3-kinase/Akt signaling affect the transcription factor FOXO?

46. If you deprived cells of growth factors, where would you expect to FOXO within cells? What effect would it have on FOXO target genes?

47. When active, how does GSK-3 affect protein synthesis in cells?

48. How does PI 3-kinase/Akt signaling promote protein synthesis in cells?

49. Why does inhibition of eIF2B by GSK-3 promote apoptosis in cells?