

Receptors

Based on the required reading (Wise, Jupe, and Rees in *Annu. Rev. Pharmacol. Toxicol.* 2004, 44:43-66) and/or any other materials available to you, answer the following questions:

1. Explain why some G-protein coupled receptors are called orphan GPCRs and why people are interested in them. (2 pts)
2. Imagine that you have just cloned an orphan GPCR gene into your favorite eukaryotic expression system and need to find out if the protein is indeed expressed in these cells. Discuss one way to confirm that the orphan GPCR protein is expressed in your expression system. (2 pts)
3. Imagine that you need to find a ligand for the orphan receptor and are looking for sources that are likely to contain the ligand for this receptor. Prepare a list of three possible such sources and briefly discuss the advantages/disadvantages of using each of the three sources. (2 pts)
4. Imagine that you have identified a compound that produces increase in Ca^{++} concentration in your expression system. Describe necessary controls to ensure that the increase in Ca^{++} concentration is mediated by the orphan receptor. (2 pts)
5. Imagine that you have identified a ligand specific to the orphan GPCR that you were studying. Propose an experiment to test a hypothesis that this receptor acts via the inhibitory $\text{G}_{\alpha i}$ protein. (2 pts)