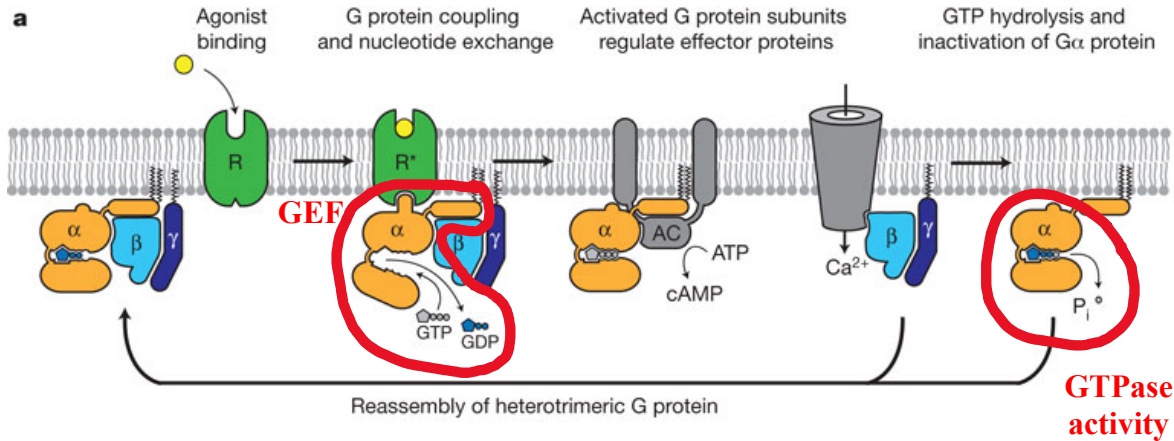


Names: _____

The scientists who determined the GPCR and heterotrimeric G protein crystal structure and its conformational changes were awarded the Nobel Prize in 2012. Below are figures from one of the papers of this work: Rasmussen *et al*, Nature 2011.

Overall Pathway

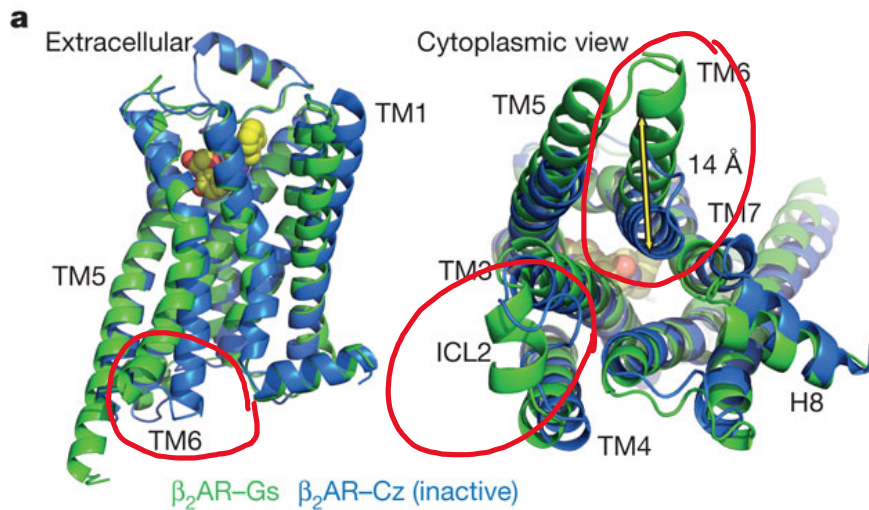
1. Where on the summary diagram is the non-catalytic guanine exchange caused by the Guanine Exchange Factor (GEF)? Where is the GTPase catalytic activity used? Circle and label these events.



- The receptor serves as a Guanine Exchange Factor (GEF) to help the Gα protein open up and release GDP. The empty Gα protein can then bind to GTP.
- The Gα protein itself is a GTPase enzyme that can cleave off a phosphate from GTP. This is a type of phosphatase reaction: $GTP \rightarrow GDP + P_i$.

The Receptor

2. Upon binding to the ligand (agonist), the transmembrane receptor protein changes conformation as shown below (green = bound to ligand, blue = no ligand). Find the parts of the receptor that change location and circle them.

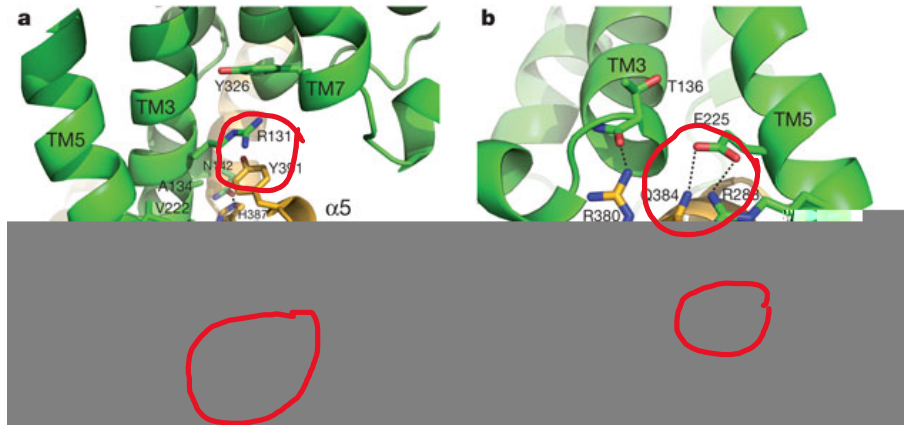


Transmembrane segment 6 (TM6) and the interconnecting loop (ICL2) move the most.

Names: _____

The Receptor's Binding to the G-alpha Protein

3. Shown is the binding between the receptor (green) and the G-alpha protein. Circle two sets of interacting amino acids and give the type of intermolecular bond (ionic, H-bond, van der Waals).



E225 with Q384 is a Glu with a Gln => H-bond. K232 with D381 is Lys with Asp => ionic bond. L394 with L230 is Leu with Leu => vdW bond.

The Receptor's Effect on the G-alpha Protein

4. Shown is the interaction between the receptor (green) and the active G-alpha protein (yellow, open, in the act of releasing the GDP) and the inactive G-alpha protein (grey, closed around the GDP analog called GTP γ S).

Circle the parts of the receptor that change conformation when ligand binds (Q2 above).
Circle the parts of the receptor that make important interactions with the G-alpha protein (Q3 above).
Note how changes in these regions affect the overall change in the G-alpha protein that allows exchange of GDP for GTP!

