With this background on the structure and general properties of the GPCRs and the G-proteins, we can now look at what happens when a signal arrives at the cell surface and binds to a GPCR. The binding of a signal molecule by the extracellular part of the G-protein linked receptor causes the cytosolic tail of the receptor to interact with, and alter the conformation of, a G-protein. This has two consequences:

- First, the alpha subunit of the G-protein loses its GDP and binds a GTP instead.
- Second, the G-protein breaks up into the GTP-bound α part and the β part.
What happens when G-proteins interact with their target proteins? That depends on what the target is. G-proteins interact with different kinds of target proteins, of which we will examine two major categories:

**Ion Channels**

Figure 8.4.6: Second Messengers
What is the effect of elevated cAMP levels?

For example, the binding of epinephrine to its receptor on the cell surface, activates, through the action of G-proteins, and subsequent activation of PKA, the phosphorylation of glycogen phosphorylase. The resulting activation of glycogen phosphorylase leads to the breakdown of glycogen, releasing glucose (in the form of glucose-1-phosphate) for use by the cell. Changes in gene expression, likewise, lead to changes in the cell by altering the production of particular proteins in response to the signal.

Although the steps described above seem complicated, they follow the simple pattern outlined at the beginning of this section:
• Binding of signal to receptor
• Several steps where the signal is passed on through intermediate molecules (G-proteins, adenylate cyclase, cAMP, and finally, PKA)
• Phosphorylation of target proteins by the kinase, leading to changes in the cell.

The IP3 and DAG produced by activated phospholipase C work together to activate a protein kinase. First, IP3 diffuses to the endoplasmic reticulum membrane where it binds to gated calcium ion channels. This causes calcium channels in the ER membrane to open and release large amounts of calcium into the cytoplasm from the ER lumen, as shown in the figure below.

The increase in cytosolic calcium ion concentration has various effects, one of which is to activate a protein kinase called protein kinase C (C for calcium), together with the DAG made in the earlier step. Like PKA, Protein kinase C phosphorylates a variety of proteins in the cell, altering their activity and thus changing the state of the cell.

The pathways leading to PKC and PKA activation following the binding of a signal to a GPCR are summarized in Figure 8.4.12.

Contributors

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