

event that elicits a cellular response. There are at least 24 adhesion GPCRs, and they have been identified in immune cells, the central nervous system, and reproductive tissue.⁴³

G-Protein-Dependent Signaling Pathways

Signal transduction requires the presence of both machinery to produce the signal and a carrier to propagate the signal itself. The telephone, for example, is well suited to produce a signal that allows for communication over long distances, but cannot function in the absence of an electrical current, which acts as the signal to create sound at each end of the communication grid. In the same sense, GPCRs are the machinery that generate the signal (i.e., the telephone), but they are of little use in the absence of a signaling molecule of some type (i.e., the electricity) that transmits the signal. The signaling molecules that transmit signals from the GPCRs to the rest of the cellular machinery are often referred to as “second messengers” and can significantly amplify the signal strength by activating downstream cellular machinery. There are two major second messenger systems, the cAMP system (Figure 3.23), which uses cyclic adenosine monophosphate (cAMP, 3'-5'-cyclic adenosine monophosphate) system as its second messenger, and the phosphatidylinositol signaling system

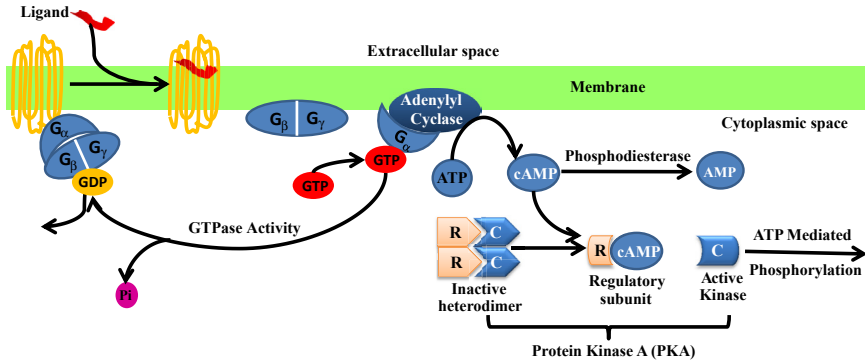


FIGURE 3.23 cAMP signaling begins with binding of a ligand to the GPCR. Conformational changes in the GPCR causes the G-protein complex to dissociate from the GPCR, the G_α protein and GDP are released, and GTP binds to the G_α protein. The GTP/ G_α protein complex binds to adenylate cyclase, activating the enzyme, which produces cAMP. Binding of cAMP to the regulatory protein (“R”) suppressing protein kinase A (RC) releases active protein kinase A (C), allowing it to phosphorylate molecular targets. The system is regulated by the GTPase activity of the G_α protein and cAMP phosphodiesterase.

(Figure 3.24), which generates inositol-1,4,5-trisphosphate (IP_3) and diacylglycerol (DAG) from phosphatidylinositol 4,5-bisphosphate to relay cellular signaling.⁴⁴