Second messanger systems

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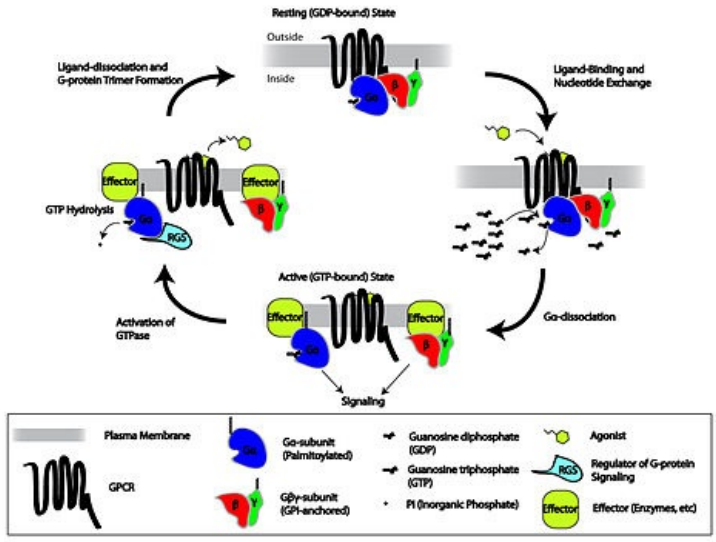
Hormones are signalling molecules that bind to a receptor and initiate a response in the cell. Second messenger systems are a link between extracellular events and chemical changes within the cell. There are two main second messenger systems: the calcium/phosphatidylinositol system and the adenyl cyclase system.

Adenylyl cyclase system

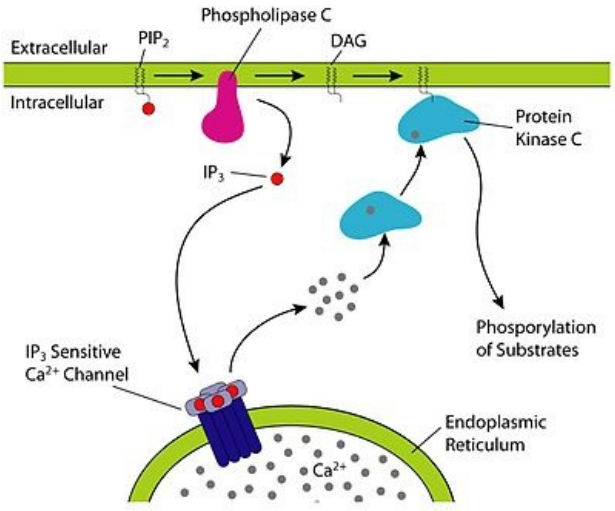
The adenylyl cyclase system in initiated by a chemical messenger binding to ß or α andrenergic receptors. ß and α andrenergic receptors are G-coupled receptors activated by norepinephrine or epinephrine. This causes either an increase or a decrease in the adenylyl cyclase, which is an enzyme responsible for converting ATP to 3'-5'-adenosine monophosphate (also called cAMP or AMP). Cells respond to more than one chemical signal and have several different receptors, each linked to adenyl cyclase. They are called more specifically G protein coupled receptors (GPCR). GPCR are composed of: extracellular ligand-binding region, seven transmembrane helices and an intracellular domain that interacts with G proteins.

The activity of GPCR is controlled by trimeric proteins (α, ß and γ). They are called G-proteins because they bind guanosine nucleotides GTP or GDP. They link adenyl cyclase with the G protein.

Usually the G protein is bound to GDP, when GTP binds, the α subunit dissociates and moves to adenylyl cyclase. This newly activated cyclic AMP activates a protein kinase, for example protein kinase A. By binding to its two regulatory subunits it causes the release of active catalytic subunits, which catalyses the transfer of phosphate from ATP to specific amino acid residues of proteins. These phosphorylated proteins can: act directly on ion channels of the cell, if they are enzymes they may be either activated or inactivated by phosphorylation or can be phosphorylated DNA binding proteins effecting gene expression.



GPCR cycle



Phosphatidylinositol system

The system is similar, but the α subunit when activated by a GTP bound to the α subunit activates the enzyme phospholipase C, instead of activating adenylyl cyclase. Phospholipase C, produces inositol triphosphate (IP3) and diacylglycerol (DAG). IP3 acts on the endoplasmic reticulum causing a release of calcium cations that activated Protein C. DAG activates directly Protein Kinase C. Protein kinase C phosphorylates cellular proteins, which produces a vast array of effects on the cell.

Bibliography

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