Signal transduction, membrane receptors and their ligands, G-proteins

Signal transduction

The conversion of signal from outside the cell to a functional change within the cell is known as signal transduction. It involves ordered sequences of reactions within the cell, carried out by enzymes, activated by second messengers resulting in an a signal transduction pathway. This pathway has many steps through which the final specific task expected by the cell is achieved.

Signal transduction pathway

1. **First messengers:** they are compounds located in the extracellular compartment destined to bind on cell plasma membrane receptors and initiate the transduction pathway. First messengers refer to hormones, neurotransmitters, growth factors and cytokines.
2. **Receptors:** they are integral proteins located on the cell plasma membrane, responsible for binding specific first messengers in order to elicit the proper intracellular response either directly or through second messengers. There are three different types of receptors specified for first messengers: Ion channel receptors, G-protein-linked receptors and Enzyme linked receptors
3. **Transducers:** it is the mean through which the first effector is activated. The term transducer usually refers to G proteins.
4. **First effectors:** They are enzymes activated by transducers or directly by receptors.The synthesize and activate second messengers in order to carry on the signal. There are many different typers of primary effectors such as: adelylyl cyclase: formation of the cAMP (cyclic adenosine monophospate) second messenger, phospolipase C: formation of IP_3 (inositol triphosphate) and 1,2 DAG (1,2 diacylglycerol) second messengers, phospholipase A_2: formation of arachidonic acid second messenger, guanylyl cyclase: formation of cGMP (cyclic guanosine monophosphate) second messenger
5. **Second messengers:** they are compounds activated by first effectors and they are responsible for activation of second effectors. Second messegers as mentioned above are cAMP, cGMP, arachidonate and phospholipases.
6. **Second effectors:** they are enzymes activated by second messengers. They are the final part of the signal transduction pathway responsible for eliciting the proper cellular response according to the specific signal.

Membrane receptors

Ion channel-linked receptors

There also referred to as ligand-gated channels which upon ligand interaction they alter their conformational arrangement and allow influx or outflux of ions of form of signal transduction in the form of ionic movement. This results in changes in the electrical potential of the cell that in turn propagates the signal along the cell. Ion channel-linked receptors usually serve synaptic signaling between neurons and electrically excitable cells.

G-protein-linked receptors

G-protein-linked receptors typically have seven membrane spanning domains. In the absence of a ligand, the heterotrimeric (α,β and γ subunits) G-protein is in an inactive GDP-bound form and probably not associated with its receptor. The G-protein complex is anchored to the the cytosolic side of the membrane through prenylated groups on the β,γ subunits. When a ligna interacts with the receptors, conformational change of the receptor occurs. Activation causes G-protein to release GDP and bind GTP. This activates the G-protein with subsequent dissociation of the α-GTP subunits from the β,γ dimer. The α-GTP subunit binds to and activates the primer effectors such as: adenylyl cyclase, guanylyl cyclase, ion channels, phospholipases and sometimes phosphodiesterases.

Enzyme-linked receptors

They are receptors that activate enzymes or have enzymatic activity themselves.

1. Receptor guanylyl cyclase: ligand binding leads to formation of cGMP second messenger which binds to and activates cGMP-dependent protein kinase (aka protein kinase G) which in turn phosphorylates substrates.
2. Receptors tyrosine kinase: surface receptors direclty linked to intracellular enzyme kinases. Ligand binding induces receptor dimerization which leads to autophosphorylation of the receptor. Phosphorylation increases tyrosine kinase activity creating specific new binding sites destined to bind proteins. Bound proteins are phosphorylated and activated at the tyrosine residues and transmit intracellular signals.
3. Receptor tyrosine phopshatase: upon ligand binding it activates and is responsible for dephosphorylation, thereby terminating signals initiated by the protein tyrosine kinase.

Links

Bibliography

MURRAY, Robert K. – BENDER, David A.. *Harper's Illustrated Biochemistry.* 29th edition. McGraw-Hill Companies, Inc., 2012. ISBN 978-0-07-176576-3.