Kinase-linked receptor

Receptors are intracellular and cell surface proteins that interact with drugs or signaling molecules and initiate a series of biochemical events in cell or organisms. The receptor plays a central part in deciding the nature of the pharmacological impact of the medicate reaction (Litalien & Beaulieu 2011). There are four receptors which is ionotropic receptors, G-protein coupled receptors, Kinase-linked receptors and nuclear receptors.

The role of kinase-linked receptors is to receive messages from the outside world, receive them and pass them on until they reach the relevant target. Proteins, enzymes, and chemical messengers inside the cell all transfer information to the intended target. The kinase link receptors do not interact with the rapid response departments of cells like ionotropic and G-protein, but instead focus on tasks and results that occur within minutes to hours. There are three main types of the task that including glucose and glycogen metabolism (motioned by insulin), inflammation response (motioned by cytokine) and the most common function is to command cell division or separation, at last prompting new tissue which are called growth factors.

Figure 1: The process of how kinase-linked receptors works (Howard 2011)

The kinase-linked receptors are membrane bound receptors with a single alpha helix coil (Hubbard 1999). In the case of receptor tyrosine kinase (RTK) or receptor serine/threonine kinase (RS/TK), the kinase-linked receptor is a complex of transmembrane proteins located in the plasma membrane, which has tyrosine Kinase or serine/threonine kinase activity. The ligands that bind to these receptors trigger the initiation of the phosphorylation cascade, which ultimately results in the transcription factor recruiting gene promoters and transcriptional activation into the target nucleus(Rotman & Wahli 2010). In other words, the receptor phosphorylates each other. The phosphorylated receptors now act as a docking site and attract
proteins from within the cell, initiating a signaling cascade (Lemmon & Schlessinger 2010). This signaling cascade leads to gene transcription and changes in the expressing of target genes. Ultimately this results in changes in cell function (Ullrich & Schlessinger 1990).

![Canonical signal transduction cascades for kinase-linked receptors](image)

**Figure 2:** Canonical signal transduction cascades for kinase-linked receptors (Rotman & Wahli 2010).

When the receptor system breaks down, the diabetes, inflammation, or bone disease can occur, and most of these diseases are cancers (Lemmon & Schlessinger 2010). The failure of protein tyrosine kinases is a hallmark of many diseases, and usually refers to its increased activity. Many nausea diseases are associated with increased activity, such as psoriasis, papilloma (Levitzki 1999).

Epidermal growth factor is one of the four members of the RTK family which is widely expressed in various ectoderm and mesoderm cells (Borg et al. 2000). Overexpression of EGFR usually occurs in many types of cancers, such as the head and neck, colon, ovarian, cervical, papillary thyroid, etc. The signal pathways through EGFR activate many features associated with cancer cells, such as proliferation, migration, stromal invasion, tumor neovascularization, and resistance to cell death suggest that the main EGFR ligands are EGF and transforming growth factor, heparin-binding EGF, regulatory protein, betaine, epiregulin (Shawver, Slamon & Ullrich 2002). Excessive expression of EGFR is accompanied by self-secretion or paracrine expression of the ligand, resulting in a continuously enhanced stimulation of the EGF dependent pathway (Levitzki 1999). The potential success of developing EGFR kinase inhibitors is an important achievement, as it may become an effective universal inhibitor.

Cetuximab is a monoclonal antibody against epidermal growth factor receptor (EGFR), which
is approved by the FDA to treat metastatic colorectal cancer and head and neck cancer. Colorectal cancer patients will show a lot of epidermal growth factor receptor, and may be one of the causes of cancer cells, cetuximab is aimed at the characteristic development of cancer cells, target drug can fully inhibit the growth of cancer cells, reduce the impact on the rest of the normal cells, thus can reduce drug treatments have side effects on cancer patients (Gonçalves et al. 2008). Although most new targeted cancer drugs have former genome origin, but people can foresee a complex wave of "smart drugs" post-genome fundamentally change all the treatment of cancer.

**Reference**


Levitzki, A. 1999, 'Protein Tyrosine Kinase Inhibitors as Novel Therapeutic', *Pharmacology and Therapeutics*, vol. 82, no. 2, pp. 231-9.


