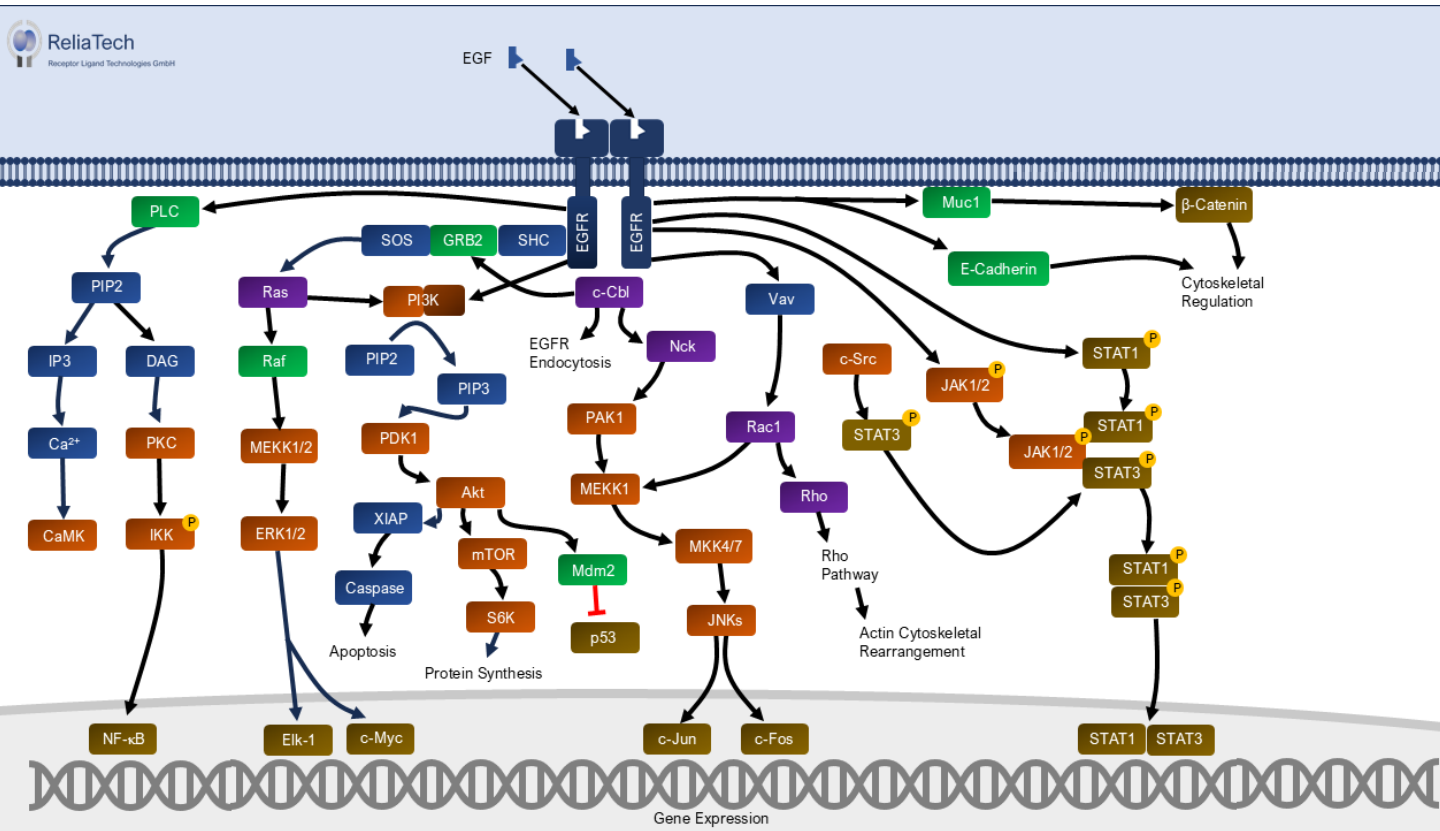
ReliaTech
Receptor Ligand Technologies GmbH

EGFR Pathway



Epidermal growth factor (EGF) is the first discovered member of the EGF protein family, which also includes amphiregulin (AREG), betacellulin (BTC), epiregulin (EPR), HB-EGF, neuregulins and other related proteins. This family is characterized by pronounced structural and functional similarities. A central feature of all members is the presence of a so-called EGF domain - a conserved structure with six cysteine residues that are connected to each other via three disulfide bridges. The basic structure of this domain consists of a two-stranded β-sheet, followed by a loop and a short C-terminal β-sheet.

In addition to the EGF domain, all members have two functional characteristics: Firstly, they trigger mitogenic (cell division-promoting) signals in EGF-sensitive cells, and secondly, they bind with high affinity to the EGF receptor (EGFR).

The biological effects of these ligands are mediated via the so-called epidermal growth factor receptor tyrosine kinases (EGFR/ErbB family). These receptors consist of three main components: an extracellular domain (ectodomain) with approximately 620 amino acids, a single transmembrane region and a cytoplasmic tyrosine kinase domain. The ectodomain enables the specific and high-affinity binding of EGF and related ligands. Chemically this portion of the receptor contains 10-11 N-linked oligosaccharide chains, high content of half-cystine residues (10%) that could give rise to as many as 25 disulfides. The region between the two half-cystine-rich clusters is involved in ligand binding. The hallmark of the cytoplasmic portion of epidermal growth factor receptor is the sequence defining the tyrosine kinase domain. Near the carboxyl terminus of the receptor are four sites of EGF-dependent autophosphorylation. Epidermal growth factor plays an important role in the regulation of cell growth, proliferation, and differentiation.