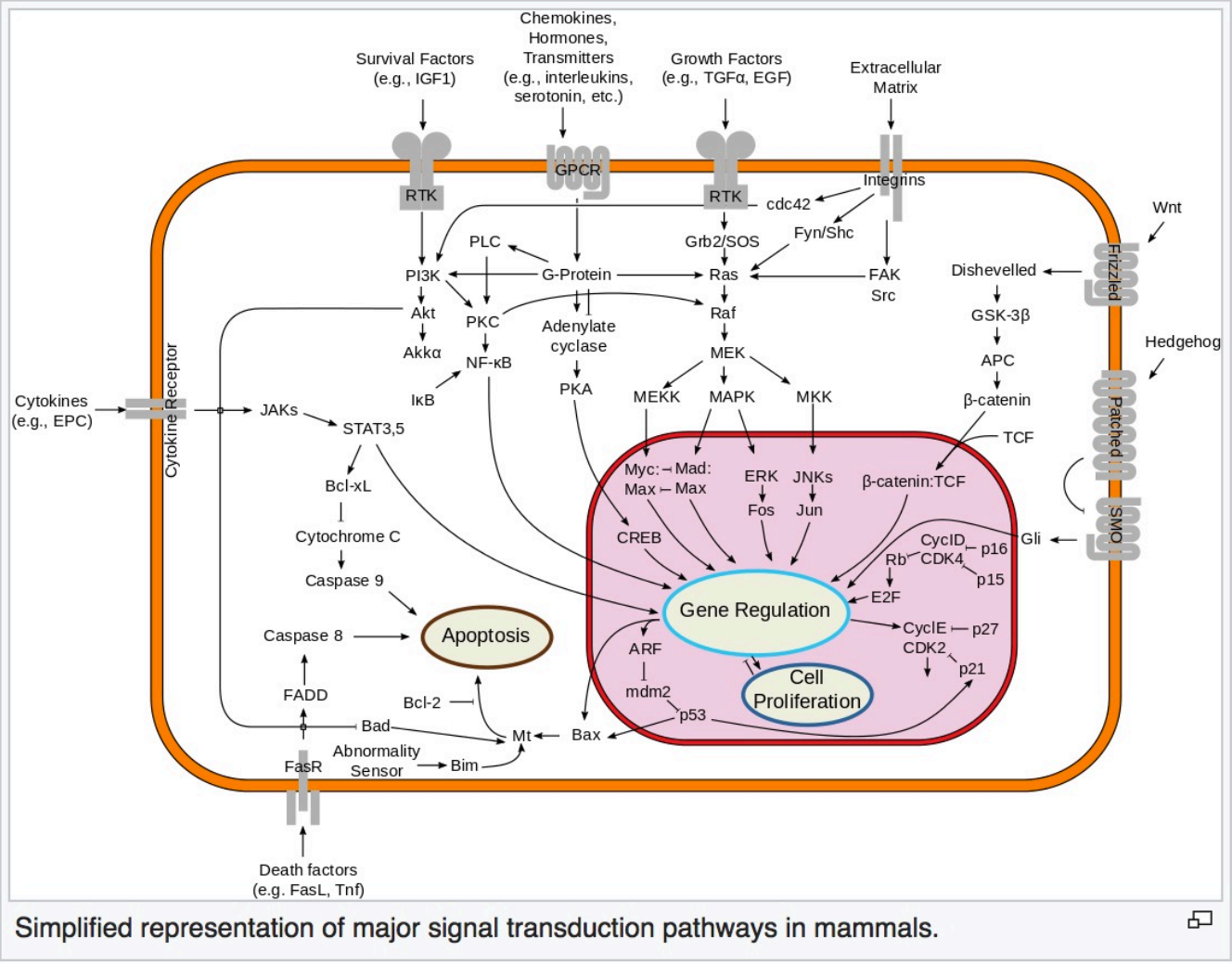
Epidermal growth factor

The epidermal growth factor (EGF) is a growth factor that stimulates cell growth, cell proliferation, and cell differentiation by binding to its receptor EGFR.

Human EGF is a 6045-Da protein with 53 amino acid residues and three intramolecular disulfide bonds.

EGF was originally described independently as a secreted peptide found in the submaxillary glands of mice and in human urine. EGF has since been found in many human tissues including submandibular gland, parotid gland.

Initially, human EGF was known as urogastrone.



Simplified representation of major signal transduction pathways in mammals.

Aberrant epidermal growth factor receptor (EGFR) signaling is widespread in cancer, making the EGFR an important target for therapy. EGFR gene amplification and mutation are common in glioblastoma (GBM), but EGFR inhibition has not been effective in treating this tumor.

Guo et al. propose that primary resistance to EGFR inhibition in glioma cells results from a rapid compensatory response to EGFR inhibition that mediates cell survival.

They show that in glioma cells expressing either EGFR wild type or the mutant EGFRvIII, EGFR inhibition triggers a rapid adaptive response driven by increased tumor necrosis factor (TNF) secretion, which leads to activation in turn of c-Jun N-terminal kinase (JNK), the Axl receptor tyrosine kinase and extracellular signal-regulated kinases (ERK). Inhibition of this adaptive axis at multiple nodes rendered glioma cells with primary resistance sensitive to EGFR inhibition. The findings provide a possible explanation for the failures of anti-EGFR therapy in GBM and suggest a new approach to the treatment of EGFR-expressing GBM using a combination of EGFR and TNF inhibition [1)]

Epidermal growth factor receptor

see Epidermal growth factor receptor.

1)
Guo G, Gong K, Ali S, Ali N, Shallwani S, Hatanpaa KJ, Pan E, Mickey B, Burma S, Wang DH, Kesari S, Sarkaria JN, Zhao D, Habib AA. A TNF-JNK-Axl-ERK signaling axis mediates primary resistance to EGFR inhibition in glioblastoma. Nat Neurosci. 2017 Jun 12. doi: 10.1038/nn.4584. [Epub ahead of print] PubMed PMID: 28604685.