

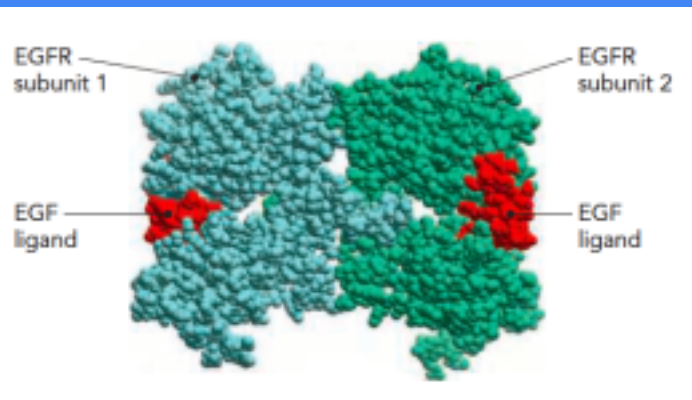
Epidermal Growth Factor

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Overview of EGF

Purpose: Downstream response of EGF is **increased cell division**

Figure 8.37



- Receptor Tyrosine Kinase
- Monomer ligand
- Binds to EGFR to create dimer (EGFR1 & EGFR2)
- Induced dimer formation on the cell surface occurs when EGF ligand is bound to each receptor
- EGF is a 53-aa protein made from larger progenitor protein resulting in a hormone with 3 disulfide bridges

Other Components of the Mechanism

SH2: Src kinase homology-2

GRB2: Growth factor receptor-bound 2

SOS: Son of Sevenless

SH3: Src kinase homology-3

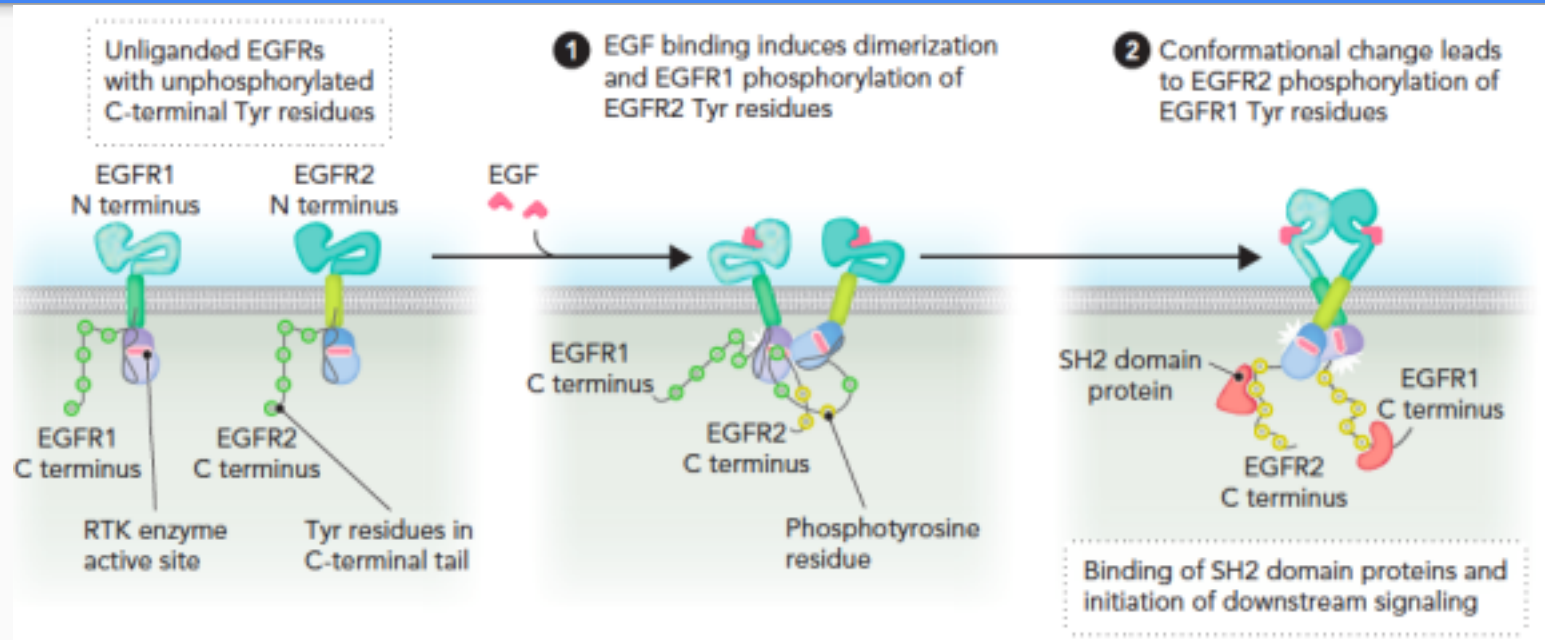
Raf- Rapid accelerated fibrosarcoma

MEK: MAP/ERK kinase

ERK: Extracellular signal-regulated kinase

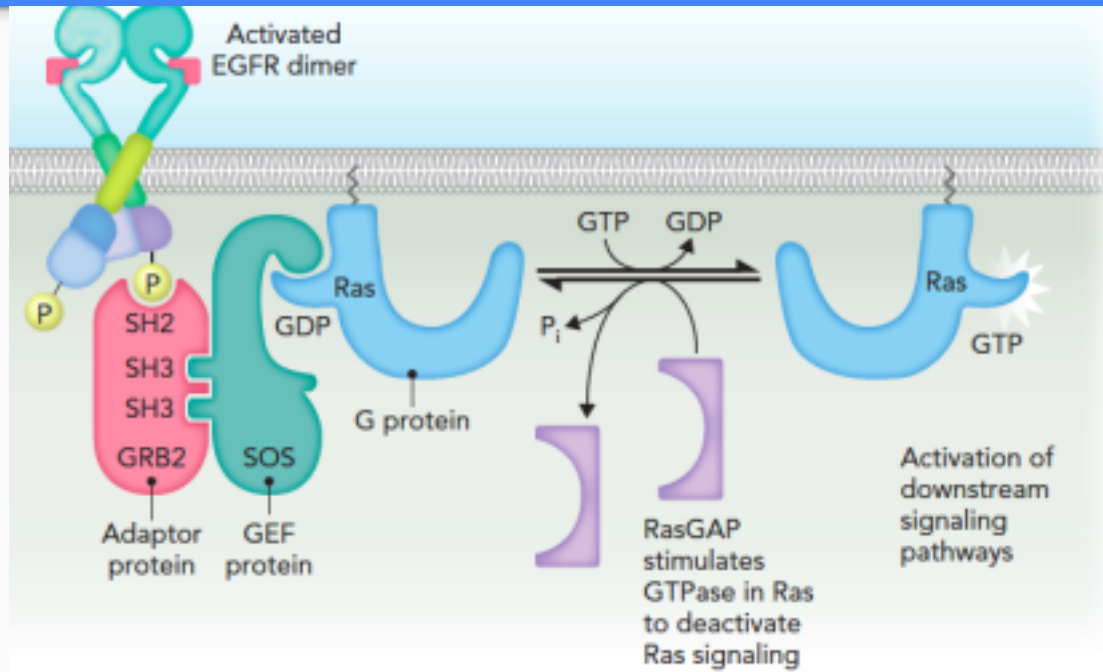
Formation of EGFR Dimer

Figure 8.36



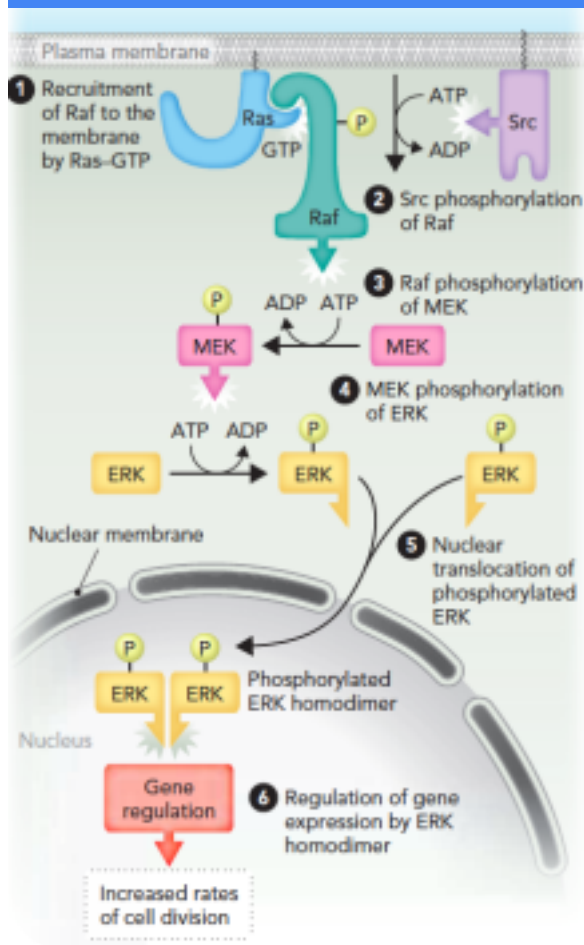
- 2 EGFs bind to the N-terminus region, creating dimerization of the receptors EGFR1 & EGFR2
- 5 tyrosine residues are phosphorylated in EGFR2 -> conformational change
- Activates EGFR2 kinase domain and tyrosine phosphorylation of EGFR1 residues

Activation of Ras-GTP



- pY residues in EGFR bind to GRB2
- SOS recruited
- SOS binds and exchanges with Ras
- GAPs inactivate Ras signaling

Regulation of gene expression



- MAP signaling pathway is stimulated by activated Ras
- Phosphorylation starts consisting of three MAP kinase proteins
- Regulation of gene expression and increased rates of cell division are the cell response

Turning off message

Normal

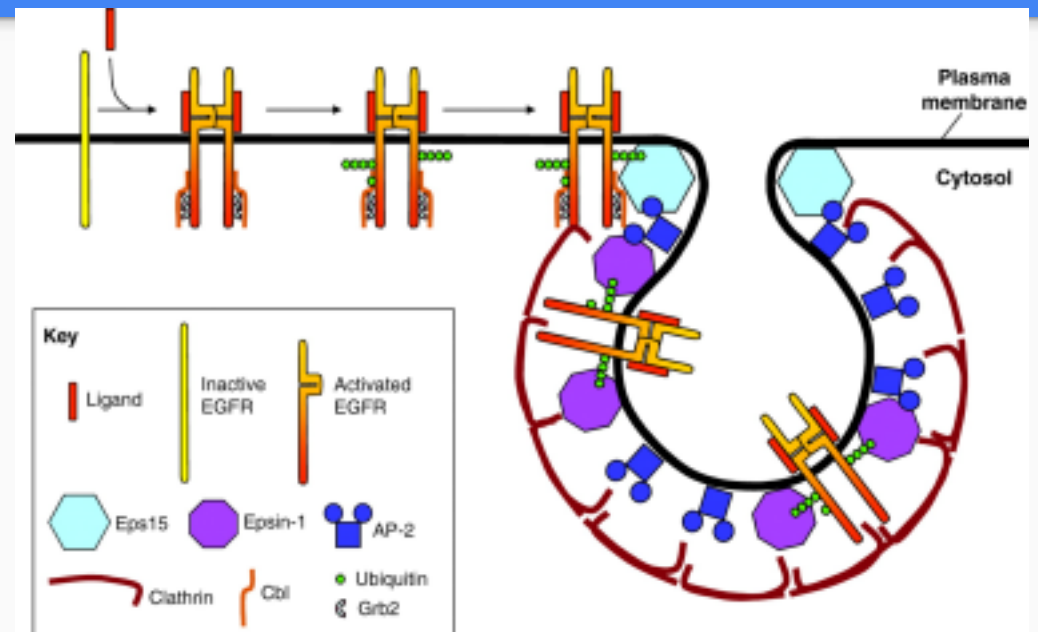
- Enzyme clips off the phosphates that are at the receptor tails when it is activated, Ex: protein tyrosine phosphatase 1B
- Ubiquitination adds ubiquitin monomers to a protein to target for degradation, Ex: CBL

EGFR- Targeted Therapies (tumorigenesis)

- Monoclonal antibodies
- Tyrosine kinase inhibitors

Recycling of signal

- Eps15 is known to back clathrin-mediated internalization of EGFR at the plasma membrane
- Research suggests it controls the structure integrity and handling of space



References

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