

Key Concept

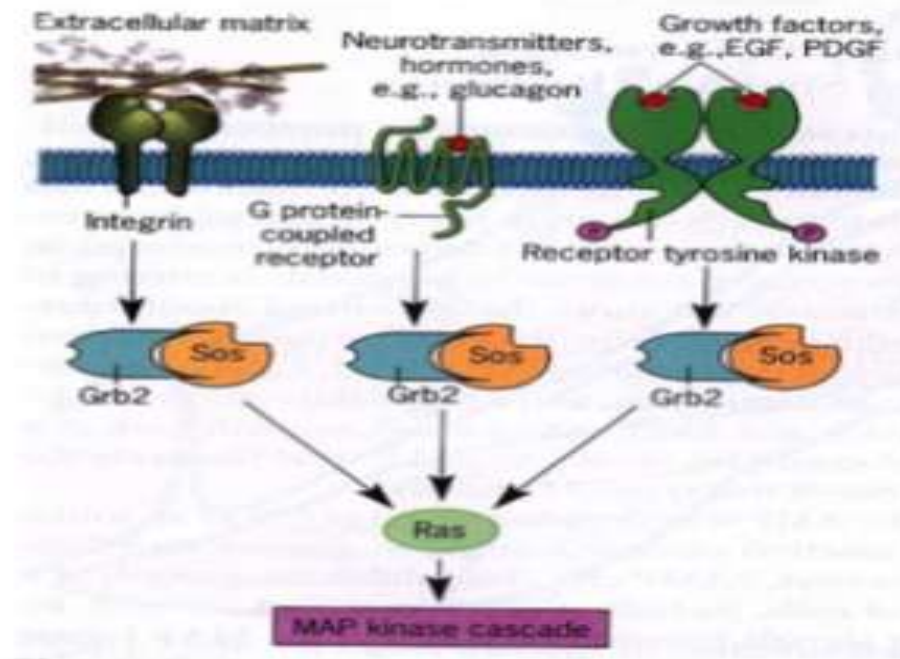


- Convergence
- Divergence
- Crosstalk
- Signaling Pathways

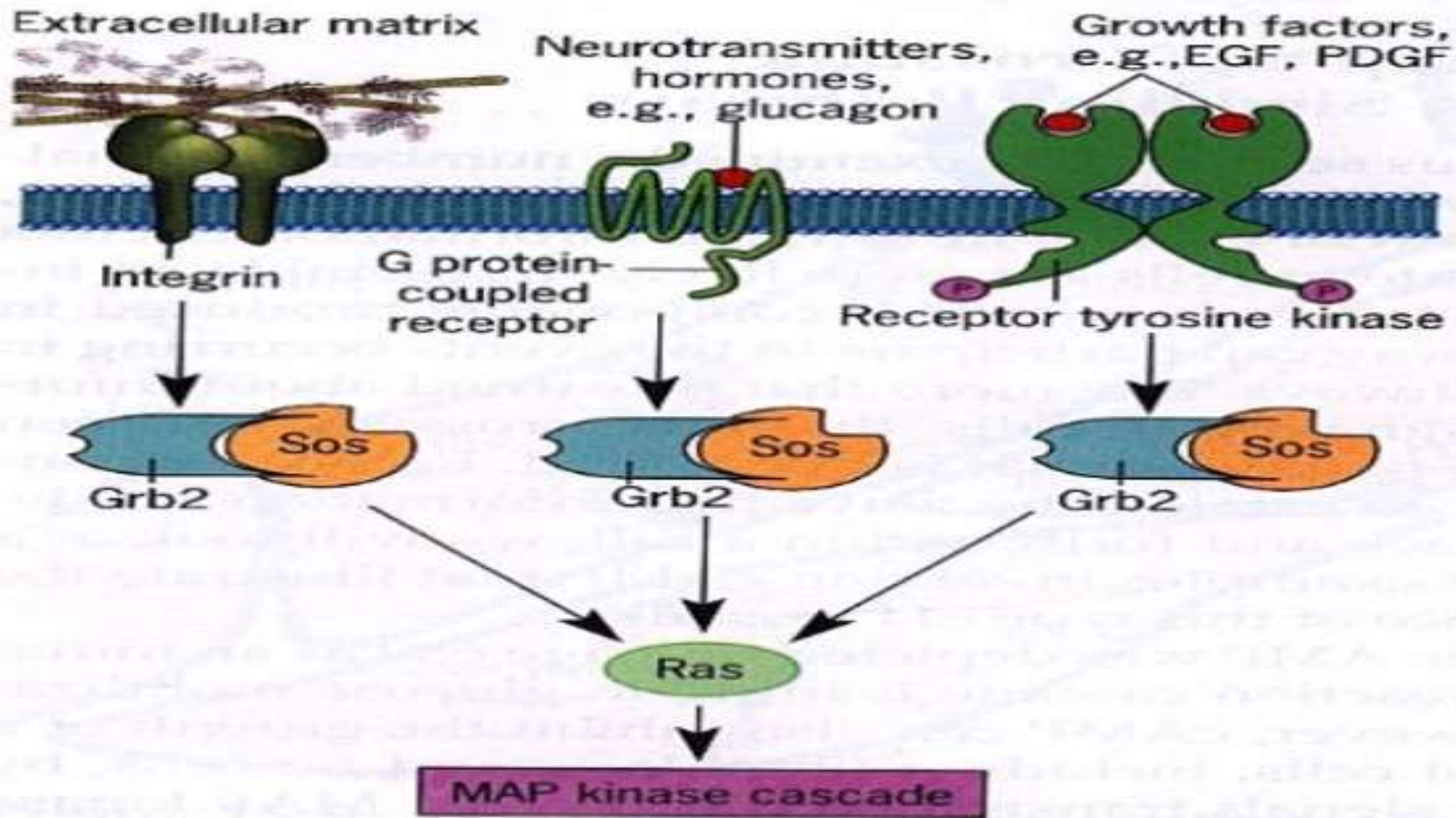


CONVERGENCE

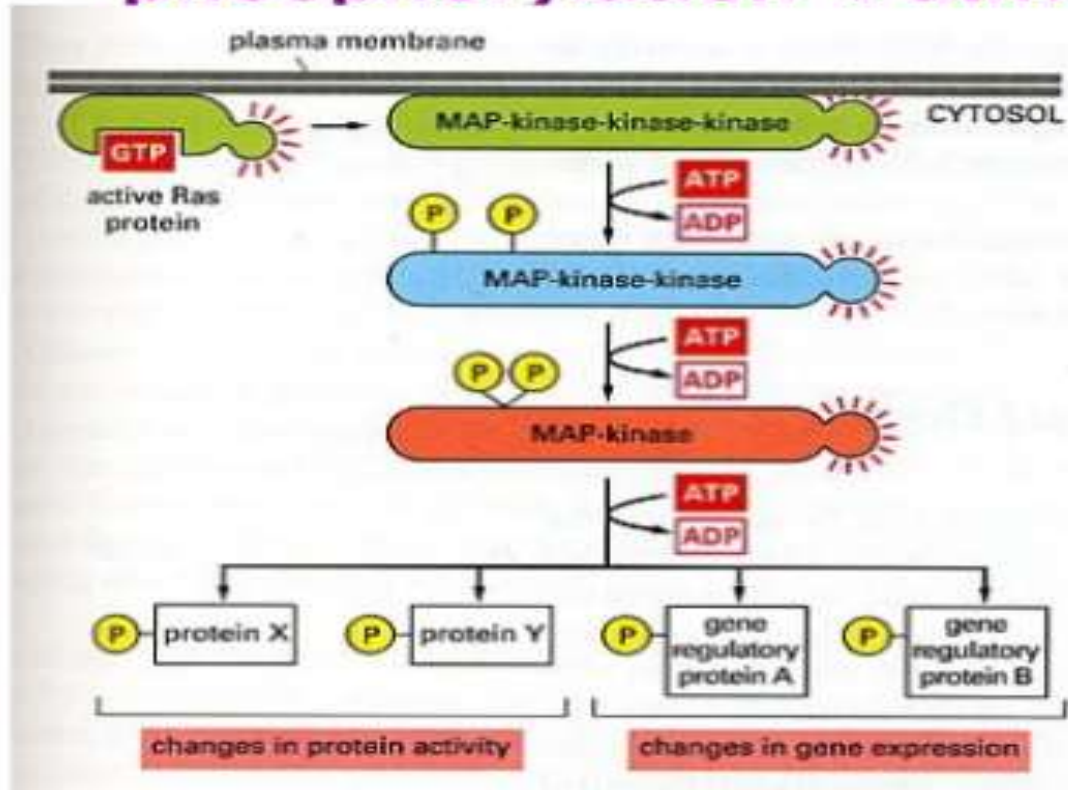
► Signals from a **VARIETY OF UNRELATED** receptors converge to activate a **COMMON EFFECTOR** after binding to their individual ligand. E.g Ras Raf.



different stimuli resulting in the same effect regardless of at which point in some internal signalling pathway the two responses 'converge'



MAP-kinase serine/threonine phosphorylation Pathway activated by



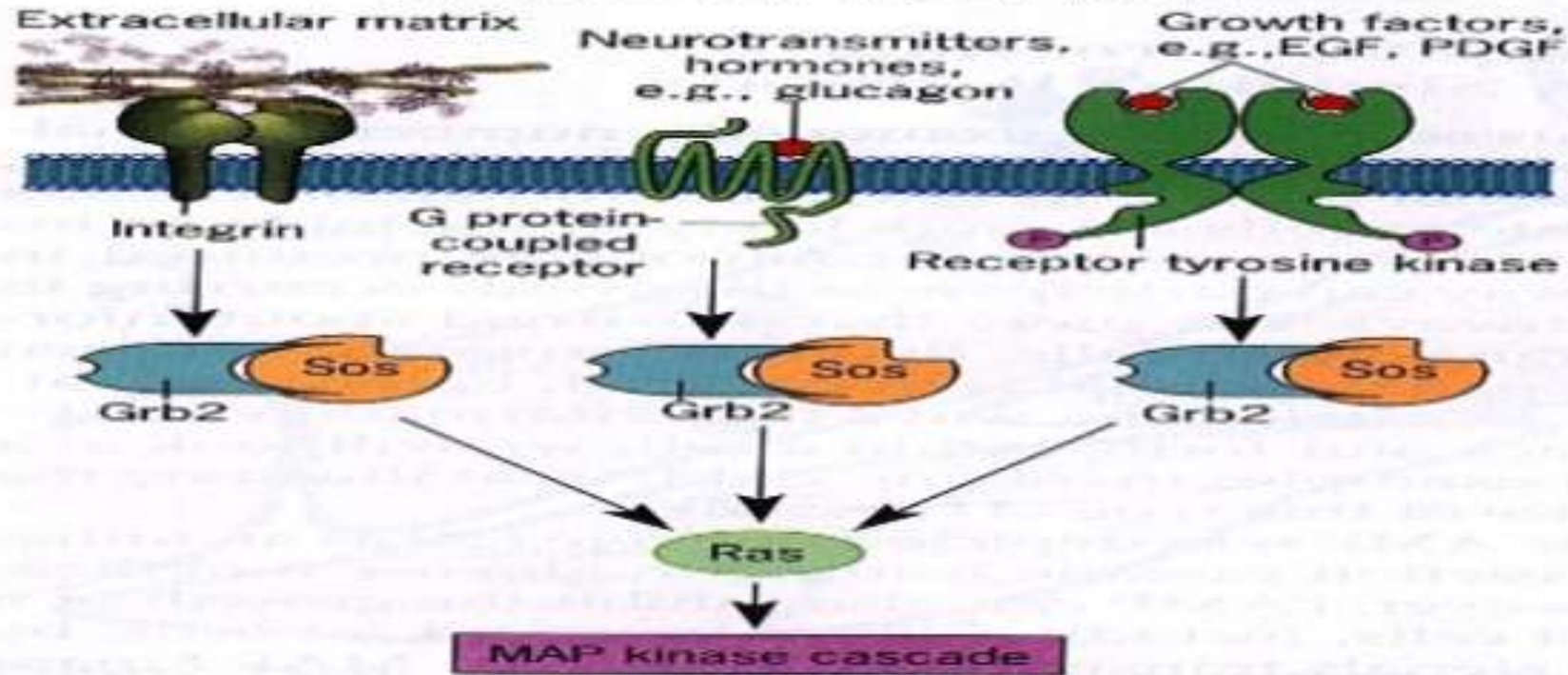
**Ras-
activated
phosphorylat
ion cascade**

CONVERGENCE

- Signals usually from **RECEPTORS**
- Examples:
 - G-protein coupled receptors
 - Receptor tyrosine kinases
 - Integrins



CONVERGENCE



Signals transmitted from a G protein-coupled receptor, an integrin and a receptor tyrosine kinase all converge on Ras and are then transmitted along the MAP kinase cascade.

CONVERGENCE

- Lead to formation of **PHOSPHOTYROSINE DOCKING** sites for SH2 domain
- Lead to **TRANSCRIPTION** and **PROMOTION** of a **SIMILAR** set of growth promoting genes in target cells.
- Signals transmitted from G-protein-coupled receptors on integrins, and a receptor tyrosine kinase all **CONVERGE** on Ras/Raf and are then transmitted along the MAP kinase cascade.
- Integrins are receptors at sites of cell-substrate and cell-cell contact.

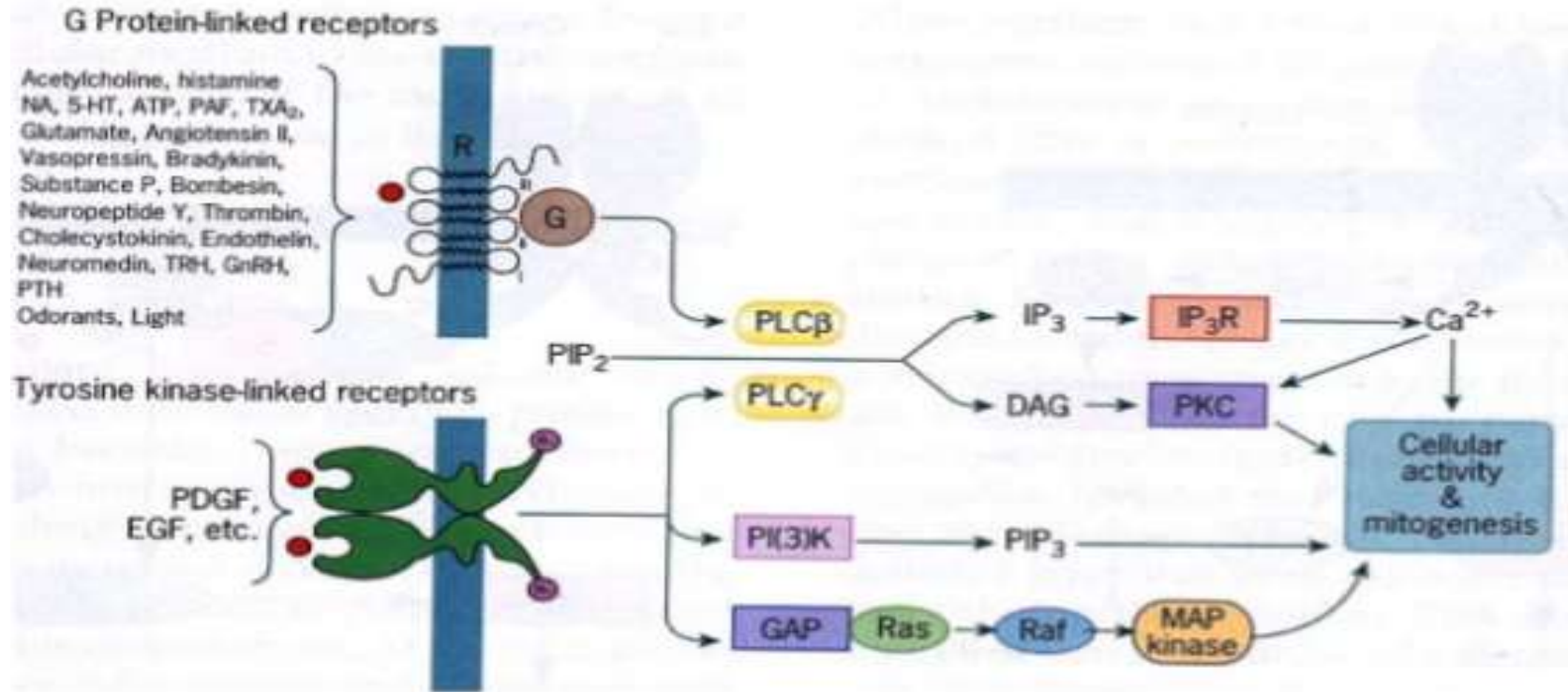
DIVERGENCE

Signals from the same ligand diverge to activate **A VARIETY OF DIFFERENT EFFECTORS** leading to diverse cellular responses.



Members Only
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DIVERGENCE



DIVERGENCE

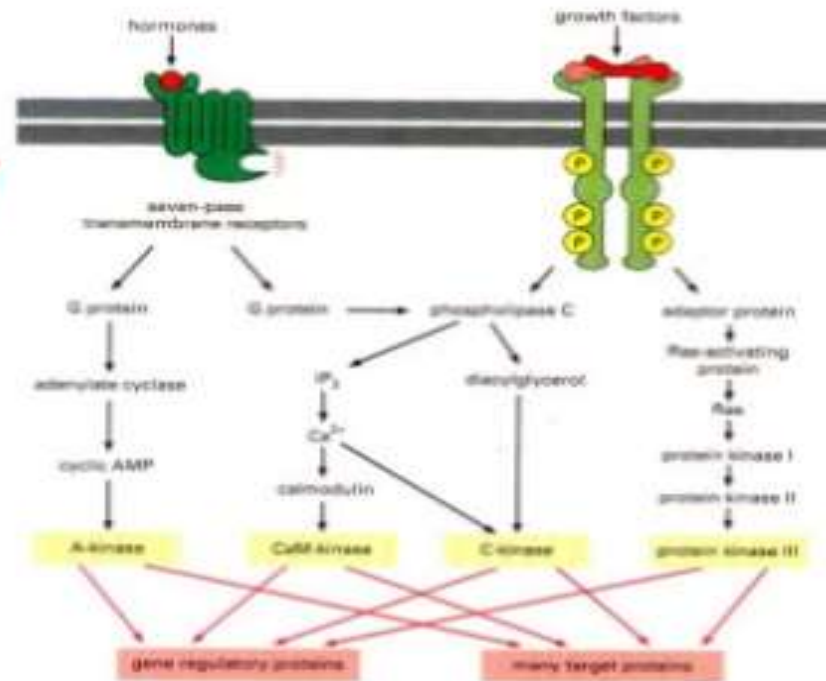
- Effects are usually LIGAND based
- Examples
 - EGF ligand
 - Insulin ligand

CROSS TALK

Signals are passed
BACK AND FORTH
between **DIFFERENT**
PATHWAYS

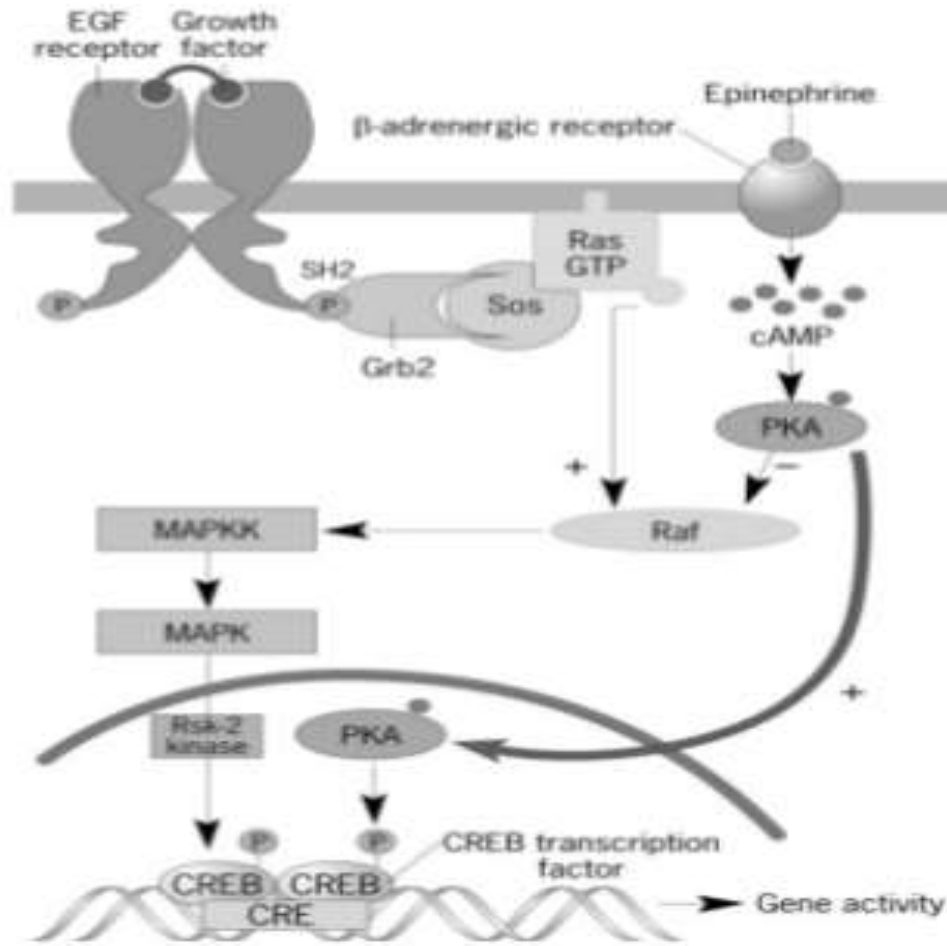
Example:

Cyclic Adenosine
Monophosphate
(cAMP)



How does cAMP block signals transmitted through the MAP kinase cascade?

- Achieves this by:
 - activating PKA (a cAMP dependent kinase)
 - PKA phosphorylates/inhibits Raf (a protein that leads the MAP kinase cascade)



Crosstalk between 2 major signaling pathways. cAMP acts in some cells via cAMP-dep.kinase, PKA, to block transmission of signals from Ras to Raf which inhibits activation of MAP kinase cascade. Also both PKA and kinases of MAP kinase cascade phosphorylate transcription factor CREB on same serine residue, activating transcription factor and allowing it to bind to specific sites on the DNA.

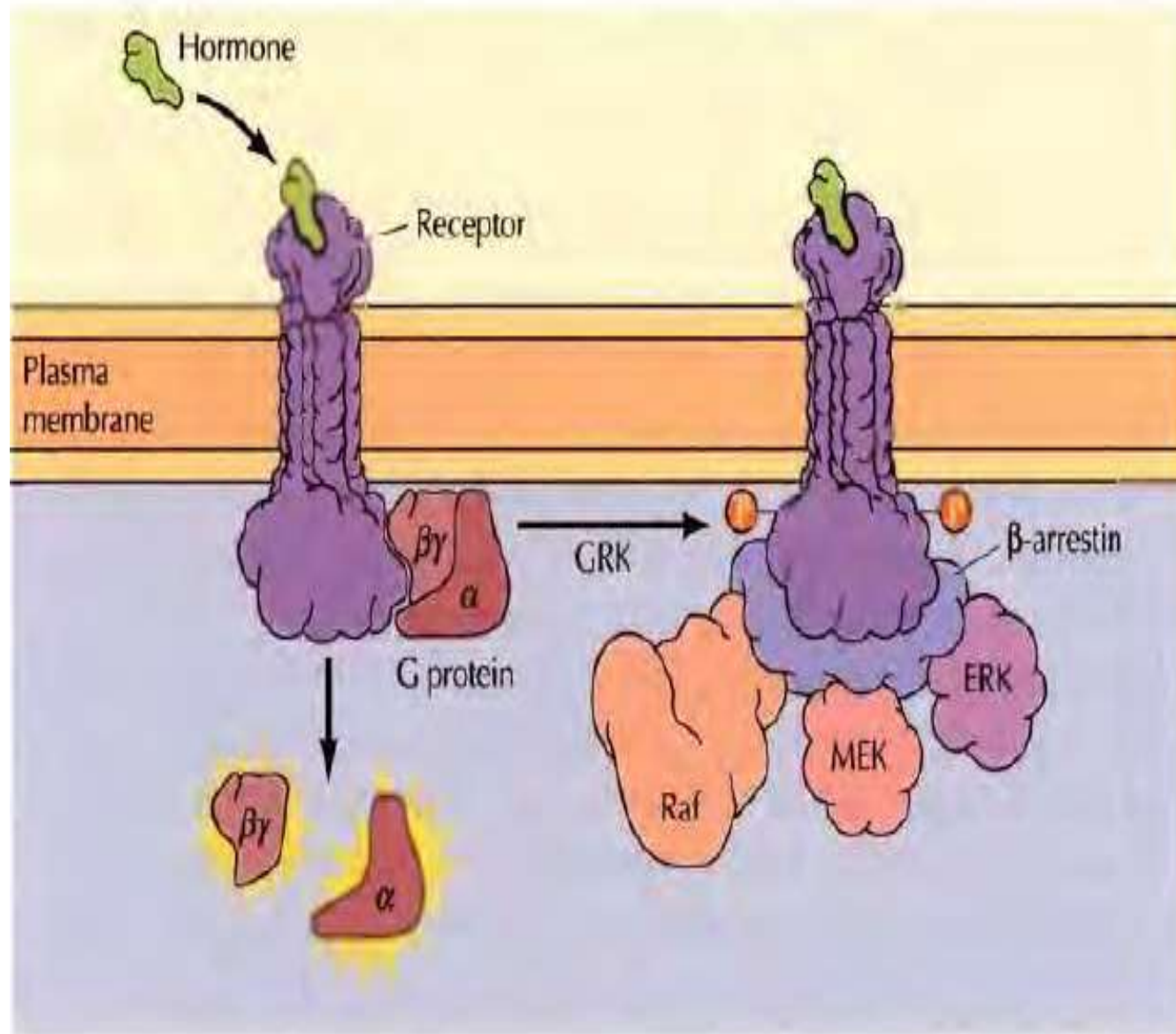


FIGURE 15.50 Crosstalk between G protein-coupled receptors and ERK signaling by β -arrestin Ligand binding stimulates G protein-coupled receptors, leading to activation of trimeric G proteins. The activity of the receptors is turned-off as a result of phosphorylation by GRKs and association of β -arrestin with the phosphorylated receptor. β -arrestin also acts as a scaffold protein for Raf, MEK, and ERK, linking G protein-coupled receptors to the ERK signaling pathway.

SURMARY

Signals from a variety of **UNRELATED RECEPTORS** can **CONVERGE** to activate a common effector, such as Ras/Raf; signals from the **SAME LIGAND** can **DIVERGE** to activate a variety of **DIFFERENT EFFECTORS**; and signals can be passed **BACK AND FORTH** between pathways (Cross talk).