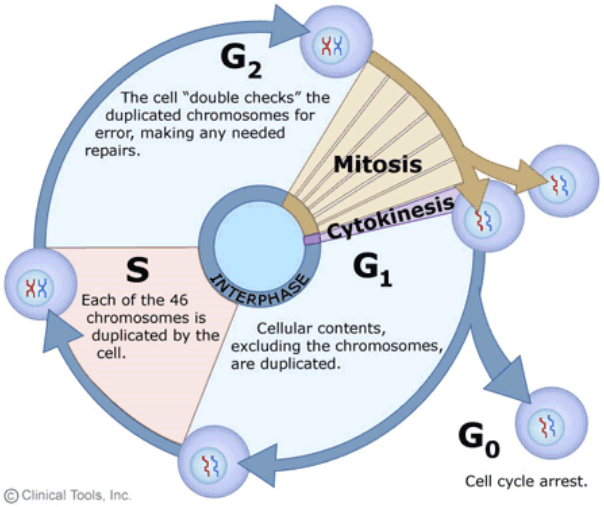
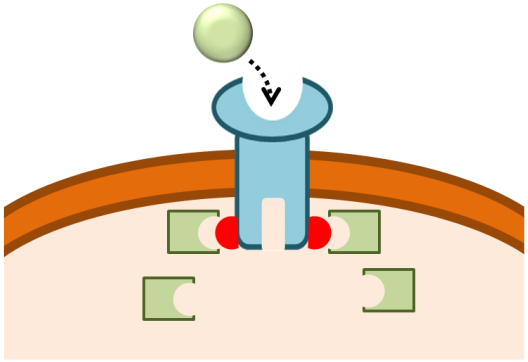
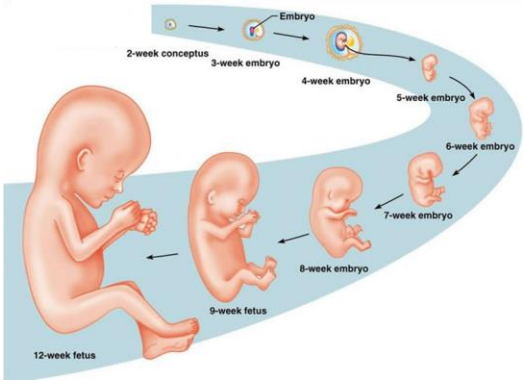
Summary; Cell growth and development

Regulation of eukaryotic cell cycle → **Signal transduction** → **Cell birth and lineage**







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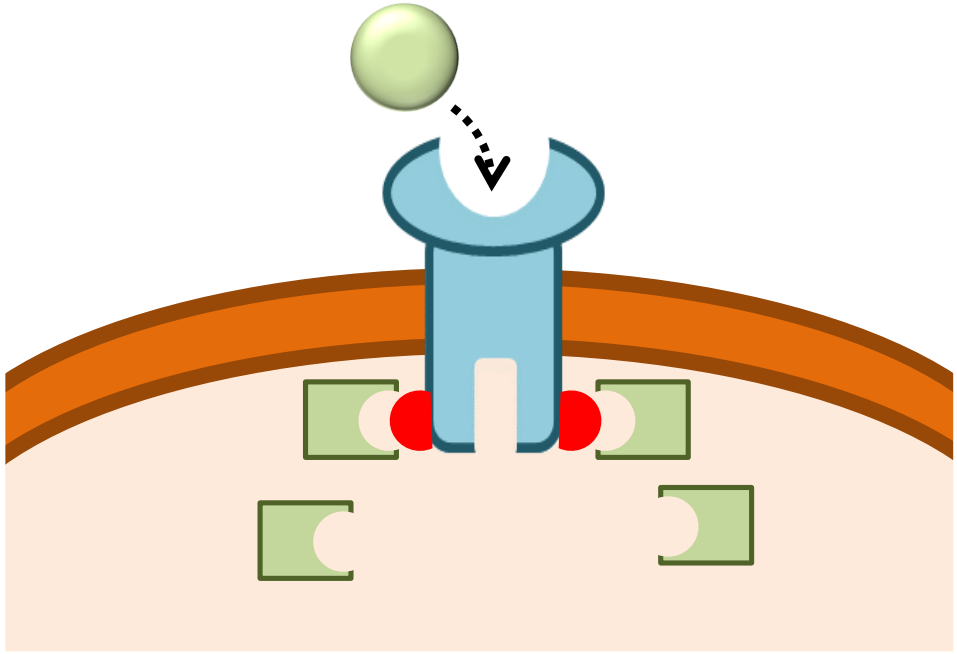
Cell growth and development;

2. Signal transduction



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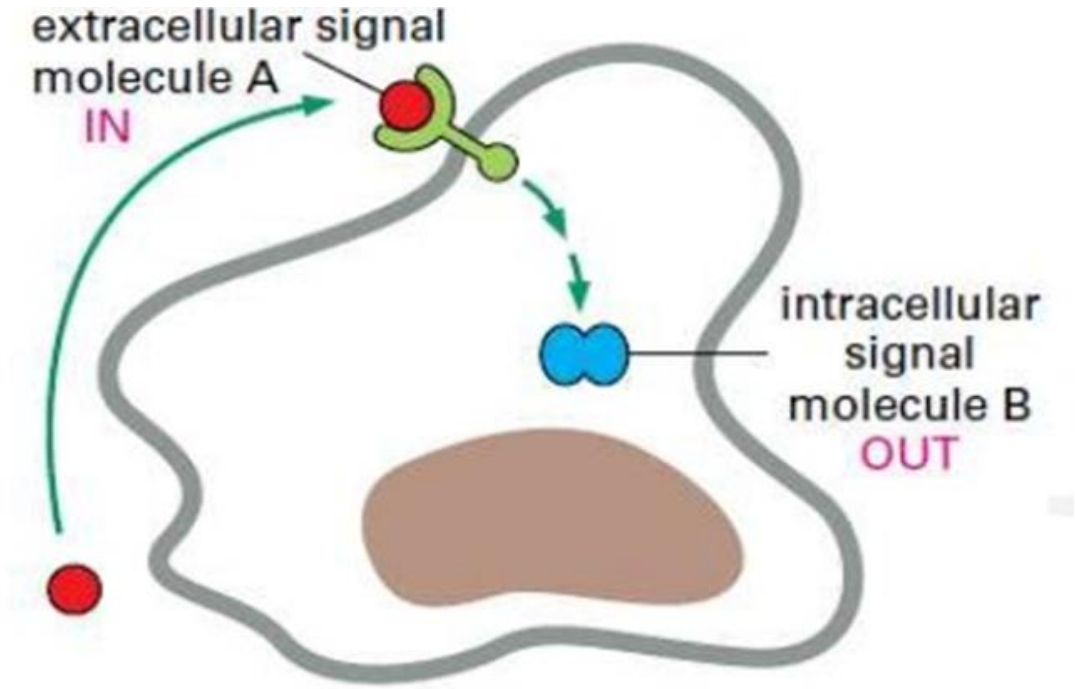
Objectives (2)

After lecture, student is capable of telling

1. **Signaling molecules and cell-surface receptors**
2. **Intracellular signal transduction**

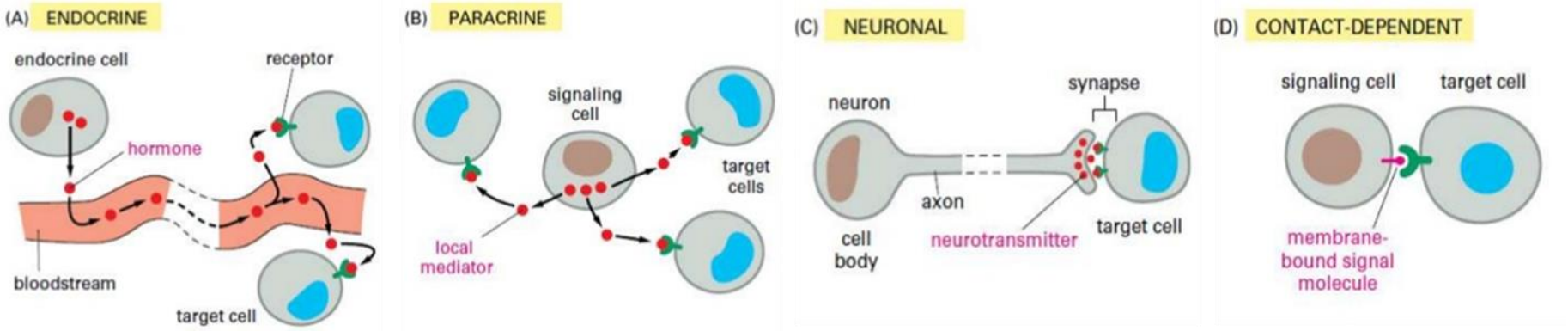
Cell signaling system

- **Cell communication begins when the receptor protein on the target cell receives an extracellular signal and converts to intracellular signal that direct cell behavior**

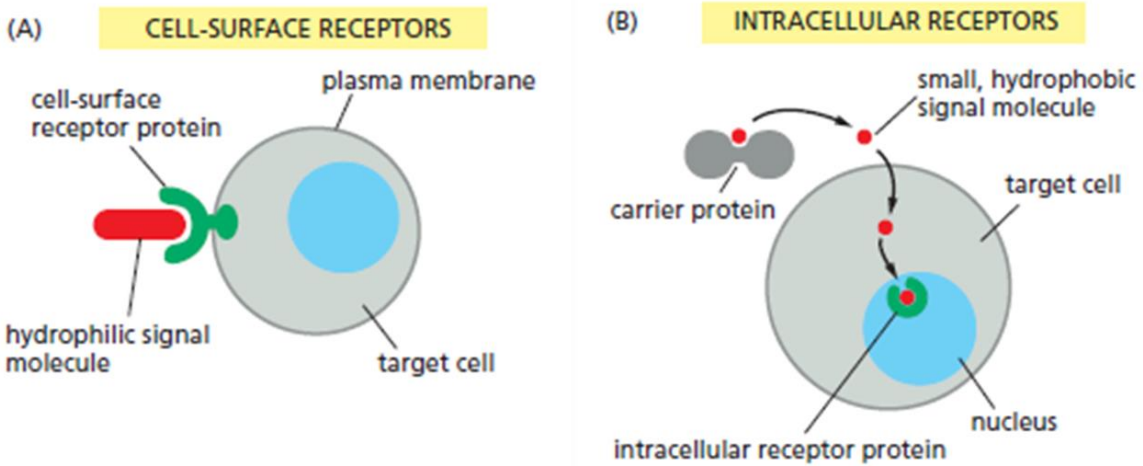


Cell Communication and signaling

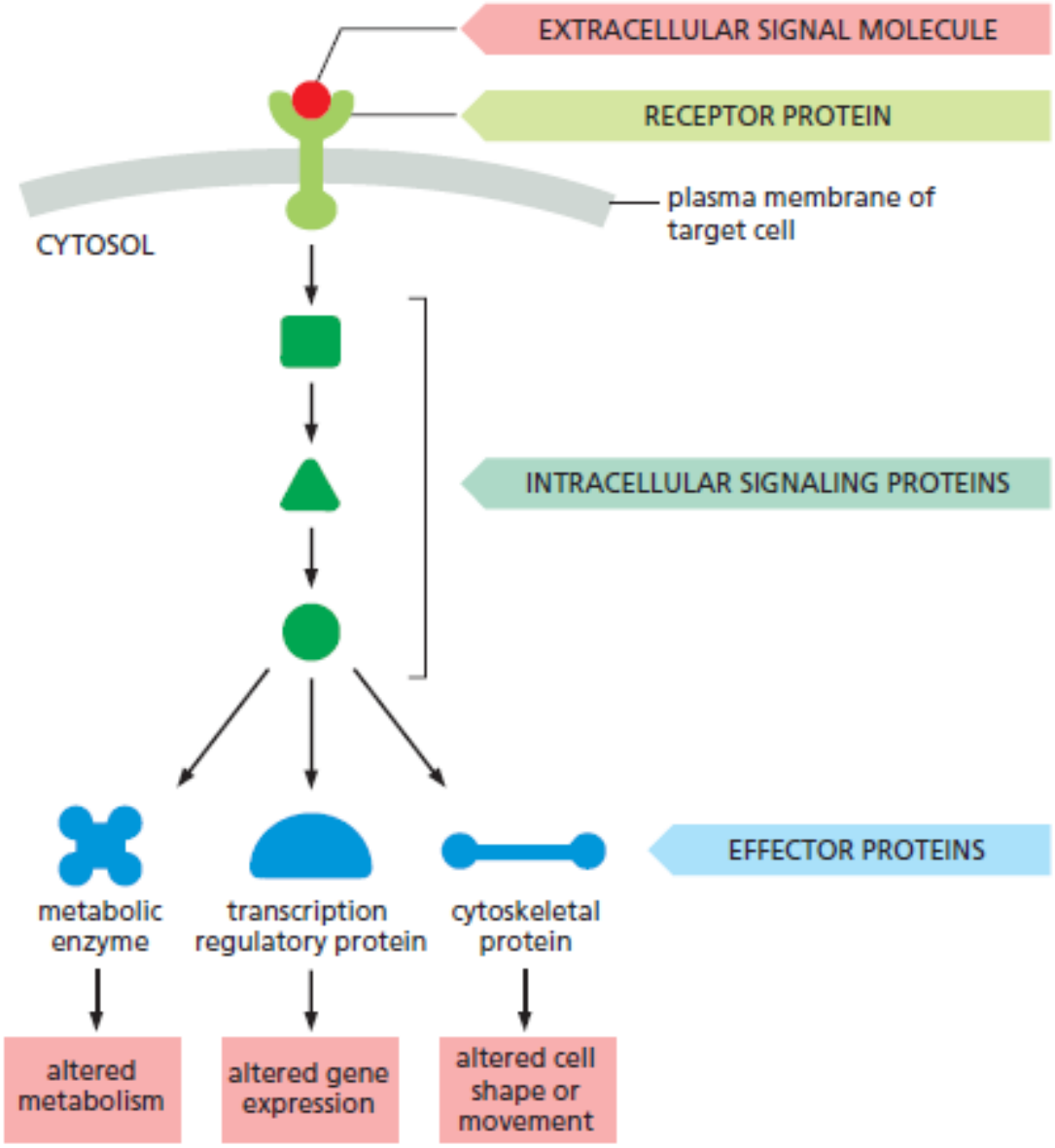
Cell Communication



Cell signaling



Intracellular Signal Transduction

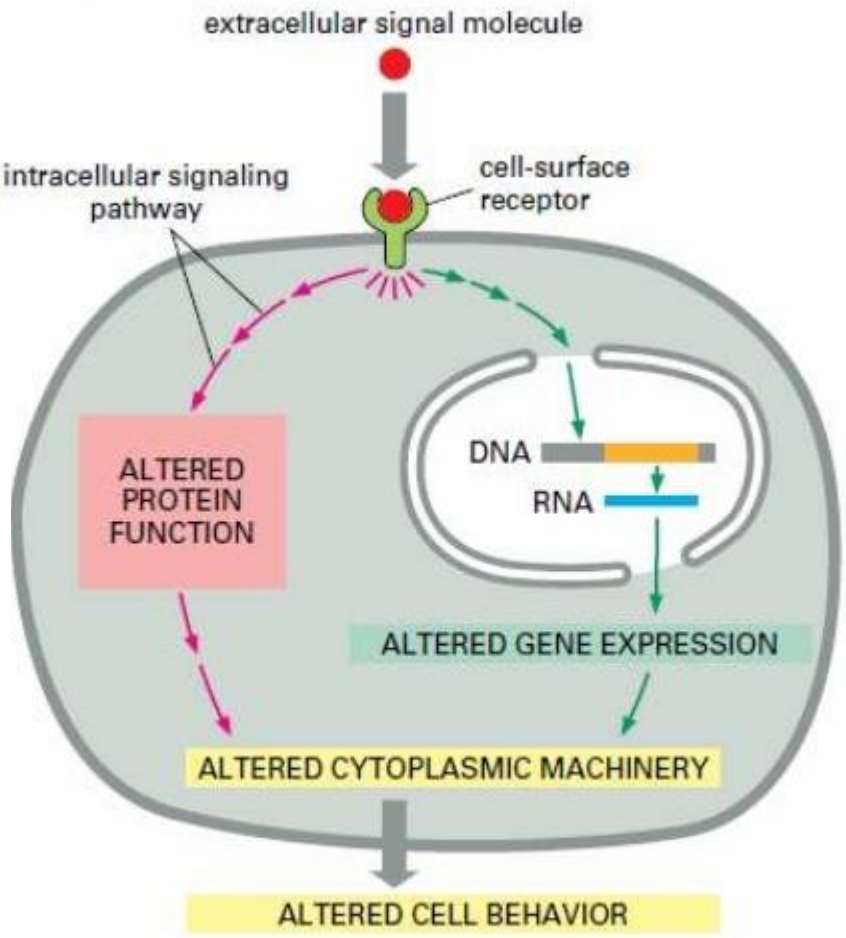


Cell behavior

Fast (sec to min)

Changes in cell activities

e.g. movement, secretion, or metabolism

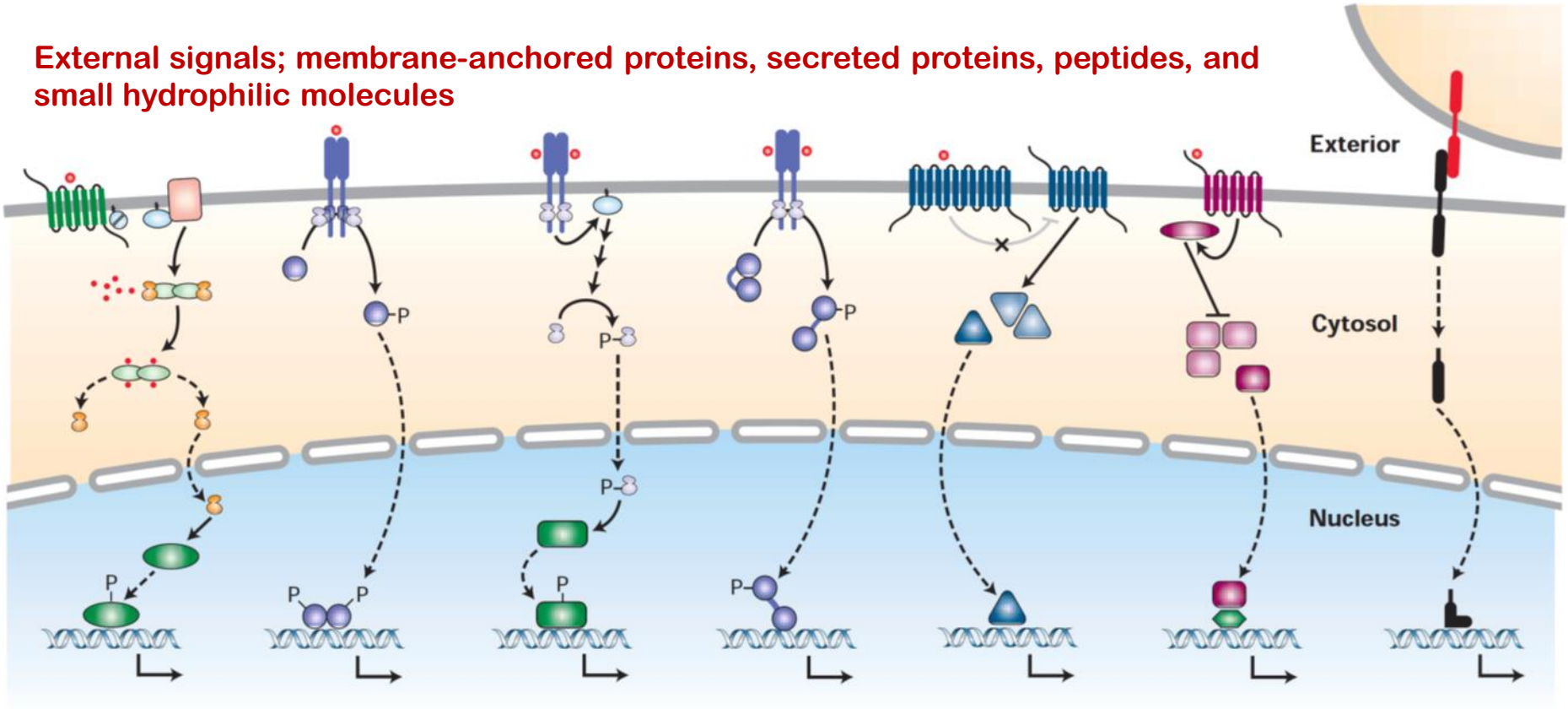


Slow (min to hr)

Involves in gene and protein expressions

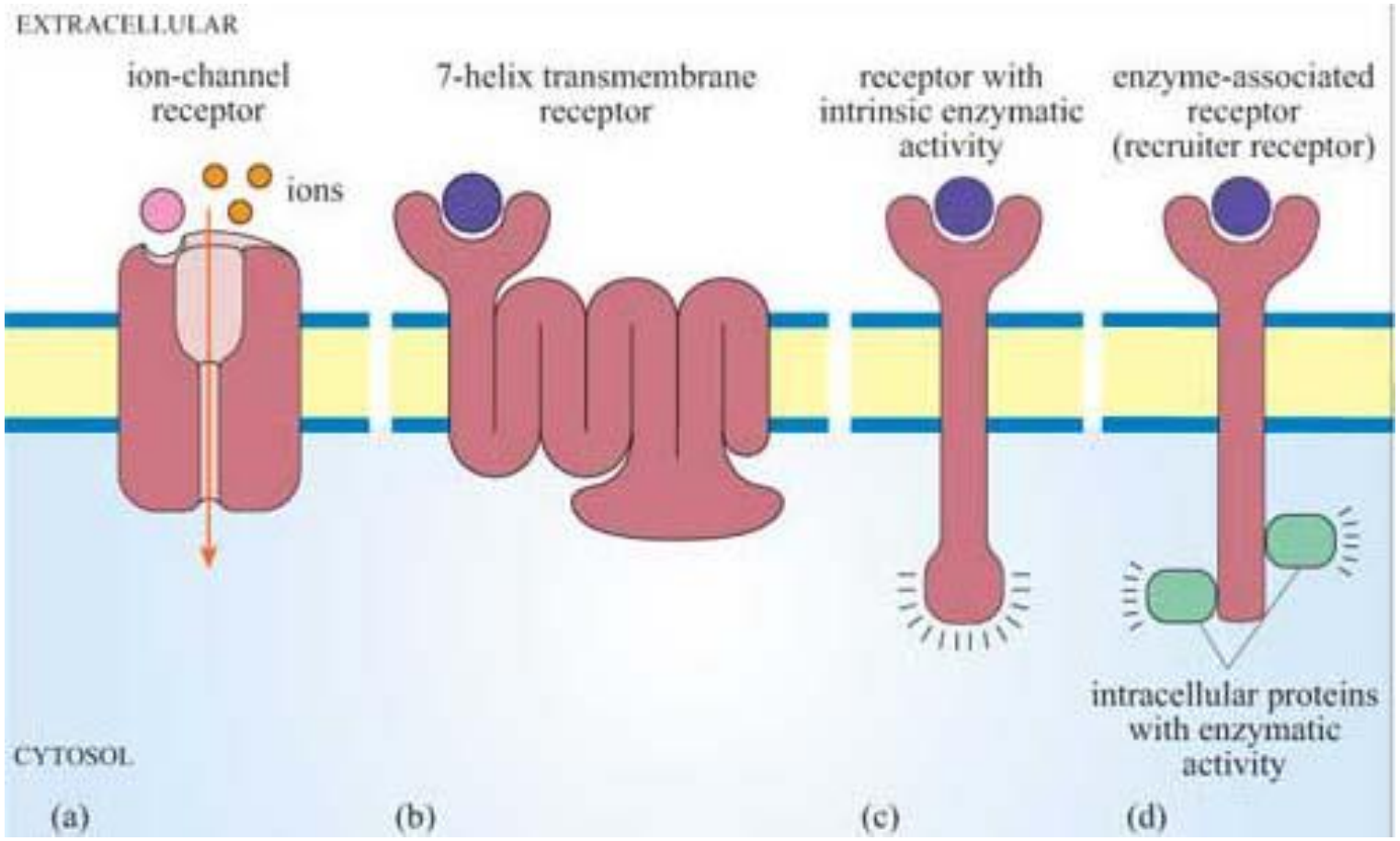
7 major classes of cell surface receptors

External signals; membrane-anchored proteins, secreted proteins, peptides, and small hydrophilic molecules

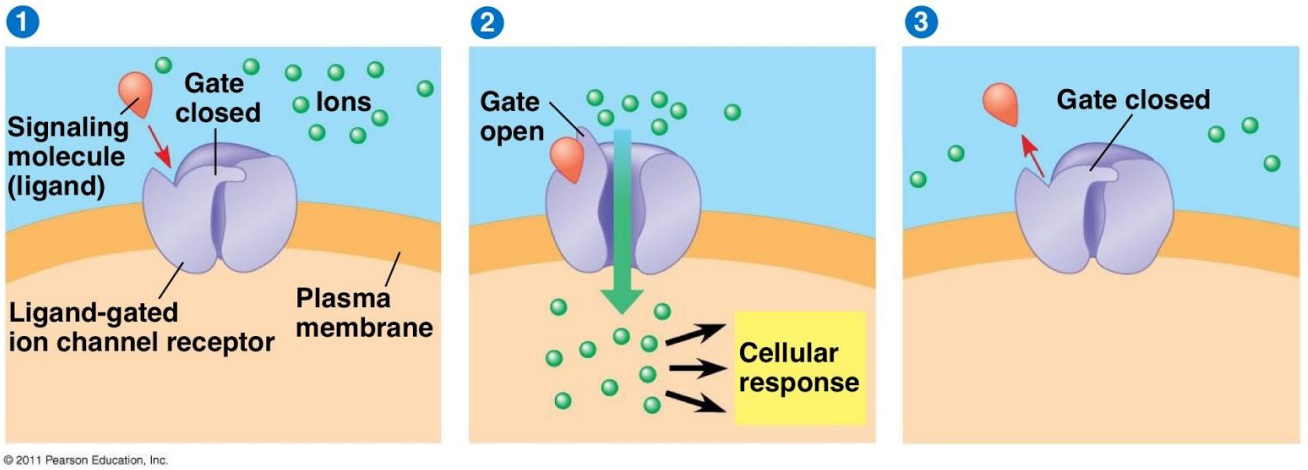


G protein-coupled receptors	Cytokine receptors	Receptor tyrosine kinases	TGFβ receptors	Hedgehog (Hh) receptors	Wnt receptors	Notch receptor
Trimeric G protein	Cytosolic JAK kinases	Tyr kinase domain	Ser/Thr kinase domain	Cytosolic complex	Pamitoylated Wnt	Delta ligand is released
Activate cytosolic or nuclear transcription factors via several pathways (here one involving protein kinase A)	Activate cytosolic STAT transcription factors by phosphorylation	Activate cytosolic kinases (here MAP kinase) that trans-locate to the nucleus and activate nuclear transcription factors by phosphorylation	Activate Smad transcription factors in the cytosol by phosphorylation	Control processing of transcription factor by proteolysis; Hh binding causes release from cytosolic complex	Release an activated transcription factor from a multiprotein complex in the cytosol	Cytosolic domain of Notch released by proteolysis acts in association with nuclear transcription factors

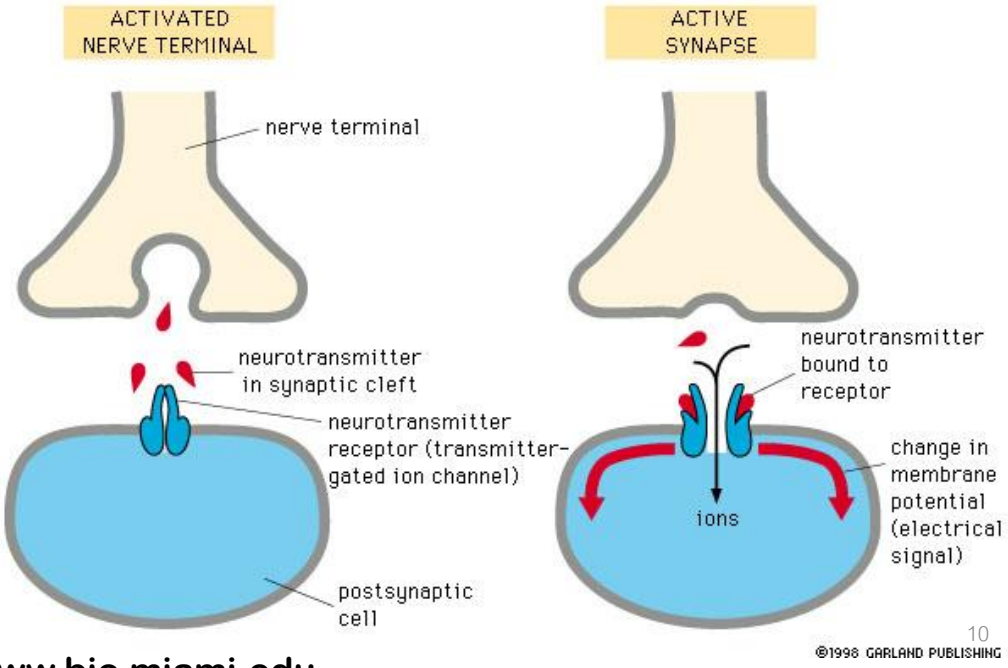
4 major classes of membrane receptors



Ion channel receptor



- Ligand-gated channels
- Converts chemical signals to electrical ones
- Essential in neuronal activities



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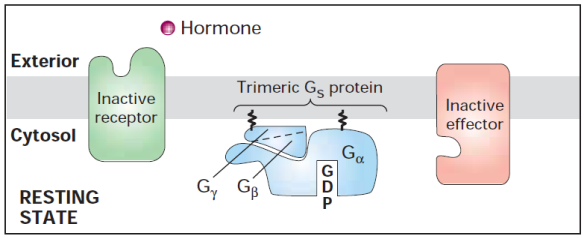
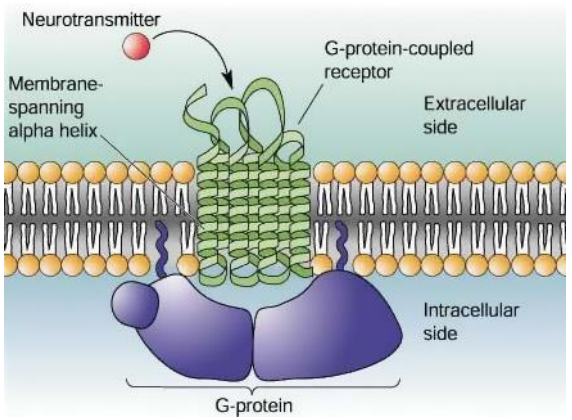
Seven-transmembrane domain receptors (7TM receptors)

- G-protein coupling receptors (GPCRs)





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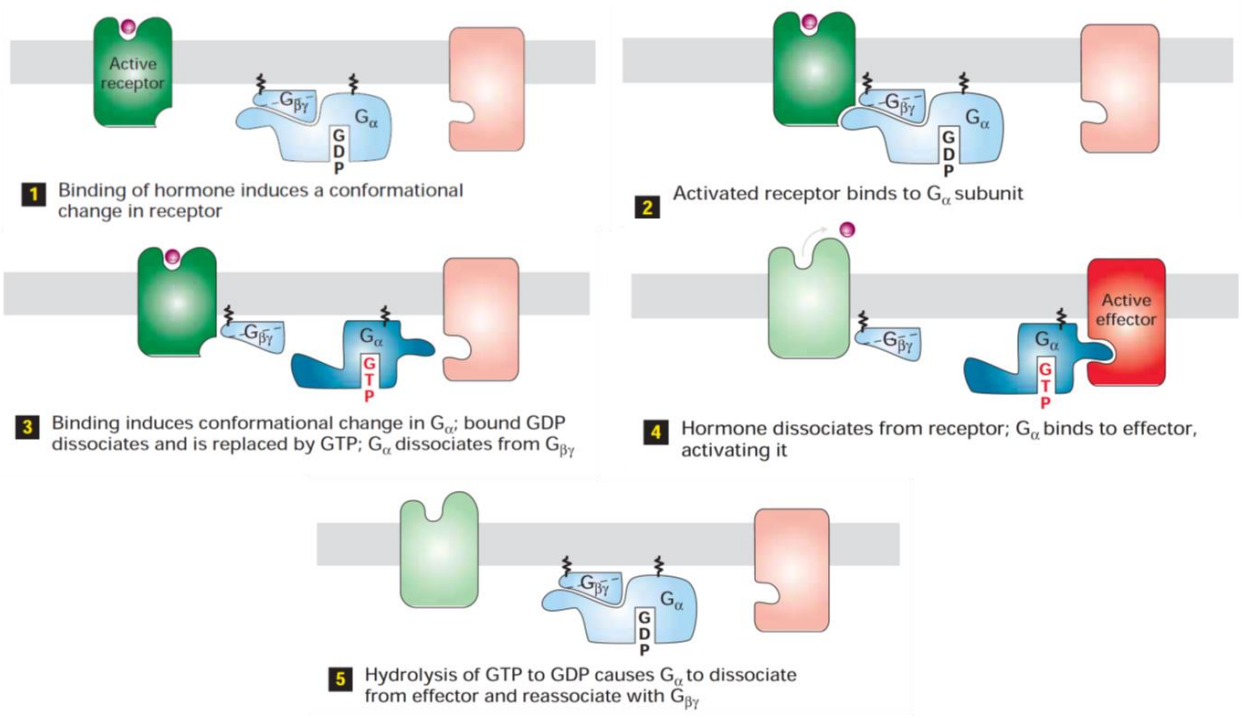


Intracellular Signal Transduction

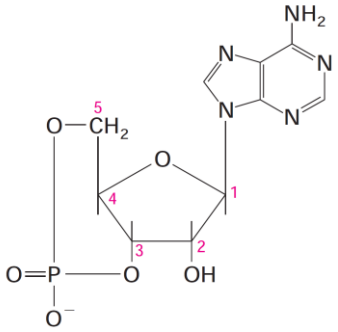
Ligand-Receptor

"first messengers"

↑ or ↓ of a intracellular signaling molecules

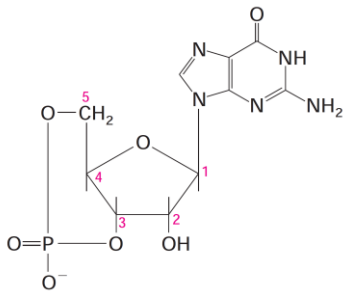
"second messengers"

3',5'-cyclic AMP (cAMP), 3',5'-cyclic GMP (cGMP), 1,2-diacylglycerol (DAG), and and inositol 1,4,5-trisphosphate (IP_3)



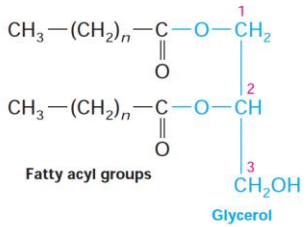
3′,5′-Cyclic AMP (cAMP)

Activates protein kinase A (PKA)



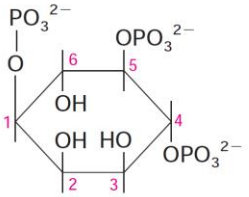
3′,5′-Cyclic GMP (cGMP)

Activates protein kinase G (PKG) and opens cation channels in rod cells



1,2-Diacylglycerol (DAG)

Activates protein kinase C (PKC)



Inositol 1,4,5-trisphosphate (IP_3)

Opens Ca^{2+} channels in the endoplasmic reticulum

4 common intracellular second messengers

G-protein coupling receptors

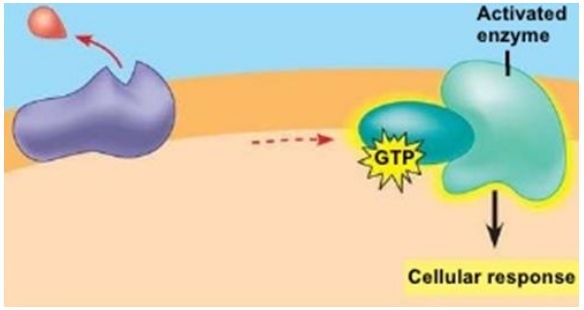
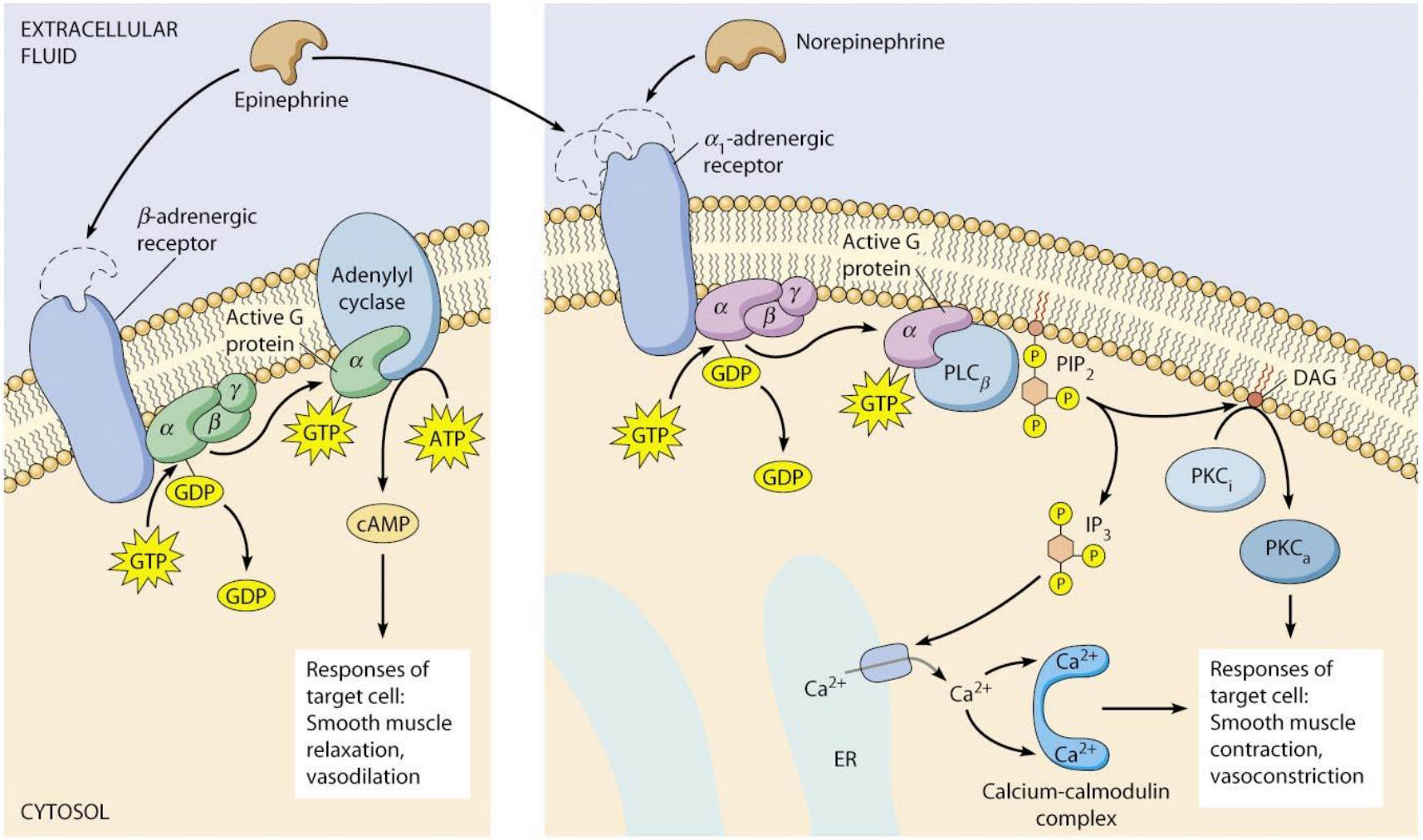


TABLE 13-1 Major Classes of Mammalian Trimeric G Proteins and Their Effectors*

G_α Class	Associated Effector	2nd Messenger	Receptor Examples
$G_{s\alpha}$	Adenylyl cyclase	cAMP (increased)	β-Adrenergic (epinephrine) receptor; receptors for glucagon, serotonin, vasopressin
$G_{i\alpha}$	Adenylyl cyclase K^+ channel ($G_{\beta\gamma}$ activates effector)	cAMP (decreased) Change in membrane potential	α_1-Adrenergic receptor Muscarinic acetylcholine receptor
$G_{olf\alpha}$	Adenylyl cyclase	cAMP (increased)	Odorant receptors in nose
$G_{q\alpha}$	Phospholipase C	IP_3, DAG (increased)	α_2-Adrenergic receptor
$G_{o\alpha}$	Phospholipase C	IP_3, DAG (increased)	Acetylcholine receptor in endothelial cells
$G_{t\alpha}$	cGMP phosphodiesterase	cGMP (decreased)	Rhodopsin (light receptor) in rod cells

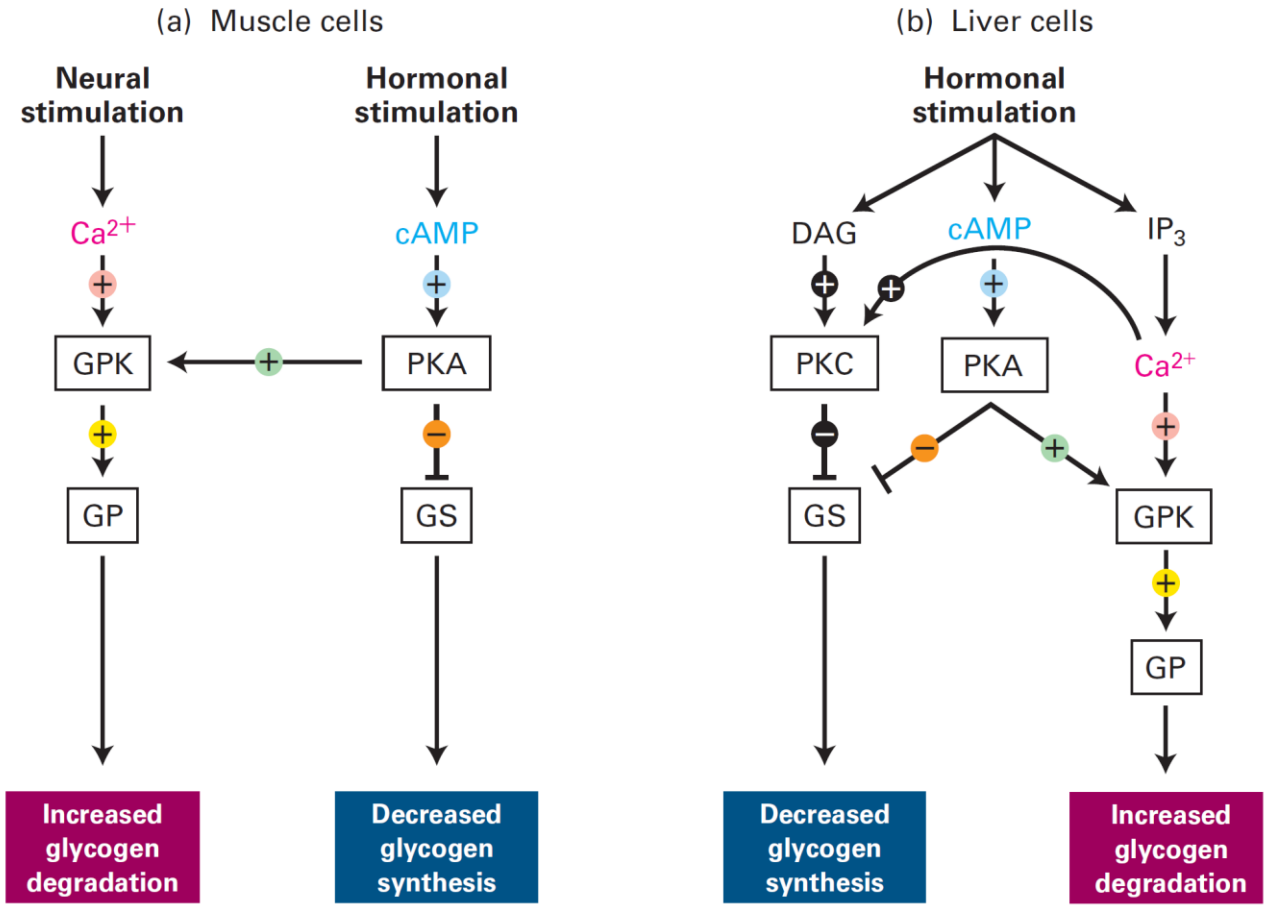
G-protein coupling receptors



(a) cAMP pathway initiated by activation of β-adrenergic receptor

(b) Inositol-phospholipid-calcium pathway initiated by activation of α_1-adrenergic receptor

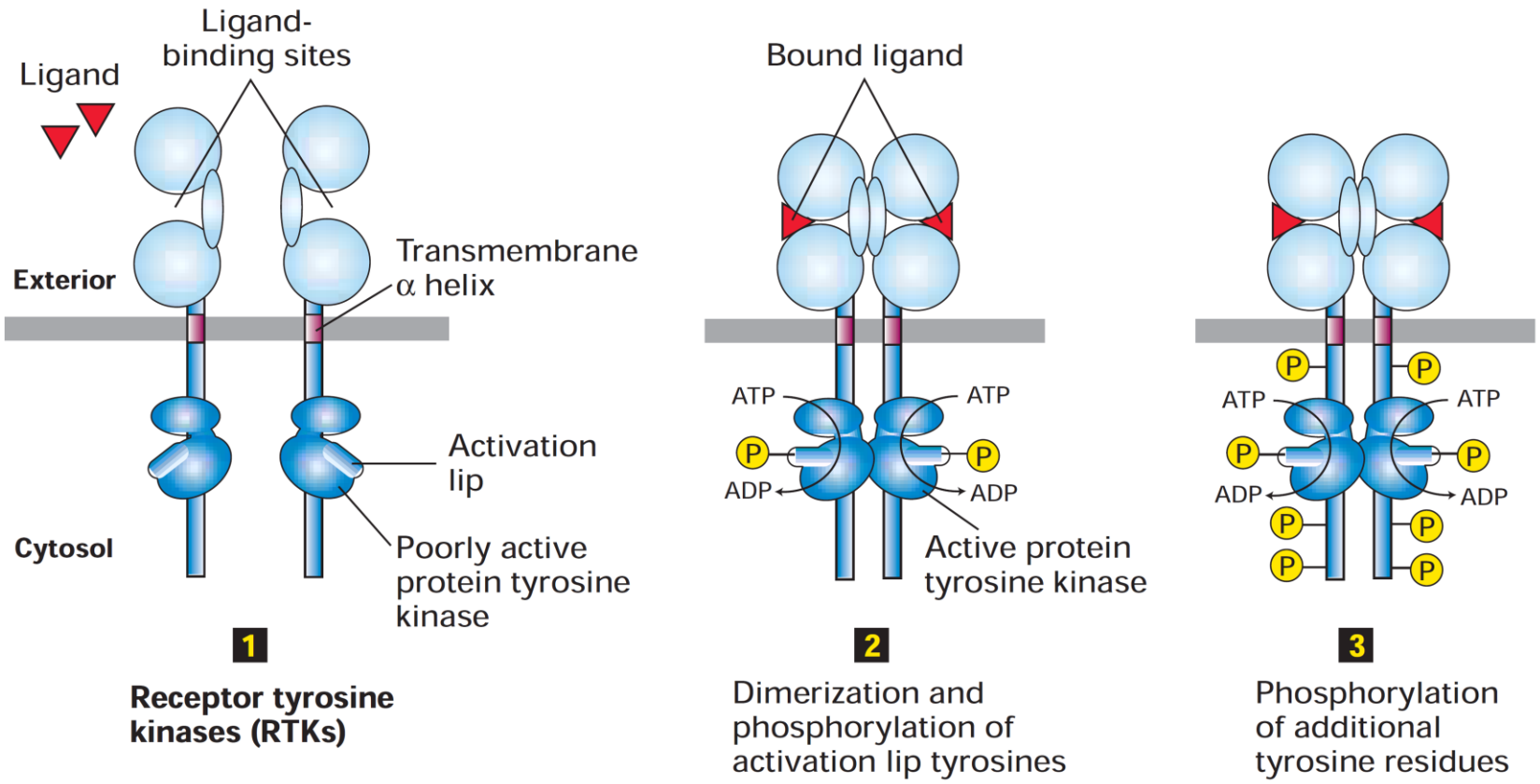
Integrated regulation mediated by several second messengers.



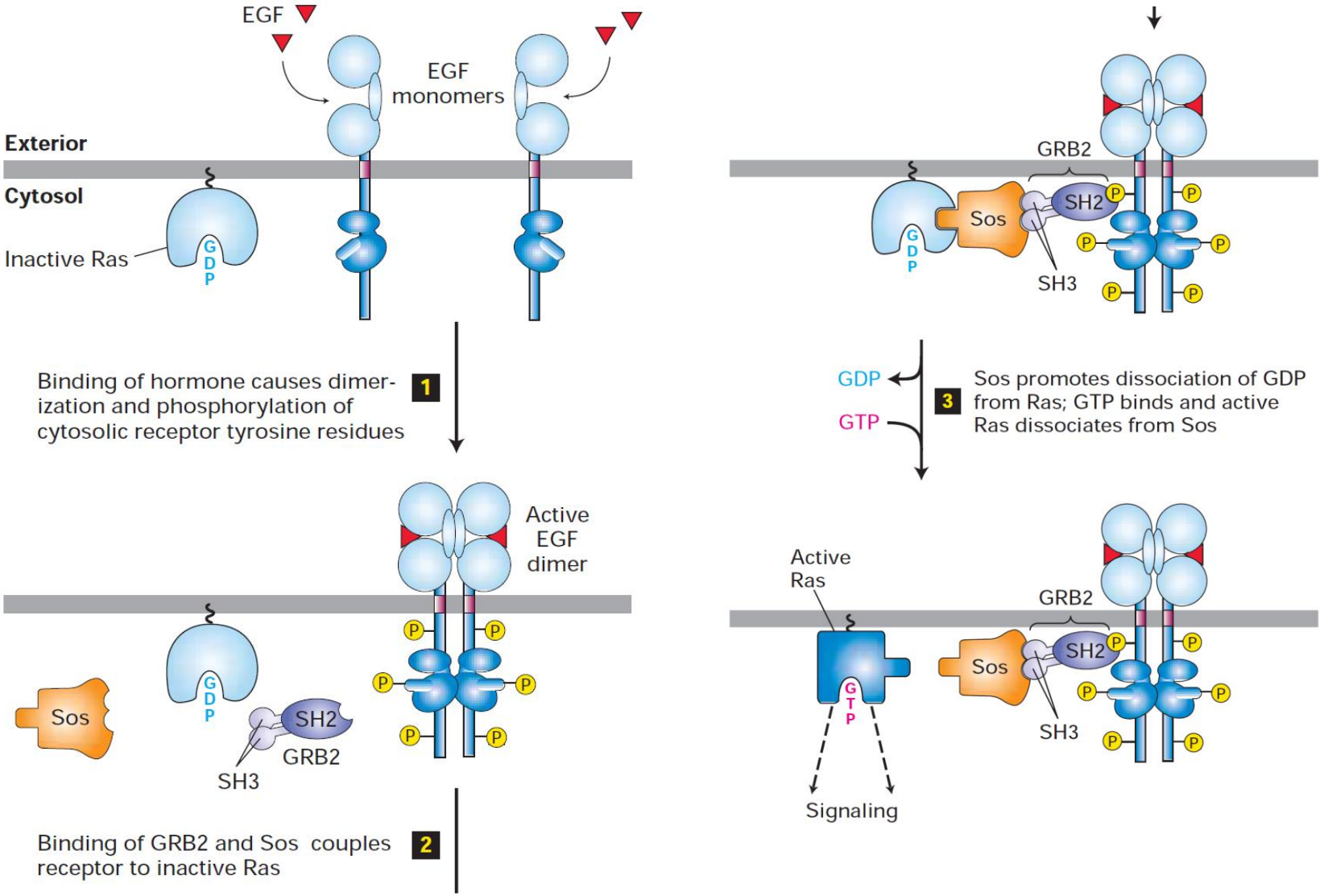
Abbreviations:

PKA	Protein kinase A	GP	Glycogen phosphorylase
GPK	Glycogen phosphorylase kinase	GS	Glycogen synthase

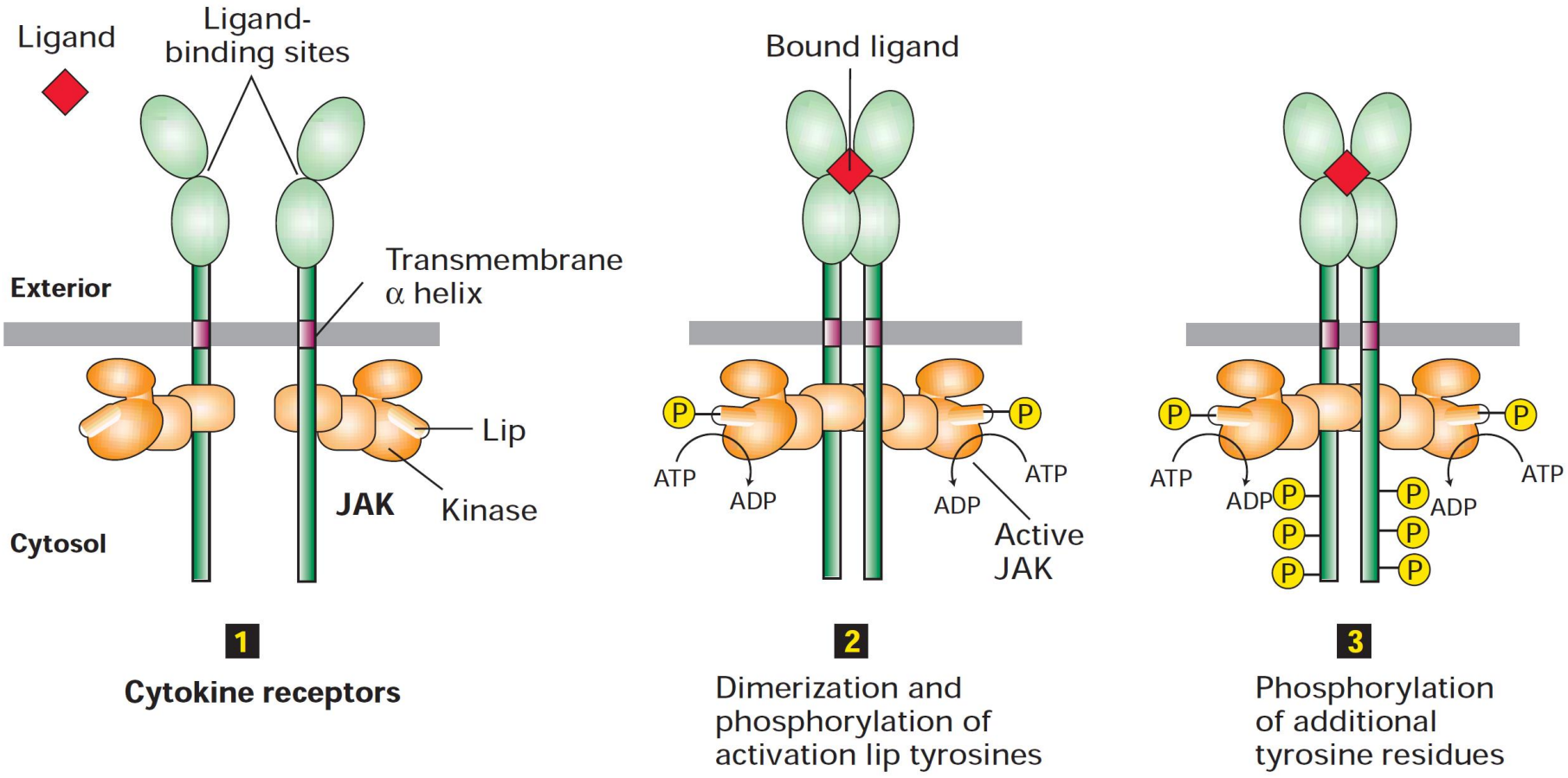
Receptor with intrinsic enzyme activity: tyrosine kinase receptor



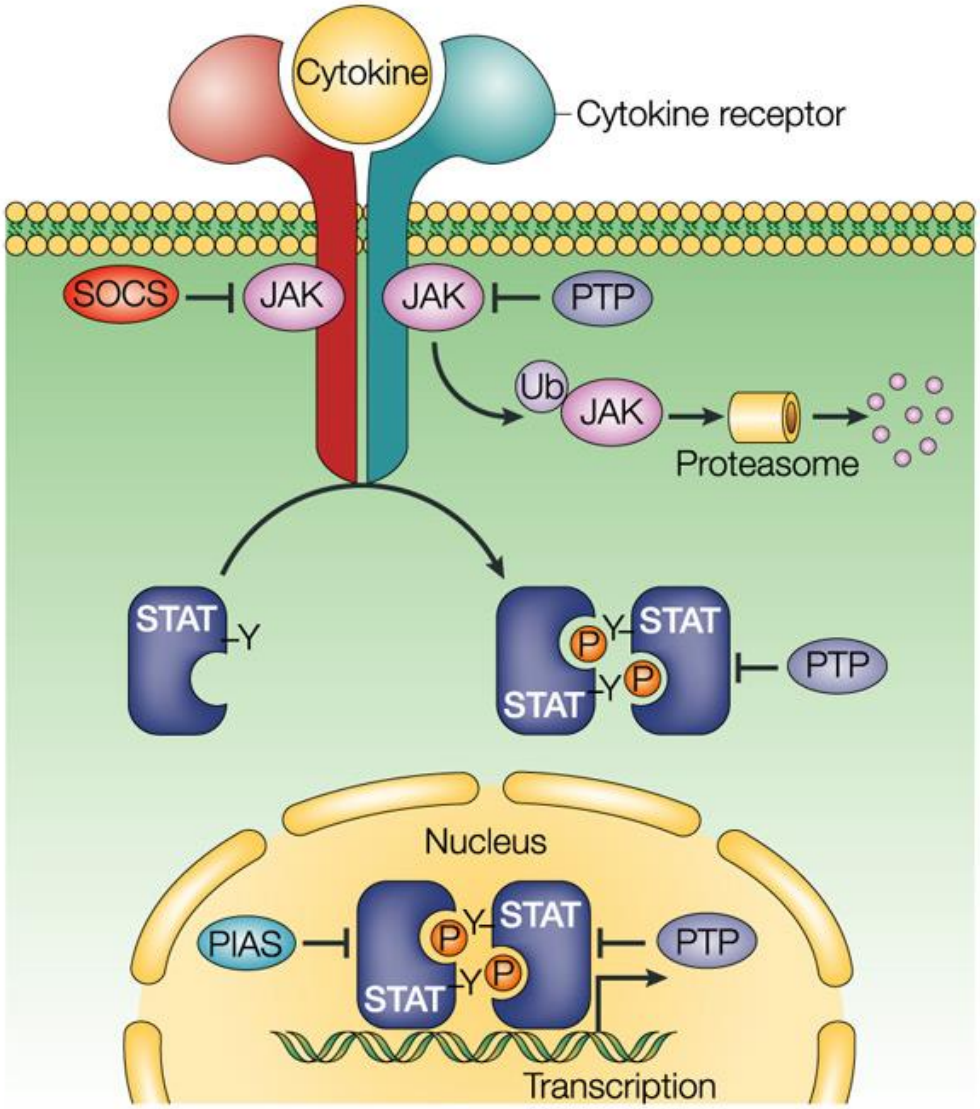
Receptor tyrosine kinases



Enzyme associated receptor: cytokine receptor



JAK-STAT signaling pathway



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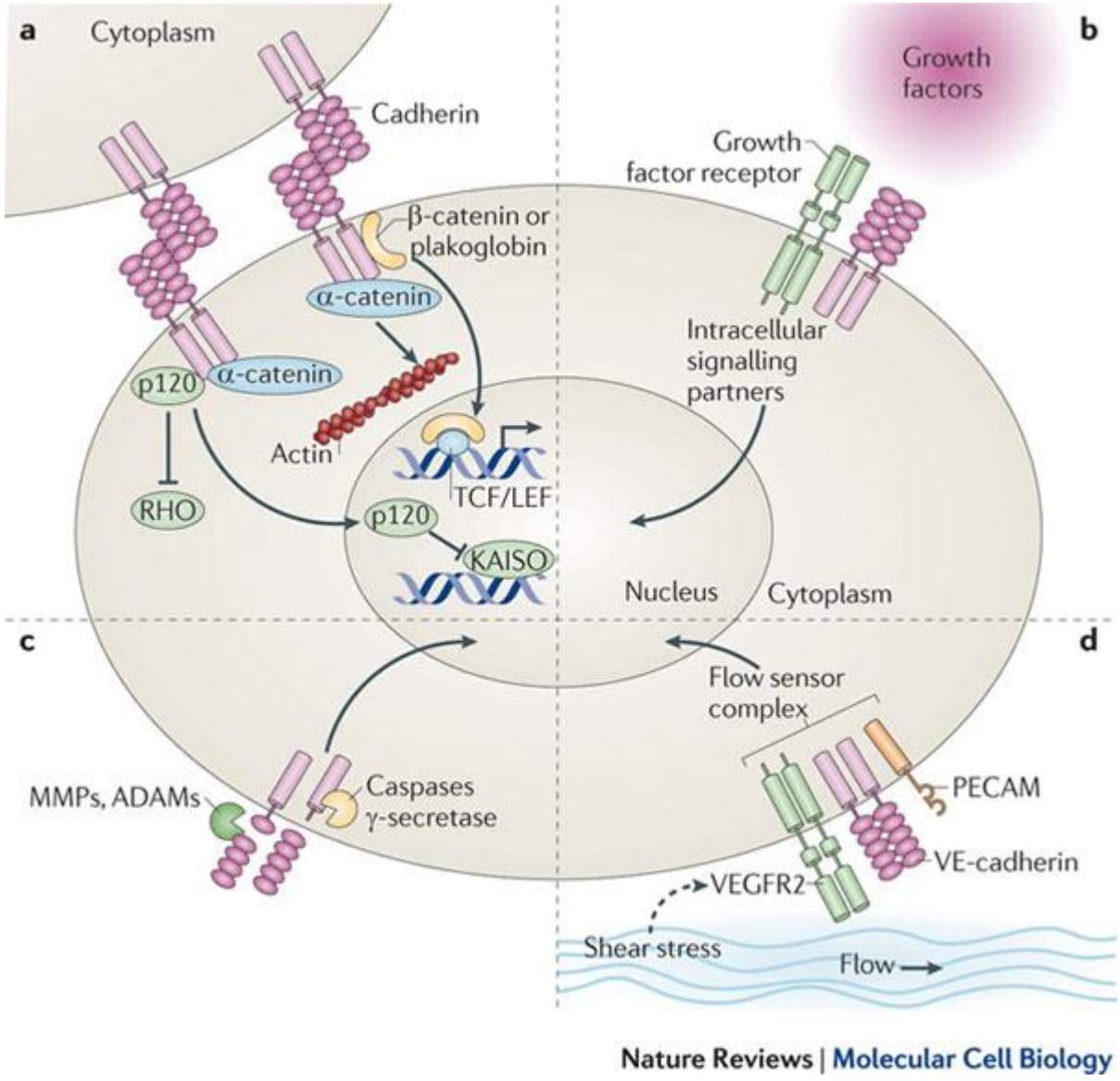
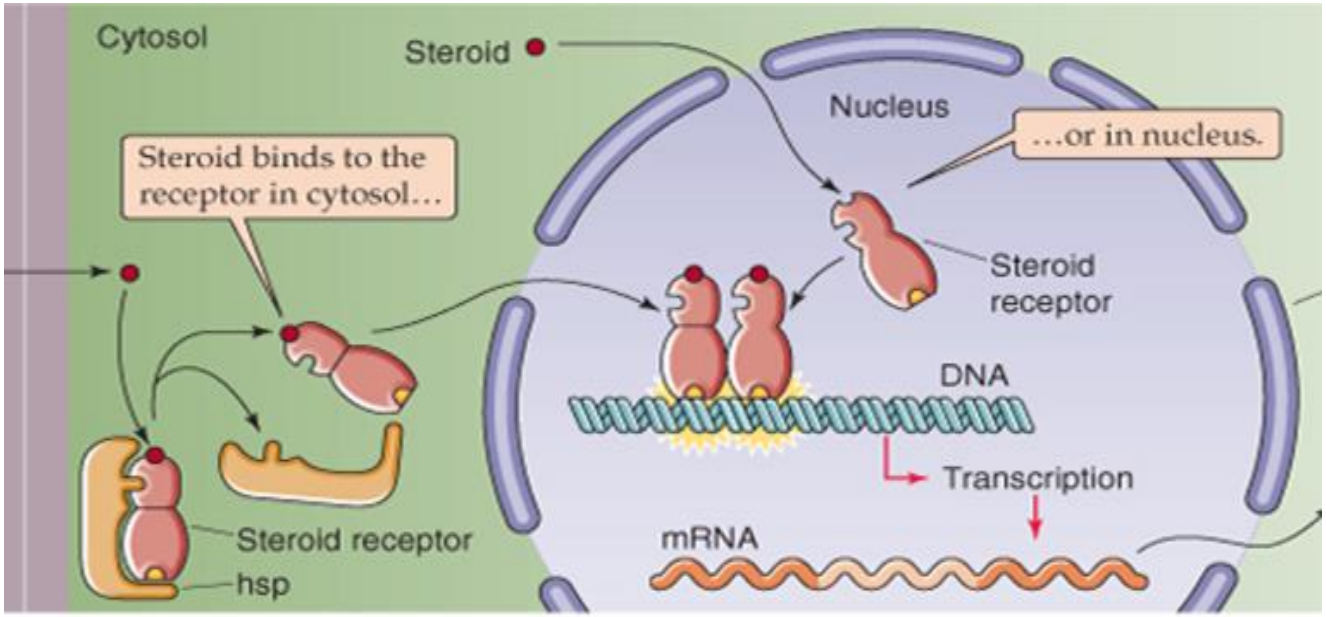
Adhesion molecule signaling



Steroid receptor signaling



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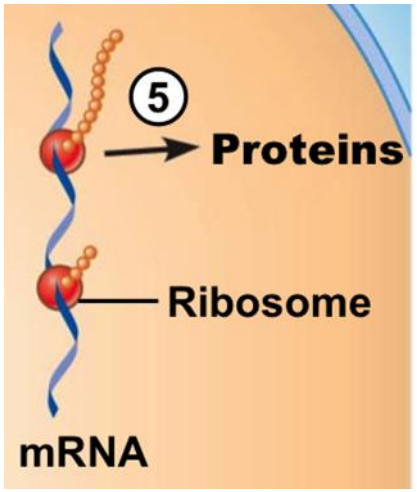
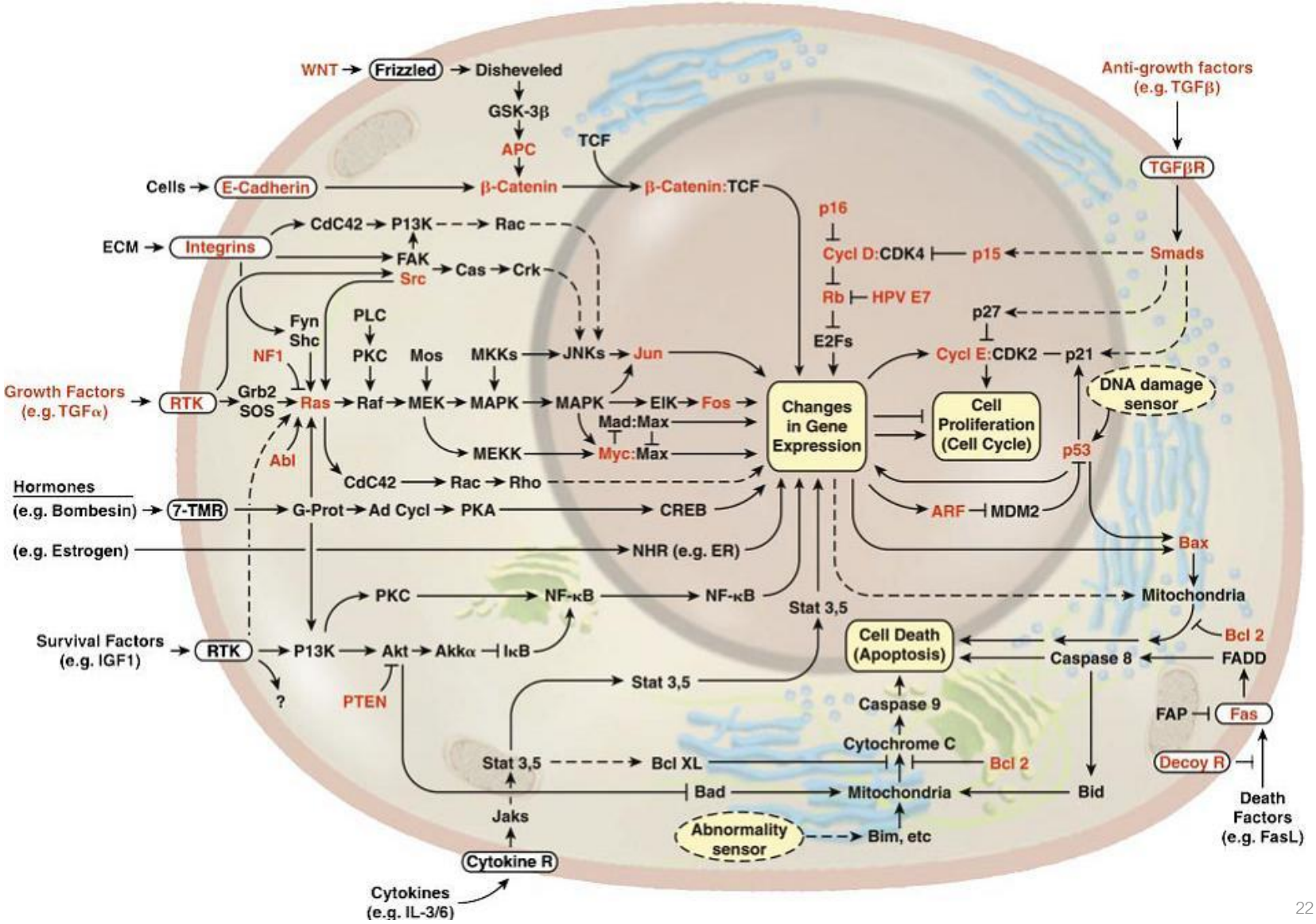


Integration of signal transduction



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