

A microscopic image showing several cells with prominent red nuclei and extensive yellow filamentous structures, likely actin or tubulin, extending between them.

# Lecture 11 Cell Communication

## Part II

### Outline

- I. G-protein-coupled receptor signaling
- II. Enzyme-linked receptor signaling

# I. G-protein-coupled receptor (GPCR) signalling

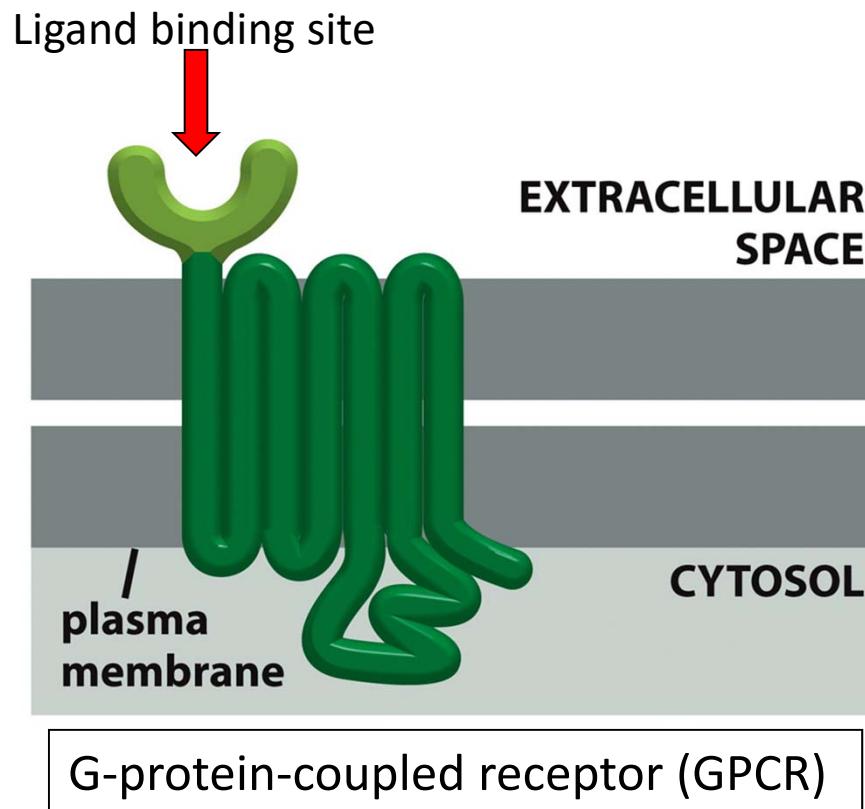
1. Facts & structure of GPCRs and G-proteins
2. Activation of G-proteins by activated GPCRs
3. Major families of G-proteins and their function
4. Mediators of GPCR signaling:
  - cAMP
  - Phospholipase C- $\beta$
  - $\text{Ca}^{2+}$
  - cAMP/cGMP-gated ion channel in olfactory and vision
5. GPCR desensitization

# 1. Facts and structure of G-protein-coupled receptor (GPCR) signalling

## Facts about GPCRs:

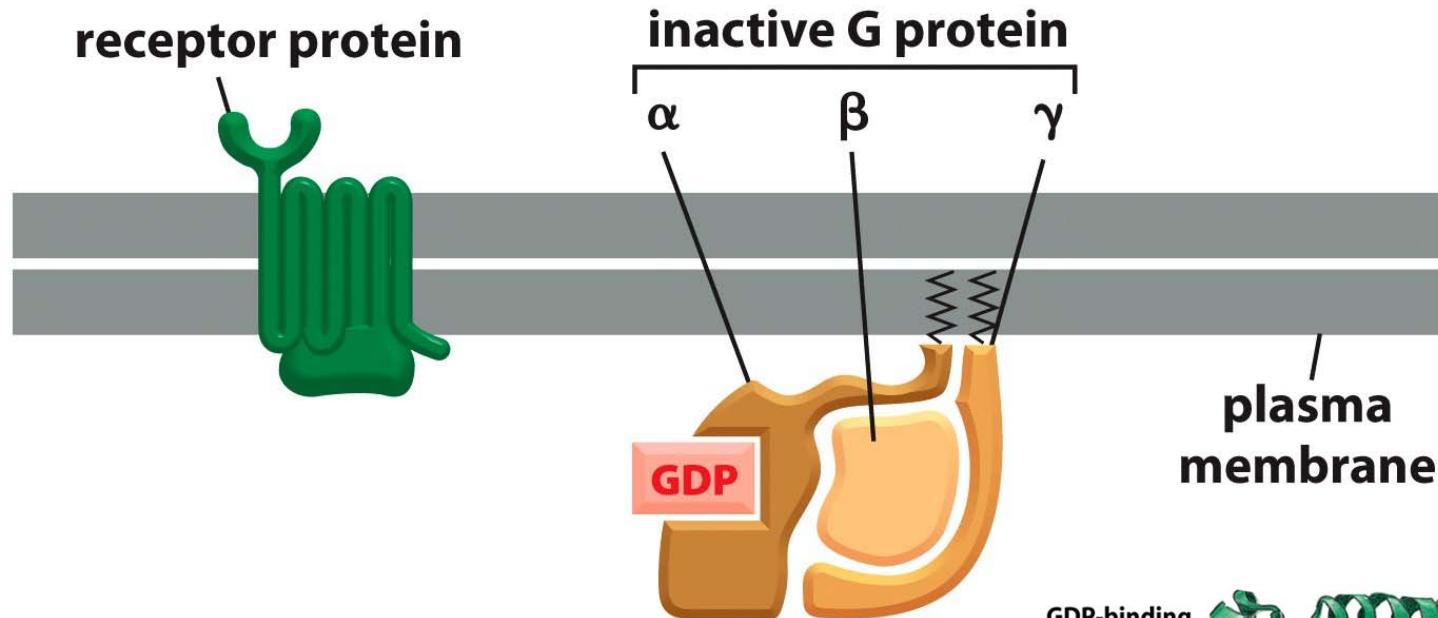
- >700 GPCRs in humans,  
(it is the largest cell surface receptor family)
- Respond to sight, smell, taste, neurotransmitters, etc.
- ~50% of drugs target GPCR signaling
- ~150 GPCR ligands known.
- All GPCRs are 7-pass transmembrane proteins
- All GPCRs need trimeric GTP-binding proteins to relay signals.

## Domain structure of G-protein-coupled receptors (GPCRs)

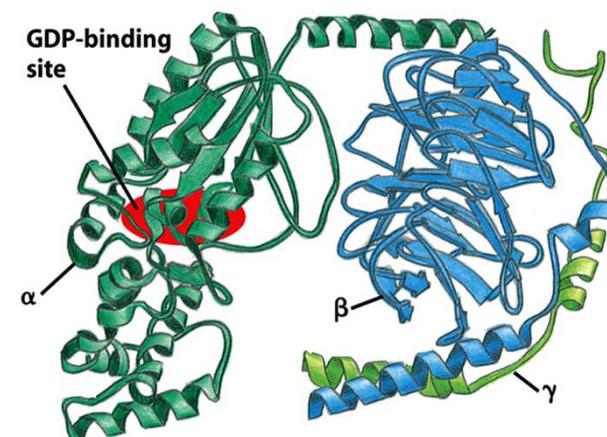


One single polypeptide, 7-pass transmembrane in a serpentine manner

G-protein function is coupled to the receptor function, therefore the name **G-protein-coupled receptor (GPCR)**



- Subunits  $\alpha$  and  $\gamma$  are tethered to PM
- Subunit  $\alpha$  binds to GTP/GDP and has GTPase activity
- $\beta$  subunit is bound by  $\alpha$  and  $\gamma$
- $\beta$  and  $\gamma$  form a functional subunit



## 2. Activation of a G-protein by an activated GPCR

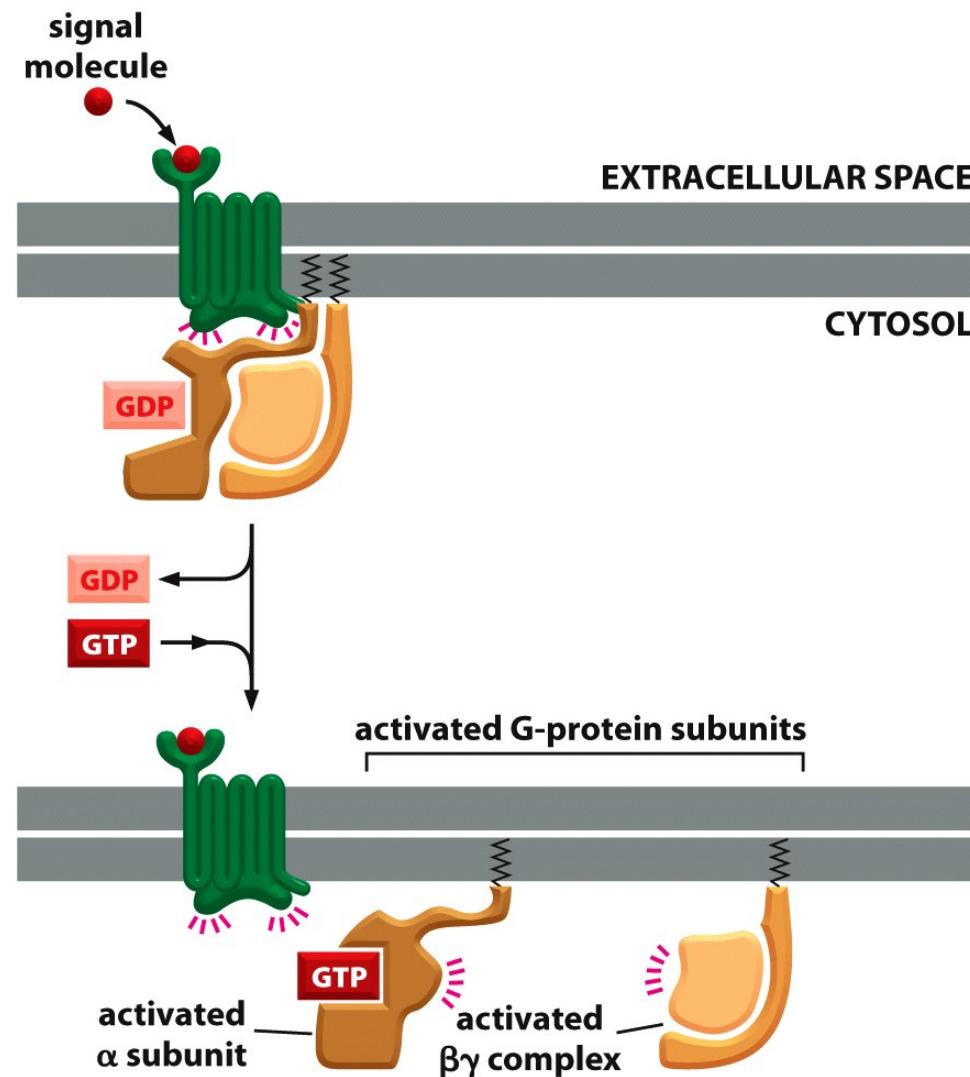


Figure 16-17b Essential Cell Biology 3/e (© Garland Science 2010)

# G-proteins can be deactivated by GTP hydrolysis

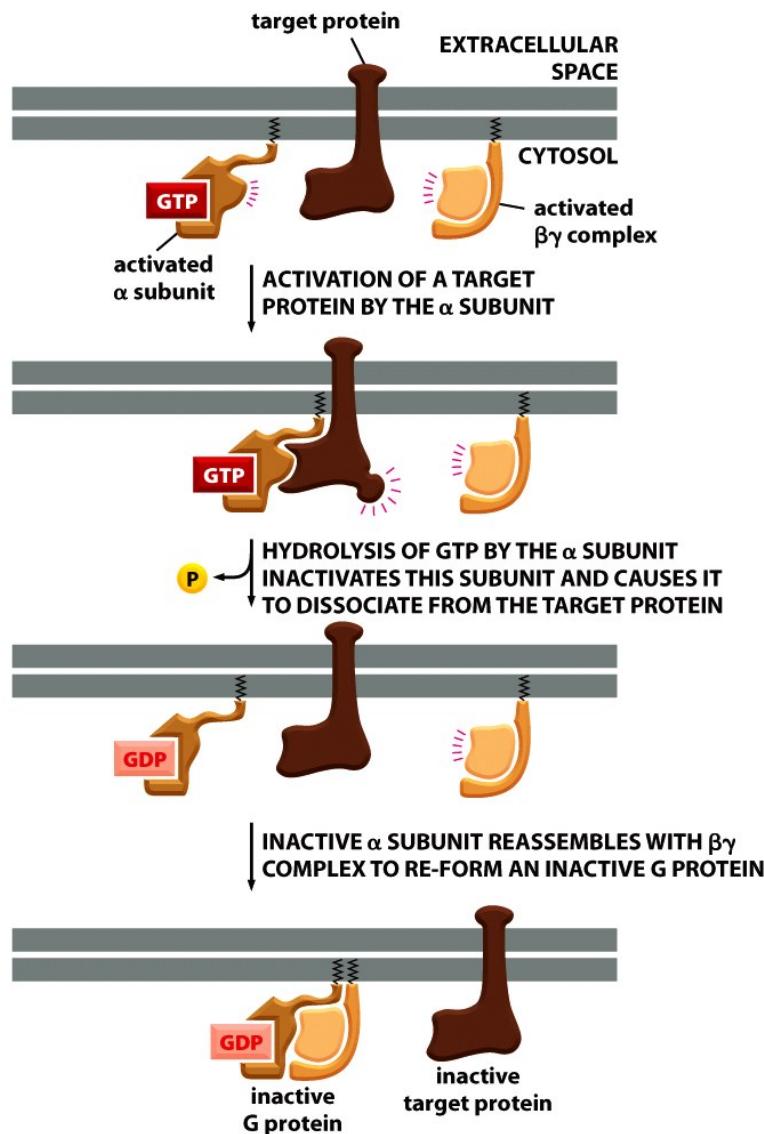


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# GPCR signaling includes the activation-deactivation cycle of the trimeric G-proteins

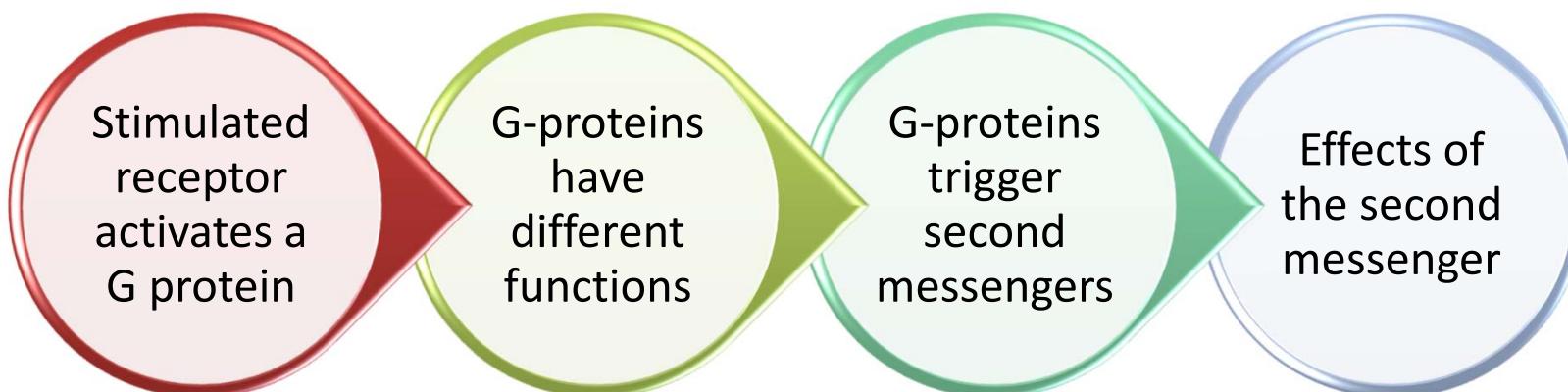
## Activation/deactivation of G-proteins:

- Ligand binding activates GPCR, which then acts as a GEF to exchange GDP for GTP and thus **activates** the G-protein
- “Activated trimeric G-proteins” dissociate into an **active  $\alpha$  subunit and an active  $\beta\gamma$  complex**
- The active complexes expose functional groups on the activated  $\alpha$  subunit and on the  $\beta\gamma$  complex.
- Subunit  $\alpha$  then acts as GTPase to hydrolyze GTP to GDP, thereby **inactivating** the G-protein.

## **Alternative inactivation:**

RGS (regulator of G-protein signaling) acts as  $\alpha$ -subunit-specific GTPase activating protein (GAP) to cause GTP hydrolysis.

# The principle of GPRC-mediated signaling



**Signaling molecule activates receptor, receptor activates trimeric G-proteins**

Active G-protein triggers then a second messenger by:  
- opening channels (Gs)  
- modulating the synthesis of the messenger:

**Gs, Gi: modulate the adenylyl cyclase ( $\rightarrow$ cAMP)**  
**Gq: phospholipase C- $\beta$  ( $\rightarrow$ DAG & IP<sub>3</sub>)**

**Second messengers:**

- Ions (Ca<sup>2+</sup>/K<sup>+</sup>) (Gs)
- cAMP (Gs, Gi)
- DAG (Gq)
- IP<sub>3</sub> (inositol 3 phosphate (Gq))

**Effects:**

- protein modification & regulation (Fast response)
- gene regulation (Slow response)
- all of the above

### 3. The members of four major families of trimeric G-proteins (I-IV) control ion channels, second messengers & GTPases

**Table 15–3 Four Major Families of Trimeric G Proteins\***

FAMILY	SOME FAMILY MEMBERS	SUBUNITS THAT MEDIATE ACTION	SOME FUNCTIONS
I	$G_s$	$\alpha$	activates adenylyl cyclase; activates $Ca^{2+}$ channels
	$G_{olf}$	$\alpha$	activates adenylyl cyclase in olfactory sensory neurons
	$G_i$	$\alpha$	inhibits adenylyl cyclase
		$\beta\gamma$	activates $K^+$ channels
	$G_o$	$\beta\gamma$	activates $K^+$ channels; inactivates $Ca^{2+}$ channels
	$G_t$ (transducin)	$\alpha$ and $\beta\gamma$	activates phospholipase C- $\beta$
III	$G_q$	$\alpha$	activates phospholipase C- $\beta$
	$G_{12/13}$	$\alpha$	activates Rho family monomeric GTPases (via Rho-GEF) to regulate the actin cytoskeleton

\*Families are determined by amino acid sequence relatedness of the  $\alpha$  subunits. Only selected examples are included. About 20  $\alpha$  subunits and at least 6  $\beta$  subunits and 11  $\gamma$  subunits have been described in humans.

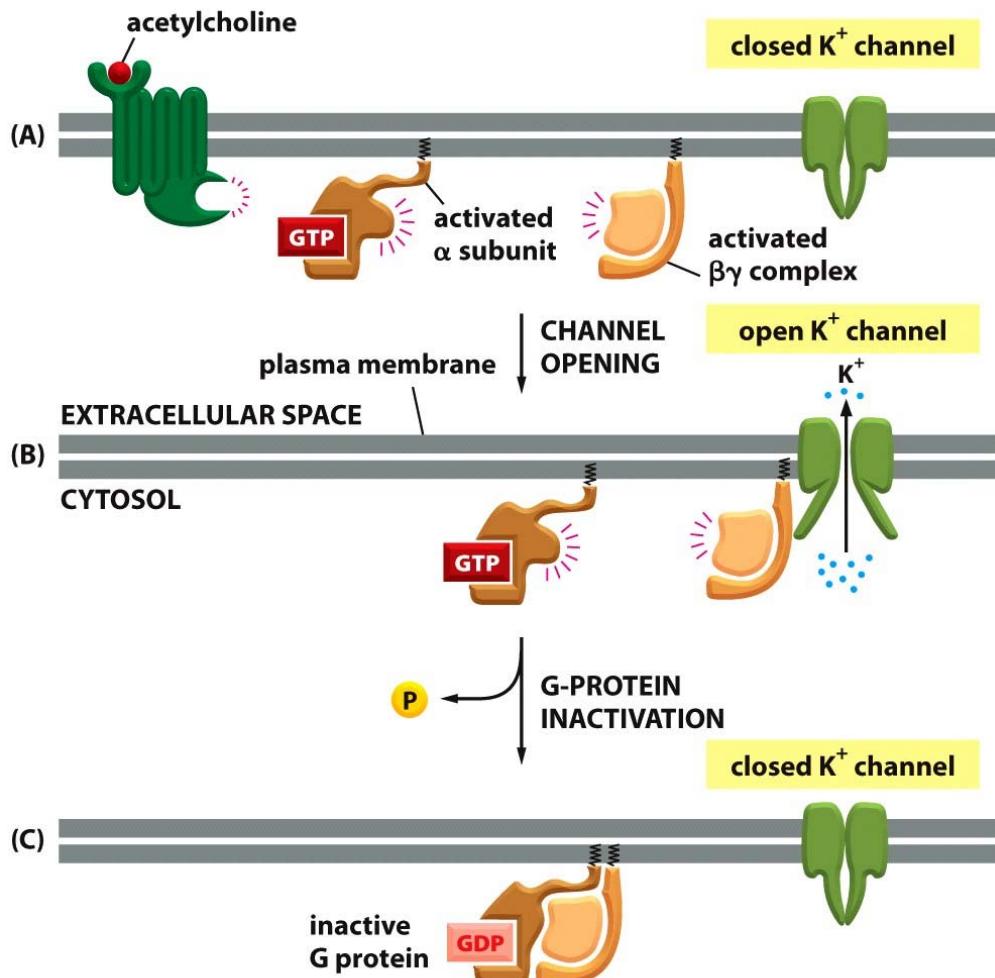
# GPCR signaling can be used to activate K<sup>+</sup> channels via the βγ subunit of the trimeric G protein G<sub>i</sub>

**Table 15–3 Four Major Families of Trimeric G Proteins\***

FAMILY	SOME FAMILY MEMBERS	SUBUNITS THAT MEDIATE ACTION	SOME FUNCTIONS
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	G <sub>olf</sub>	α	activates adenylyl cyclase in olfactory sensory neurons
II	G <sub>i</sub>	α	inhibits adenylyl cyclase
		βγ	activates K <sup>+</sup> channels
	G <sub>o</sub>	βγ	activates K <sup>+</sup> channels; inactivates Ca <sup>2+</sup> channels
	G <sub>t</sub> (transducin)	α and βγ	activates phospholipase C-β
III	G <sub>q</sub>	α	activates cyclic GMP phosphodiesterase in vertebrate rod photoreceptors
IV	G <sub>12/13</sub>	α	activates phospholipase C-β
			activates Rho family monomeric GTPases (via Rho-GEF) to regulate the actin cytoskeleton

\*Families are determined by amino acid sequence relatedness of the α subunits. Only selected examples are included. About 20 α subunits and at least 6 β subunits and 11 γ subunits have been described in humans.

# GPCR signaling activates K<sup>+</sup> channels via the βγ subunit of the trimeric G-protein G<sub>i</sub>



Slowing down heartbeat:

A) Binding of **acetylcholine** to its **GPCR** on the heart cells **activates** the **G-protein, G<sub>i</sub>**.

B) The activated **βγ complex** directly **opens** a **K<sup>+</sup> channel** in the plasma membrane, increasing its permeability to K<sup>+</sup> and thereby making the membrane harder to activate and slowing the heart rate.

C) **Inactivation** of the **α-subunit** by **GTP hydrolysis** inactivates the G-protein, the channel closes

Figure 16-19 Essential Cell Biology 3/e (© Garland Science 2010)

# GPCR signaling can activate small second messenger molecules

## Small messengers:

- cAMP ( $\rightarrow$ produced by **adenylyl cyclase**)
- DAG (diacylglycerol) and IP<sub>3</sub> (inositol 1,4,5 triphosphate) ( $\rightarrow$ produced by **phospholipase C-β**)
- Ca<sup>2+</sup> ( $\rightarrow$ levels are controlled by **gated channels**)
- cGMP/cAMP (to trigger gated ion channels in smell and vision)

Table 15–3 Four Major Families of Trimeric G Proteins\*

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#### 4. GPCR signaling can activate small messenger molecules

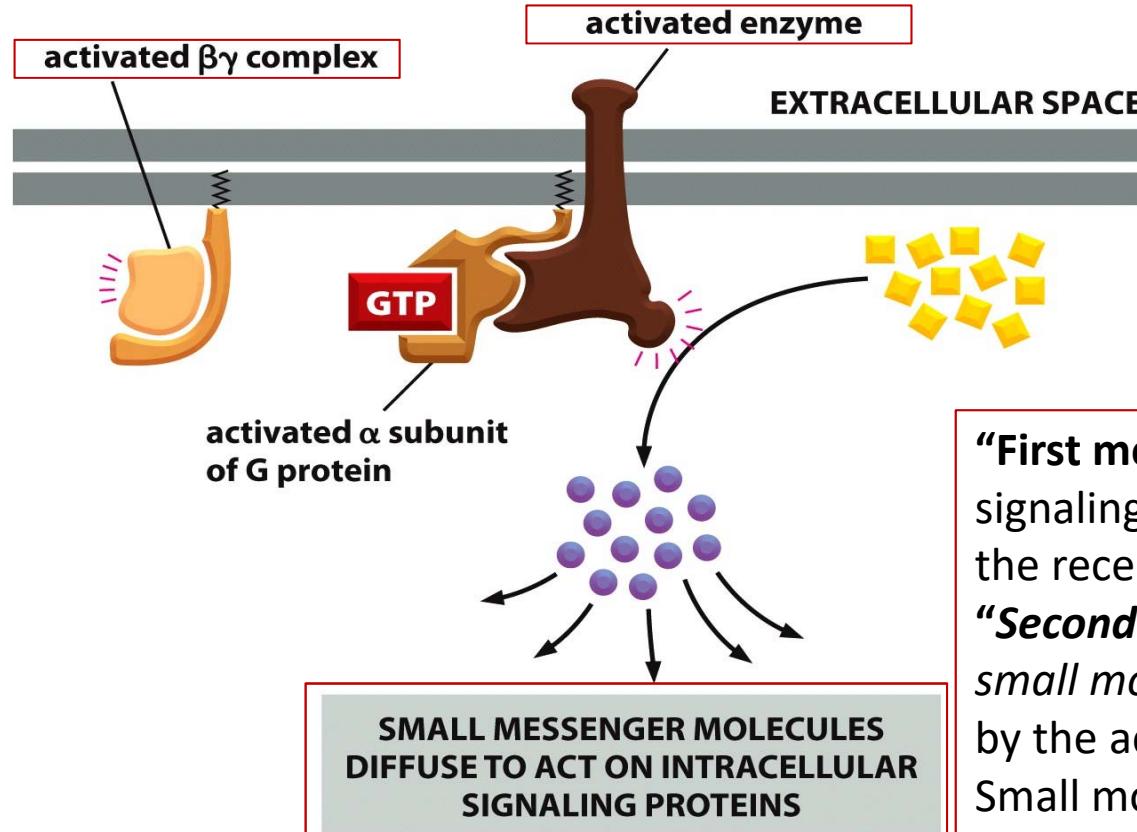


Figure 16-20 Essential Cell Biology 3/e (© Garland Science 2010)

**"First messengers":**  
signaling molecules that activate the receptor  
**"Second messengers":**  
*small molecules* that are produced by the activated enzymes  
Small molecules rapidly diffuse away from their source, thereby amplifying and spreading the intracellular signal

# Activation/regulation of cAMP synthesis by GPCR signaling: the G-proteins $G_s$ and $G_i$

**Table 15–3 Four Major Families of Trimeric G Proteins\***

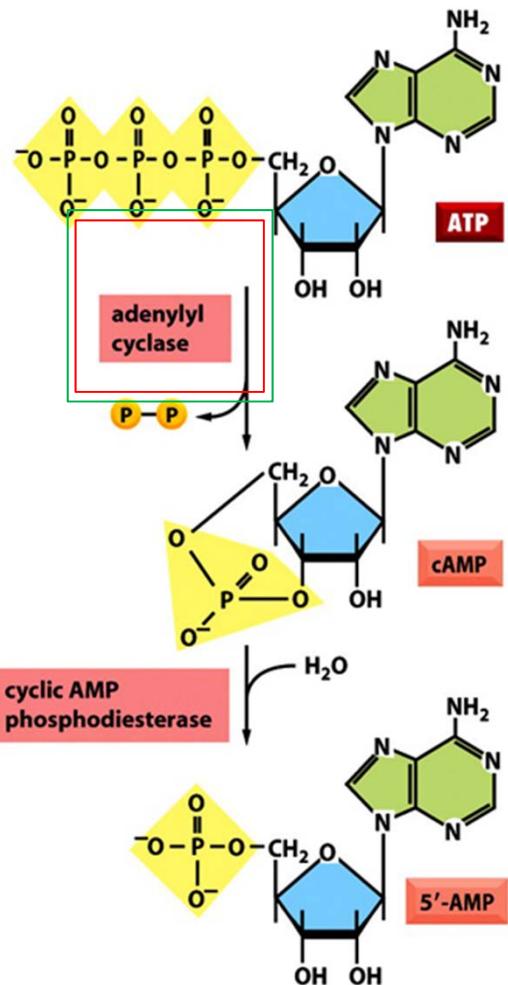
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Mediators of GPCR signaling:

## 4. Mediators of GPCRs: cAMP

cAMP is an important second messenger that relays signals and is synthesized from ATP by the adenylyl cyclase



1. cAMP levels are balanced by two enzymes: **adenylyl cyclase** and **cyclic AMP phosphodiesterase**
2. **Adenylyl cyclase** is a plasma-membrane-bound enzyme
3. **Two different G-proteins influence cAMP synthesis:** **Gs** (stimulatory G-protein) **activates** adenylyl cyclase but **Gi** (inhibitory G-protein) **inhibits** adenylyl cyclase

**$\alpha$ -subunits of Gs and Gi are target of the cholera toxin**  
 **$\alpha$ -subunits of Gi is target of the pertussis toxin**

**see below.....**

## Neuron cells **sense** serotonin and produce cAMP instantly

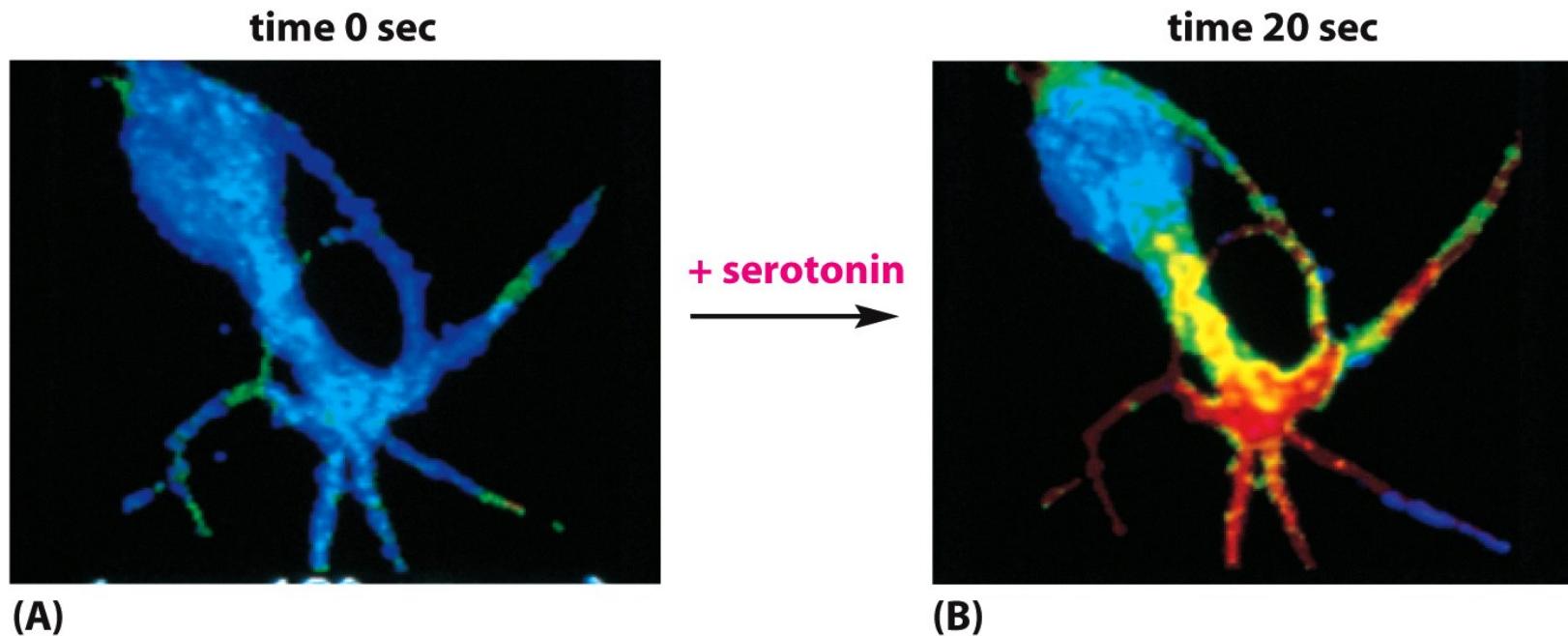


Figure 16-22 Essential Cell Biology 3/e (© Garland Science 2010)

**Detection of cAMP using a fluorescent protein whose fluorescence changes color when it binds cyclic AMP: Blue indicates low level of cAMP, yellow an intermediate level, and red a high level.**

**In 20 seconds:**

**concentration of cAMP has risen more than twentyfold (to  $> 10^{-6}$  M)  
in the parts of the cell where the serotonin receptors are concentrated**

## Most of the cAMP signals are executed by the cAMP-dependent protein kinase PKA

PKA (cAMP-dependent protein kinase)-executed cAMP signaling can trigger **fast and slow responses**:

- PKA is a serine/threonine **protein kinase**.  
By phosphorylation of substrates (protein modification), PKA mediates GPCR signaling **in a fast manner/response**
- PKA also **phosphorylates CREB (CRE-binding protein)**, which then recruits CBP (**CREB-binding protein**) and **activates gene transcription** (gene regulation) **in a slow manner/response**

## PKA triggers fast response:

### Adrenaline-induced glycogen breakdown:

In skeletal muscle, glycogen breakdown occurs within seconds of adrenaline binding to its receptor (activated by the *second messenger* cAMP)

1. **Receptor activates adenyl cyclase to produce cAMP**
2. **cAMP activates PKA**
3. activated **PKA phosphorylates the phosphorylase kinase**
4. **phosphorylase kinase phosphorylates glycogen phosphorylase**
5. **glycogen phosphorylase triggers glycogen breakdown**

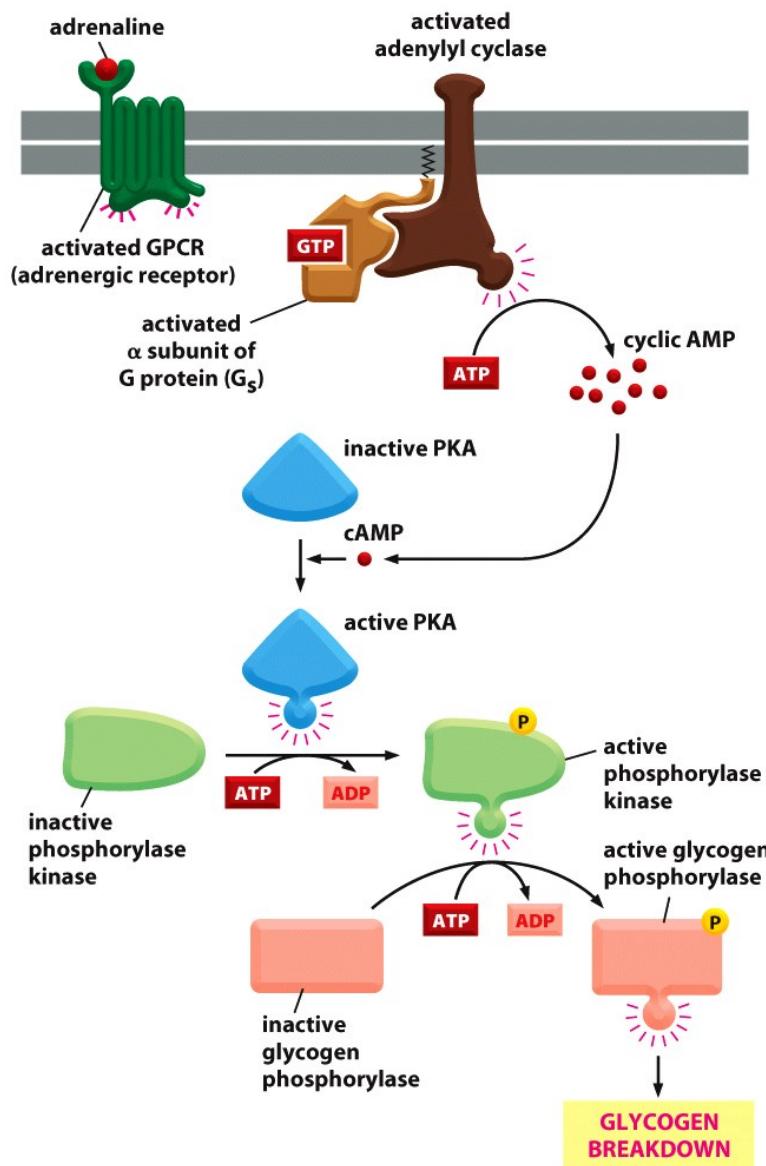
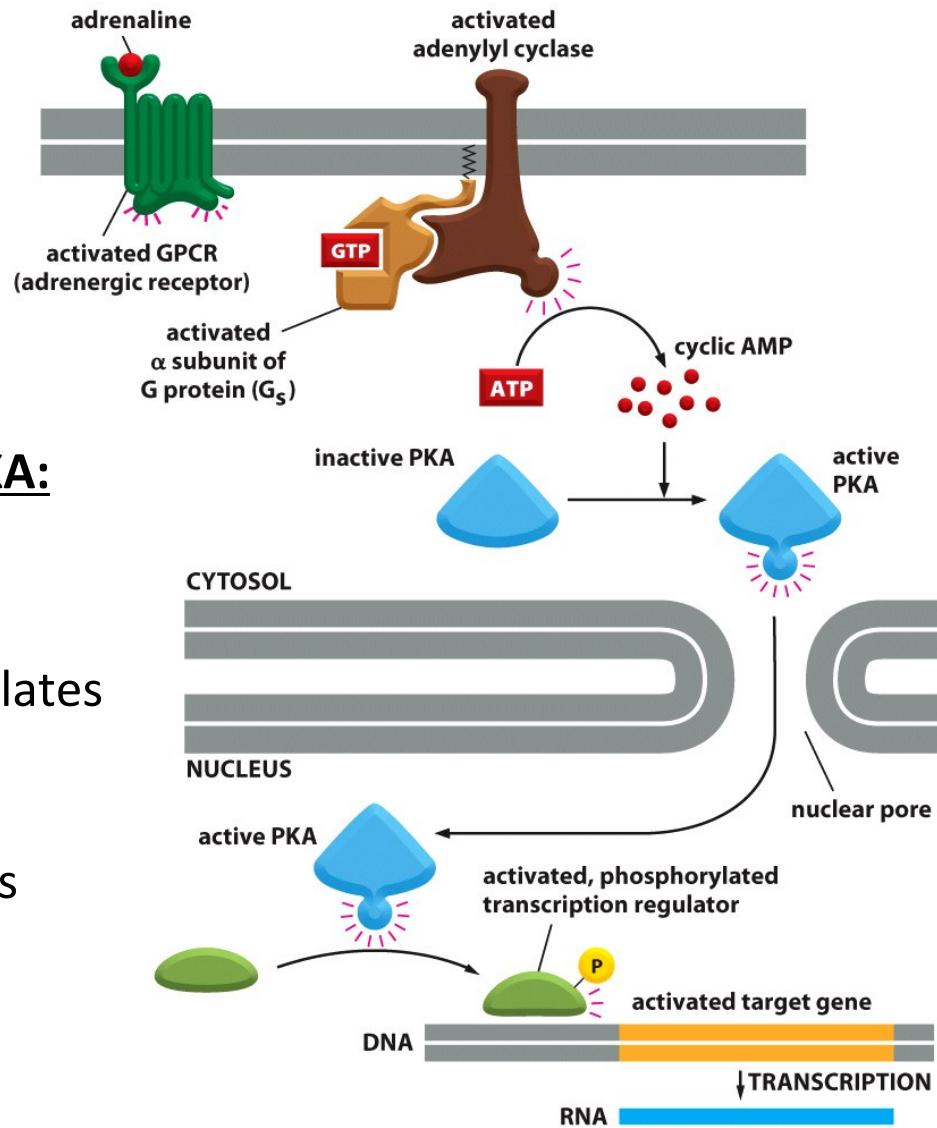


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## PKA triggers slow response:



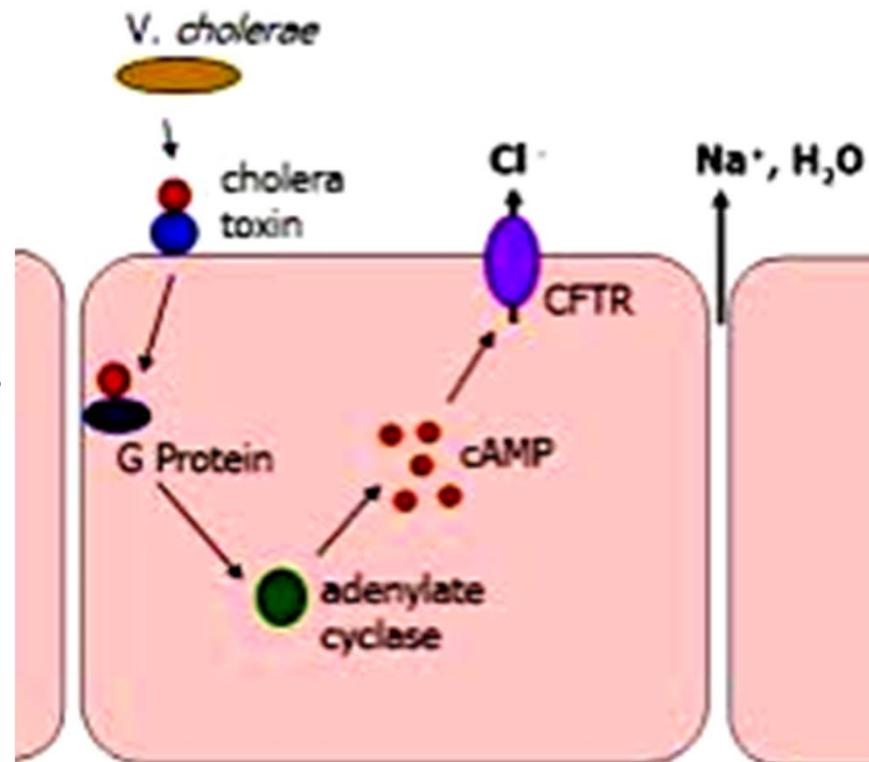
### Transcription regulation by PKA:

- activation of PKA by cAMP
- active PKA moves into the nucleus and phosphorylates transcription regulators to stimulate transcription many different target genes

Figure 16-24 Essential Cell Biology 3/e (© Garland Science 2010)

## Mechanism of cholera toxin: prolonged elevation of cAMP concentrations

- Catalyzes the transfer of ADP ribose from intracellular NAD<sup>+</sup> to the  **$\alpha$  subunit of Gs**.
- ADP ribosylation alters the  $\alpha$  subunit so that it can **no longer hydrolyze its bound GTP**, causing it to remain in an active state
- **This indefinitely stimulates the adenylyl cyclase.**
- The **prolonged elevation in cAMP concentration** causes **influx of Cl<sup>-</sup> and water from intestinal epithelial cells into the gut**, thereby causing the severe diarrhea that characterizes cholera.



The opposite is true for the mechanism of pertussis toxin:  
**permanent inactivation** of G-proteins

- Catalyzes the ADP ribosylation of  $\alpha$  subunit of the G-protein  $G_i$ .
- Locks the G-protein in the GDP (inactive) state.
- Leads to an increase in mucus secretion in the lung.
- Syndrome: whooping cough

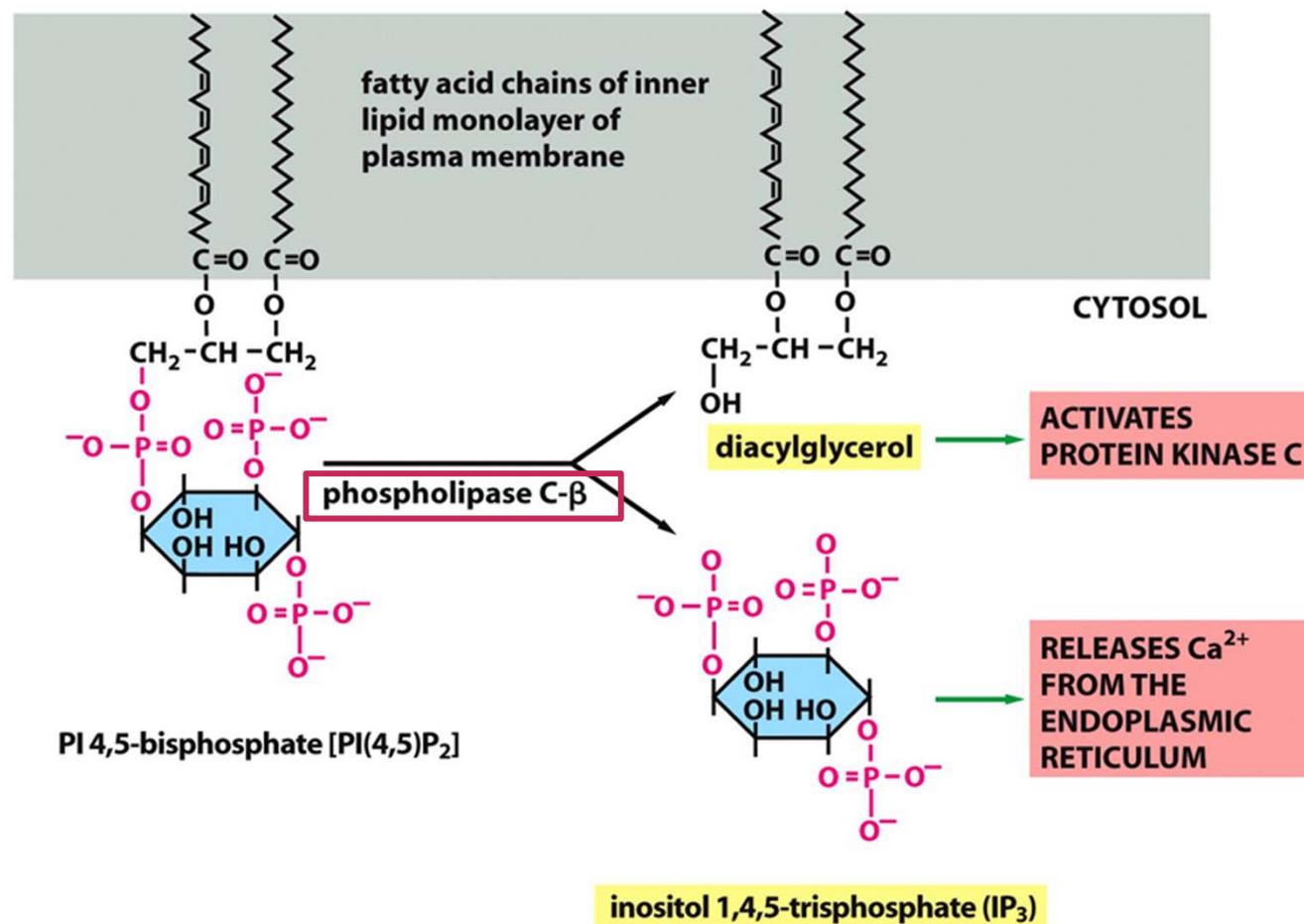
## Mediators of GPCRs: signaling via the phospholipase C- $\beta$

- The **trimeric G-protein Gq activates phospholipase C- $\beta$ .**
- **Substrates for phospholipase C- $\beta$  is PI(4,5)P<sub>2</sub>**
- Cleavage of PIP<sub>2</sub> results in production of the two **second messengers 1,4,5-triphosphate (IP<sub>3</sub>) and diacylglycerol (DAG)**

**Table 15–2 Some Cell Responses in Which GPCRs Activate PLC $\beta$**

TARGET TISSUE	SIGNAL MOLECULE	MAJOR RESPONSE
Liver	vasopressin	glycogen breakdown
Pancreas	acetylcholine	amylase secretion
Smooth muscle	acetylcholine	muscle contraction
Blood platelets	thrombin	platelet aggregation

# Production and action of the second messengers diacylglycerol and inositol 1,4,5-triphosphate ( $\text{IP}_3$ ) by phospholipase C- $\beta$ from PI4,5-biphosphate



## Mediators of GPCRs: $\text{Ca}^{2+}$

- The activated phospholipase C hydrolyzes PI(4,5)P<sub>2</sub> and releases the two messengers: DAG and IP<sub>3</sub>. IP<sub>3</sub> triggers release of  $\text{Ca}^{2+}$ .
- Together,  $\text{Ca}^{2+}$  and DAG activate the protein kinase C (PKC)

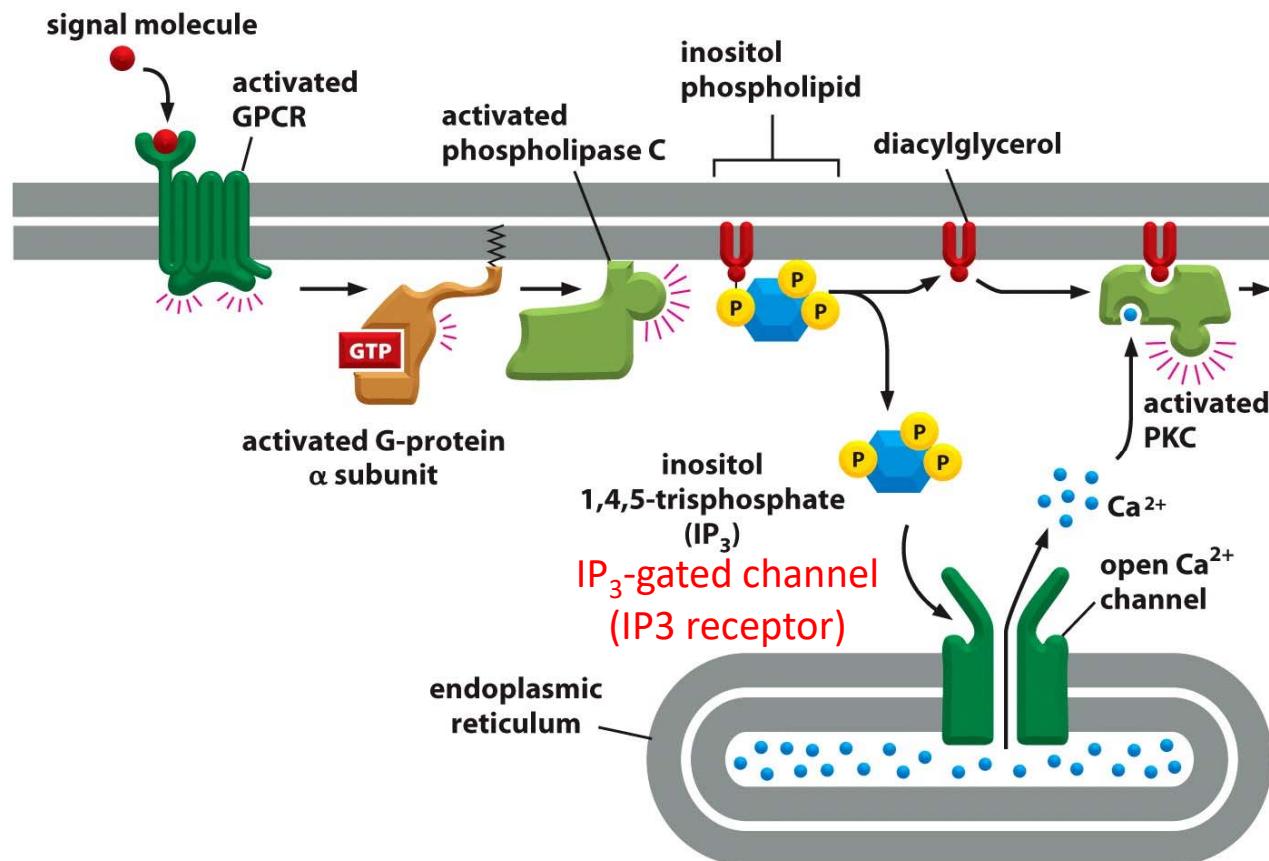


Figure 16-25 Essential Cell Biology 3/e (© Garland Science 2010)

## $\text{Ca}^{2+}$ functions as universal intracellular mediator

- Rise in  $\text{Ca}^{2+}$  in fertilized egg cytosol initiates embryonic development (and prevents entry of other sperm cells)
- Triggers muscle contraction
- Triggers secretion of secretory vesicle

Fertilized egg shows waves of  $\text{Ca}^{2+}$  from the site of sperm entry

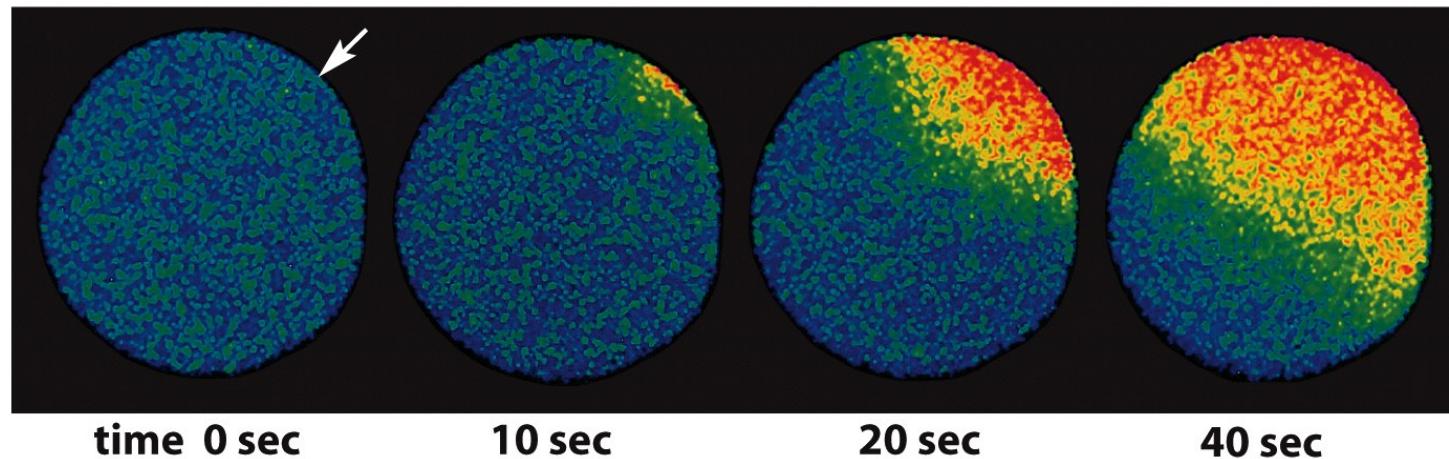
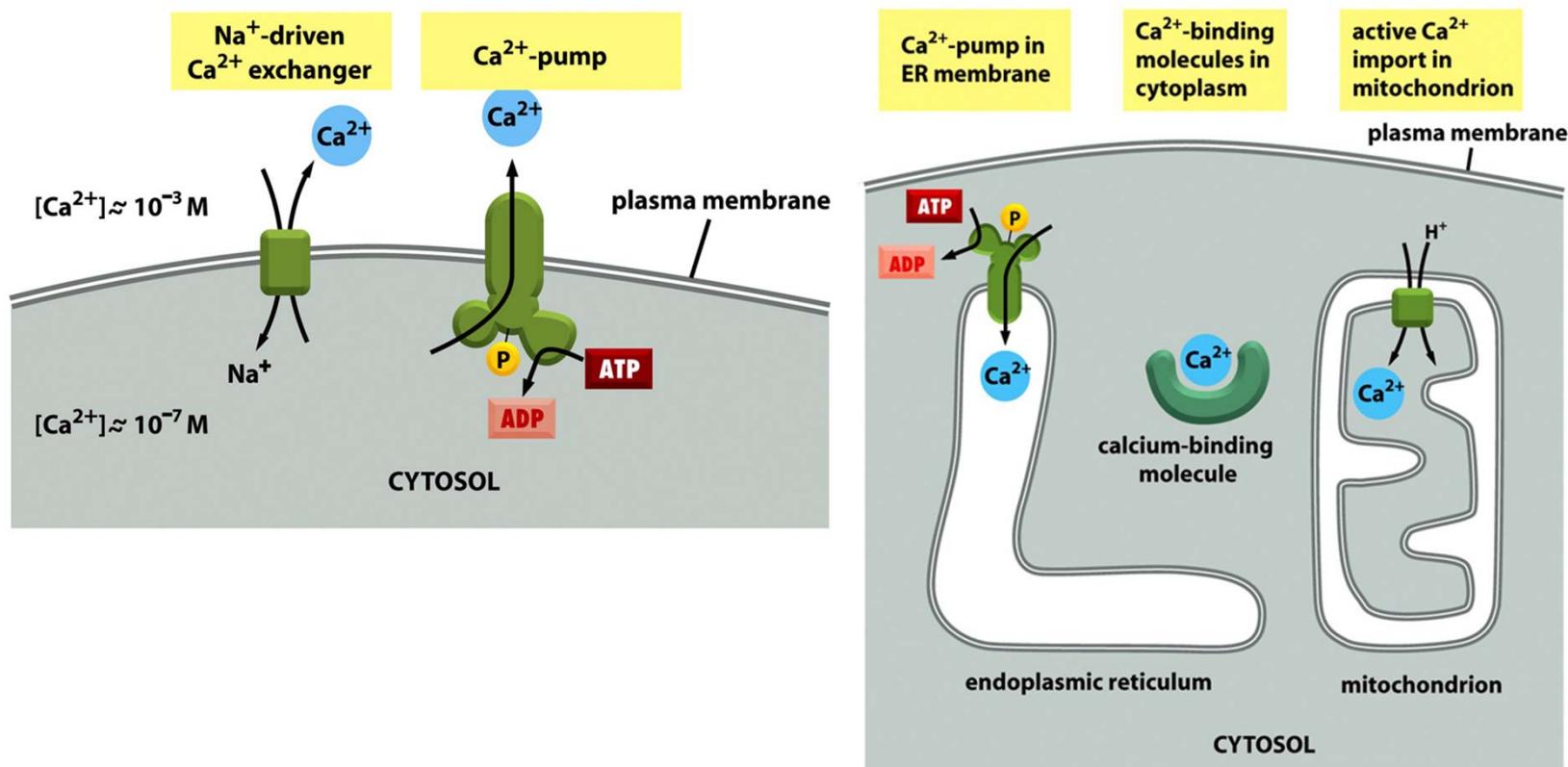


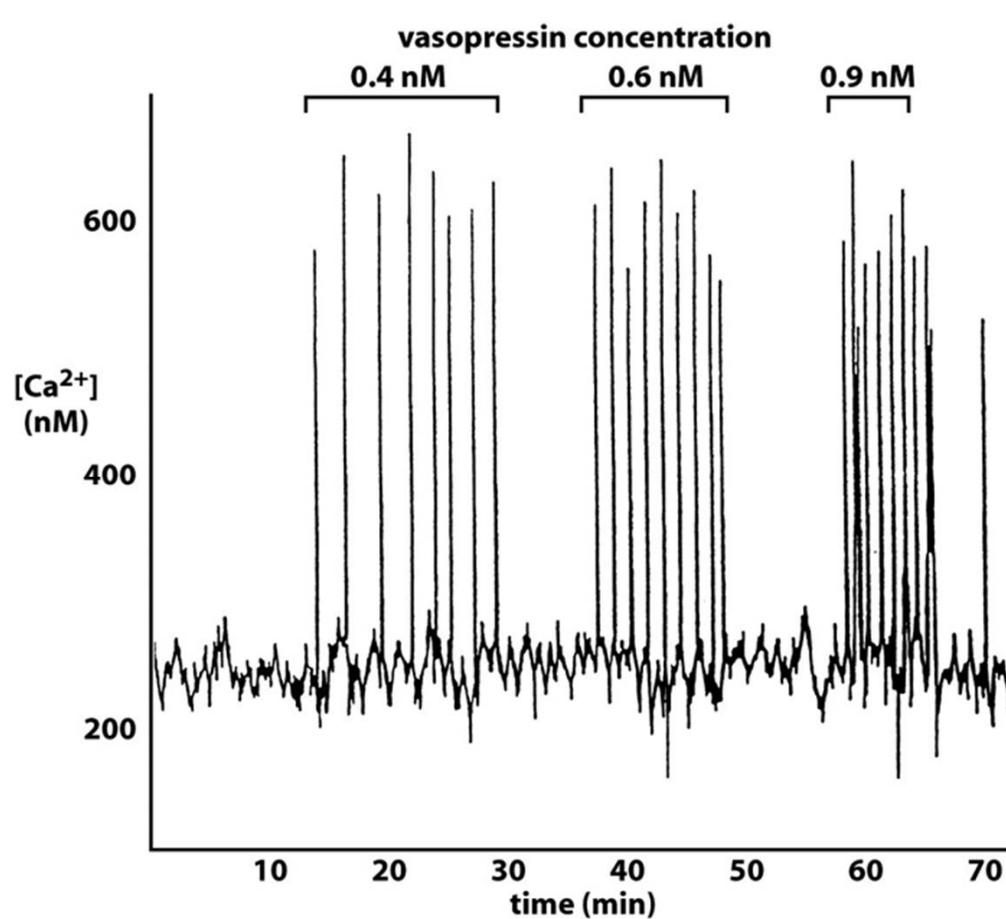
Figure 16-26 Essential Cell Biology 3/e (© Garland Science 2010)

# How do cells keep low $\text{Ca}^{2+}$ concentrations in the cytosol?

5 different ways to keep cytosolic  $\text{Ca}^{2+}$  concentrations low:



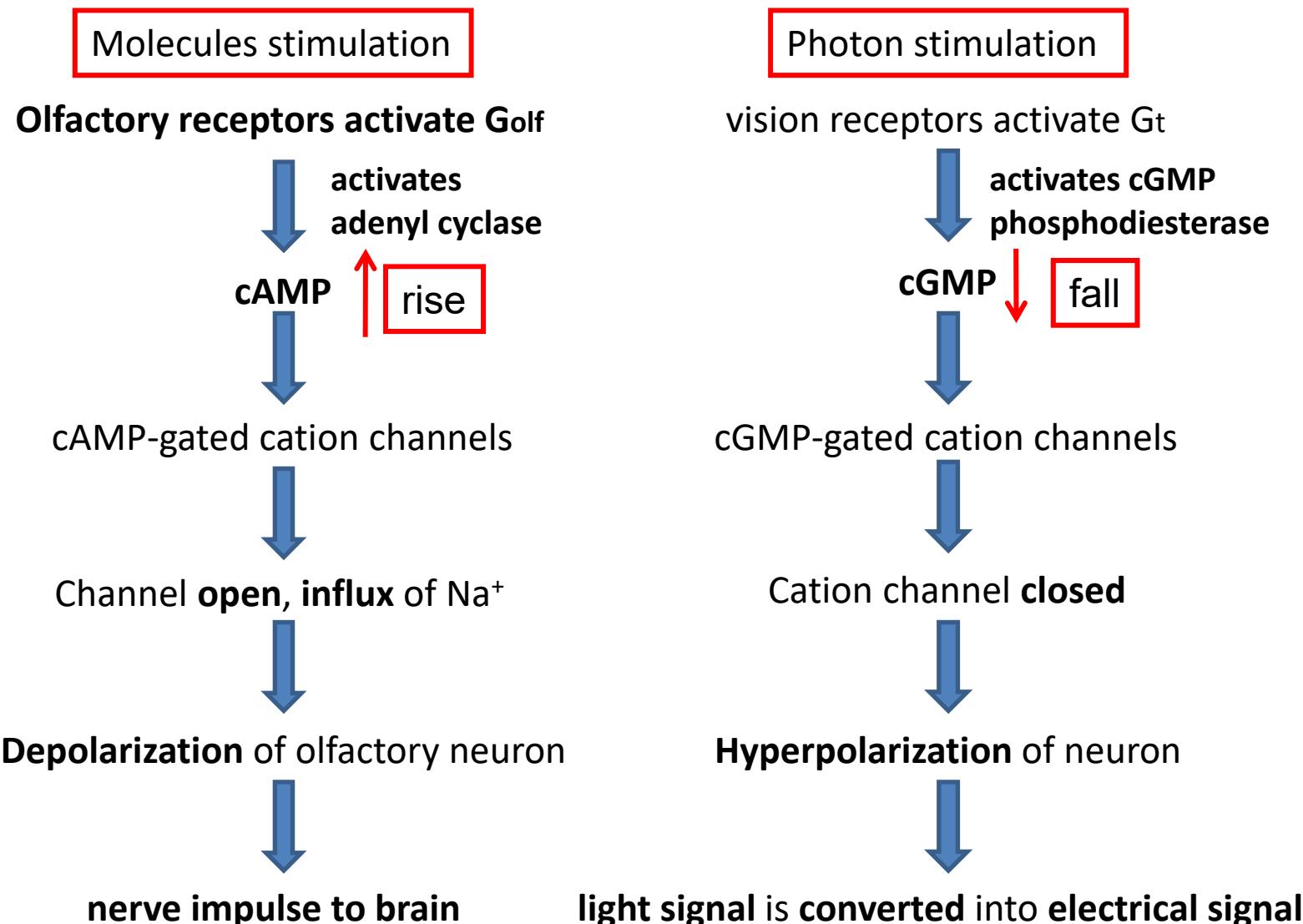
# $\text{Ca}^{2+}$ oscillation in cells in response to stimuli as consequence of positive and negative feedback



The peptide signal molecule **vasopressin** activates a GPCR and thereby PLC $\beta$ , that triggers  $\text{Ca}^{2+}$  release.  
Initial **release of  $\text{Ca}^{2+}$  triggers further release (pos. feedback)**  
At **high concentration,  $\text{Ca}^{2+}$  triggers inhibits further release**  
**delayed neg. feedback**  
→ oscillation

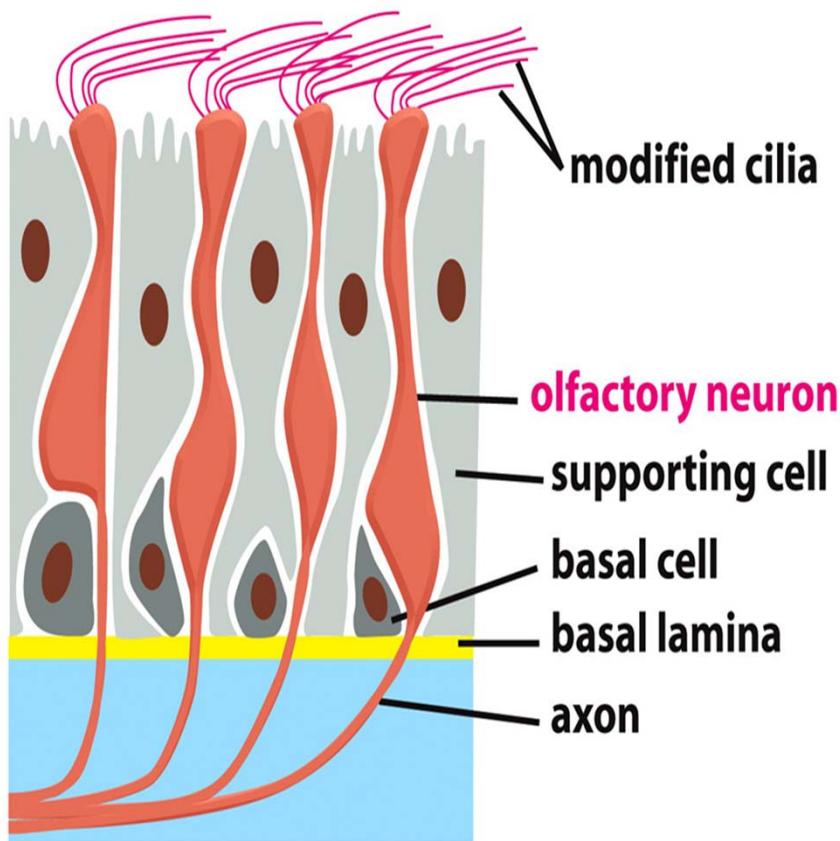
**Note:**  
Only the frequency of the  $\text{Ca}^{2+}$  spikes increases with increasing concentration of vasopressin  
**but the amplitude of the spikes is not affected**

## Mediators of GPCR signaling: cyclic-nucleotide-gated ion channels downstream of GPCRs operate in **smell** and **vision**

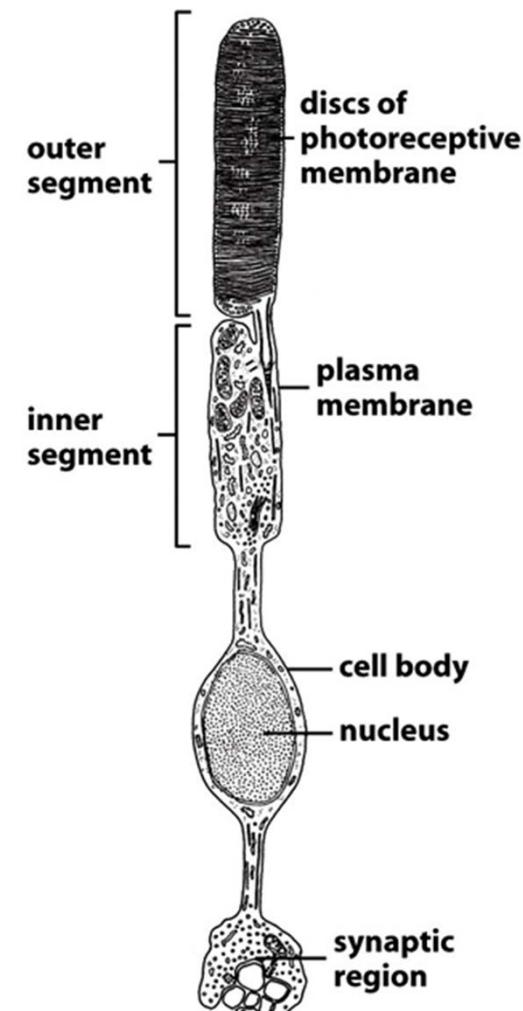


# Receptors for smell and vision

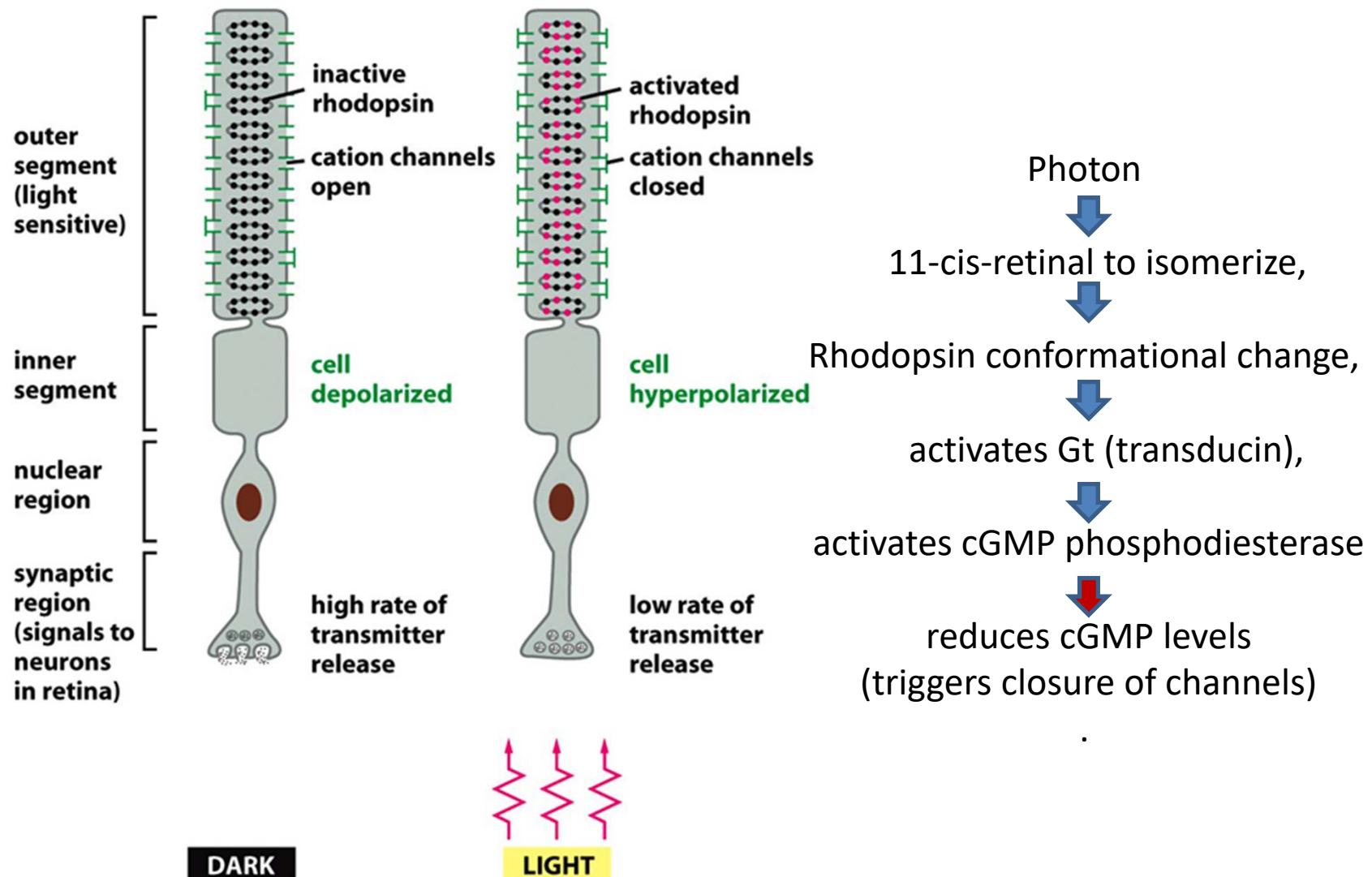
Over 10,000 smells can be differentiated by ~ 350 distinct receptors for human.



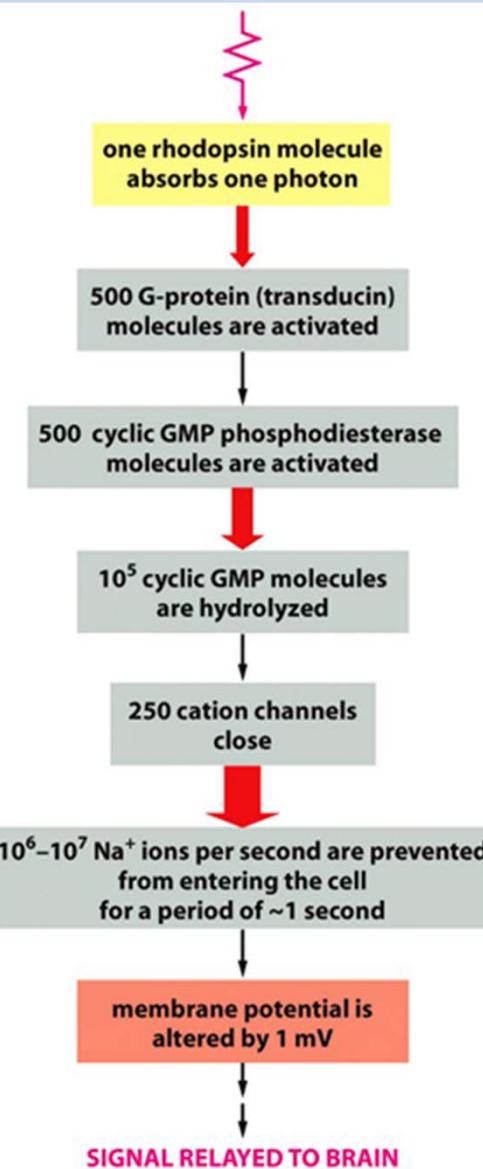
photoreceptor cells sense color



# Response of a rod photoreceptor cell to light



# Signal amplification in transduction



A catalytic cascade due to enzymatic activity

## 5. GPCR desensitization

**Six strategies to terminate the signaling (desensitization):**

1. **G-protein  $\alpha$ -subunit** is stimulated by its target protein or RGS to hydrolyse GTP into GDP ( $\rightarrow$ deactivation of G protein)
2. **IP<sub>3</sub>** is dephosphorylated by lipid phosphatase or phosphorylated by lipase kinase. ( $\rightarrow$ elimination of second messenger)
3. **cAMP/cGMP** is hydrolyzed by activated phosphodiesterases. ( $\rightarrow$ elimination of second messenger)
4. **Ca<sup>2+</sup>** is pumped out of cytosol. ( $\rightarrow$ elimination of second messenger)
5. **Phosphorylated** protein is dephosphorylated by phosphatases. ( $\rightarrow$ elimination of mediator)
6. **GPCRs** are phosphorylated by **GPCR kinases**, triggering **arrestin binding, uncoupling receptors** from G proteins and promotes their endocytosis. ( $\rightarrow$ elimination of receptors)

## II. Signaling by enzyme-coupled cell surface receptors

### Facts about enzyme-coupled cell surface receptors:

- All these receptors are **single transmembrane receptors**, which **are either an enzyme themselves or are directly associated with an enzyme**.
- Enzyme-coupled receptors are divided into 6 classes:
  1. Receptor tyrosine kinases (RTKs)
  2. Tryosine-kinase-associated receptors
  3. Receptor Ser/Thr kinases
  4. Histidine-kinase-associated receptors
  5. Receptor guanylyl cyclases---produce cGMP
  6. Receptor-like tyrosine phosphatases

# 1. Receptor tyrosine kinases (RTKs)

## - outline -

- Domain structure of receptor tyrosine kinases RTKs
- Activation of RTKs and signal relay
- Major pathways downstream of RTKs
  - Ras signaling pathway
  - Rho signaling pathway
  - PI<sub>3</sub>K/Akt signaling pathway

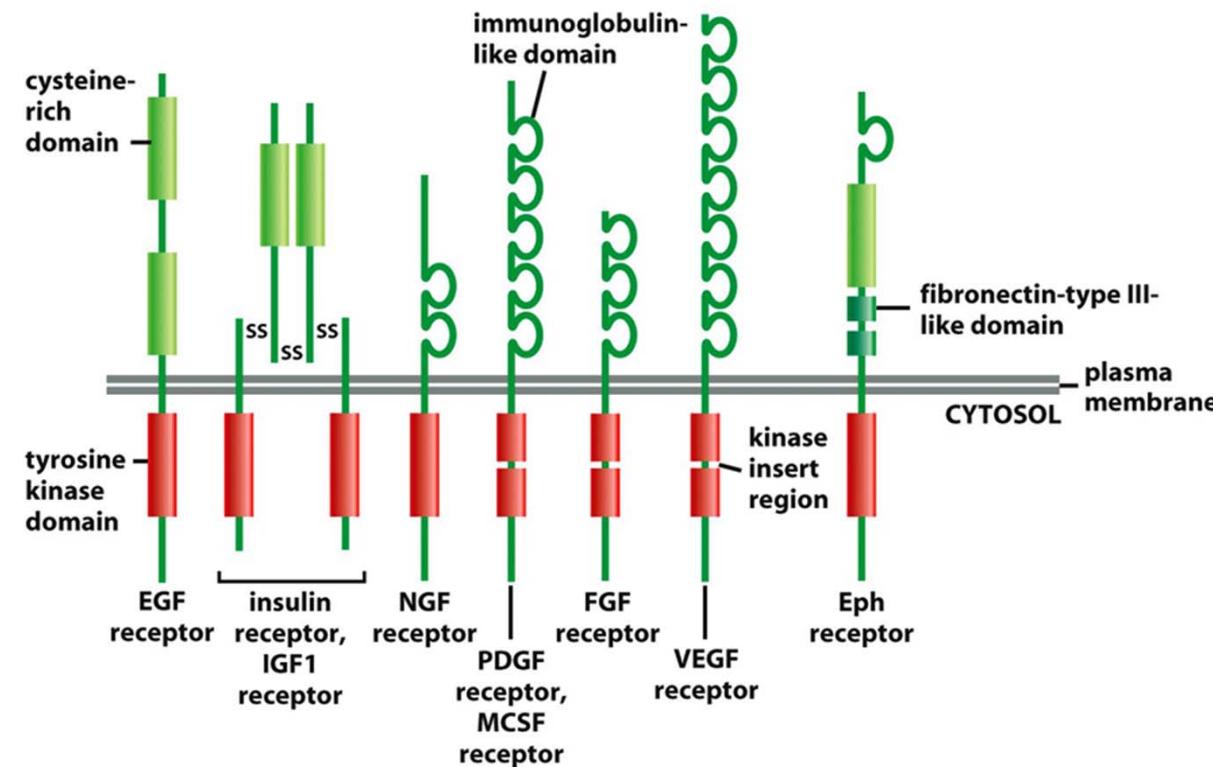
# Domain structure of some RTKs

RTKs are kinases themselves and possess three domains:

- **Extracellular region:** interact with ligand
- One single **transmembrane domain**
- **Intracellular region:** tyrosine kinase activity

Human genome encodes ~ 60 RTK genes

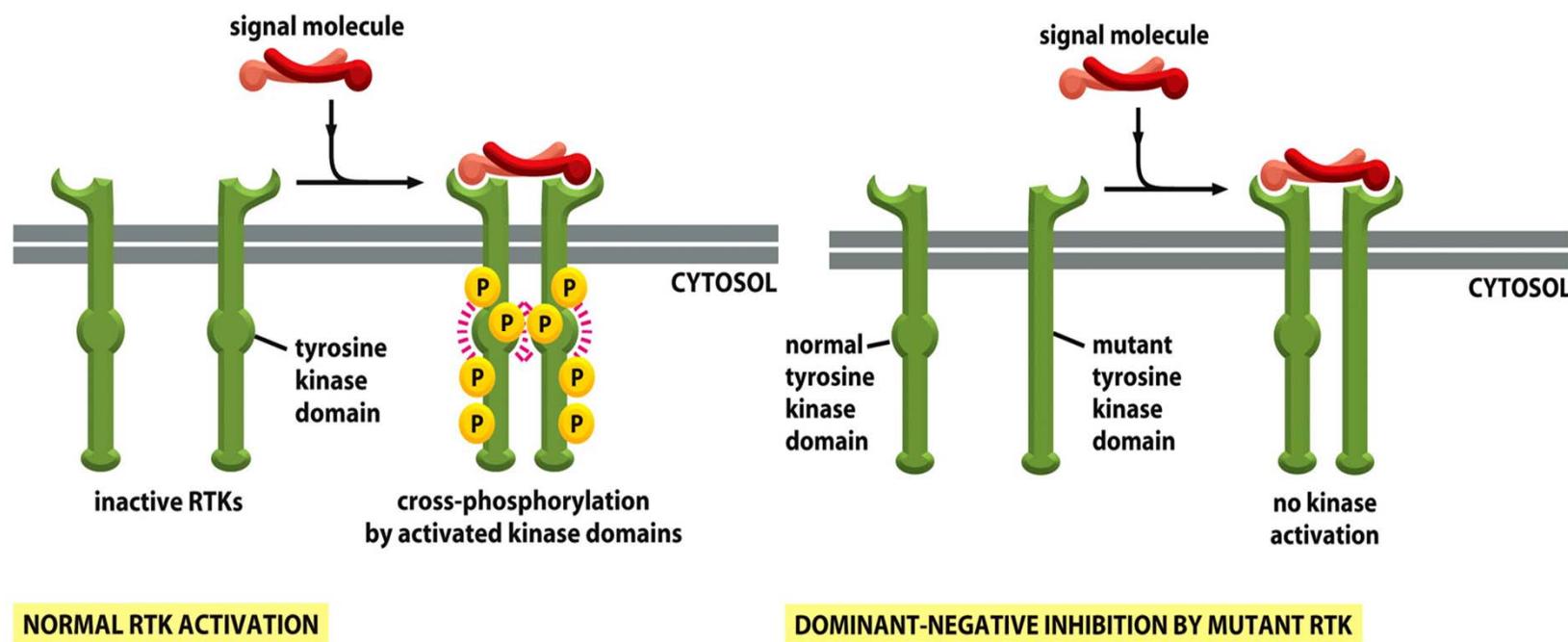
Upon ligand binding, RTK usually **dimerize** and trans-autophosphorylate themselves



# Mutant RTKs can act in a dominant negative manner

## Dominant negative mutant:

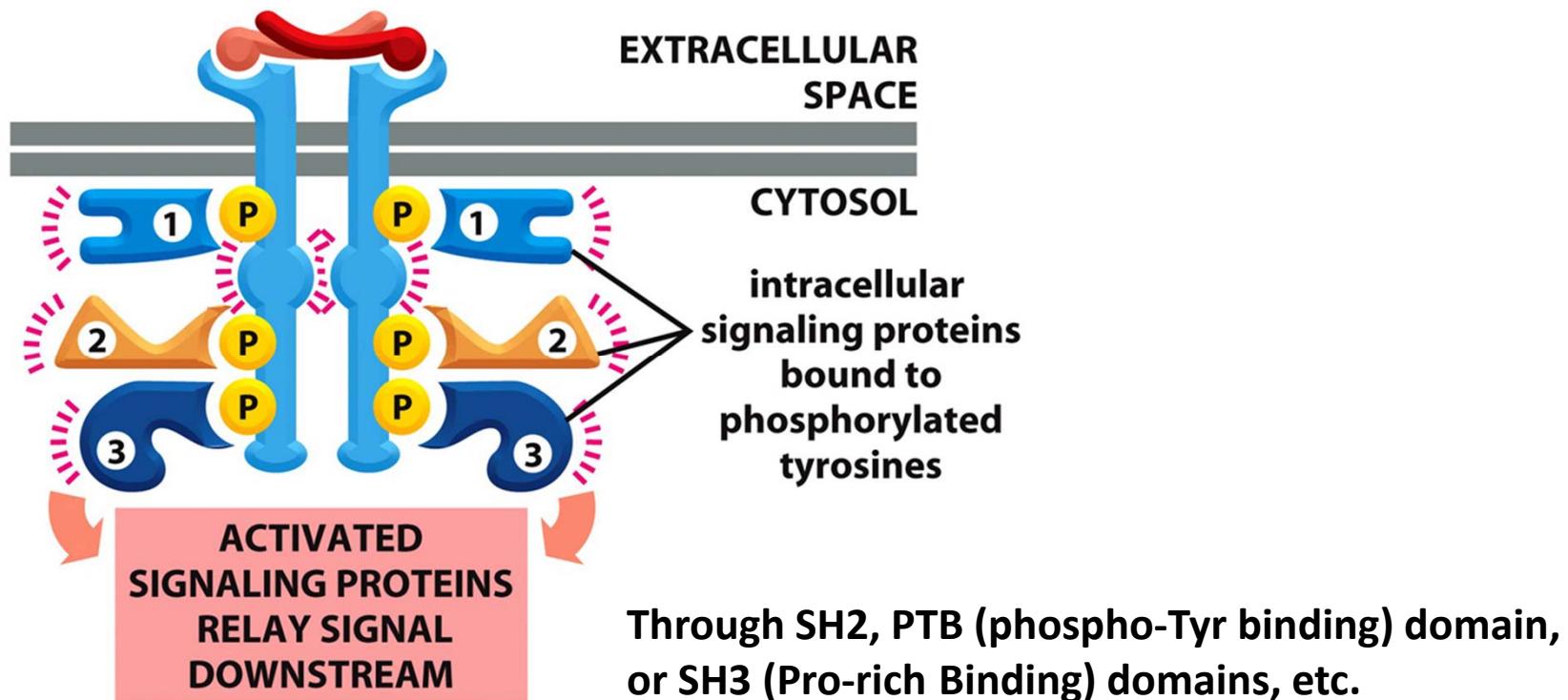
- a mutant protein that exhibits an inhibitory effect on the wild type protein



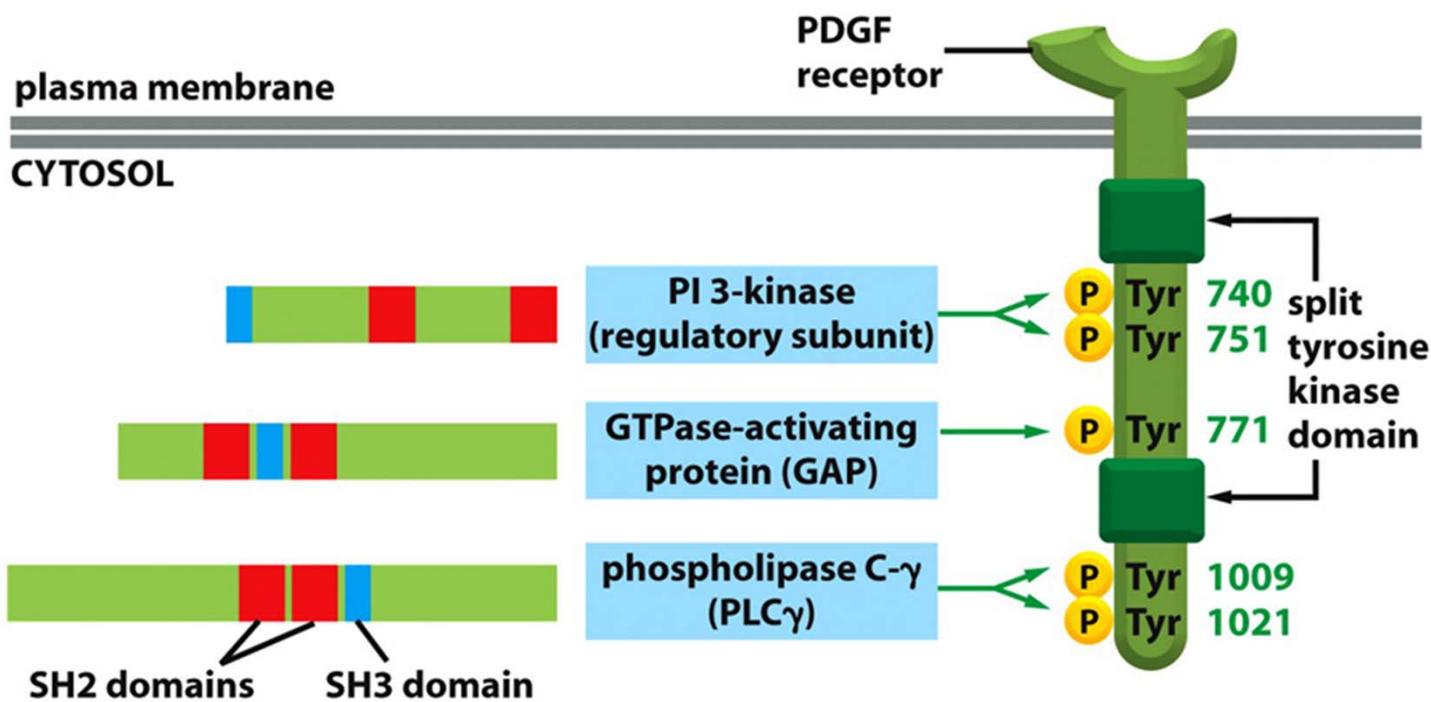
# Activation of RTKs and signal relay

Phosphorylation on RTK has dual roles:

- Activates RTK kinase activity
- Introduce phospho-Tyr that can recruit other protein factors to relay signals



# The PDGF (platelet-derived growth factor)-receptor



# Signaling pathways downstream of RTKs: -the Ras pathway-

- Ras: name **derived from** *Rat sarcoma virus*, found by RSV infection.
- Small monomeric GTPase, ~20KD, weak GTP hydrolysis activity.
- Highly mutated in human cancers, ~ 30%, in pancreatic cancer, mutation rate 95%.
- Pivotal roles in cell proliferation, survival, motility, etc.
- tethered on lipid membrane.

**Table 15–5 The Ras Superfamily of Monomeric GTPases**

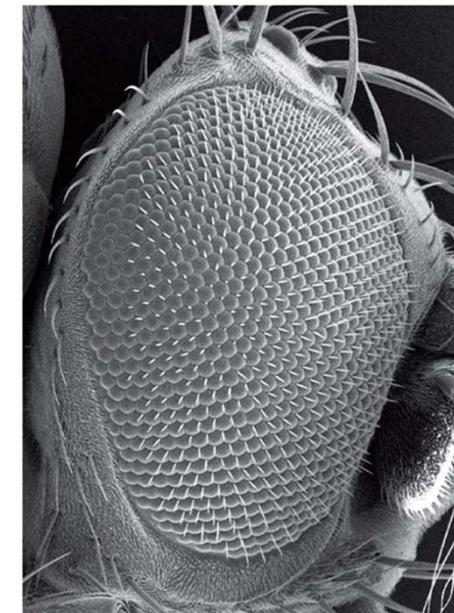
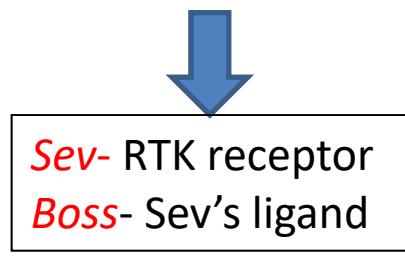
FAMILY	SOME FAMILY MEMBERS	SOME FUNCTIONS
Ras	H-Ras, K-Ras, N-Ras	relay signals from RTKs
	Rheb	activates mTOR to stimulate cell growth
	Rep1	activated by a cyclic-AMP-dependent GEF; influences cell adhesion by activating integrins
Rho*	Rho, Rac, Cdc42	relay signals from surface receptors to the cytoskeleton and elsewhere
ARF*	ARF1–ARF6	regulate assembly of protein coats on intracellular vesicles
Rab*	Rab1–60	regulate intracellular vesicle traffic
Ran*	Ran	regulates mitotic spindle assembly and nuclear transport of RNAs and proteins

\*The Rho family is discussed in Chapter 16, the ARF and Rab proteins in Chapter 13, and Ran in Chapters 12 and 17. The three-dimensional structure of Ras is shown in Figure 3–72.

# The Ras pathway was discovered by analysis of *Drosophila* eye development

## Observations:

- Lack of *sevenless (Sev)* causes failure to detect UV light by R7 photoreceptor
- Deficiency of *bride of sevenless (Boss)* causes this failure, too

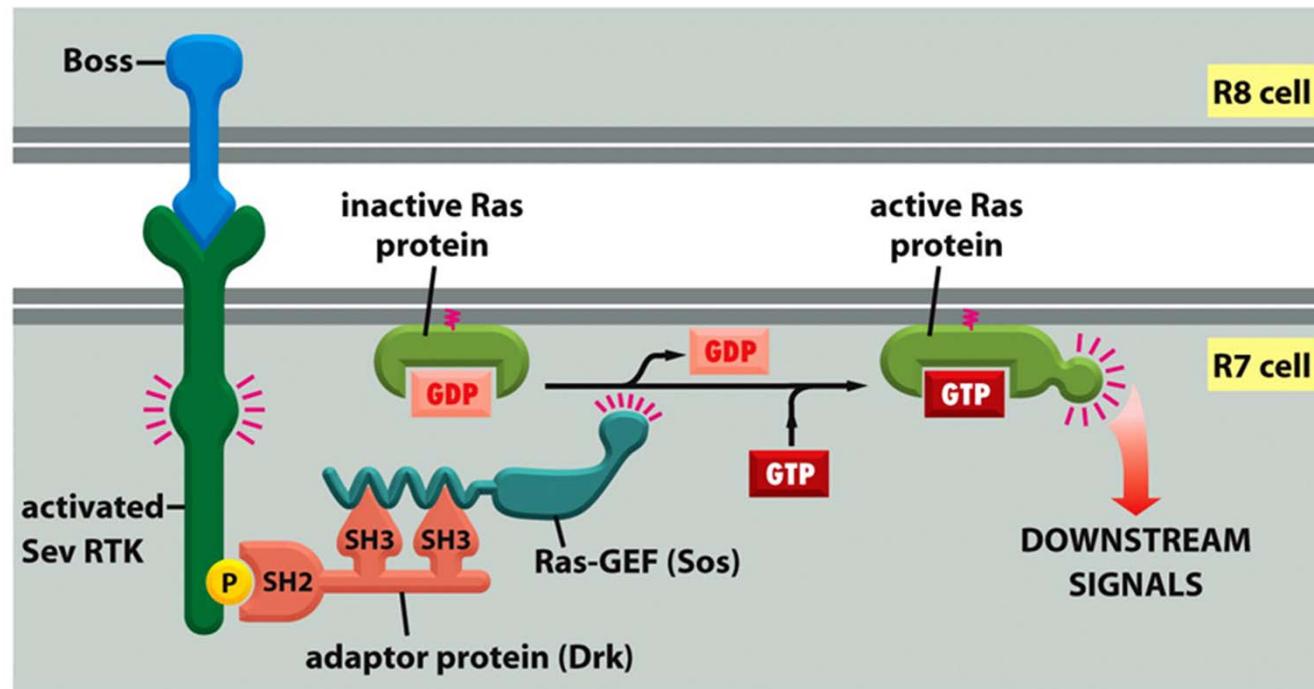


Genetic screens of *Sev/Boss* partial mutant strains revealed that mutation of Ras leads to loss of R7; while hyperactive Ras rescues deficiency of both *Sev/Boss*

Further genetic screen identified *Son of sevenless(Sos)* AND *Drk*

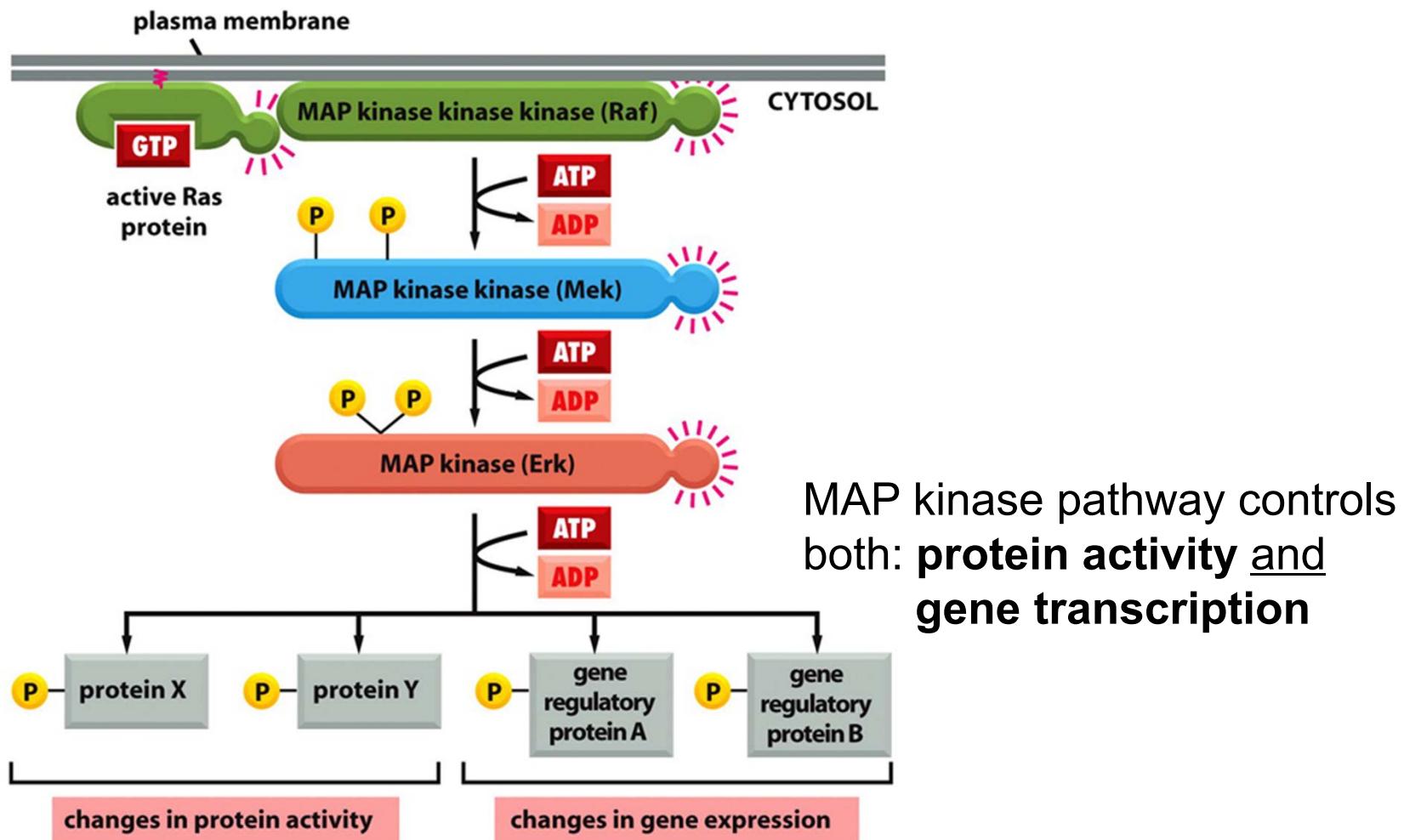
## Activation of Ras downstream of Sev RTK requires an adaptor protein Grb2 and the GEF Sos

- Activation of Ras is mediated by the Ras GEF Sos (Son of sevenless) (Ras-GDP → Ras-GTP)
- Sos the adaptor protein Grb2 (growth factor receptor binding protein 2) /Drk and Sos (Son of sevenless)

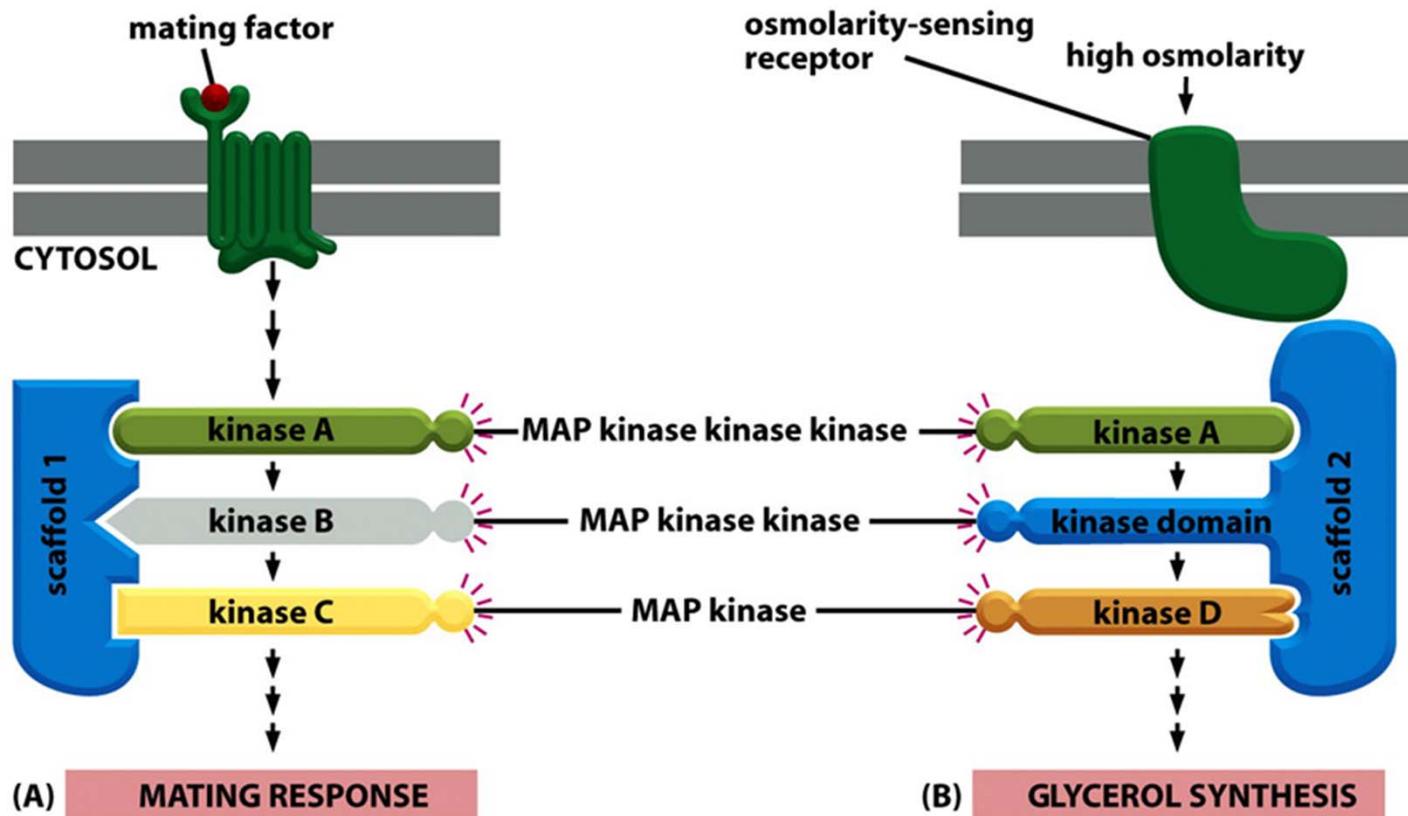


In human, Grb2 is homolog for Drk: adaptor protein

# Ras activates a MAP (mitogen-activated protein) kinase signaling module (Ras – Raf – Mek – Erk)



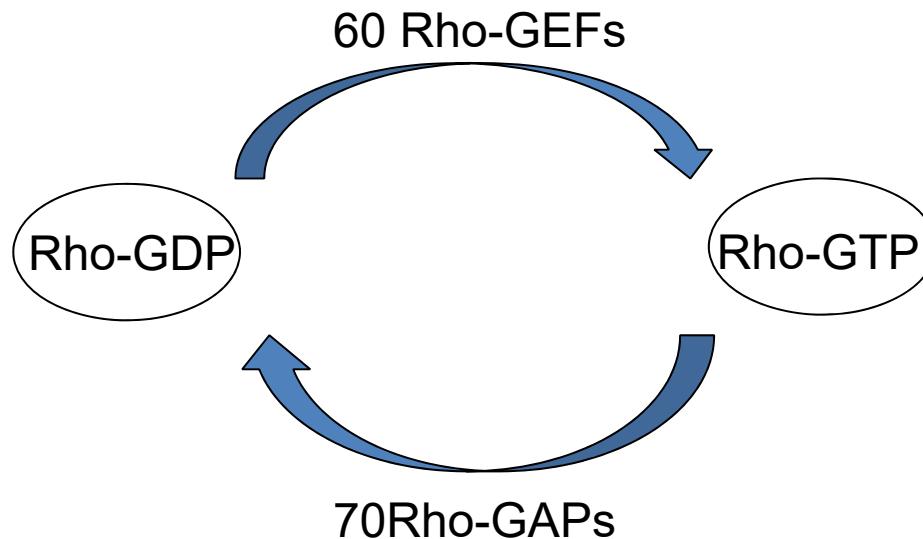
## Scaffold proteins provide precision and prevent cross-talk between parallel/neighboring MAP kinase modules



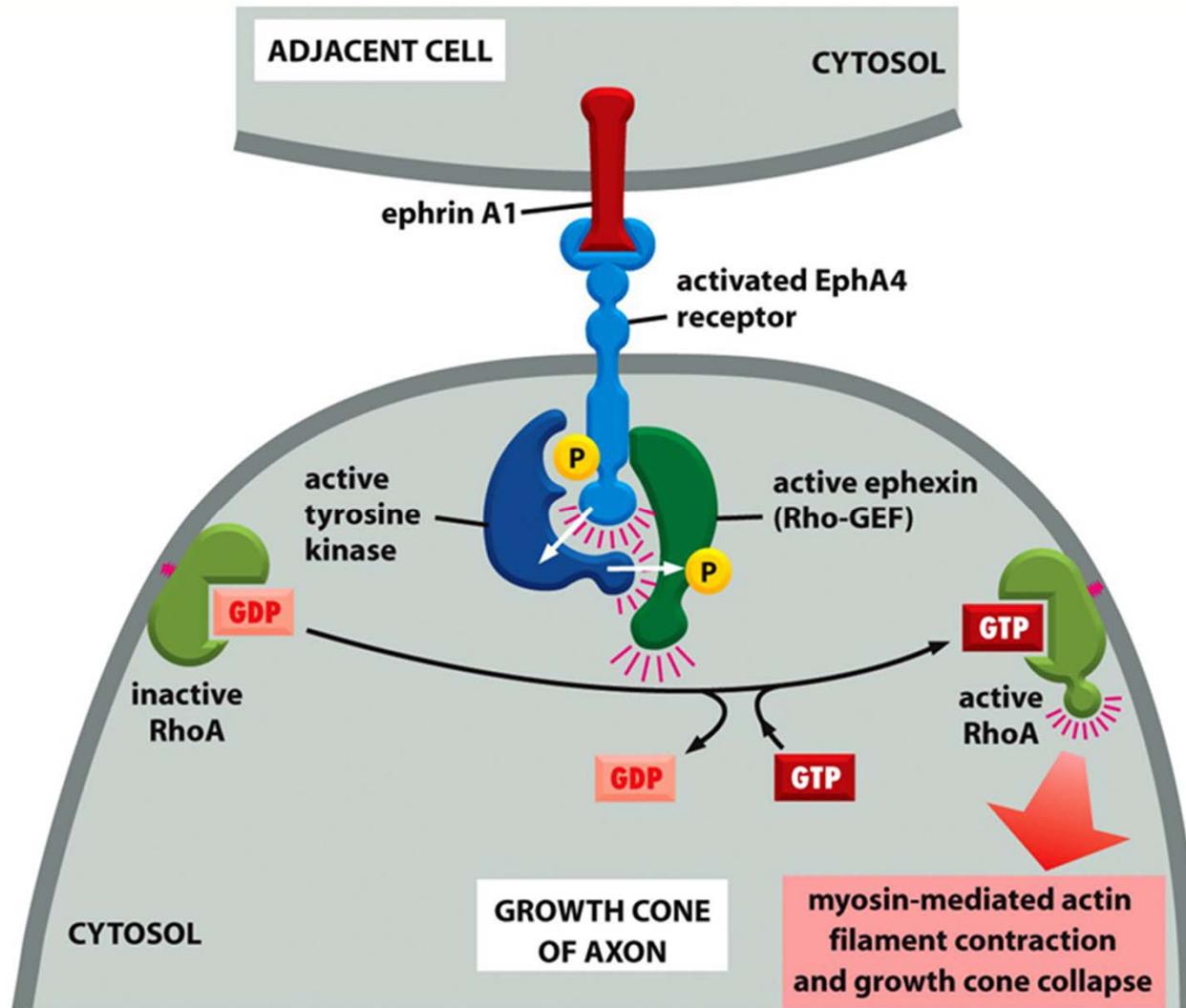
# Signaling pathways downstream of RTKs: -the Rho-GTPase pathway-

## Facts and function:

- Couples cell surface receptors to the cytoskeleton
- Controls cell shape, polarity, migration, and adhesion.
- When inactive Rho (Rho-GDP), usually associates with a guanine nucleotide dissociation inhibitor (GDI)
- Three major Rho family members: **Rho, Rac, Cdc42**



For example: ephrin induces growth cone collapse



# Signaling pathways downstream of RTKs: -the PI3K pathway-

## Functions of the PI3K pathway:

- promotes signals for cell growth and survival
- produces lipid binding/docking sites for proteins at the PM

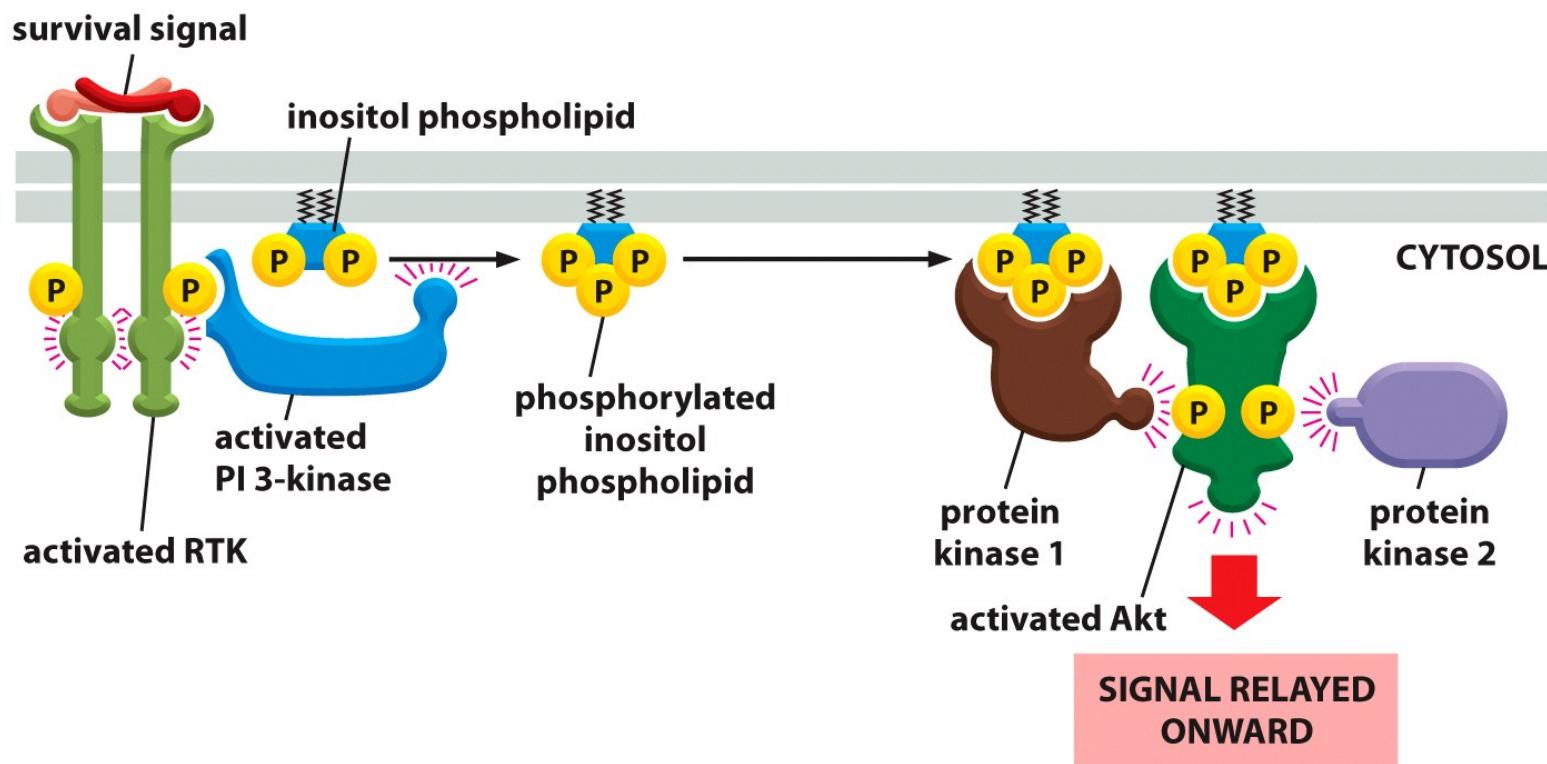
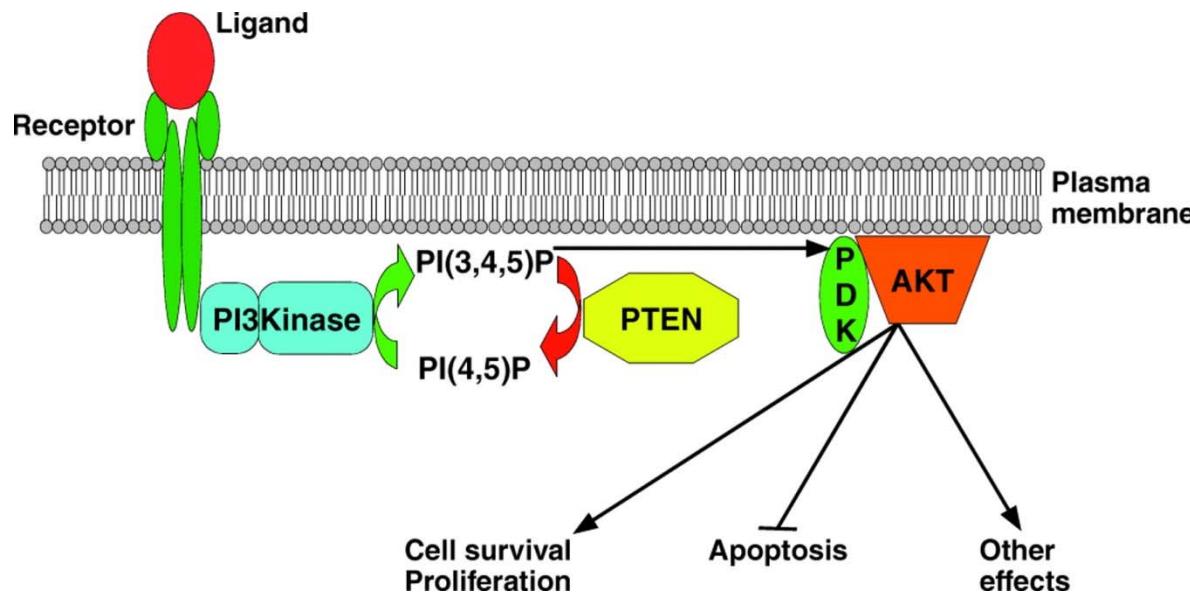


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# The PI3K and the phosphatase and tensin homolog PTEN control PIP3 levels at the PM



PI3K hyperactivation and PTEN loss of function occur frequently in human cancers.

## 2. Tyrosine-kinase-associated receptors

### 2.1 overview

### 2.2 major types of non-receptor tyrosine kinases

2.2.1 JAK-STAT signaling pathway

2.2.2 Src family proteins

2.2.3 Focal adhesion kinase

## 2. Tyrosine-kinase-associated receptors

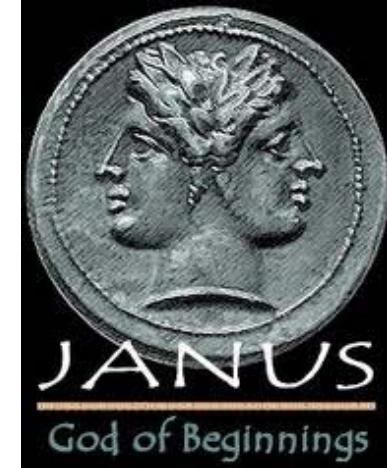
- Tyrosine-kinase-associated receptors do not possess a kinase domain.
- Tyrosine-kinase-associated receptors recruit cytosolic tyrosine kinases to relay the signal
- Form dimers upon ligand binding
- This receptor family includes receptors for:
  - Antigens
  - Integrins
  - Interleukins
  - Cytokines
  - growth hormones

# Major types of cytosolic non-receptor tyrosine kinases

- **Janus kinases (JAKs):**
  - named after the two-faced Roman God Janus
  - cytosolic tyrosine kinases
  - they **phosphorylate** and **activate** gene regulatory proteins, called STATs (signal transducers and activators of transcription)
  - mediates cytokine signaling
- **Scr (sarcoma virus) tyrosine kinase protein family:**
  - cytosolic tyrosine kinases
  - proto-oncogenes
  - controls cytoskeleton assembly, growth and proliferation.
- **Focal adhesion kinase:**
  - mediates integrin signaling to the cytoskeleton during cell adhesion.

# JAK-STAT signaling pathway

- JAK-Janus kinase  
(cytosolic tyrosine kinase)
- STAT-Signal transducers and activators of transcription (transcription factors)



**Table 15–6 Some Extracellular Signal Proteins That Act Through Cytokine Receptors and the JAK–STAT Signaling Pathway**

SIGNAL PROTEIN	RECEPTOR-ASSOCIATED JAKs	STATS ACTIVATED	SOME RESPONSES
γ-interferon	JAK1 and JAK2	STAT1	activates macrophages
α-interferon	Tyk2 and JAK2	STAT1 and STAT2	increases cell resistance to viral infection
Erythropoietin	JAK2	STAT5	stimulates production of erythrocytes
Prolactin	JAK1 and JAK2	STAT5	stimulates milk production
Growth hormone	JAK2	STAT1 and STAT5	stimulates growth by inducing IGF1 production
GMCSF	JAK2	STAT5	stimulates production of granulocytes and macrophages

# How does prolactin promote milk production?

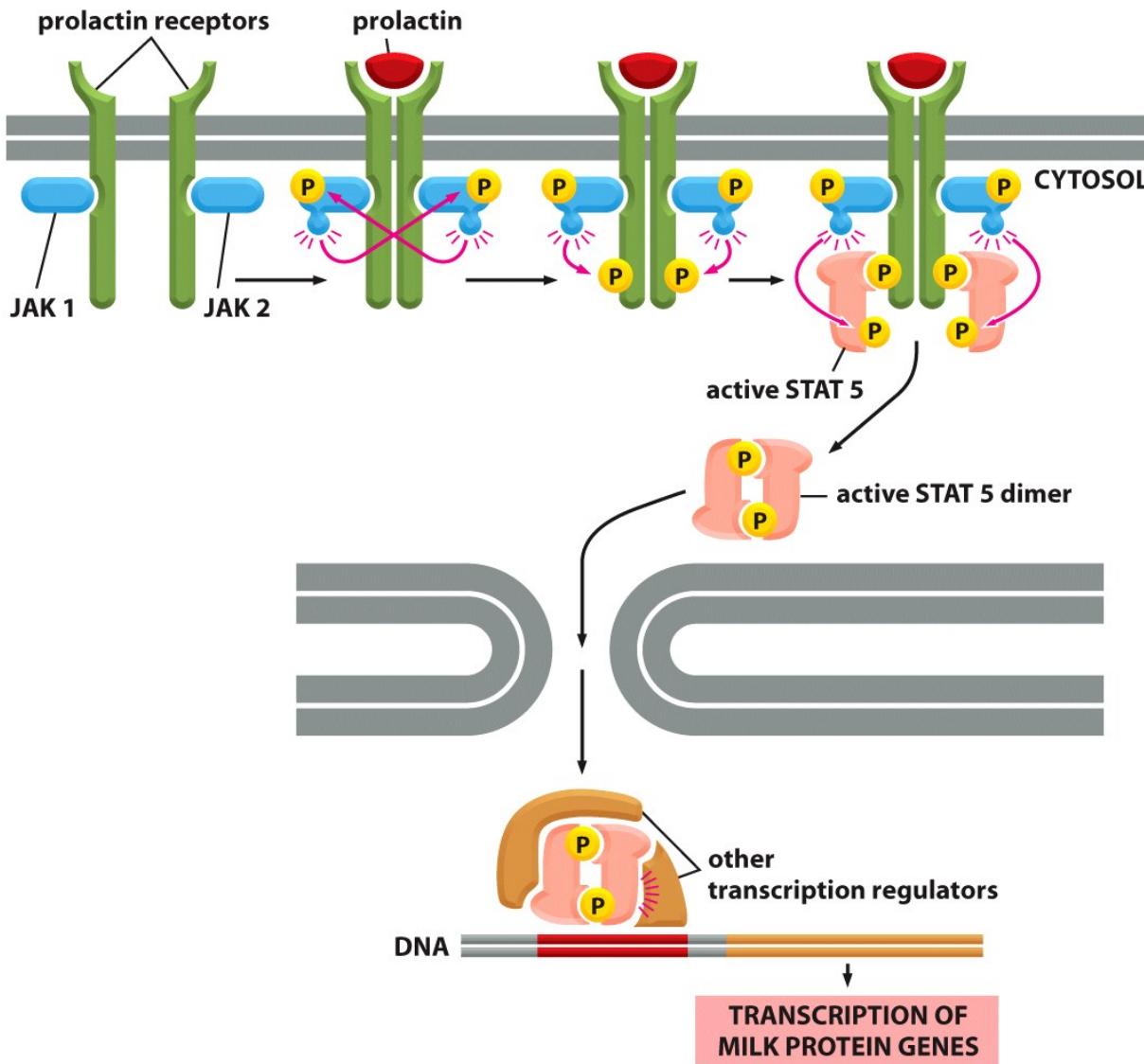
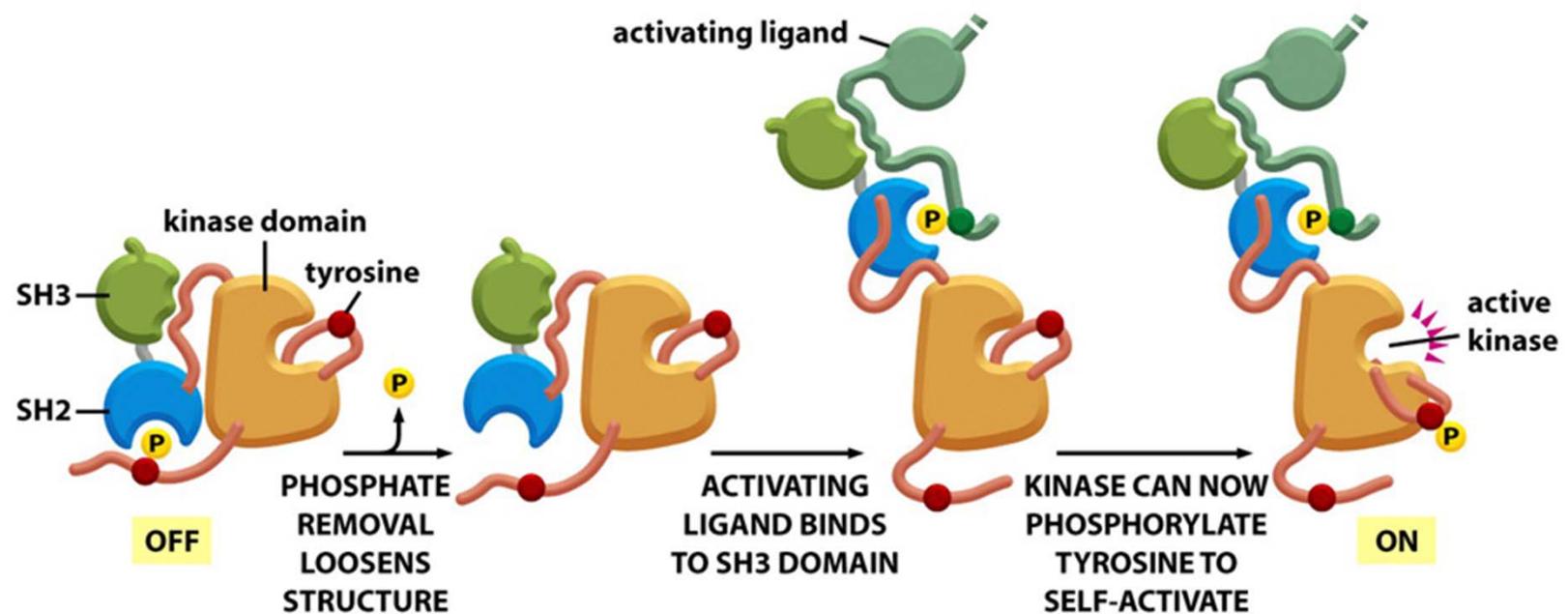


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## Src tyrosine kinase protein family

- The largest family of cytoplasmic tyrosine kinases
- Family members: Src, Yes, Fgr, Fyn, Lck, Lyn, Hck, Blk, etc
- All contain conserved SH2, SH3 and kinase domains.
- All within the cytoplasmic region

# Src kinase has “on” and “off” states, as have many kinases



Three distinct domains: SH2, SH3, kinase domain

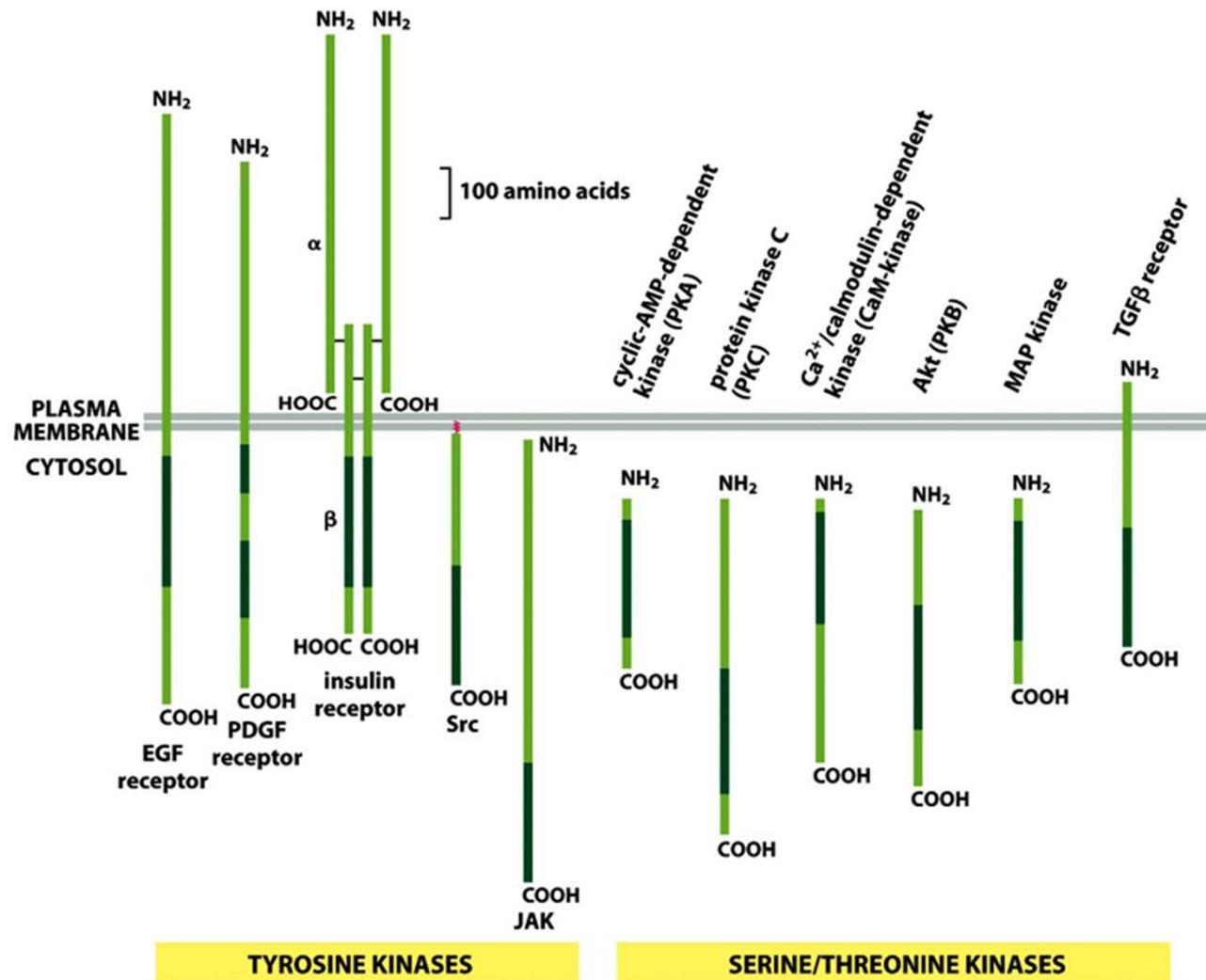
## How to deactivate phosphorylated tyrosines?

- Phosphorylated tyrosines are dephosphorylated / deactivated by tyrosine phosphatases
- ~100 protein tyrosine phosphatases in human genome, each has exquisite specificity for a subset of proteins

### 3. Serine/Threonine kinase receptor

- Single transmembrane receptor and Ser/Thr kinase.
- Two classes: Type I and Type II which form homodimers (upon activation by ligand)
- Type II dimer phosphorylates Type I dimer to form active tetramer.
- They are receptors for :
  - **transforming growth factor-  $\beta$  (TGF $\beta$ )** protein superfamily (derived from Tumor growth factor):
    - Secreted and dimeric proteins,
    - ~30-40 members for human
    - two categories:
      - TGF $\beta$ /ativin family
      - bone morphogenetic protein (BMP) family
  - Control diverse activity in differentiation, proliferation, cell death, development, etc.

# A summary and comparison for Tyrosine kinase and Ser/Thr kinase



## 4. Histidine-kinase-associated receptors

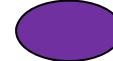
Mediates Bacterial chemotaxis response

Sugars  
Amino acids  
Peptides,

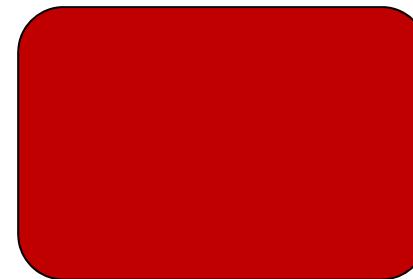


Attractants

bacteria



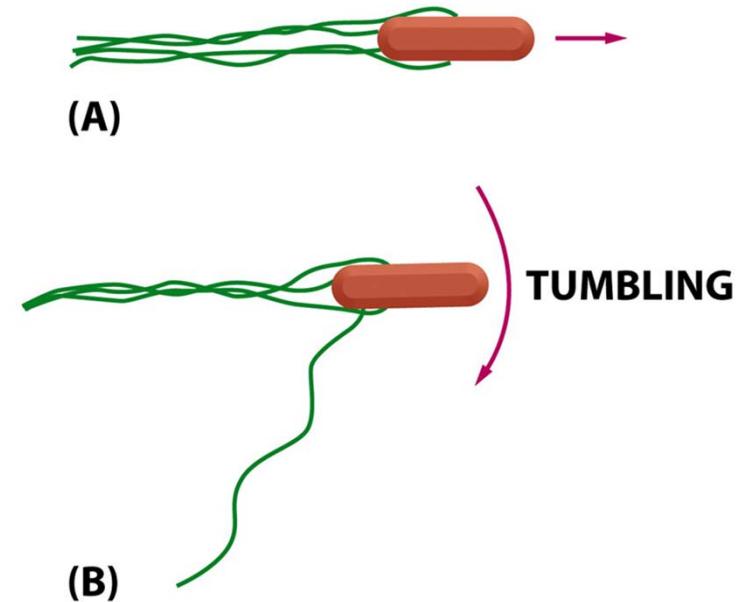
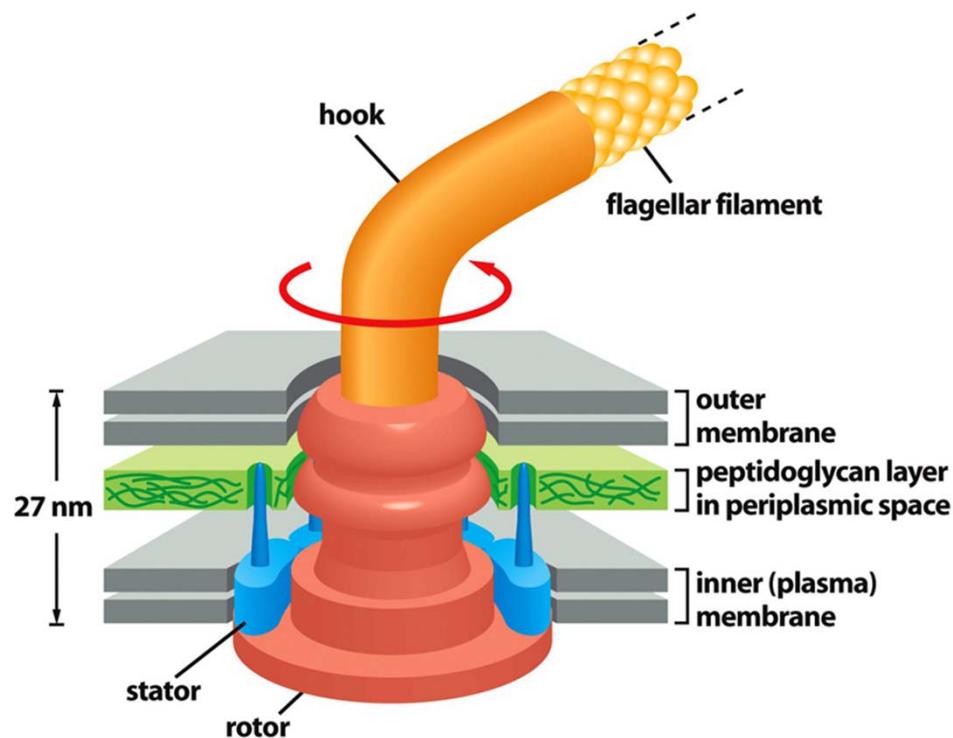
Noxious chemicals



repellents

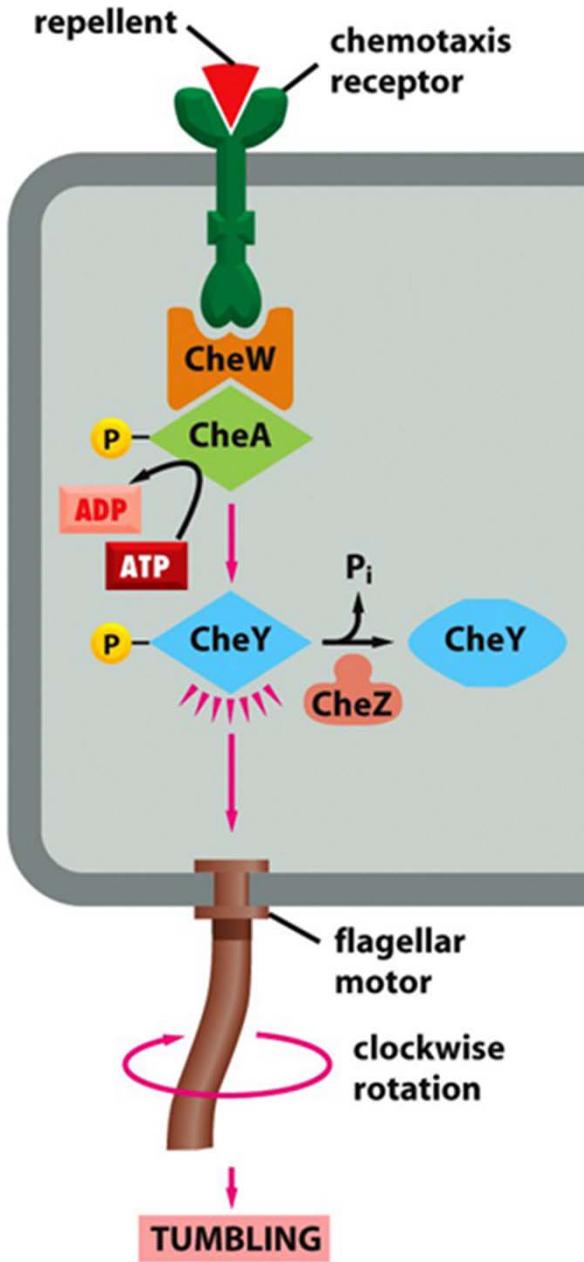
# Bacteria movement through flagella

- Proton pumps couple proton gradient to motor rotation
- Normally all motor rotate counterclockwise
- Every sec or two, some motor rotate clockwise resulting in tumbling



# Mechanism for chemotaxis by chemotaxis receptors--- histidine-kinase-associated receptors

The histidine kinase CheA can phosphorylate itself on a histidine  
CheA then transfers phosphate group to Asp on CheY



# Similar signaling pathways exist in plants to regulate plant growth

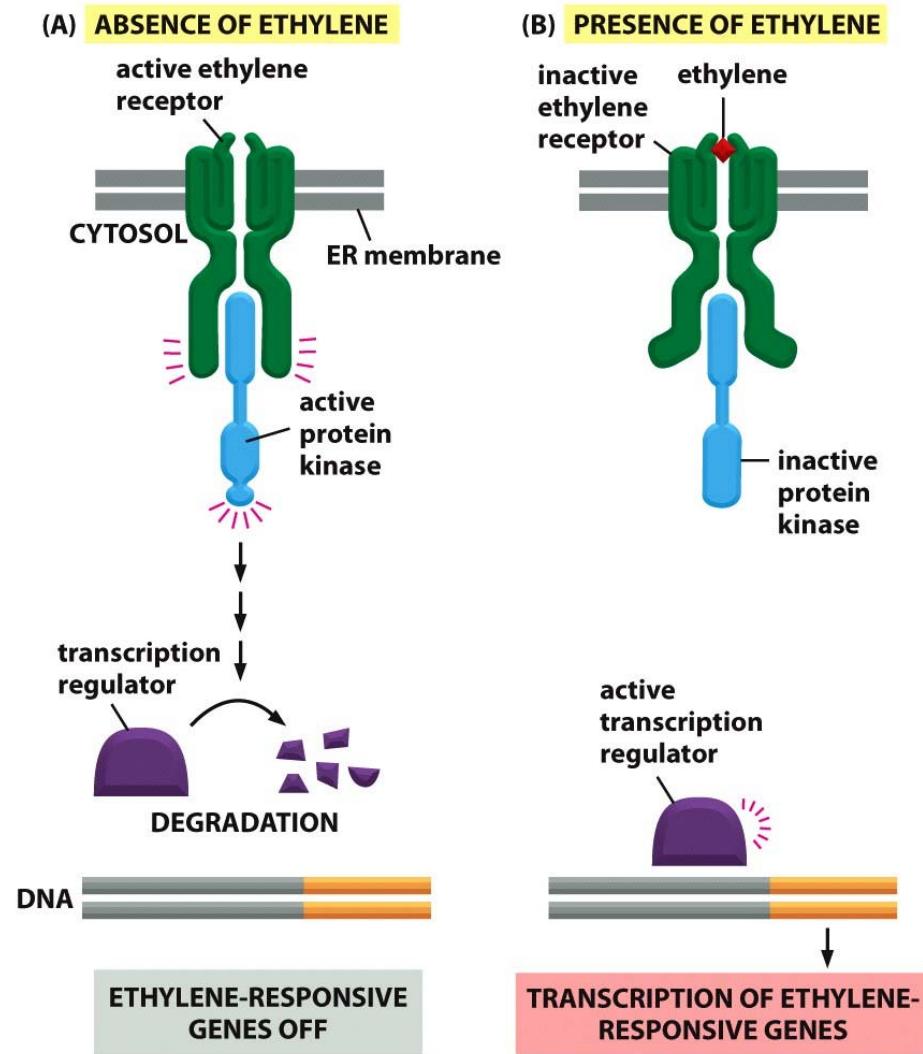


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