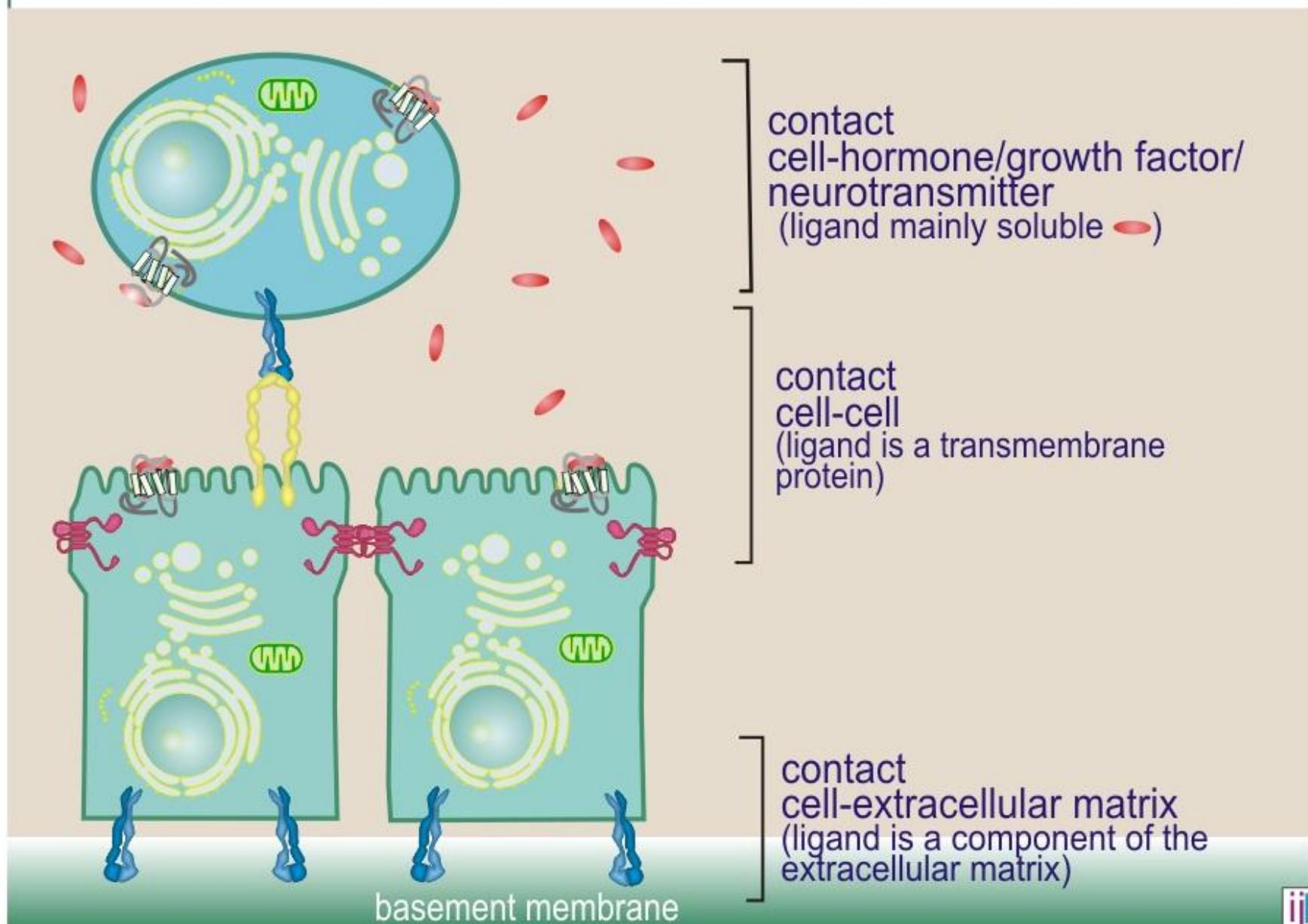
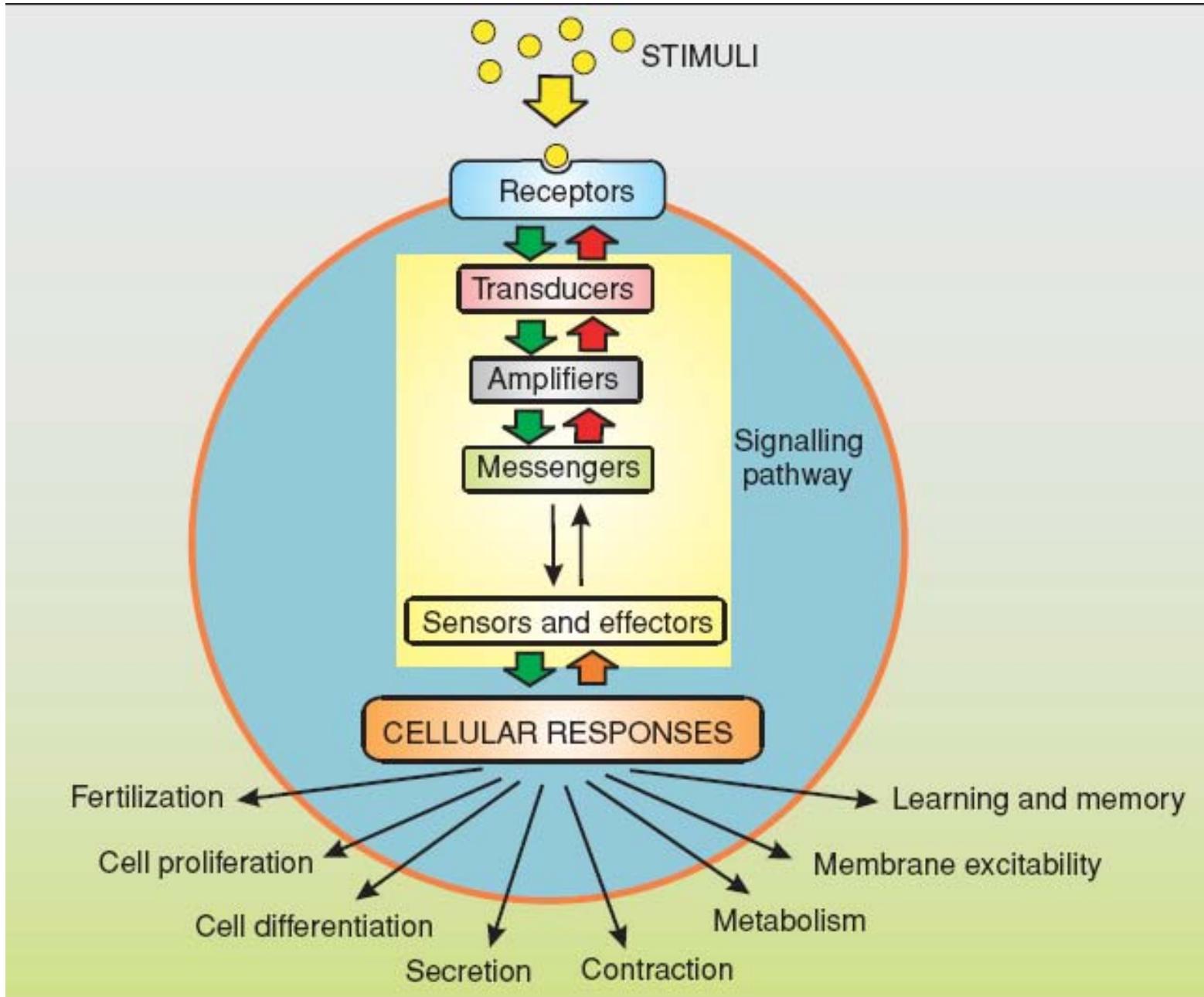


**“COMUNICACION  
CELULAR:  
Sistemas de Transducción  
de Señales”**

## modes of communication between the cell and its environment (organism)

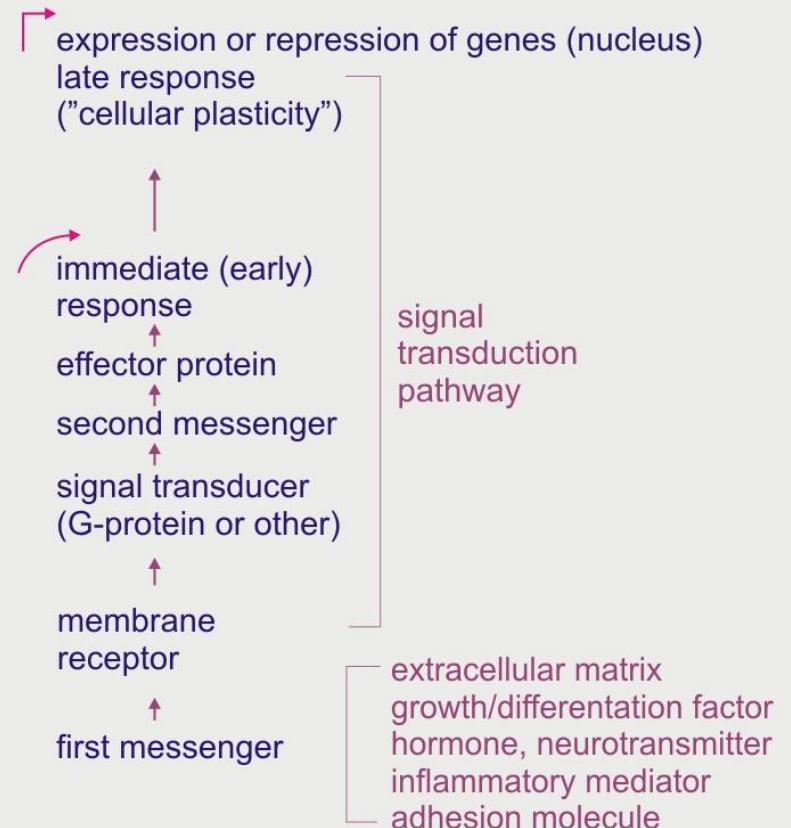
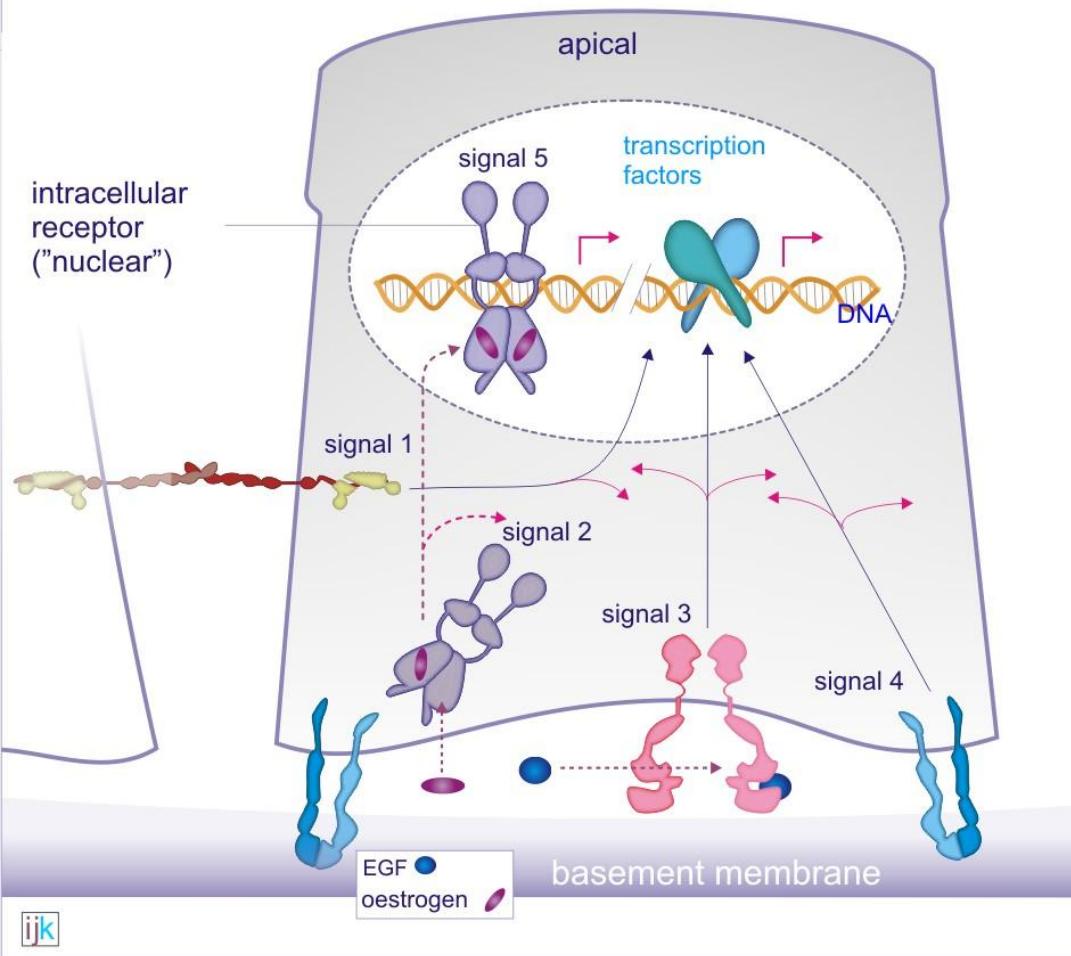


# SIGNAL TRANSDUCTION



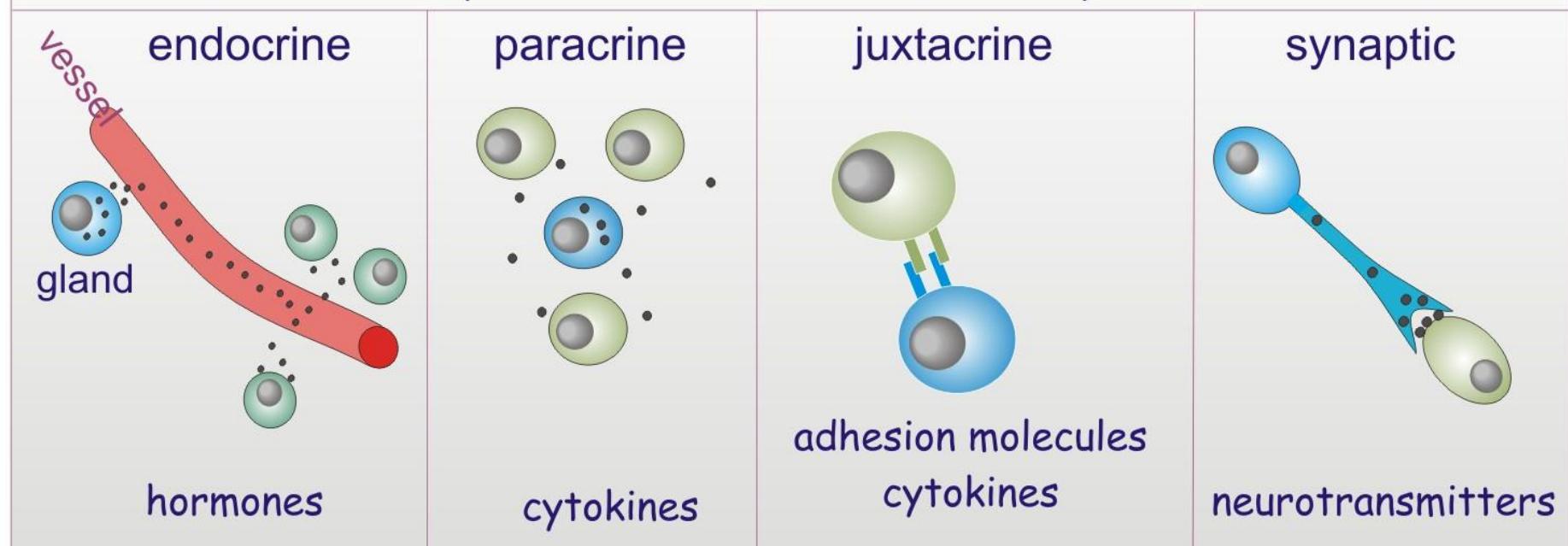
## signal transduction

comprises all processes whereby engaged receptors (both membrane and intracellular) transmit signals into the cell. Collectively, these provide a symbolic representation of the environment and allow cells to respond appropriately to changes (early and late responses)



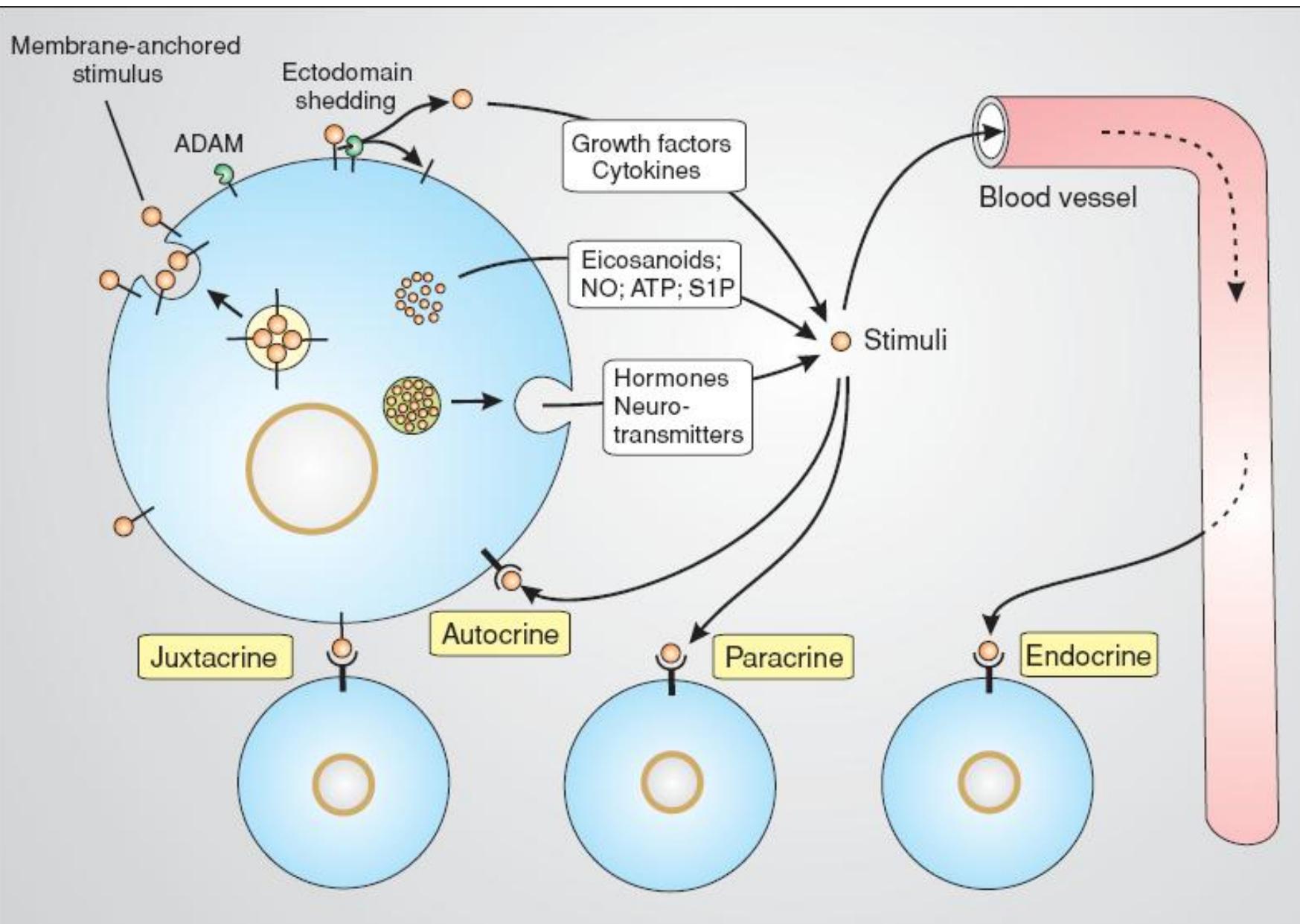
# TIPOS DE COMUNICACION

four modes of communication by first messengers  
(secreted or membrane bound)



- growth/differentiation factors
- inflammatory mediators
- interleukins

# TIPOS DE COMUNICACION



# Comunicación Celular y Respuesta Celular

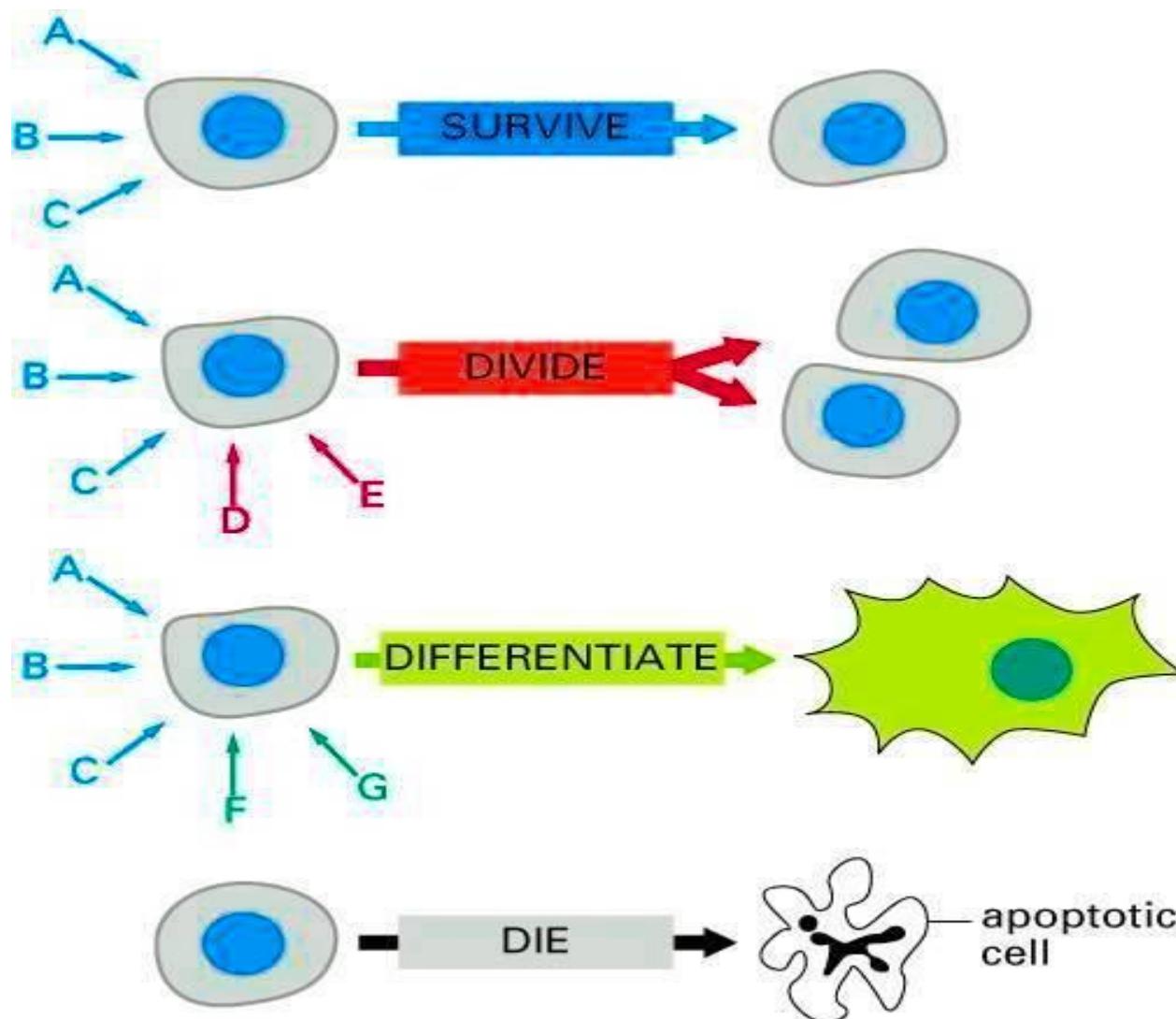


Figure 15–8. Molecular Biology of the Cell, 4th Edition.

# Sistemas de Comunicación Celular en la Escala Filogenética

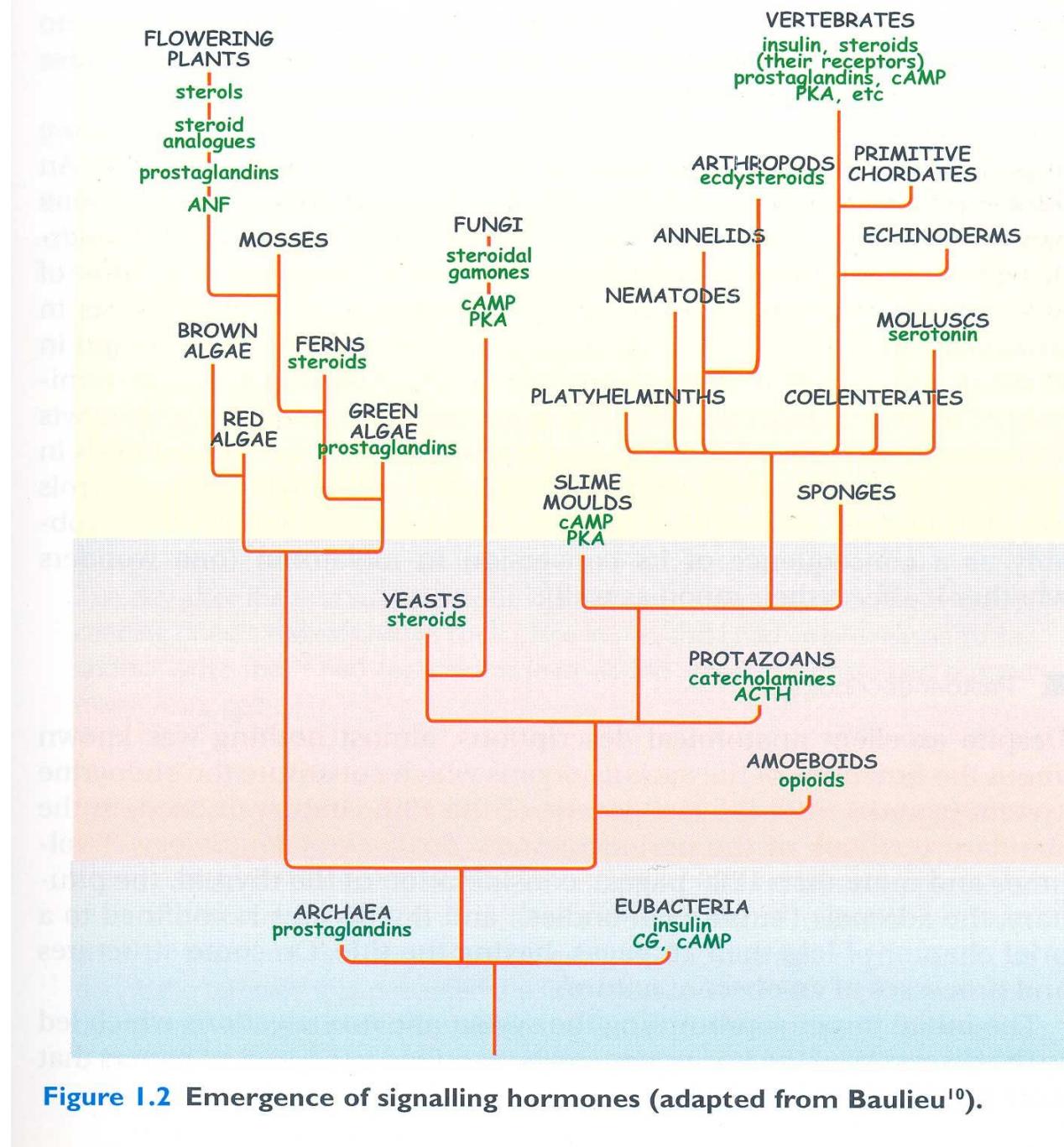


Figure 1.2 Emergence of signalling hormones (adapted from Baulieu<sup>10</sup>).

# Características de los Componentes de un Sistema de Transducción de Señales

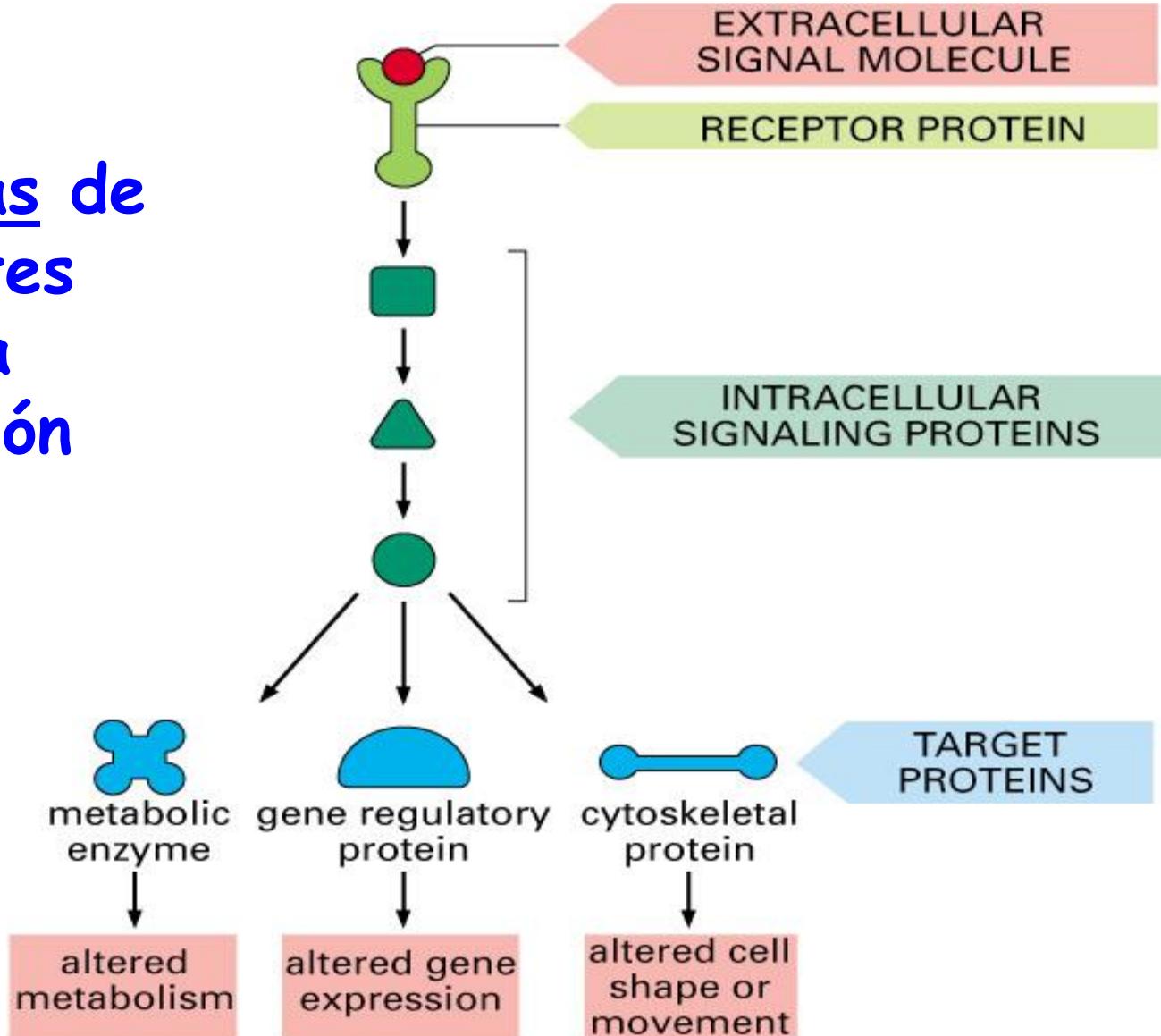


Figure 15–1. Molecular Biology of the Cell, 4th Edition.

• LIGANDO es una molécula extracelular que une a un receptor en la membrana plásmatica o en el interior de la célula, y en consecuencia causa un cambio en el citoplasma o núcleo.

- Lípidos
- Polipéptidos (proteínas)
- Nucleótidos
- Aminas
- Aminoácidos
- Luz, olores, sabores, etc.

**table 13–1**

## **Some Signals to Which Cells Respond**

---

Antigens

Cell surface glycoproteins/oligosaccharides

Developmental signals

Extracellular matrix components

Growth factors

Hormones

Light

Mechanical touch

Neurotransmitters

Odorants

Pheromones

Tastants

# MENSAJEROS QUÍMICOS

- **FACTOR DE CRECIMIENTO** es un ligando, usualmente un péptido pequeño, que activa a un receptor en la membrana plasmática para estimular el crecimiento de la célula blanco.
- **CITOCINA** es un polipéptido pequeño que afecta el crecimiento de ciertos tipos de células (sistema inmune).
- **HORMONA** sustancia secretada al torrente sanguíneo, por las células de una glándula, que afecta la función de sus células blanco.
- **NEUROTRANSMISOR** mensajero químico del sistema nervioso

# Naturaleza Química de los Ligandos

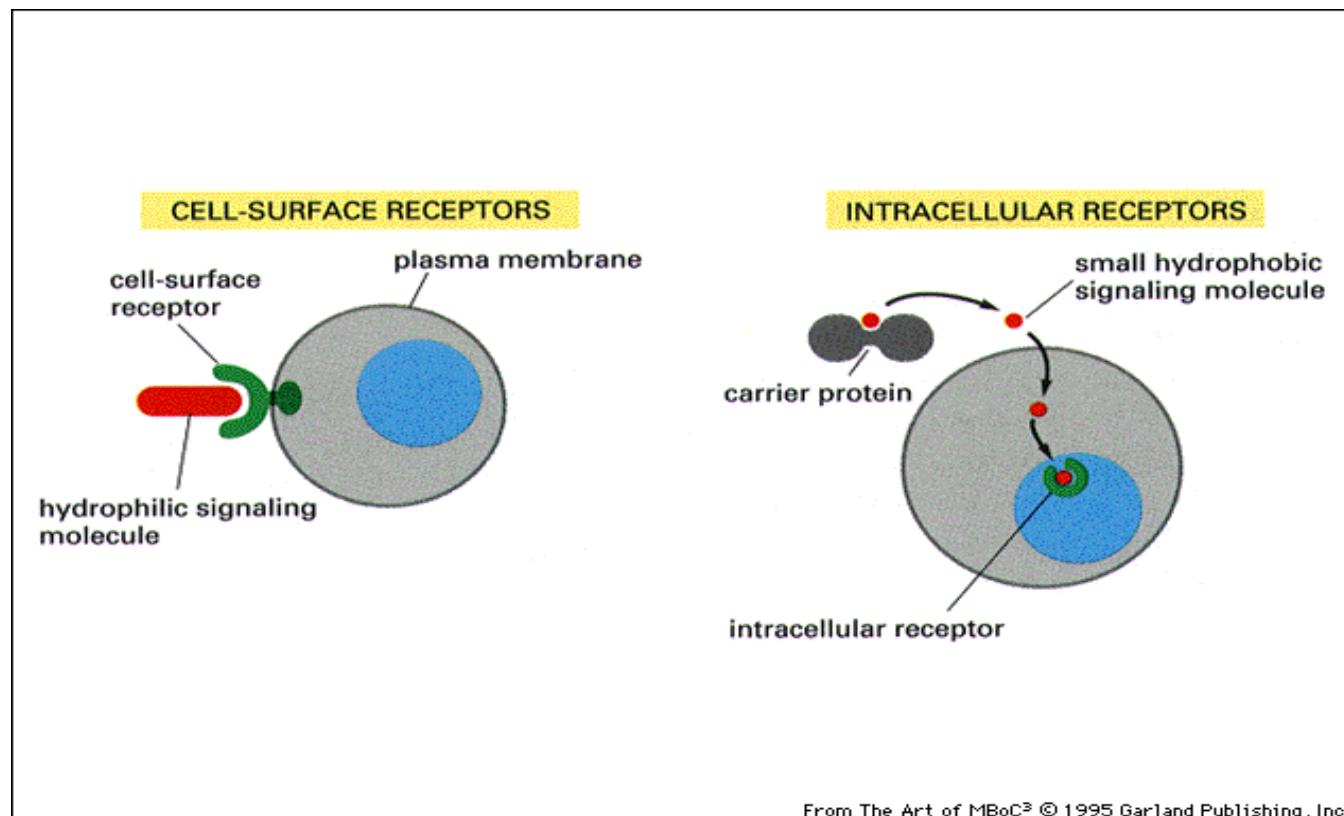
table 23–6

## Classes of Hormones

Type	Example	Parent /origin	Synthetic path	Mode of action
Peptide	Leu-enkephalin	Tyr–Gly–Gly–Phe–Leu	Proteolytic processing of proenzyme	Plasma membrane receptors; second messengers
Catecholamine	Epinephrine	Tyrosine		
Eicosanoid	PGE <sub>1</sub>	20:4 Fatty acid		
Steroid	Testosterone	Cholesterol		
Retinoid	Retinoic acid	Vitamin A		Nuclear receptors; transcriptional regulation
Thyroid	Triiodothyronine (T <sub>3</sub> )	Tyr in thyroglobulin		
Vitamin D	1,25-dihydroxycholecalciferol	Cholesterol or vitamin D		
Nitric oxide	Nitric oxide	NO•	Arginine + O <sub>2</sub>	Cytosolic receptor (guanylate cyclase) and second messenger (cGMP)

• **RECEPTOR** es una proteína transmembranal, localizada en la membrana plasmática, que une a un ligando a través de su dominio extracelular, y como resultado hay un cambio de actividad en el dominio citoplásmico (excepto los receptores nucleares).

- Selectividad
- Afinidad
- Actividad



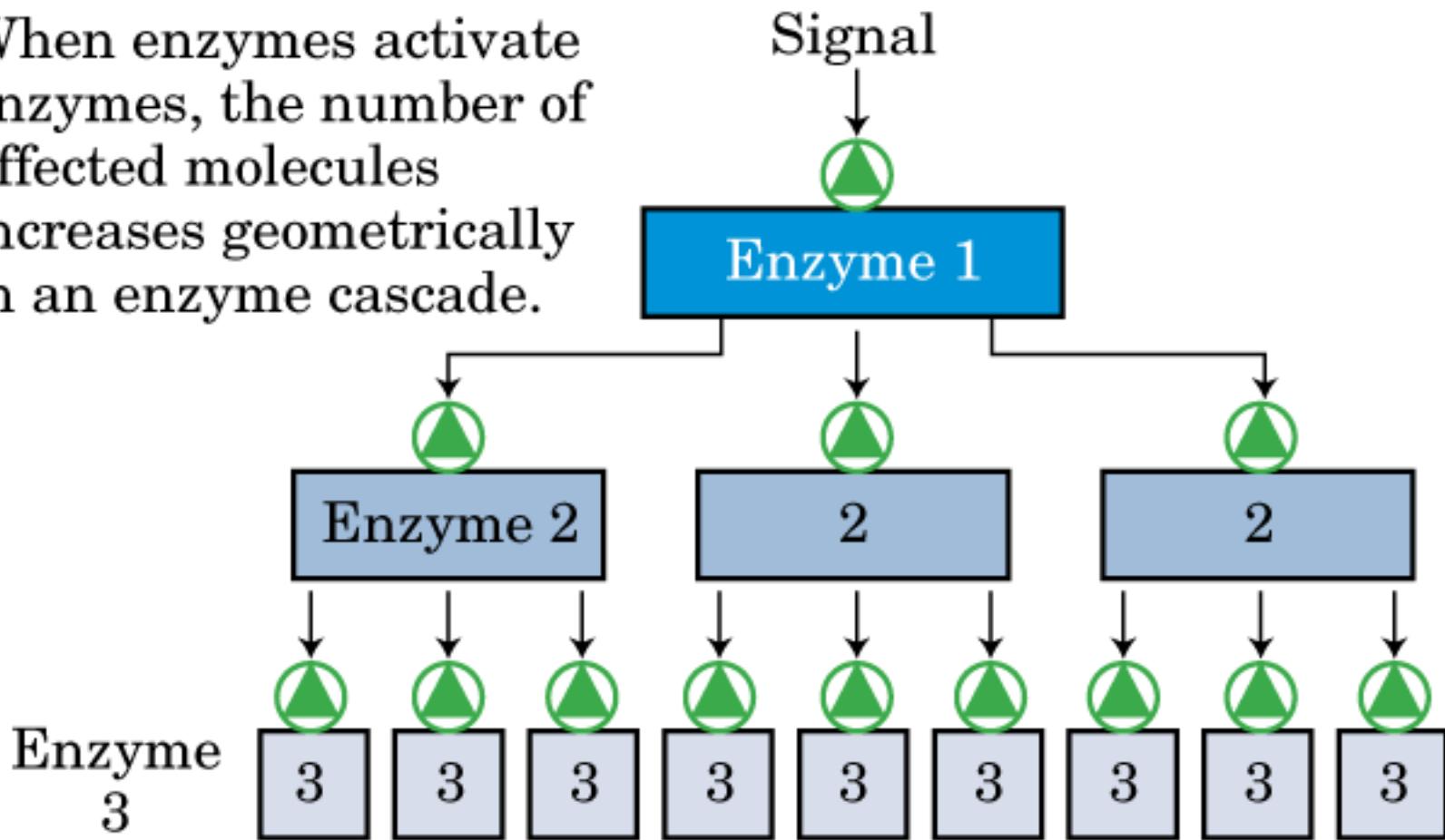
**SEGUNDO MENSAJERO** es una molécula pequeña que es generada cuando un sistema de transducción de señales es activado.

El segundo mensajero clásico es el AMP cíclico, el cual es generado cuando la adenilato ciclasa es activada por una proteína G (la cual es activada previamente por un receptor). Otros ejemplos son el GMPC, el IP3, el DAG, etc.

# TRANSDUCCION DE LAS SEÑALES

## (b) Amplification

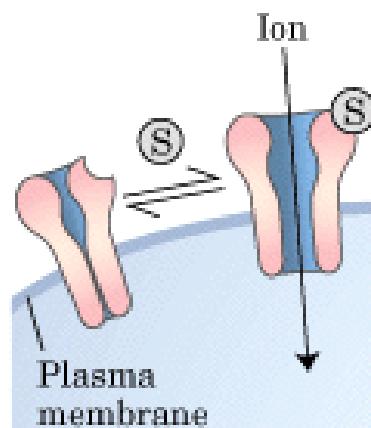
When enzymes activate enzymes, the number of affected molecules increases geometrically in an enzyme cascade.



# TIPOS DE RECEPTORES

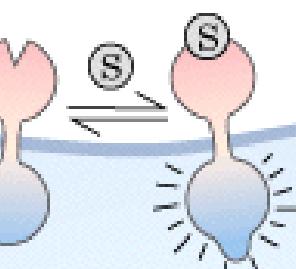
## Gated ion channel

Opens or closes in response to concentration of signal ligand (S) or membrane potential.



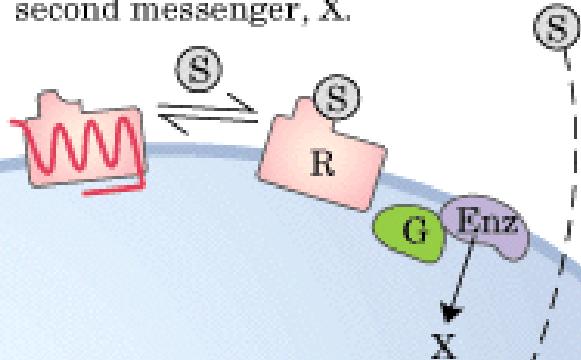
## Receptor enzyme

Ligand binding to extracellular domain stimulates enzyme activity in intracellular domain.



## Serpentine receptor

External ligand binding to receptor (R) activates an intracellular GTP-binding protein (G), which regulates an enzyme (Enz) that generates an intracellular second messenger, X.



## Steroid receptor

Steroid binding to a nuclear receptor protein allows the receptor to regulate the expression of specific genes.

DNA



Nuclear envelope

# G-Protein Coupled Receptors

**GPCR**

(Receptores acoplados a proteínas G  
o  
receptores serpentina)

## NEUROTRANSMITTERS

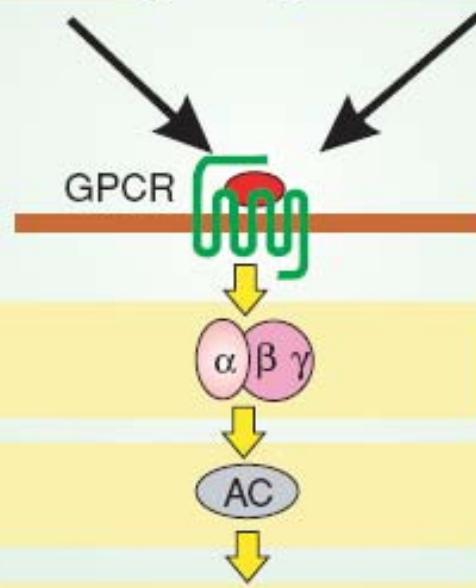
Acetylcholine (Muscarinic)  
Amylin  
Adrenomedullin (ADM)  
Calcitonin gene-related peptide (CGRP)  
Corticotropin-releasing factor (CRF)  
Dopamine  
Noradrenaline  
 $\Delta$ -Tetrahydrocannabinol  
 $\gamma$ -Aminobutyric acid (GABA)  
Galanin

Glutamate  
5-Hydroxytryptamine (5-HT)  
Melanocyte stimulating hormone ( $\alpha$ -MSH;  $\gamma$ -MSH)  
Neuropeptide Y  
Opioids (Met-enk; Leu-enk; dynorphins;  $\beta$ -endorphin)  
Somatostatin  
Pituitary adenylyl cyclase activating peptide (PCAP)  
Vasoactive intestinal peptide (VIP)

## HORMONES

Adenine nucleotides (ATP, ADP)  
Adenosine  
Adrenaline  
Adrenocorticotropic hormone (ACTH)  
Angiotensin  
Chemokines  
Glucagon  
Glucagon-like peptide 1 (GLP-1)  
Histamine

Lysophosphatidic acid (LPA)  
Sphingosine 1-phosphate (S-1-P)  
Melatonin  
Prostaglandins  
Uridine triphosphate (UTP)  
Vasopressin



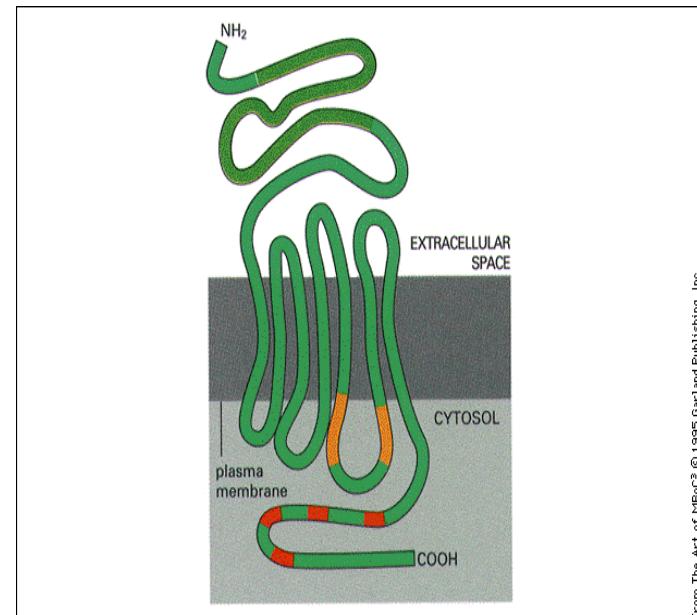
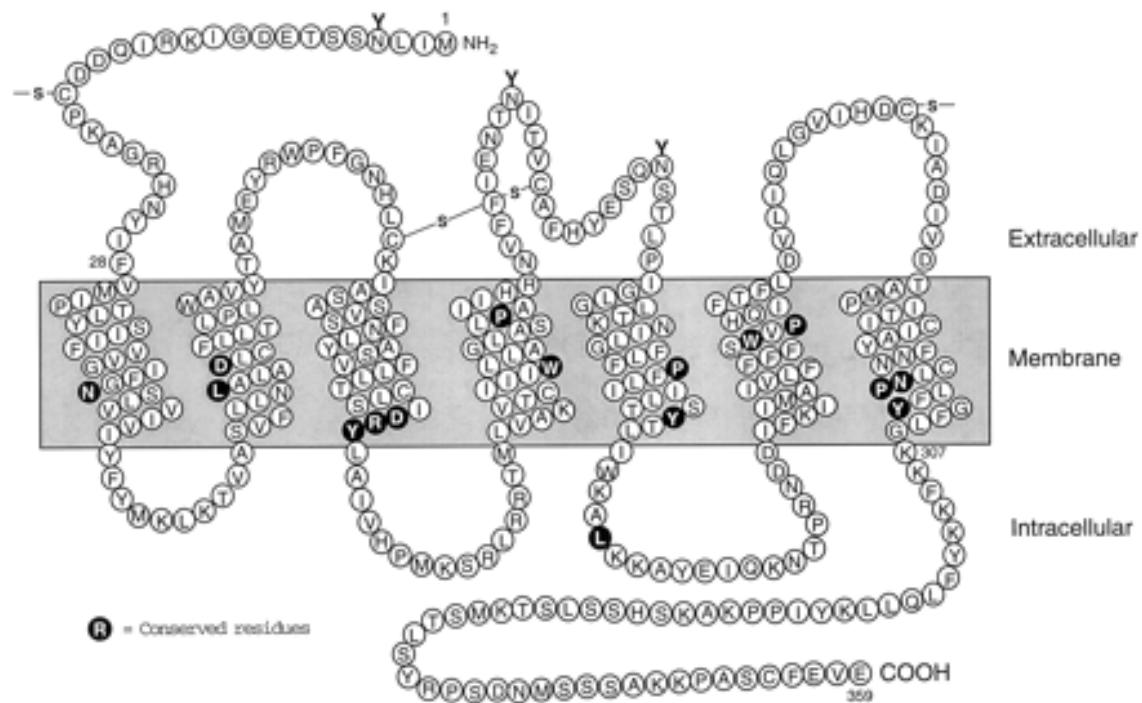
Transducer

Amplifier

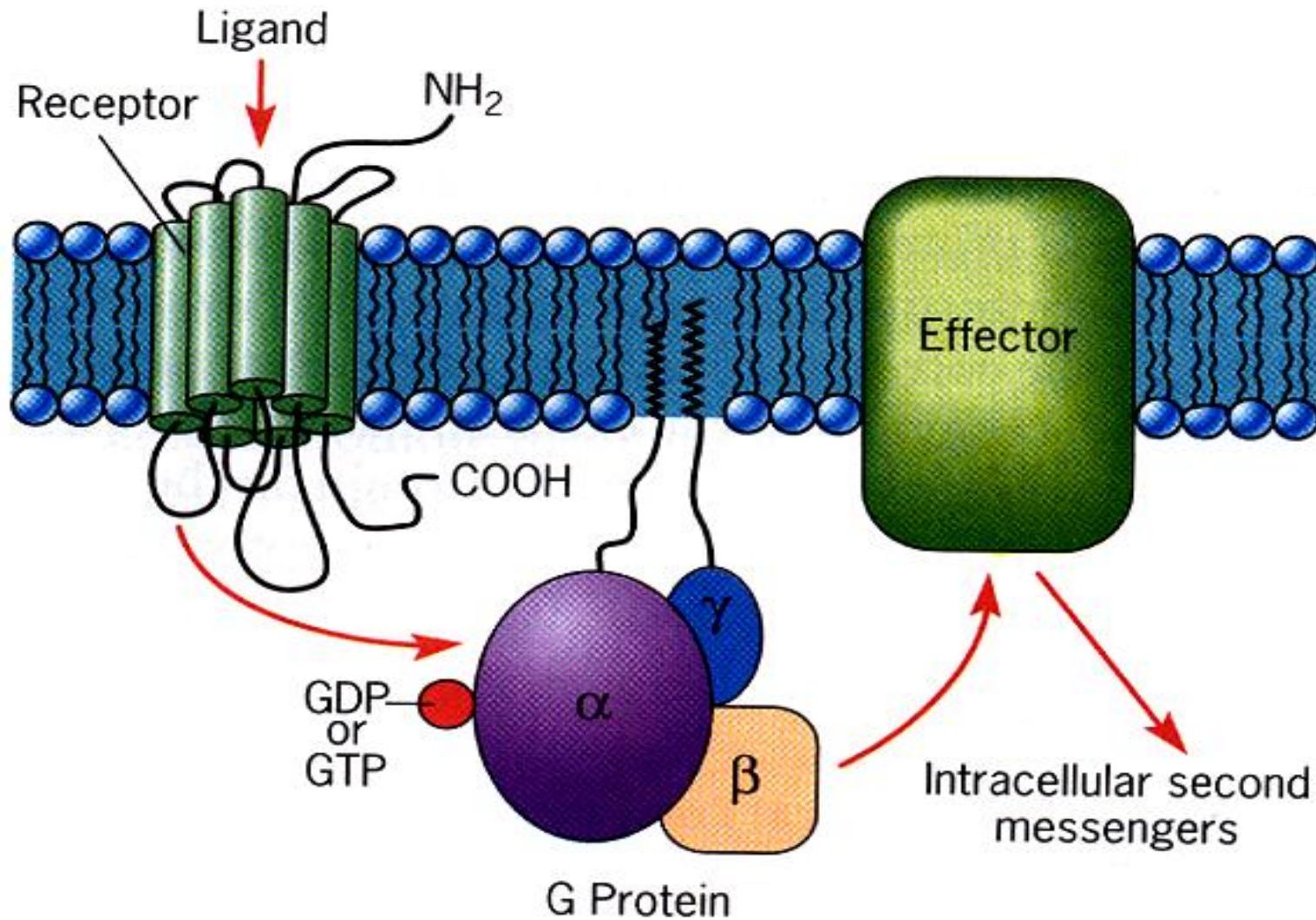
Messenger

Cyclic AMP

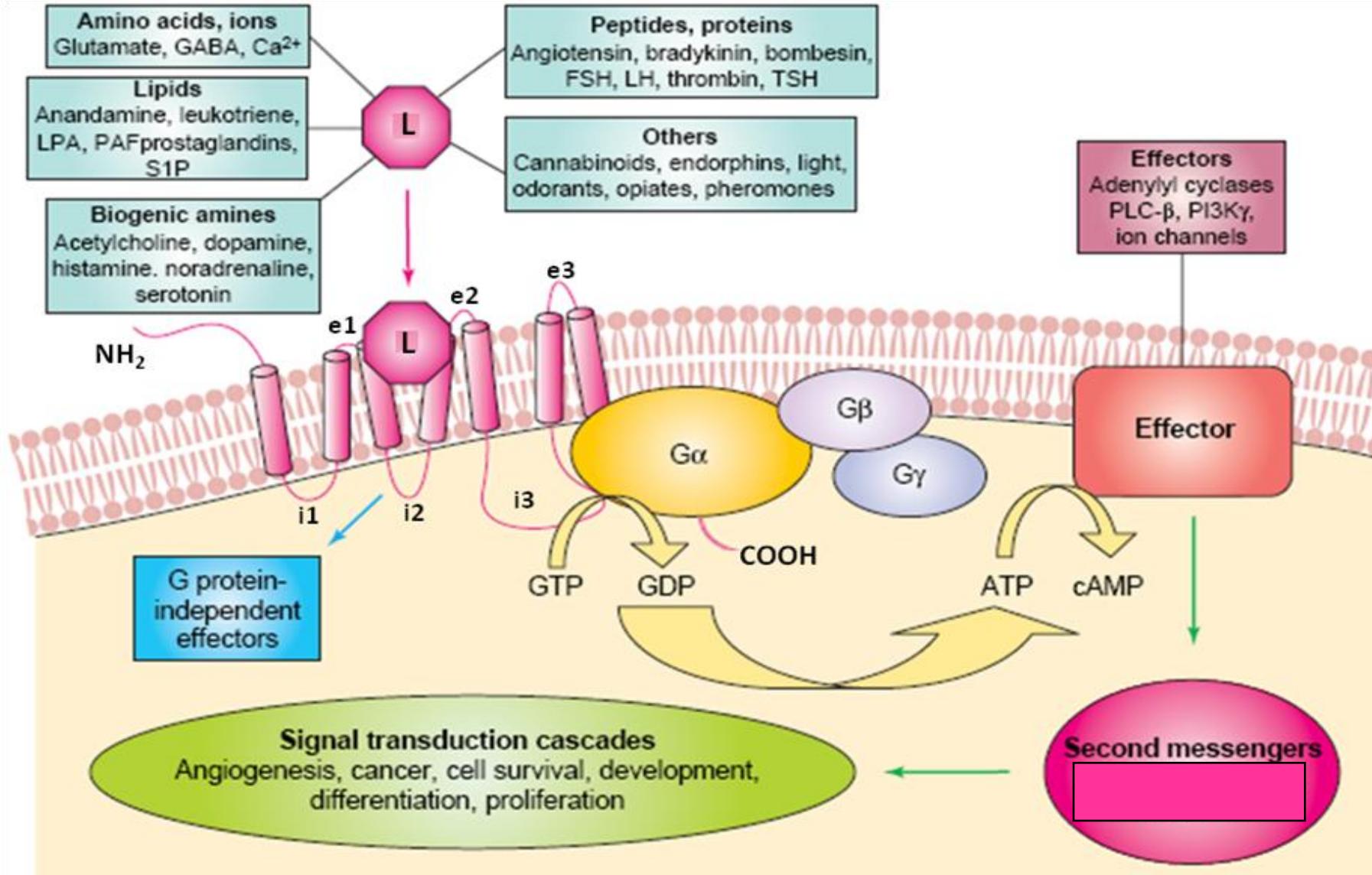
# Receptores con siete dominios transmembranales (Receptores serpentina o acoplados a proteínas G/GPCR)



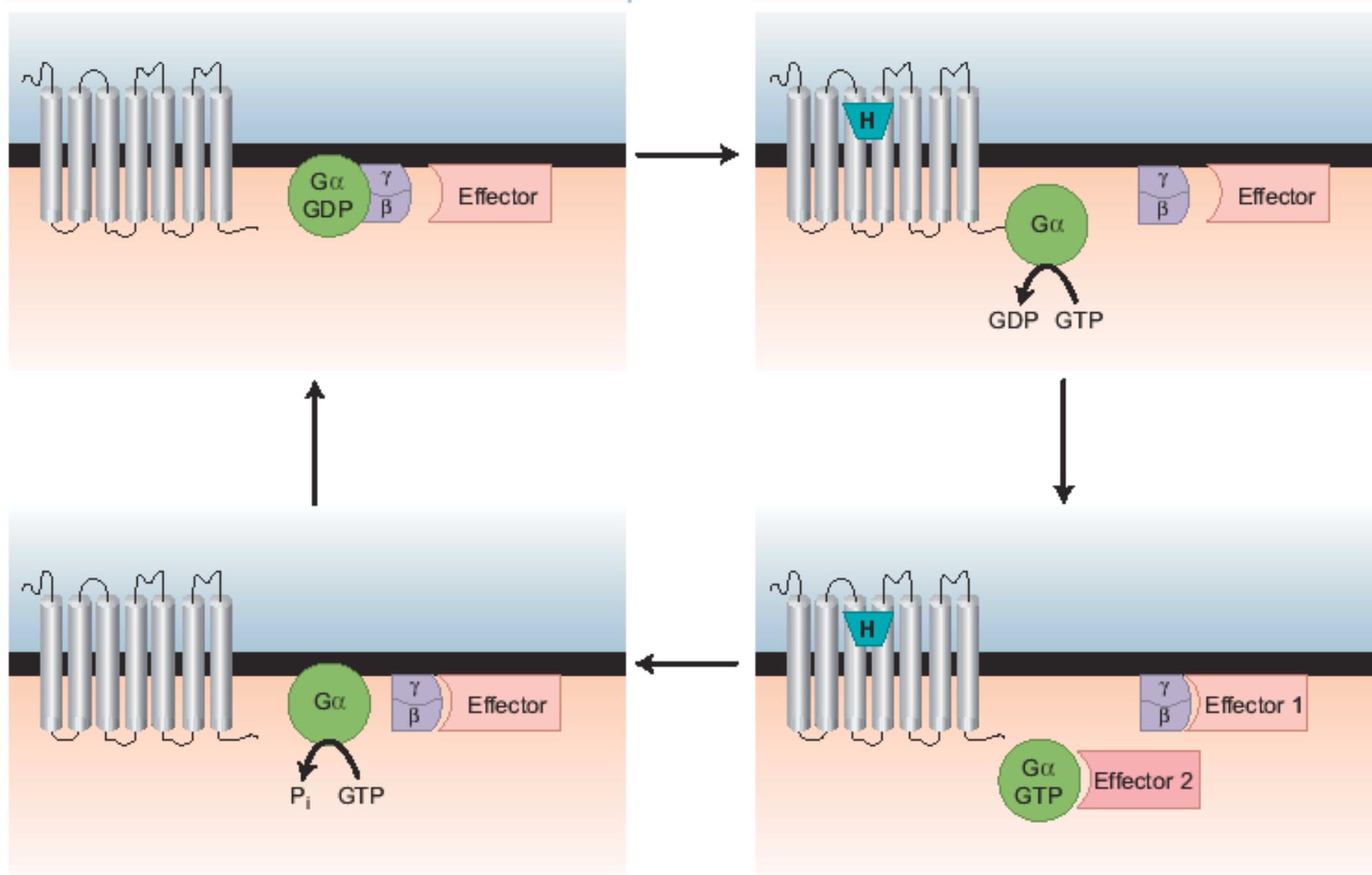
# Sistemas de Transducción de los GPCRs

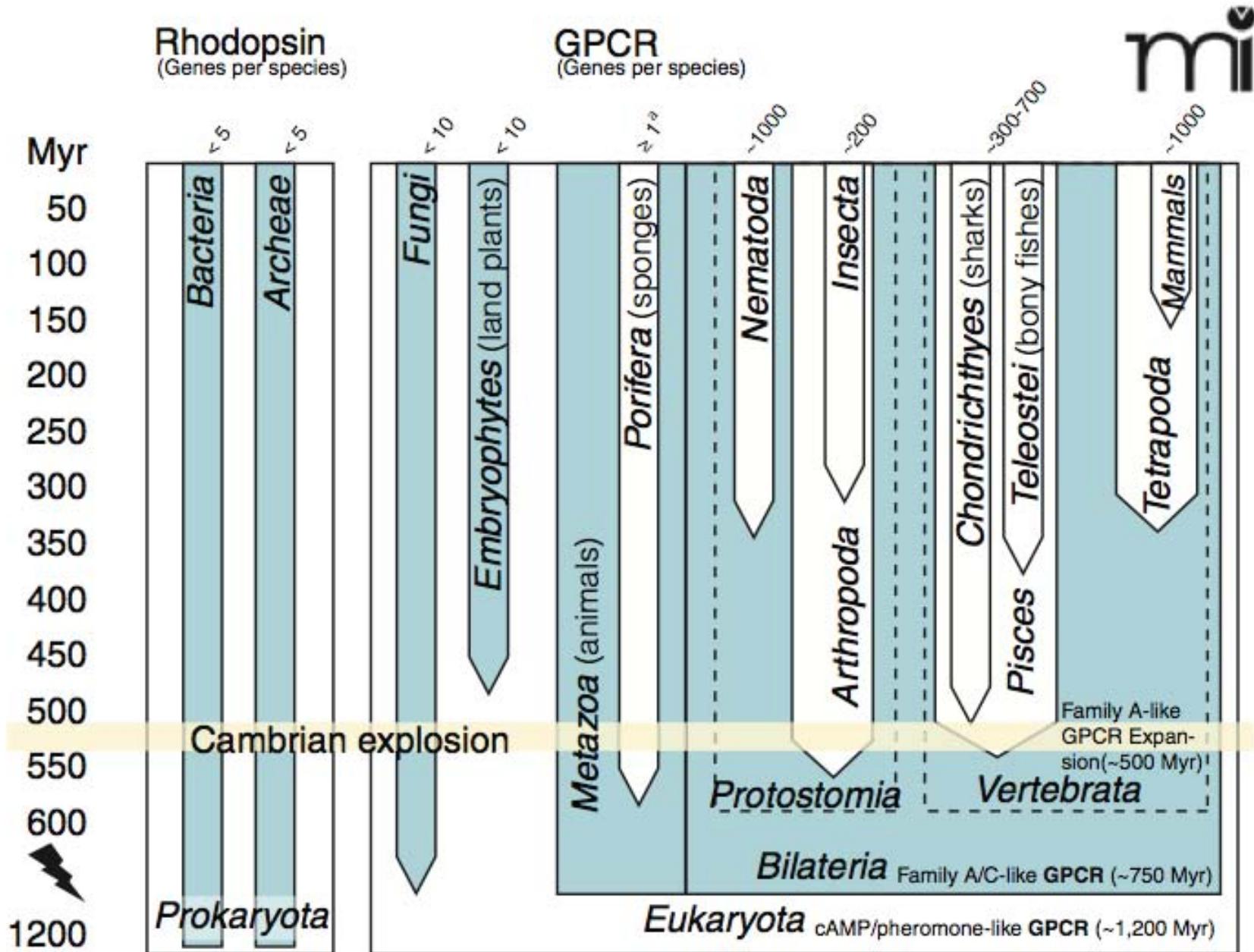


# SISTEMA DE TRANSDUCCION DE LOS GPCRs



# SISTEMA DE TRANSDUCCION DE LOS GPCRs

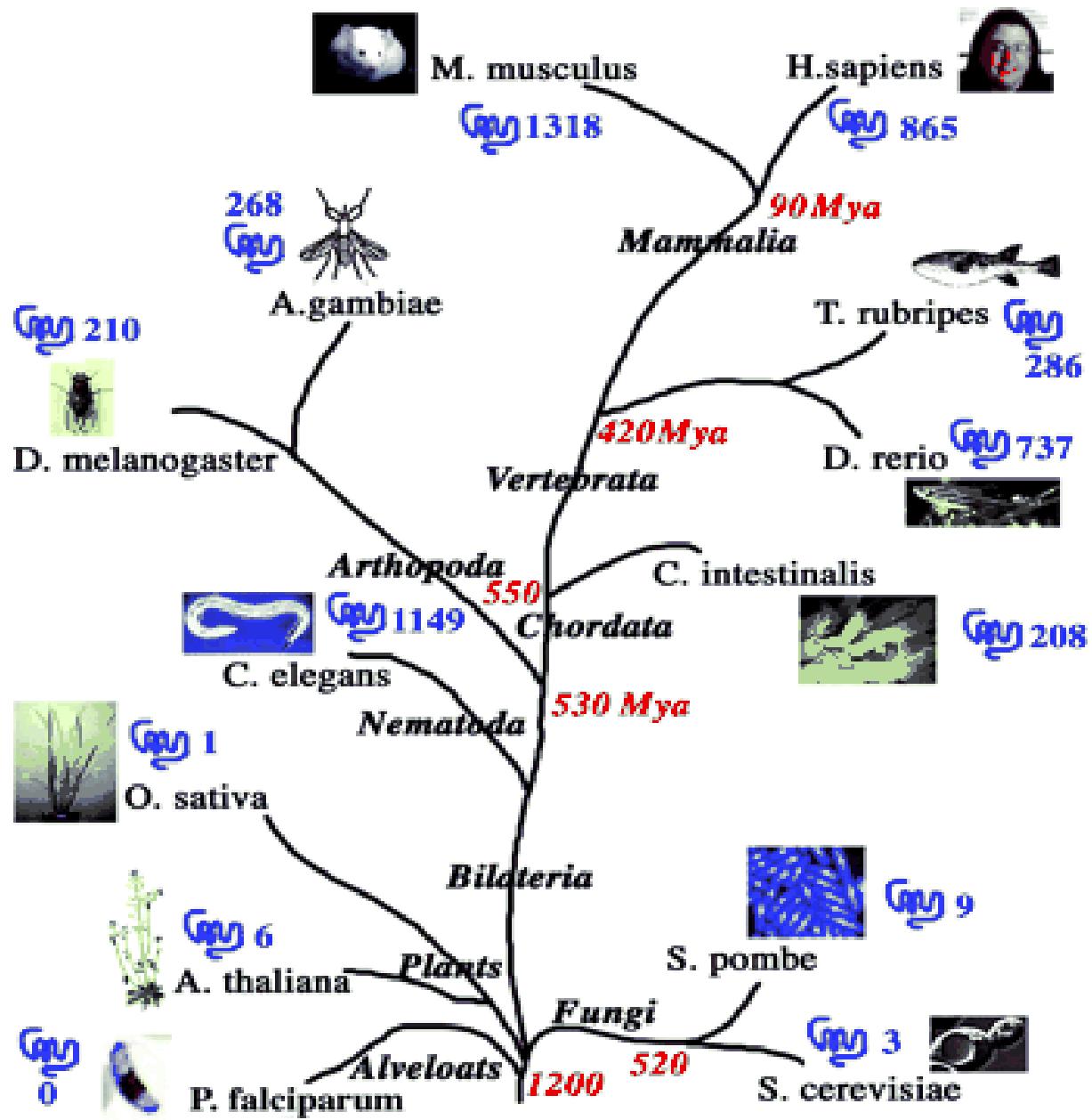




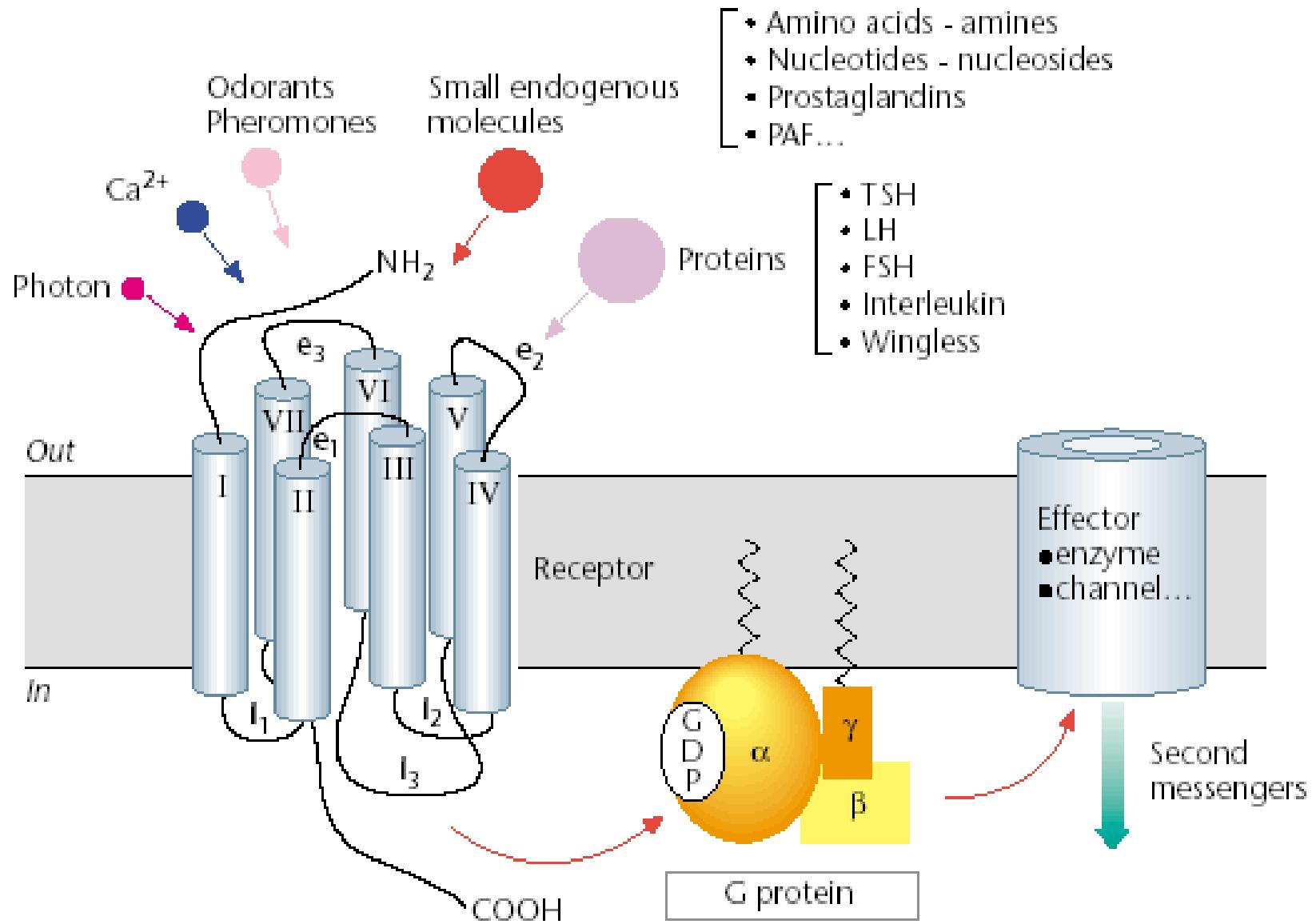
**Figure 1. Representation of GPCRs in major evolutionary lineages.**

# GPCRs en la escala filogenética

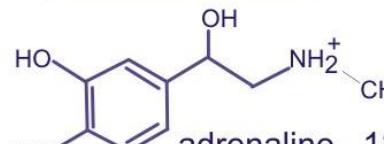
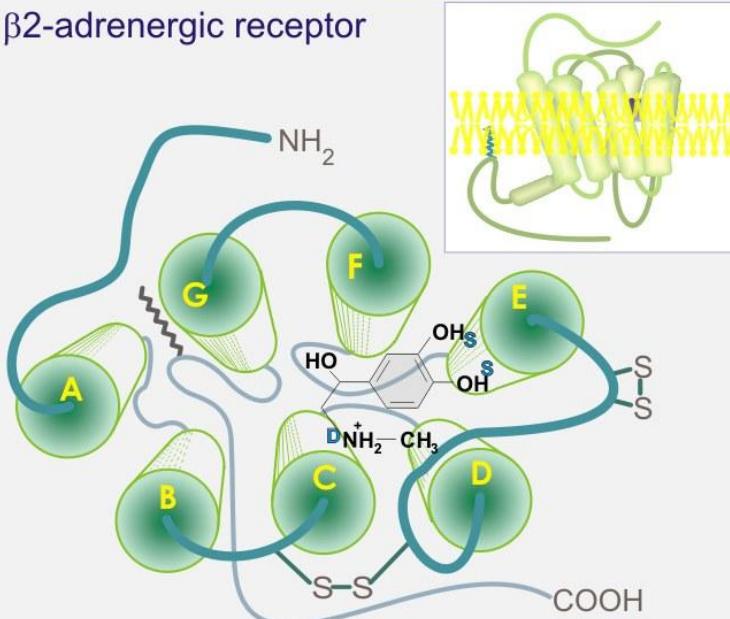
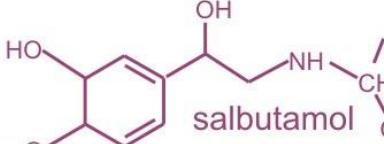
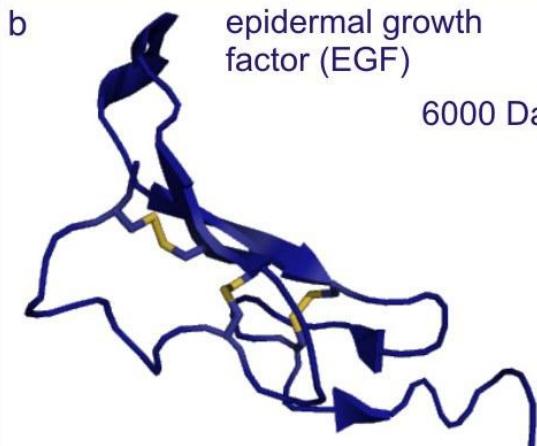
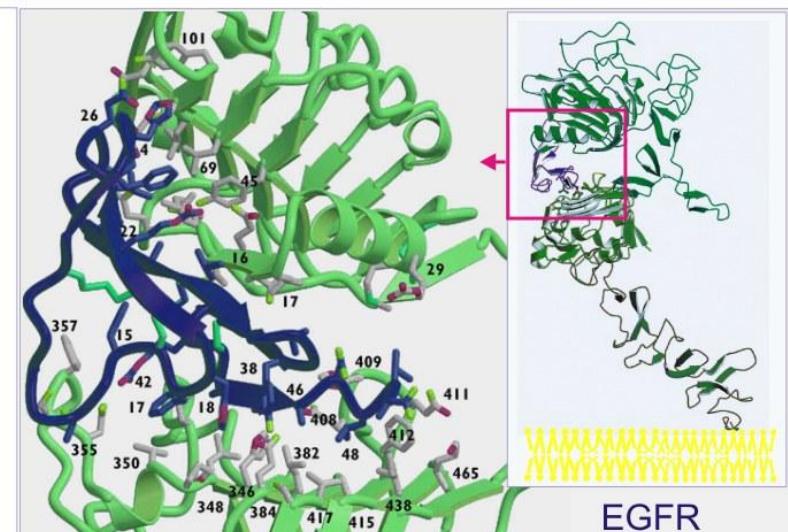
## GPCR "Tree of Life"



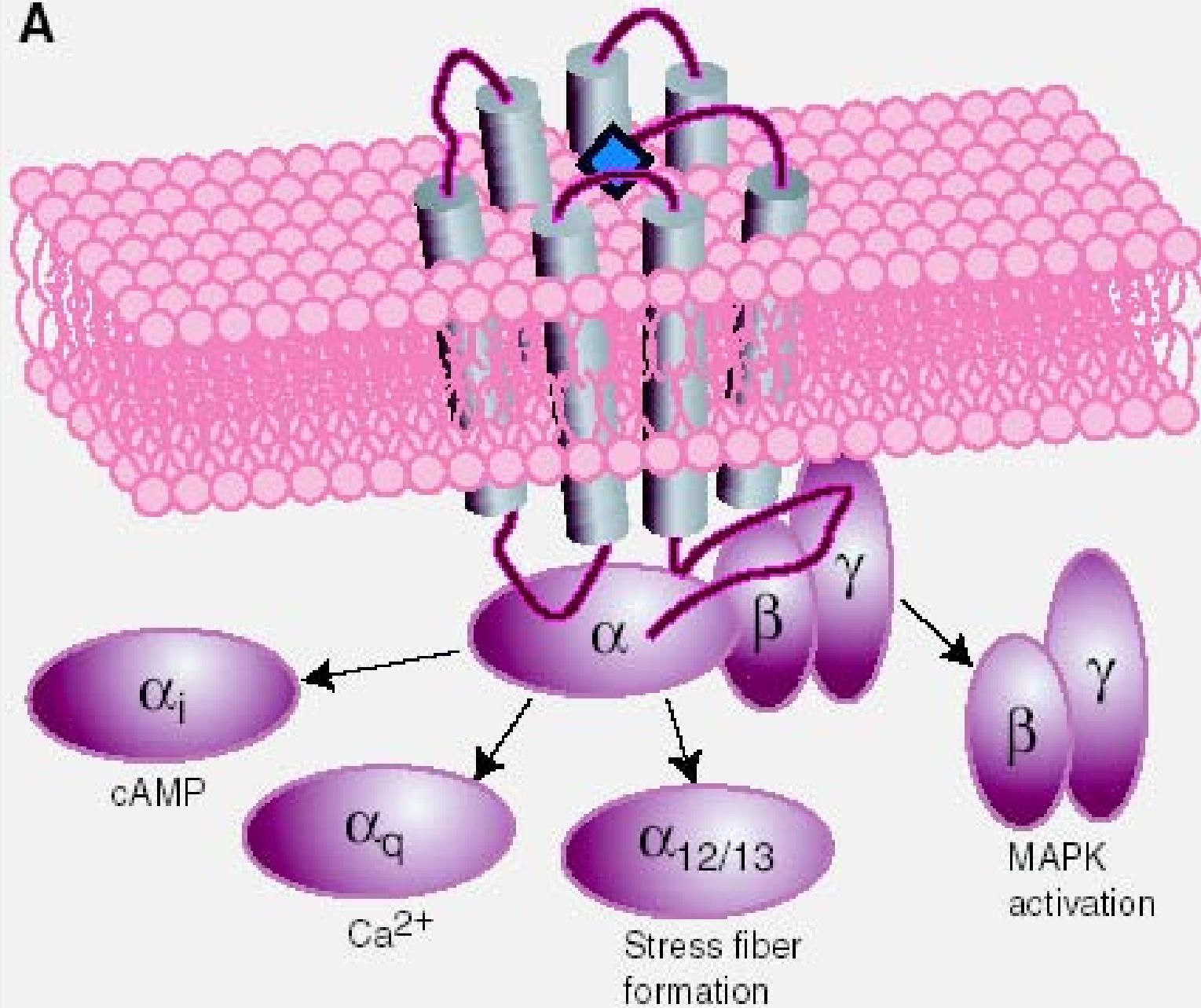
# Sistemas de Transducción de los GPCRs



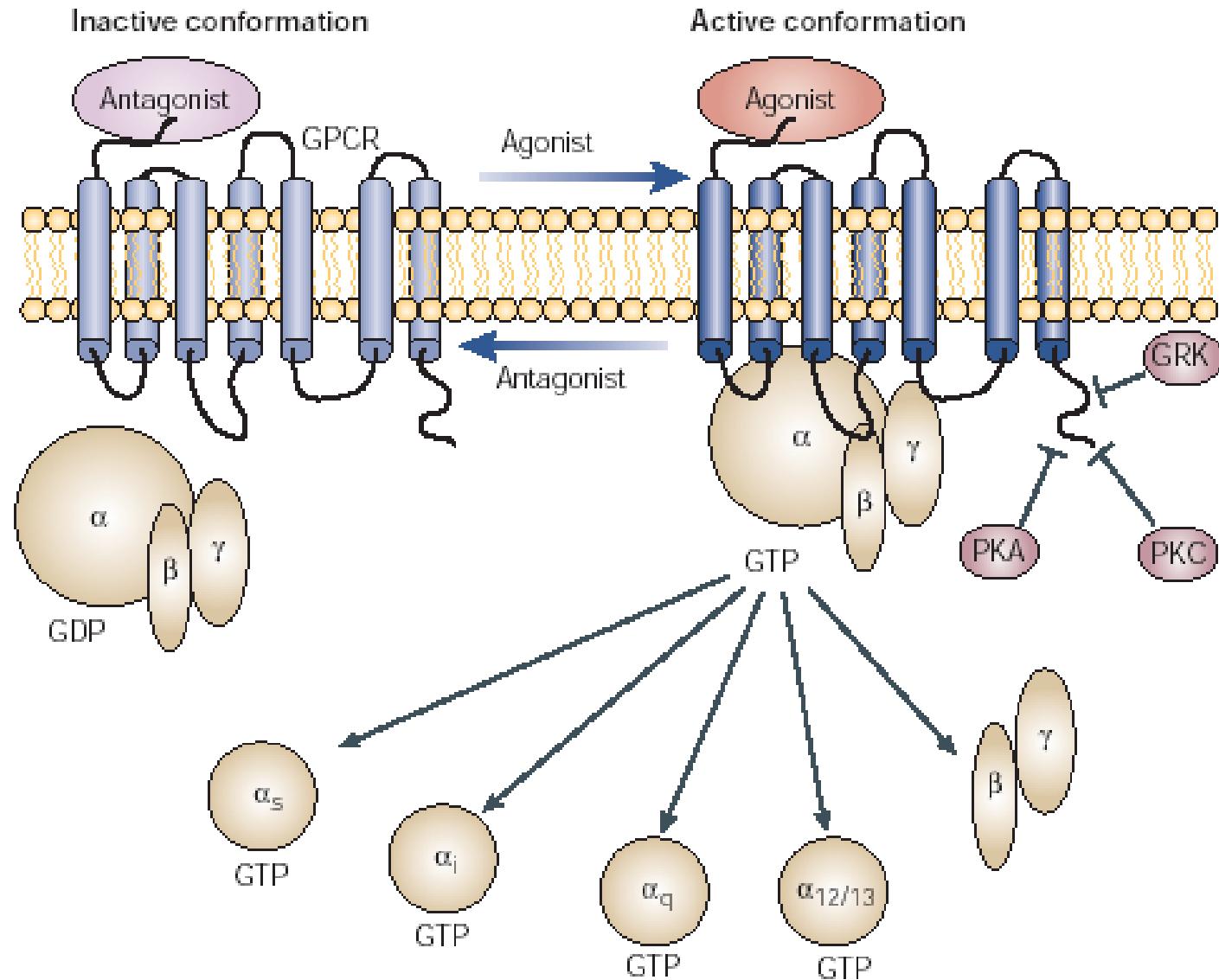
two examples of low and high molecular mass ligands and their receptors  
 (note the numerous interaction sites between EGF and its receptor)

ligands	receptor (+ ligand)
<b>a</b>  adrenaline 184 Da	<b>β2-adrenergic receptor</b> 
 salbutamol β1/β2-agonist	
 propranolol β1/β2-antagonist	
<b>b</b>  epidermal growth factor (EGF) 6000 Da	 EGFR

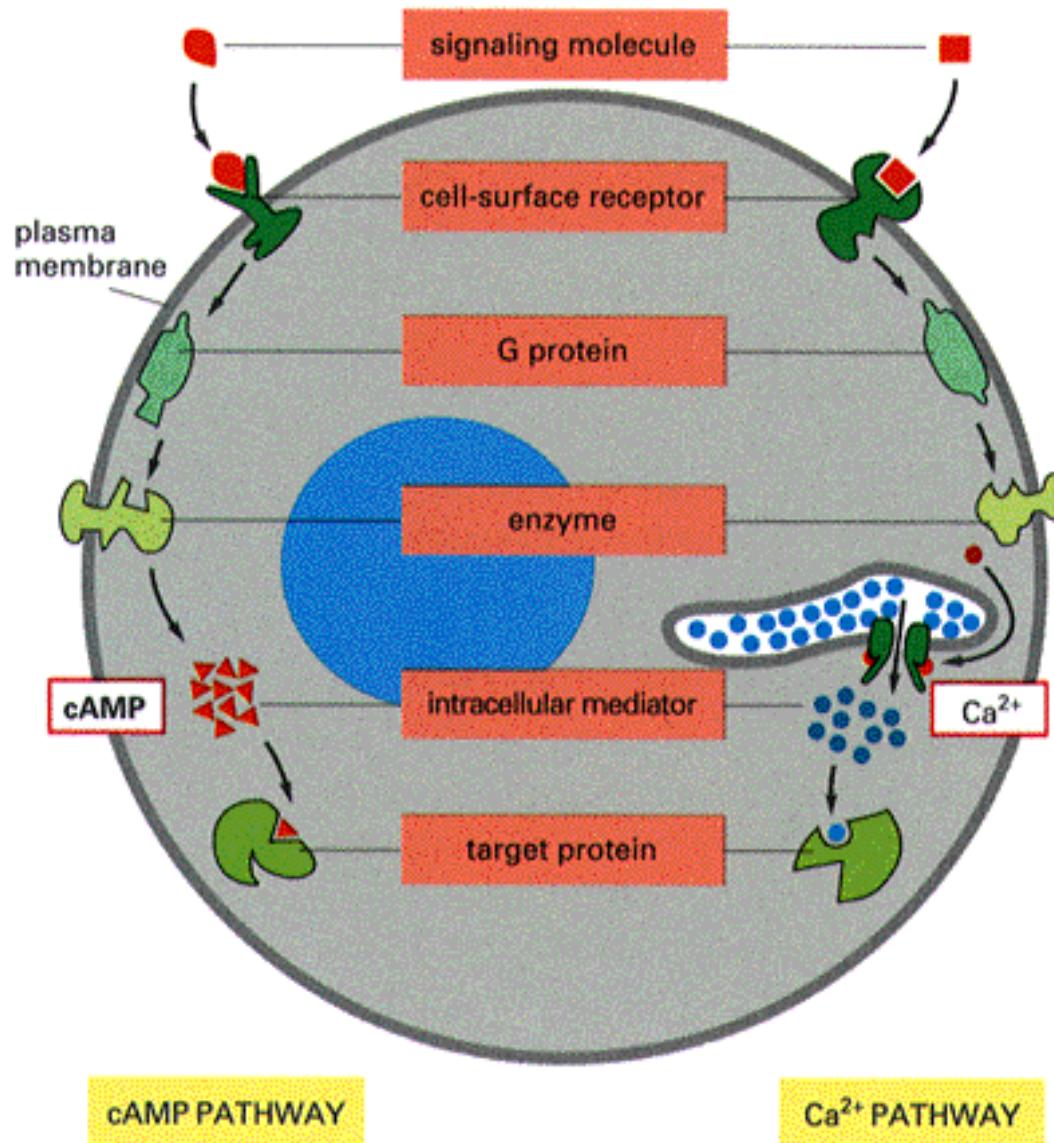
ijk

**A**

# DIVERSIDAD DE PROTEINAS G



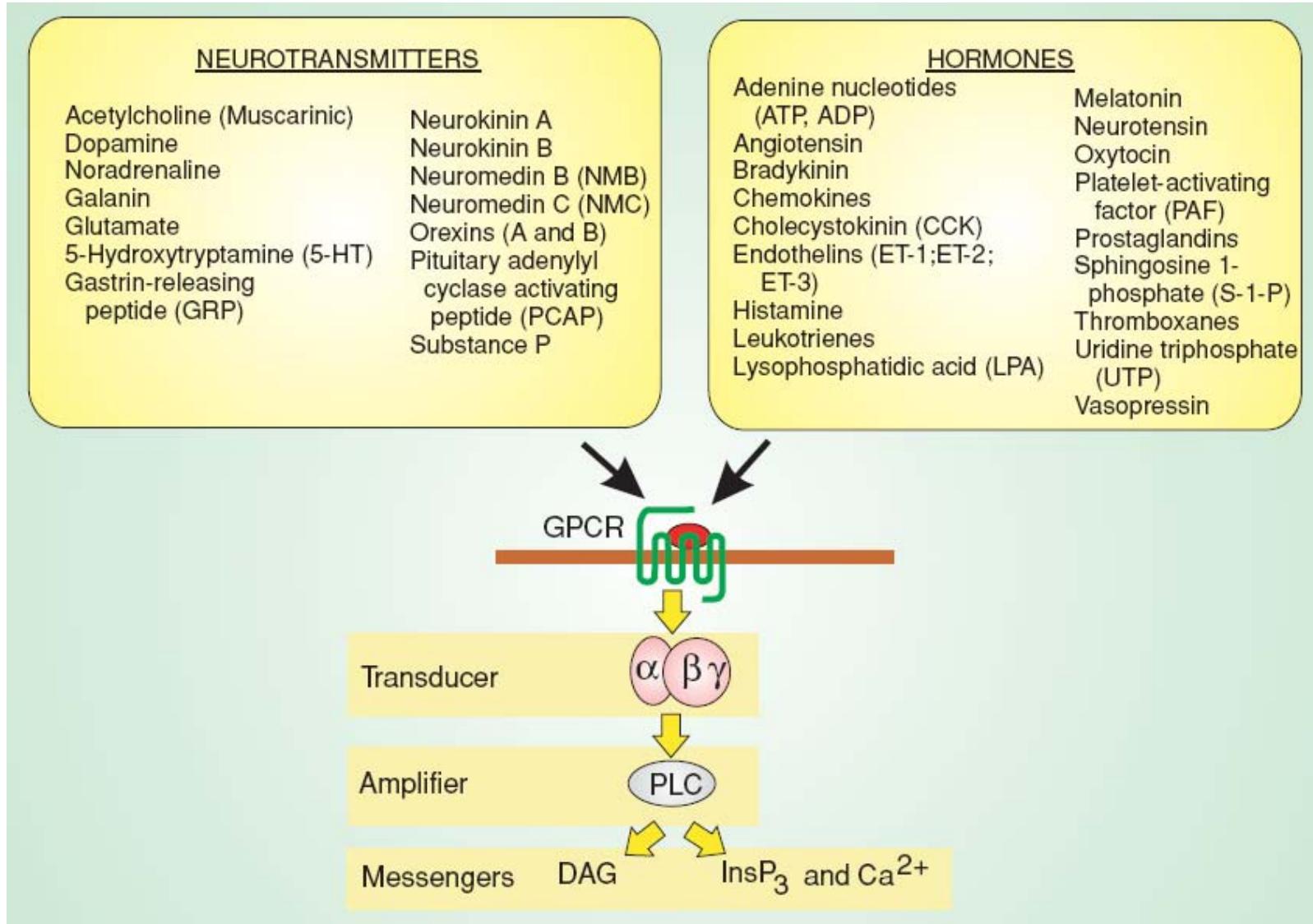
# TRANSDUCCION DE LAS SEÑALES



**GPCRs:**

**"SISTEMA DE RECAMBIO DE  
FOSFOINOSITIDOS (PI)/  
CALCIO "**

# SISTEMA DE RECAMBIO DE FOSFOINOSITIDOS/CALCIO



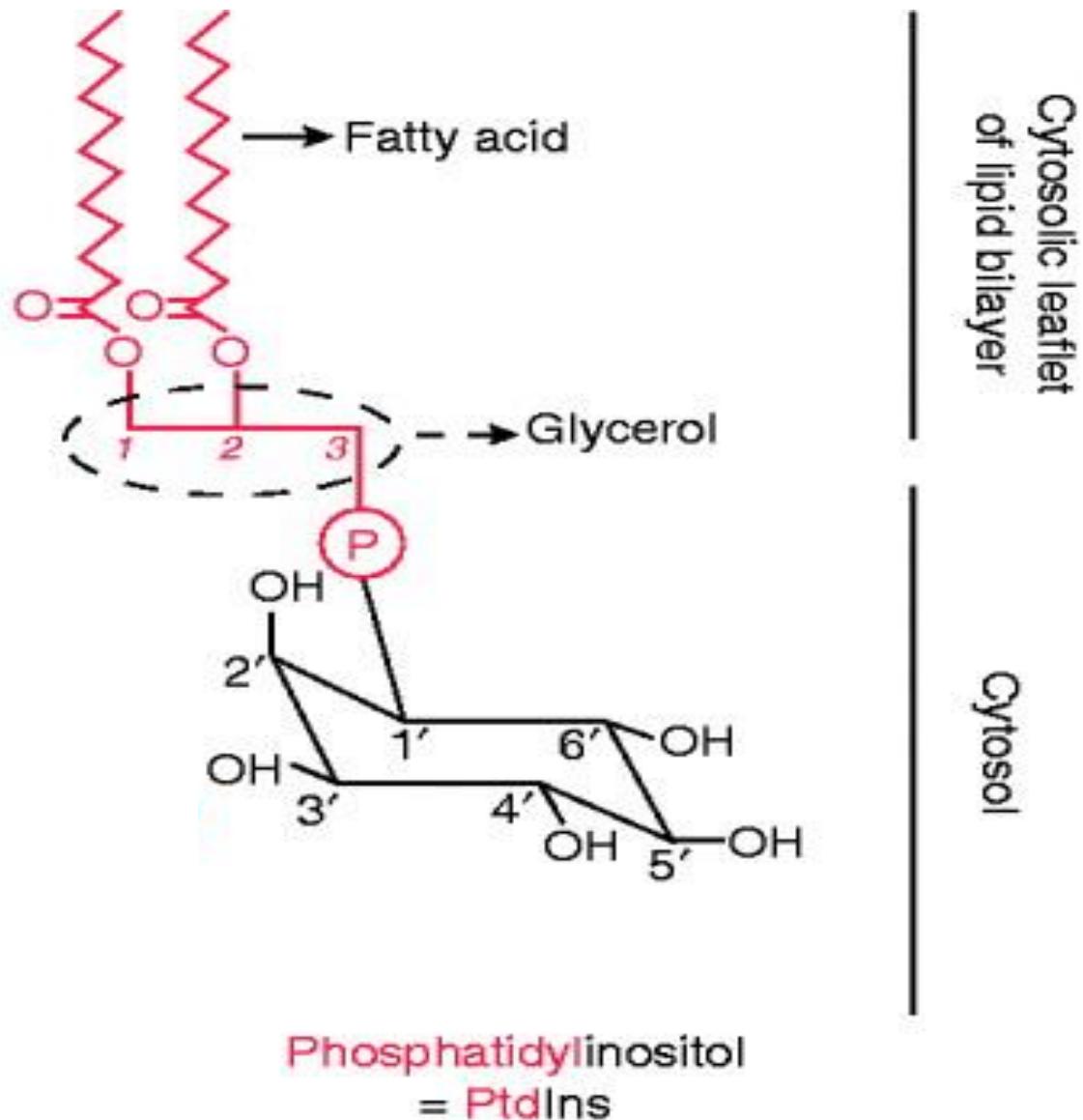
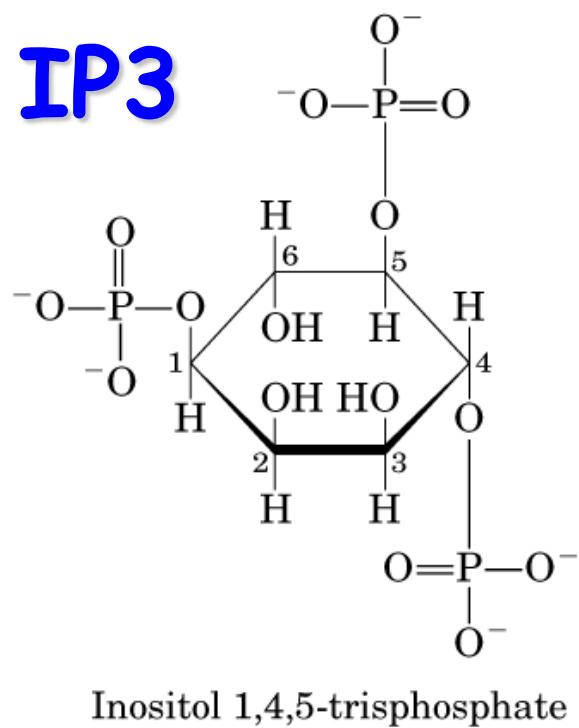
## table 13–5

### Some Signals That Act through Phospholipase C and IP<sub>3</sub>

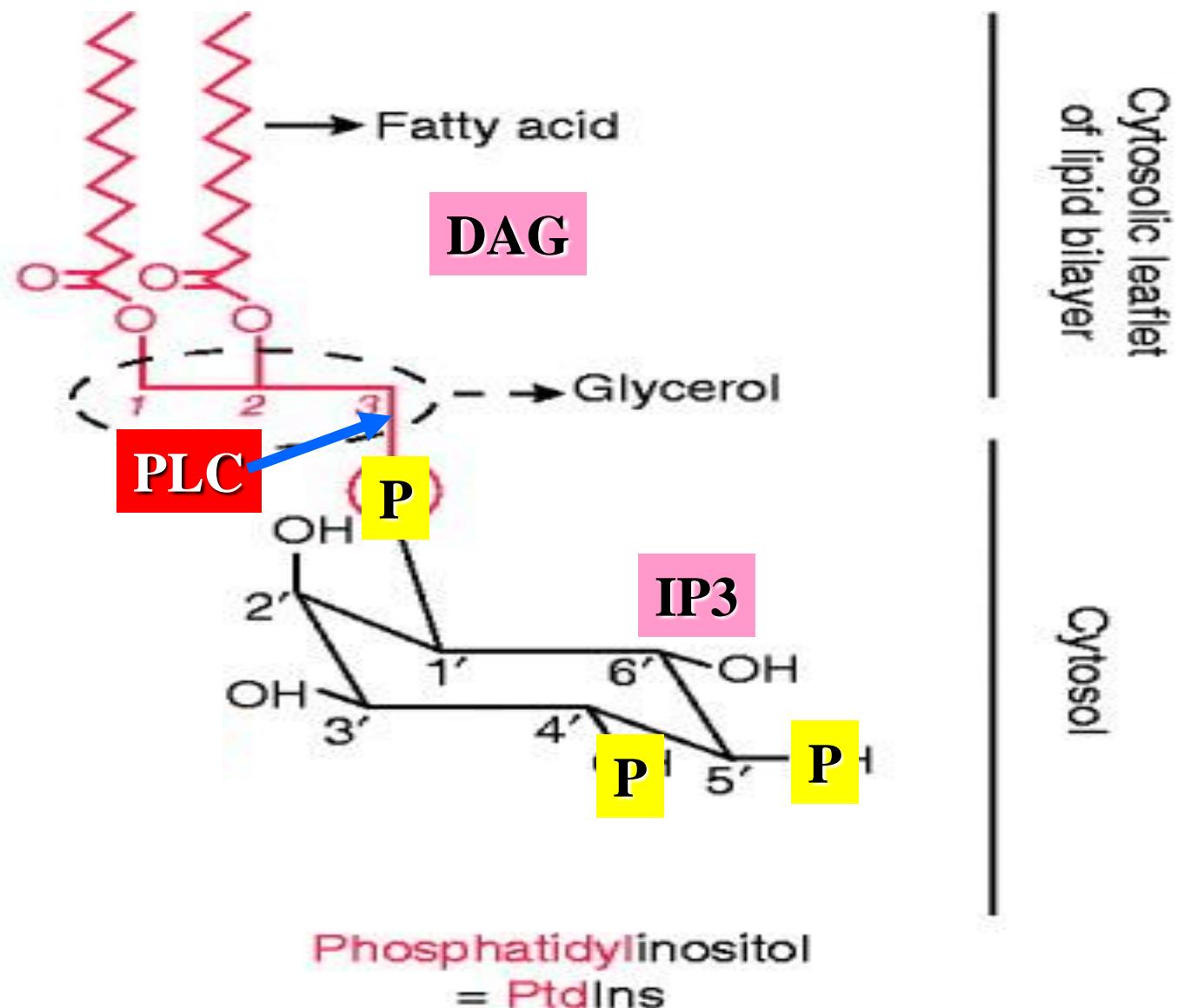
- Acetylcholine [muscarinic M<sub>1</sub>]
- $\alpha_1$ -Adrenergic agonists
- Angiogenin
- Angiotensin II
- ATP [P<sub>2x</sub> and P<sub>2y</sub>]\*
- Auxin
- Gastrin-releasing peptide
- Glutamate
- Gonadotropin-releasing hormone (GnRH)
- Histamine [H<sub>1</sub>]\*
- Light (*Drosophila*)
- Oxytocin
- Platelet-derived growth factor (PDGF)
- Serotonin [5-HT-1c]\*
- Thyrotropin-releasing hormone (TRH)
- Vasopressin

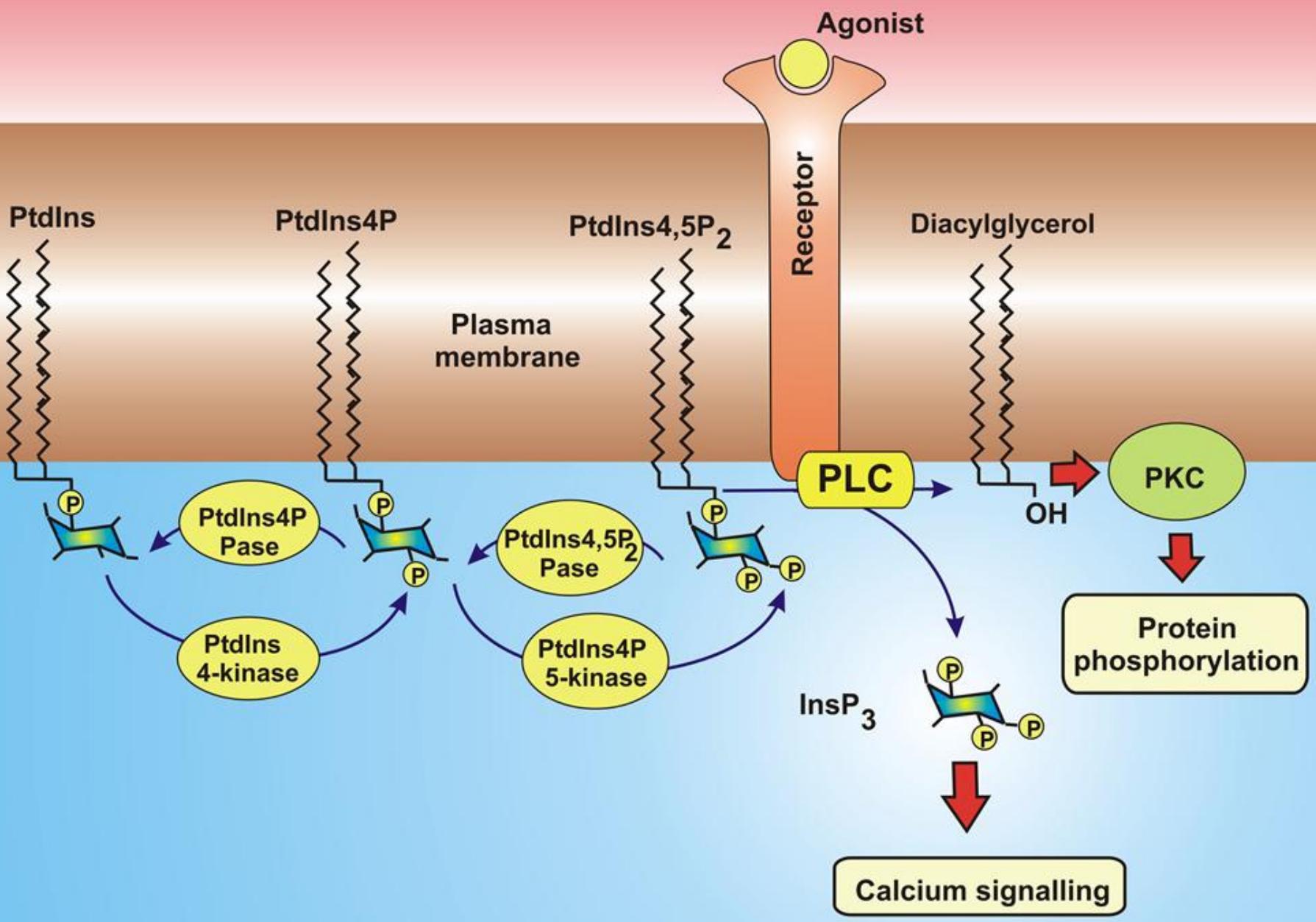
\*Receptor subtypes are in square brackets; see footnote to Table 13–4.

# PtdIns (FOSFATIDILINOSITOL)- PIP2

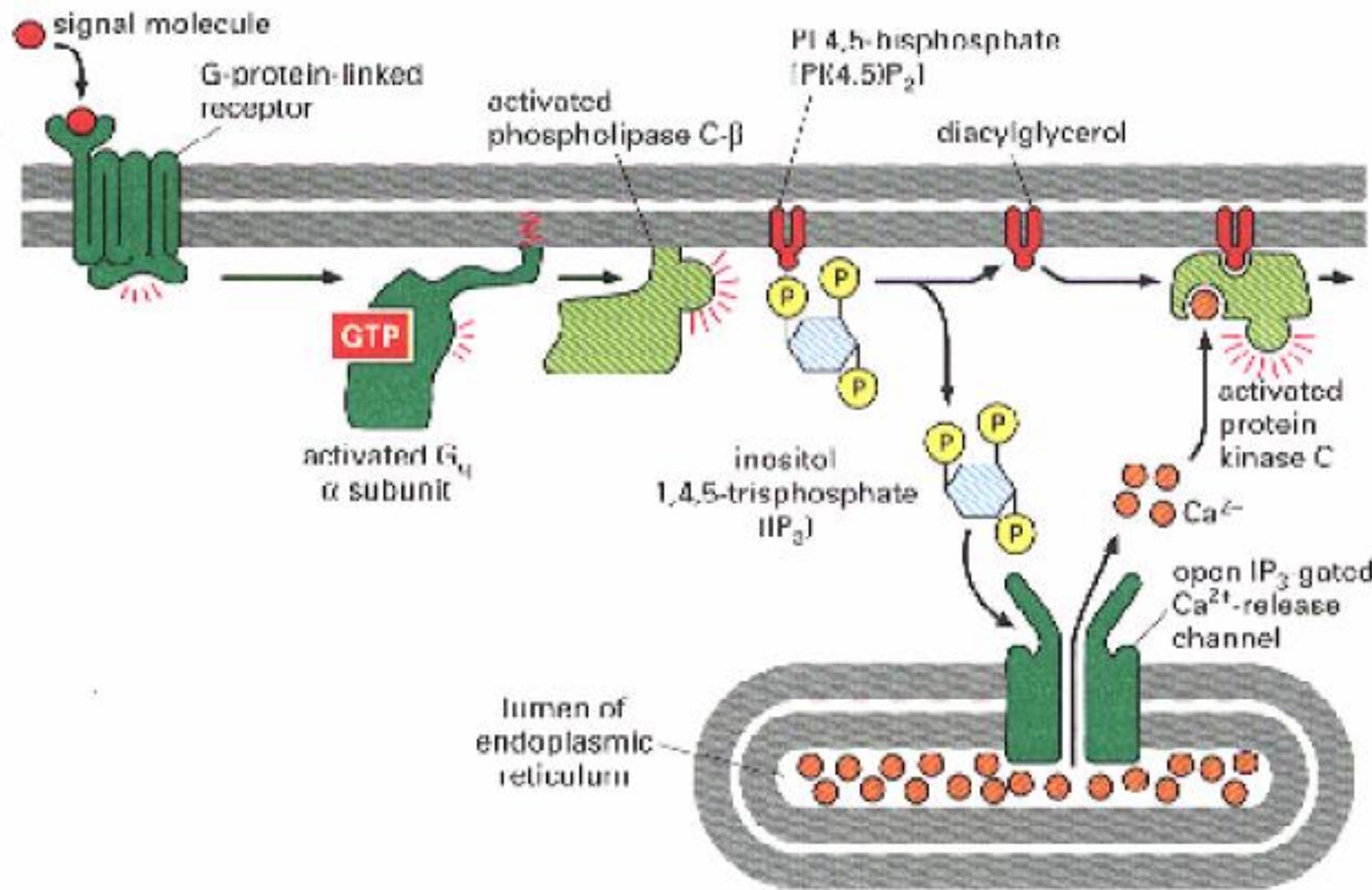


## PI 4,5 P<sub>2</sub> (FOSFATIDILINOSITOL)

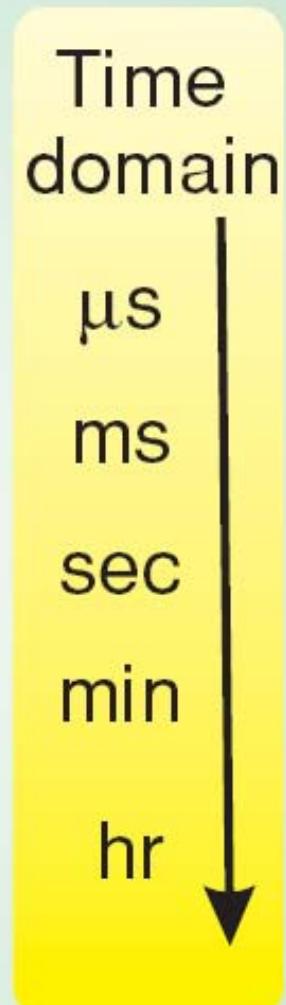
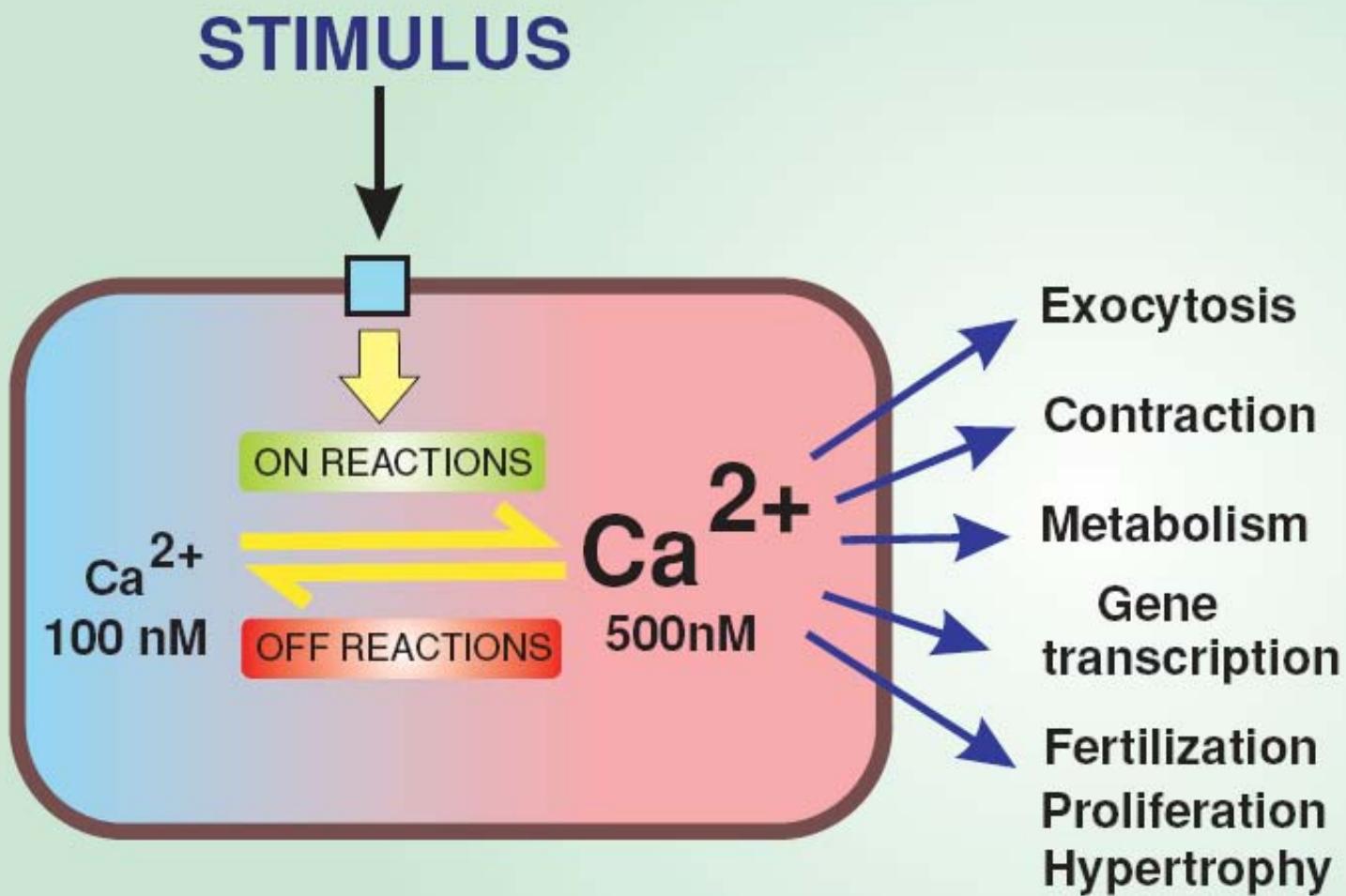




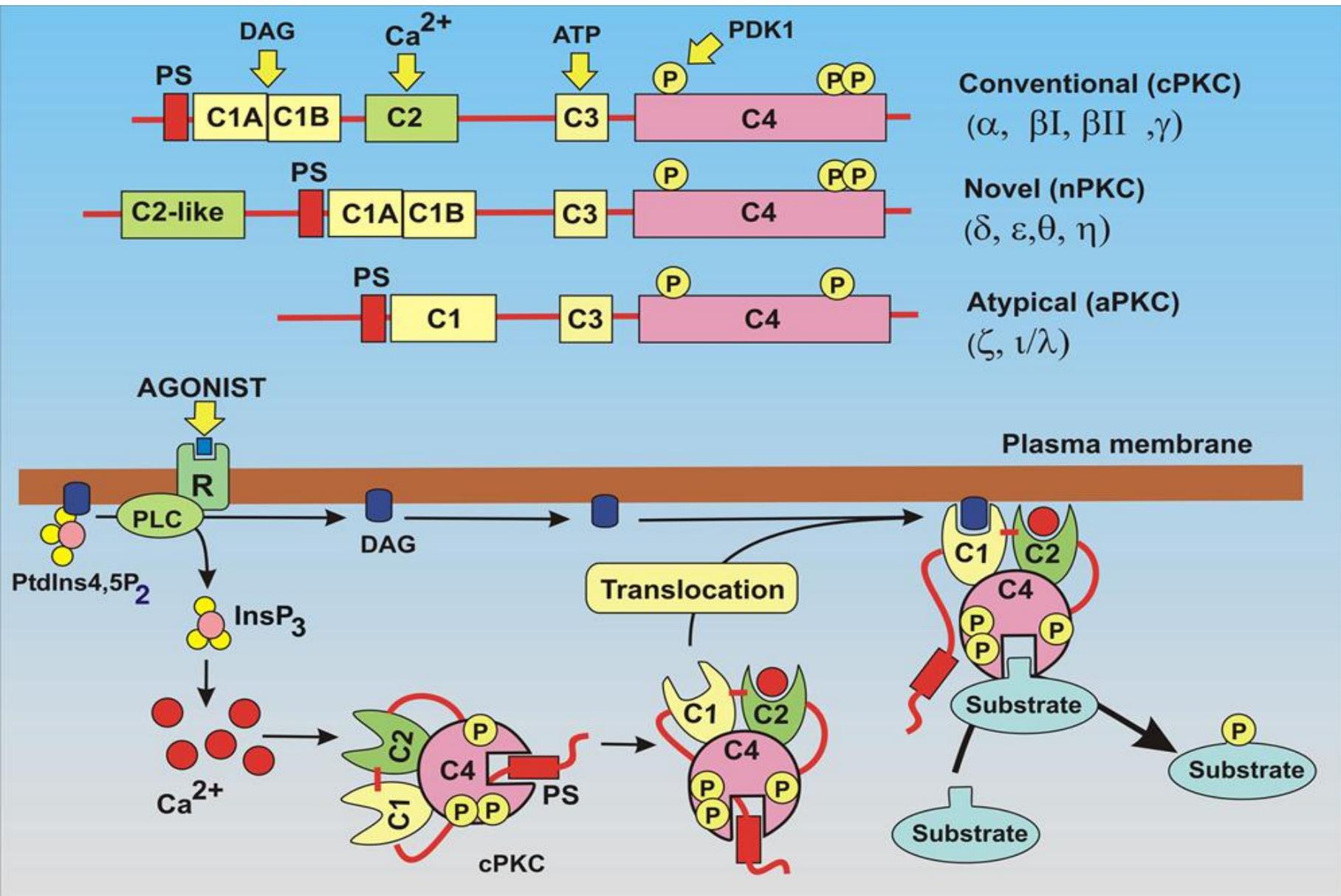
# SISTEMA DE RECAMBIO DE FOSFOINOSITIDOS/CALCIO



# Calcio intracelular

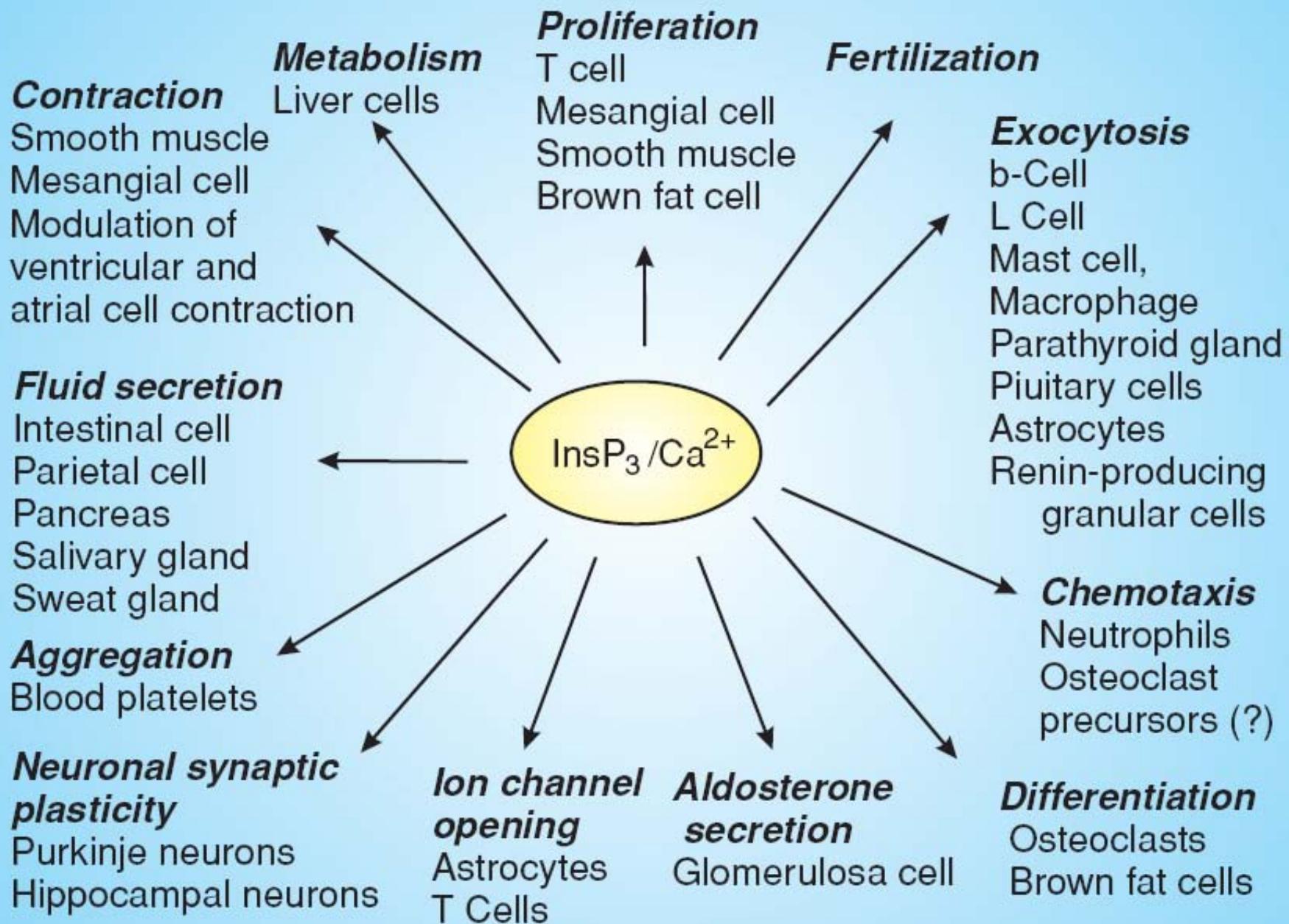


# Activación de la PKC



**Table 15.5****Examples of Responses Mediated by Protein Kinase C**

<b>Tissue</b>	<b>Response</b>
Blood platelets	Serotonin release
Mast cells	Histamine release
Adrenal medulla	Secretion of epinephrine
Pancreas	Secretion of insulin
Pituitary cells	Secretion of GH and LH
Thyroid	Secretion of calcitonin
Testes	Testosterone synthesis
Neurons	Dopamine release
Smooth muscle	Increased contractility
Liver	Glycogen hydrolysis
Adipose tissue	Fat synthesis

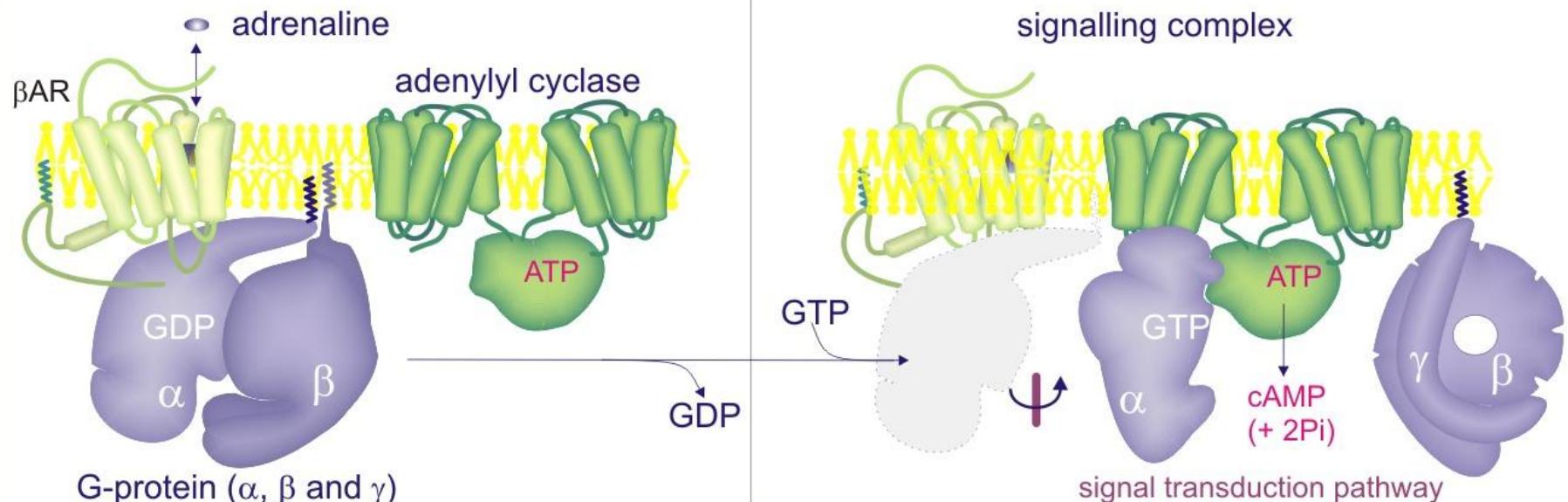


**GPCRs:**

**"SISTEMA DE LA ADENILATO  
CICLASA Y EL AMP CICLICO"**

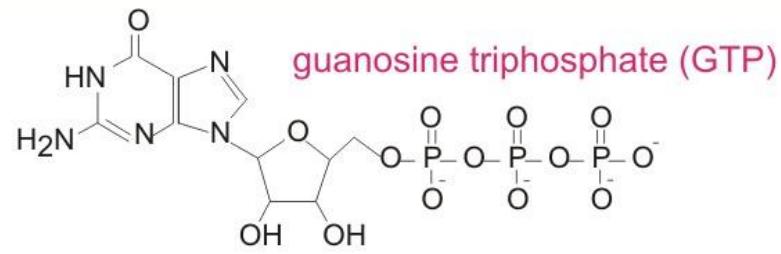
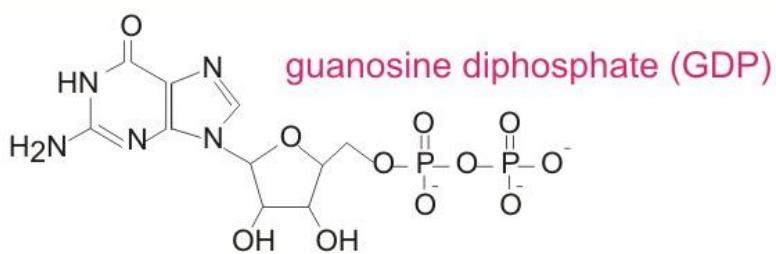
## ligand binding to its receptor induces the formation of signalling complexes

Here, adrenaline binding causes GTP exchange and subsequent binding of the G-protein  $\alpha$ -subunit to adenylyl cyclase, initiating the production of the second messenger cAMP

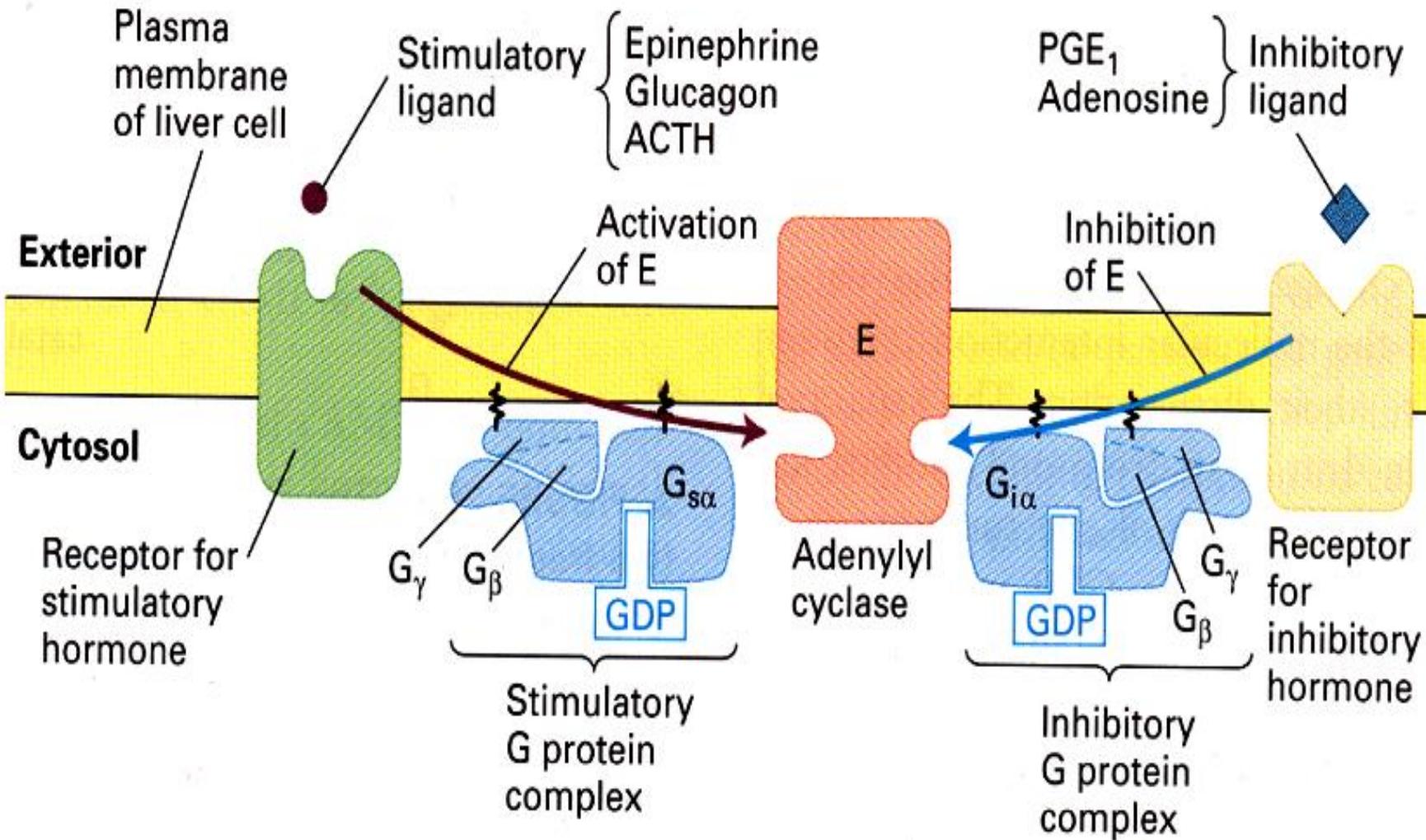


binding of adrenaline to its receptor causes an exchange of GDP for GTP in the  $\alpha$ -subunit of the G-protein

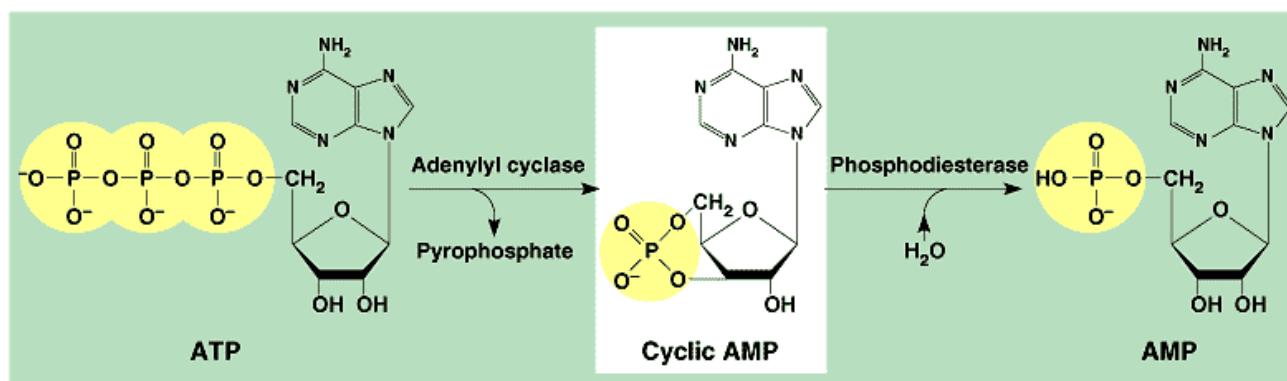
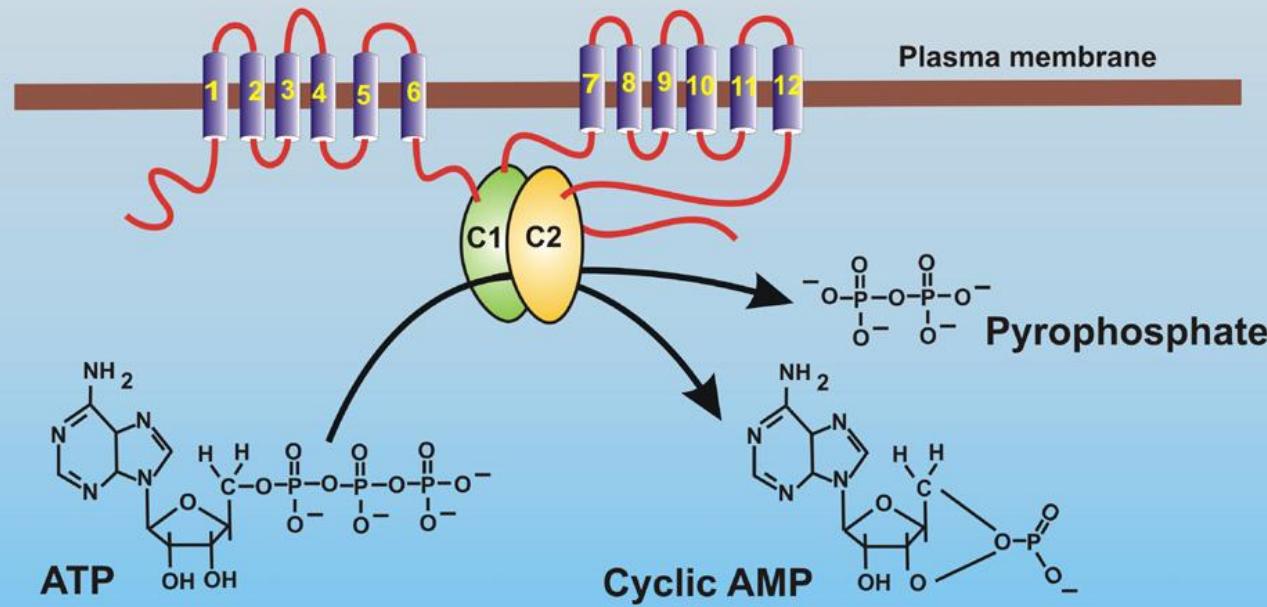
the GTP-bound  $\alpha$ -subunit switches its attention to adenylyl cyclase, thus inducing the production of cAMP (second messenger)

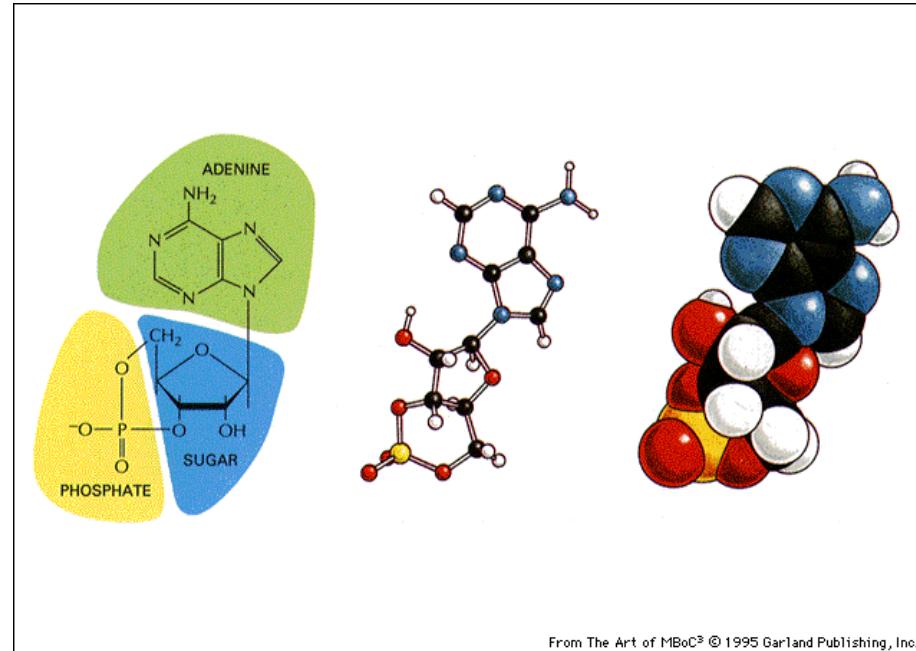
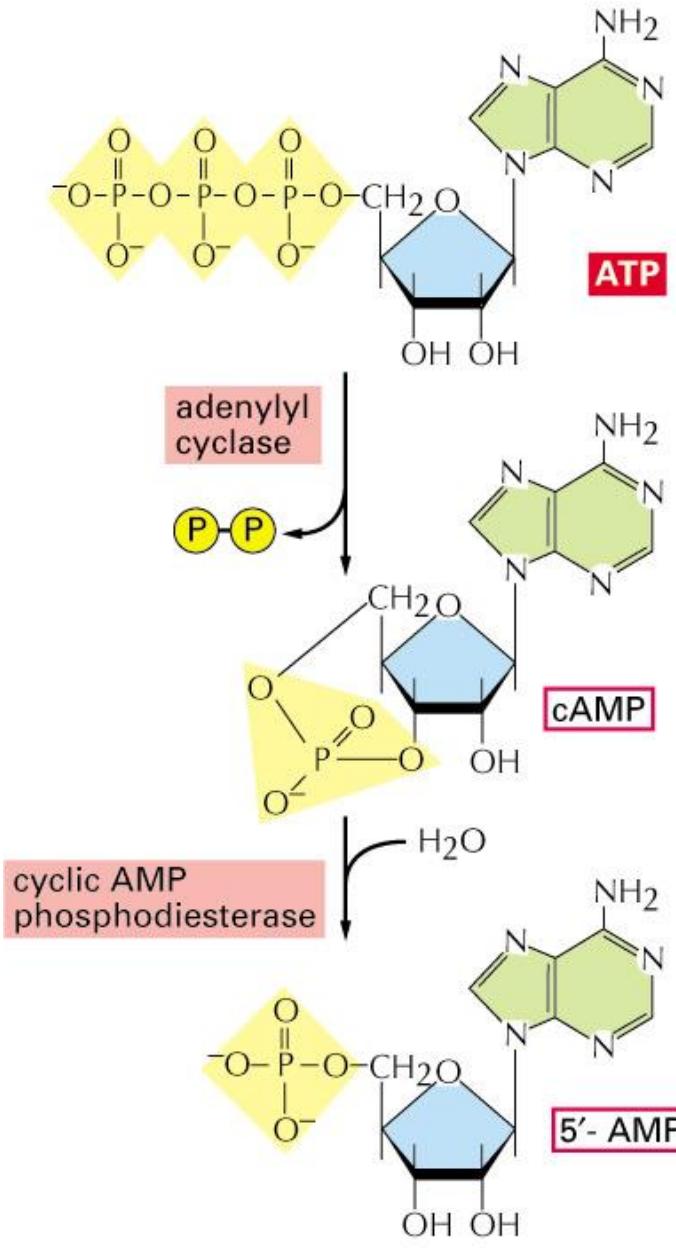


# ESTIMULACION E INHIBICION DE LA ADENILATO CICLASA



# ADENILATO CICLASA





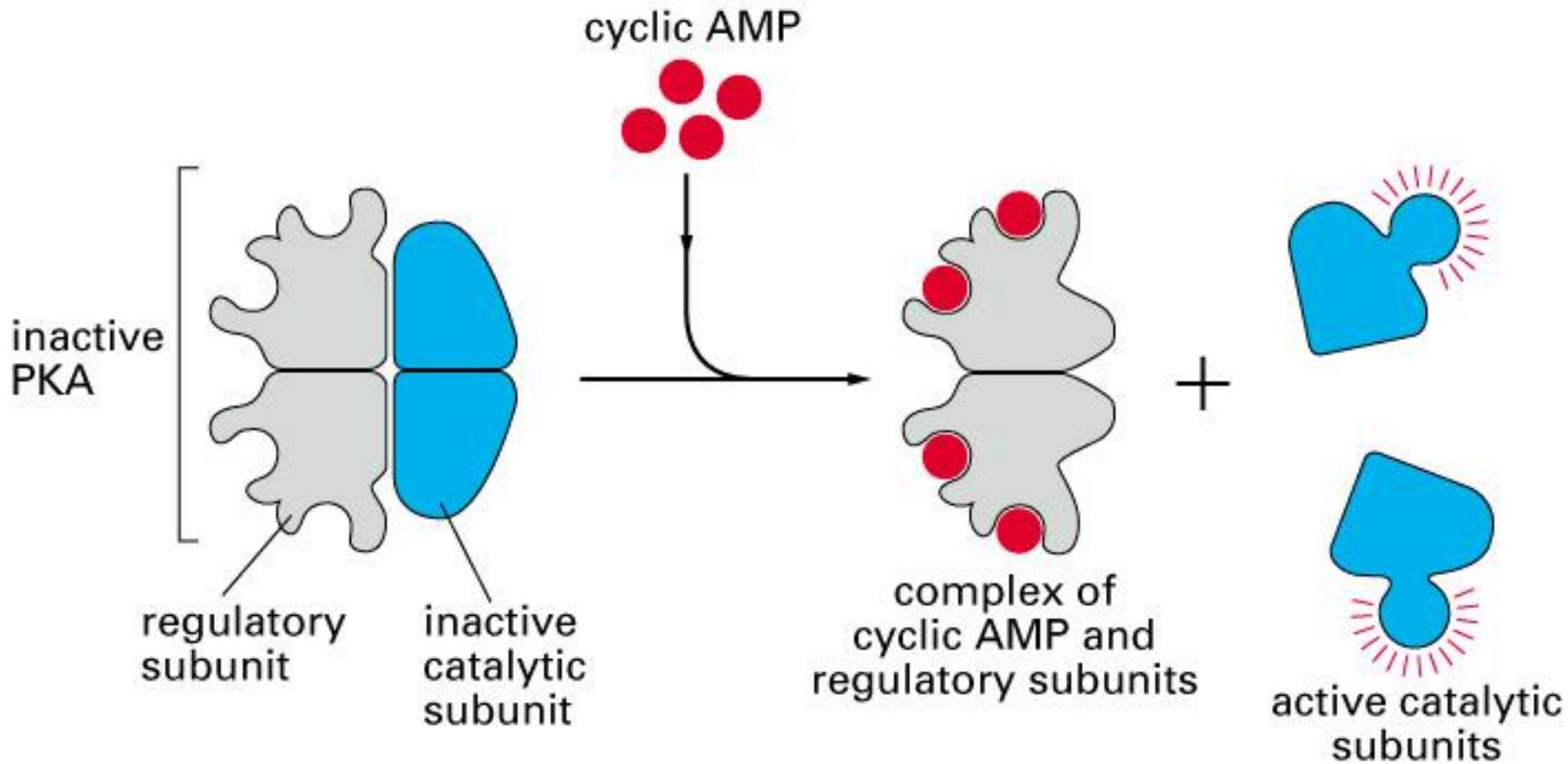
From The Art of MBoC<sup>®</sup> © 1995 Garland Publishing, Inc.

## Inhibidores de PDE (metilxantinas):

- Teofilina (té)
- Cafeína (café)
- Teobromina (chocolate)

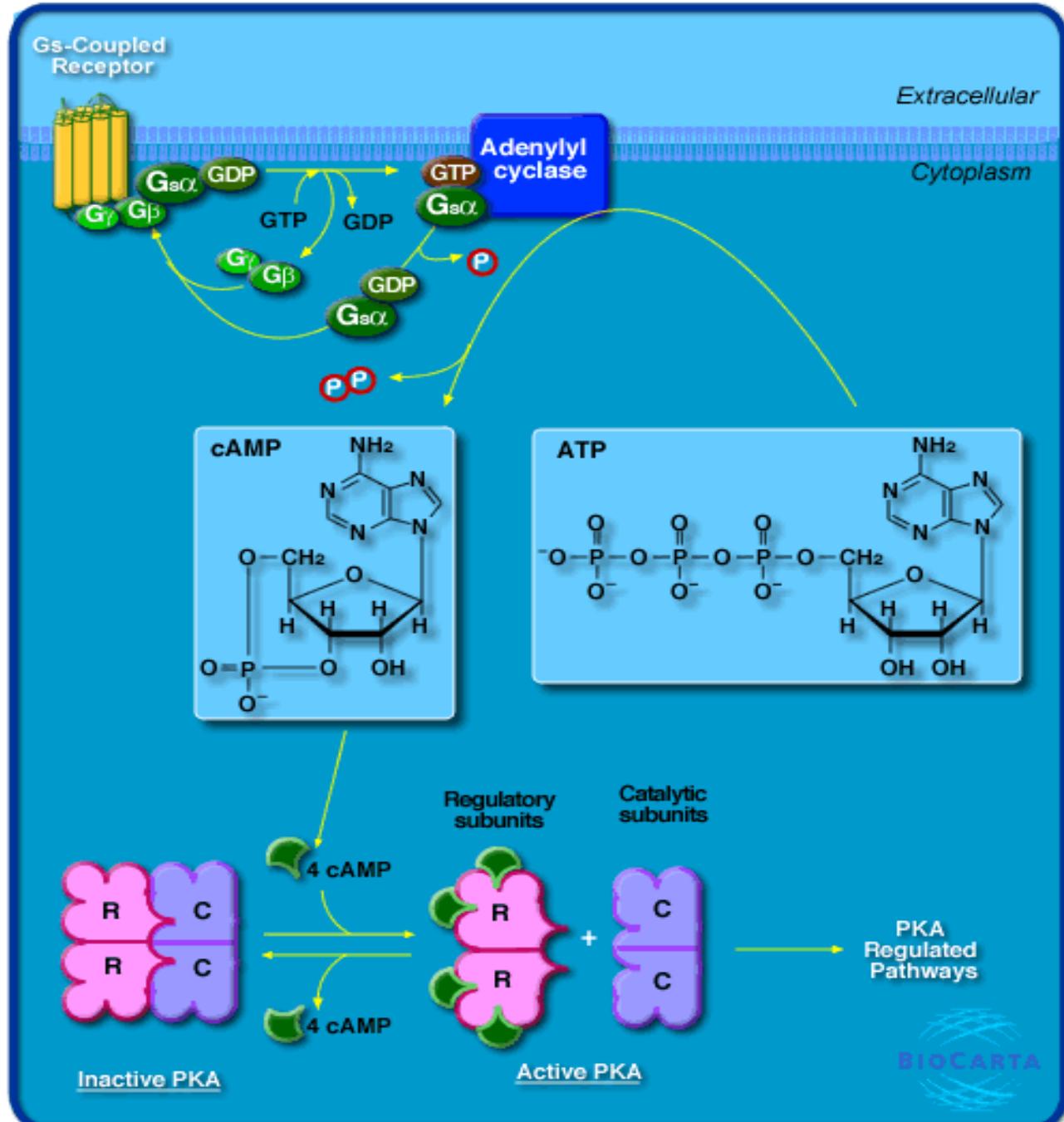
Figure 15–31. Molecular Biology of the Cell, 4th Edition.

# PROTEINA CINASA A (PKA)



La PKA fosforila residuos de Serina y Treonina

# Sistema de Transducción de la Adenilato Ciclase



## Activación del factor de transcripción CREB ("cyclic AMP Response Element Binding") por PKA

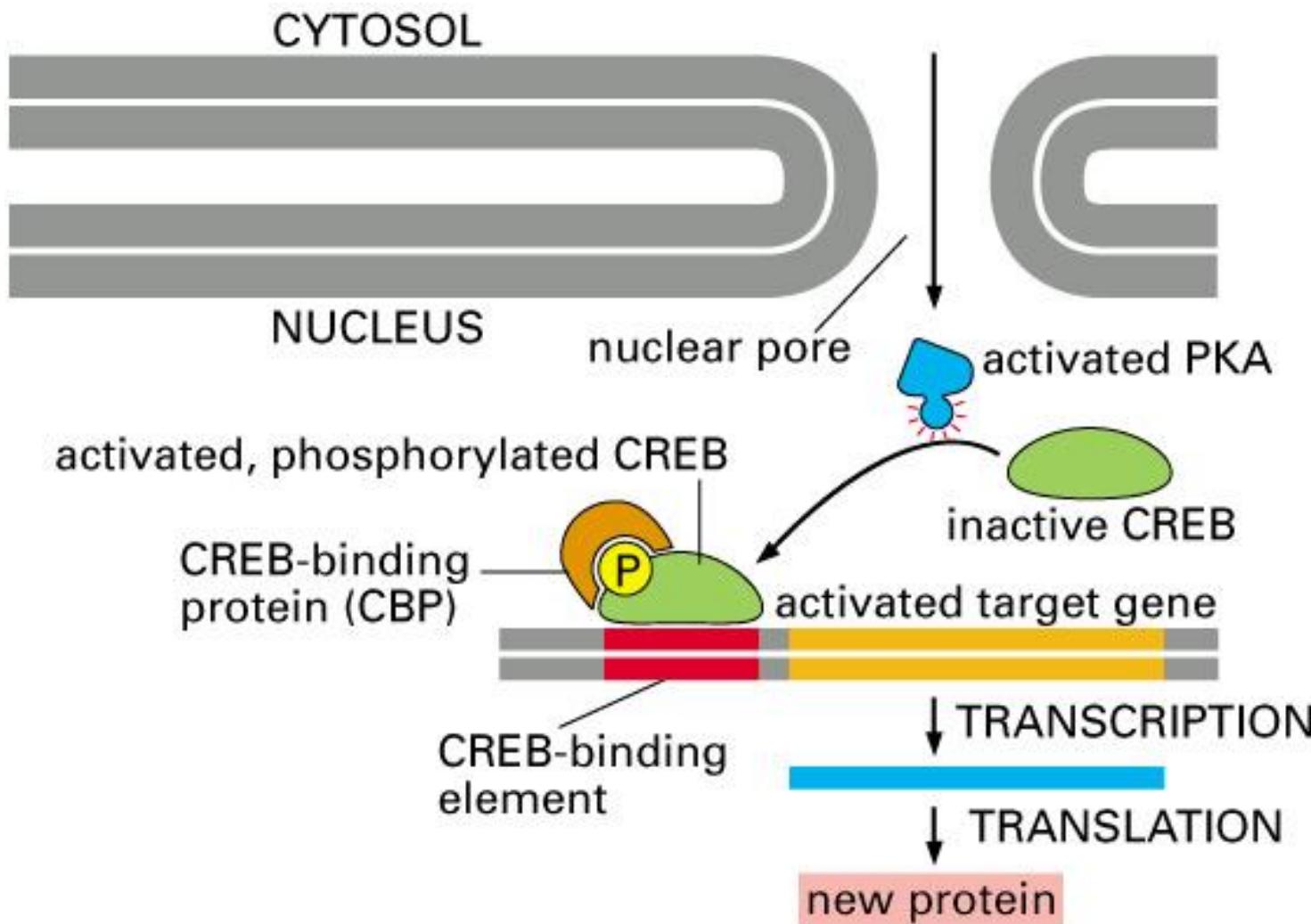
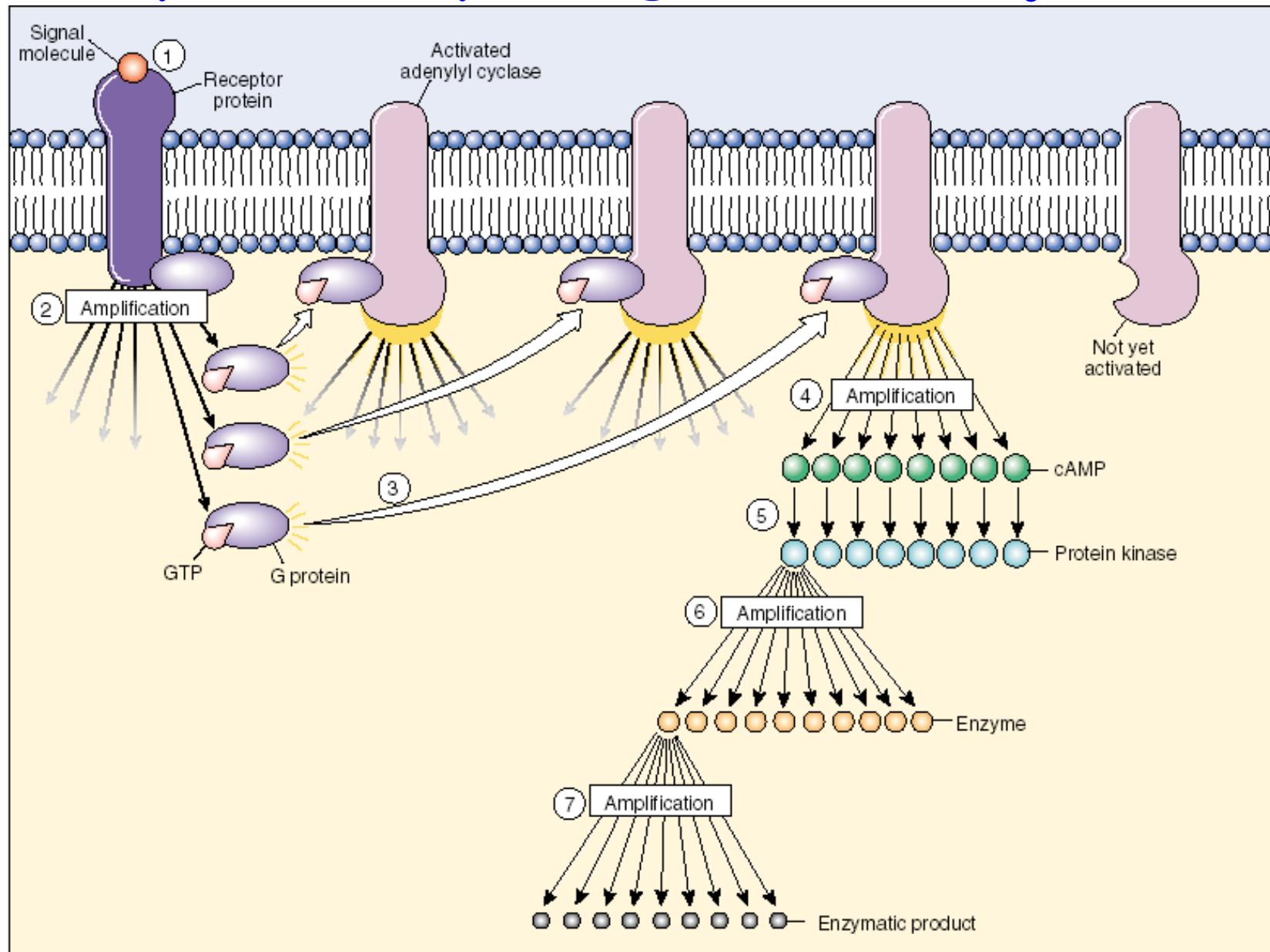
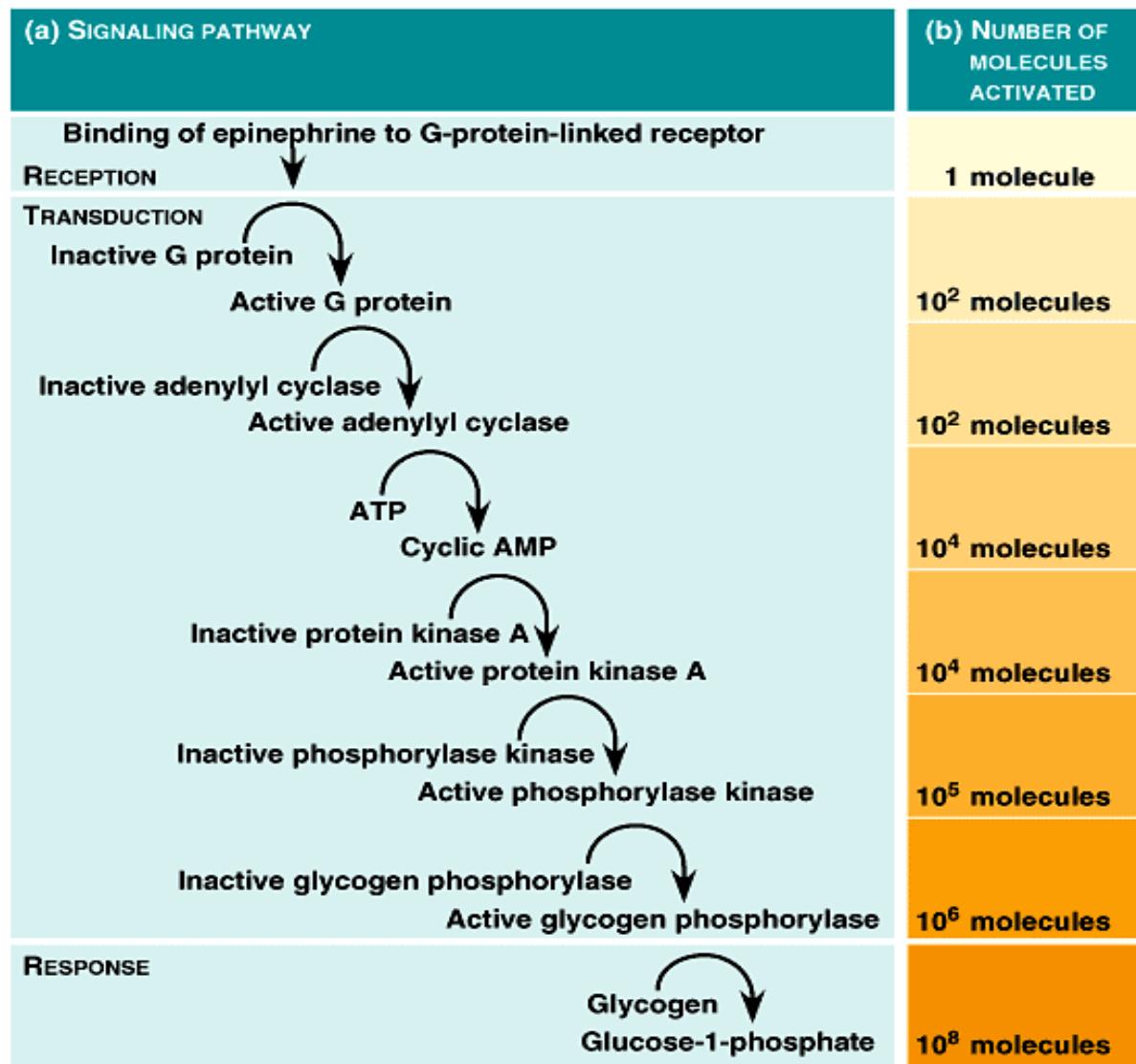


Figure 15–33 part 2 of 2. Molecular Biology of the Cell, 4th Edition.

# Amplificación por Segundos Mensajeros



# Aumento de los niveles de glucosa en sangre por adrenalina (epinefrina)

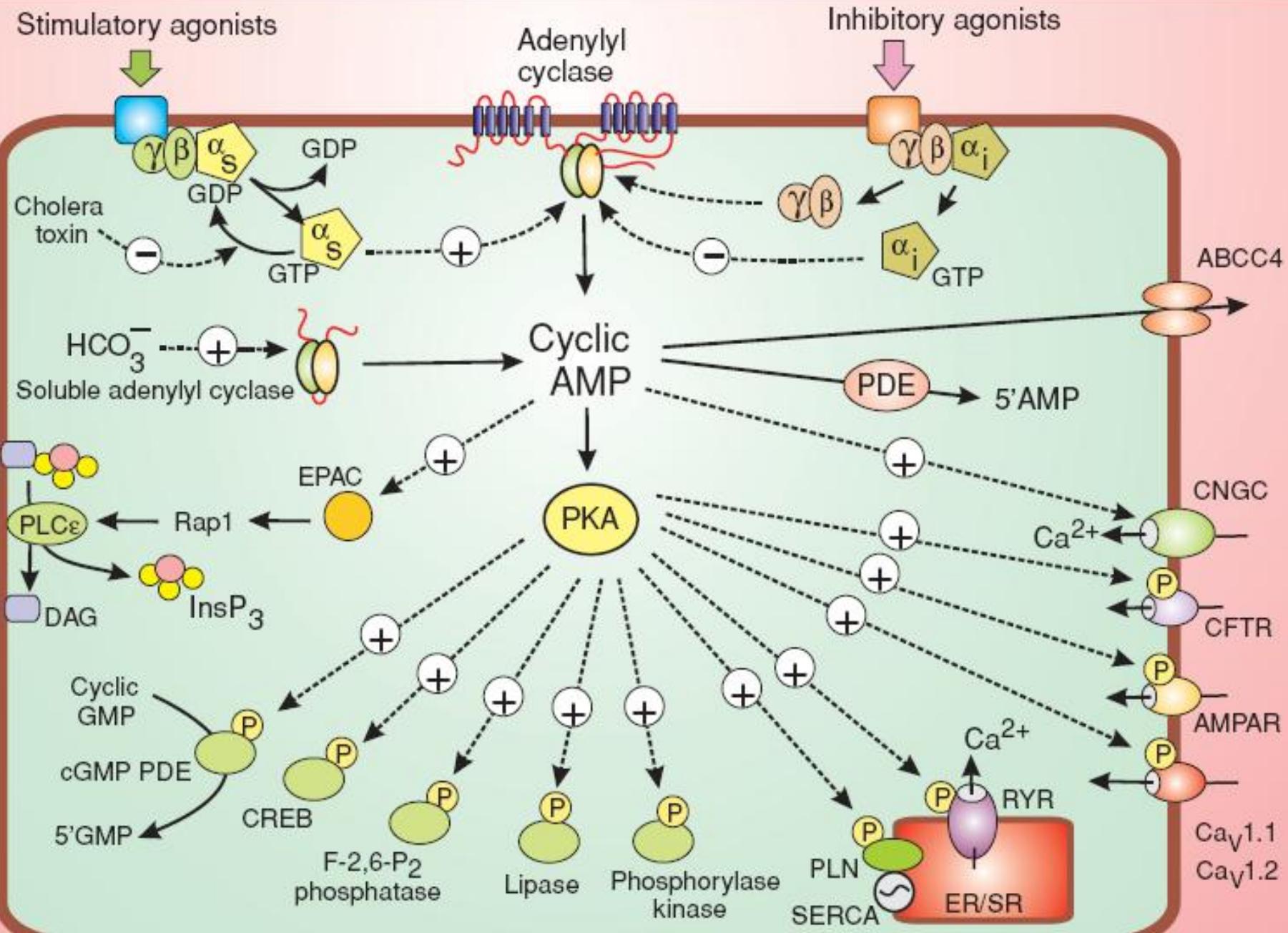


## Glucogenólisis

**TABLE 20-3** Metabolic Responses to Hormone-Induced Rise in cAMP in Various Tissues

Tissue	Hormone Inducing Rise in cAMP	Metabolic Response
Adipose	Epinephrine; ACTH; glucagon	Increase in hydrolysis of triglyceride; decrease in amino acid uptake
Liver	Epinephrine; norepinephrine; glucagon	Increase in conversion of glycogen to glucose; inhibition of synthesis of glycogen; increase in amino acid uptake; increase in gluconeogenesis (synthesis of glucose from amino acids)
Ovarian follicle	FSH; LH	Increase in synthesis of estrogen, progesterone
Adrenal cortex	ACTH	Increase in synthesis of aldosterone, cortisol
Cardiac muscle cells	Epinephrine	Increase in contraction rate
Thyroid	TSH	Secretion of thyroxine
Bone cells	Parathyroid hormone	Increase in resorption of calcium from bone
Skeletal muscle	Epinephrine	Conversion of glycogen to glucose
Intestine	Epinephrine	Fluid secretion
Kidney	Vasopressin	Resorption of water
Blood platelets	Prostaglandin I	Inhibition of aggregation and secretion

SOURCE: E. W. Sutherland, 1972, *Science* 177:401.

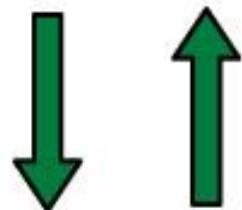


**GLUCAGON**

GLUCÓGENO

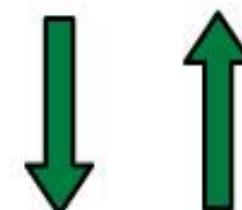
**INSULINA**

Glucogenólisis



Glucogenogénesis

Glucólisis



Gluconeogénesis

**INSULINA**

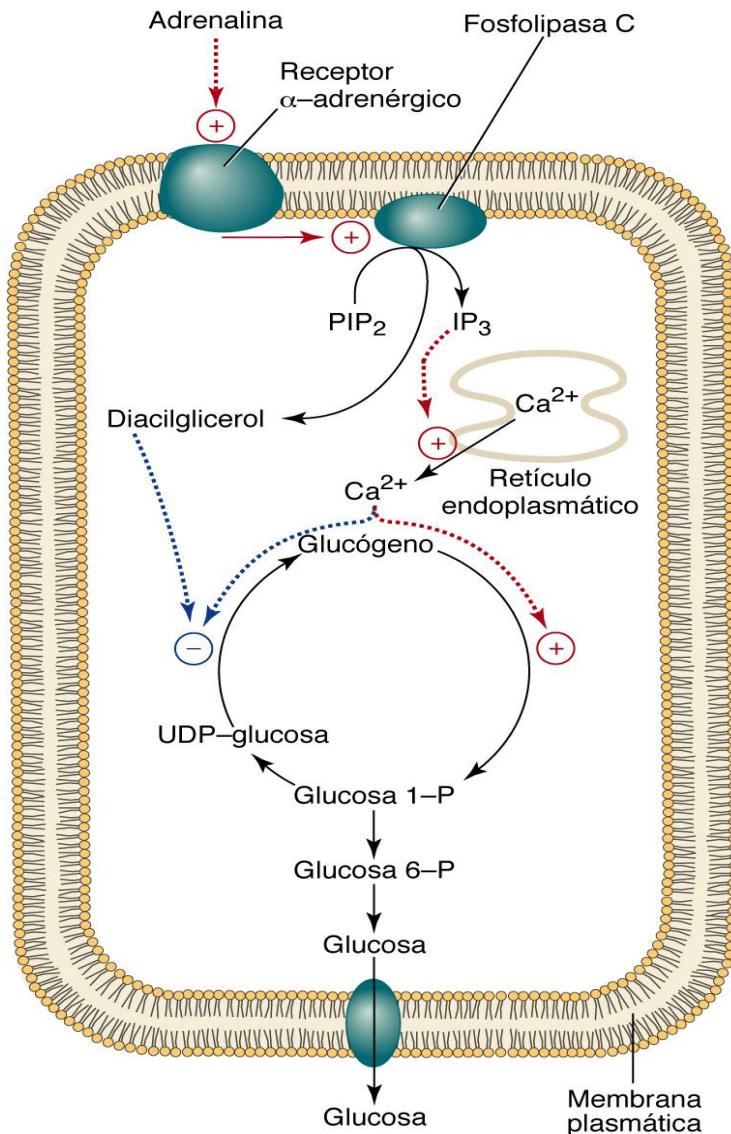
**GLUCAGON**

## FIGURA 14.1

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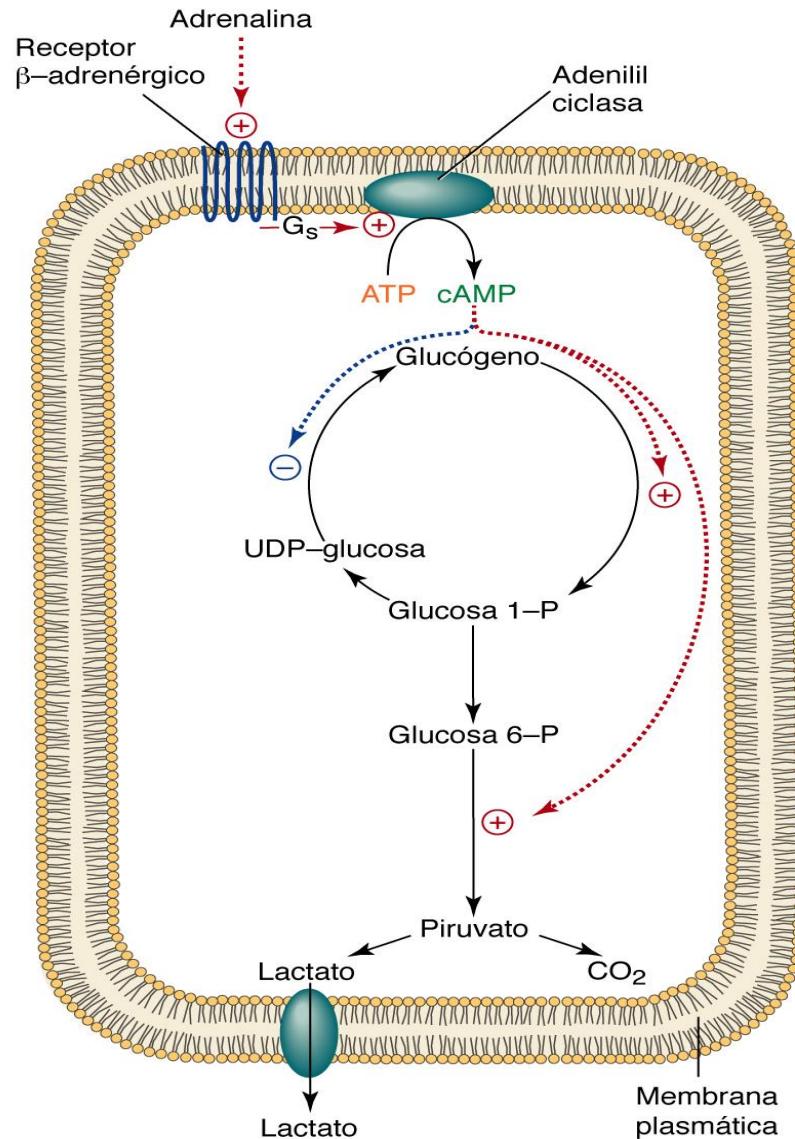
*Bioquímica. Libro de texto con aplicaciones clínicas 4<sup>a</sup> Ed.*

# ADRENALINA



**FIGURA 14.62**

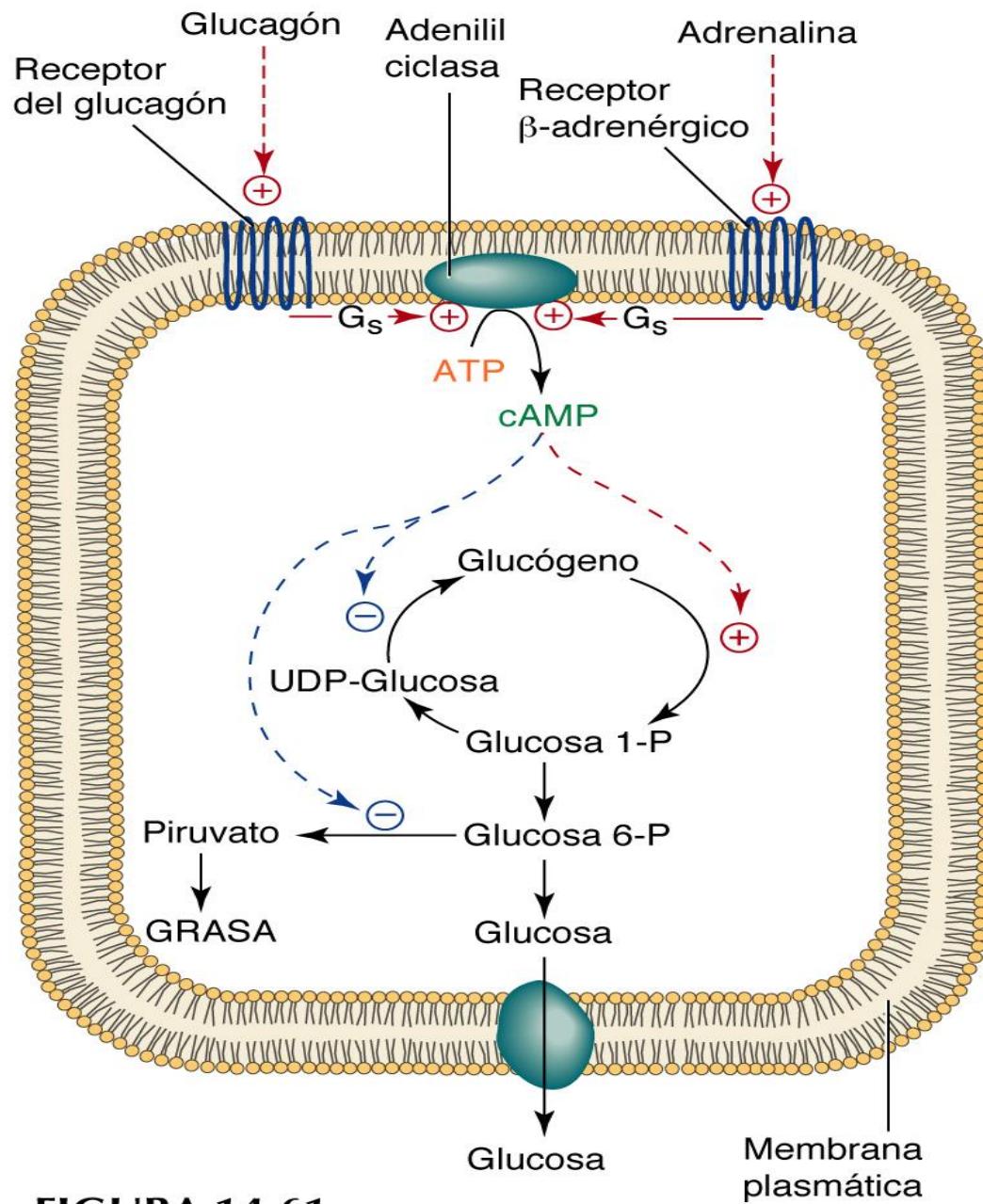
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**FIGURA 14.64**

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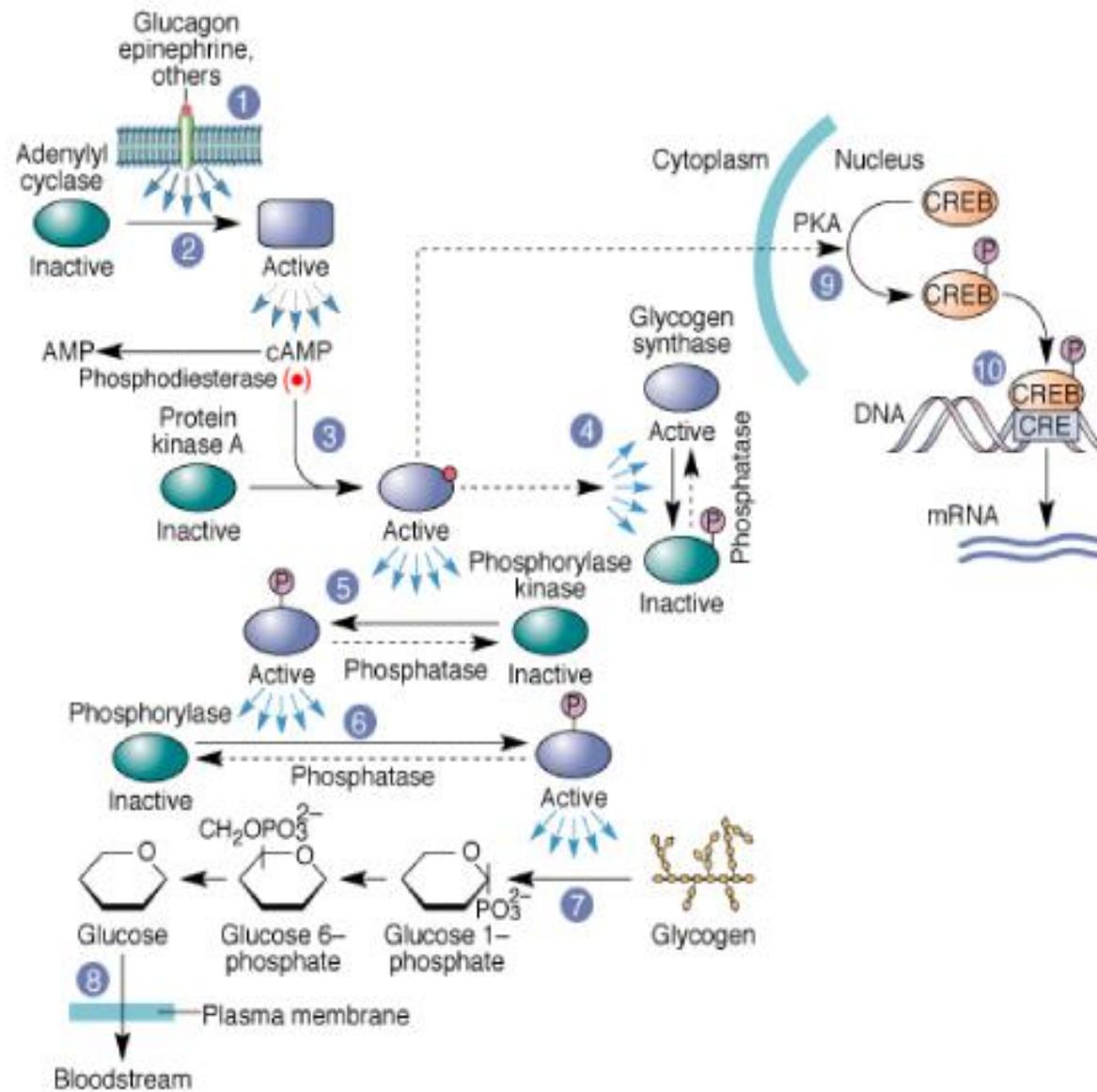
# ADRENALINA y GLUCAGÓN



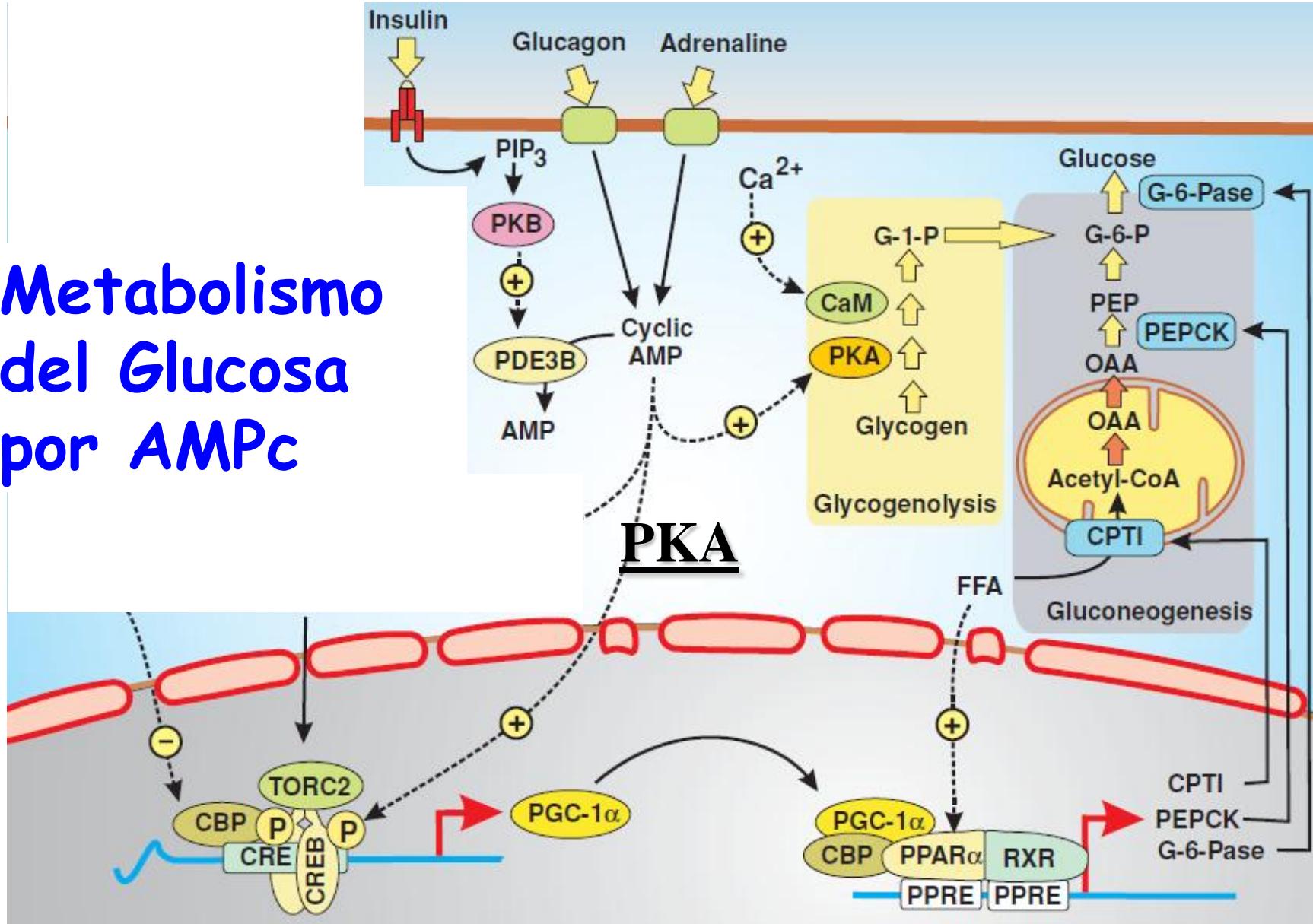
**FIGURA 14.61**

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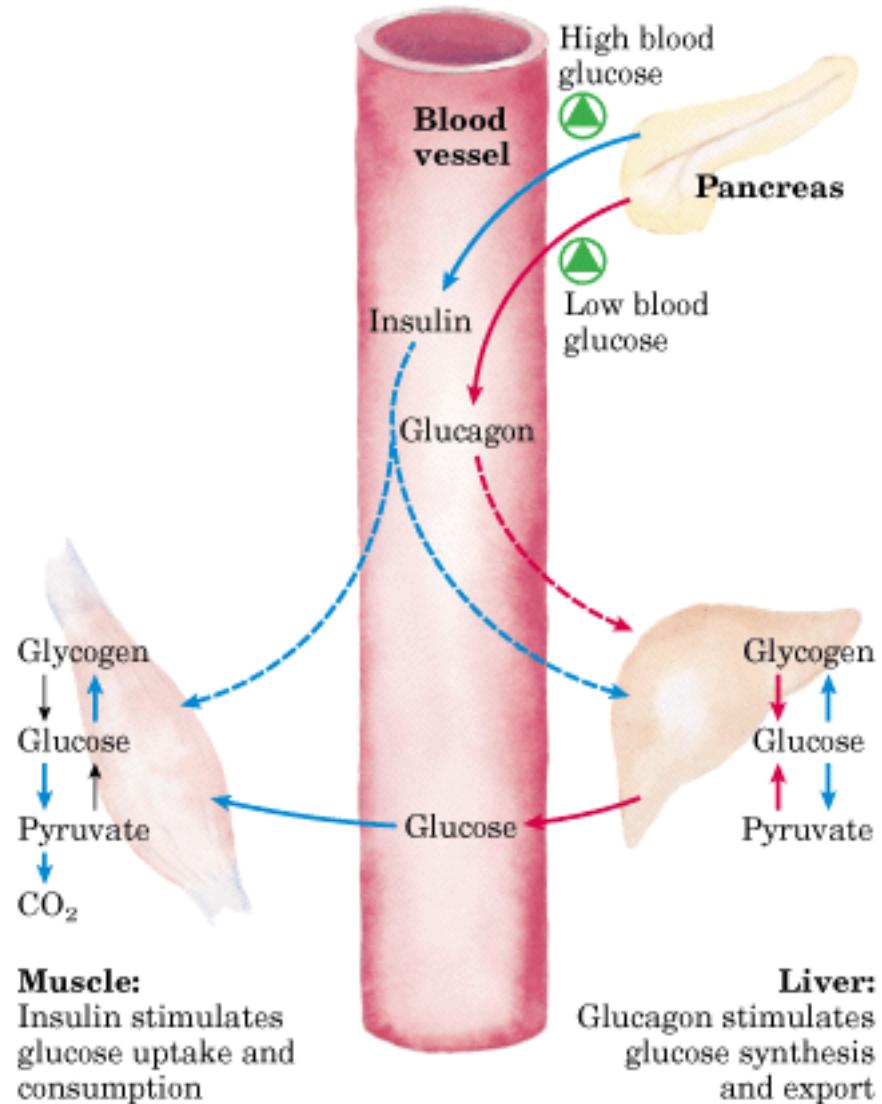
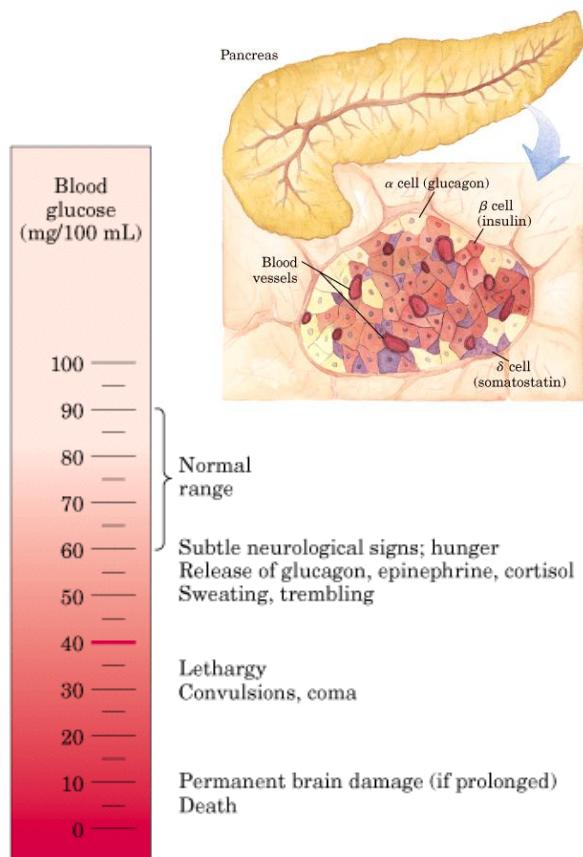
# PKA activa la glucogenólisis



# Metabolismo del Glucosa por AMPc



# Comunicación Celular en la regulación del metabolismo



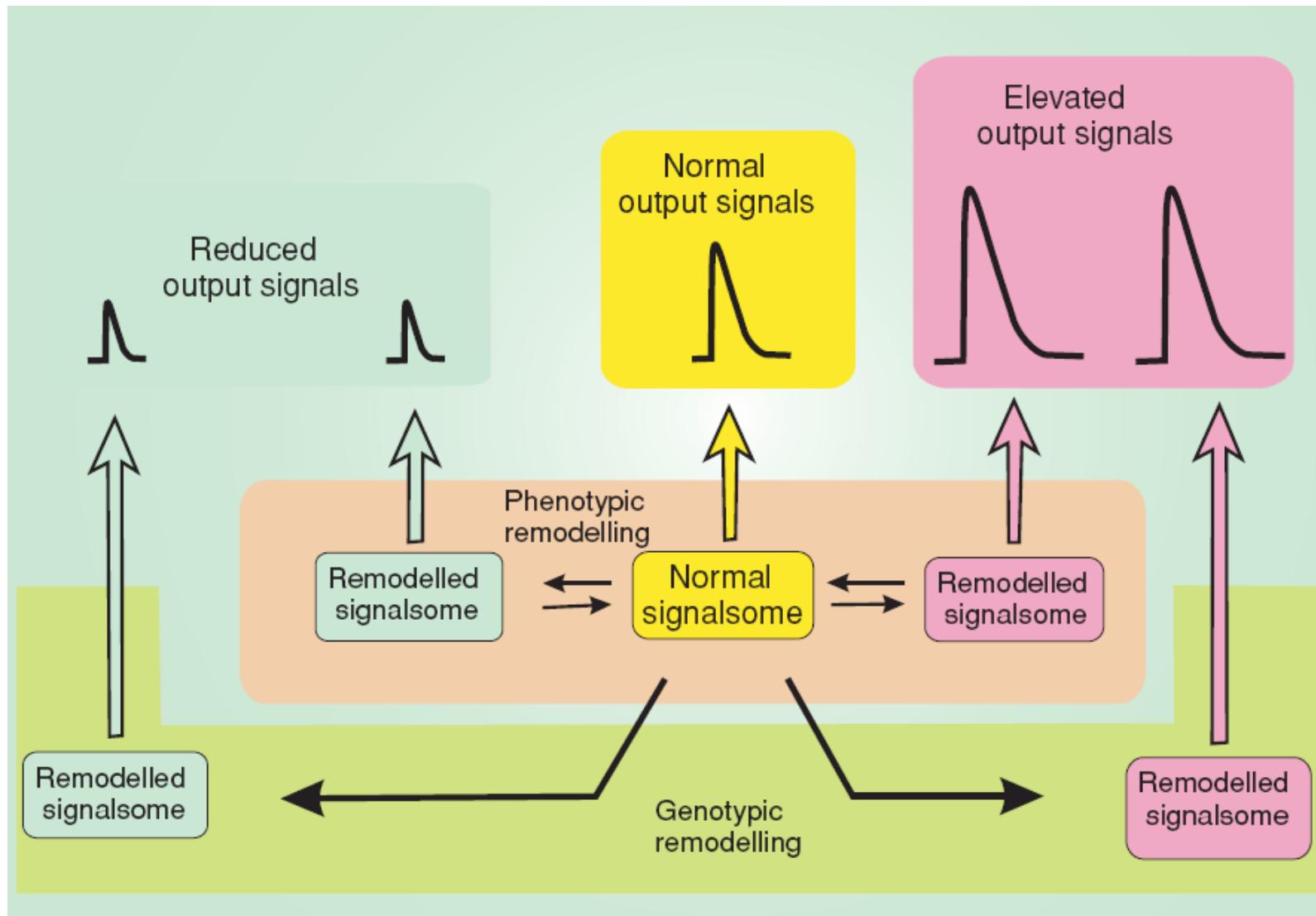
# **DESENSIBILIZACION**

## **(TOLERANCIA)**

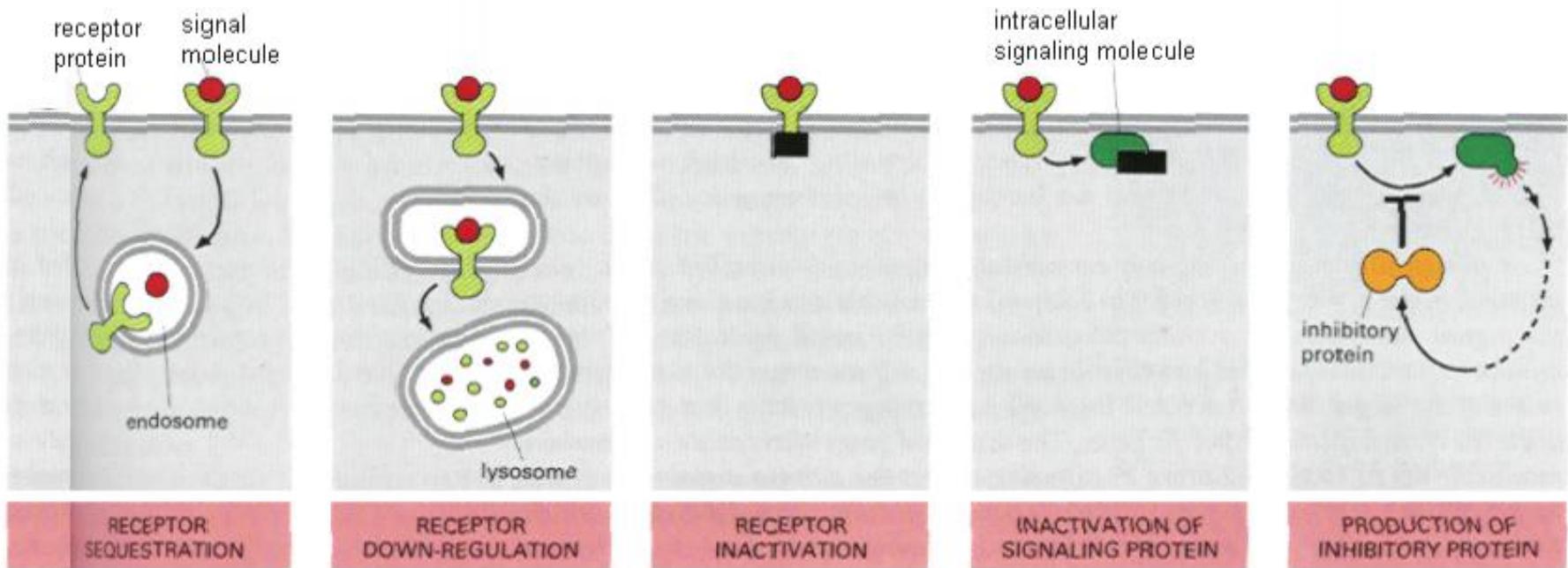
## TIPOS de Desensibilización:

- Desensibilización homóloga  
(disminución de la señal por el mismo ligando)
- Desensibilización heteróloga  
(disminución de la señal por un ligando o vía diferente)

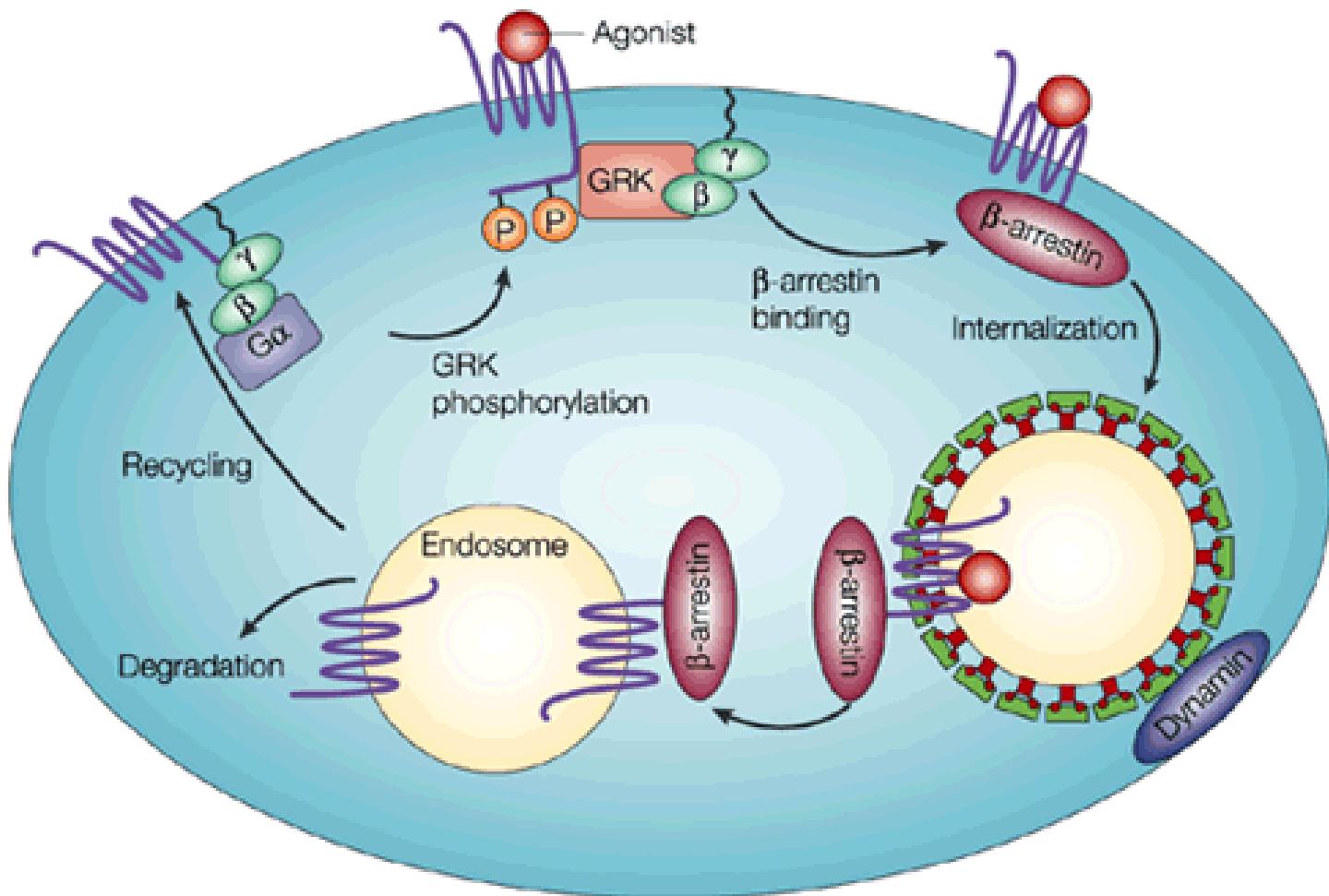
# Señalosoma

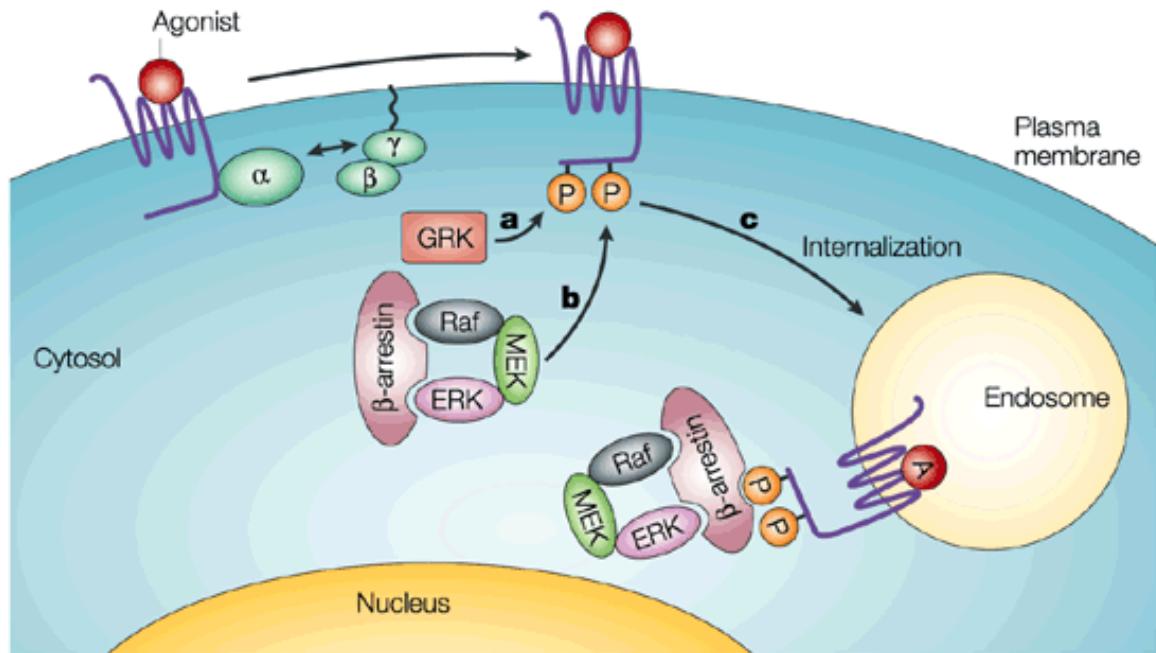


# Desensibilización de los GPCRs



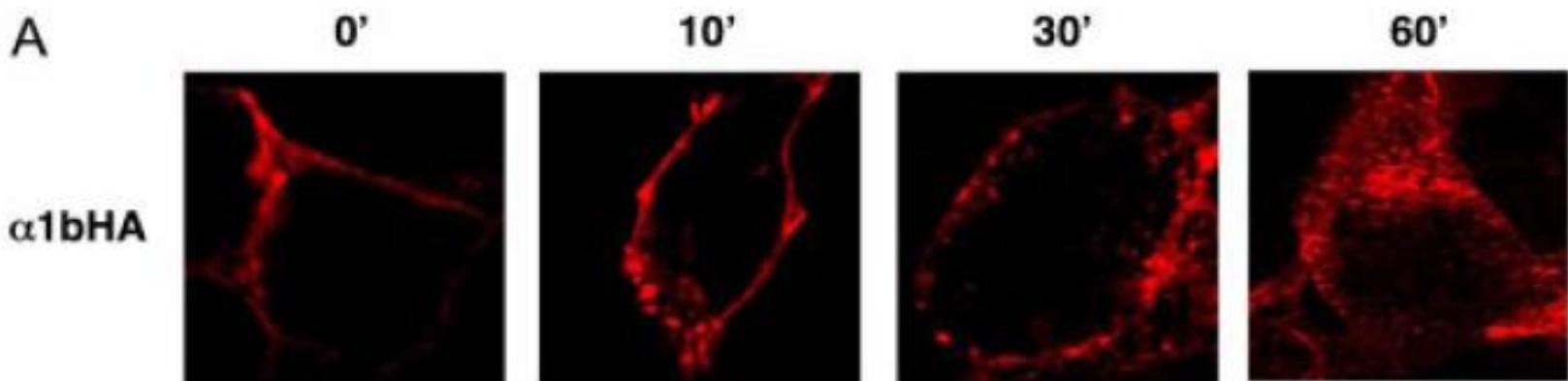
# Desensibilización de los GPCRs



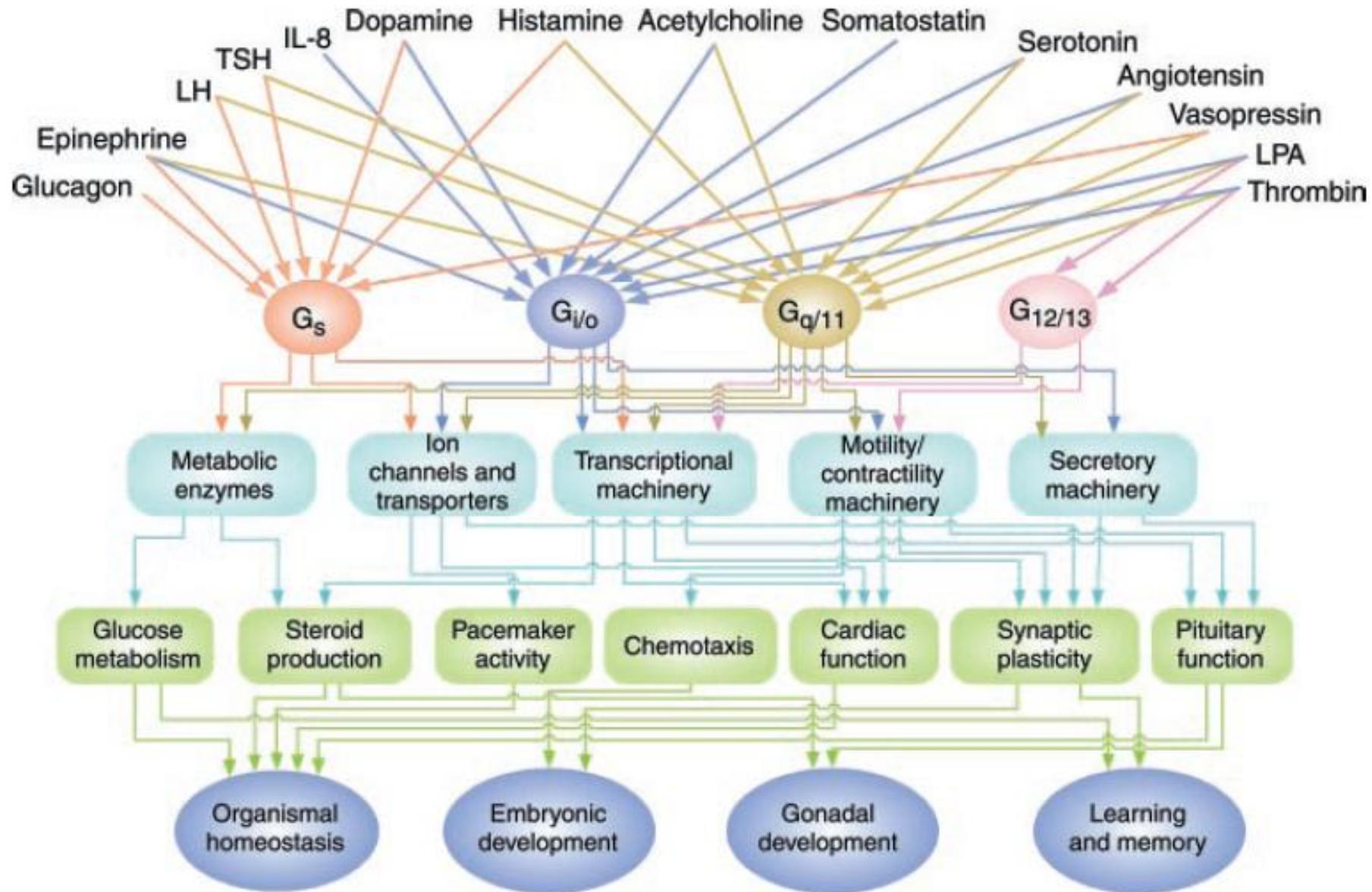


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# Sistemas de Transducción de los GPCRs



# Signaling Receptome: A Genomic and Evolutionary Perspective of Plasma Membrane Receptors Involved in Signal Transduction

