

# **SEÑALIZACION CELULAR**

**Organismos unicelulares semejantes a las bacterias actuales se conocen desde hace unos 3,5 billones de años**

**La aparición de los primeros organismos multicelulares tomó mas de 2,5 billones de años.**

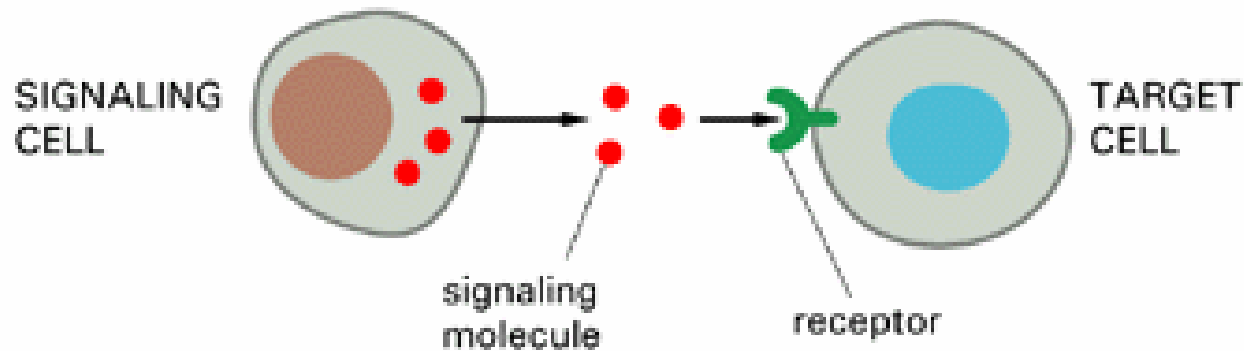
**¿Por qué la multicelularidad tomó tantos años en desarrollarse?**

**Elaboración de mecanismos de señalización intercelulares que permitan una conversación entre células diversas (célula capaz de generar una señal y una célula blanco)**

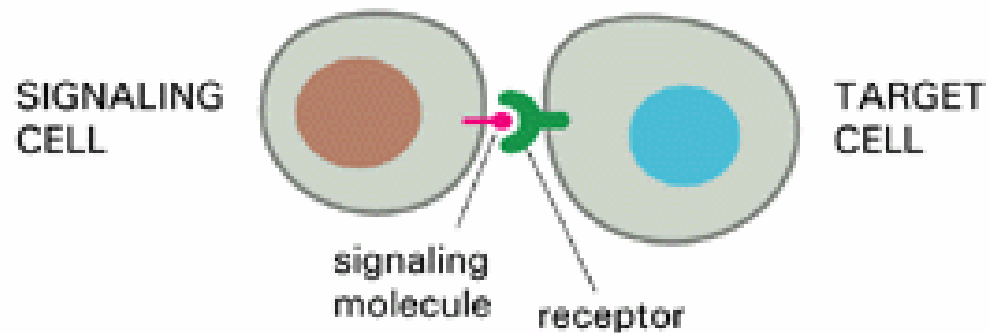
**Maquinaria compleja de elaboración de señales para posicionar y determinar una función de una célula en un organismo (célula blanco)**

# Señalización intercelular en organismos animales

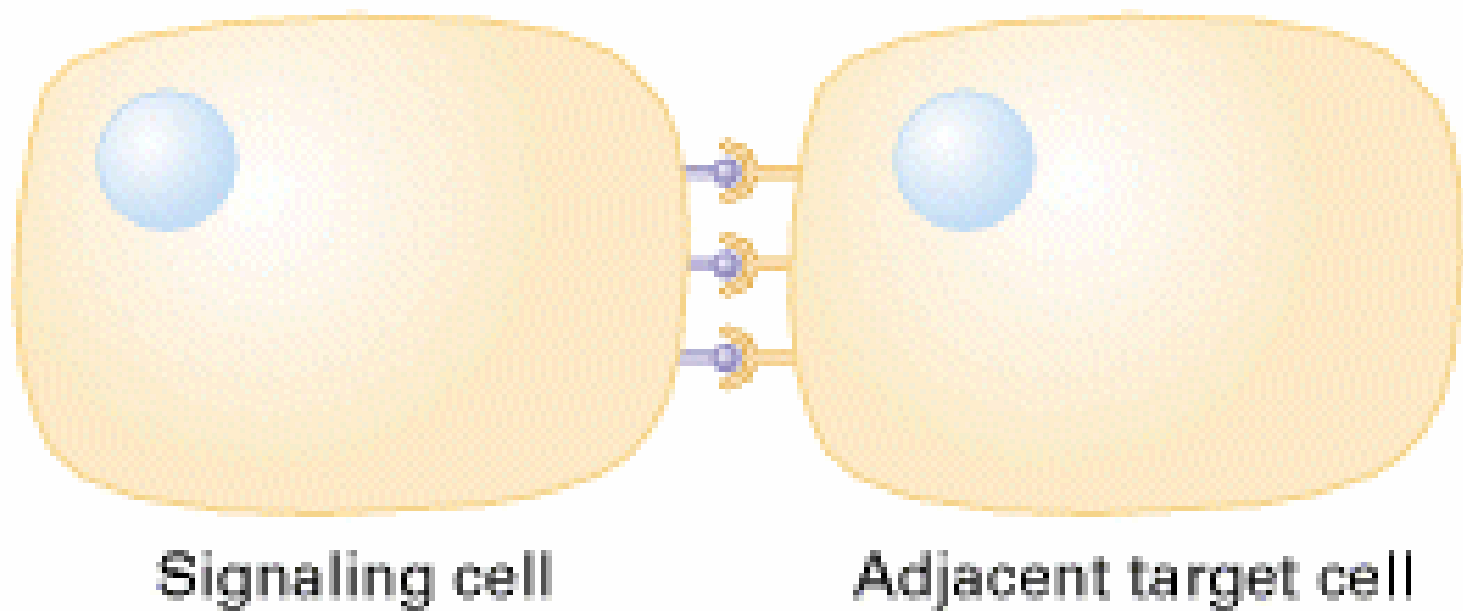
## SIGNALING BY SECRETED MOLECULES



## SIGNALING BY PLASMA-MEMBRANE-BOUND MOLECULES

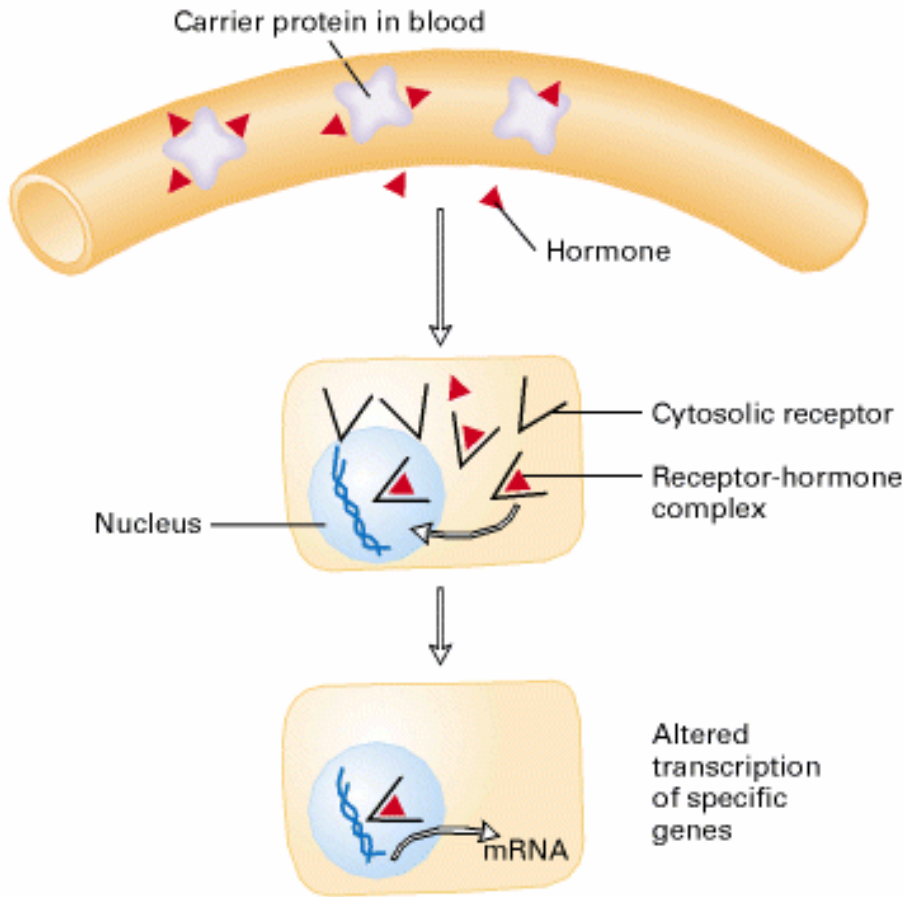


(d) Signaling by plasma membrane-attached proteins

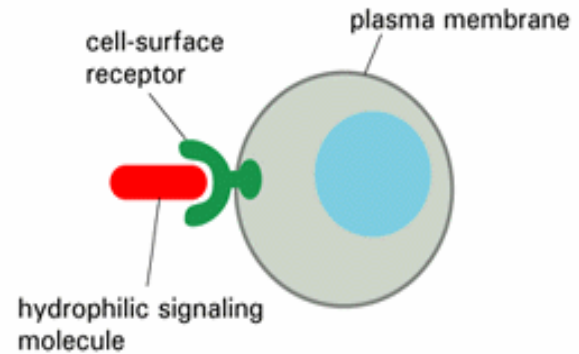


# Receptores de superficie o citoplasmáticos reciben señales externas

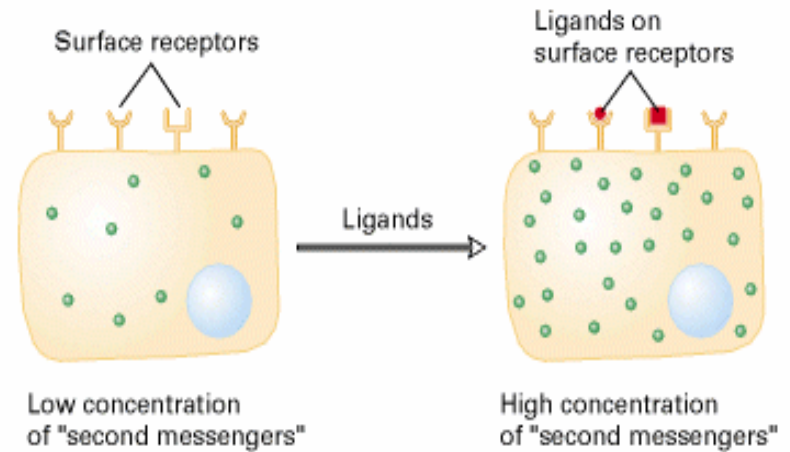
(a) Intracellular receptors



CELL-SURFACE RECEPTORS

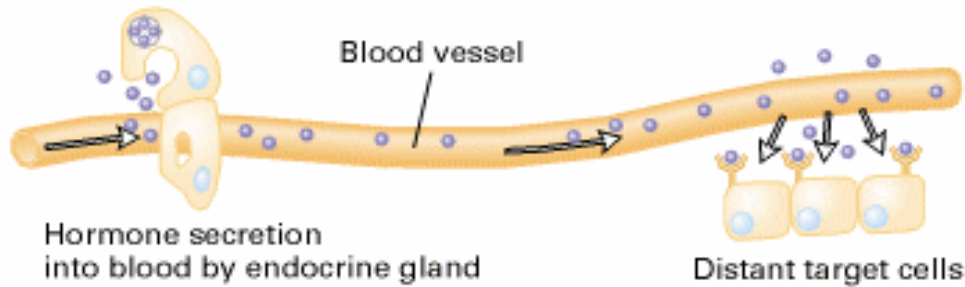


(b) Cell surface receptors

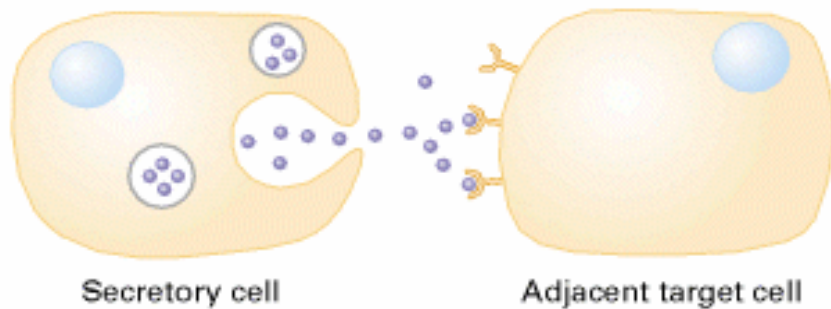


# Diferentes formas de señalización mediada por moléculas secretadas

## (a) señal endocrina



## (b) Paracrine signaling



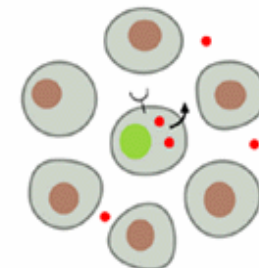
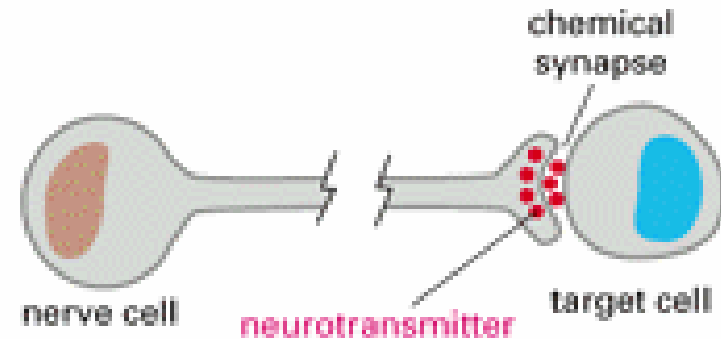
## (c) Autocrine signaling



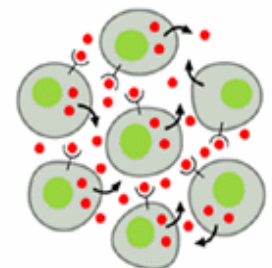
Key:

- Extracellular signal
- Y Receptor
- Membrane-attached signal

## SYNAPTIC



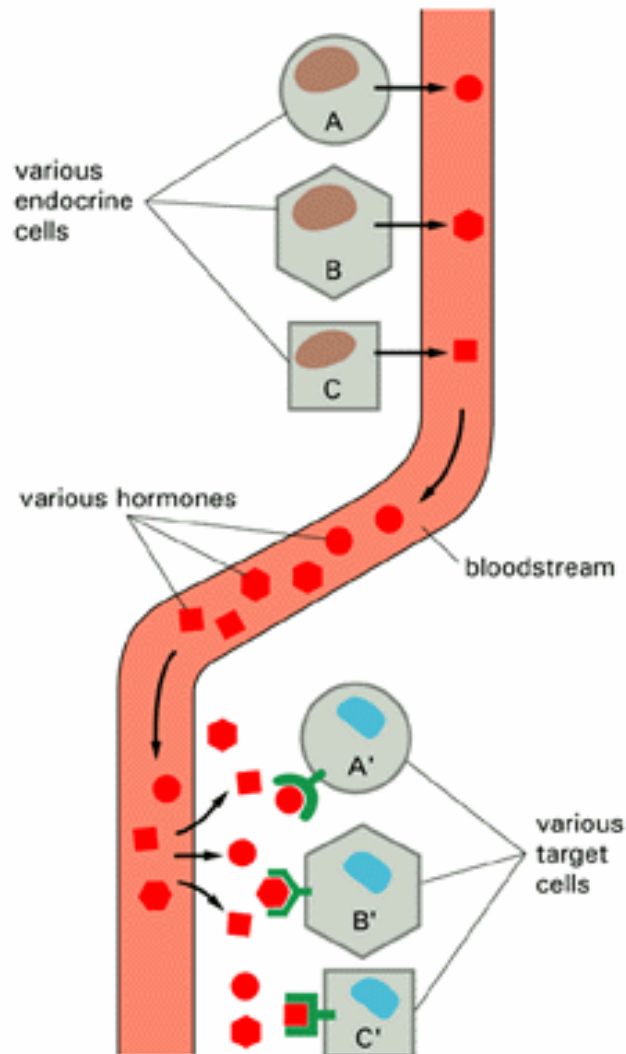
A SINGLE SIGNALING CELL RECEIVES WEAK AUTOCRINE SIGNAL



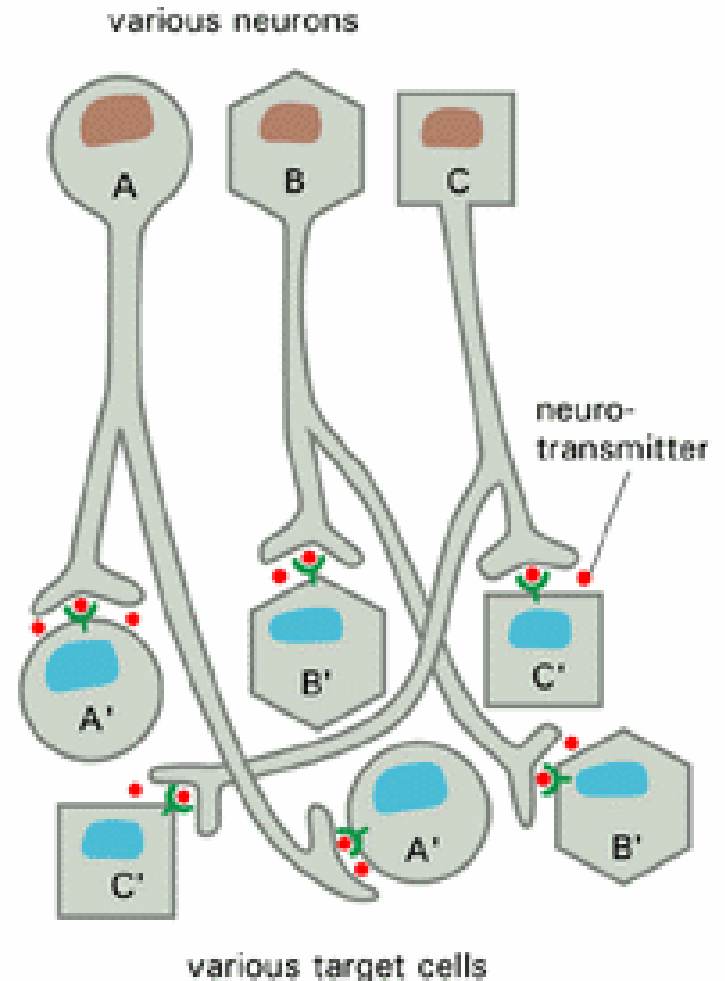
IN A GROUP OF IDENTICAL SIGNALING CELLS, EACH CELL RECEIVES A STRONG AUTOCRINE SIGNAL

# Contraste entre la señalización sináptica y endocrina

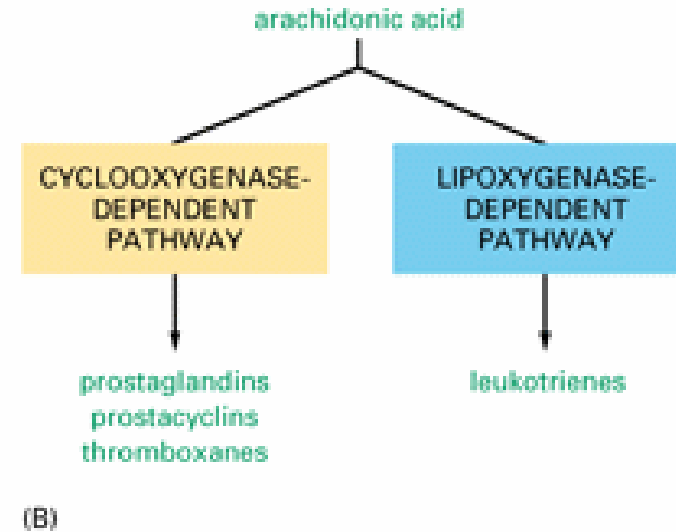
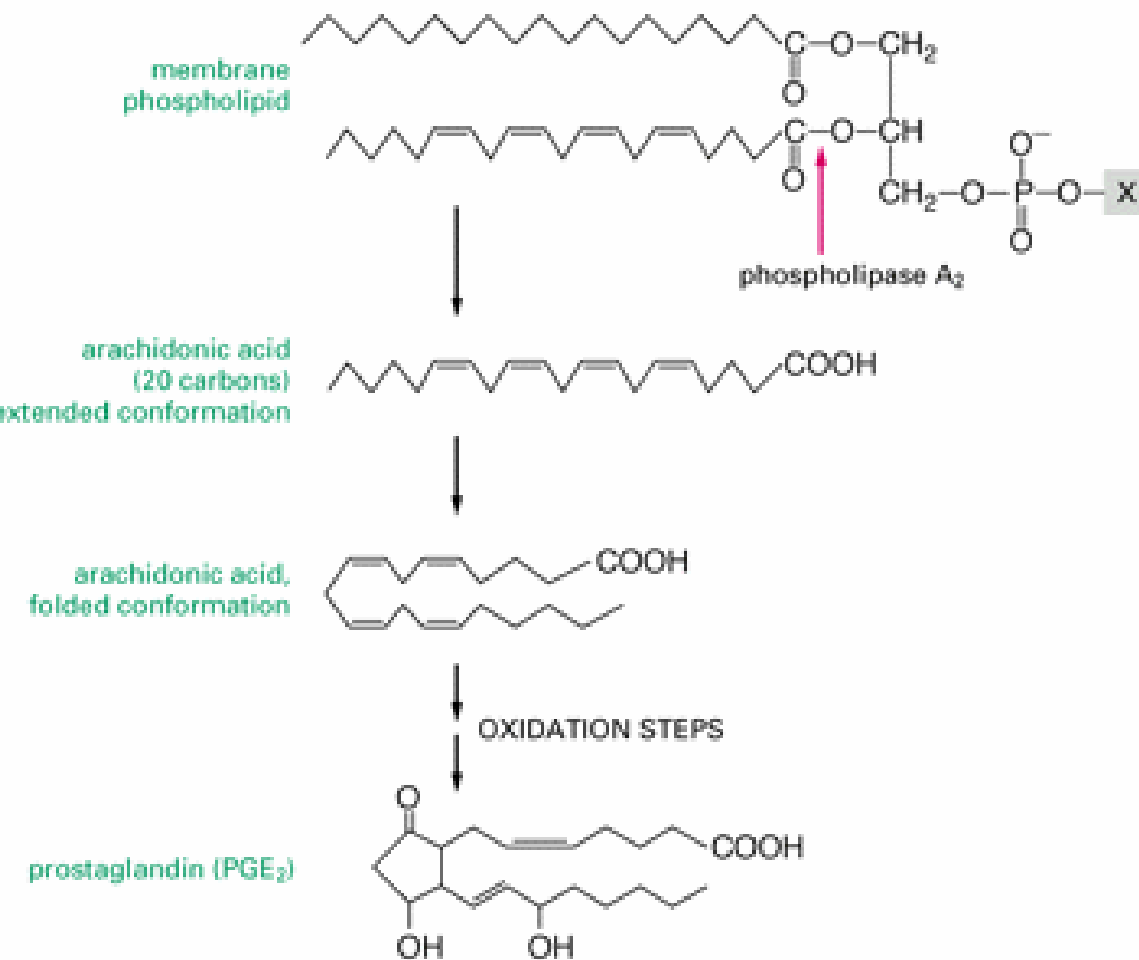
(A) ENDOCRINE SIGNALING

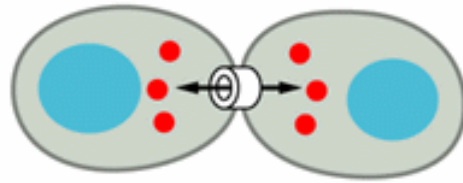


(B) SYNAPTIC SIGNALING



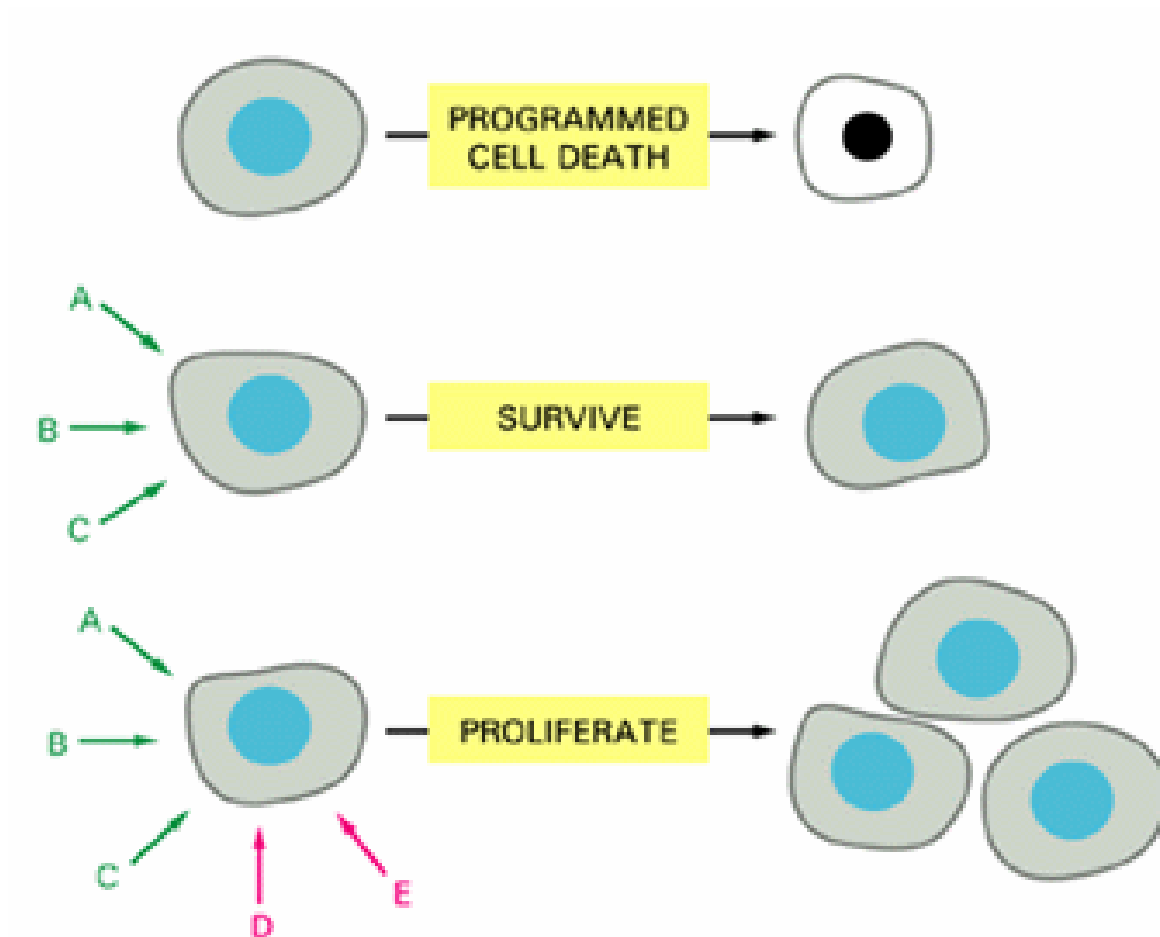
# Síntesis de Eicosanoides





## Uniones Gap

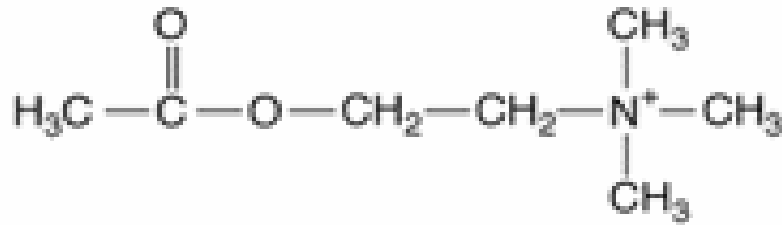
### Combinación de señales y respuesta funcional de la célula





# Una misma señal puede inducir diferentes respuestas en diferentes células blanco

(D) acetylcholine



(A) skeletal muscle cell

acetylcholine

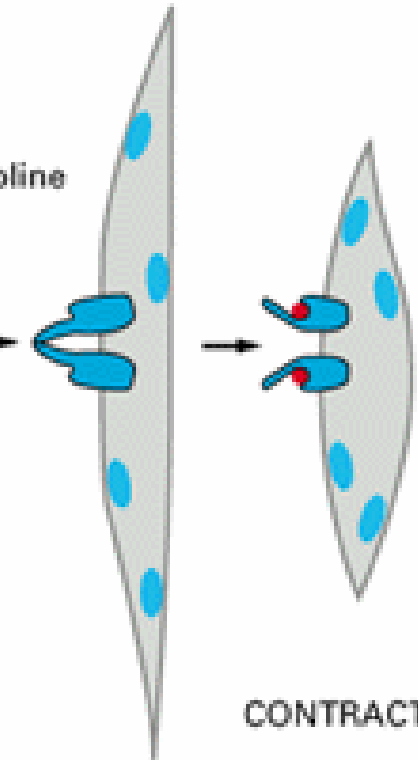
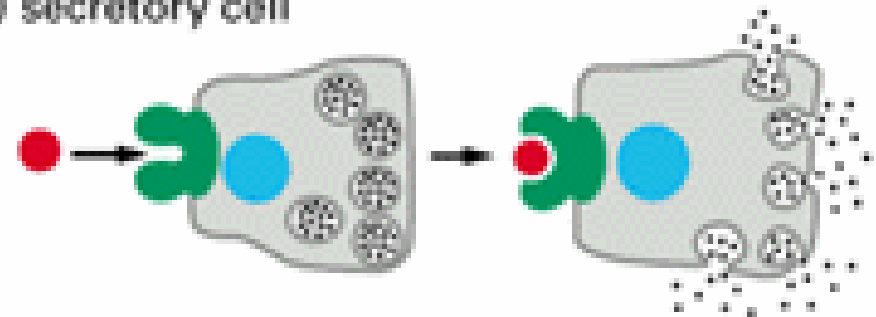
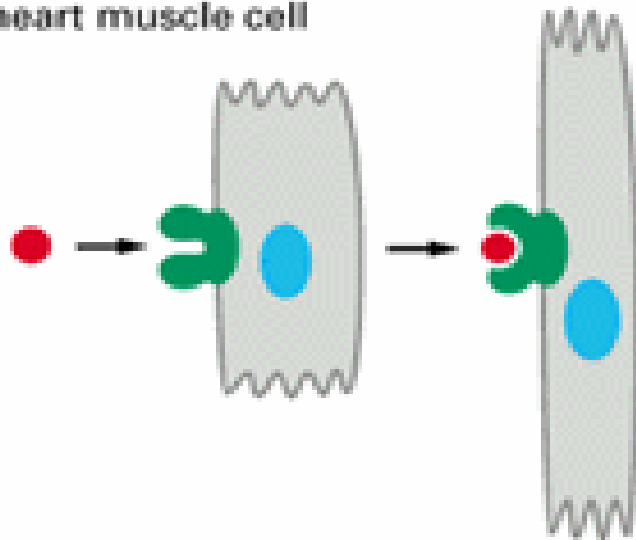
CONTRACTION

RELAJACION

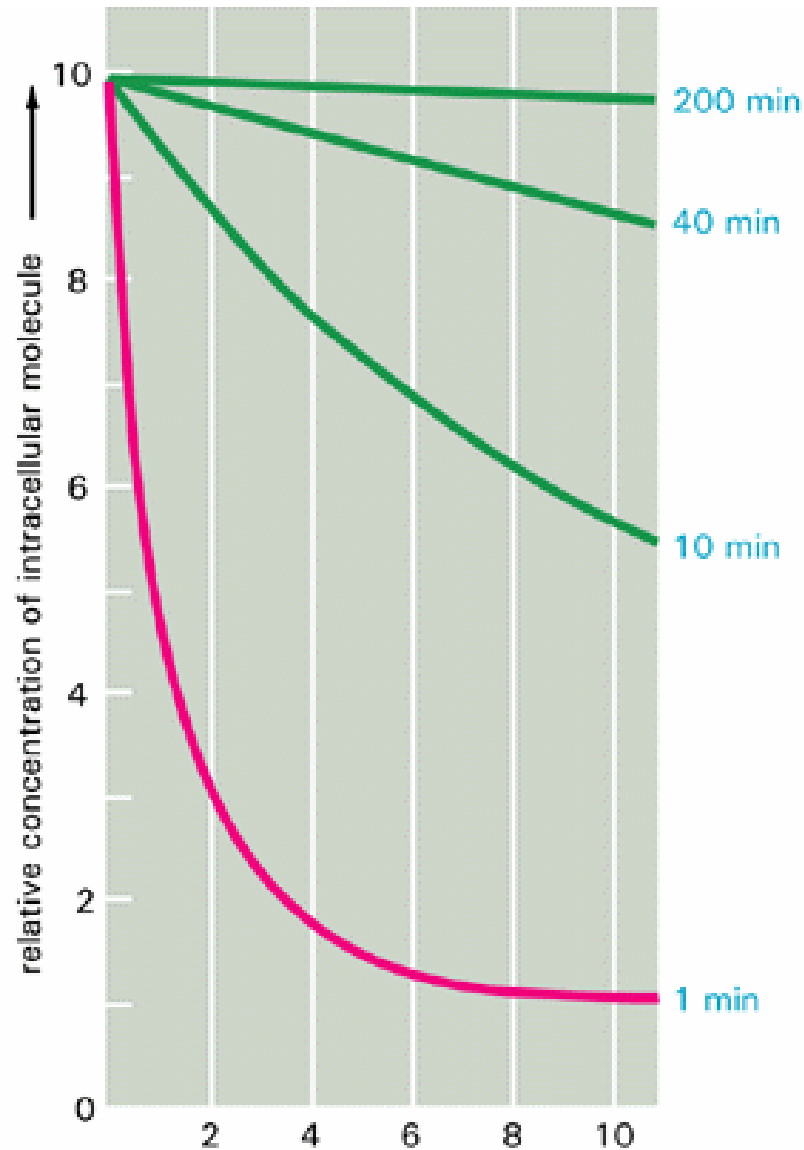
(C) secretory cell

SECRETION

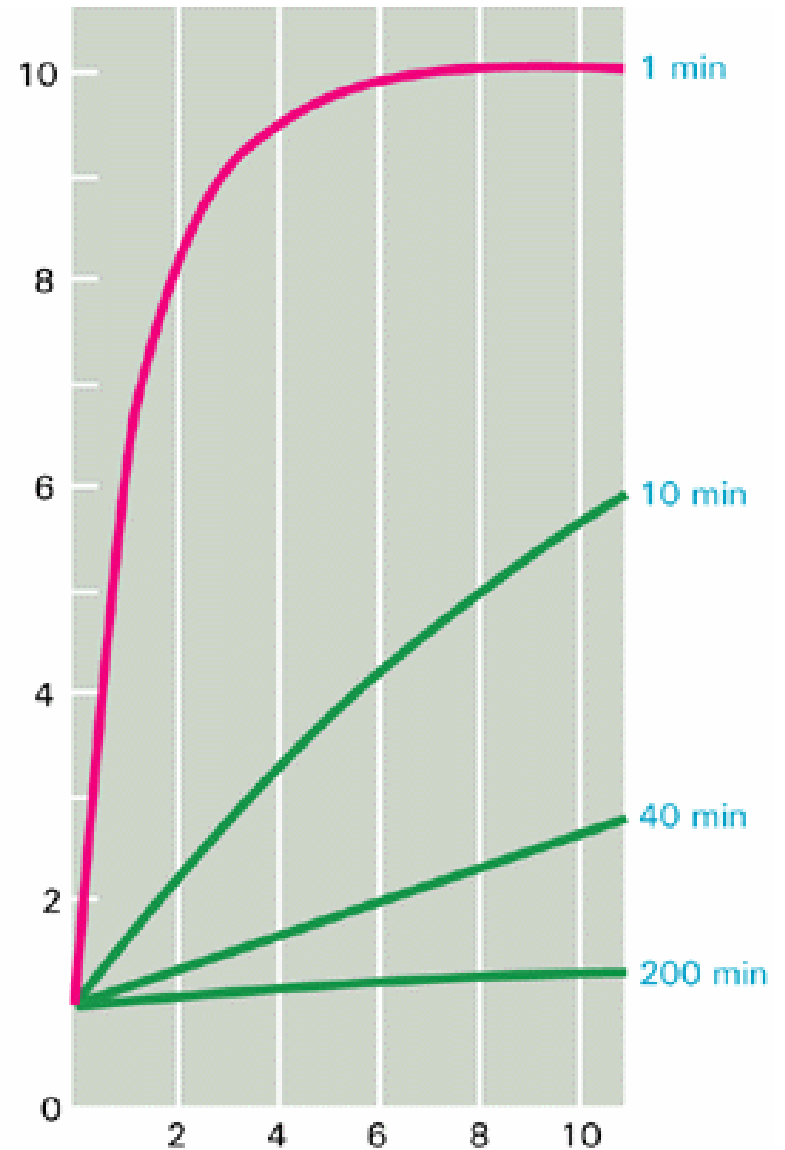
(B) heart muscle cell



# La importancia de un recambio rápido de moléculas

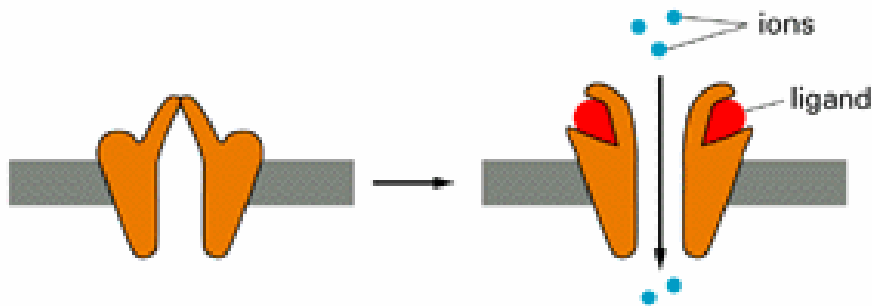


minutes after the synthesis rate has been *decreased* by a factor of 10



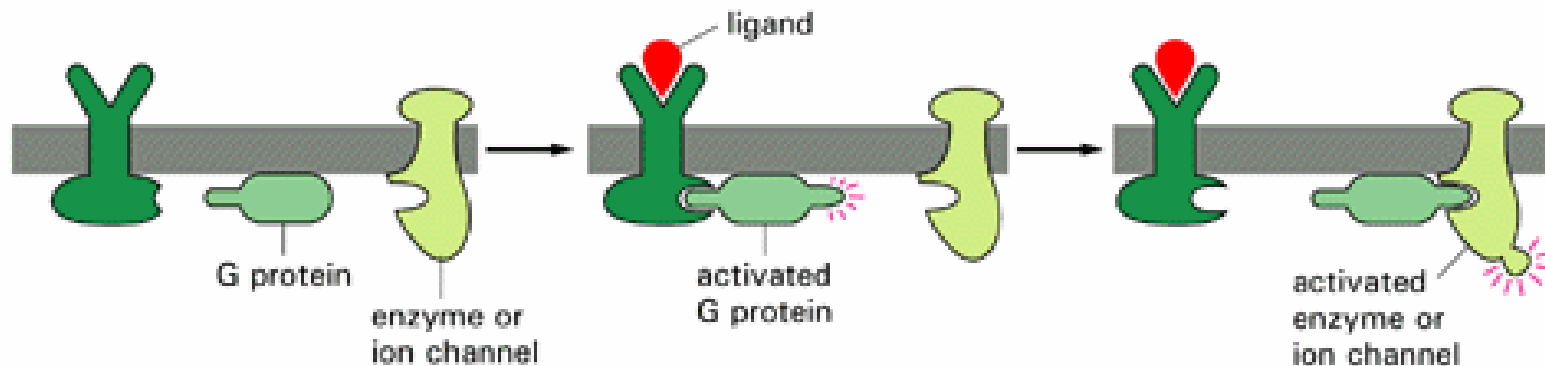
minutes after the synthesis rate has been *increased* by a factor of 10

(A) ION-CHANNEL-LINKED RECEPTOR

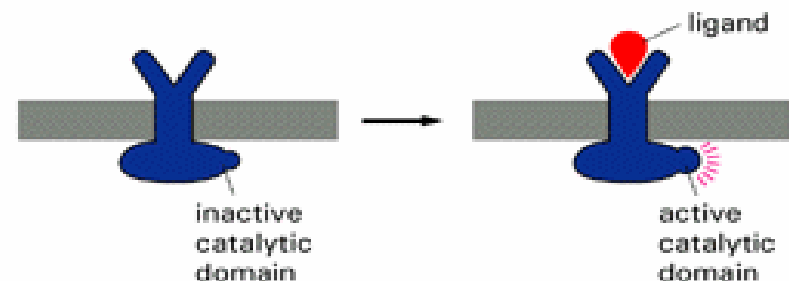


Tres tipos de receptores celulares de superficie y presentes en la membrana plásmatica de la célula

(B) G-PROTEIN-LINKED RECEPTOR

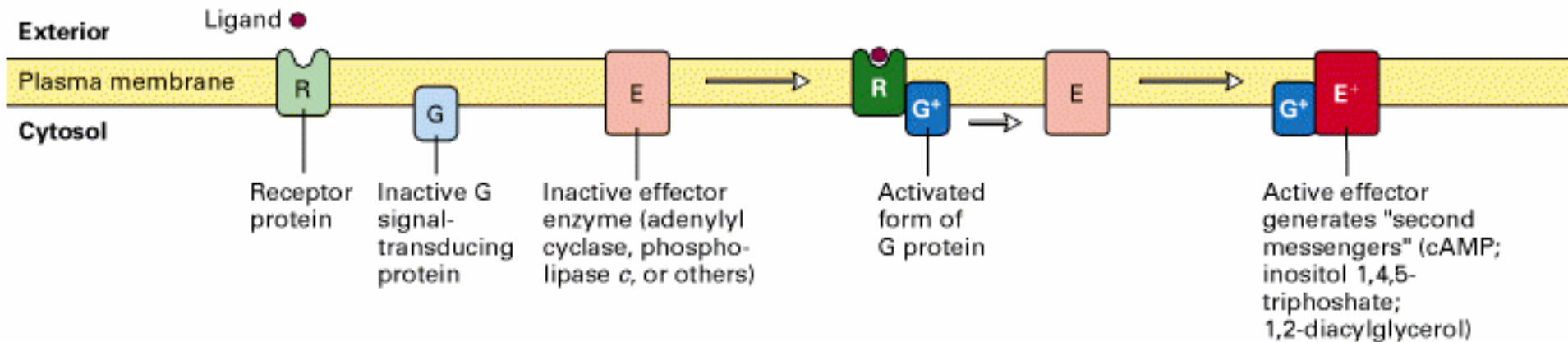


(C) ENZYME-LINKED RECEPTOR

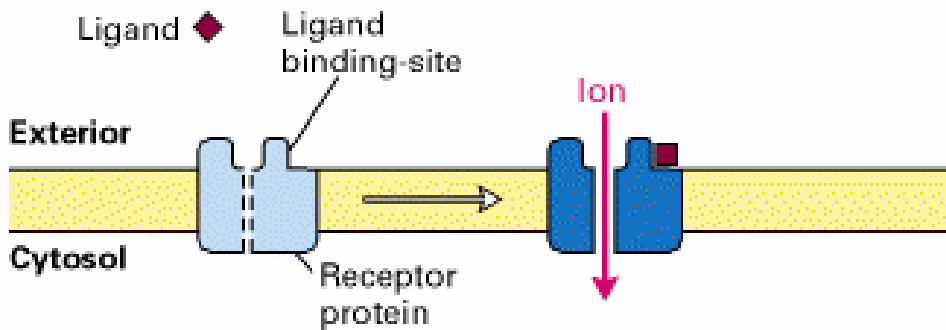


# Receptores de membrana y vías de transducción de la señal

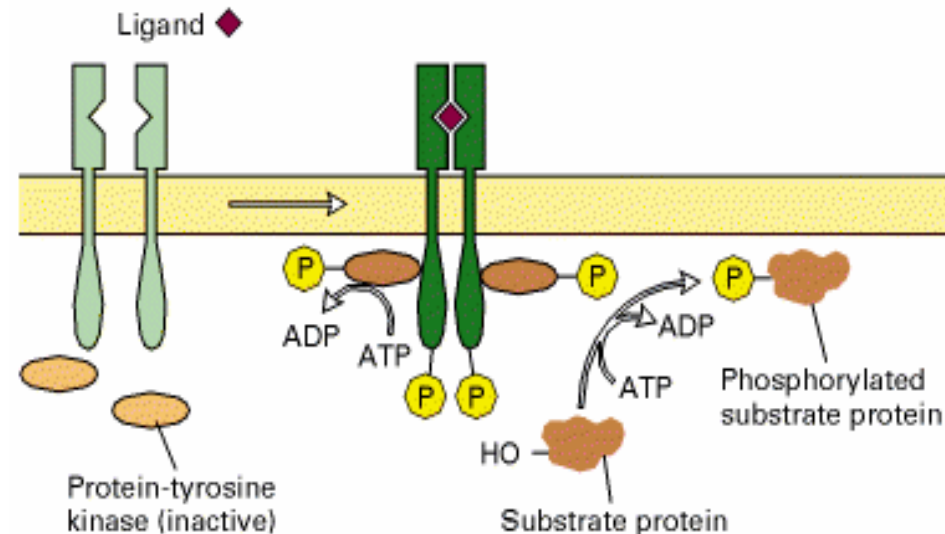
(a) **G protein-coupled receptors** (epinephrine, glucagon, serotonin)



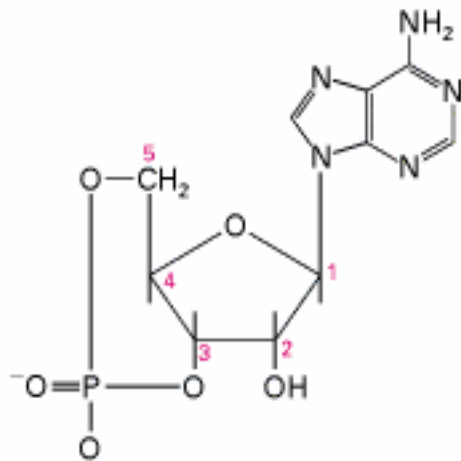
(b) **Ion-channel receptors** (acetylcholine)



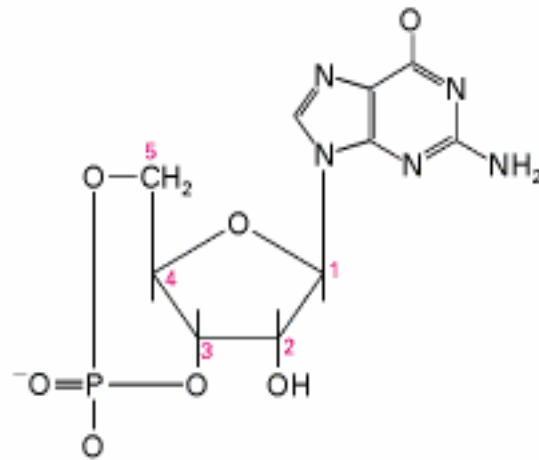
(c) **Tyrosine kinase-linked receptors** (erythropoietin, interferons)



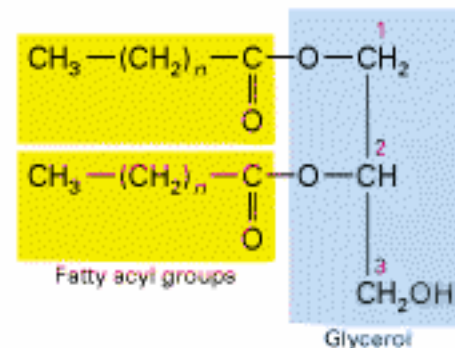
# Diversos mediadores intracelulares



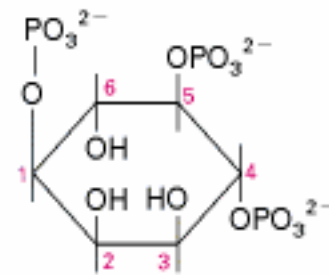
3',5'-Cyclic AMP  
(cAMP)



3',5'-Cyclic GMP  
(cGMP)

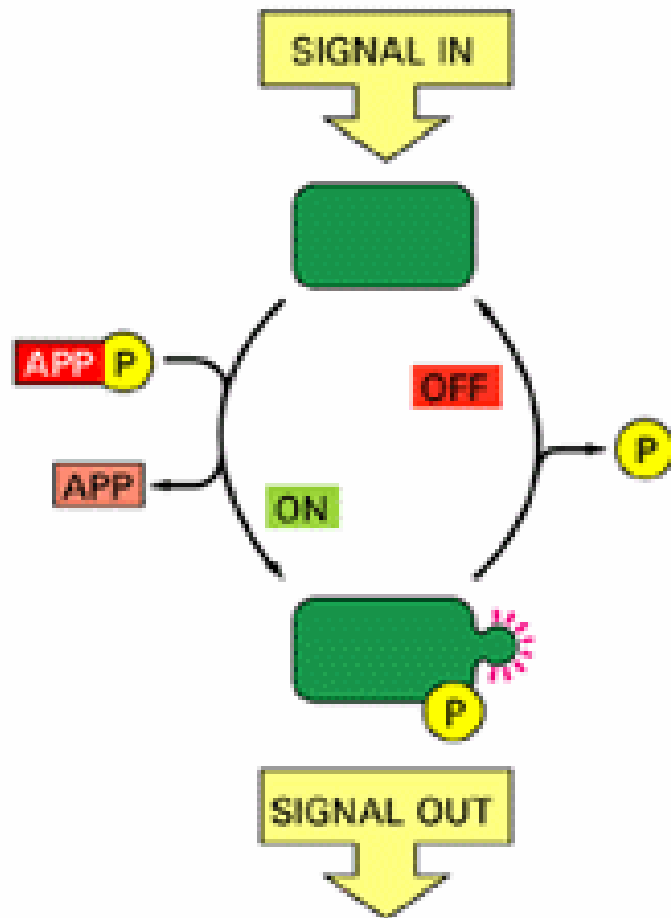


1,2-Diacylglycerol  
(DAG)

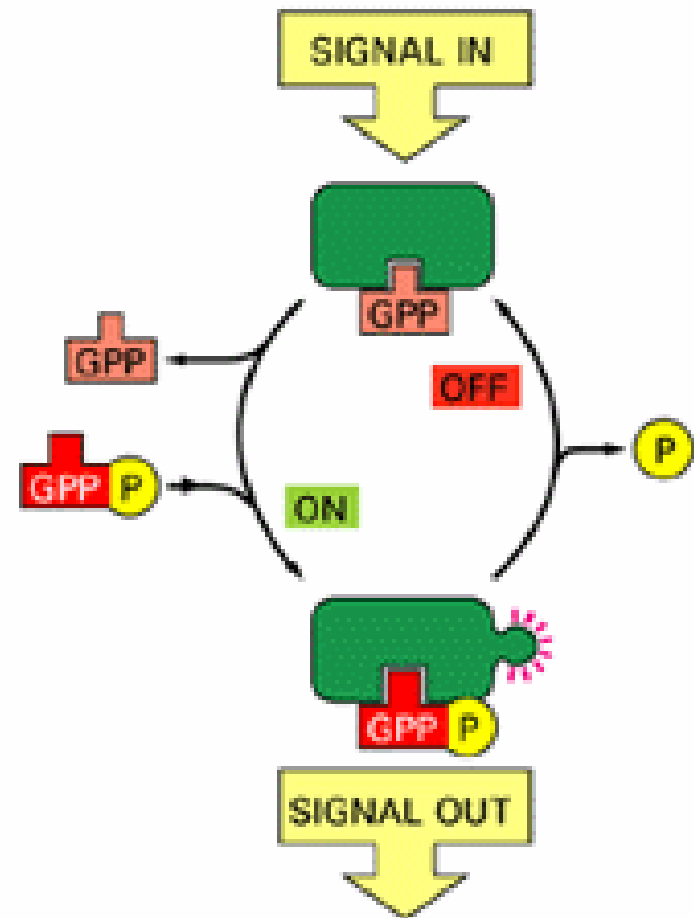


Inositol  
1,4,5-trisphosphate  
(IP<sub>3</sub>)

# Los dos mas importantes mecanismos de señalización intracelular comparten características comunes



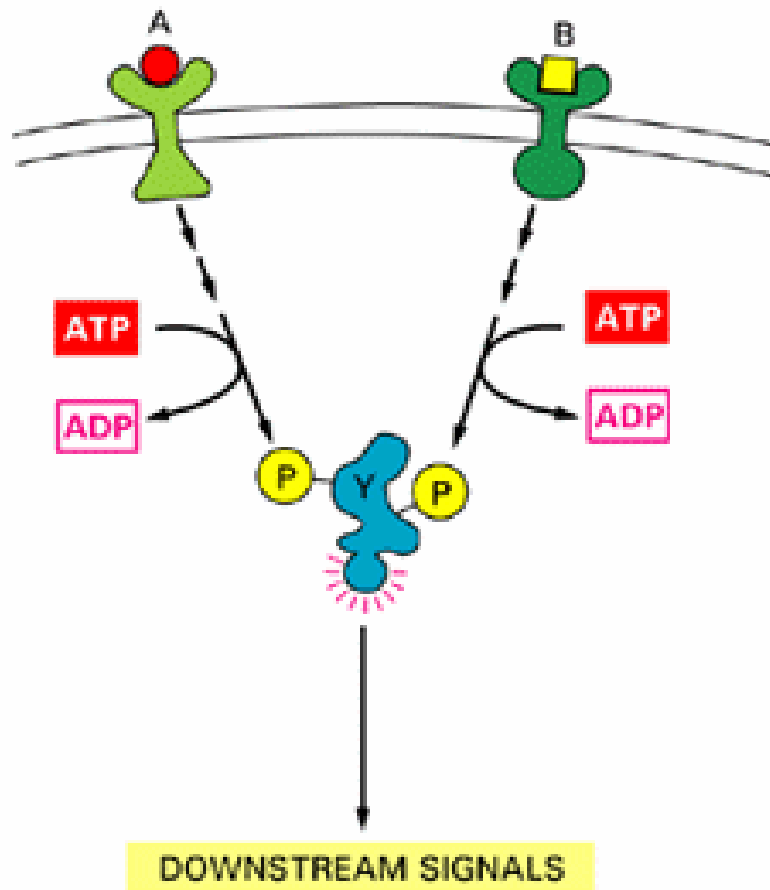
(A) SIGNALING BY PHOSPHORYLATION



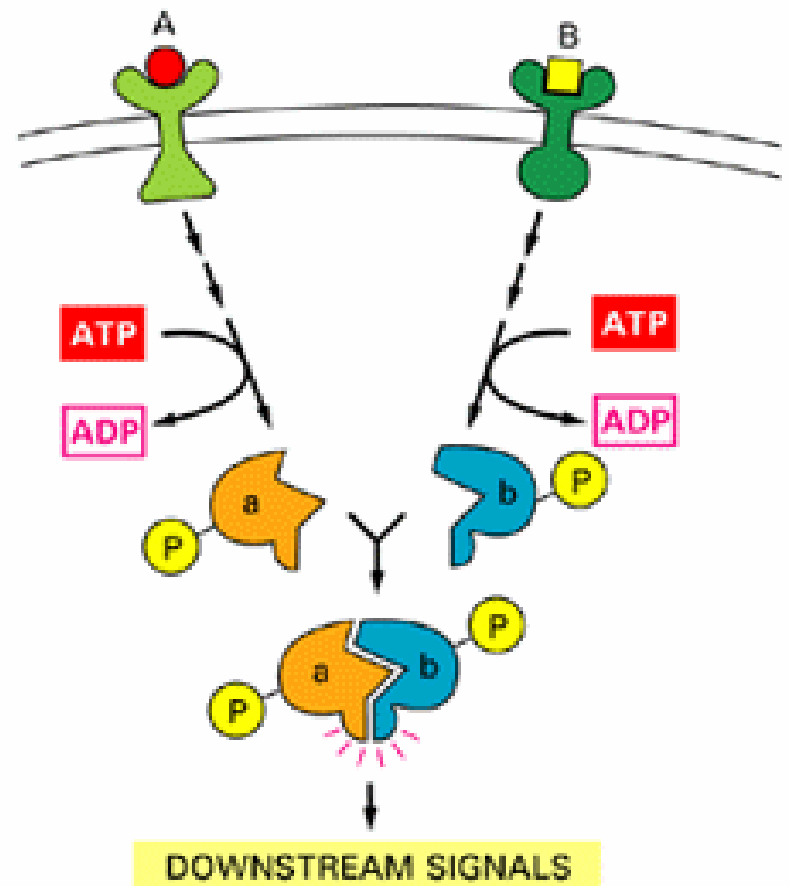
(B) SIGNALING BY GTP-BINDING PROTEIN

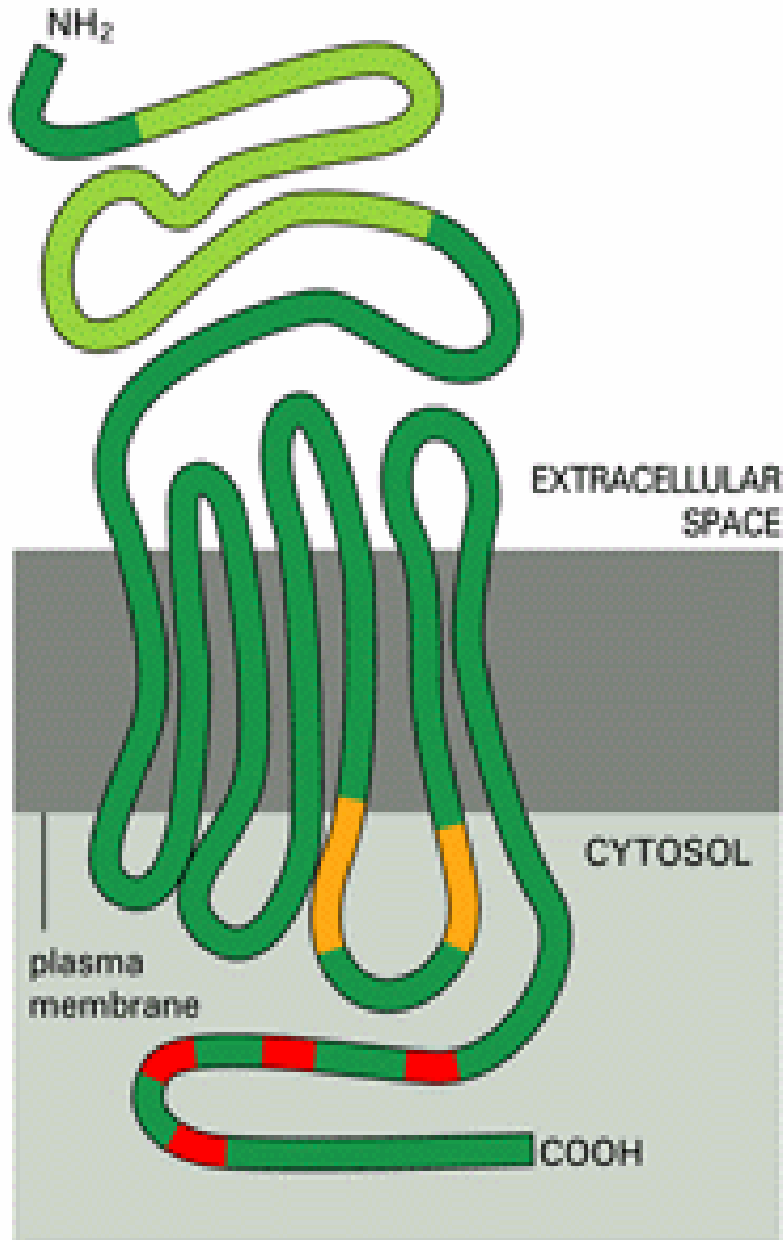
# Integración de señales externas a nivel intracelular

(A)



(B)





## Receptor unido a proteína G.

Siete segmentos trans membrana (verde osc.)

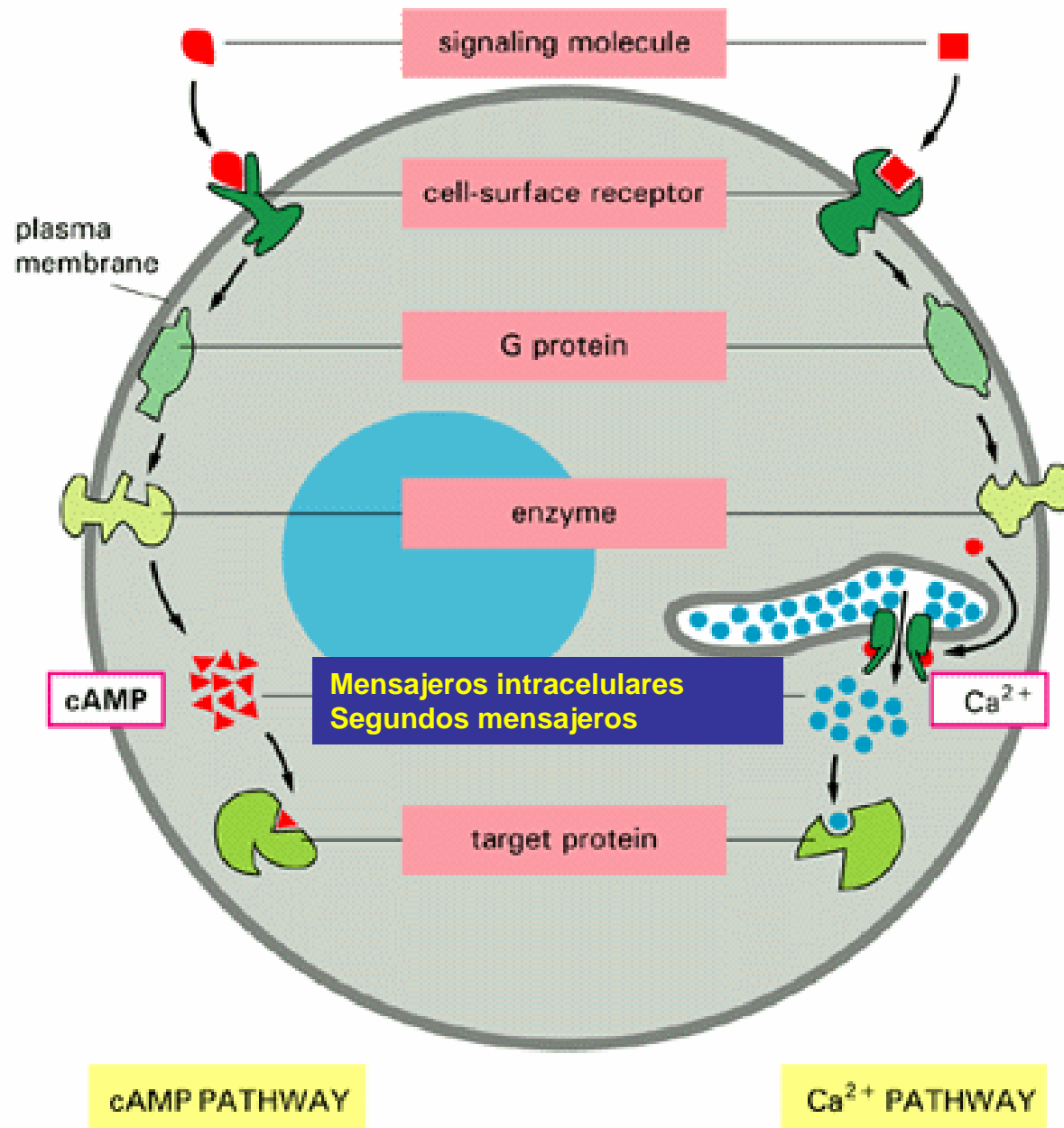
Dominio de unión a la señal externa (ligando; verde claro)

Dominios de unión a proteína G (naranja)

Sitios de fosforilación para la desensibilización del receptor (rojo)



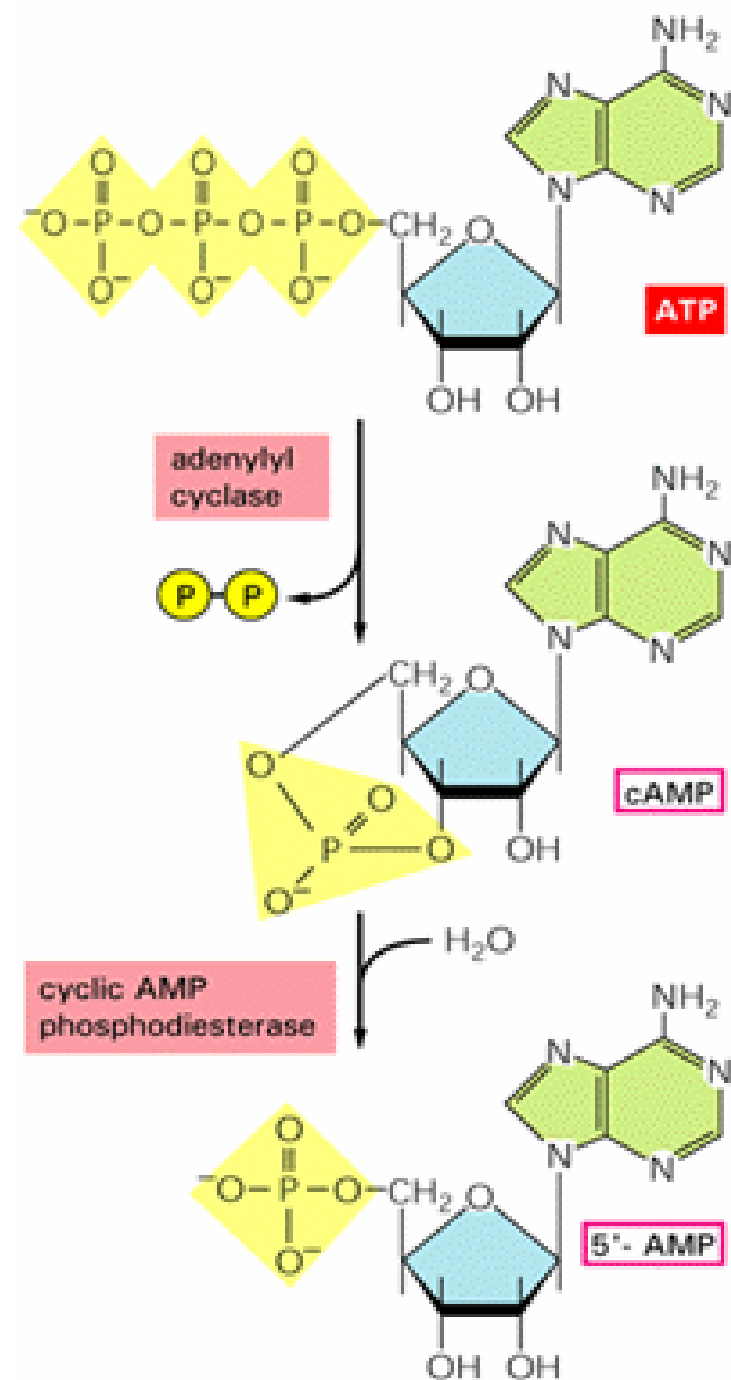
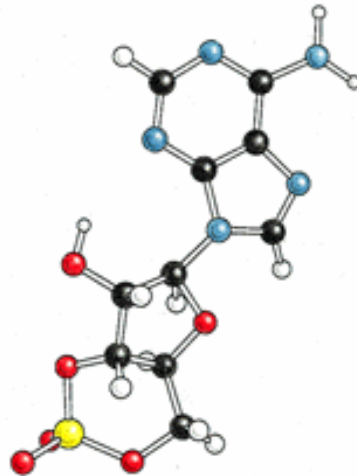
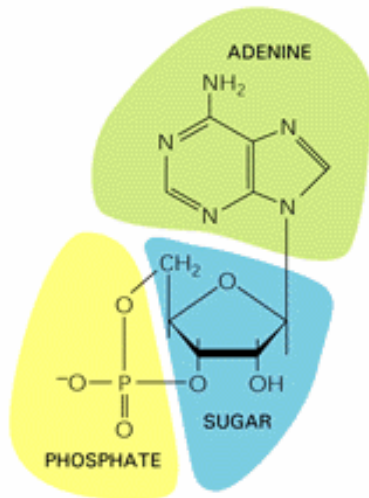
# Generación de mediadores intracelulares de bajo P.M.



# AMP cíclico

## Características

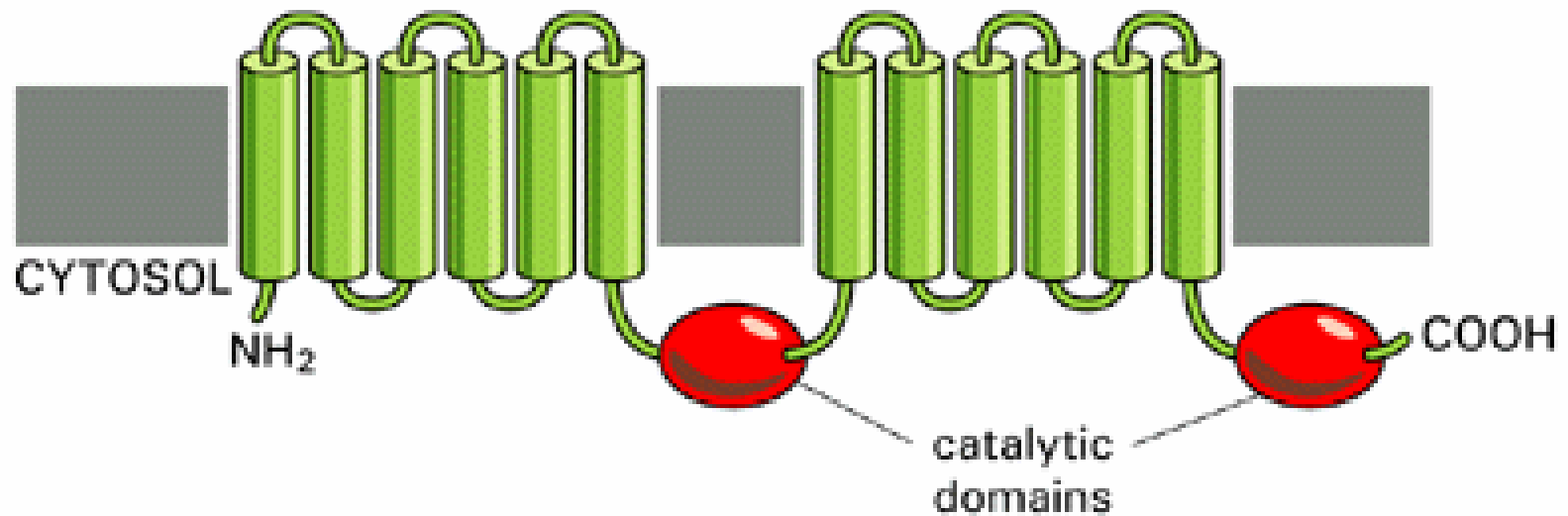
## Síntesis y Degradación



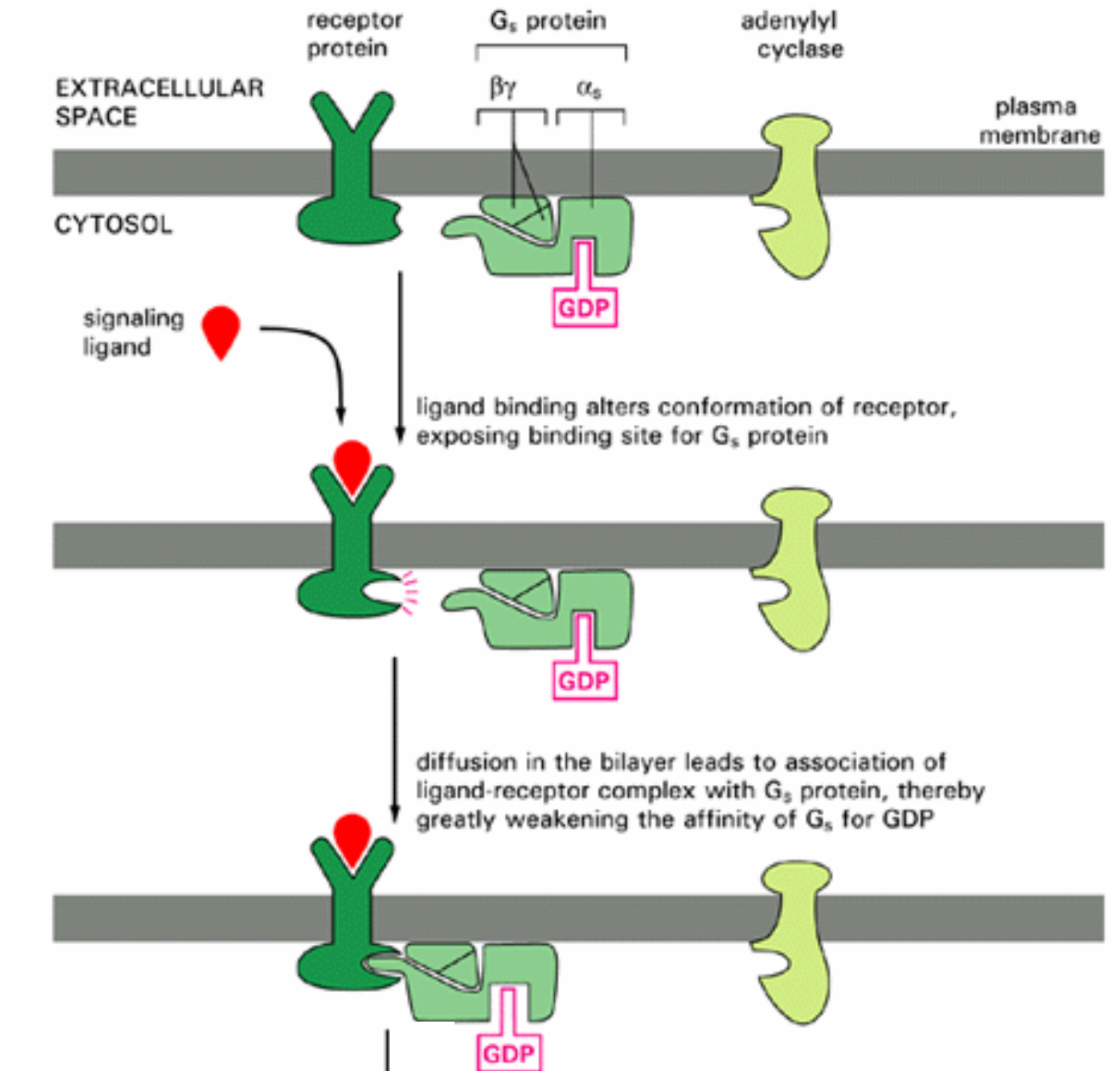
## Algunas respuestas celulares inducidas por hormonas y mediadas por acción de AMPc

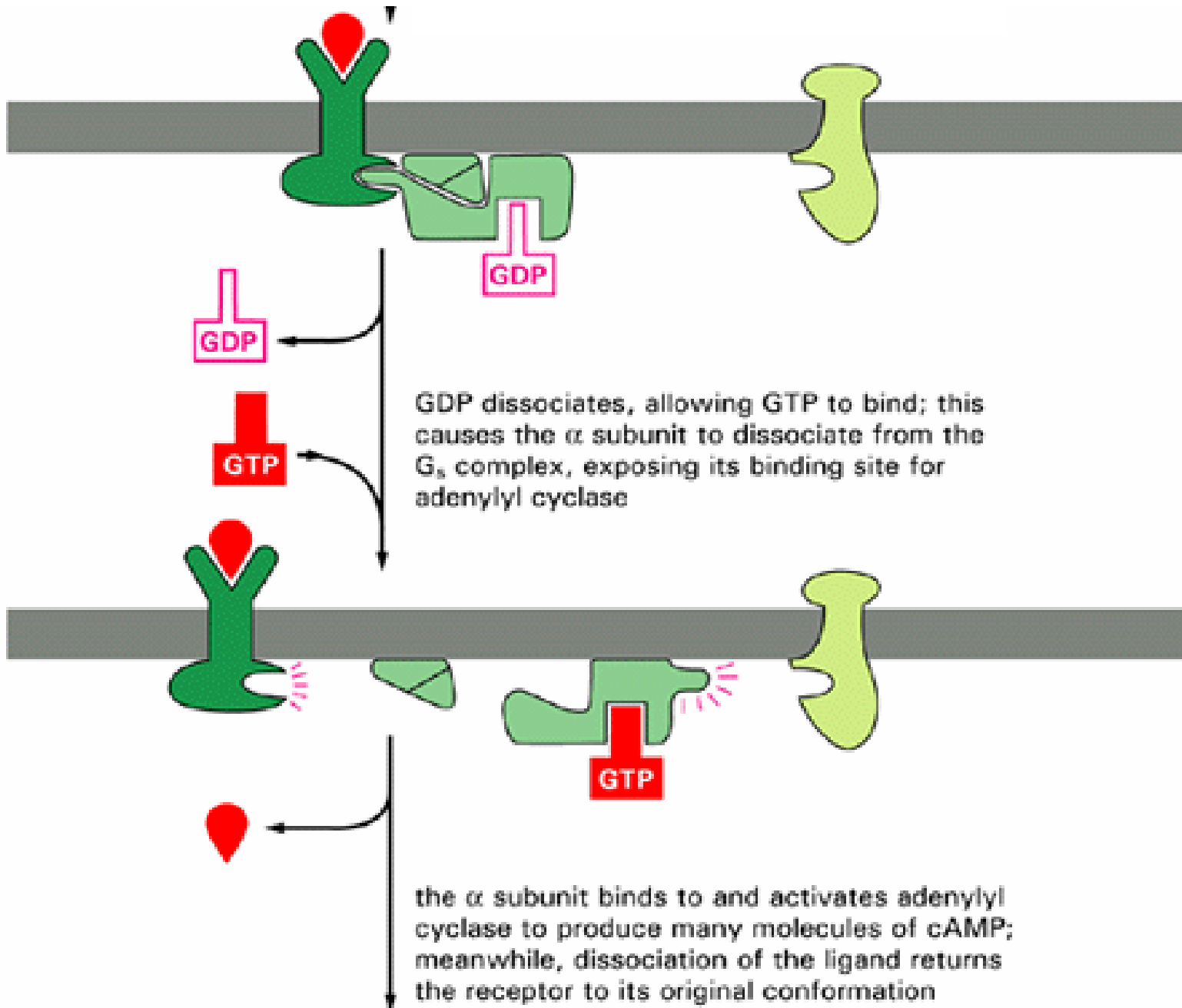
Target Tissue	Hormone	Major Response
Thyroid gland	thyroid-stimulating hormone (TSH)	thyroid hormone synthesis and secretion
Adrenal cortex	adrenocorticotrophic hormone (ACTH)	cortisol secretion
Ovary	luteinizing hormone (LH)	progesterone secretion
Muscle	adrenaline	glycogen breakdown
Bone	parathormone	bone resorption
Heart	adrenaline	increase in heart rate and force of contraction
Liver	glucagon	glycogen breakdown
Kidney	vasopressin	water resorption
Fat	adrenaline, ACTH, glucagon, TSH	triglyceride breakdown

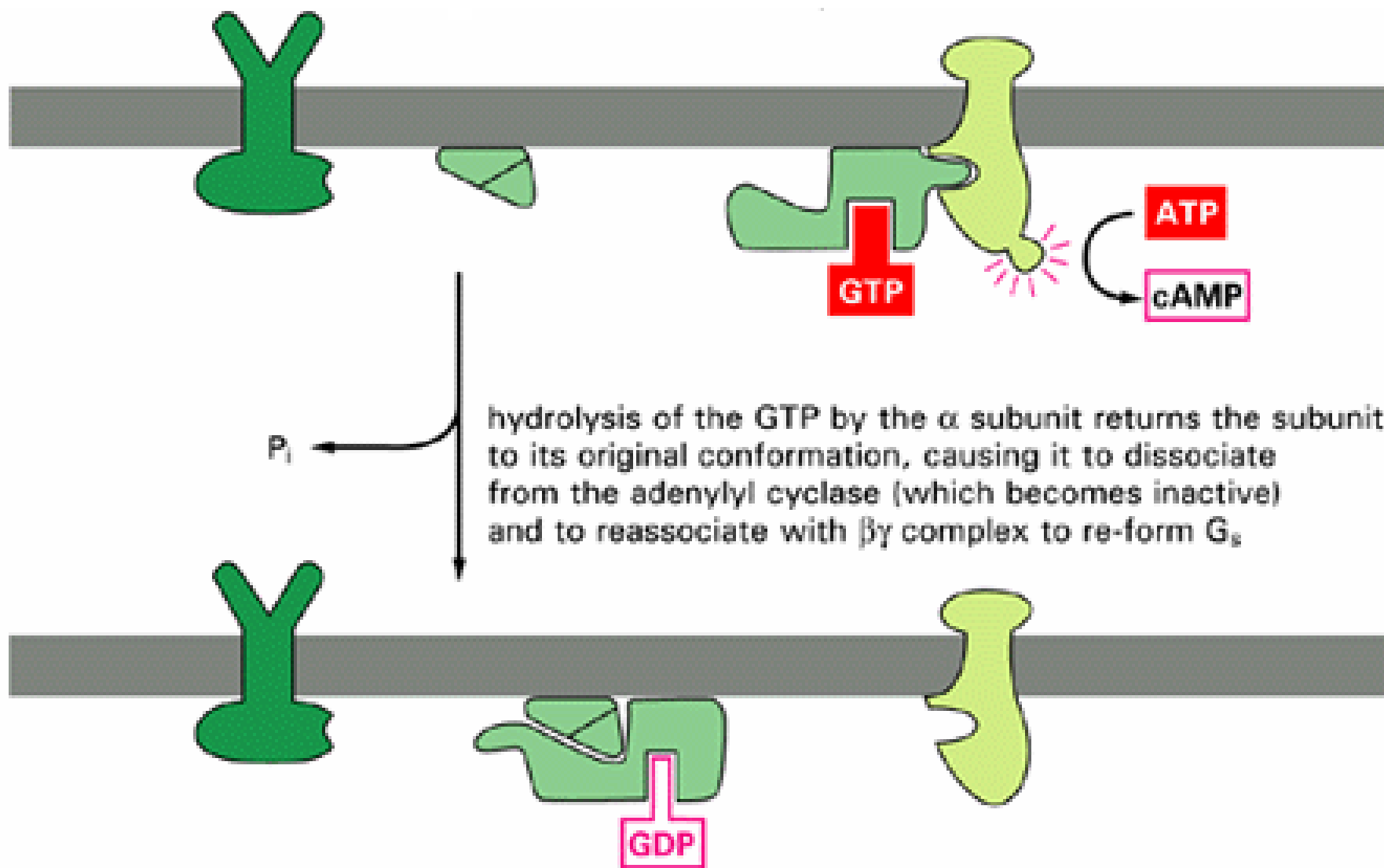
# Adenilato Ciclasa



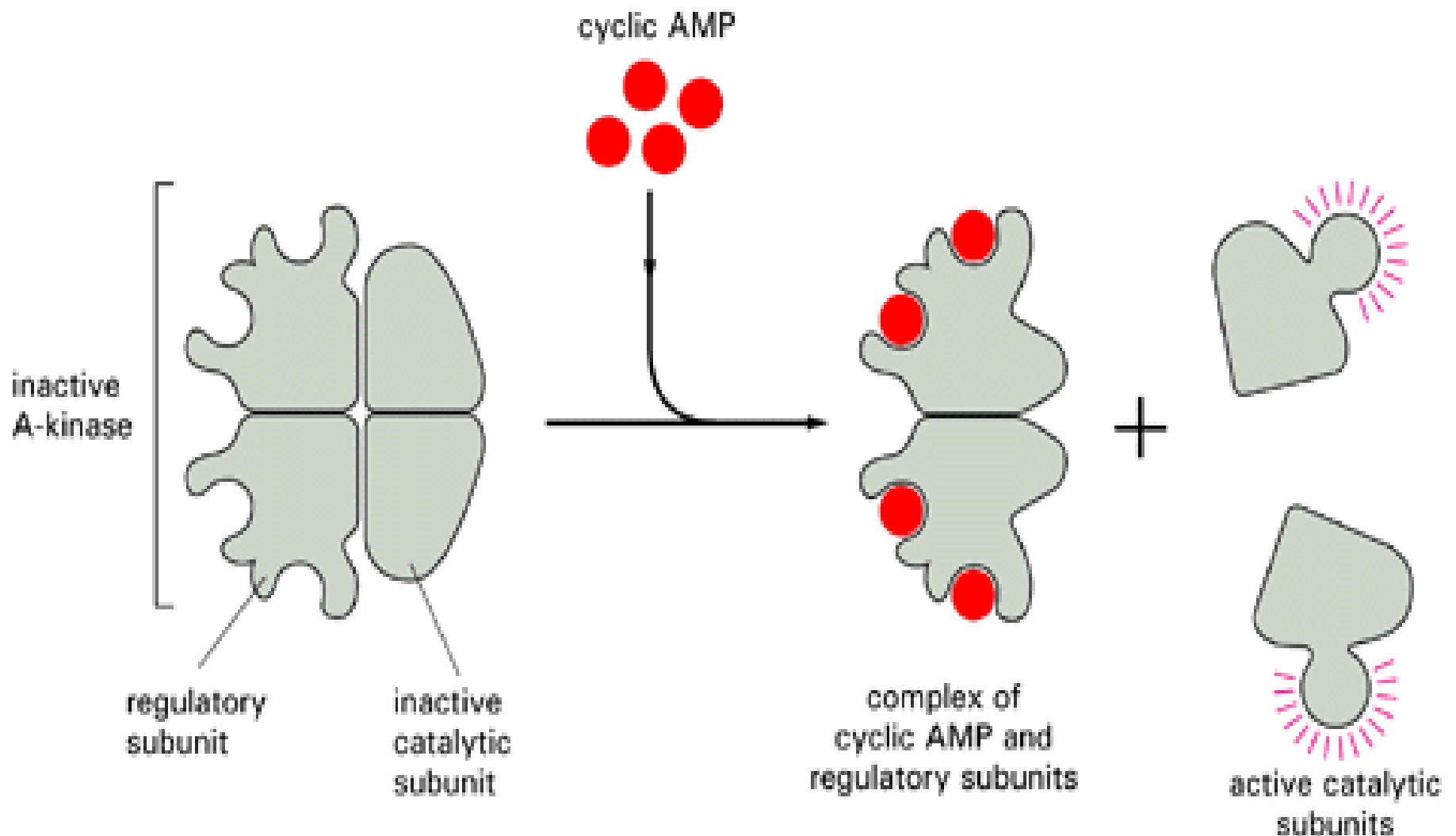
# Modelo de activación de adenilato ciclasa por proteína G





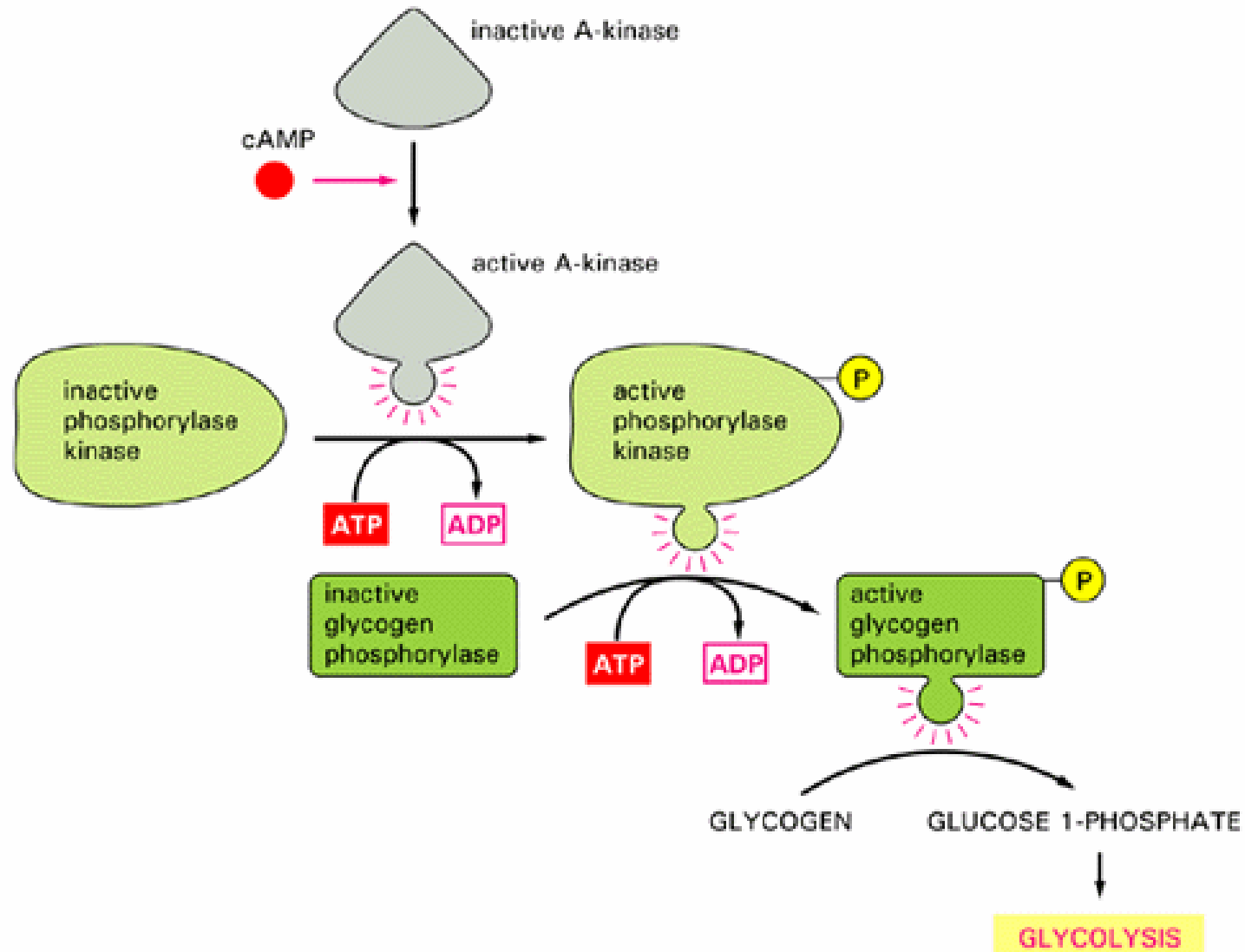


# Activación de la proteína quinasa A dependiente de AMPc

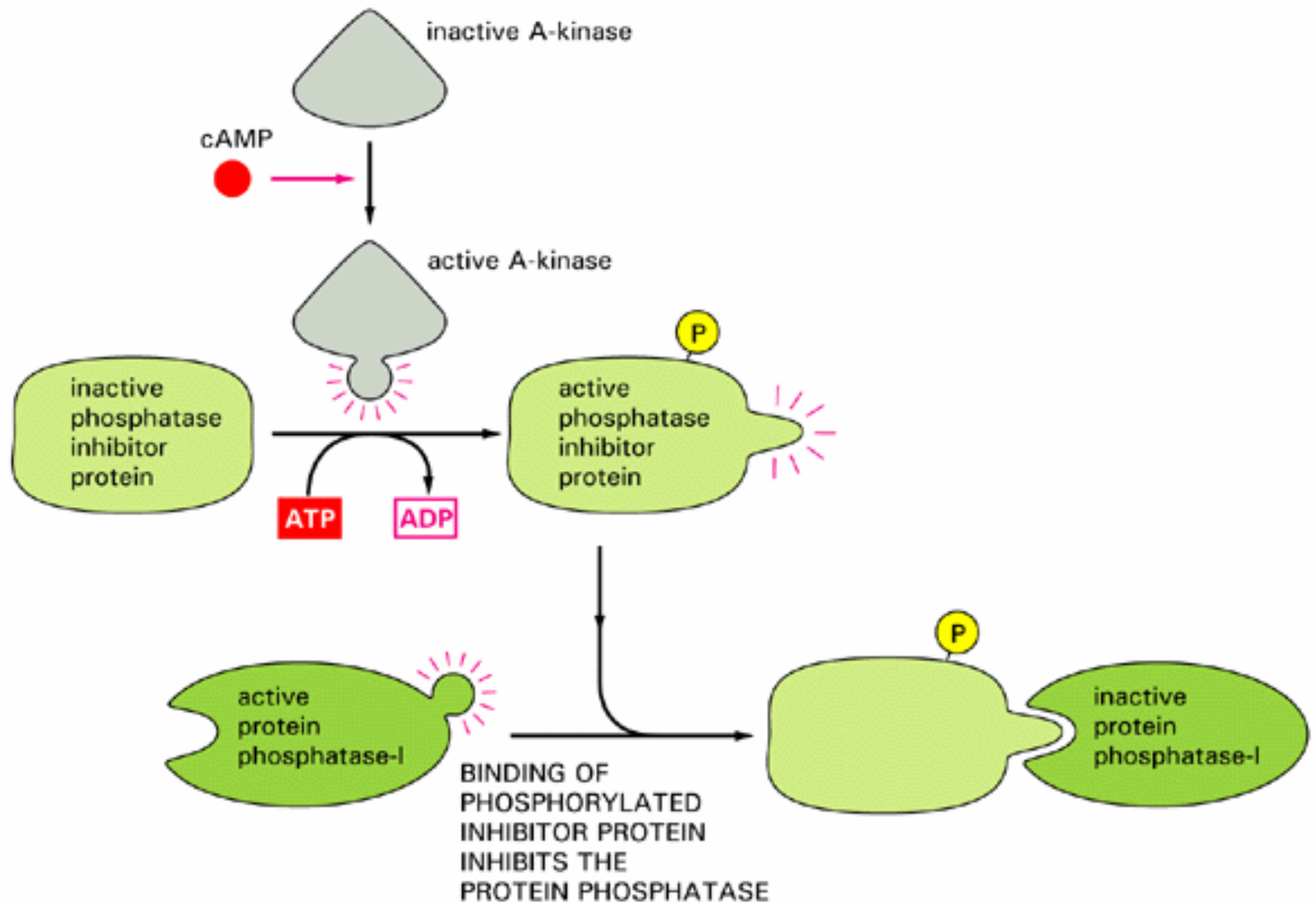




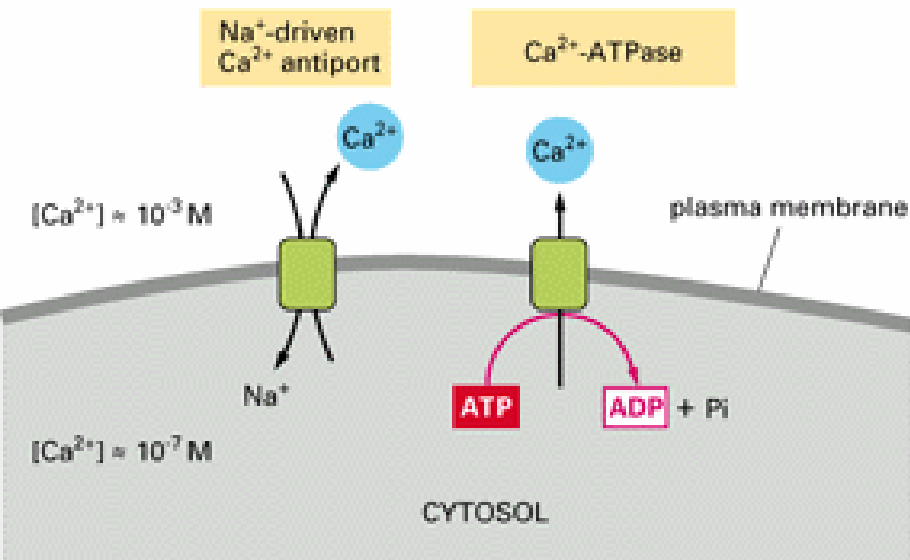
# Estimulación de la hidrólisis de glicogeno por AMPc en células de músculo esquelético



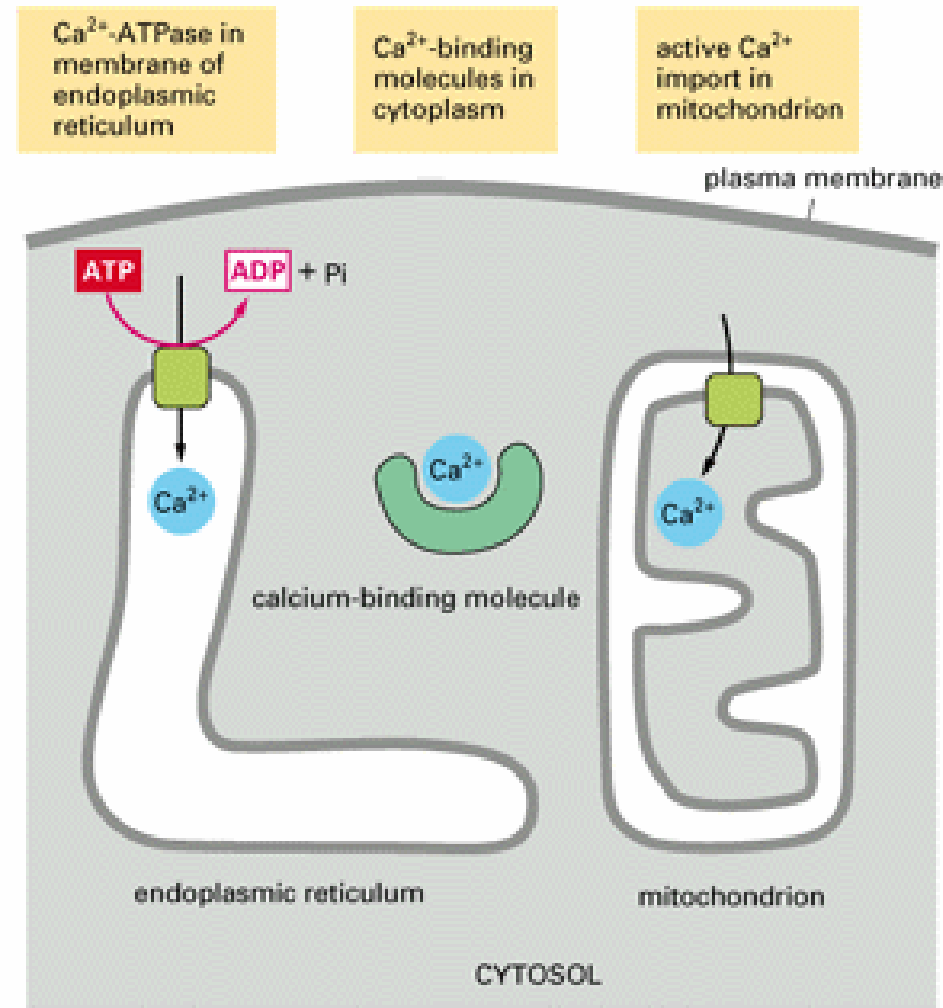
# Función de la fosfatasa-I en la regulación del metabolismo del glicógeno por AMPc



# Control de la concentración de $\text{Ca}^{2+}$ citosólico libre

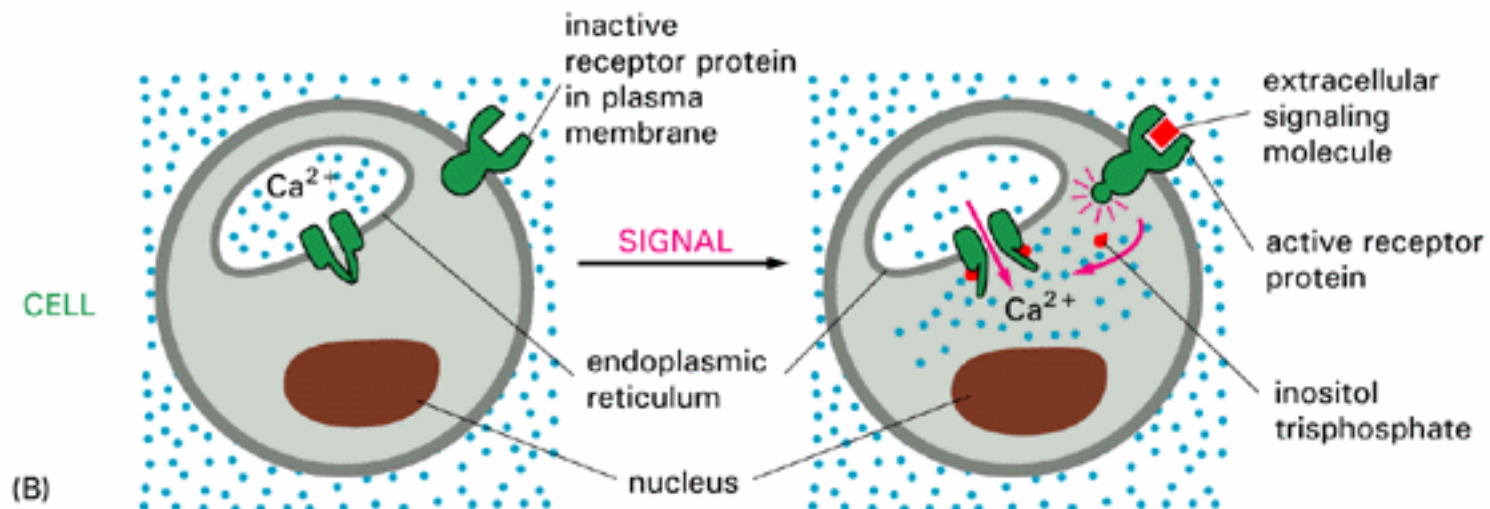
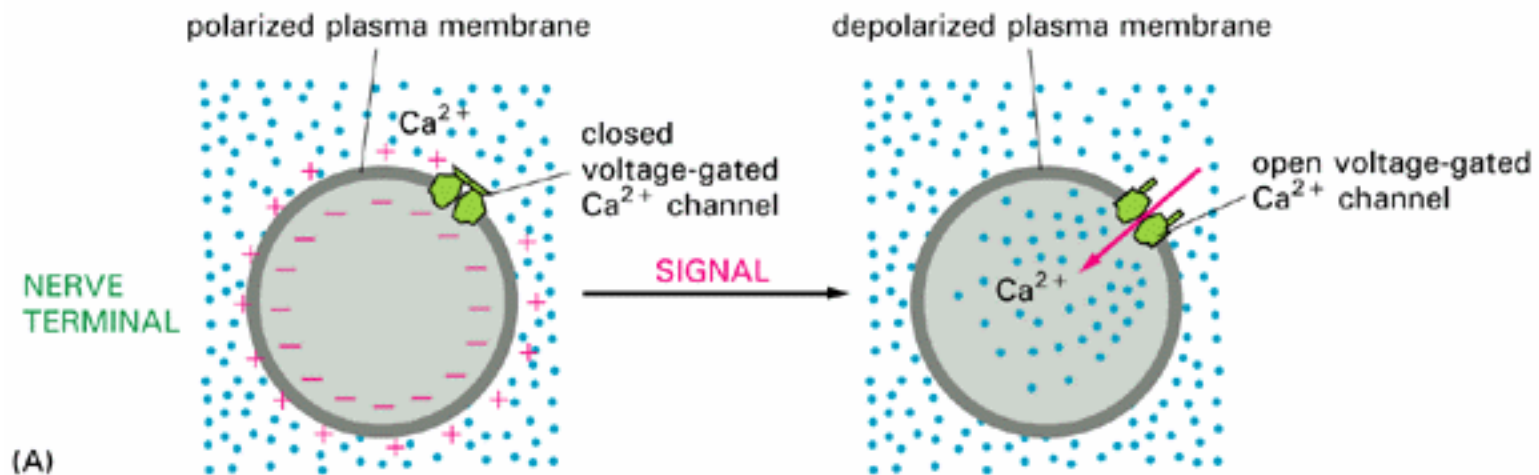


(A)

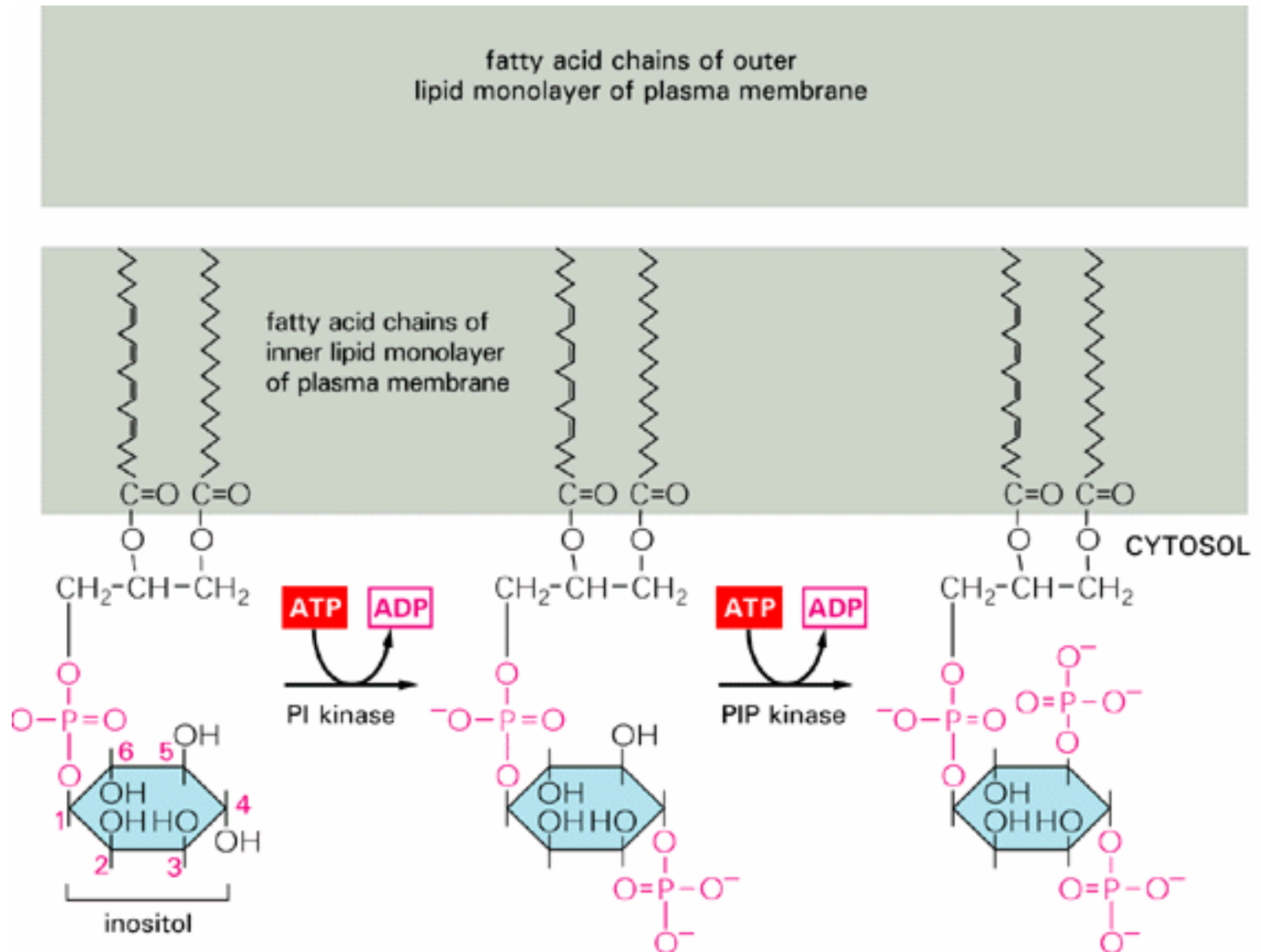


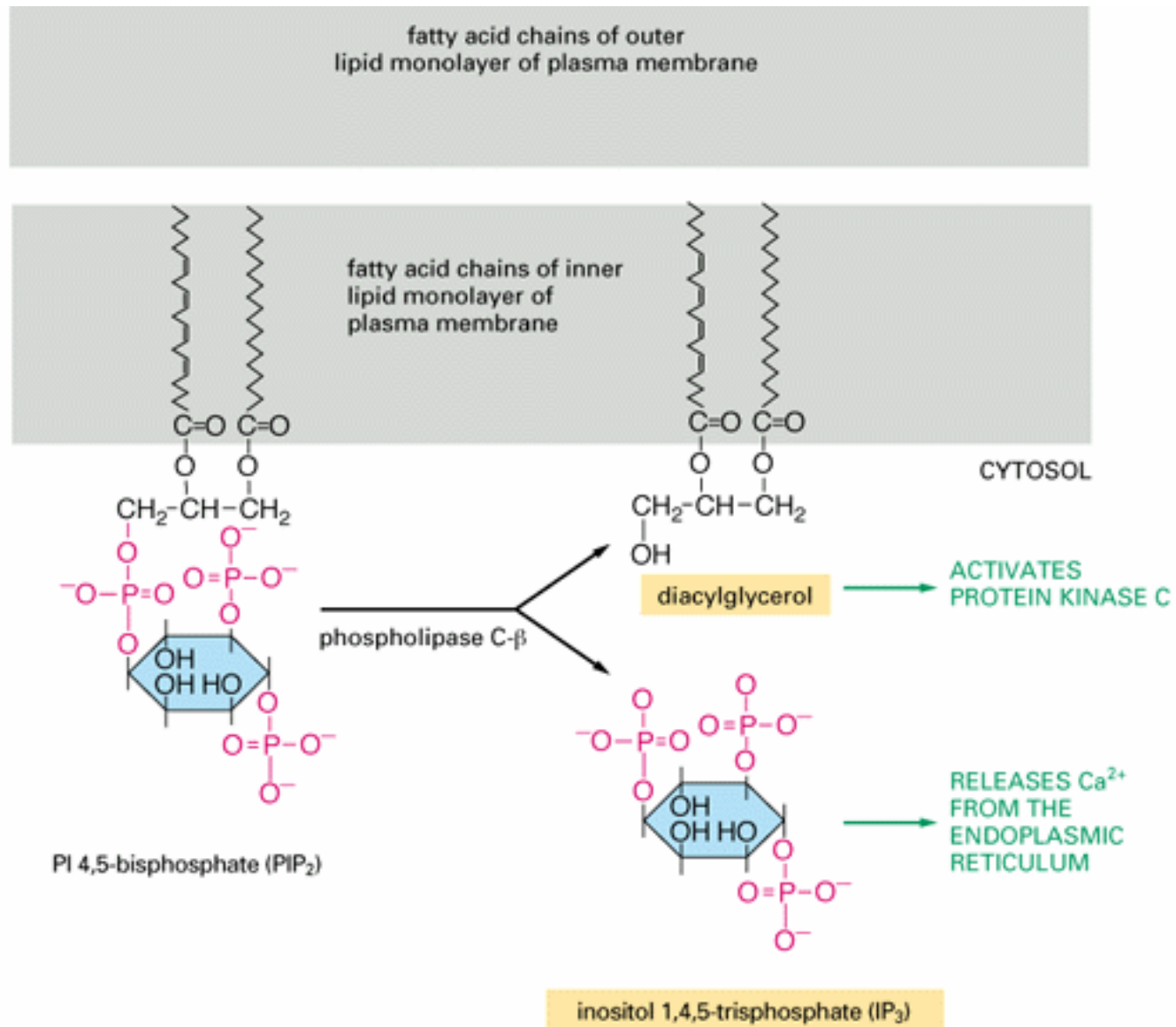
(B)

# Aumento de $\text{Ca}^{2+}$ citosólico estimulado por señales externas



# Fosfoinositidos: PI, PIP, PIP<sub>2</sub>





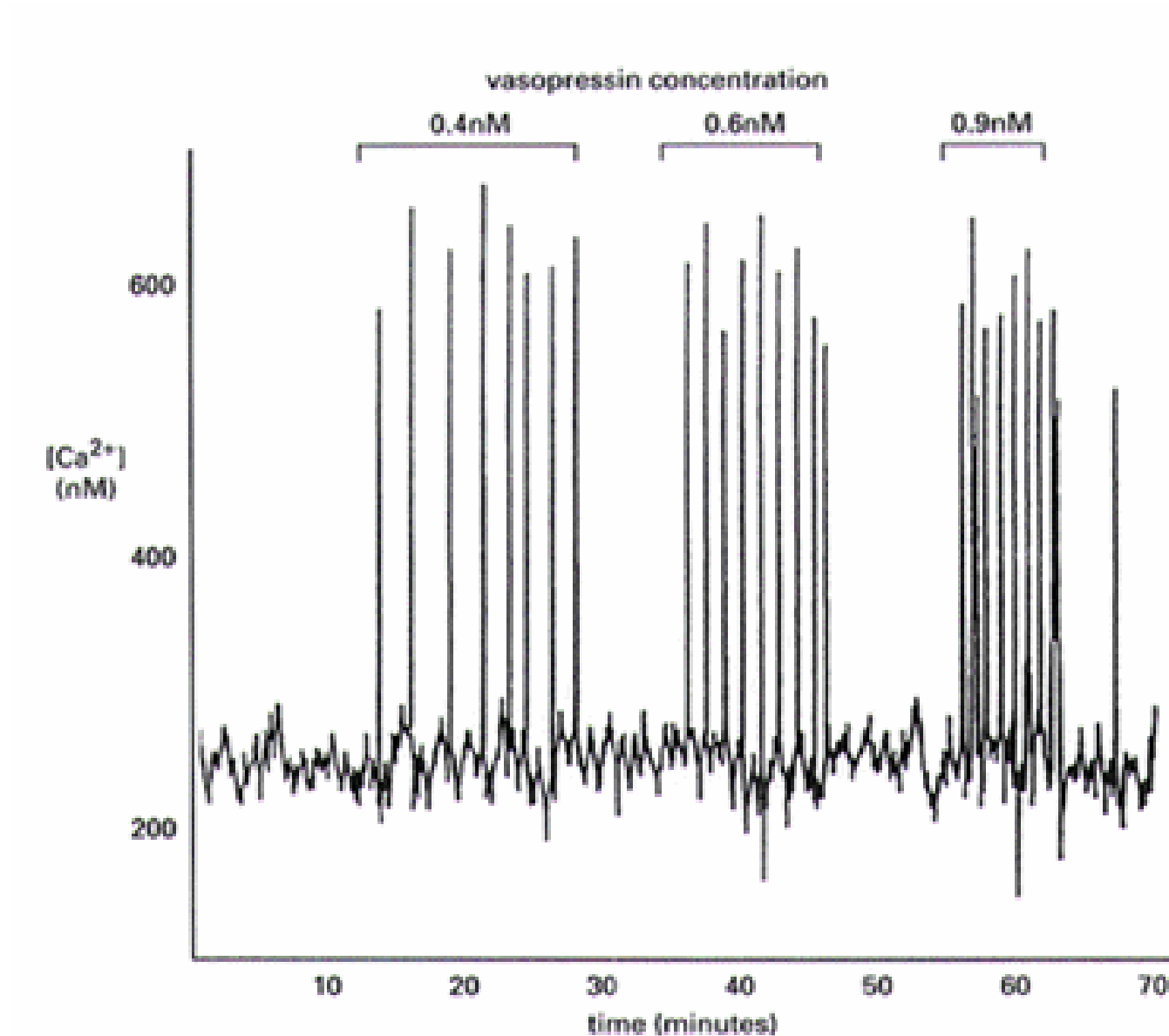
## Algunas respuestas celulares mediadas por receptores vinculados a proteína G y acoplados a la trayectoria de señalización por PIP<sub>2</sub>

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Target Tissue	Signaling Molecule	Major Response
Liver	vasopressin	glycogen breakdown
Pancreas	acetylcholine	amylase secretion
Smooth muscle	acetylcholine	contraction
Mast cells	antigen	histamine secretion
Blood platelets	thrombin	aggregation

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# Oscilaciones de $\text{Ca}^{2+}$ en hígado inducidas por vasopresina

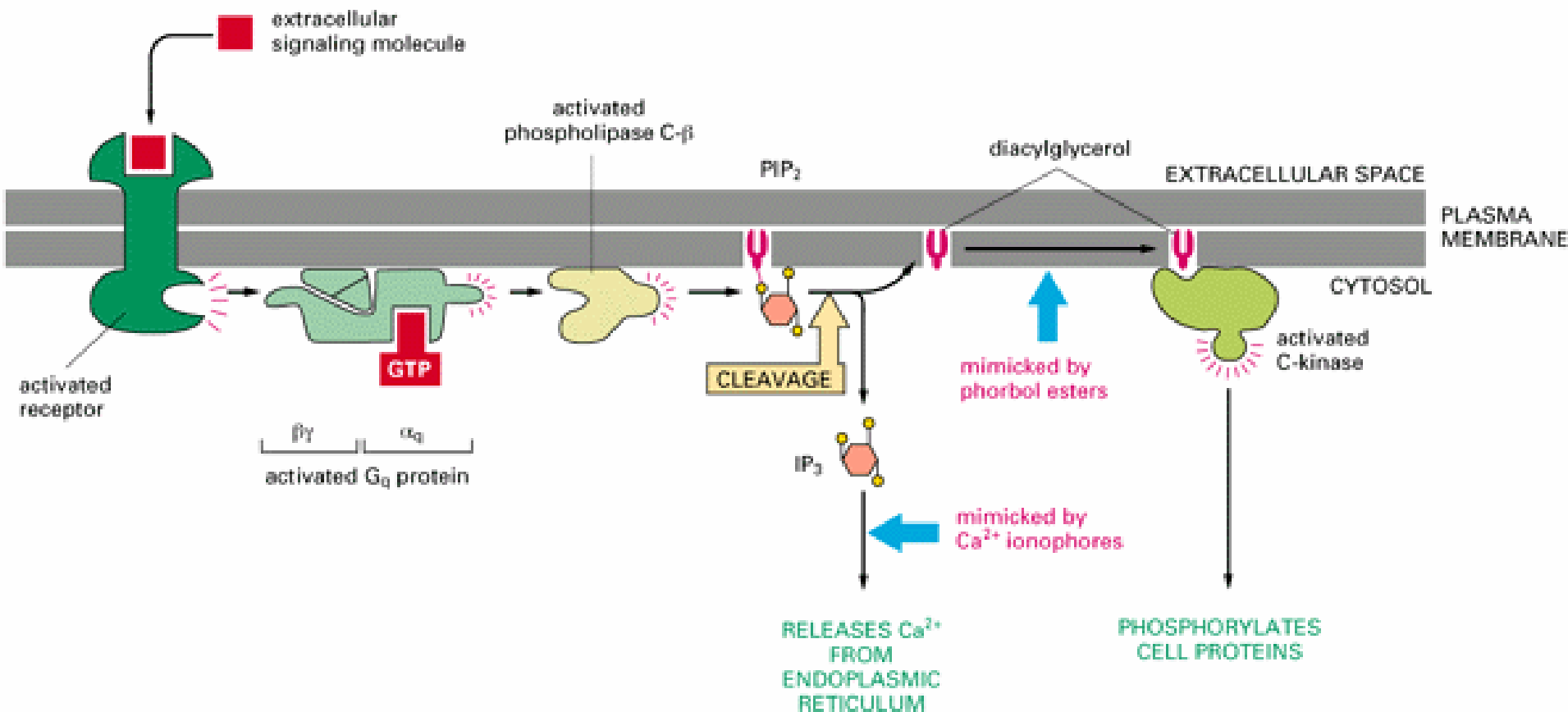




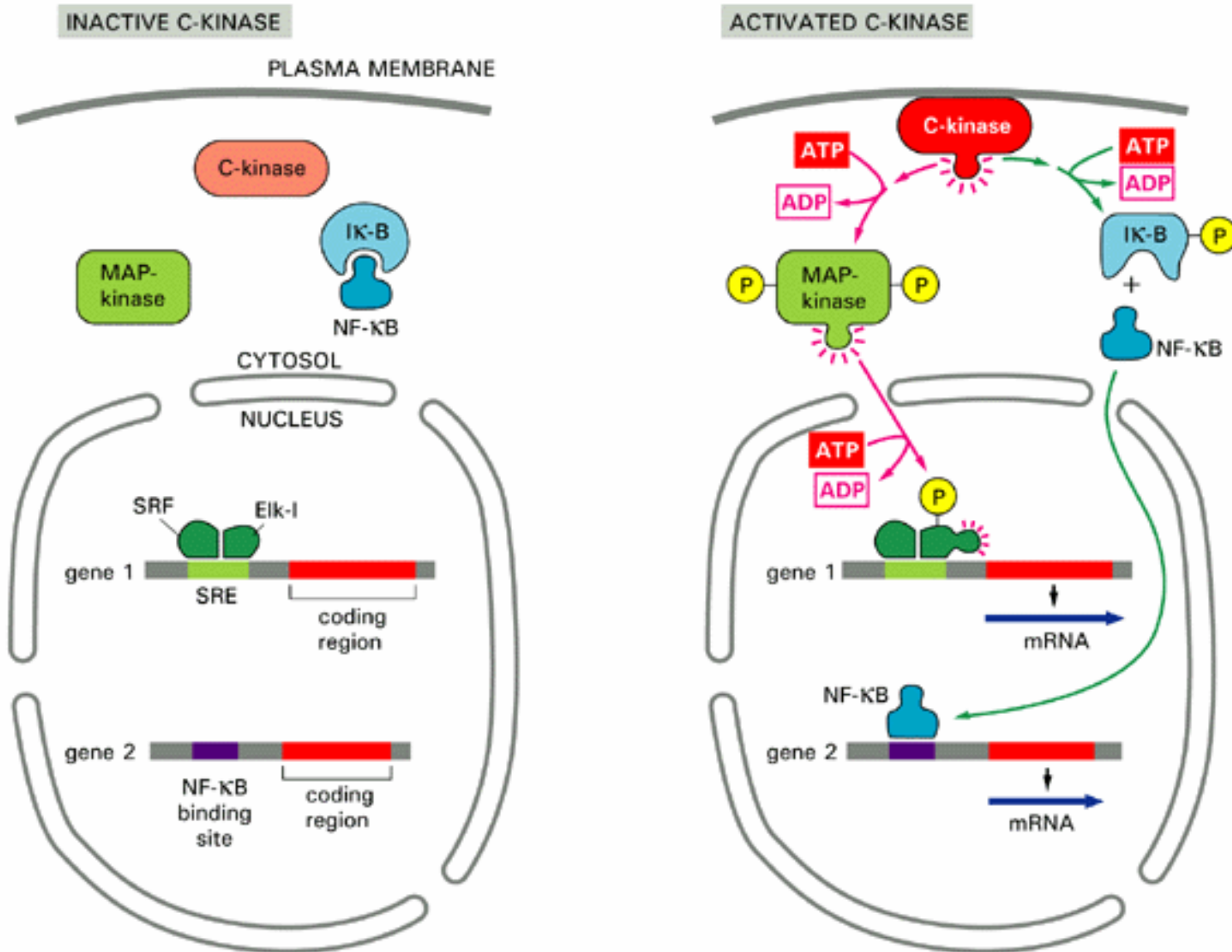
**Table 15-3. The Major Families of Trimeric G proteins\***

Family	Some Family Members	$\alpha$ Subunits	Functions	Modified by Bacterial Toxin
I	$G_s$	$\alpha_s$	activates adenylyl cyclase; activates $Ca^{2+}$ channels	cholera activates
	$G_{olf}$	$\alpha_{olf}$	activates adenylyl cyclase in olfactory sensory neurons	cholera activates
II	$G_i$	$\alpha_i$	inhibits adenylyl cyclase; activates $K^+$ channels	pertussis inhibits
	$G_o$	$\alpha_o$	activates $K^+$ channels; inactivates $Ca^{2+}$ channels; activates phospholipase C-b	pertussis inhibits
	$G_t$ (transducin)	$\alpha_t$	activates cyclic GMP phosphodiesterase in vertebrate rod photoreceptors	cholera activates and pertussis inhibits
III	$G_q$	$\alpha_q$	activates phospholipase C-b	no effect

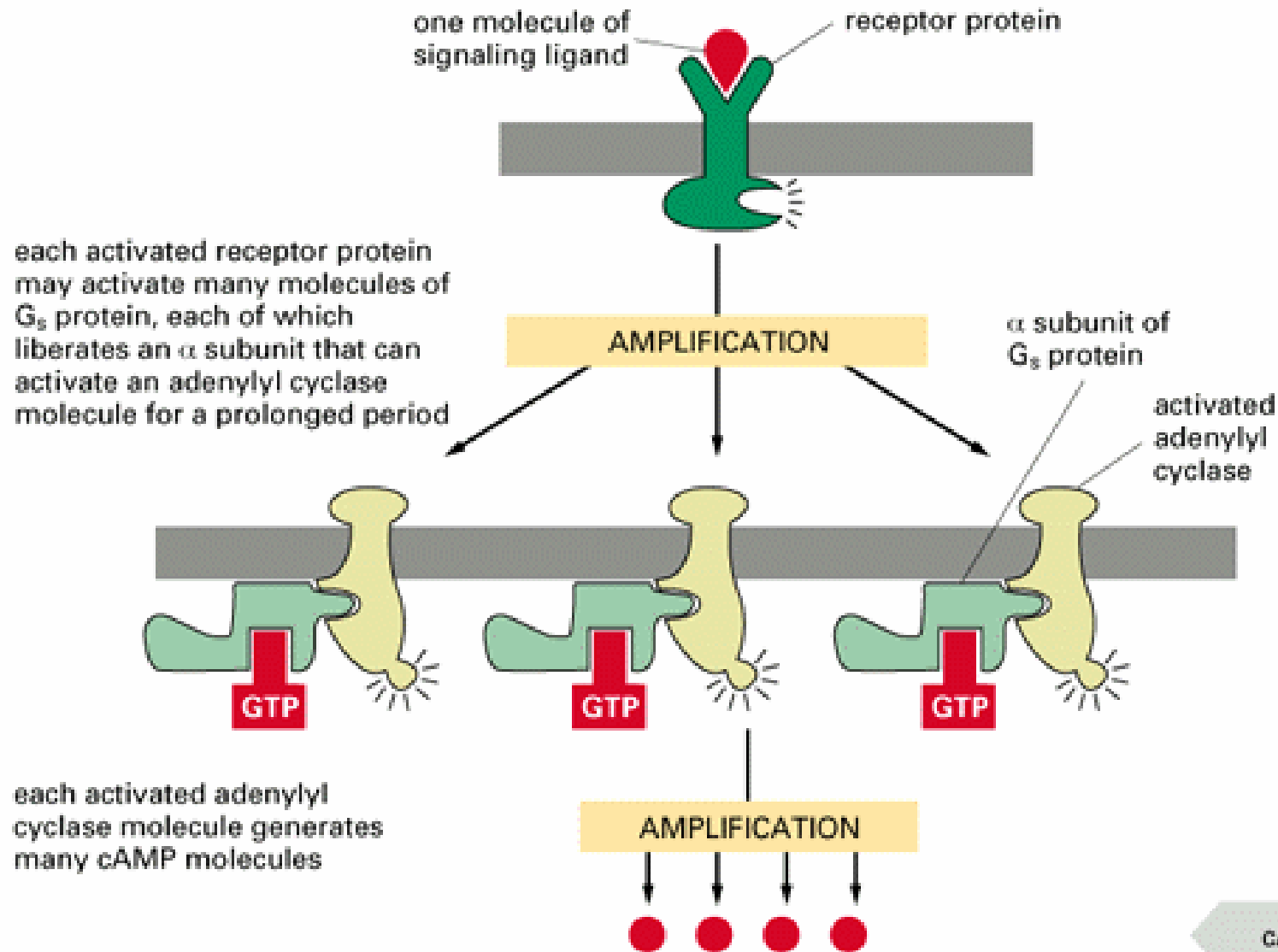
# Las dos ramas originadas por la hidrólisis de $\text{PIP}_2$



# Quinasa C activa la transcripción de genes específicos



# Amplificación de una cascada catalítica inducida por ligando



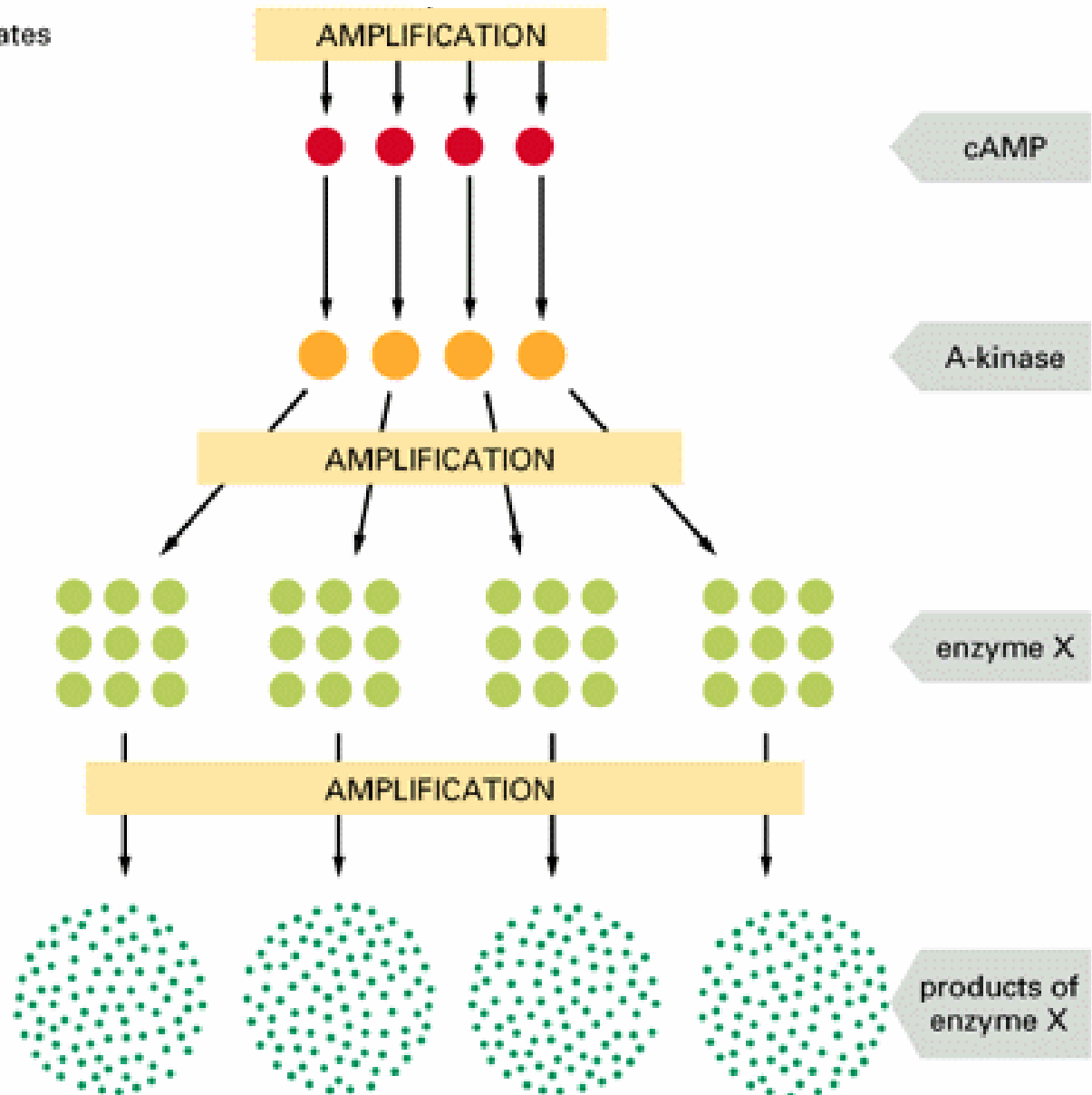
# Amplificación final

each activated adenylyl cyclase molecule generates many cAMP molecules

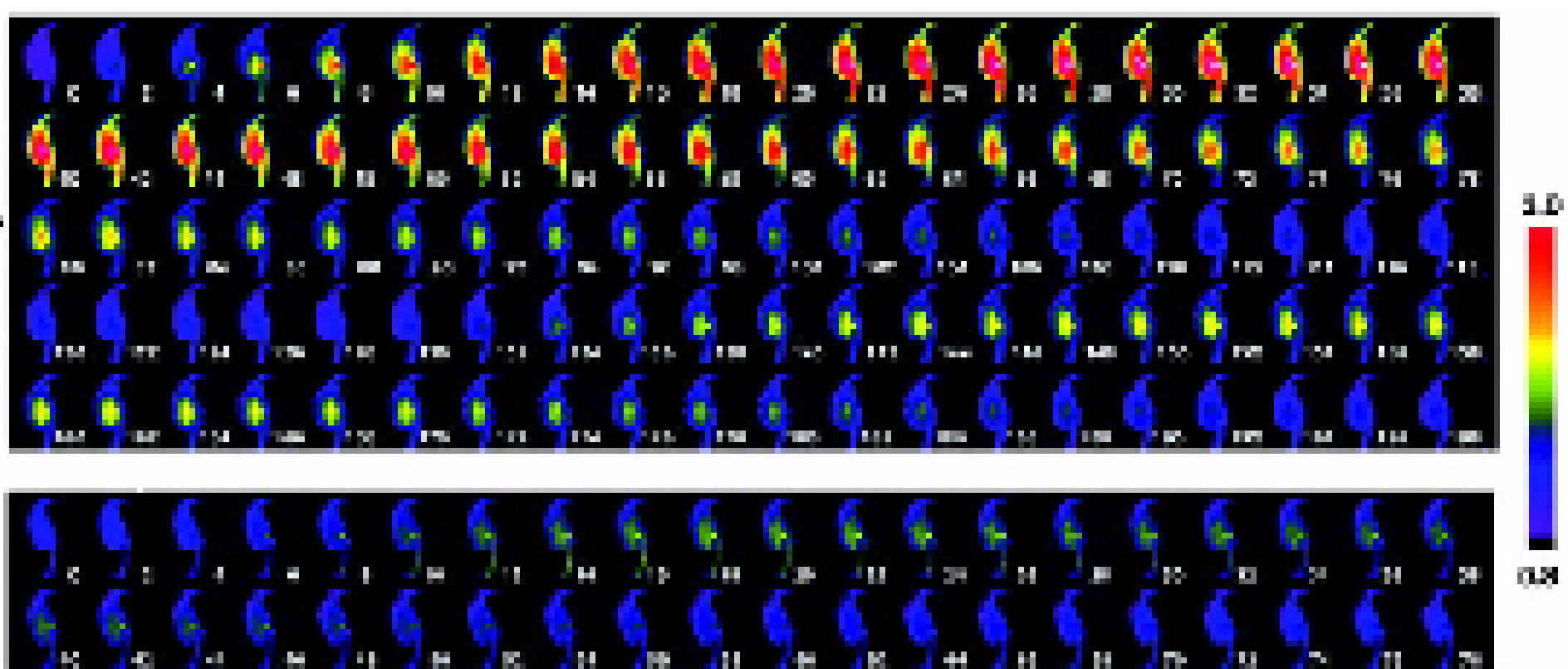
cAMP molecules activate A-kinase

each A-kinase molecule can phosphorylate and thereby activate many copies of enzyme X

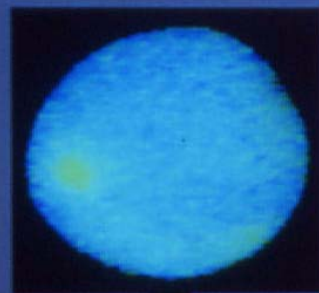
each copy of enzyme X produces many molecules of product



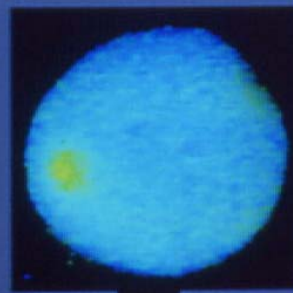
# Calcio intraespermático. Variación de sus concentraciones. Análisis de imagen de una sola célula.



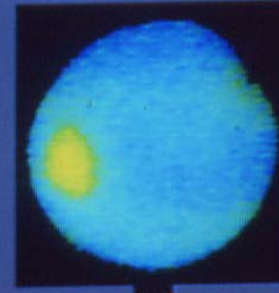
# FERTILIZATION-TRIGGERED CALCIUM WAVE IN A XENOPUS EGG



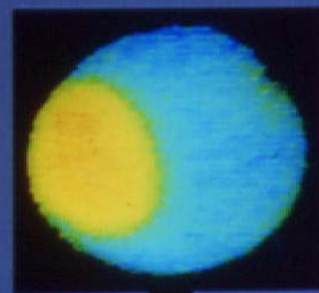
0'



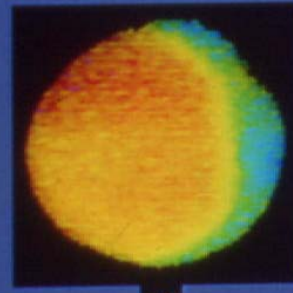
30"



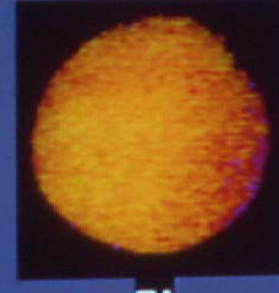
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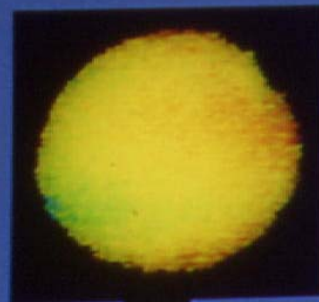
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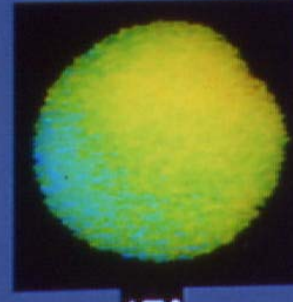
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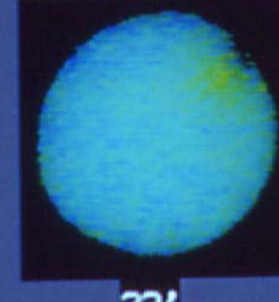
7'



14'



17'



23'





# Onda de calcio post-fertilización en huevo de rana

