

I processi fondamentali di un organismo pluricellulare

Omeostasi

“Mantenimento di condizioni stabili mediante meccanismi fisiologici coordinati”

- 1) Comunicazione tra cellule (chimica ed elettrica)
- 2) Interazione con l'esterno
- 3) Reazione agli stimoli

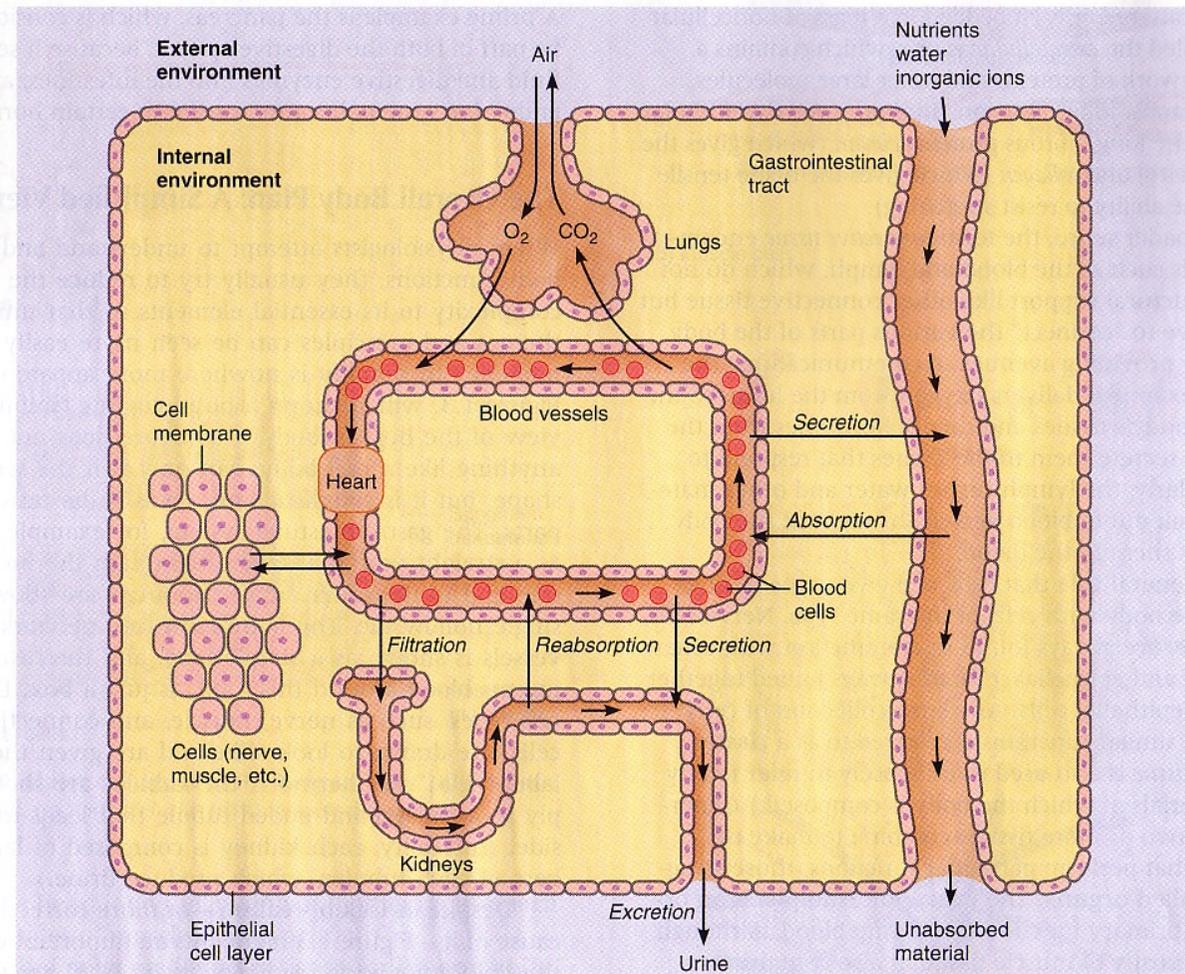
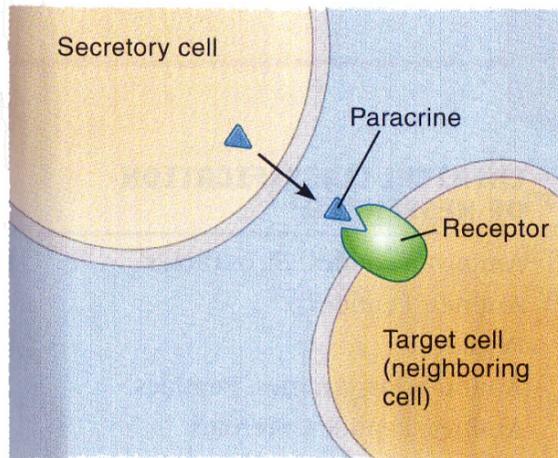
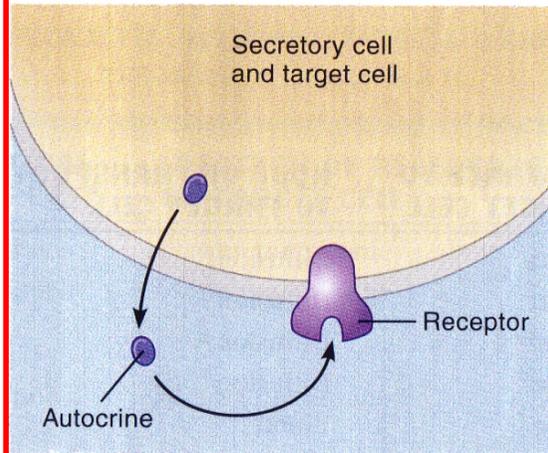


FIGURE 1.3 A highly simplified view of the overall plan of the human body. Flows of material are indicated by arrows.

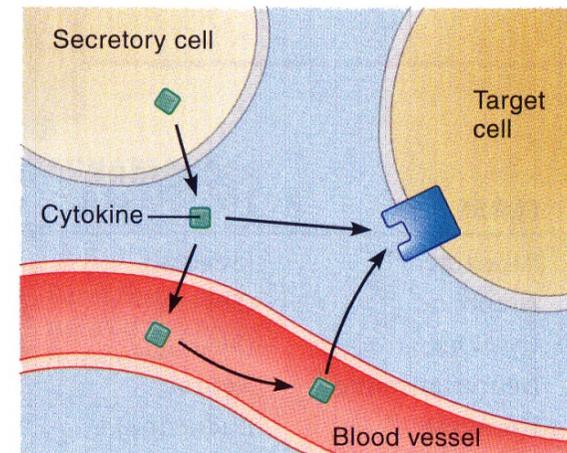
La comunicazione chimica tra le cellule



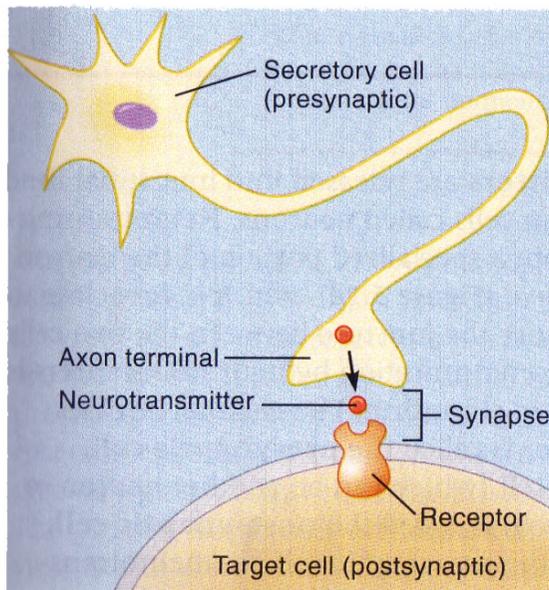
(a) Paracrine



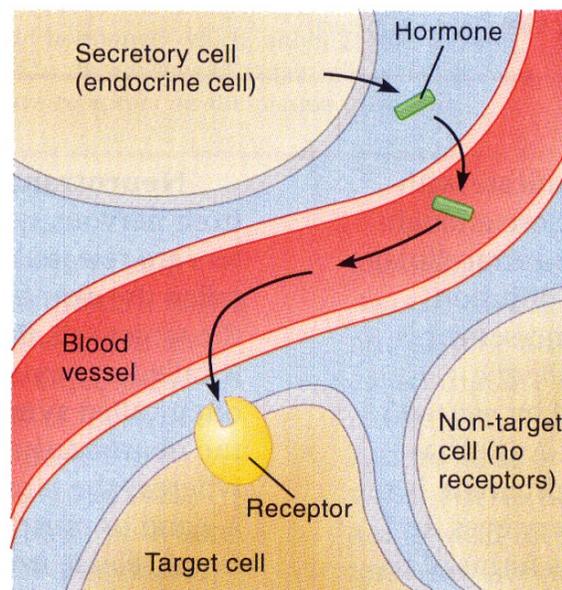
(b) Autocrine



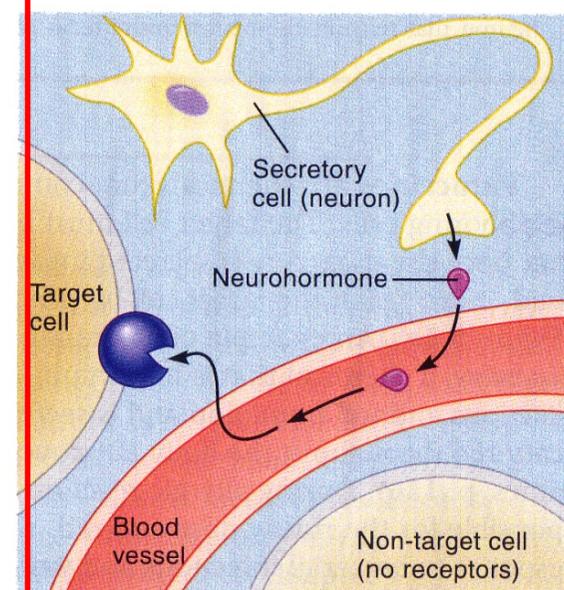
(c) Cytokines



(d) Neurotransmitters

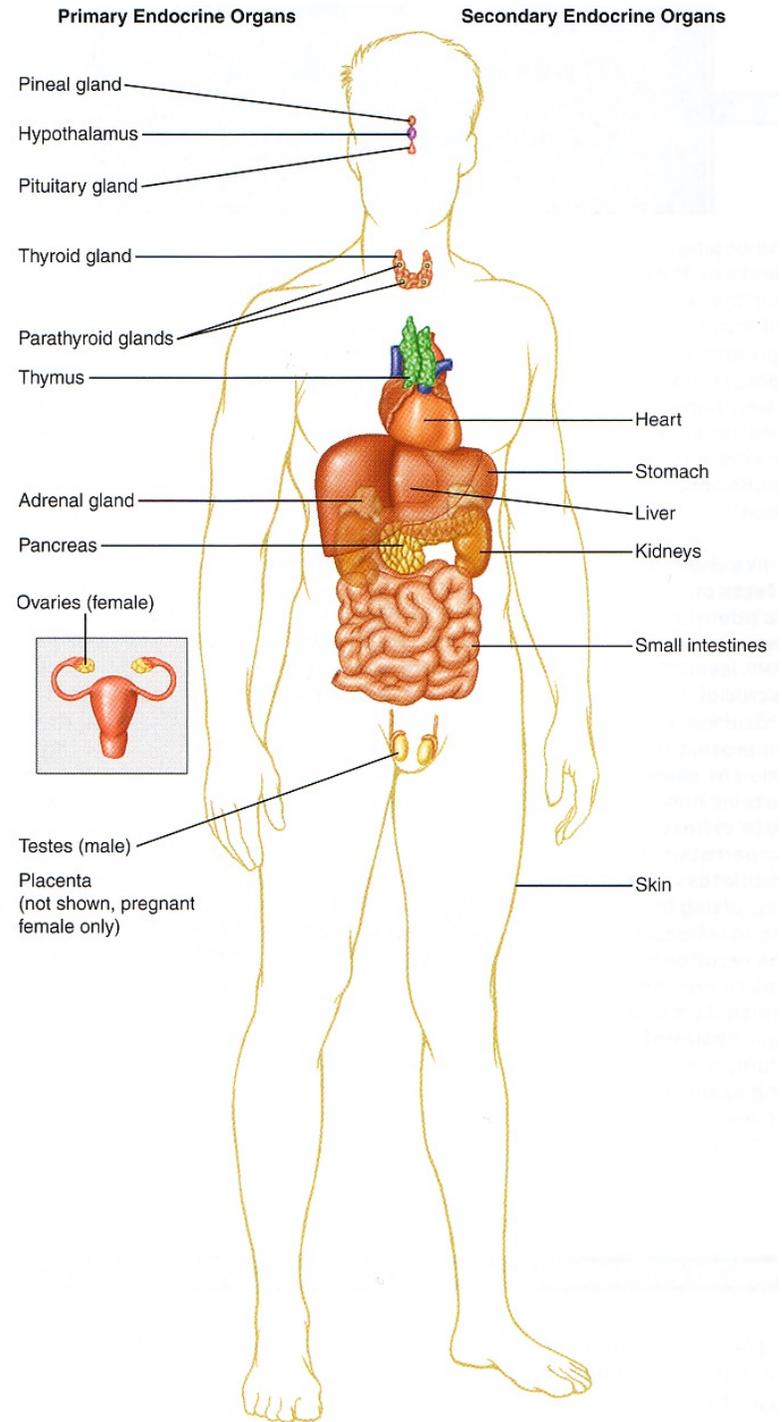


(e) Hormones



(f) Neurohormones

Le ghiandole endocrine



Il recettore e la specificità di risposta

- Il recettore è in genere una glicoproteina
- La sua attivazione si basa su un meccanismo “chiave-serratura” (sito di legame specifico)

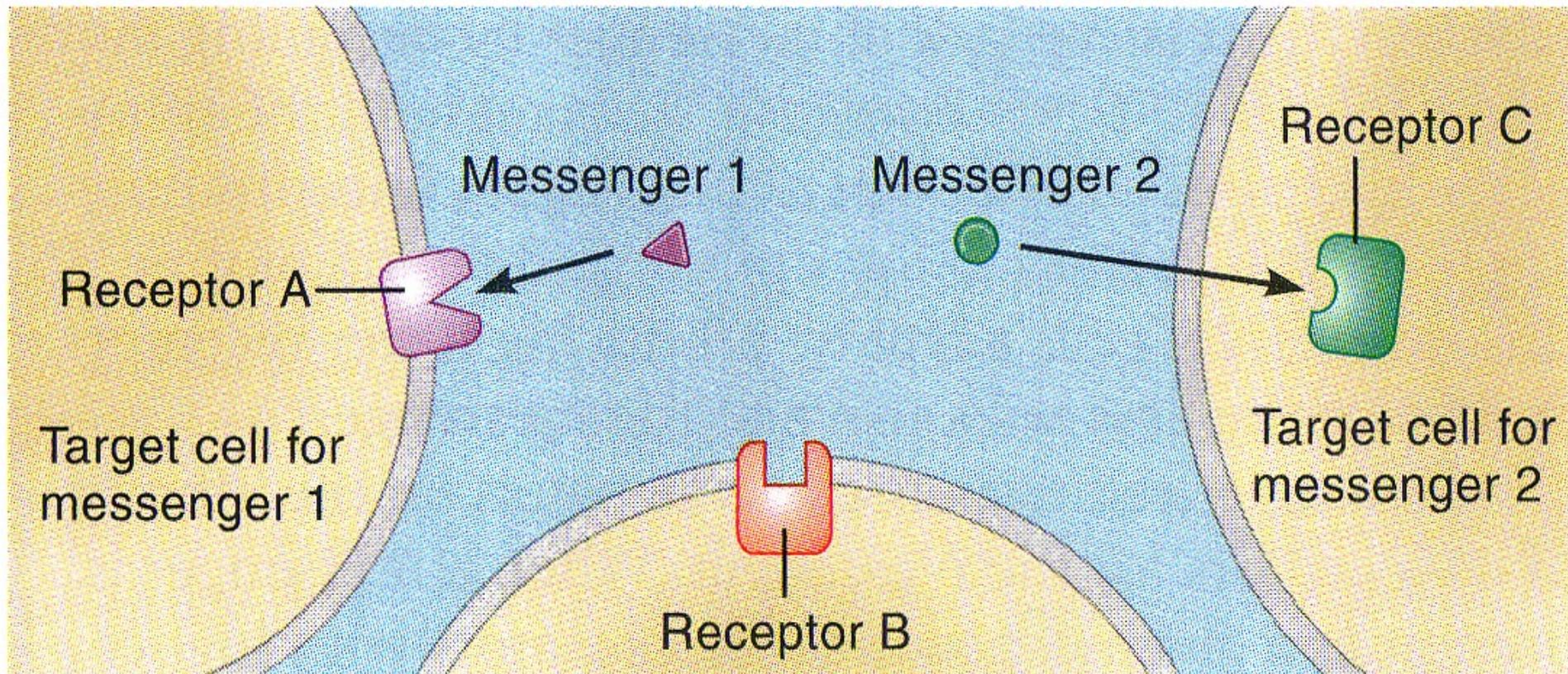


FIGURE 5.8 Receptor specificity. Receptor A is specific for messenger 1, receptor C is specific for messenger 2, and neither messenger can bind to receptor B. Note that receptors can be located either on the plasma membrane (receptors A and B) or inside the cell (receptor C).

La localizzazione del recettore è funzione delle proprietà chimico fisiche del segnale extracellulare

TABLE 5.2 CHEMICAL CLASSIFICATION OF MESSENGERS

CLASS	CHEMICAL PROPERTY	LOCATION OF RECEPTORS ON TARGET CELL	FUNCTIONAL CLASSIFICATION
Amino acids	<u>Lipophobic</u>	<u>Plasma membrane</u>	Neurotransmitters
Amines*	<u>Lipophobic</u>	<u>Plasma membrane</u>	Paracrines, autocrines, neurotransmitters, hormones
Peptides	<u>Lipophobic</u>	<u>Plasma membrane</u>	Paracrines, autocrines, cytokines, neurotransmitters, hormones
Steroids	<u>Lipophilic</u>	<u>Cytosol[†]</u>	Hormones
Eicosanoids	<u>Lipophilic</u>	<u>Cytosol</u>	Paracrines

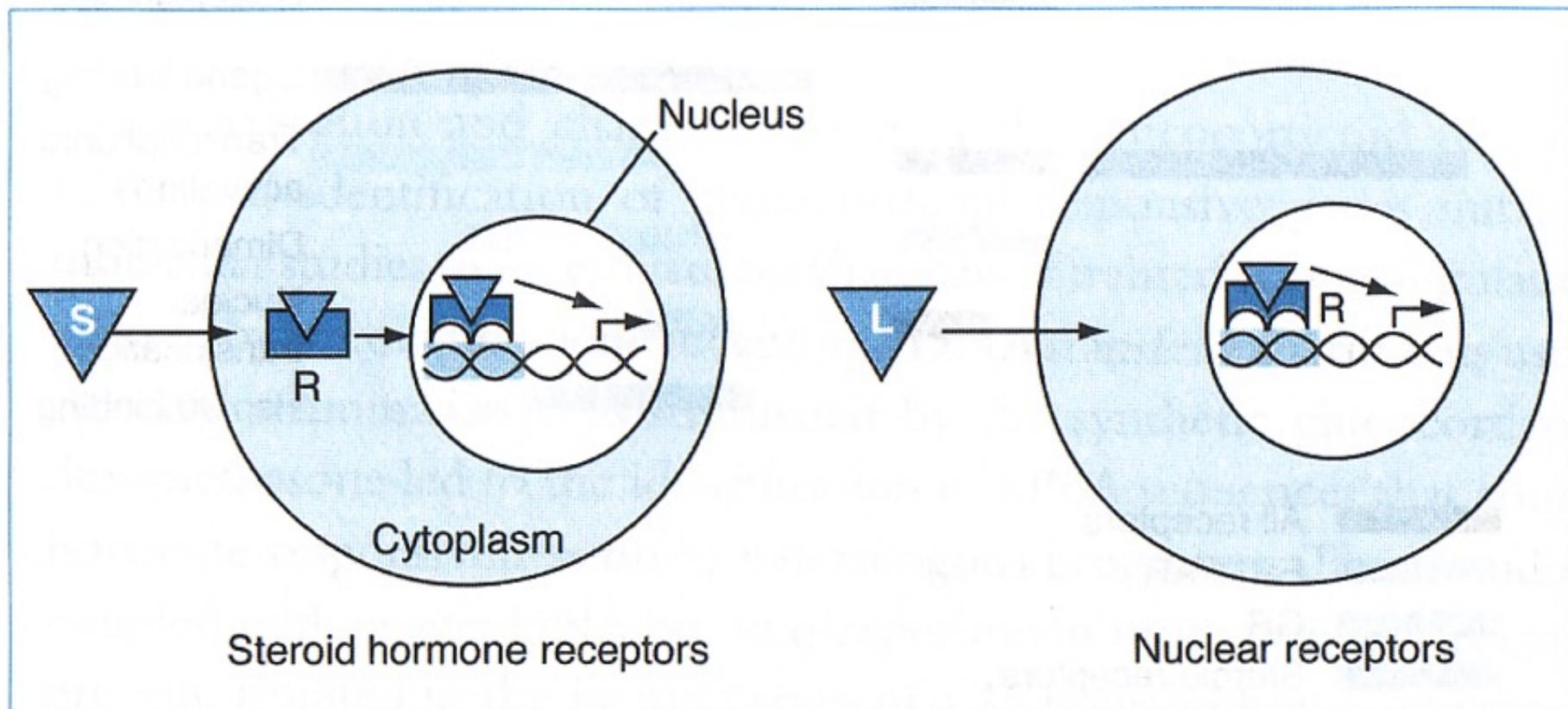
*One exception is the thyroid hormones, which, although amines, are lipophilic and have receptors in the nucleus of target cells.

[†]A few steroid hormones have receptors on the plasma membrane.

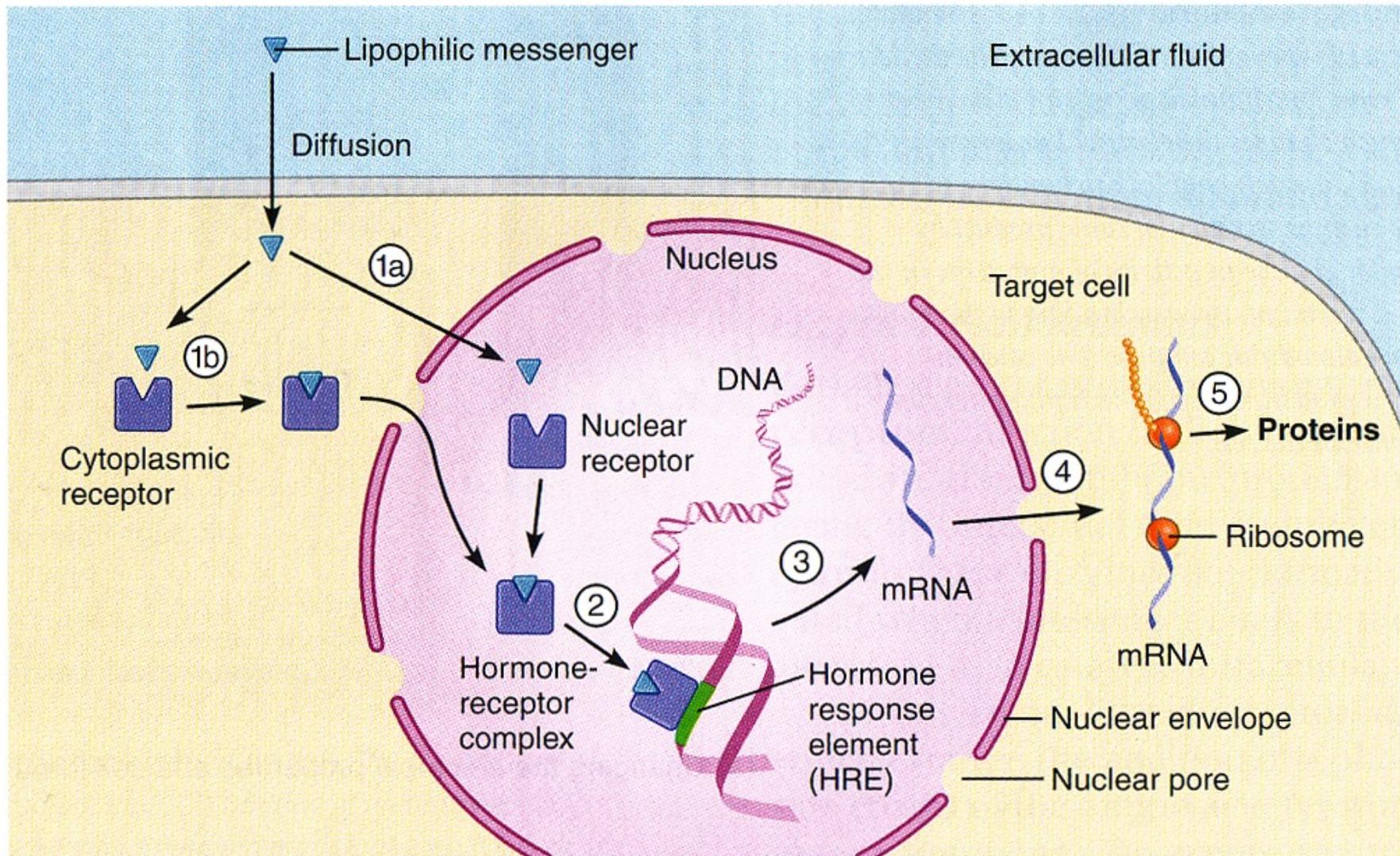
Se il segnale extracellulare (o ligando) è lipofilo i recettori sono intracellulari

I recettori intracellulari possono essere:

- citoplasmatici
- nucleari



Il complesso ligando-recettore (intracellulare) riconosce specifiche sequenze di DNA



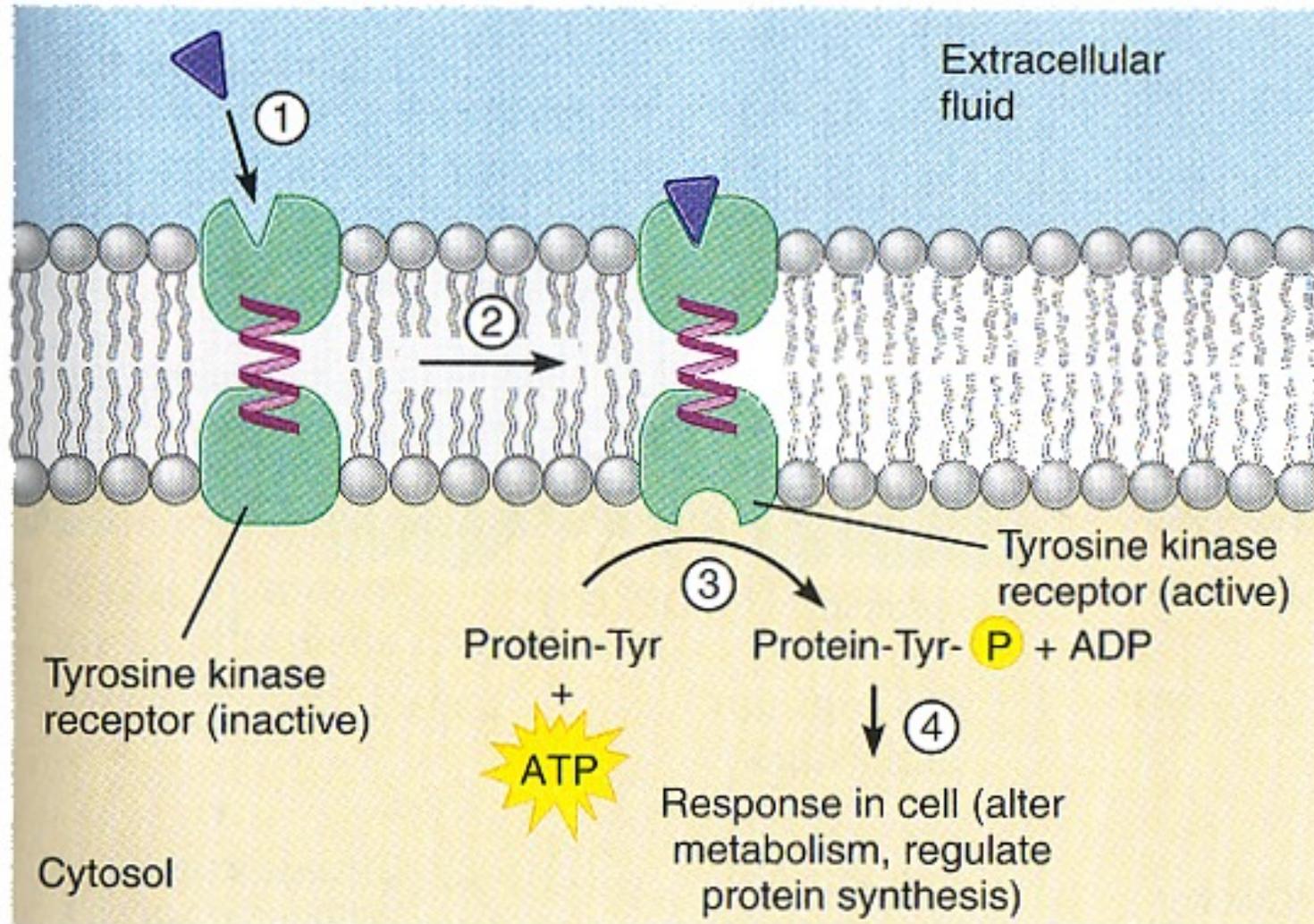
Se il segnale extracellulare (o ligando) è idrofilo
i recettori sono inseriti nella membrana plasmatica

I recettori di membrana possono essere:

recettori dotati di attività enzimatica

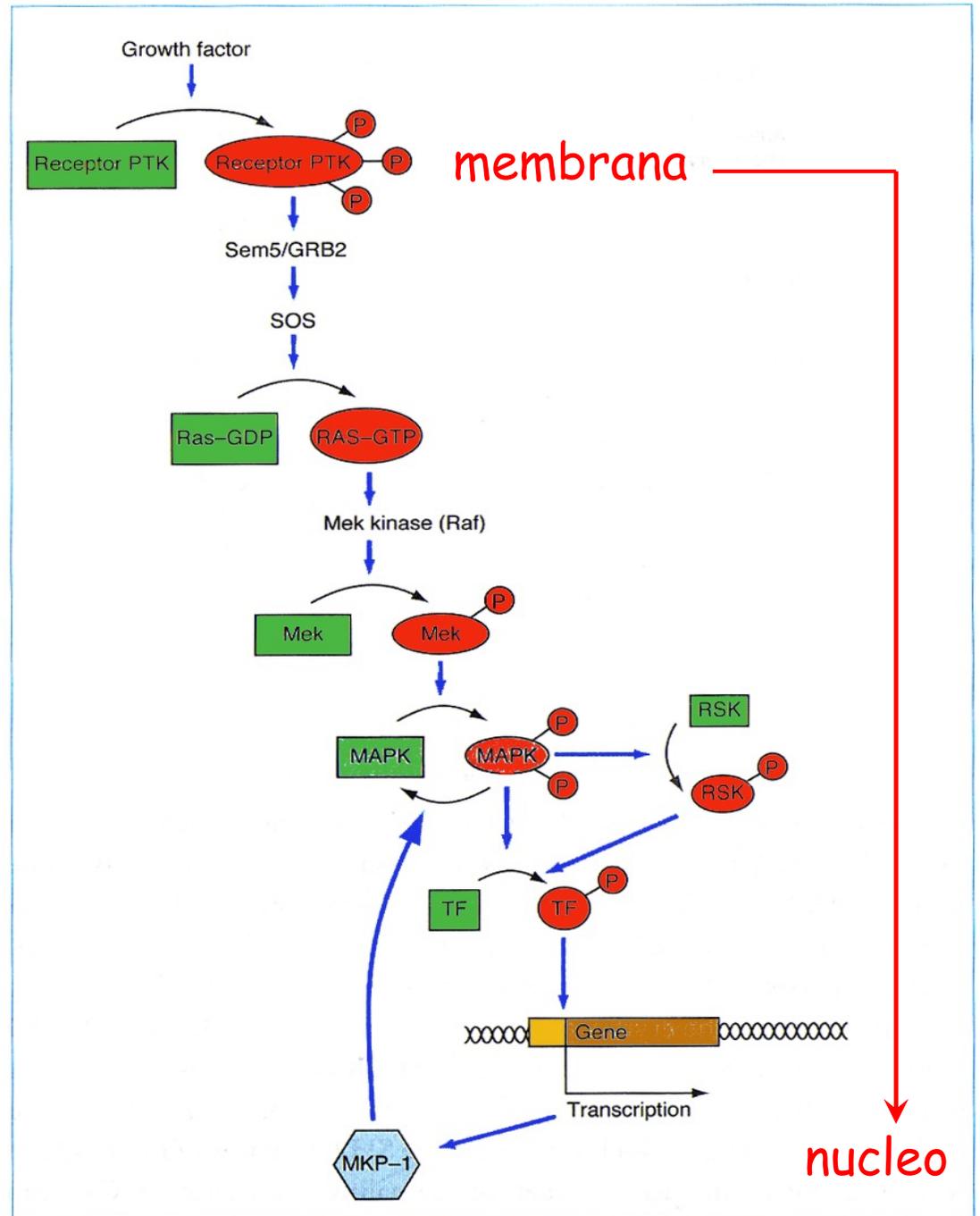
recettori accoppiati a proteine G

I recettori con attività enzimatica (protein-chinasi): i recettori tirosina chinasi



Una cascata

Figure 17.2 A signaling pathway triggered by growth factor receptor PTKs. Following activation of a growth factor receptor PTK by binding to its cognate ligand, autophosphorylation of the receptor creates docking sites that recruit the adaptor protein Grb2, leading to activation of Sos, the GDP-GTP exchanger for Ras. Then a cascade of phosphorylation is triggered, leading to activation of mitogen-activated protein kinase (MAPK). MAPK in turn phosphorylates transcription factors (TF), either directly or through activation of another Ser/Thr kinase, Rsk, thus promoting the transcription of genes required for the growth response. One of the genes induced by growth factor stimulation, presumably through the MAPK pathway, encodes a MAPK phosphatase (MKP-1). As denoted by the filled arrow, MKP-1 may feed back on the pathway by dephosphorylating and inactivating MAPK, thus attenuating the signaling response. [Reproduced with permission from Sun, H. and Tonks, N.K. (1994) *Trends Biochem. Sci.*, 19, 480-5.]



I recettori accoppiati a proteine G

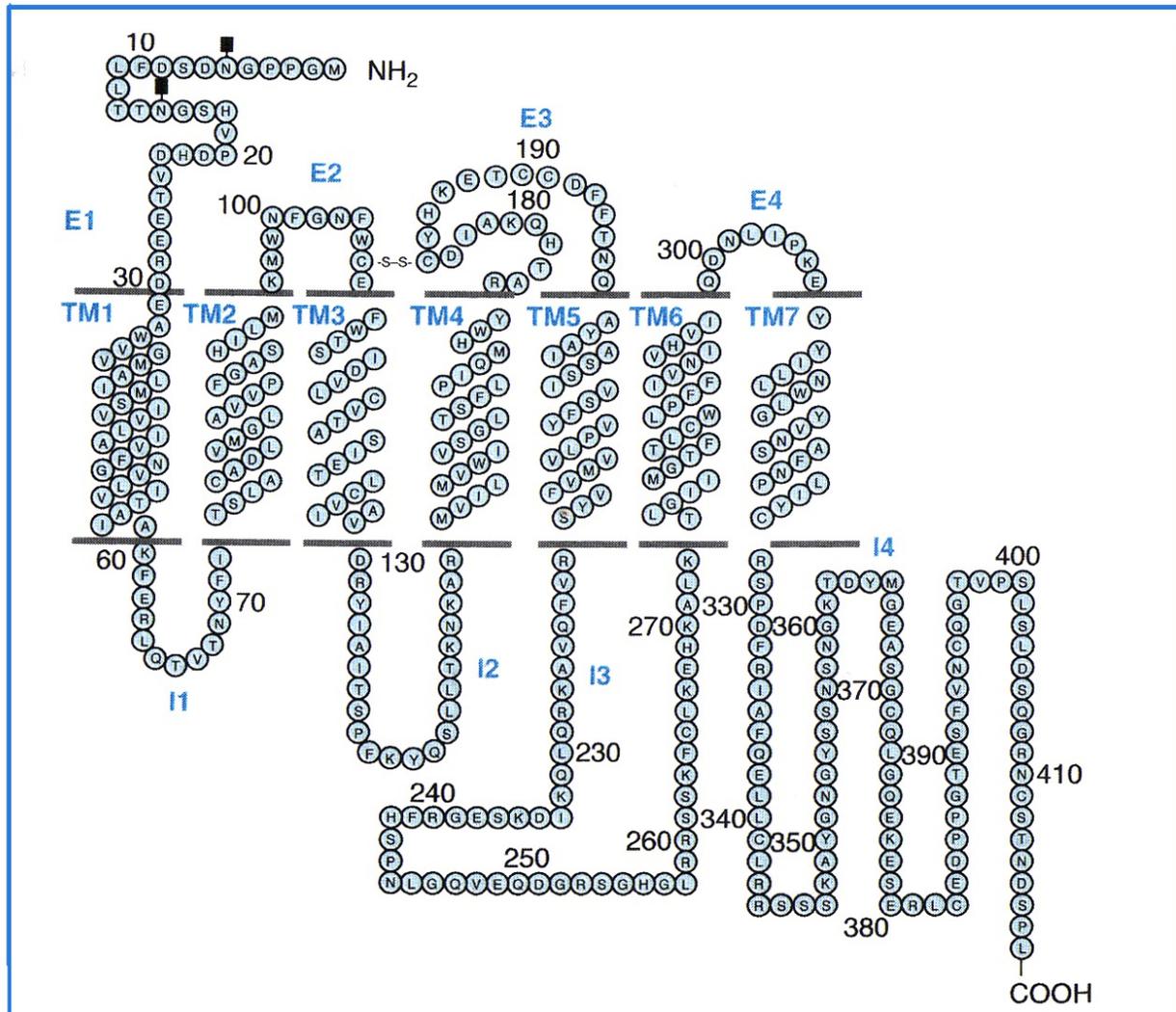


Figure 7.1 Model depicting the transmembrane topology of the β_2 -adrenergic receptor. The positioning of the seven transmembrane domains was accomplished by hydrophathy analysis of the primary amino acid sequence. Extended domains of hydrophobic amino acids were assigned as putative transmembrane spanning regions. Further examination of these sequences by Chou–Fasman analysis suggests that the transmembrane domains exist in an α -helical conformation. The putative transmembrane domains are labeled TM1–TM7, the extracellular domains E1–E4 and the intracellular domains I1–I4.

L'effettore è un enzima (o un canale ionico)

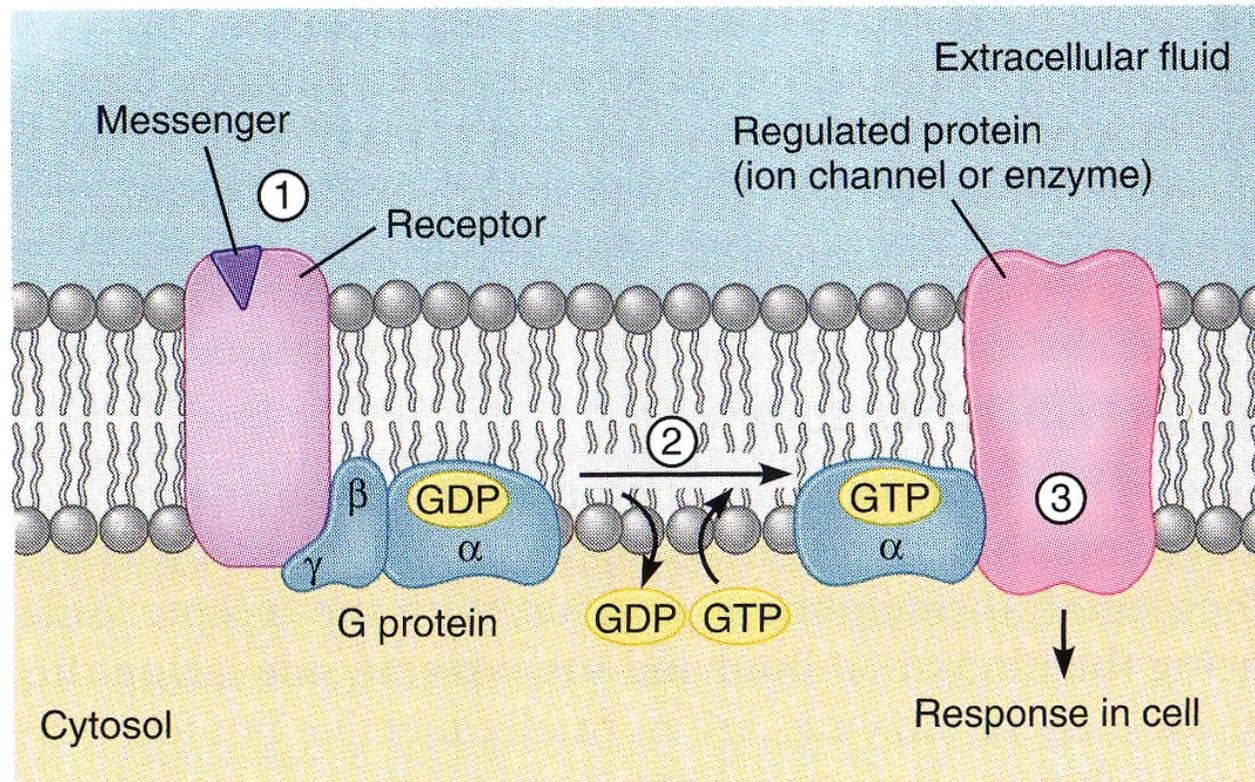
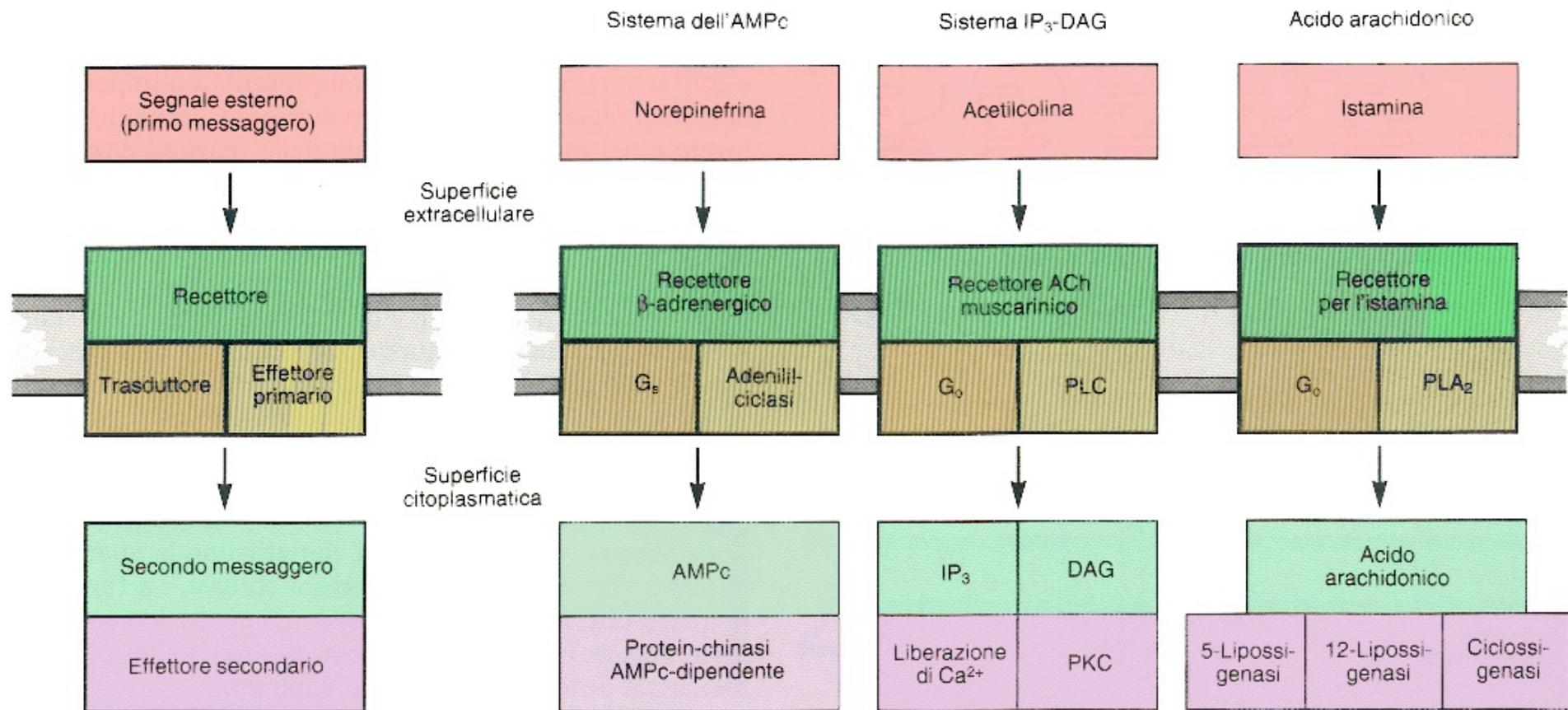
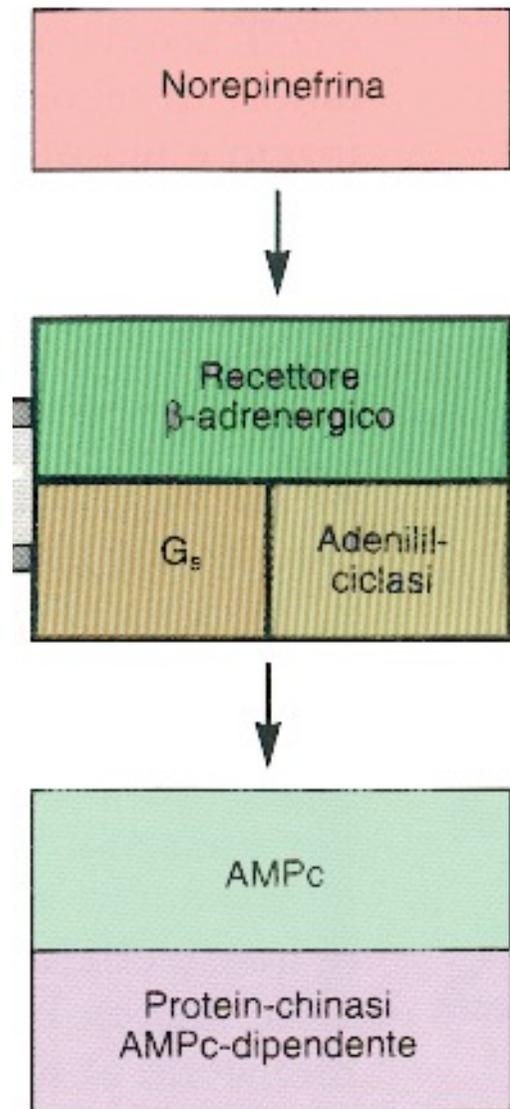


FIGURE 5.14 Actions of G proteins. *G proteins have three subunits: alpha, beta, and gamma. The alpha subunit has binding sites for guanosine nucleotides. In the inactive state, GDP is bound to the alpha subunit. ① Binding of a messenger to a G-protein-linked receptor activates the G protein. ② The GDP is released as the alpha subunit moves laterally within the membrane and binds a GTP. ③ The alpha unit then activates another membrane protein, producing a response in the cell.*

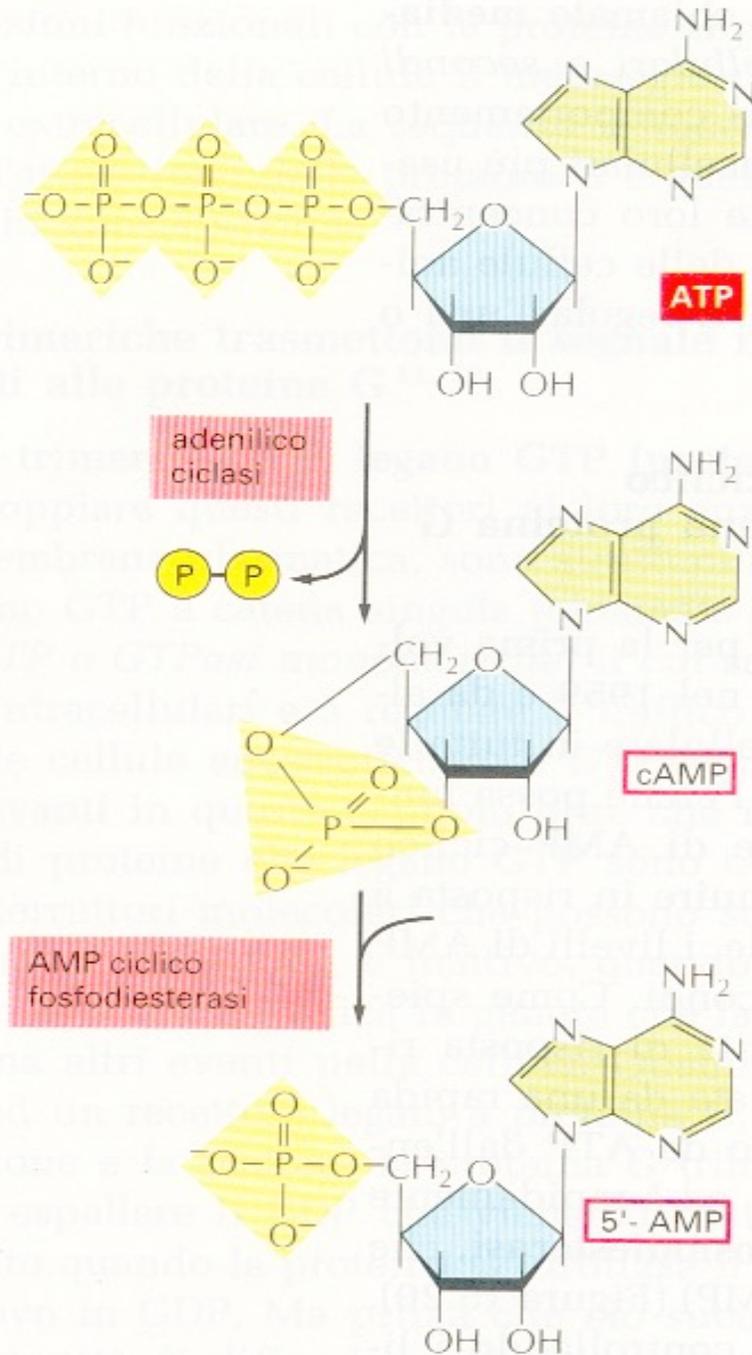
I secondi messaggeri



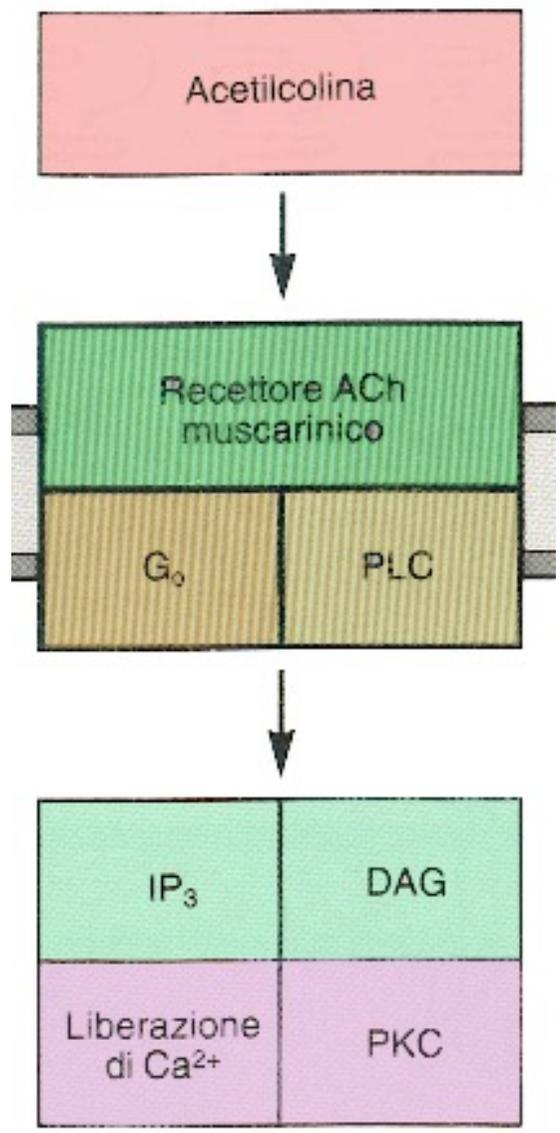
Sistema dell'AMPC



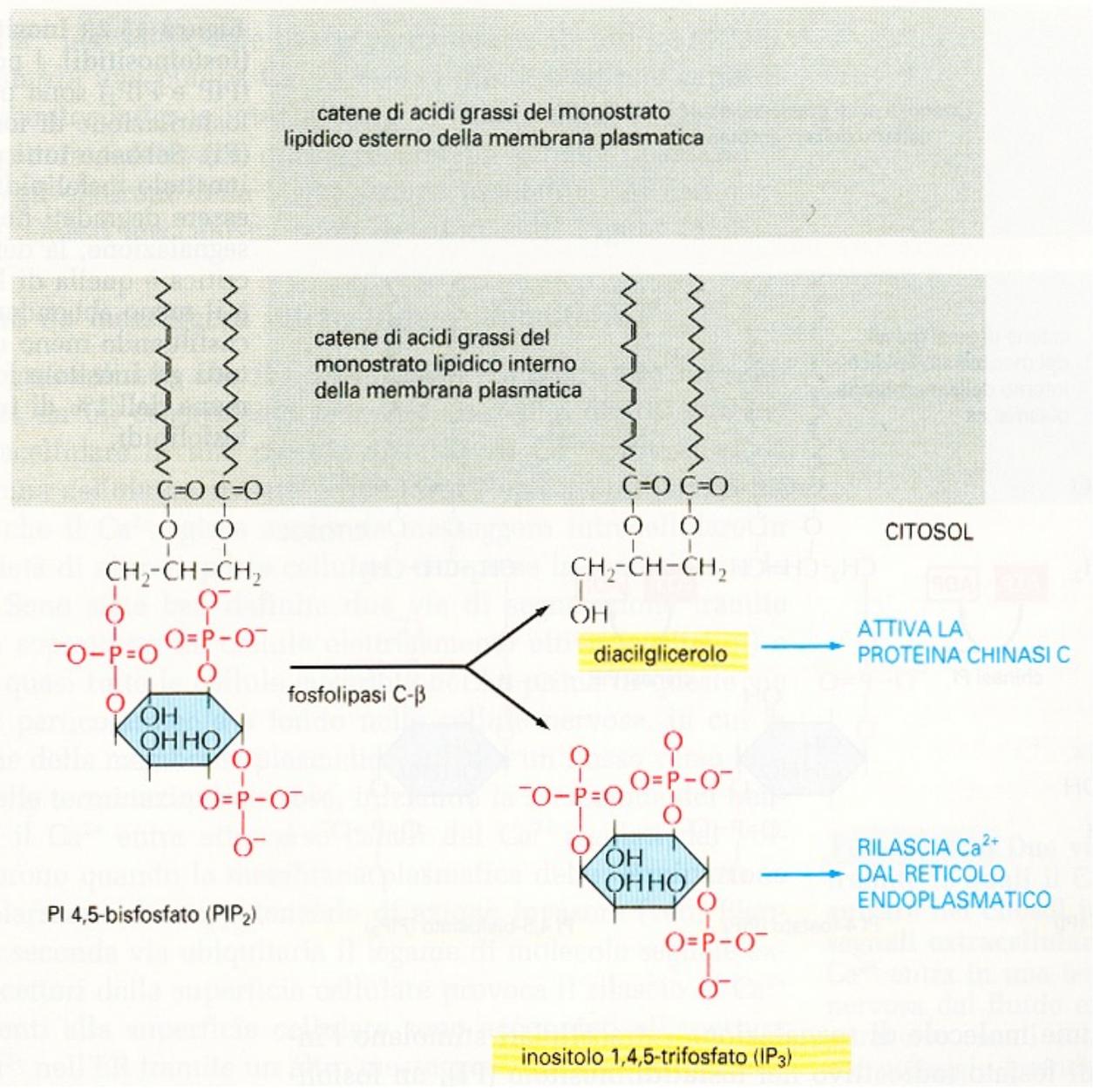
La sintesi dell' AMPC

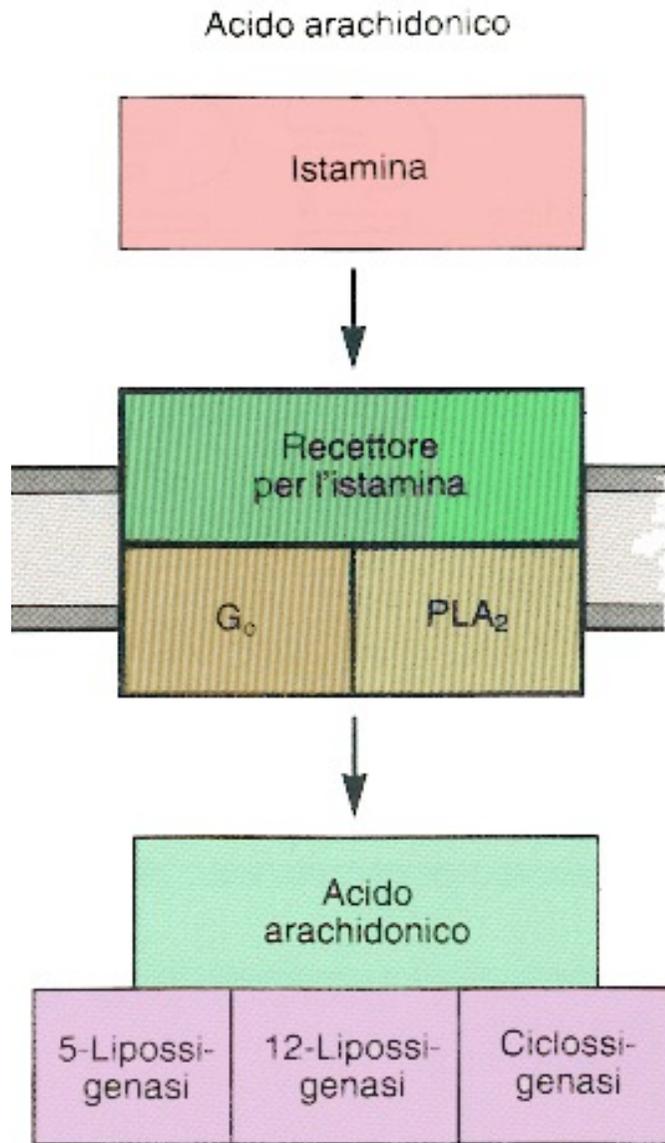


Sistema IP₃-DAG

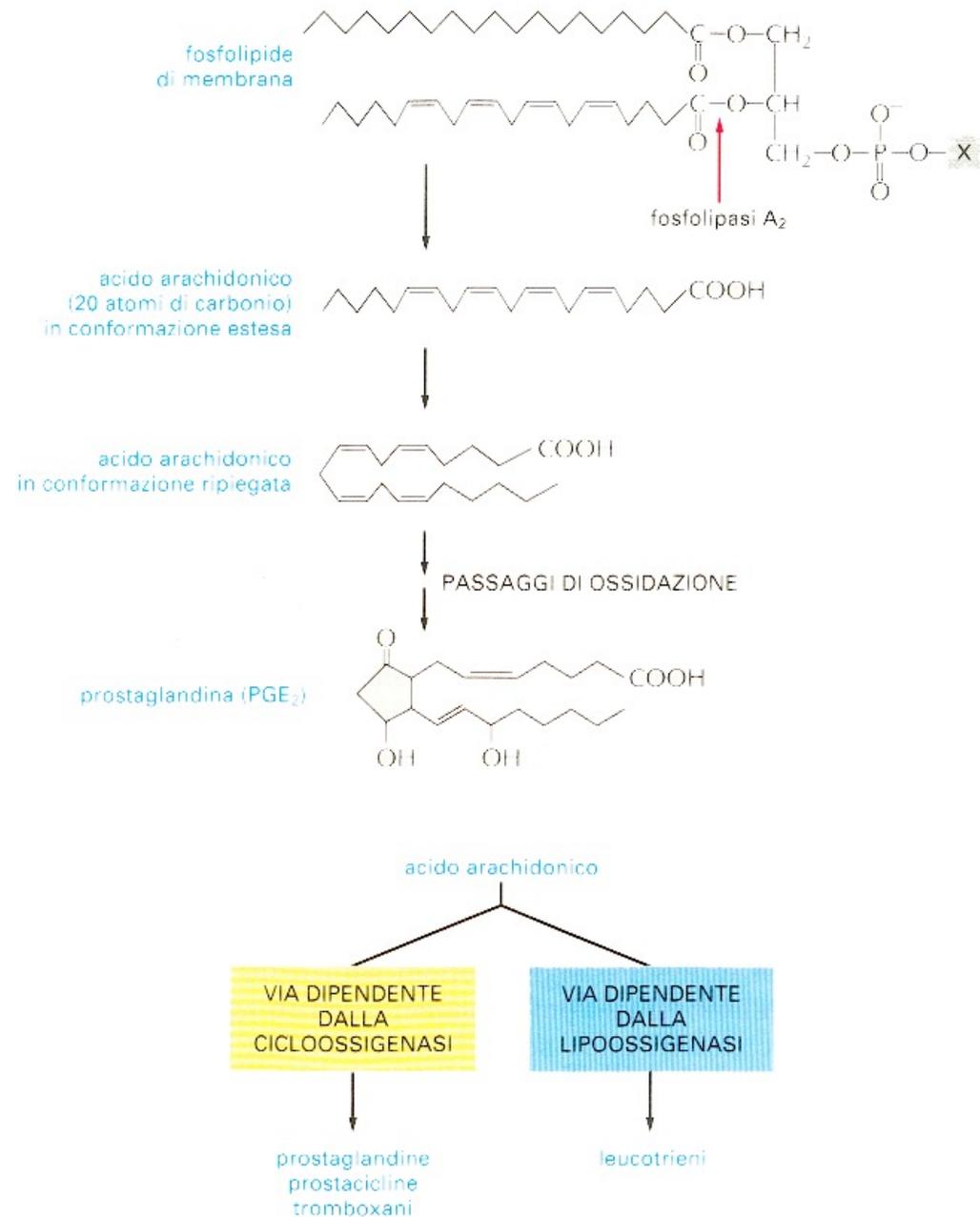


La sintesi dell' IP₃

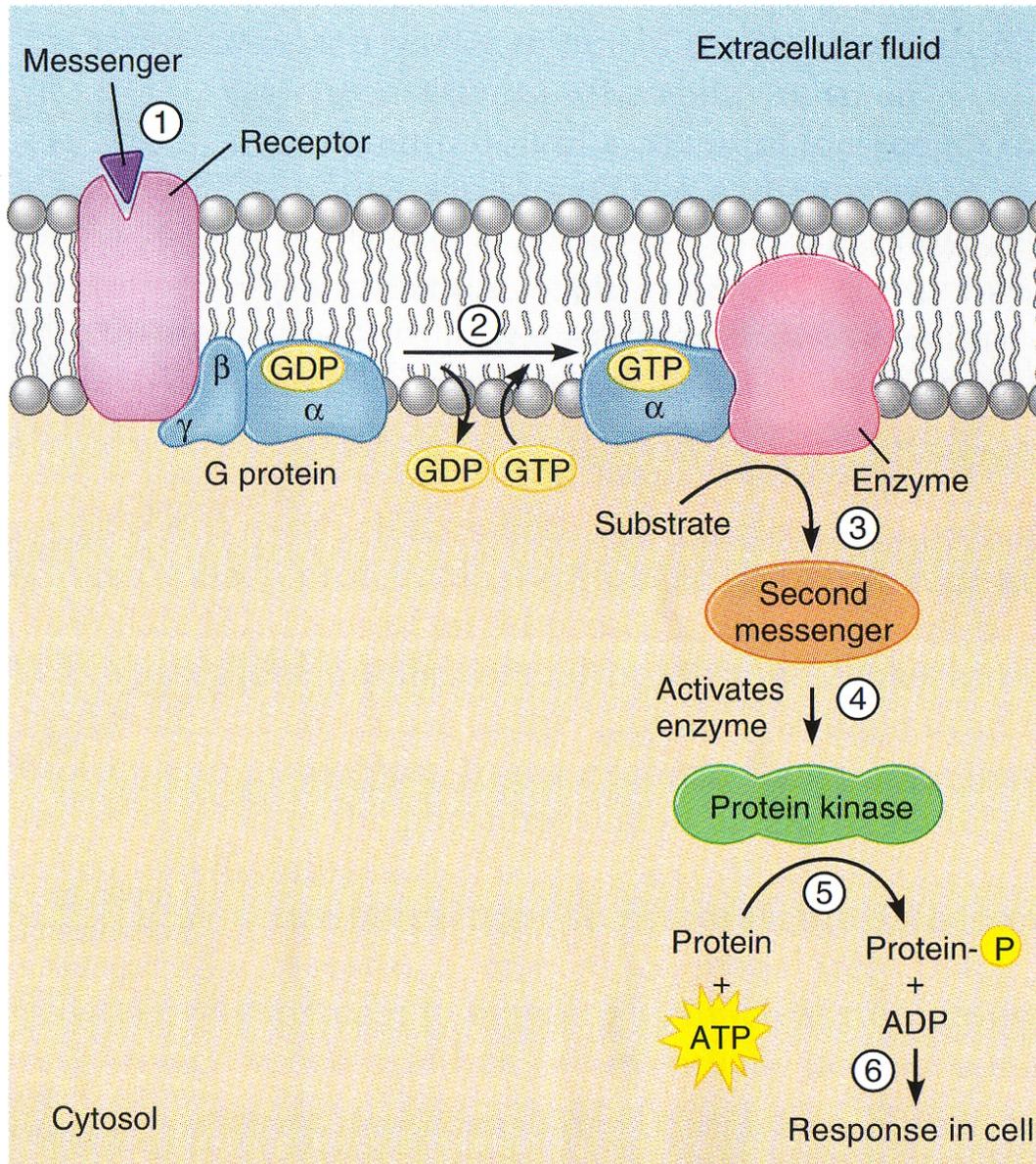




La sintesi dell'acido arachidonico



Il secondo messaggero attiva le protein-chinasi



Fosforilazione delle proteine

strategia “universale”
di attivazione cellulare

Protein-chinasi A (PKA)

Attivate da AMPc

Protein-chinasi C (PKC)

Attivate da Ca^{2+}

FIGURE 5.16 G-protein-regulated enzymes and second messengers. In this example the G protein is coupled to an enzyme in the plasma membrane. ① Binding of the messenger to its receptor activates the G protein. ② The alpha subunit moves to and activates an enzyme in the membrane. ③ The activated enzyme catalyzes formation of a second messenger in the cytosol. ④ The second messenger activates a protein kinase, which ⑤ catalyzes phosphorylation of a protein, which ⑥ initiates a response in the cell.

Il vantaggio della cascata attivata da secondi messaggeri

L' amplificazione del segnale

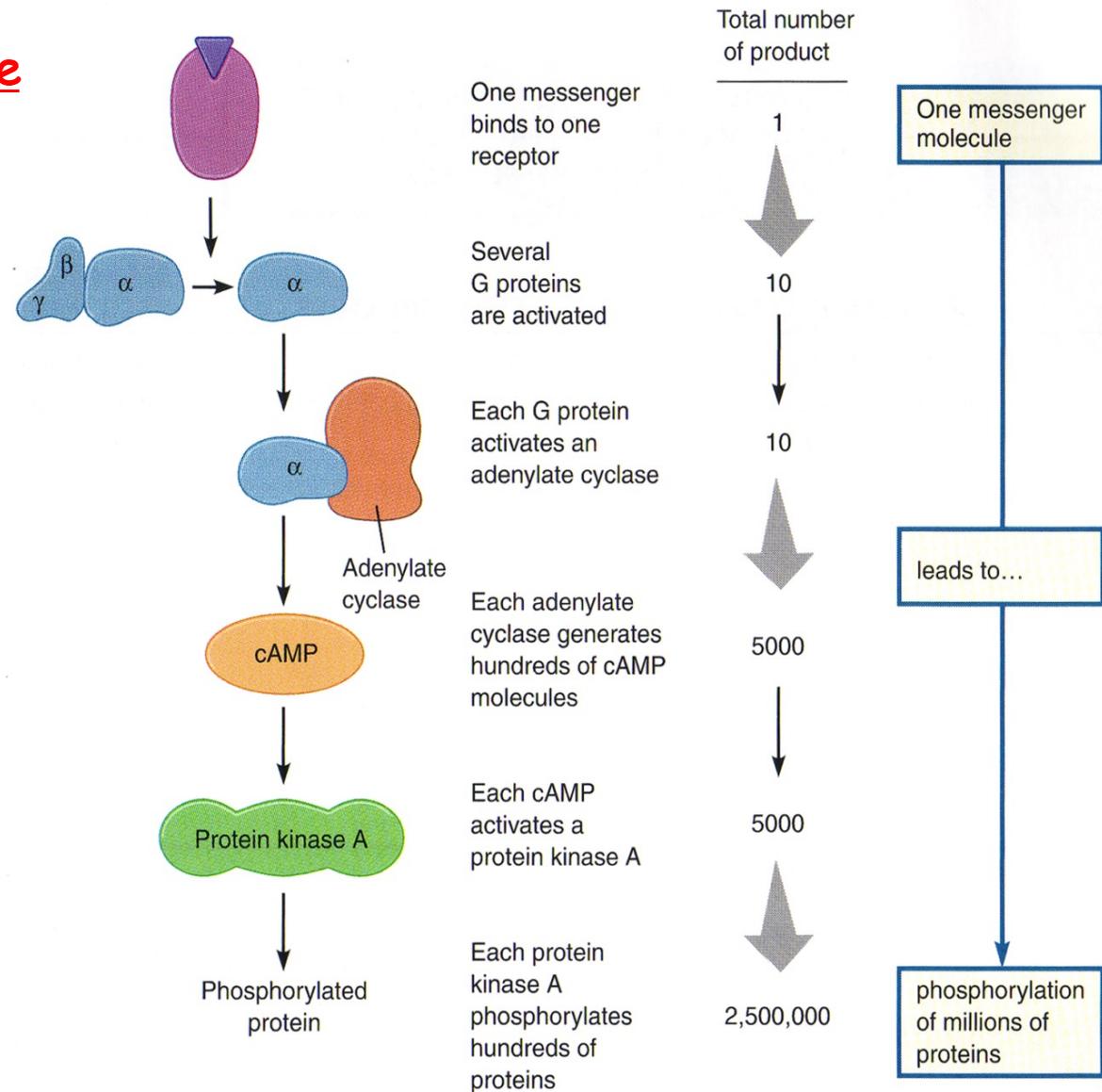


FIGURE 5.18 Signal amplification, in this case by the second messenger cAMP.