L'organismo pluricellulare necessita di comunicazione intercellulare

Omeostasi

"Mantenimento di condizioni stabili mediante
meccanismi fisiologici coordinati"

1) Comunicazione tra cellule
2) Interazione con l'esterno
3) Reazione agli stimoli
4) Autoritmicità (cuore, respiro)

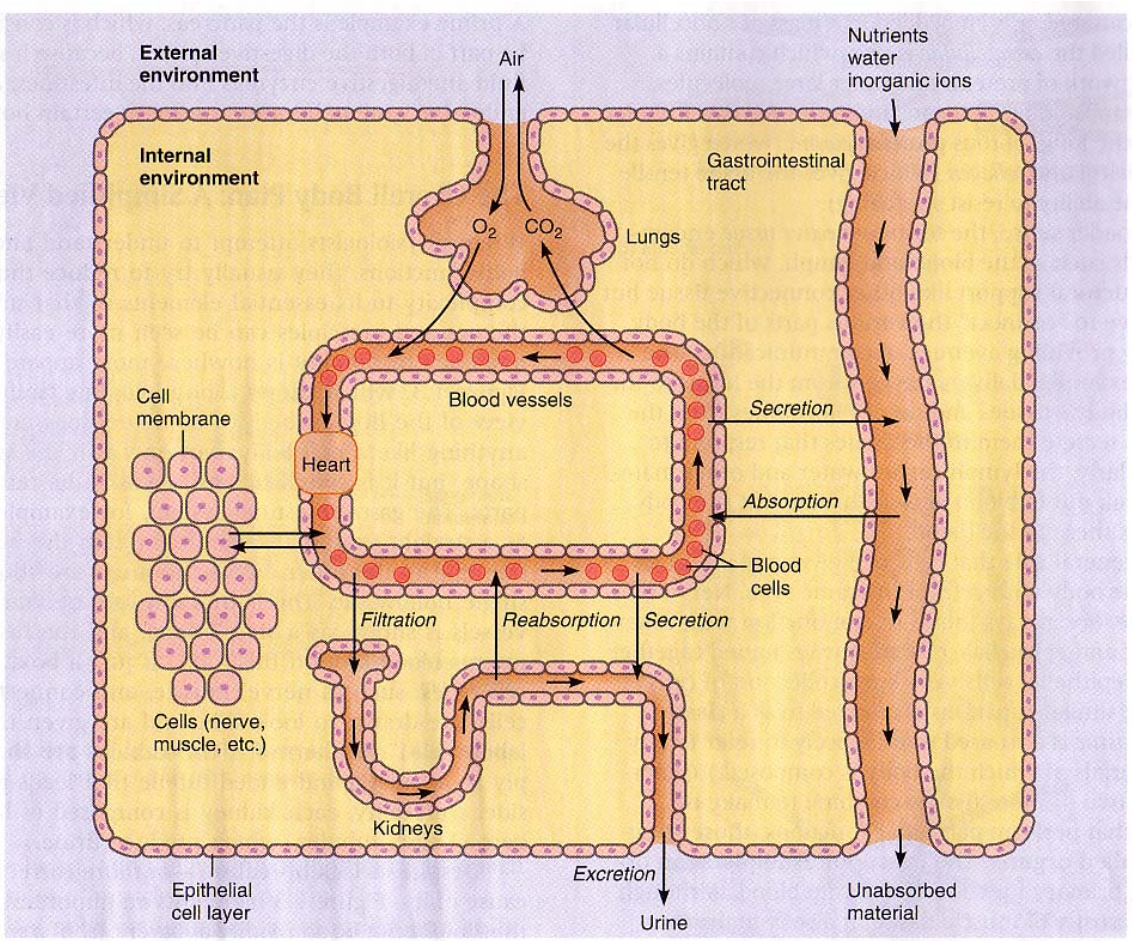
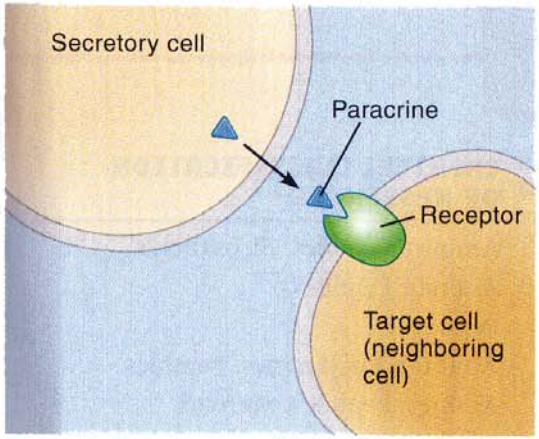
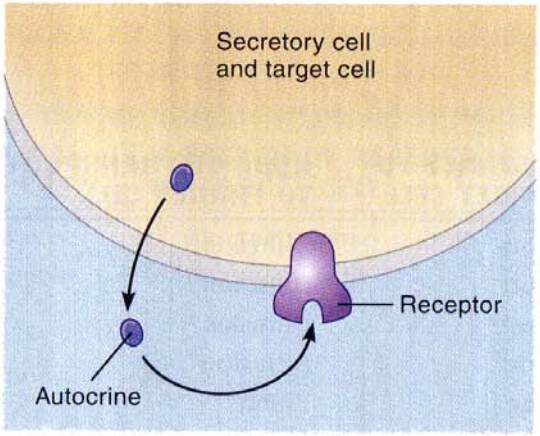


FIGURE 1.3 **A highly simplified view of the overall plan of the human body.**
Flows of material are indicated by arrows.

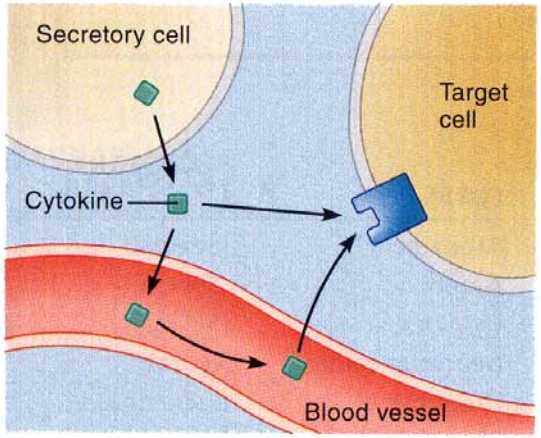
La comunicazione chimica tra le cellule



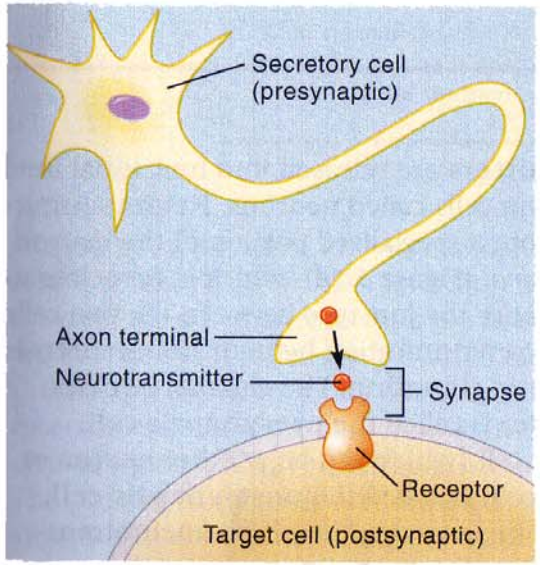
(a) Paracrines



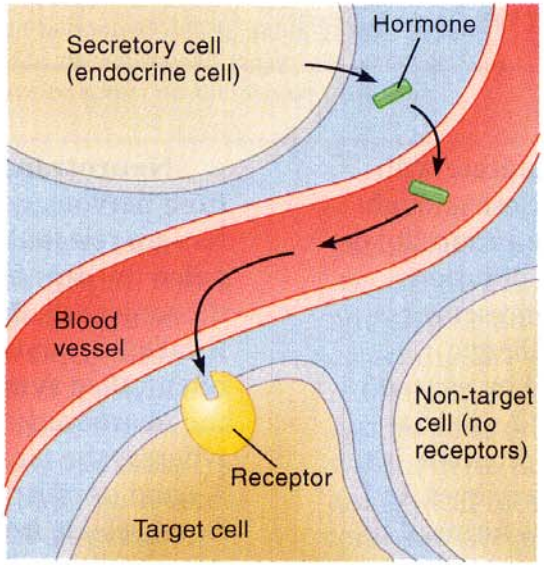
(b) Autocrines



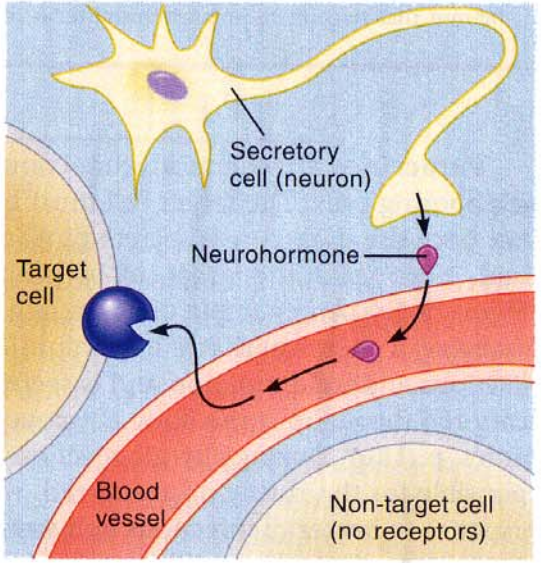
(c) Cytokines



(d) Neurotransmitters

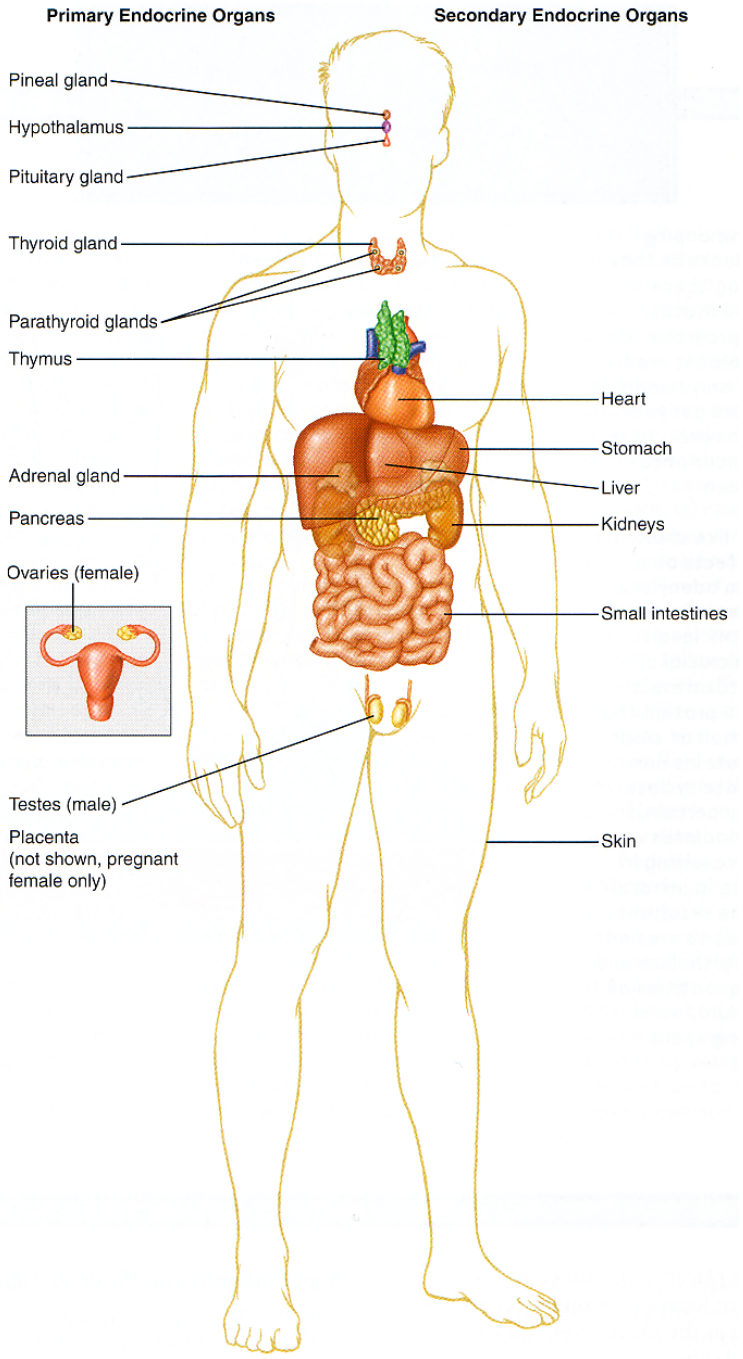


(e) Hormones



(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)

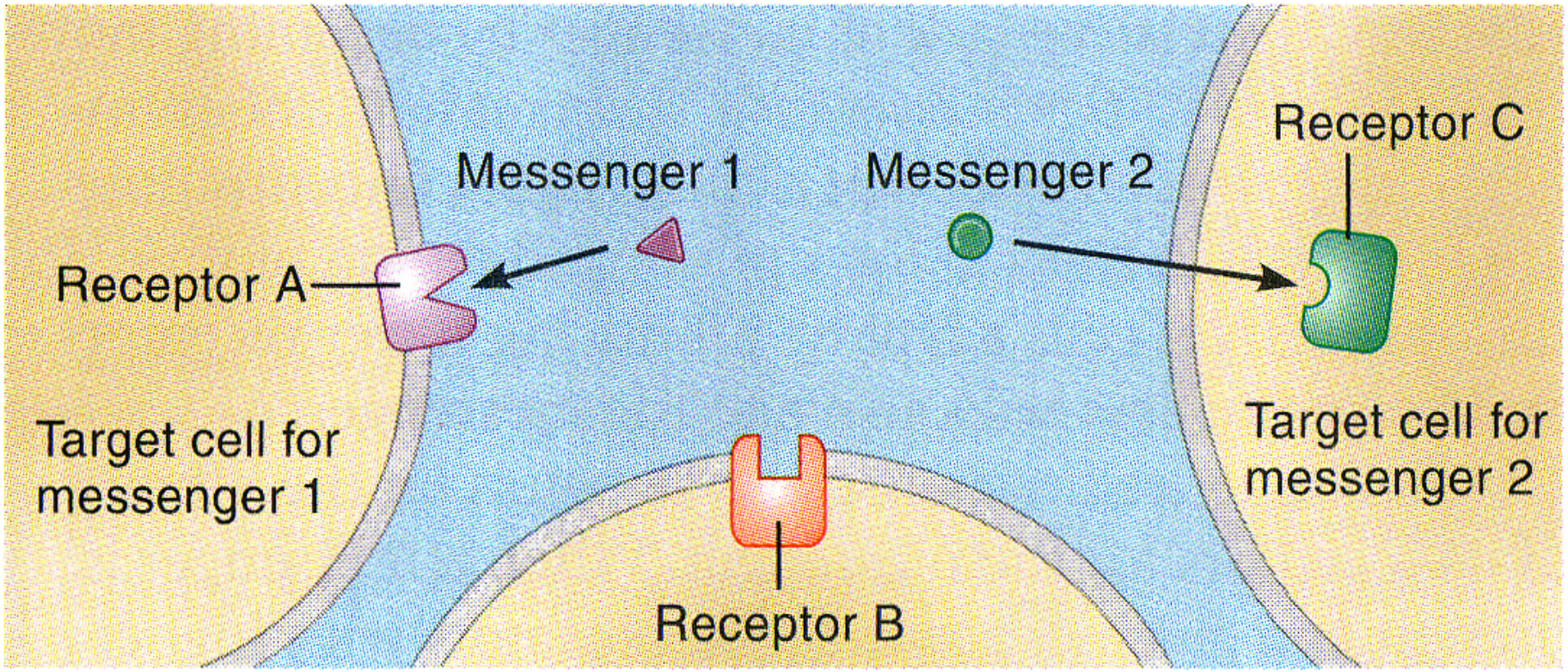


FIGURE 5.8 Receptor specificity. *Receptor A is specific for messenger 1, receptor C is specific for messenger 2, and neither messenger can bind to receptor B. Note that receptors can be located either on the plasma membrane (receptors A and B) or inside the cell (receptor C).*

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

TABLE 5.2 CHEMICAL CLASSIFICATION OF MESSENGERS

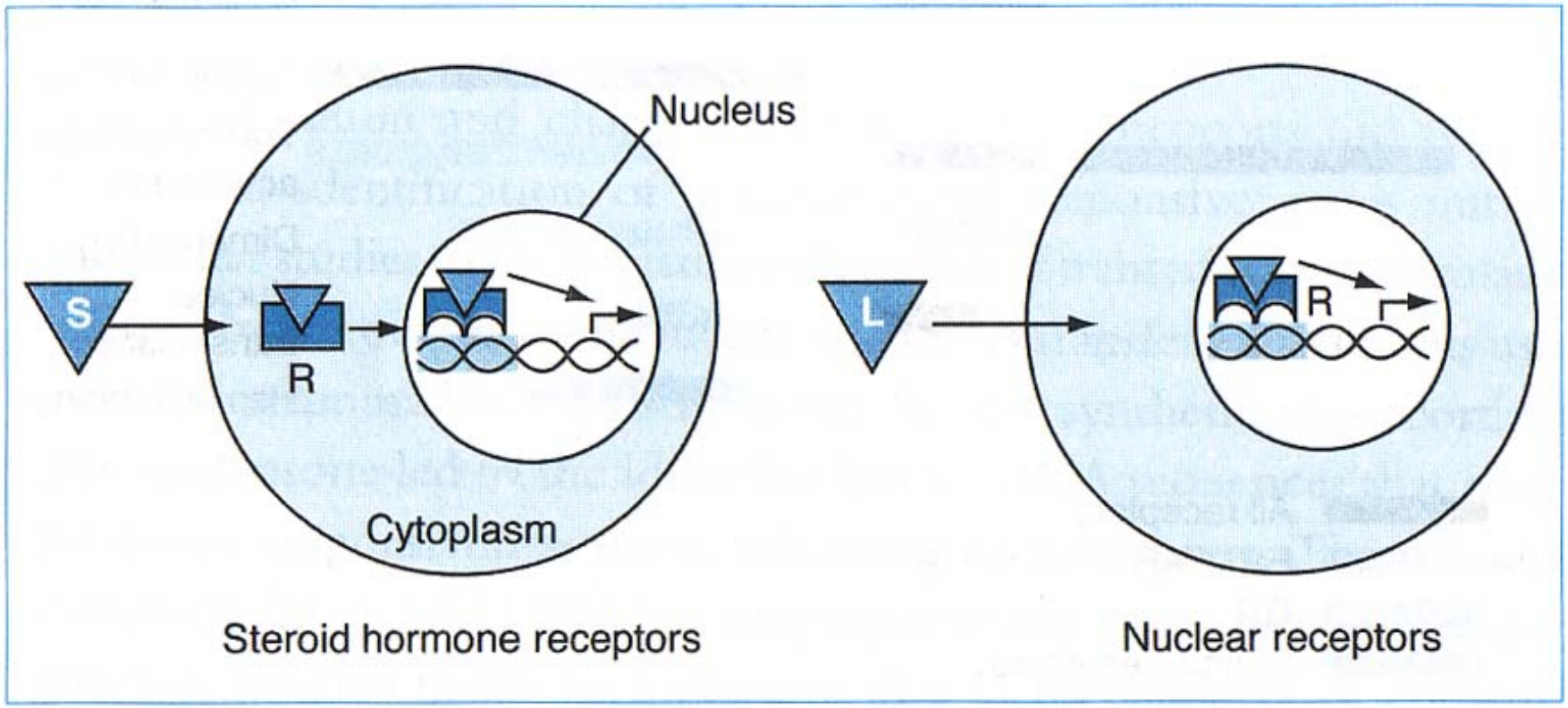
CLASS	CHEMICAL PROPERTY	LOCATION OF RECEPTORS ON TARGET CELL	FUNCTIONAL CLASSIFICATION
Amino acids	Lipophobic	Plasma membrane	Neurotransmitters
Amines*	Lipophobic	Plasma membrane	Paracrines, autocrines, neurotransmitters, hormones
Peptides	Lipophobic	Plasma membrane	Paracrines, autocrines, cytokines,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

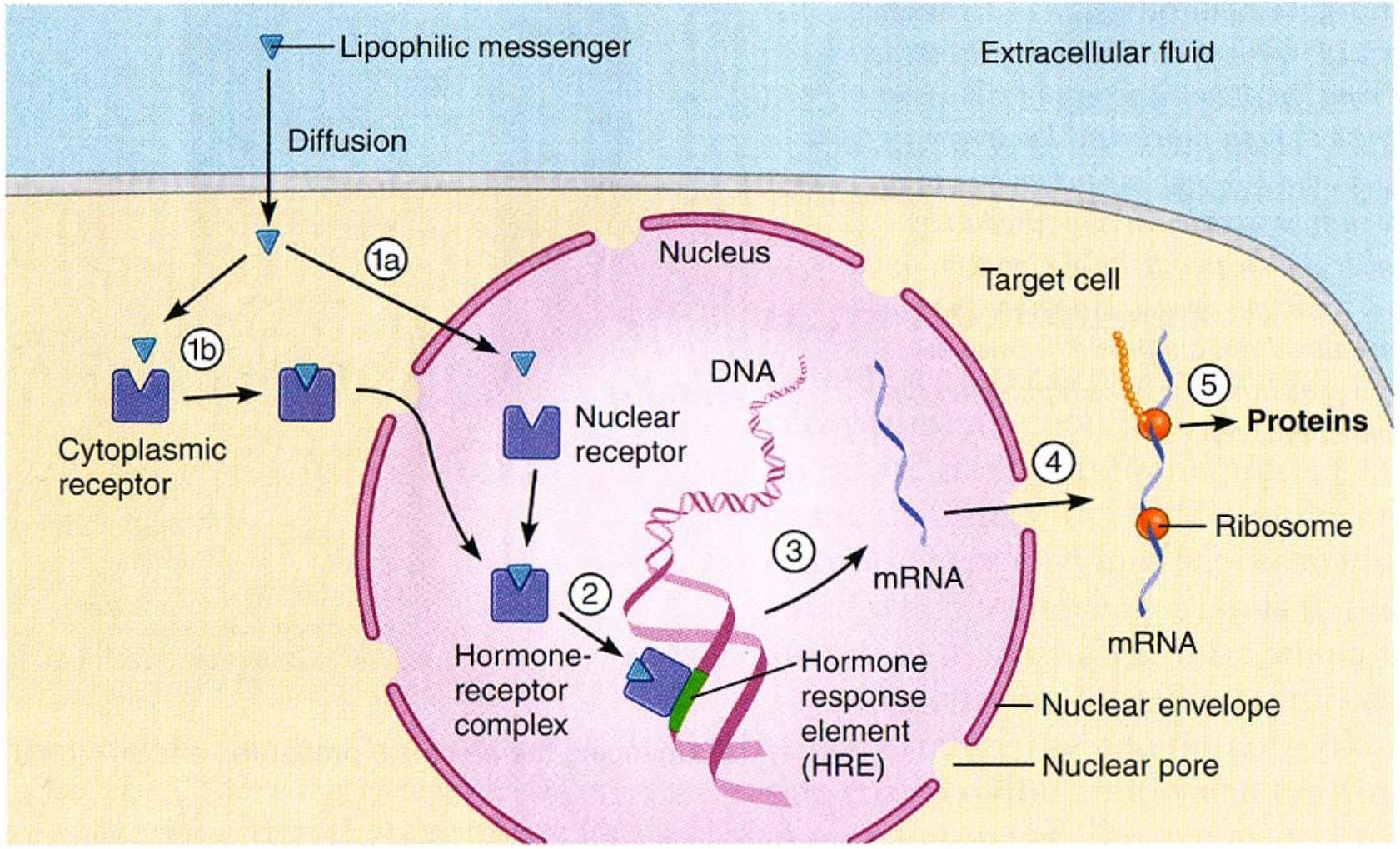
Se il segnale extracellulare (o ligando) è lipofilo i recettori sono intracellulari

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

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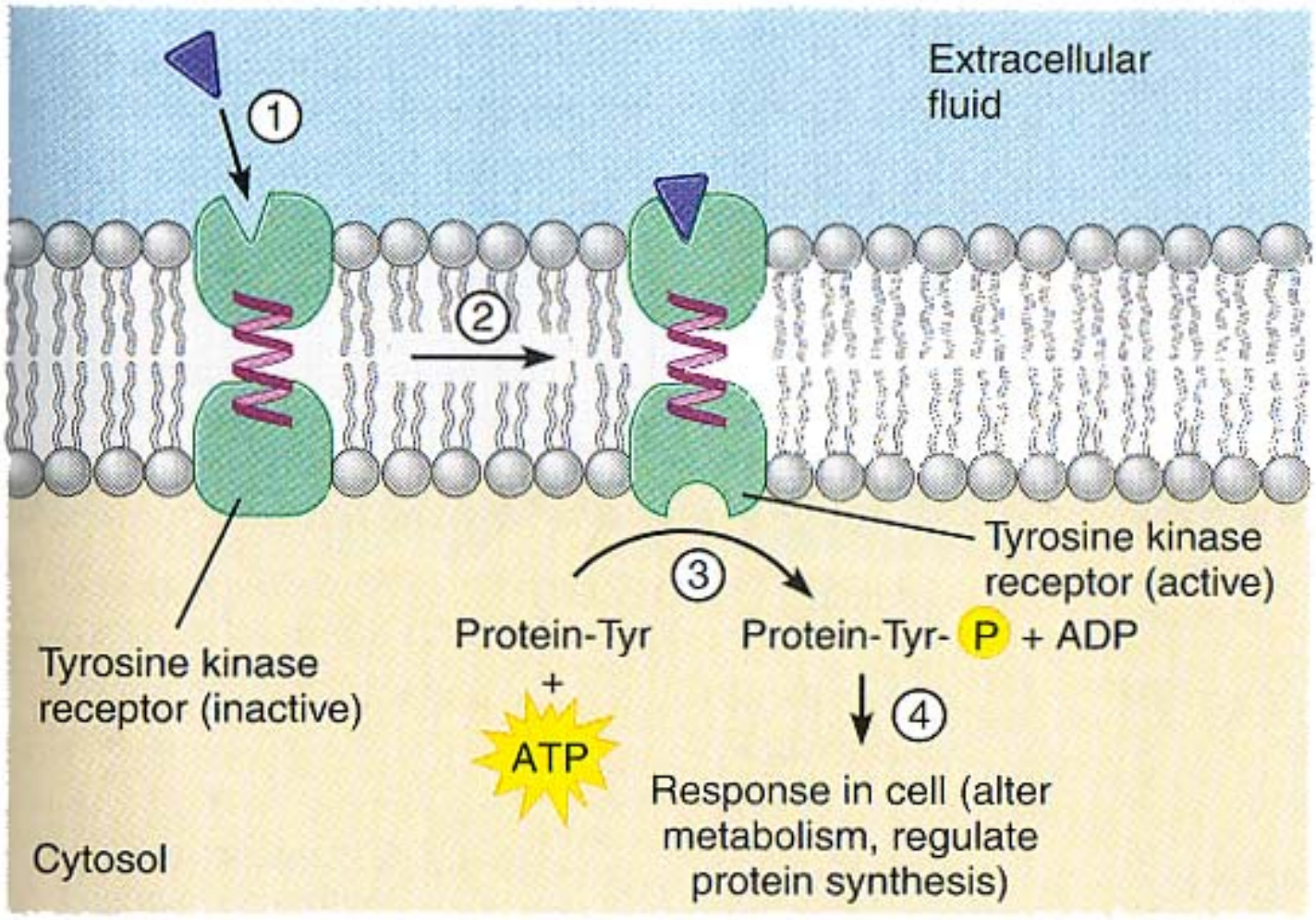
I recettori di membrana possono essere:

recettori dotati di attività enzimatica

recettori accoppiati a proteine G

I recettori con attività enzimatica: i recettori tirosina chinasi



La dimerizzazione dei recettori tirosina chinasi

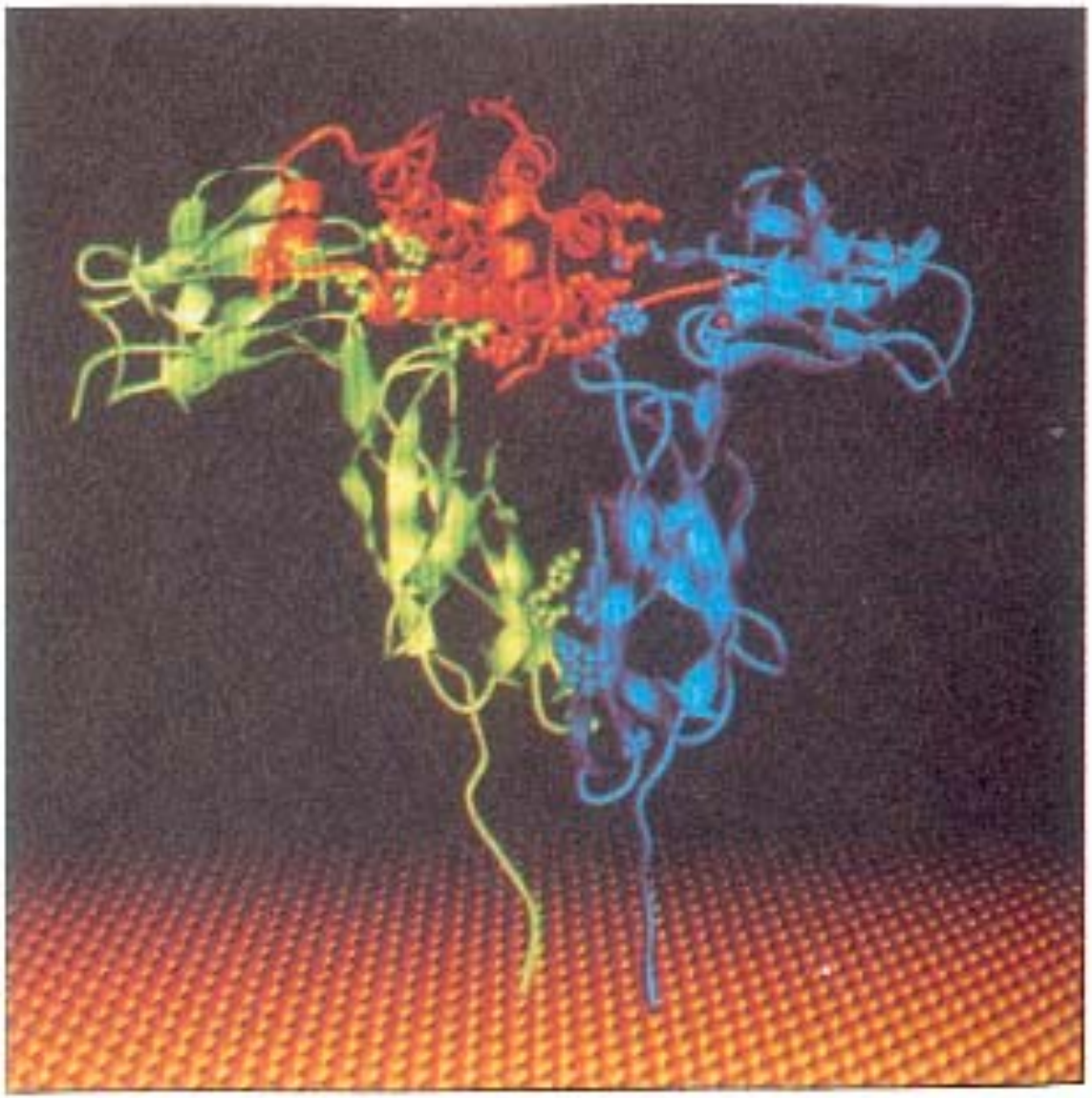
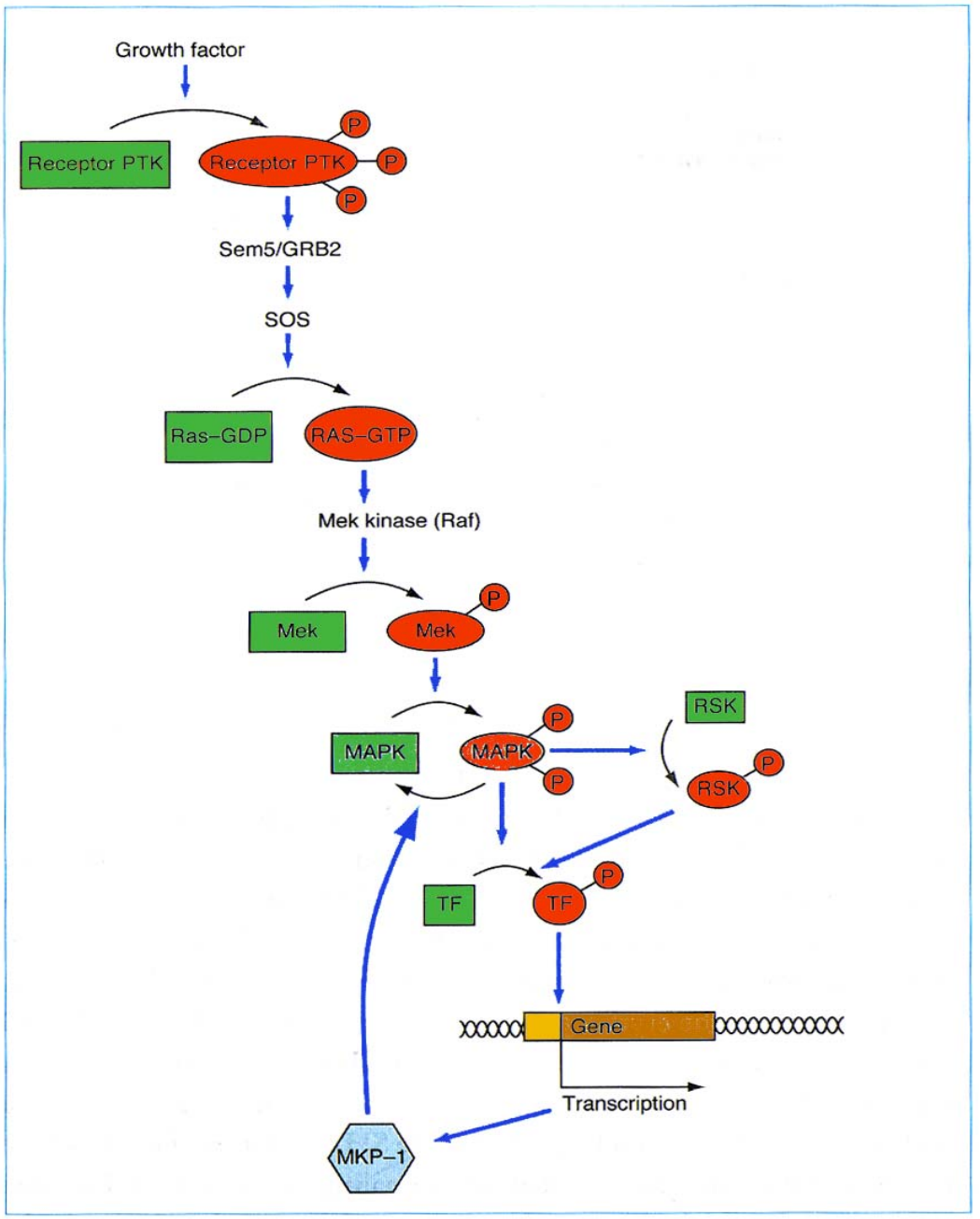


Figura 15.55 Struttura tridimensionale dell'ormone della crescita umano legato al suo recettore. L'ormone (*rosso*) ha legato insieme due recettori identici (uno rappresentato in *verde* e l'altro in *blu*) per formare un omodimero. (Non ci si aspettava assolutamente che un ligando monomerico come un ormone della crescita legasse insieme i suoi recettori, perché ciò richiede che i due recettori identici riconoscano parti diverse dell'ormone.)

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

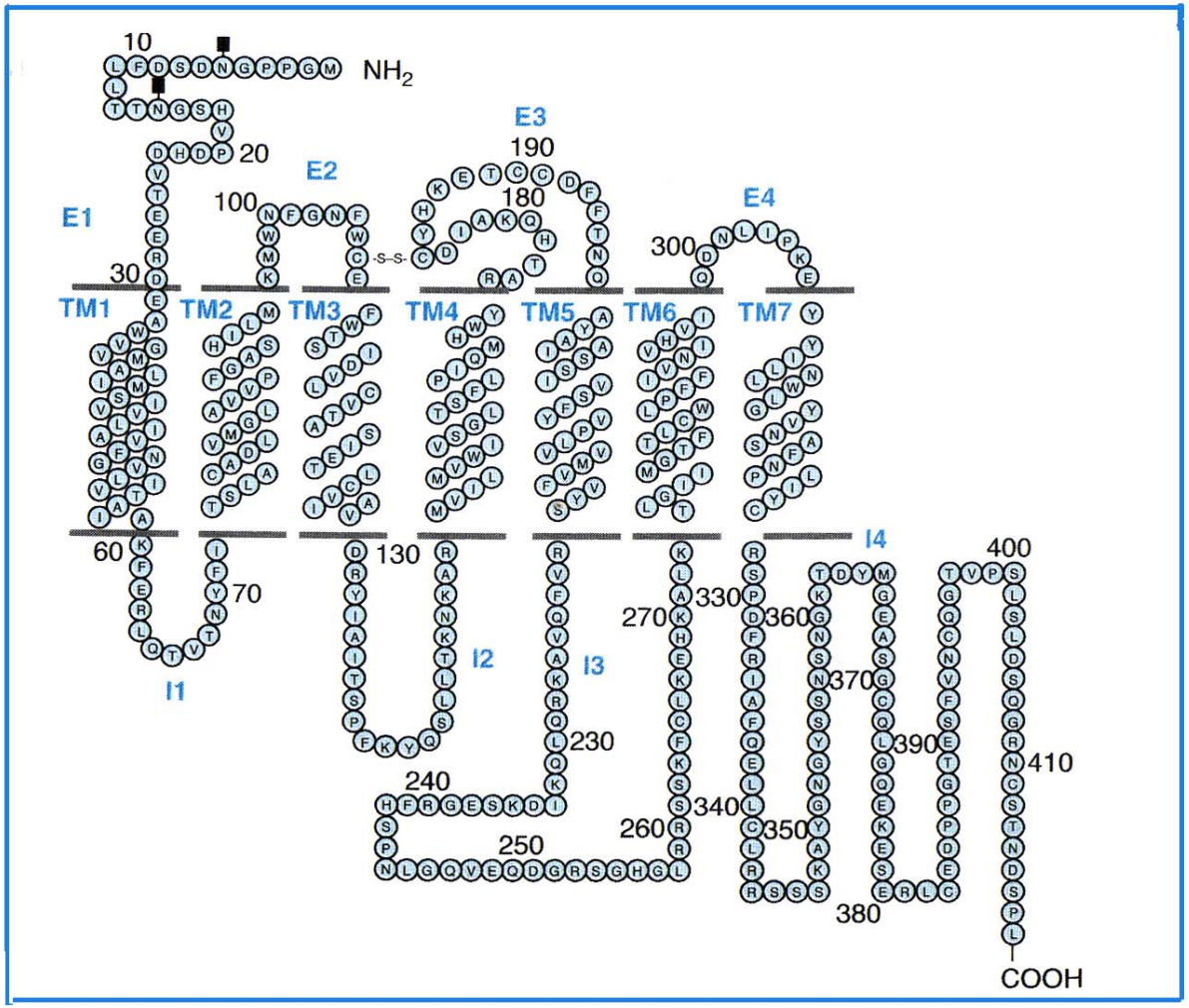


Figure 7.1 Model depicting the transmembrane topology of the β_2-adrenergic receptor. The positioning of the seven transmembrane domains was accomplished by hydropathy analysis of the primary amino acid sequence. Extended domains of hydrophobic amino acids were assigned as putative transmembrane spanning 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.

Gli elementi caratterizzanti
la trasduzione via recettori accoppiati a proteine G

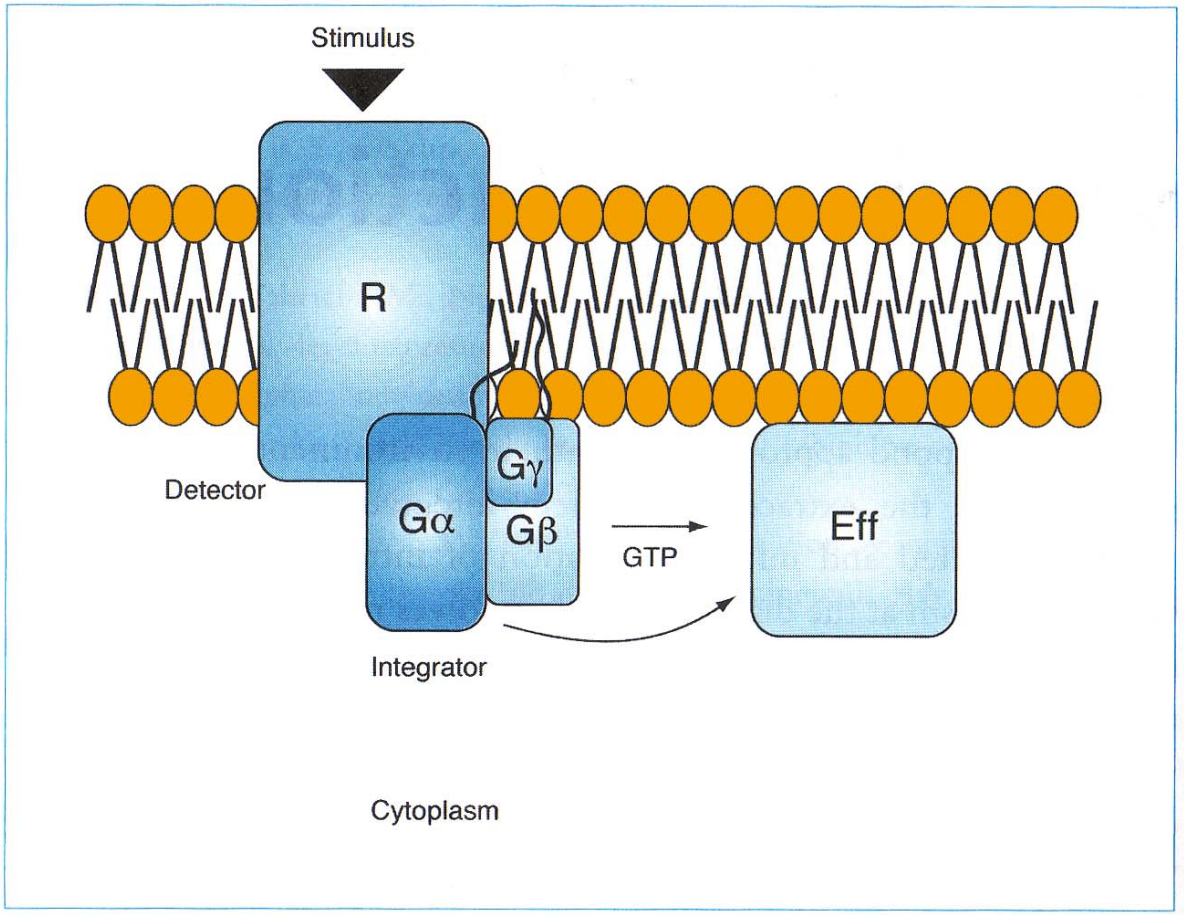


Figure 19.1 Basic pathway for G-protein-dependent signal transduction. Stimulation of receptors initiates a vectorial signaling cascade that results in the production of an amplified intracellular signal. See text for details. Abbreviations: R, receptor; G, G protein; Eff, effector.

Gli elementi caratterizzanti
la trasduzione via recettori accoppiati a proteine G

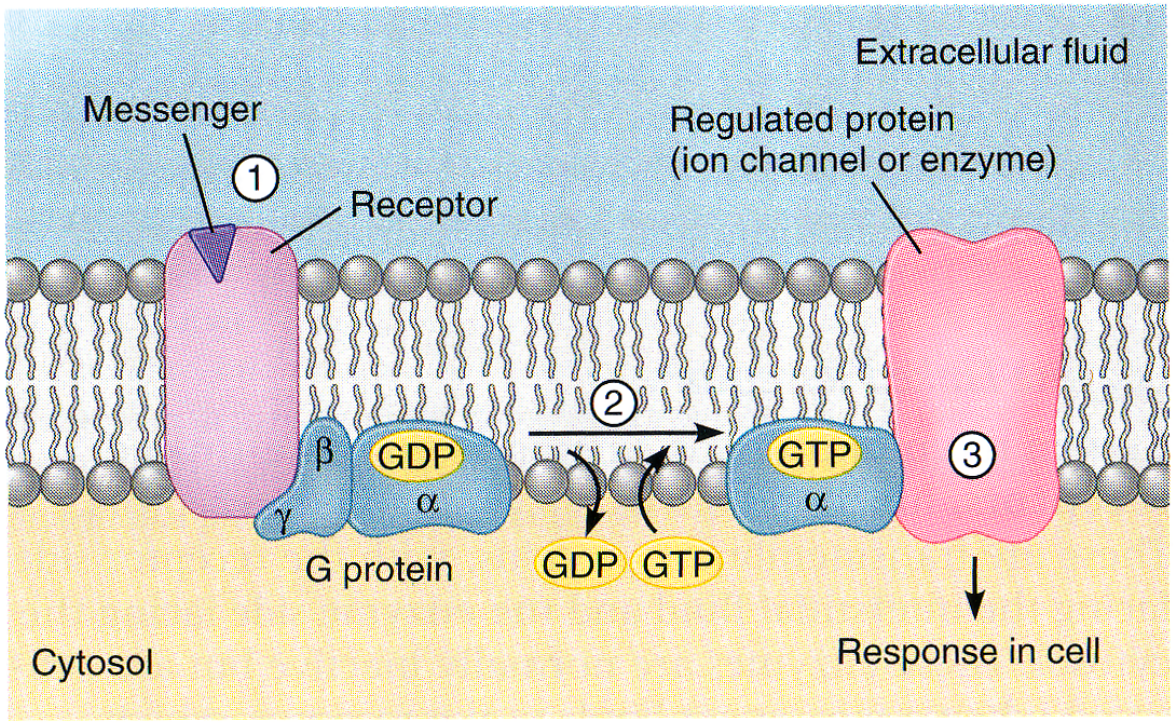
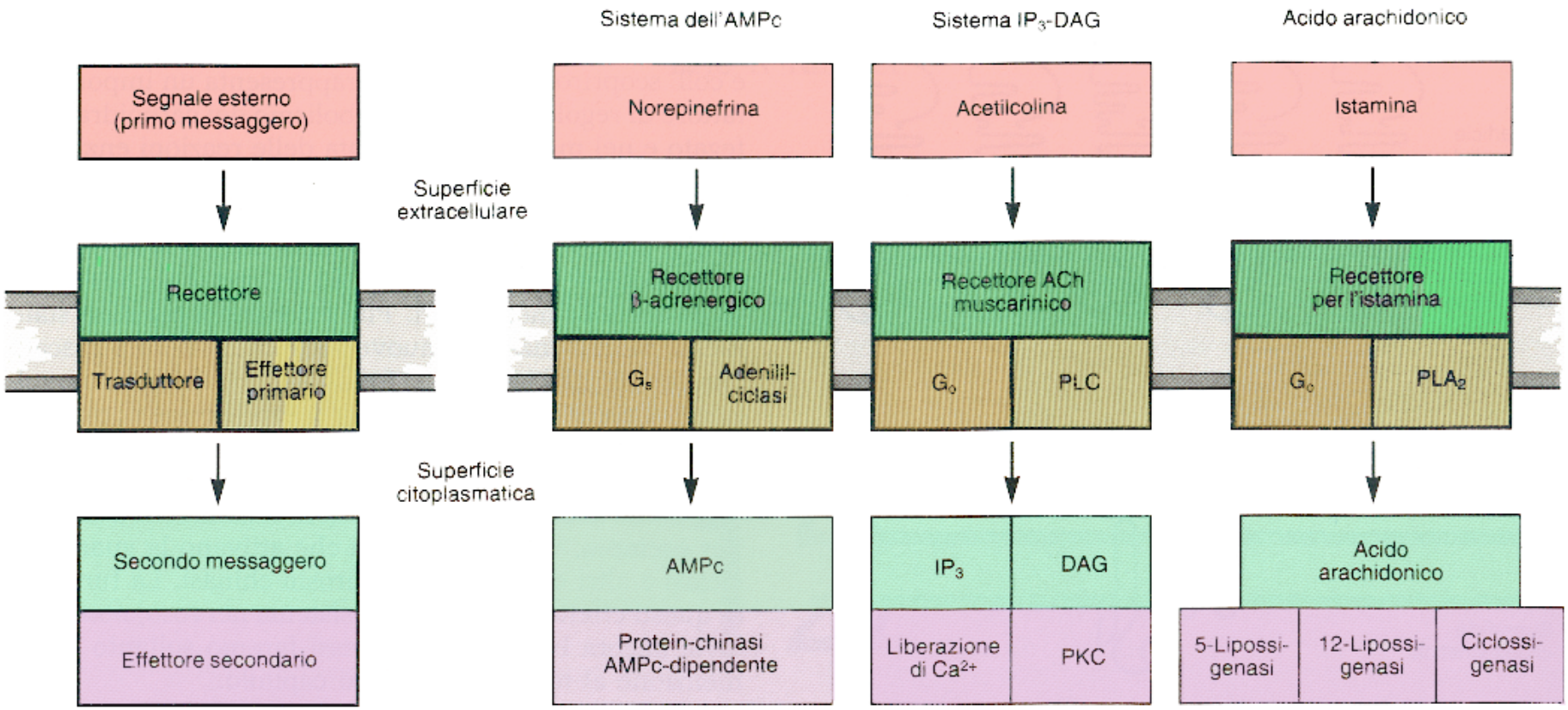
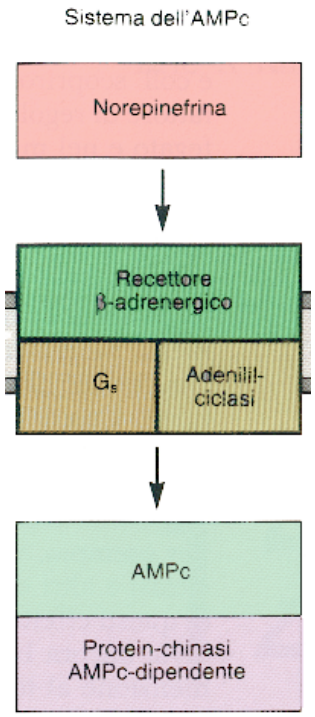
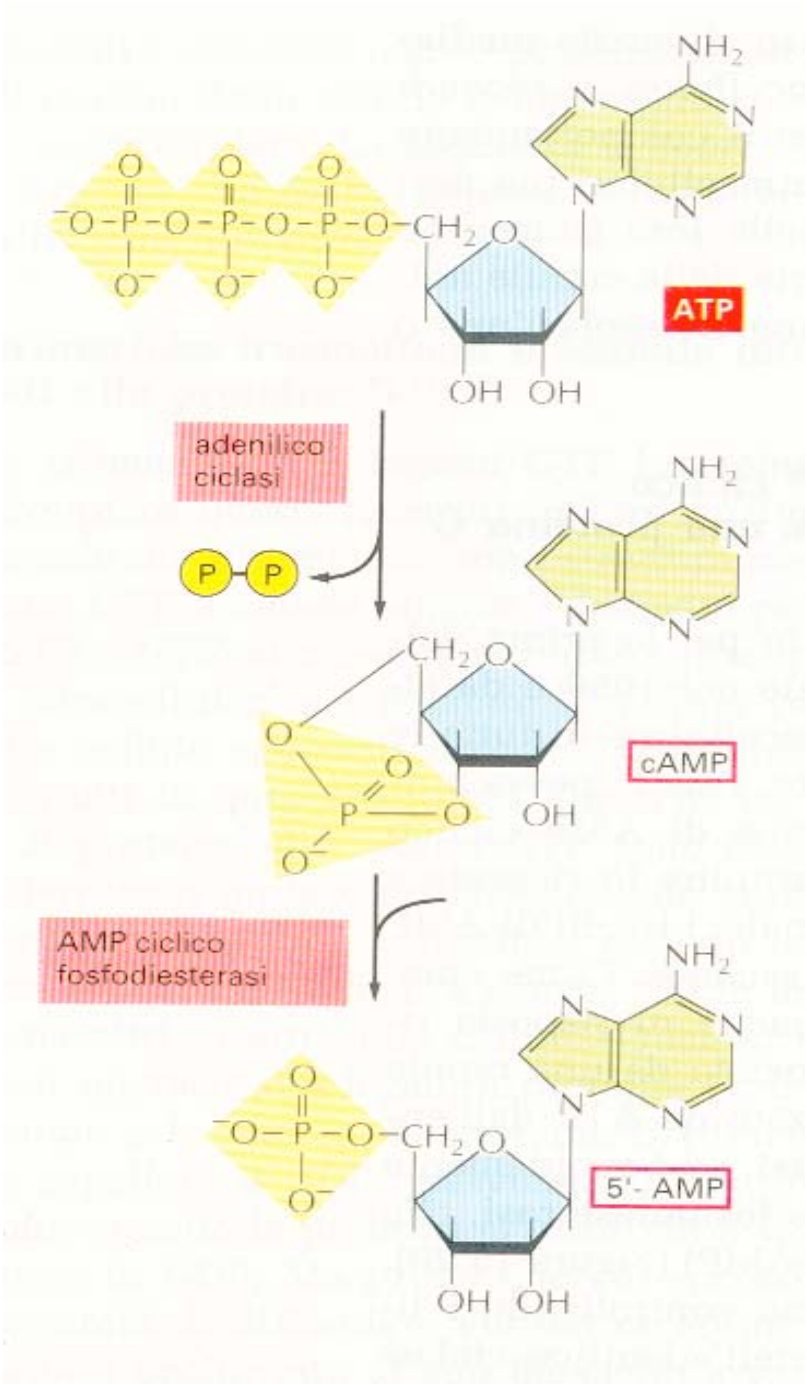


FIGURE 5.14 Actions of G proteins. *G proteins have three subunits: alpha, beta, and gamma. The alpha subunit has binding sites for guanosine nucleotides. In the inactive state, GDP is bound to the alpha subunit. (1) Binding of a messenger to a G-protein-linked receptor activates the G protein. (2) The 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.*

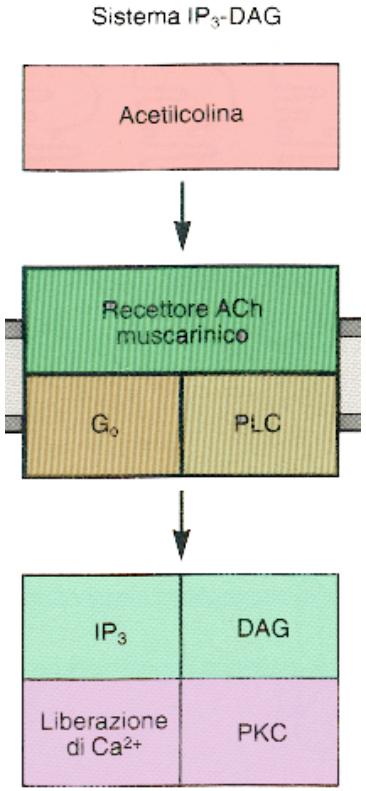
I secondi messaggeri

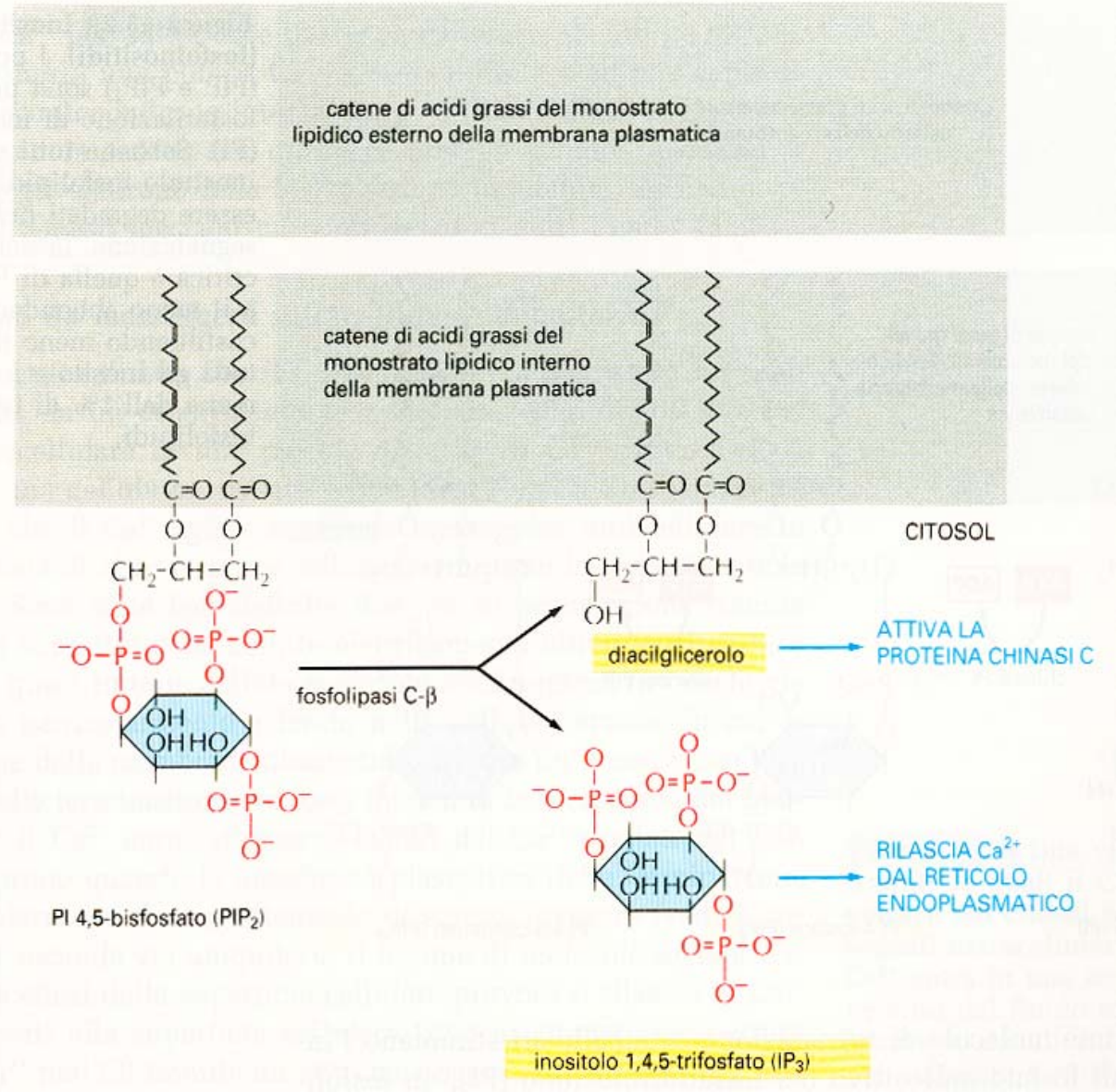




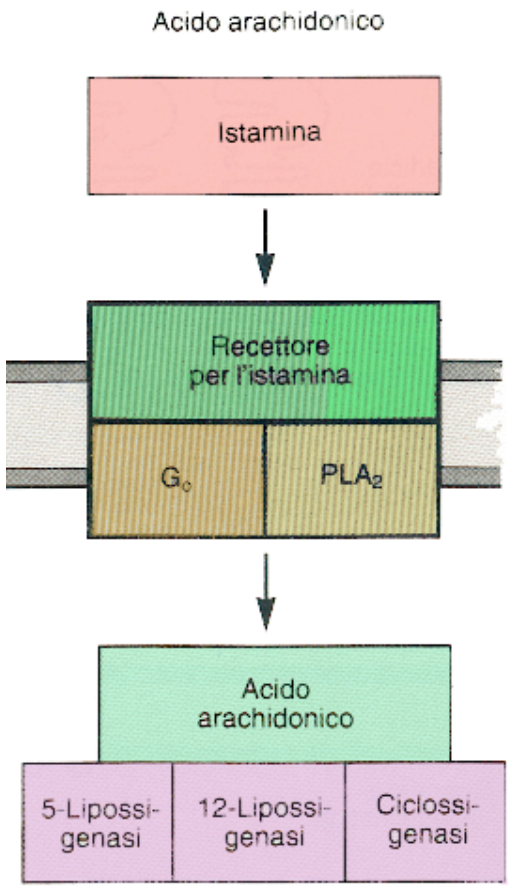


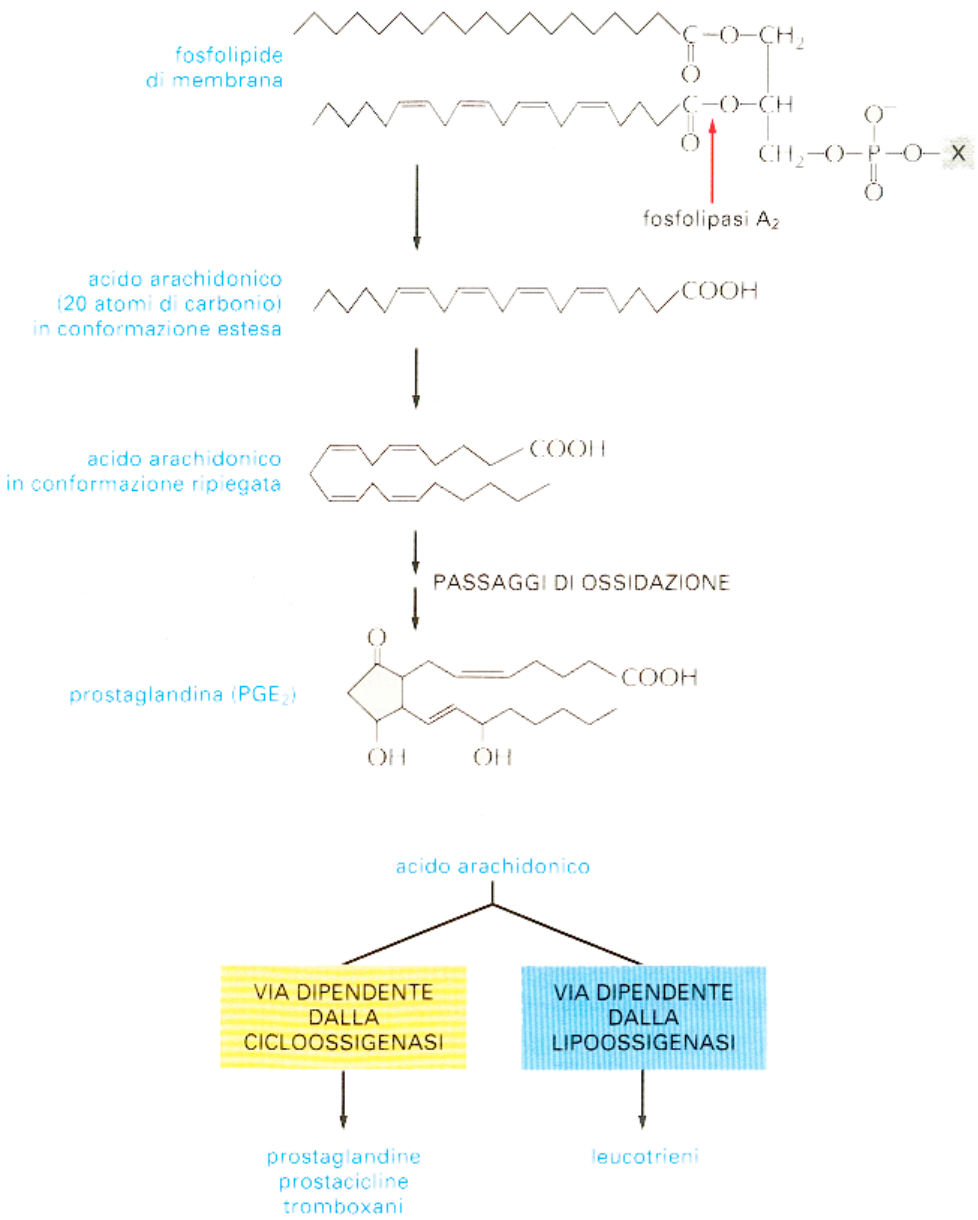
La sintesi dell'AMPc





La sintesi dell'IP_3





La sintesi dell'acido arachidonico

Il secondo messaggero attiva le protein chinasi

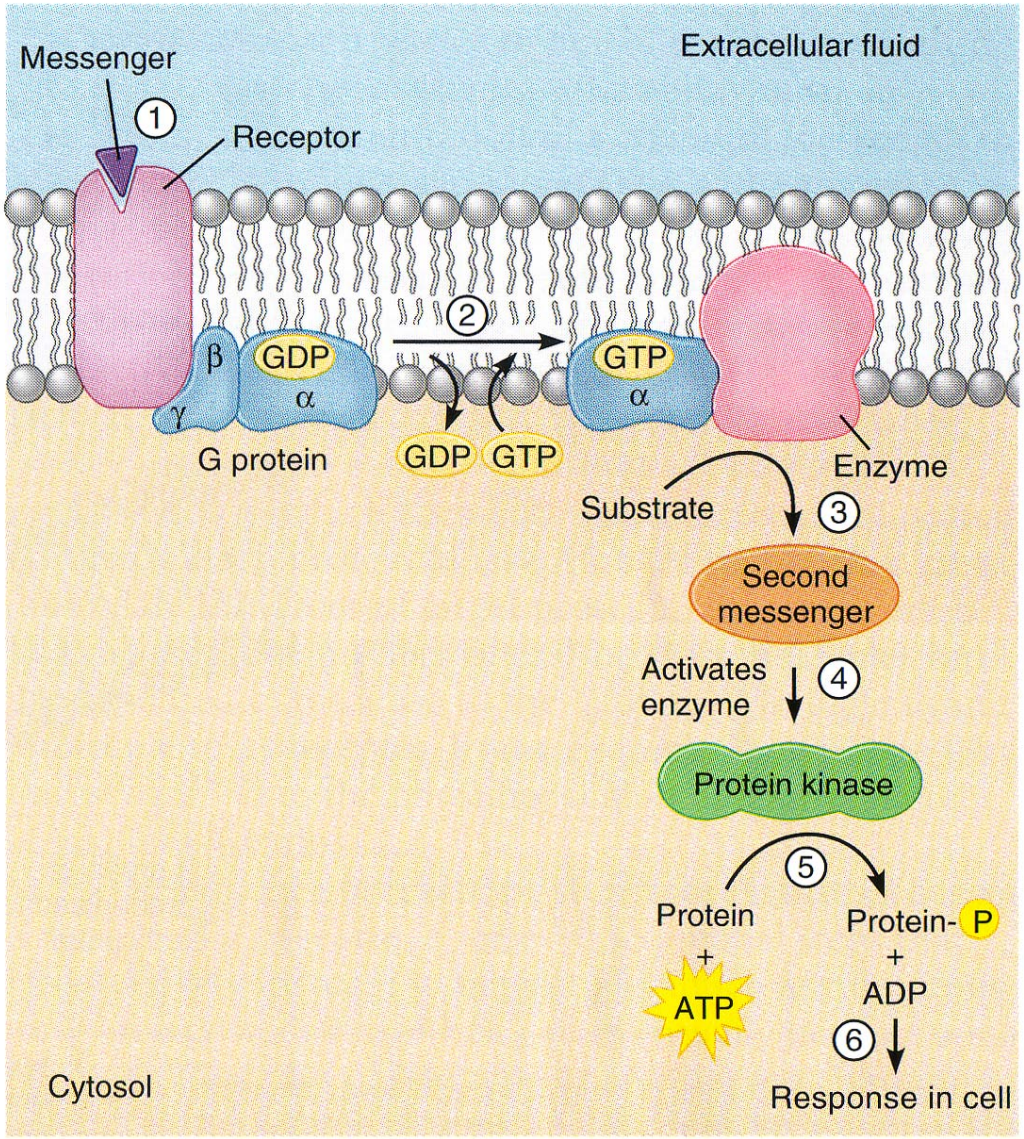


FIGURE 5.16 G-protein-regulated enzymes and second messengers. *In this example the G protein is coupled to an enzyme in the plasma membrane. ① Binding of the messenger to its receptor activates the G protein. ② The alpha subunit moves to and activates an enzyme in the membrane. ③ The activated enzyme 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.*

Fosforilazione

strategia "universale"
di attivazione cellulare

Il vantaggio della cascata attivata da secondi messaggeri

L'amplificazione del segnale

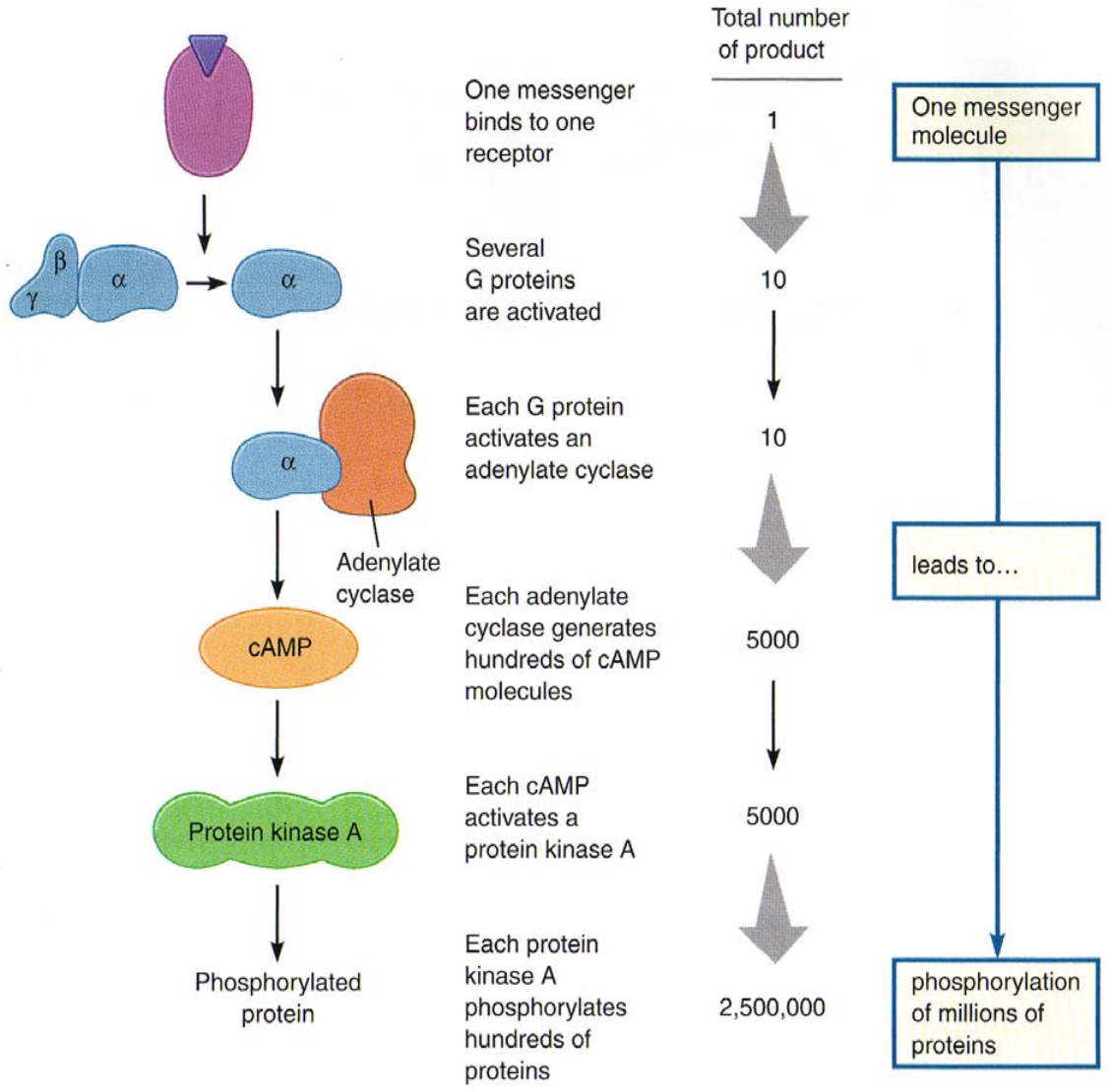


FIGURE 5.18 **Signal amplification, in this case by the second messenger cAMP.**