Celično signaliziranje

Celično signaliziranje pomeni prenos informacije iz zunajceličnega prostora v celico. Temeljne lastnosti celičnega signaliziranja:

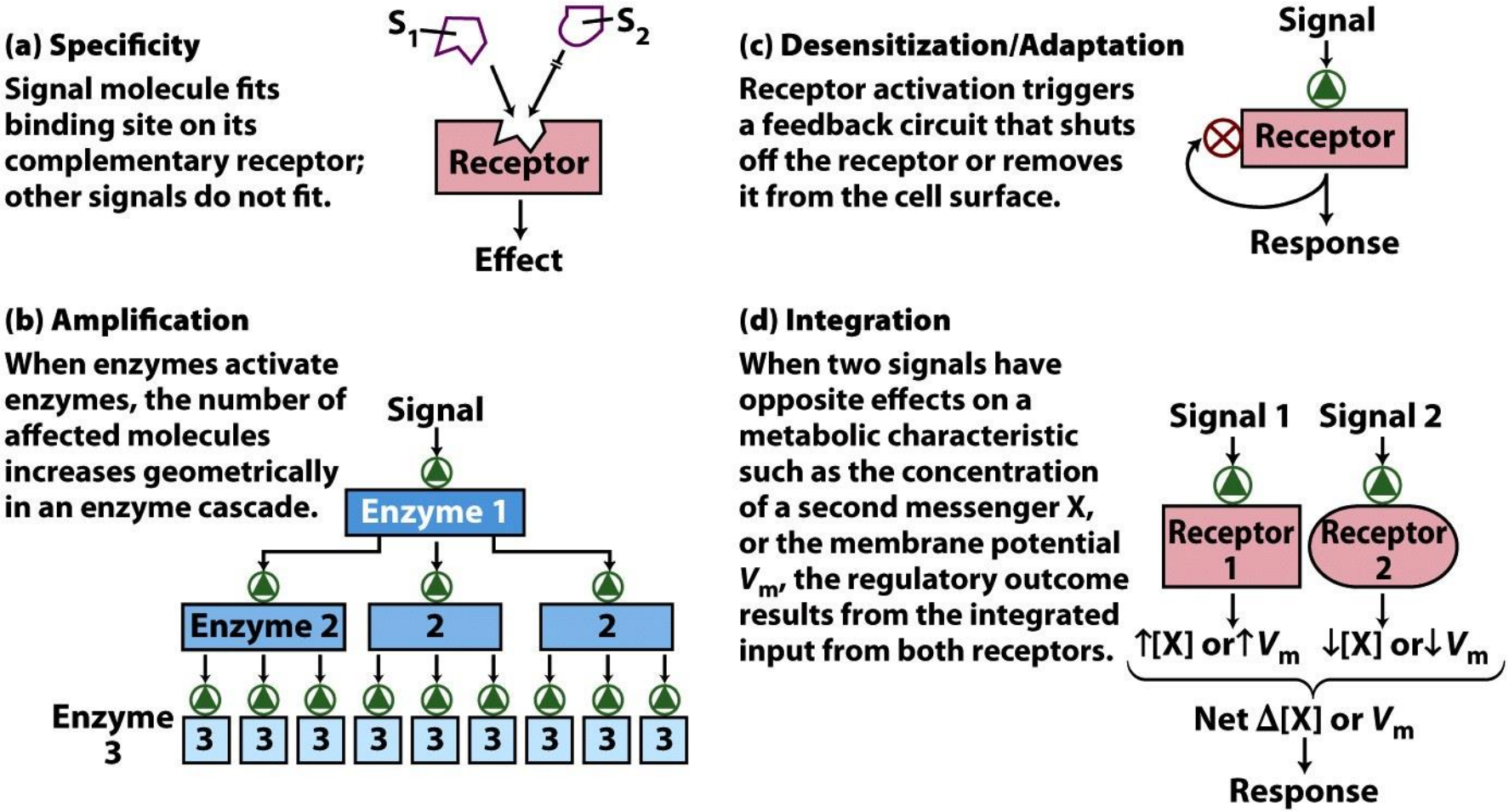


Figure 12-1
Lehninger Principles of Biochemistry, Fifth Edition

Celično signaliziranje

Zunanje molekule, ki sprožijo signal (*primarni obveščevalci*) lahko delujejo:

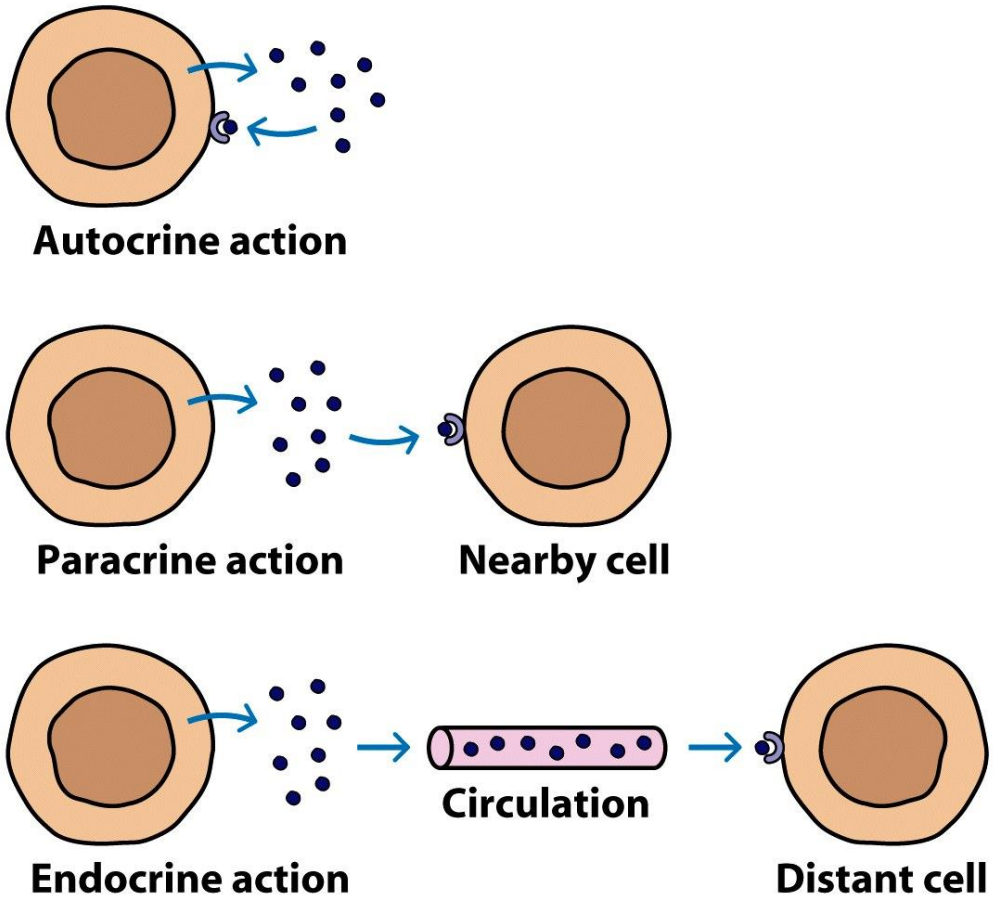
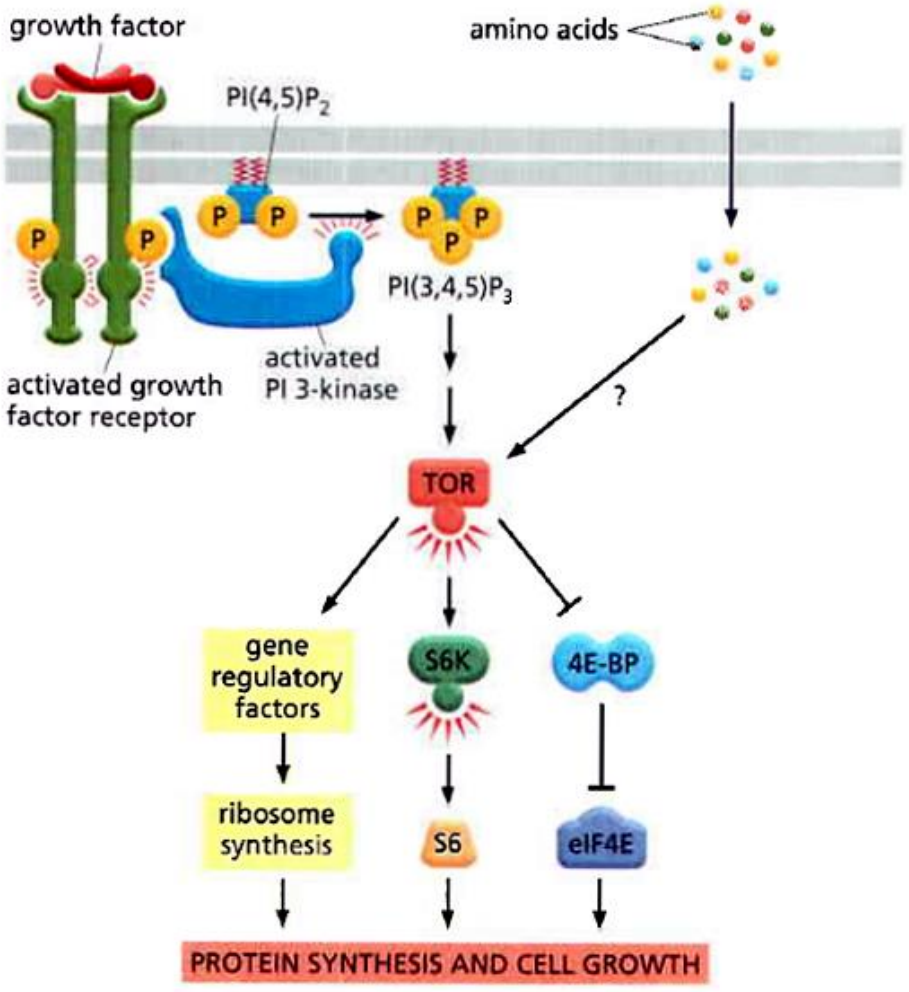
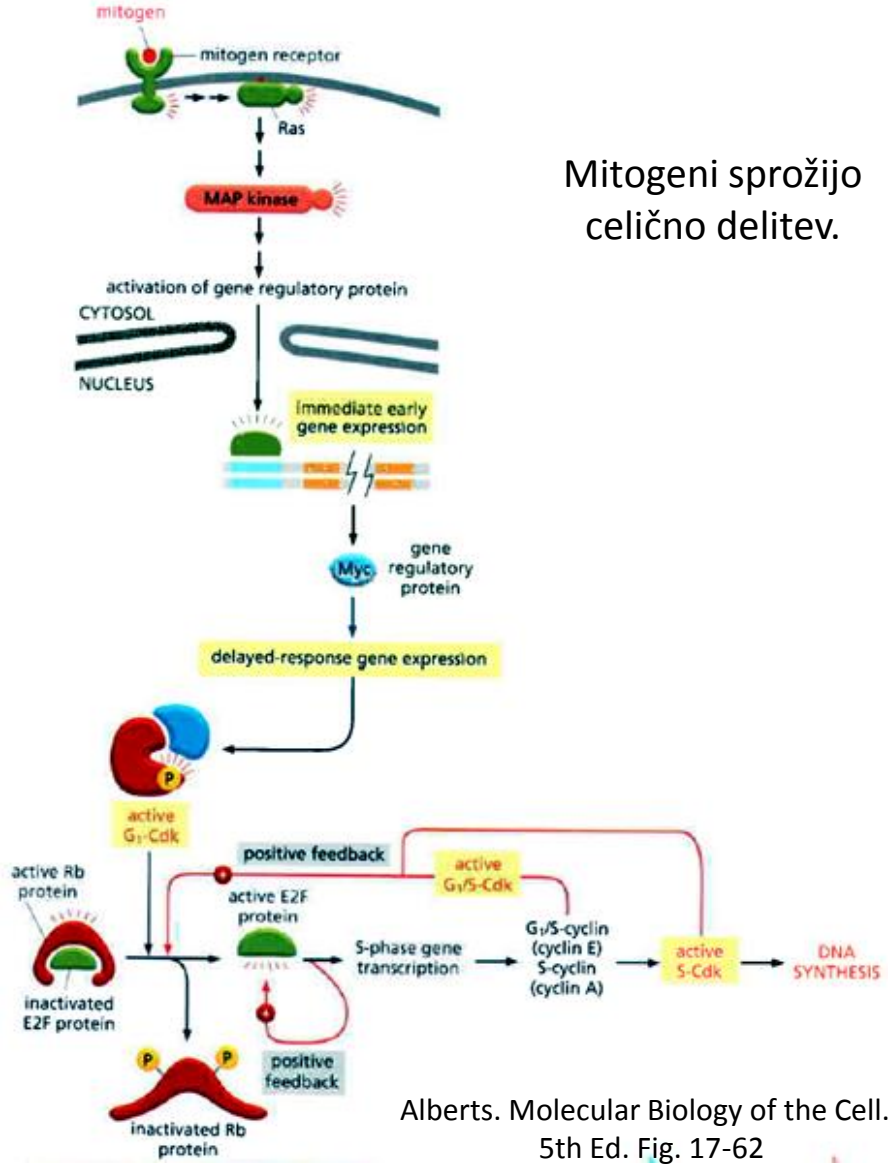


Figure 12-1b
Kuby IMMUNOLOGY, Sixth Edition

Celično signaliziranje

Dve pogosti vrsti signalnih molekul so mitogeni in rastni faktorji.





Mitogeni sprožijo celično delitev.

Rastni faktorji sprožijo sintezo proteinov in celično rast.

Alberts. Molecular Biology of the Cell. 5th Ed. Fig. 17-62

Načini prenosa signala

Šest osnovnih načinov prenosa signala v celico:

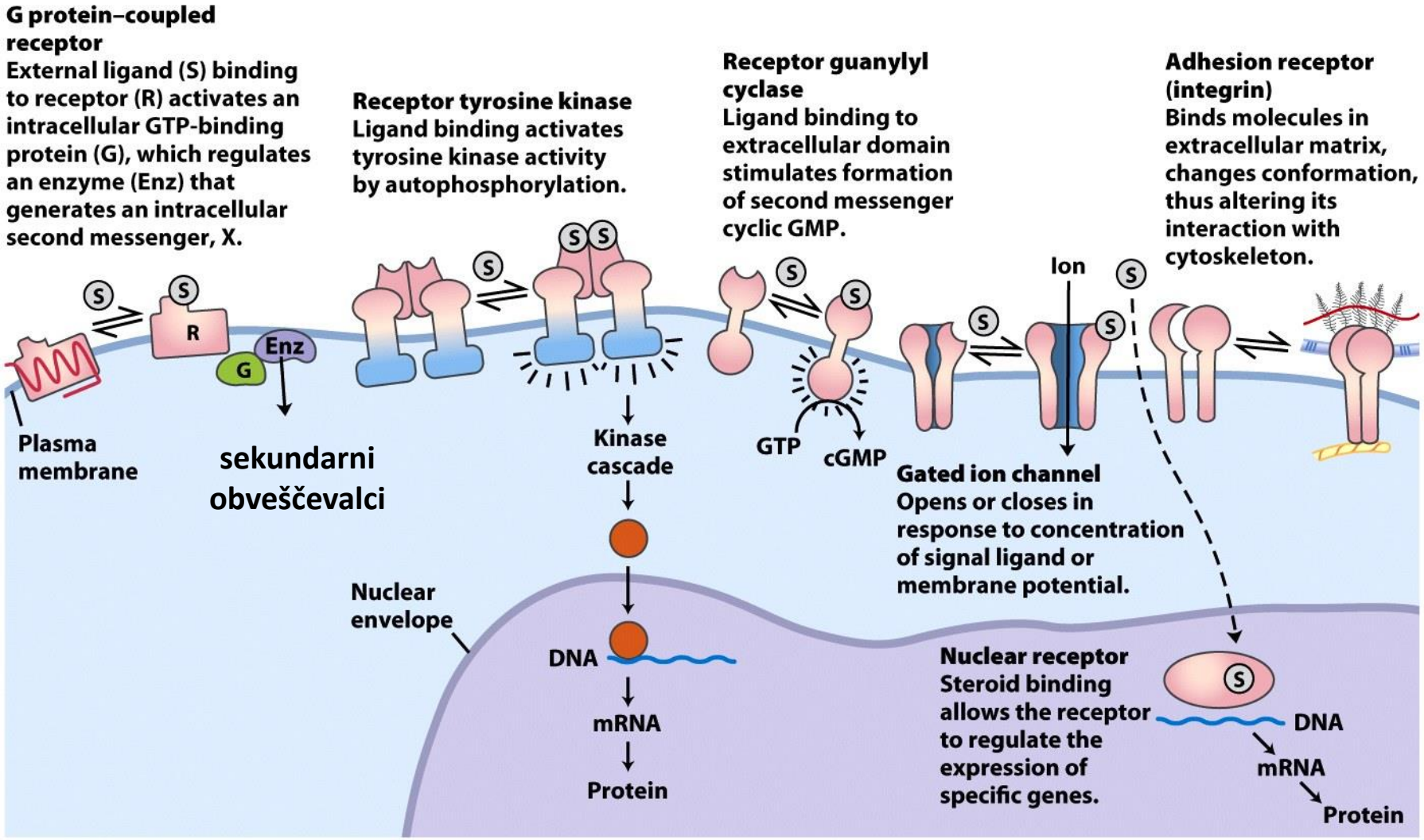


Figure 12-2
Lehninger Principles of Biochemistry, Fifth Edition

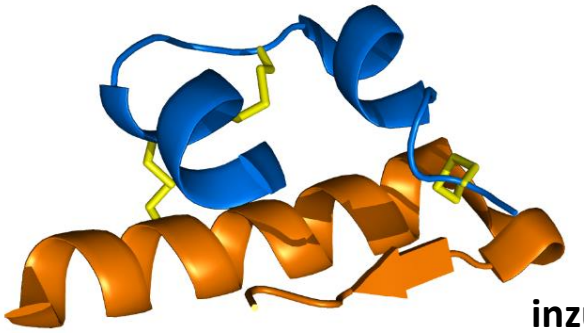
Metabolični hormoni

Hormoni, ki uravnavajo metabolizem goriv:

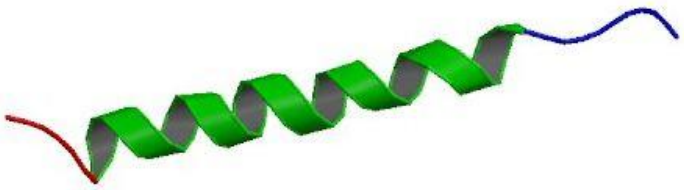
receptorske tirozinske kinaze

z G proteini sklopljeni receptorji

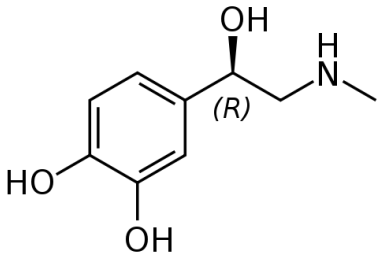
hormon	biokemijsko delovanje: povečanje ali stimulacija	biokemijsko delovanje: zmanjšanje ali inhibicija
inzulin	prenos glukoze v mišice in maščobno tkivo	glukoneogeneza
	glikoliza v jetrih	hidroliza triacilglicerolov
	sinteza glikogena	razgradnja glikogena
	sinteza triacilglicerolov	koncentracija krvne glukoze
glukagon	koncentracija cikličnega AMP v jetrih in maščobnem tkivu	sinteza glikogena
	razgradnja glikogena	glikoliza
	glukoneogeneza v jetrih	
	koncentracija krvne glukoze	
adrenalin	koncentracija cikličnega AMP v skeletni mišici	sinteza glikogena
	hidroliza triacilglicerolov	
	razgradnja glikogena	
	koncentracija krvne glukoze	



inzulin



glukagon



adrenalin

Z G proteini sklopljeni receptorji

Z G proteini sklopljeni receptorji imajo tipično zgradbo s sedmimi transmembranskimi vijačnicami. Velika skupina G proteinov sproži signaliziranje preko sekundarnega obveščevalca cAMP.

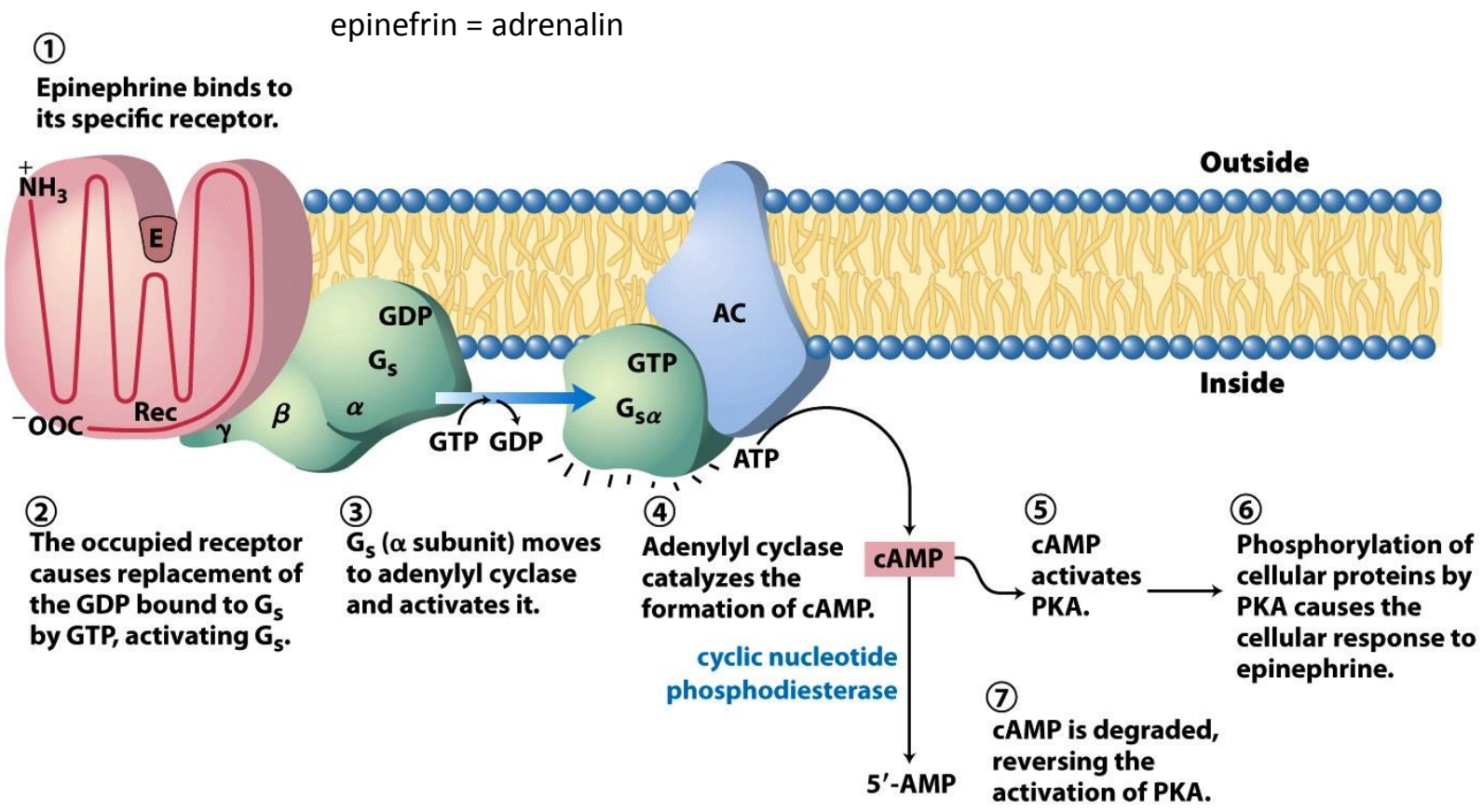


Figure 12-4a
Lehninger Principles of Biochemistry, Fifth Edition

Z G proteini sklopljeni receptorji

TABLE 12–3	Some Signals That Use cAMP as Second Messenger
Corticotropin (ACTH)	
Corticotropin-releasing hormone (CRH)	
Dopamine [D_1, D_2]	
Epinephrine (β-adrenergic)	
Follicle-stimulating hormone (FSH)	
Glucagon	
Histamine [H_2]	
Luteinizing hormone (LH)	
Melanocyte-stimulating hormone (MSH)	
Odorants (many)	
Parathyroid hormone	
Prostaglandins E_1, E_2 (PGE_1, PGE_2)	
Serotonin [5-HT-1a, 5-HT-2]	
Somatostatin	
Tastants (sweet, bitter)	
Thyroid-stimulating hormone (TSH)	

Note: Receptor subtypes in square brackets. Subtypes may have different transduction mechanisms. For example, serotonin is detected in some tissues by receptor subtypes 5-HT-1a and 5-HT-1b, which act through adenylyl cyclase and cAMP, and in other tissues by receptor subtype 5-HT-1c, acting through the phospholipase C–IP_3 mechanism (see Table 12–4).

Table 12-3

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Delovanje G proteinov

G protein se aktivira ob aktivaciji receptorja z izmenjavo vezanega GDP za GTP. Ko se molekula GTP hidrolizira (Gα je GTPaza), se G protein inaktivira in vrne v izhodno stanje.

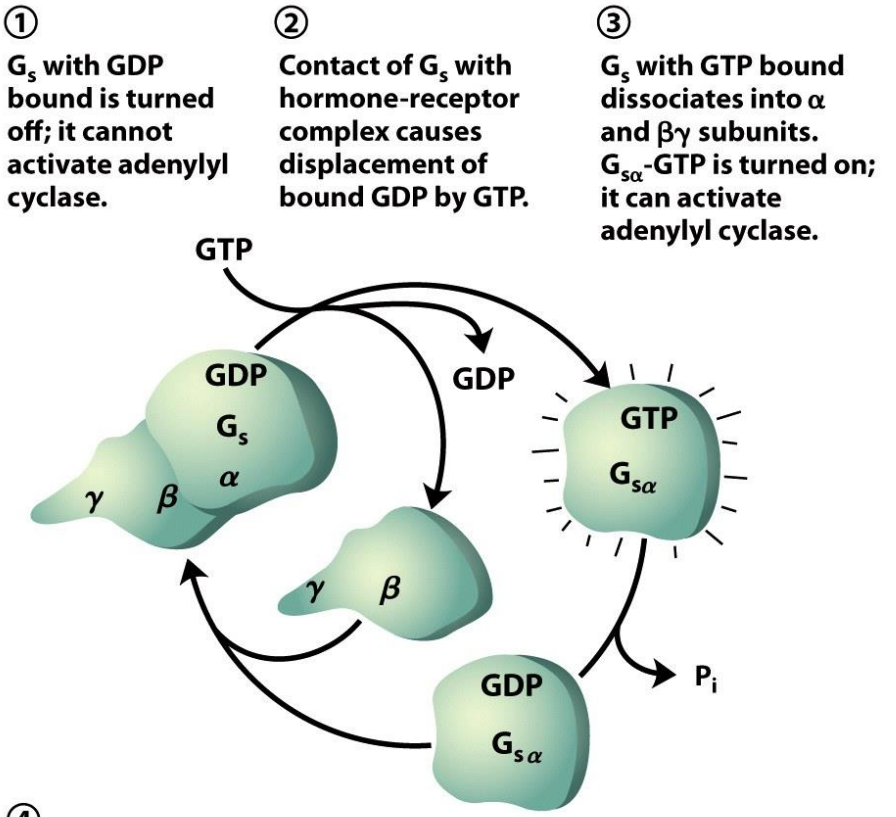


Figure 12-5
Lehninger Principles of Biochemistry, Fifth Edition

Amplifikacija signala epinefrina

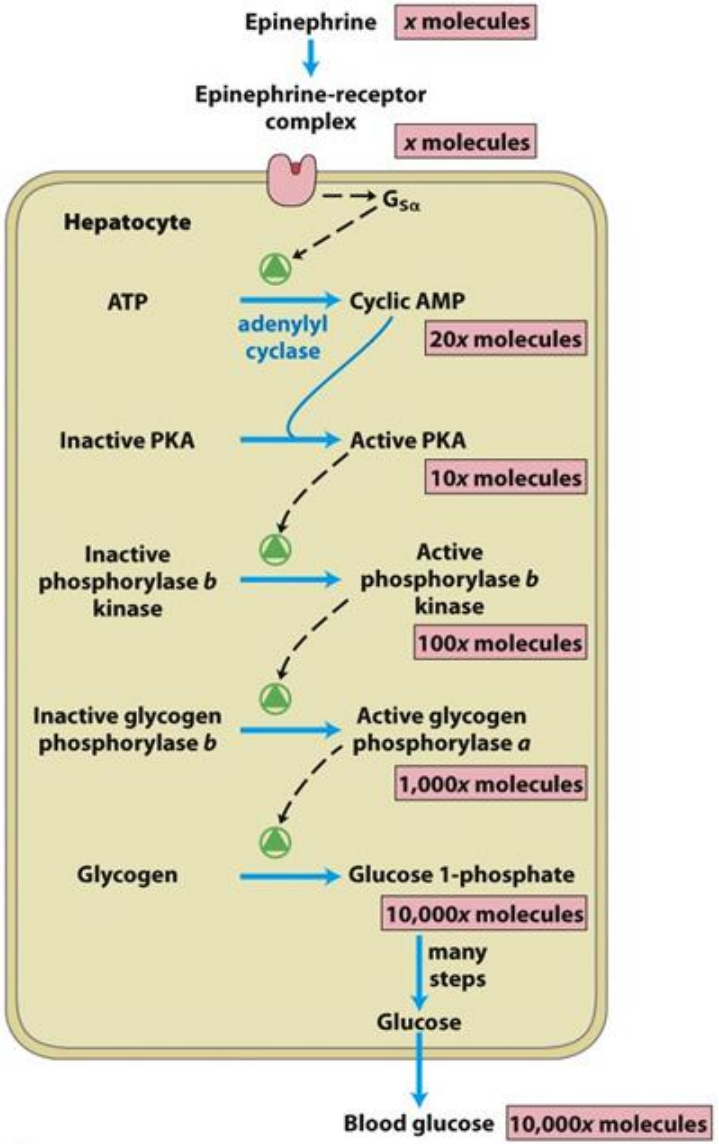


Figure 12-7
Lehninger Principles of Biochemistry, Fifth Edition

Z G proteini sklopljeni receptorji

Druga velika skupina z G proteini sklopljenih receptorjev sproži signaliziranje preko fosfolipaze C in inozitol 1,4,5-trisfosfata (IP3).

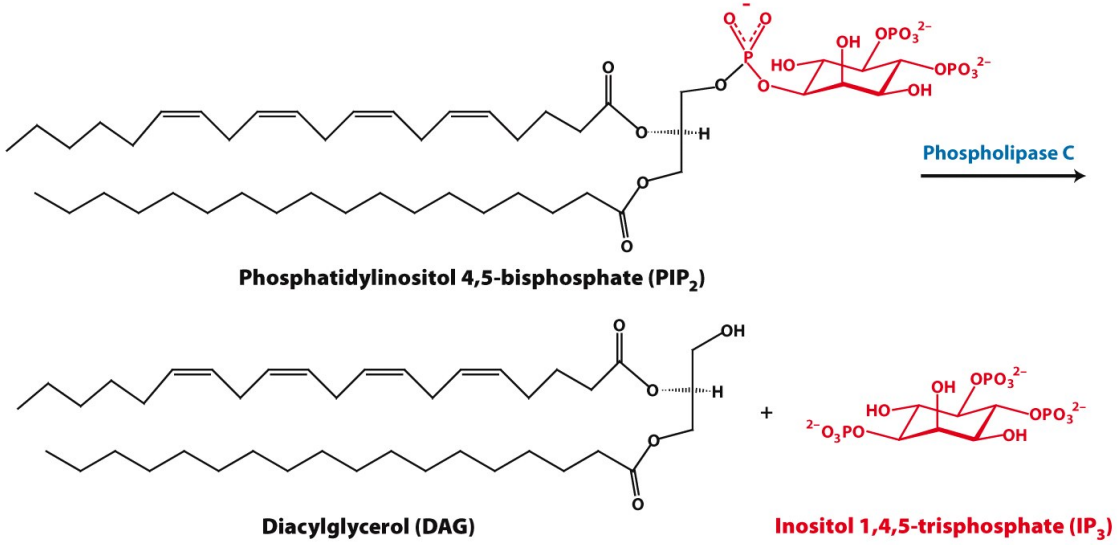


Figure 14.12
Biochemistry, Seventh Edition

TABLE 12–4 Some Signals That Act through Phospholipase C, IP_3, and Ca^{2+}

Acetylcholine [muscarinic M_1]	Gastrin-releasing peptide	Oxytocin
α_1-Adrenergic agonists	Glutamate	Platelet-derived growth factor (PDGF)
Angiogenin	Gonadotropin-releasing hormone (GRH)	Serotonin [5-HT-1c]
Angiotensin II	Histamine [H_1]	Thyrotropin-releasing hormone (TRH)
ATP [P_{2x}, P_{2y}]	Light (*Drosophila*)	Vasopressin
Auxin		

Note: Receptor subtypes are in square brackets; see footnote to Table 12–3.

Table 12-4
Lehninger Principles of Biochemistry, Fifth Edition

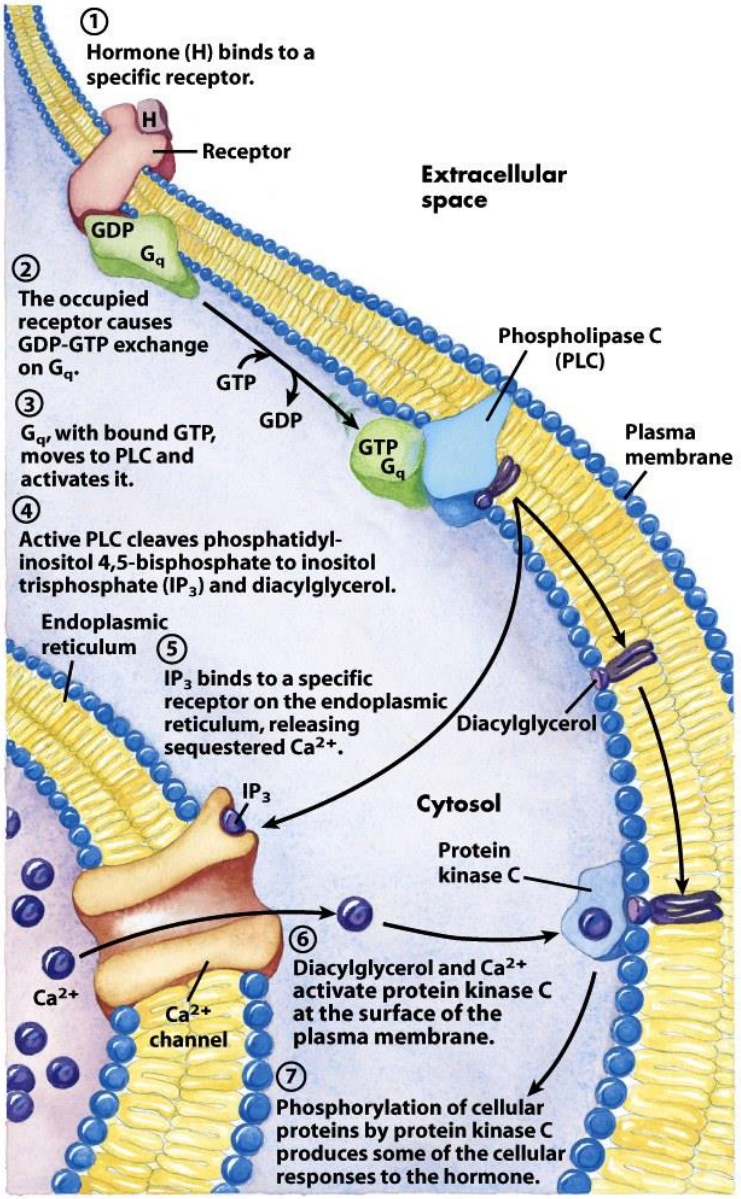
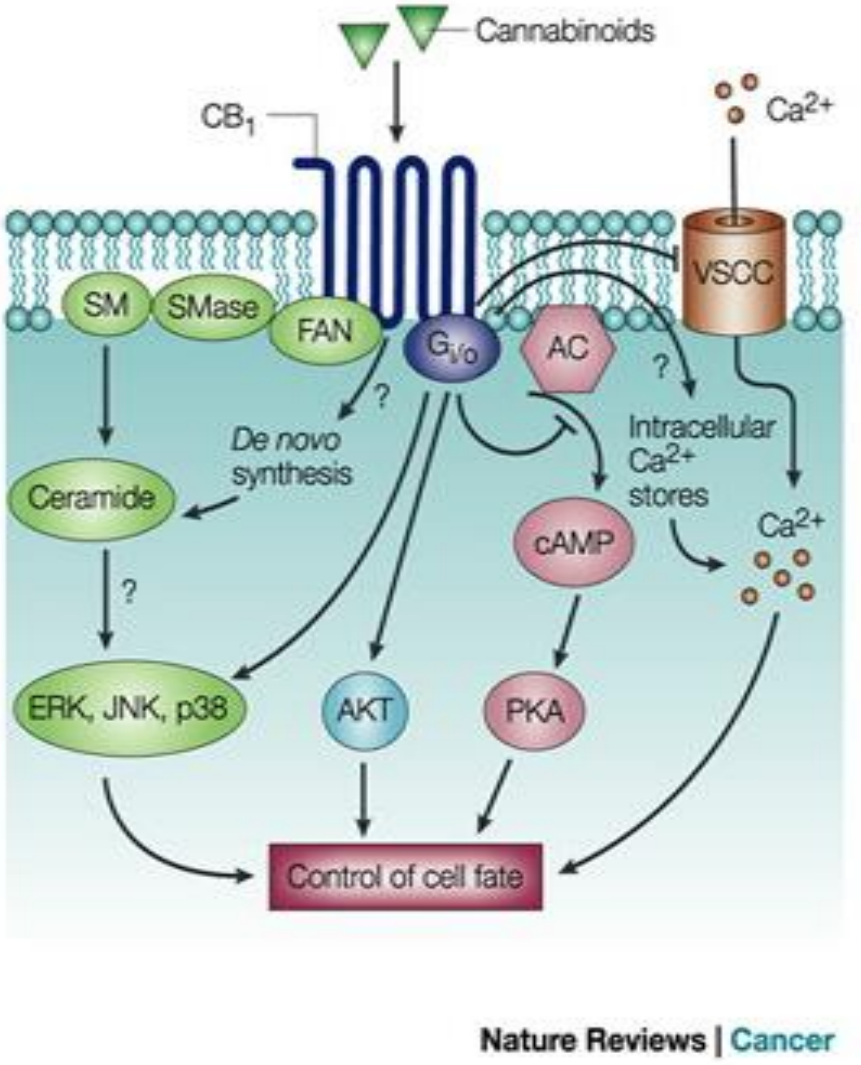
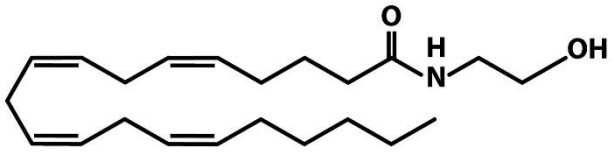


Figure 12-10
Lehninger Principles of Biochemistry, Fifth Edition

Z G proteini sklopljeni receptorji

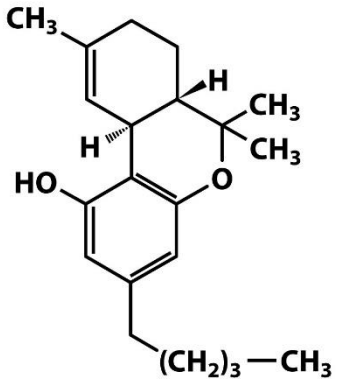
V to družino spadajo tudi kanabinoidni receptorji v možganih, ki regulirajo stimulacijo celice – ščitijo pred pretiranih vzburjanjem.





Anandamide (arachidonylethanolamide, an endogenous cannabinoid)

Unnumbered 12 p442b
Lehninger Principles of Biochemistry, Fifth Edition
© 2008 W.H. Freeman and Company



Δ9-Tetrahydrocannabinol (THC)

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Lehninger Principles of Biochemistry, Fifth Edition
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THC sproži tudi signaliziranje preko protein kinaze B – občutek lakote.

Receptorske tirozinske kinaze

Vezava inzulina na receptorsko tirozinsko kinazo povzroči avtofosforilacijo dimera le-te. S tem se kinaza aktivira in s fosforilacijo aktivira druge proteine.

ERK spada med MAP kinaze – kinaze aktivirane z mitogeni – sprožijo delitev celice.

Na podoben način delujejo številni rastni faktorji.

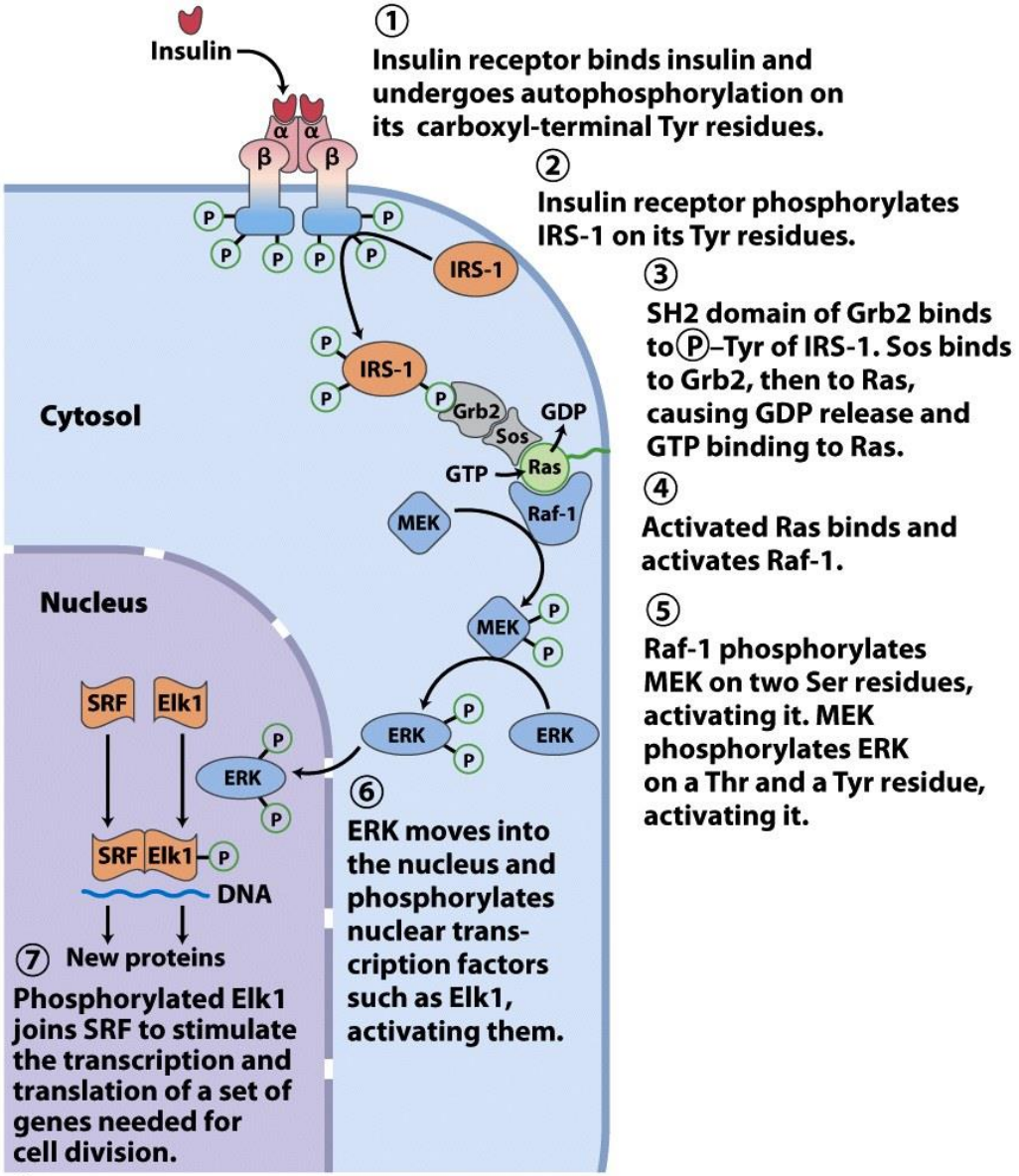


Figure 12-15
Lehninger Principles of Biochemistry, Fifth Edition

Receptorske tirozinske kinaze

V mišicah in jetrih inzulin aktivira sintezo glikogena in vnos glukoze.

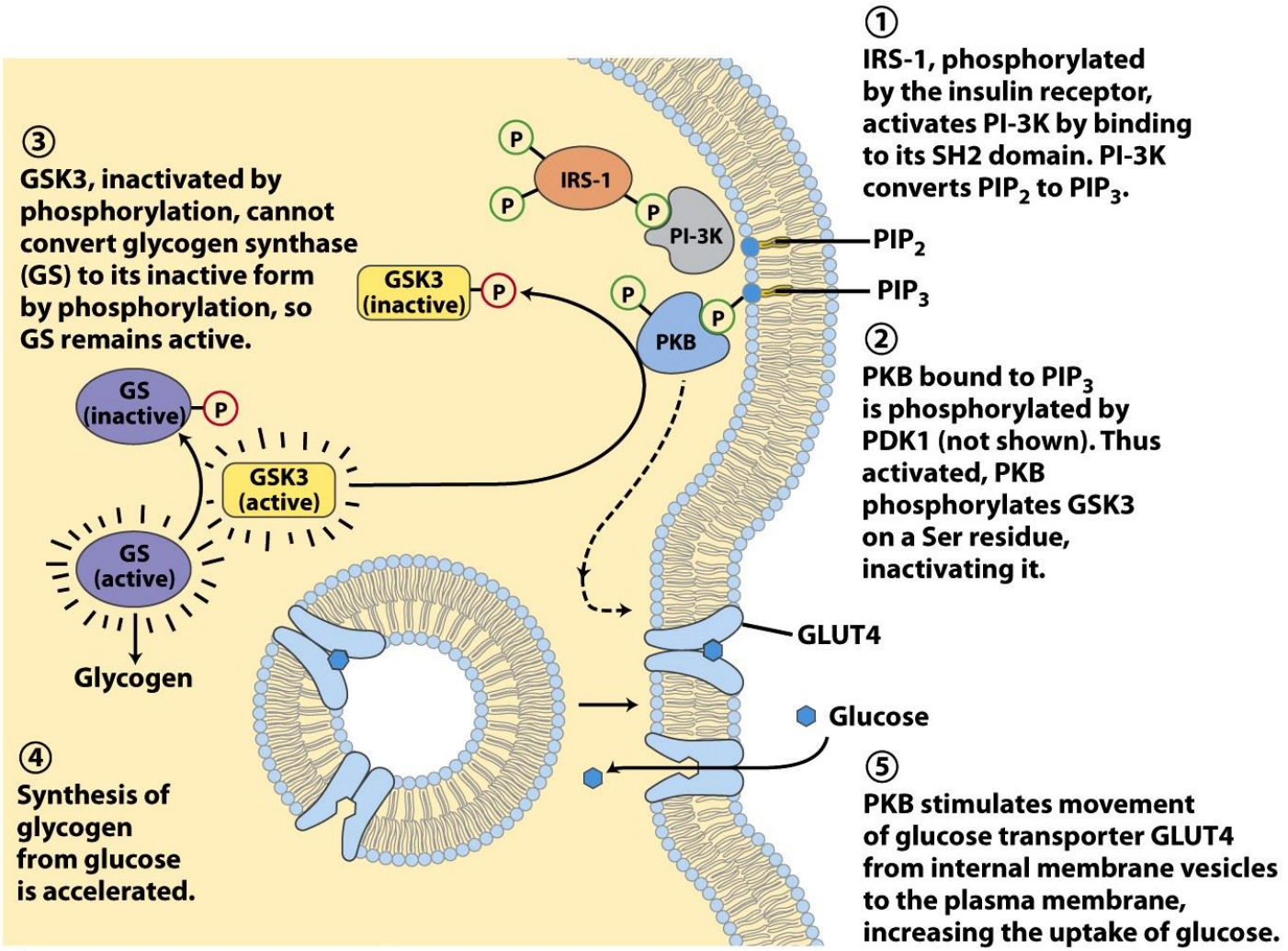
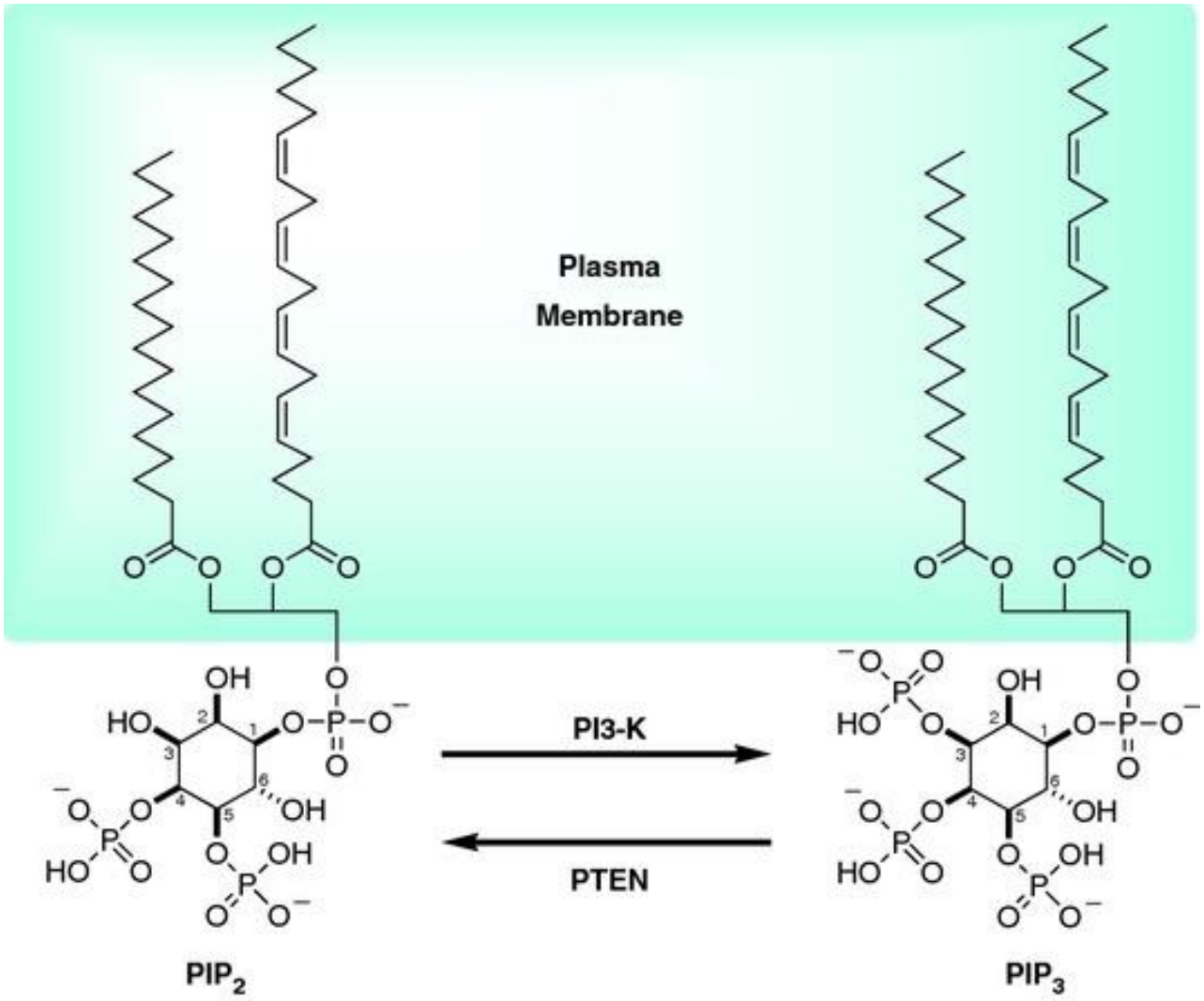


Figure 12-16
Lehninger Principles of Biochemistry, Fifth Edition

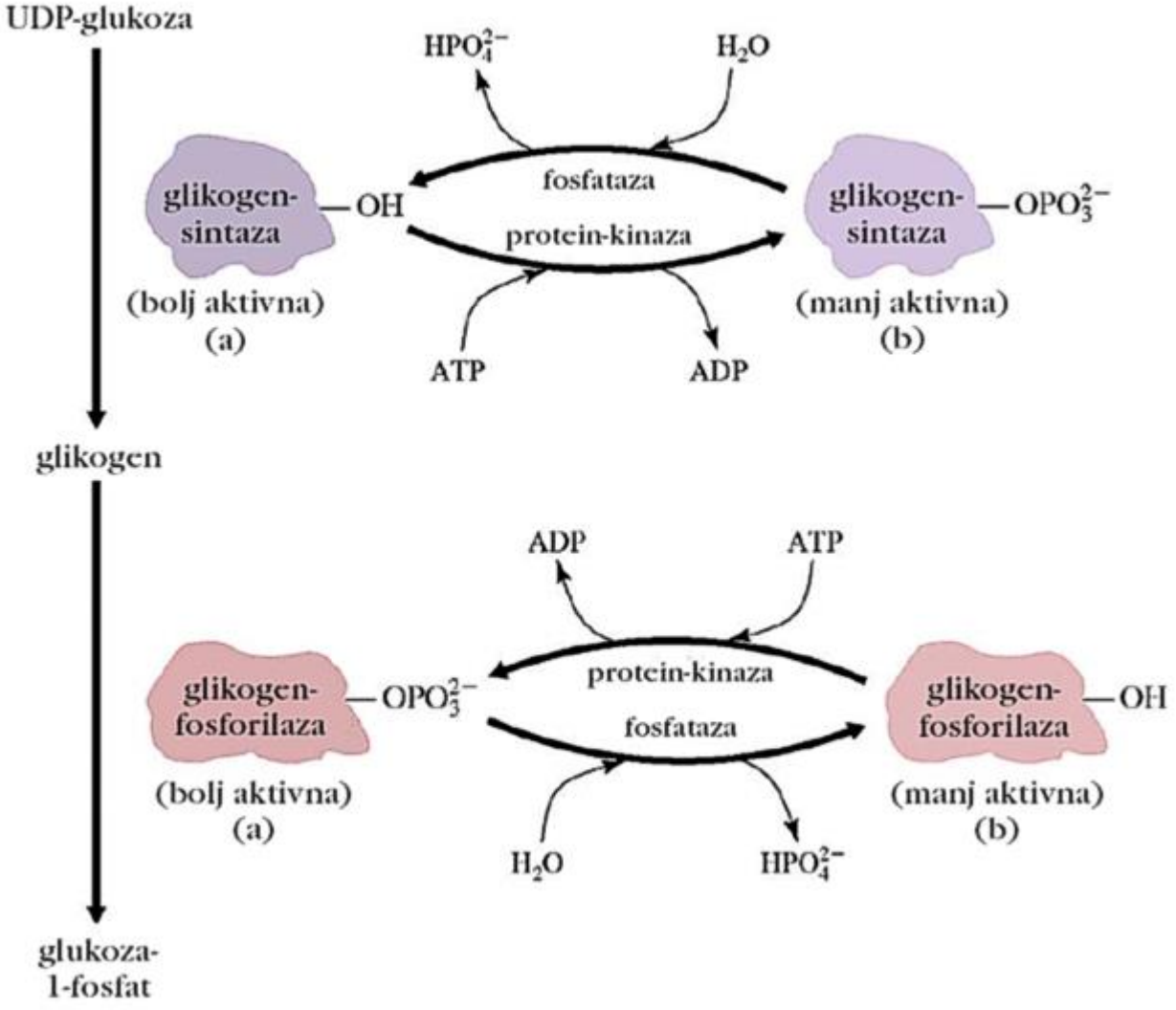
Receptorske tirozinske kinaze

V mišicah in jetrih inzulin aktivira sintezo glikogena in vnos glukoze.



Receptorske tirozinske kinaze

V mišicah in jetrih inzulin aktivira sintezo glikogena in vnos glukoze.



Signalizacijska pot JAK-STAT

Vezava liganda povzroči dimerizacijo receptorja, kar povzroči aktivacijo JAK kinaze, ki aktivira transkripcijske faktorje iz družine STAT – ekspresija specifičnih genov in celična delitev.

Pot je zlasti pogosta v imunskih celicah in drugih krvnih celicah.

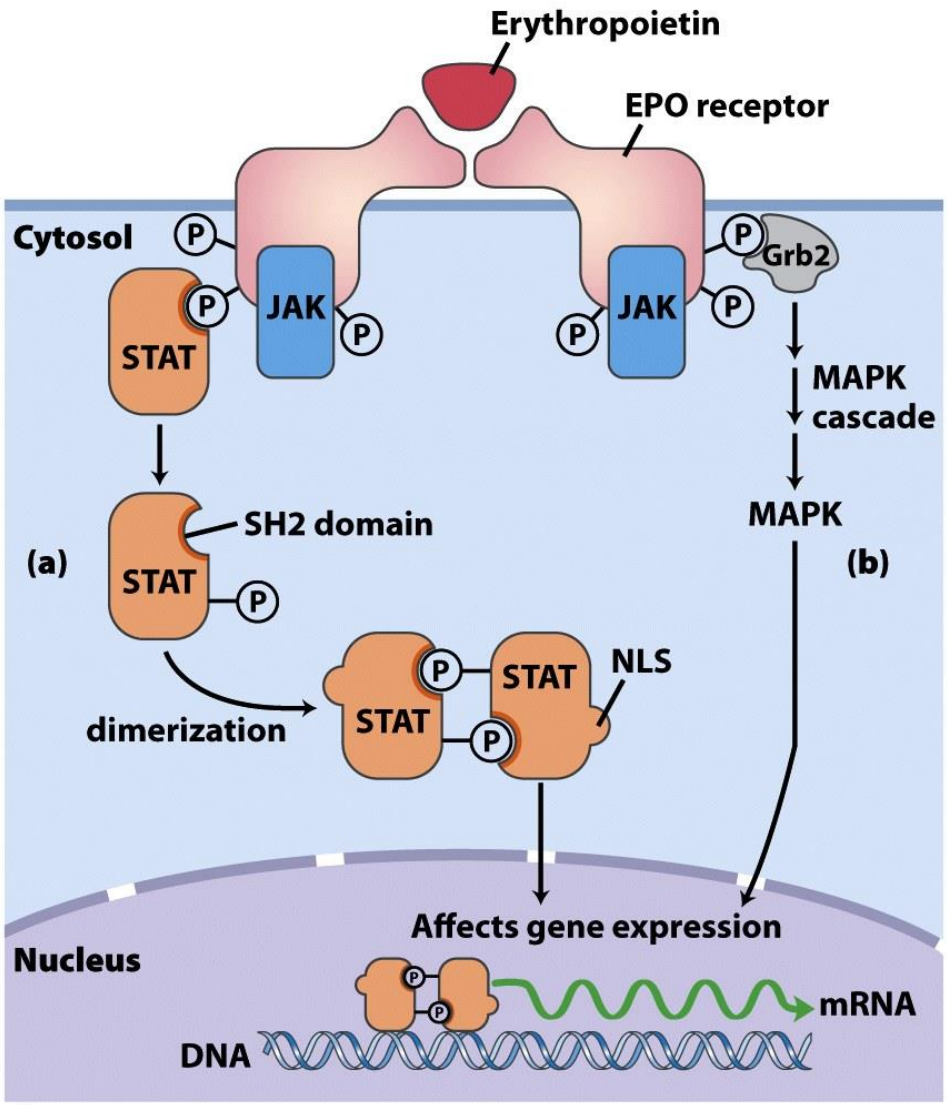


Figure 12-18
Lehninger Principles of Biochemistry, Fifth Edition

Receptorske gvanilat ciklaze

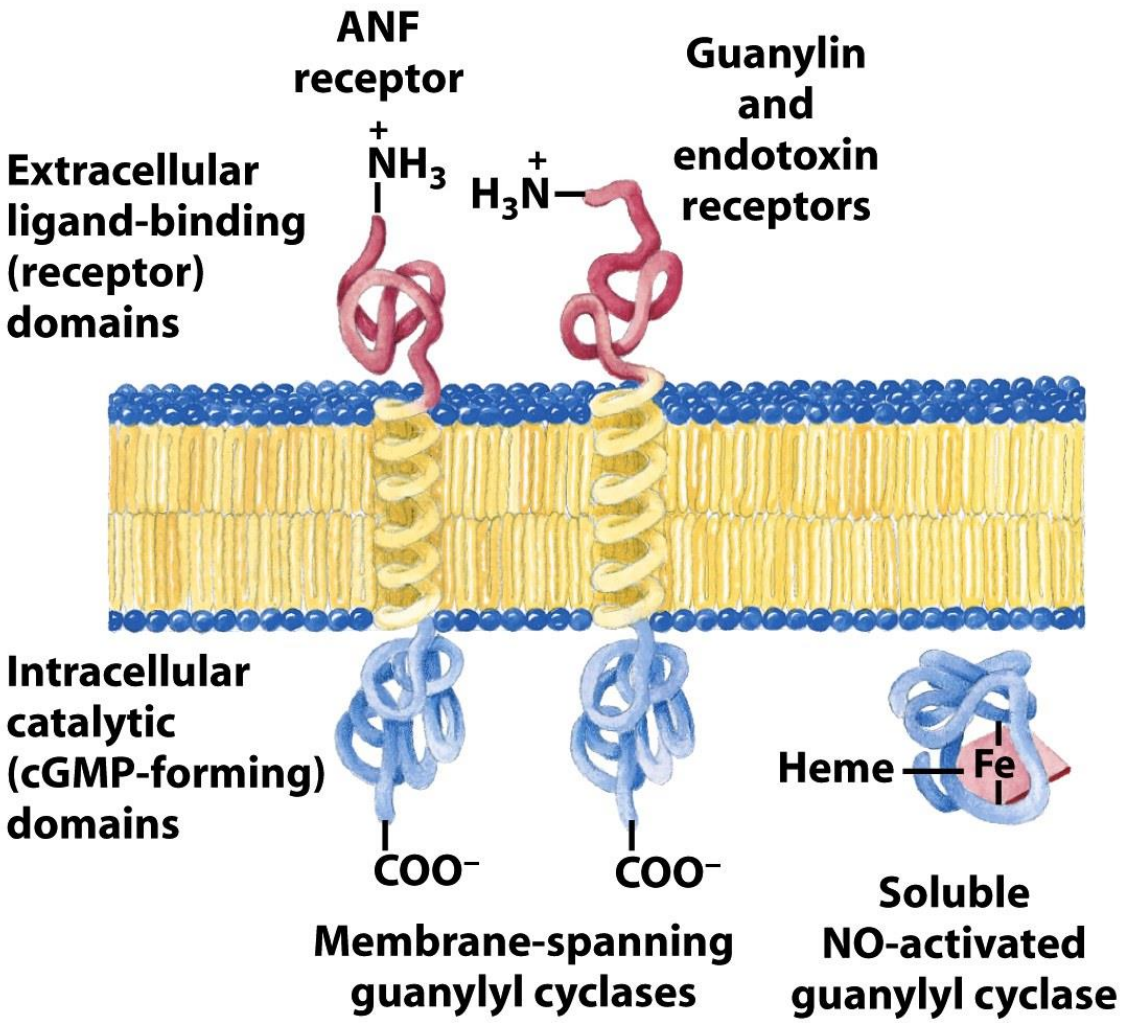
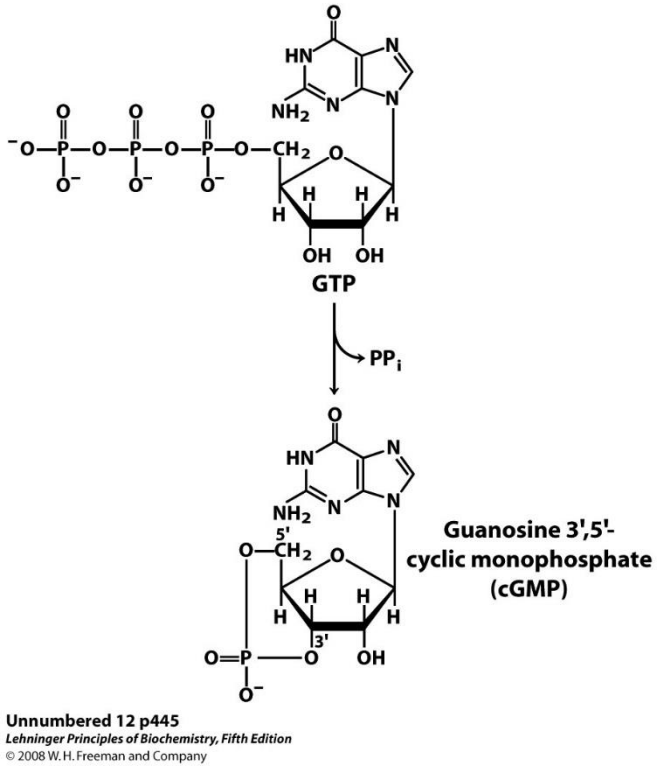


Figure 12-20
Lehninger Principles of Biochemistry, Fifth Edition

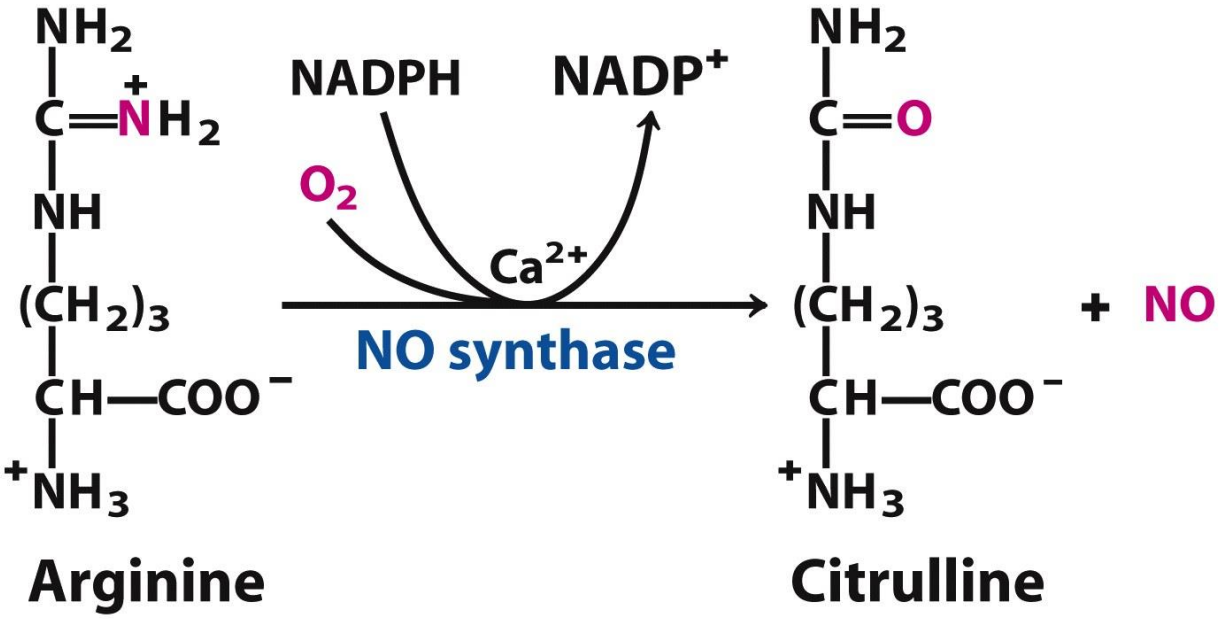


Unnumbered 12 p445
Lehninger Principles of Biochemistry, Fifth Edition

Regulirajo nekatere procese v ledvicah (izločanje Na^+), relaksacijo gladkih mišic.

Receptorske gvanilat ciklaze

Citosolno gvanilat ciklazo aktivira NO, ki ga sintetizira NO sintaza.



Unnumbered 12 p446a
Lehninger Principles of Biochemistry, Fifth Edition

NO je pomemben regulator krvnega tlaka, ker povzroča širjenje žil in umirja intenzivnost bitja srca. Je dovolj majhen, da lahko prosto difundira preko membran.

Od napetosti odvisni ionski kanalčki

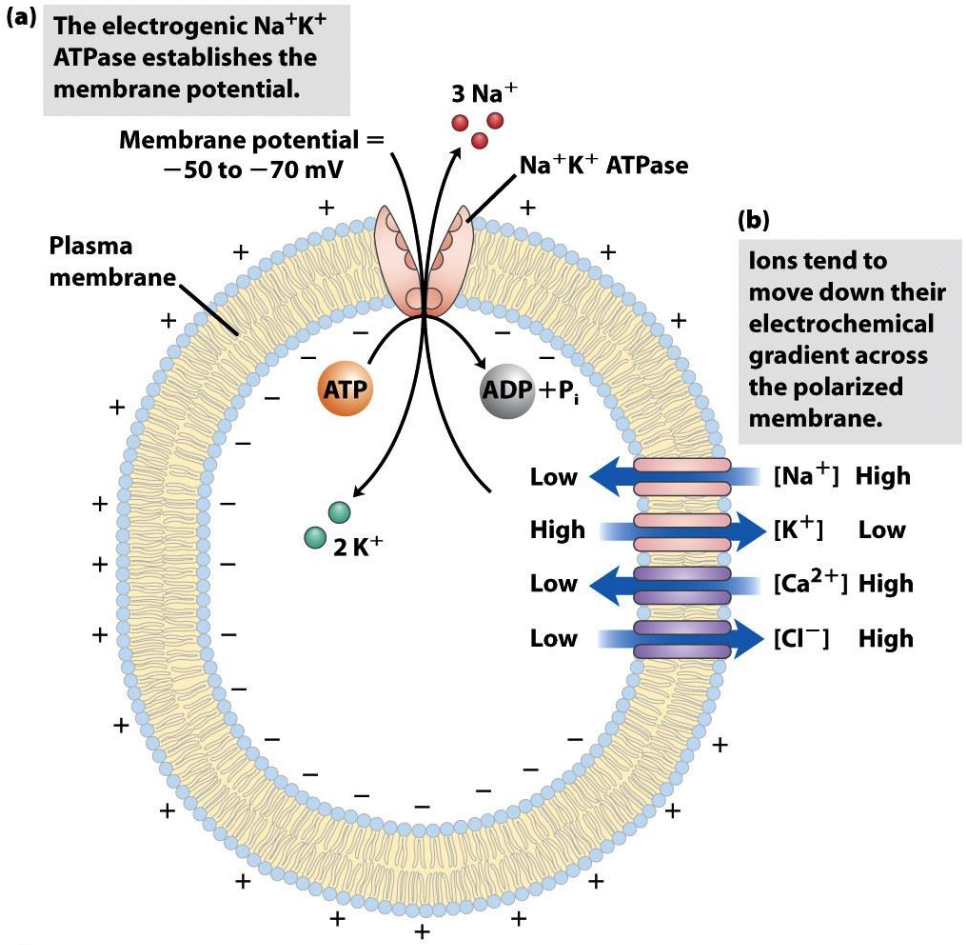


Figure 12-24
Lehninger Principles of Biochemistry, Fifth Edition

Na^+/K^+ ATPaza ustvarja membranski potencial zaradi črpanja 2 K^+ *vs* 3 Na^+.

TABLE 12–6 Ion Concentrations in Cells and Extracellular Fluids (mM)

	K^+		Na^+		Ca^{2+}		Cl^-	
Cell type	In	Out	In	Out	In	Out	In	Out
Squid axon	400	20	50	440	≤0.4	10	40–150	560
Frog muscle	124	2.3	10.4	109	<0.1	2.1	1.5	78

Table 12-6
Lehninger Principles of Biochemistry, Fifth Edition

Od napetosti odvisni ionski kanalčki

Od napetosti odvisni kanalčki omogočajo širjenje akcijskega potenciala (valu depolarizacije/repolarizacije) vzdolž aksona.

Na^+ kanalčki so vzdolž celotnega aksona. Odprejo se ob depolarizaciji, ki jo sprožijo nevtrotransmiterji (npr. acetilholin). Povzročijo **depolarizacijo** membrane.

Podobno so K^+ kanalčki vzdolž celotnega aksona. Odprejo se zaradi spremembe potenciala kot posledice odprtja Na^+ kanalčkov. Povzročijo **repolarizacijo** membrane.

Ca^{+2} kanalčki so le na distalnem koncu aksona. Ko jih doseže val depolarizacije/repolarizacije, se aktivirajo in povzročijo izločanje veziklov z acetilholinom v sinaptično režo.

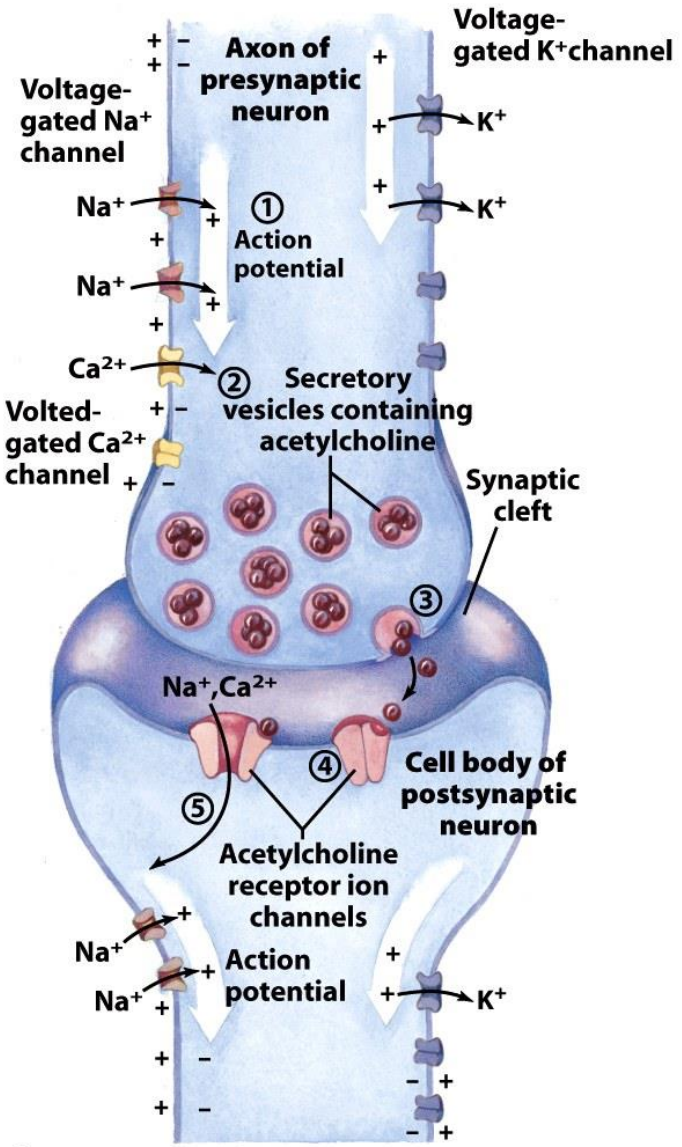


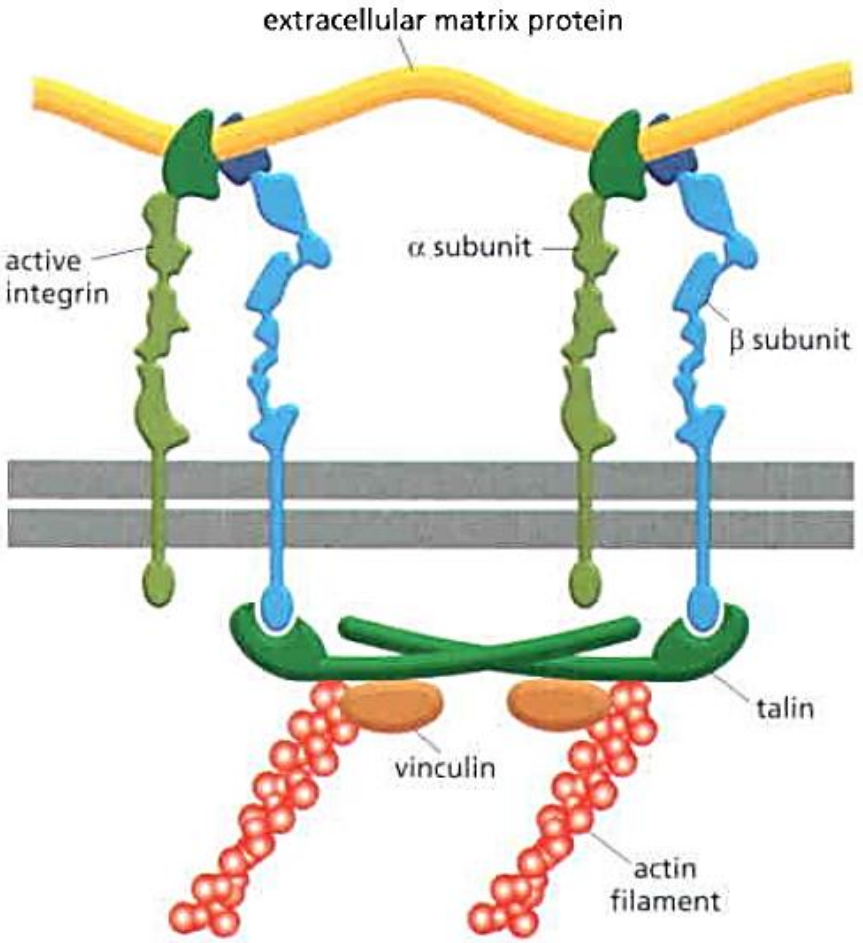
Figure 12-25
Lehninger Principles of Biochemistry, Fifth Edition

Integrini

So poglavitna skupina molekul, ki regulira vezavo celic na zunajcelični matriks. So $\alpha\beta$ heterodimeri. Imajo pomembne vloge pri prenosih signalov povezanih z diferenciacijo in proliferacijo celic, migracijo celic, celično smrtjo, itd.

Zunajcelični del se povezuje z elementi ECM.

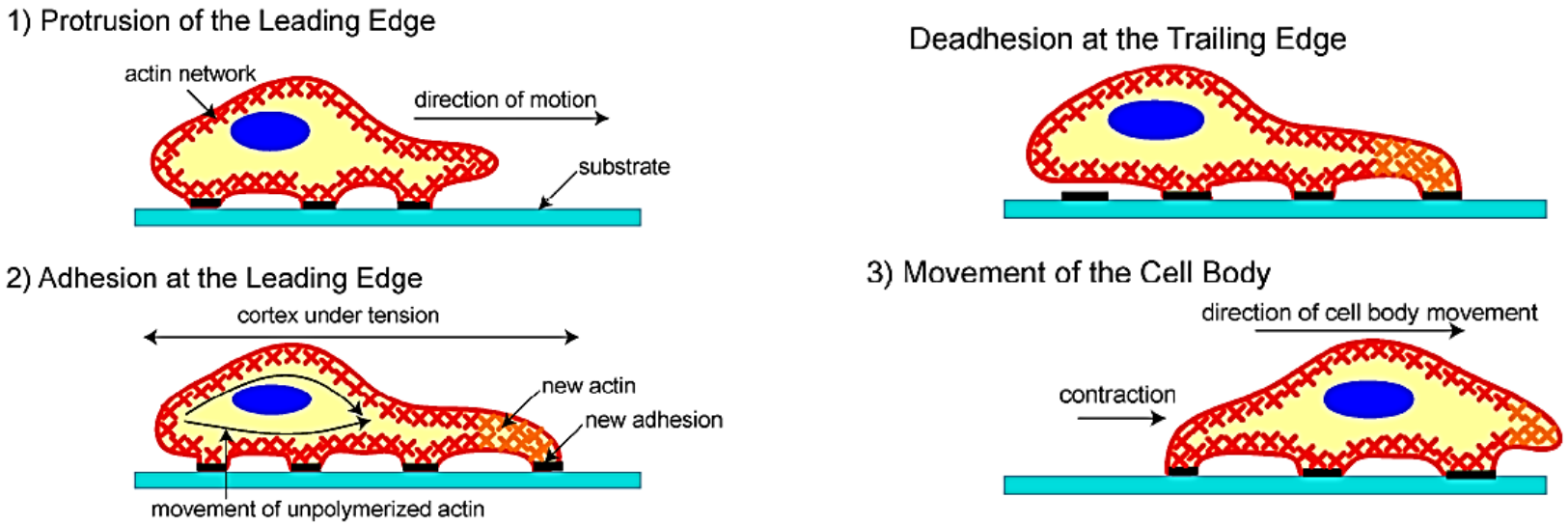
Znotrajcelični del se povezuje z elementi citoskeleta.

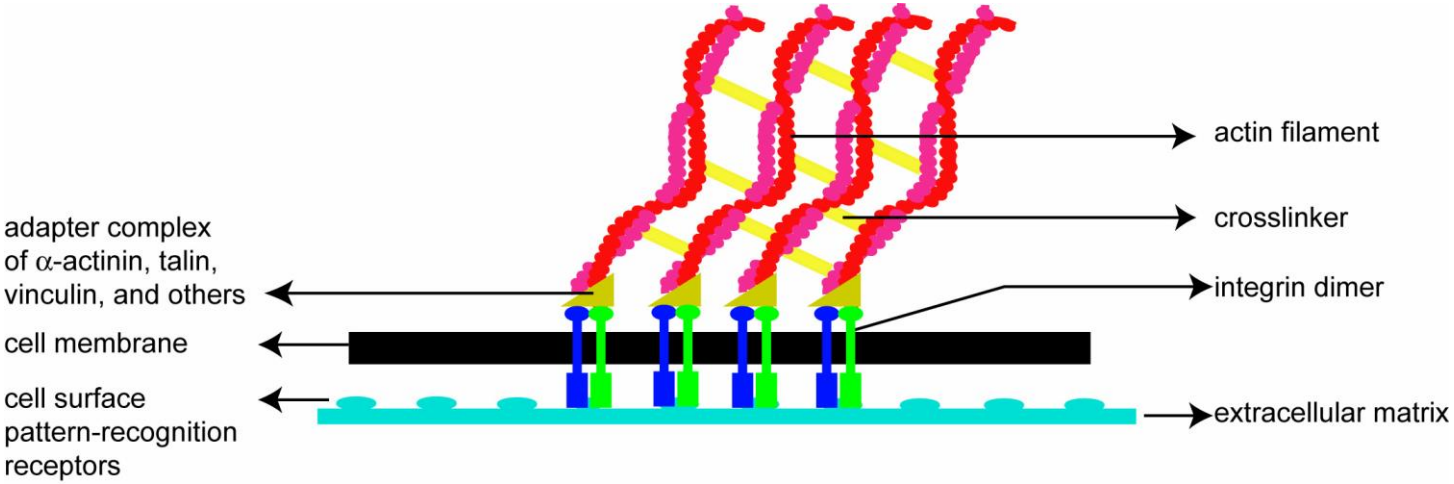


Alberts. Molecular Biology of the Cell. 5th Ed. Fig. 19-45

Integrini

Integrini sodelujejo pri **migraciji** celic.

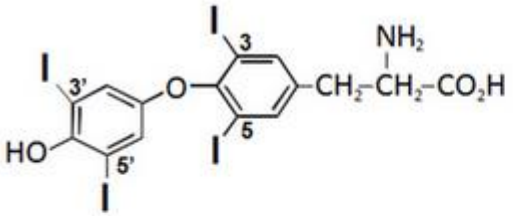




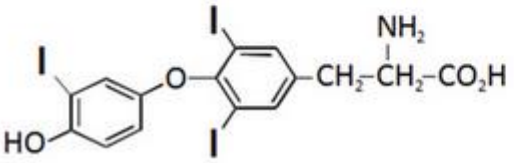
Ananthakrishnan and Ehrlicher. 2007. *Int J Biol Sci*. 3

Ščitnični hormoni

Integrini lahko delujejo tudi kot receptorji primarnih obveščvalcev, npr. hormonov ščitnice.



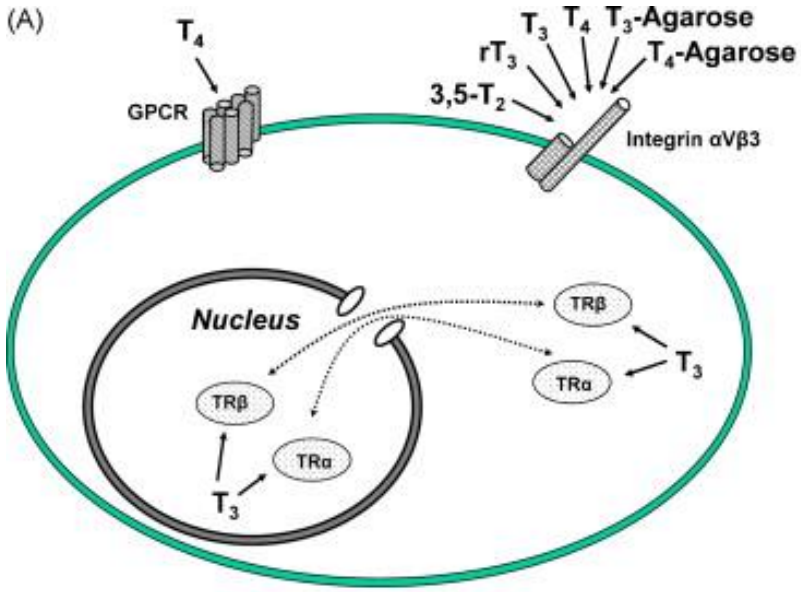
L-Thyroxine (T_4)

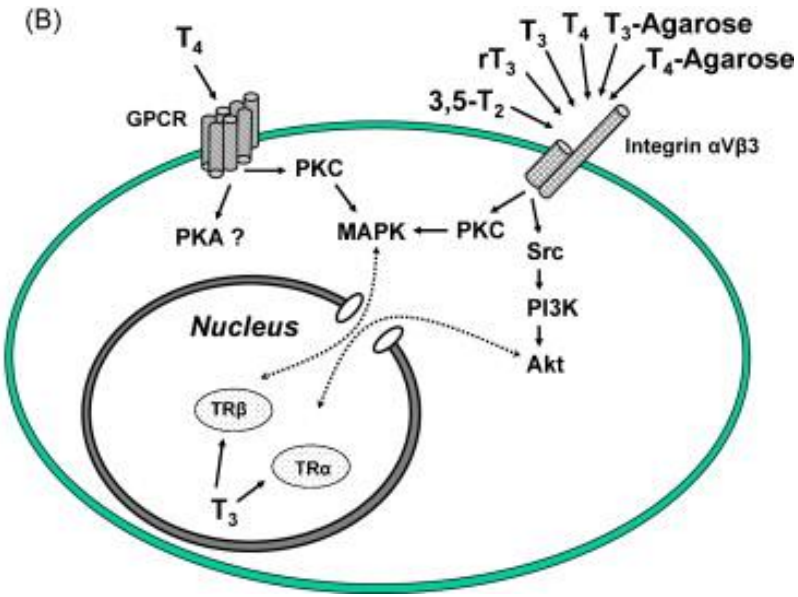


3,5,3'-Triiodo-L-thyronine (T_3)

<u>Efekt ščitničnih hormonov:</u>

- povišan katabolizem AK in OH
- hitrejše bitje srca
- povišan bazalni metabolizem
- hitrejše dihanje





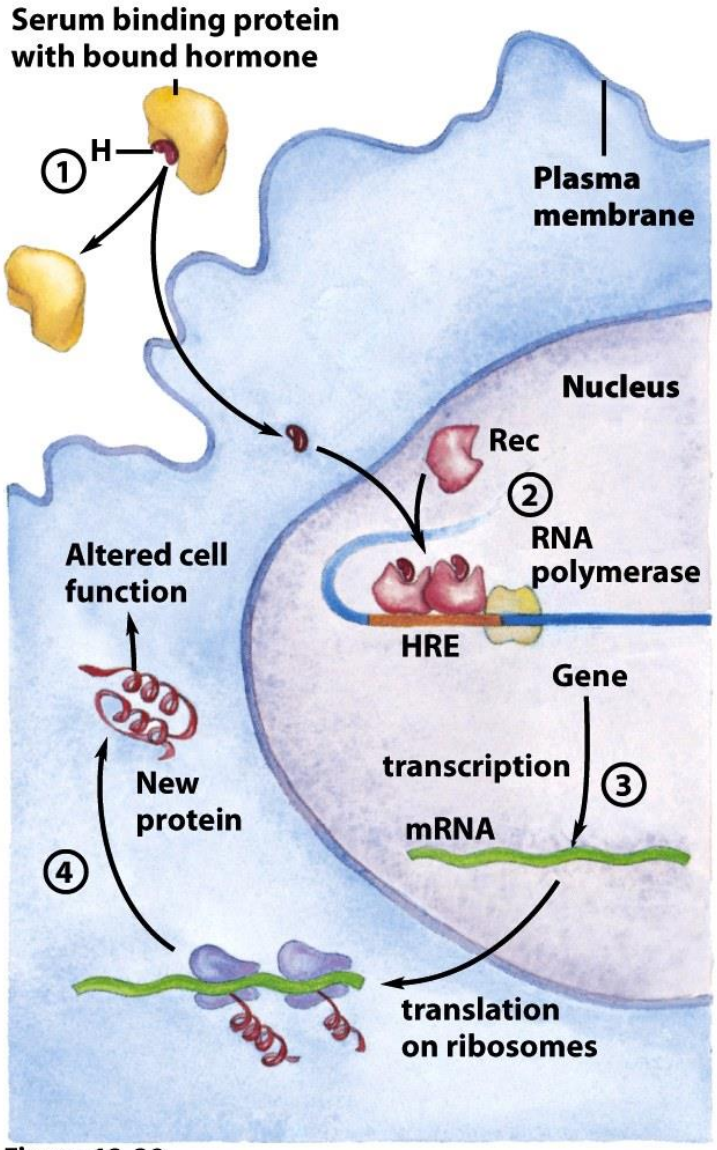
Ščitnični hormoni

Simptomi: povečana ščitnica, povečan metabolizem, izguba telesne teže kljub povečanemu apetitu, slabše prenašanje vročine, povečano znojenje, hitro in močno utripanje srca, nemirnost, razdražljivost, tremor, eksoftalmus – nenormalen pomik očesa iz očesne votline (posebna značilnost Gravesove bolezni), mehka, vlažna in topla koža, mišična šibkost, pri ženskah tudi neredni menstruacijski cikli, znižan libido (*vir: www.viva.si*)

vir: www.suite101.com

vir: www.thachers.org

Steroidni hormoni



1
Hormone (H), carried to the target tissue on serum binding proteins, diffuses across the plasma membrane and binds to its specific receptor protein (Rec) in the nucleus.

2
Hormone binding changes the conformation of Rec; it forms homo- or heterodimers with other hormone-receptor complexes and binds to specific regulatory regions called hormone response elements (HREs) in the DNA adjacent to specific genes.

3
Binding regulates transcription of the adjacent gene(s), increasing or decreasing the rate of mRNA formation.

4
Altered levels of the hormone-regulated gene product produce the cellular response to the hormone.

Figure 12-29
Lehninger Principles of Biochemistry, Fifth Edition

Senzorični signali

Prenašanje senzoričnih signalov poteka preko receptorjev sklopljenih z G proteini.

Vid:

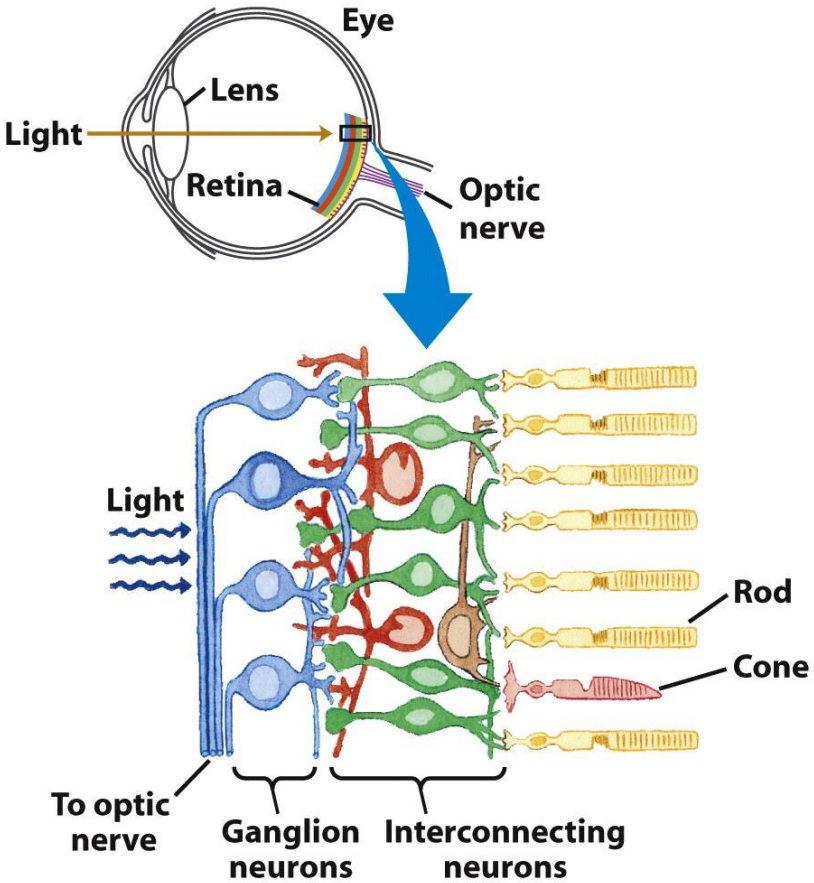


Figure 12-35
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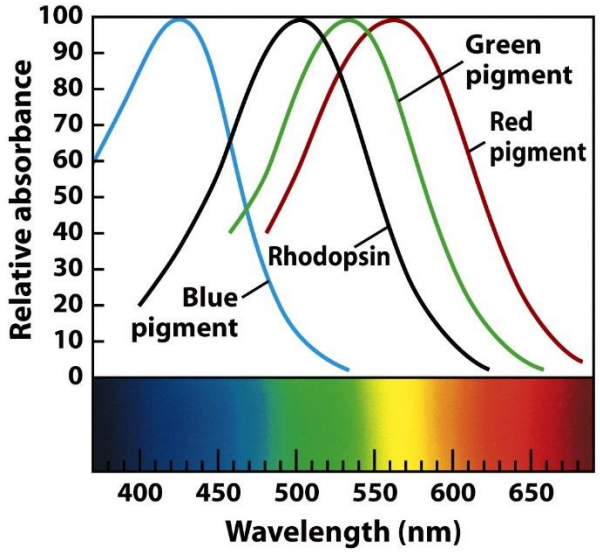
paličnice zaznavajo intenziteto svetlobe

čepnice zaznavajo barve

V obeh vrstah celic so pigmenti, ki absorbirajo svetlobo.



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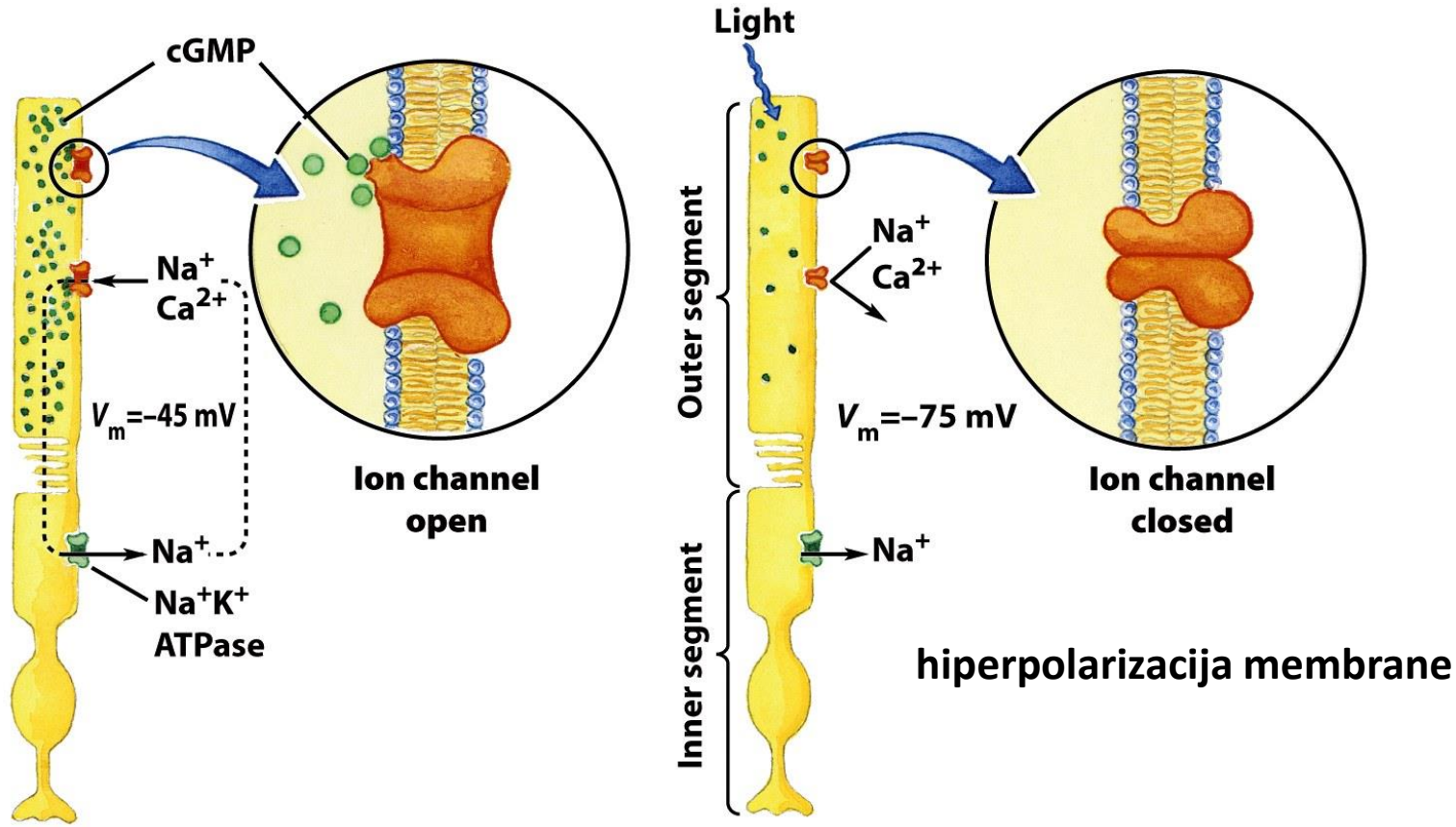
Senzorični signali

Prenašanje senzoričnih signalov poteka preko receptorjev sklopljenih z G proteini.

Vid:



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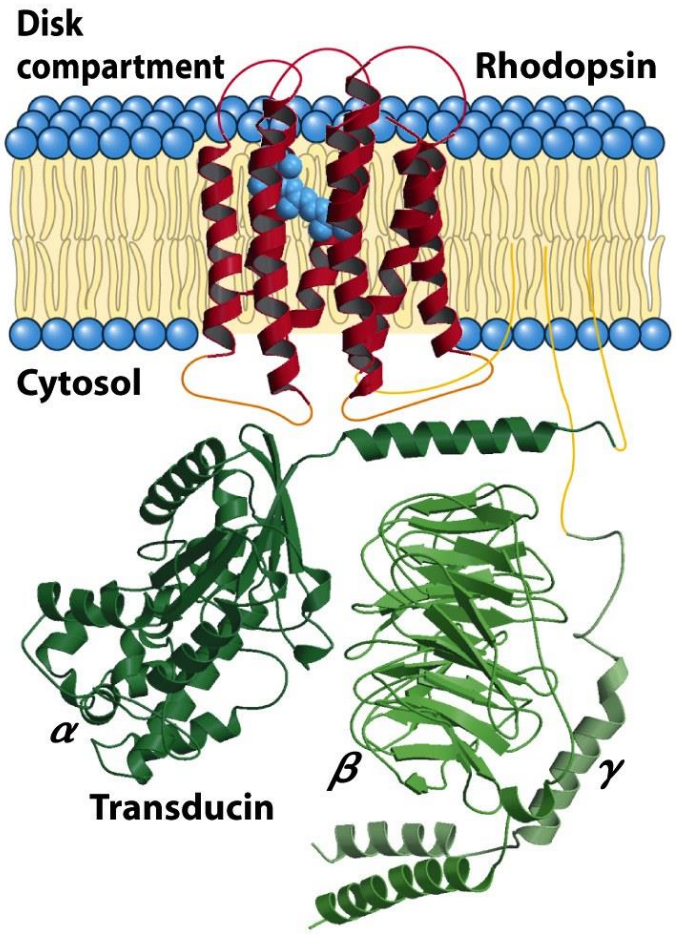
Senzorični signali

Prenašanje senzoričnih signalov poteka preko receptorjev sklopljenih z G proteini.

Vid:



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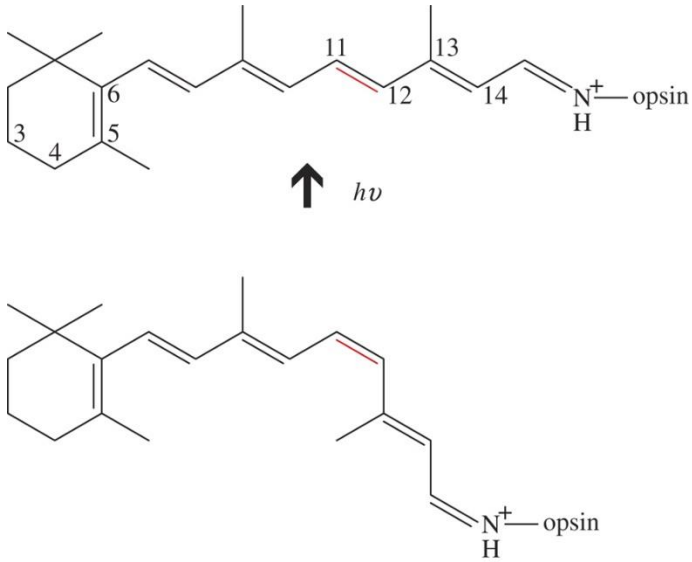

Izomerizacija retinala povzroči konformacijsko spremembo rodopsina, kar povzroči aktivacijo G proteina transducina.

Senzorični signali

Vid:

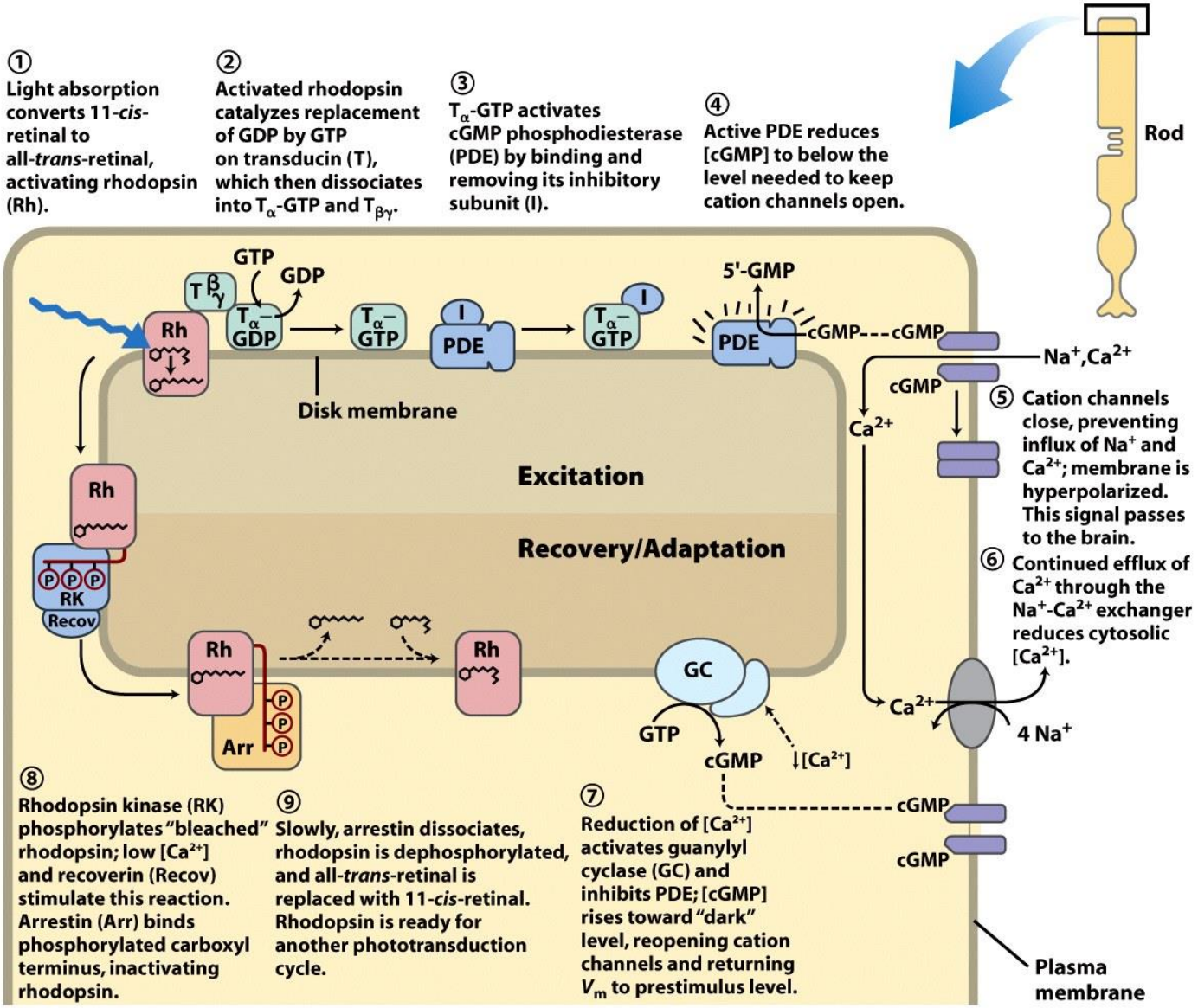

Figure 12-38

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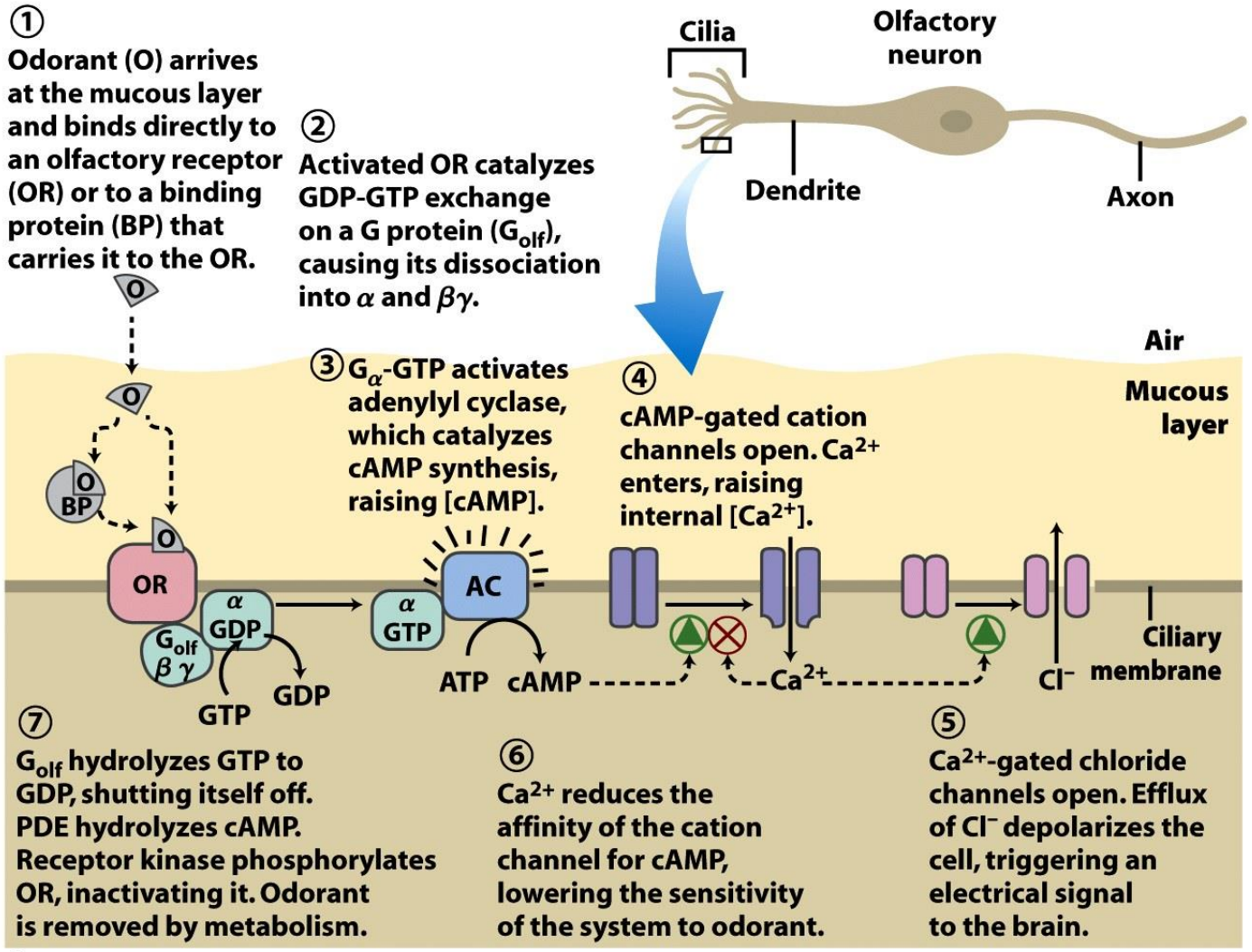
Senzorični signali

Prenašanje senzoričnih signalov poteka preko receptorjev sklopljenih z G proteini.

Vonj:



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Senzorični signali

Prenašanje senzoričnih signalov poteka preko receptorjev sklopljenih z G proteini.

Okus:

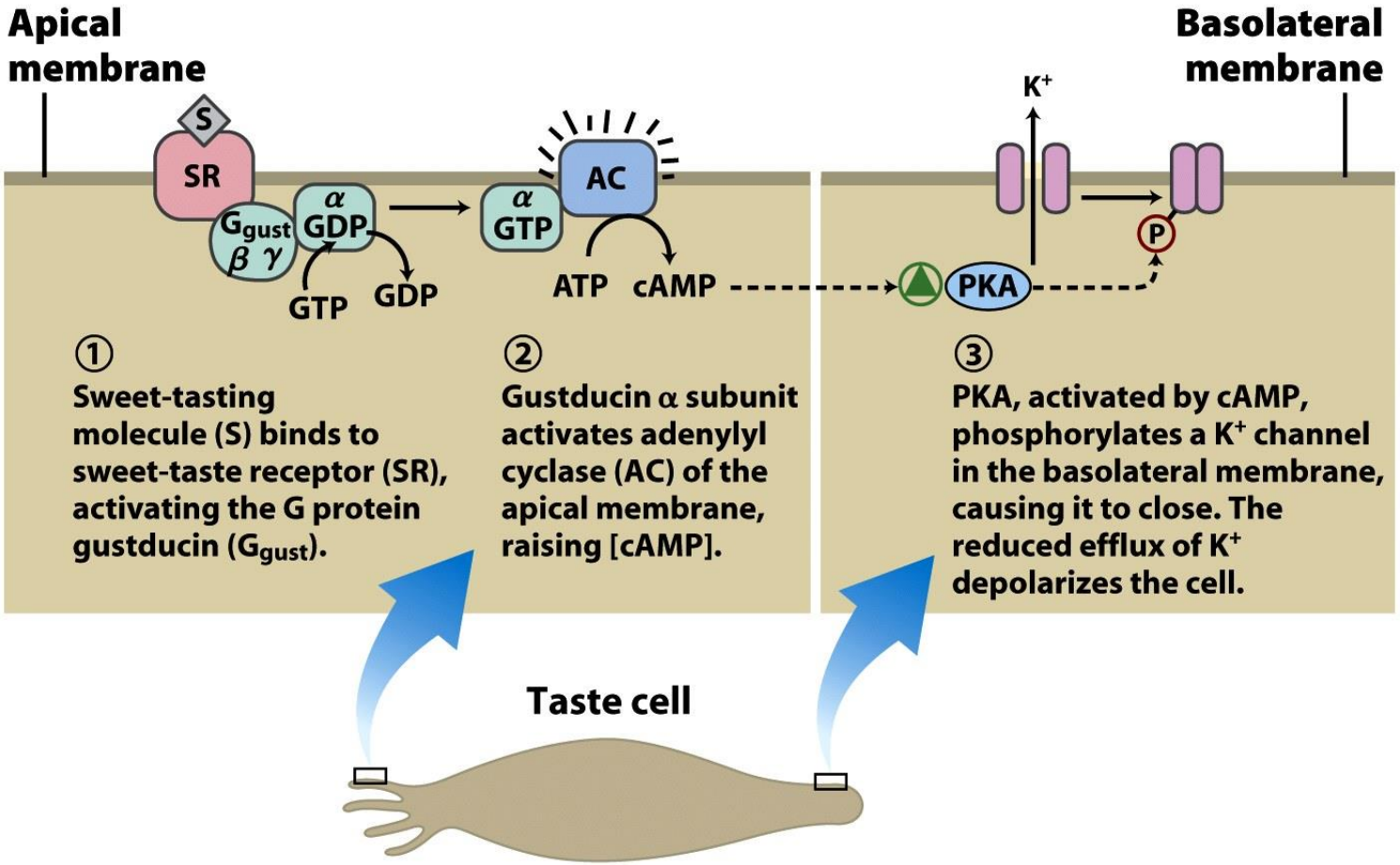

Figure 12-41
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