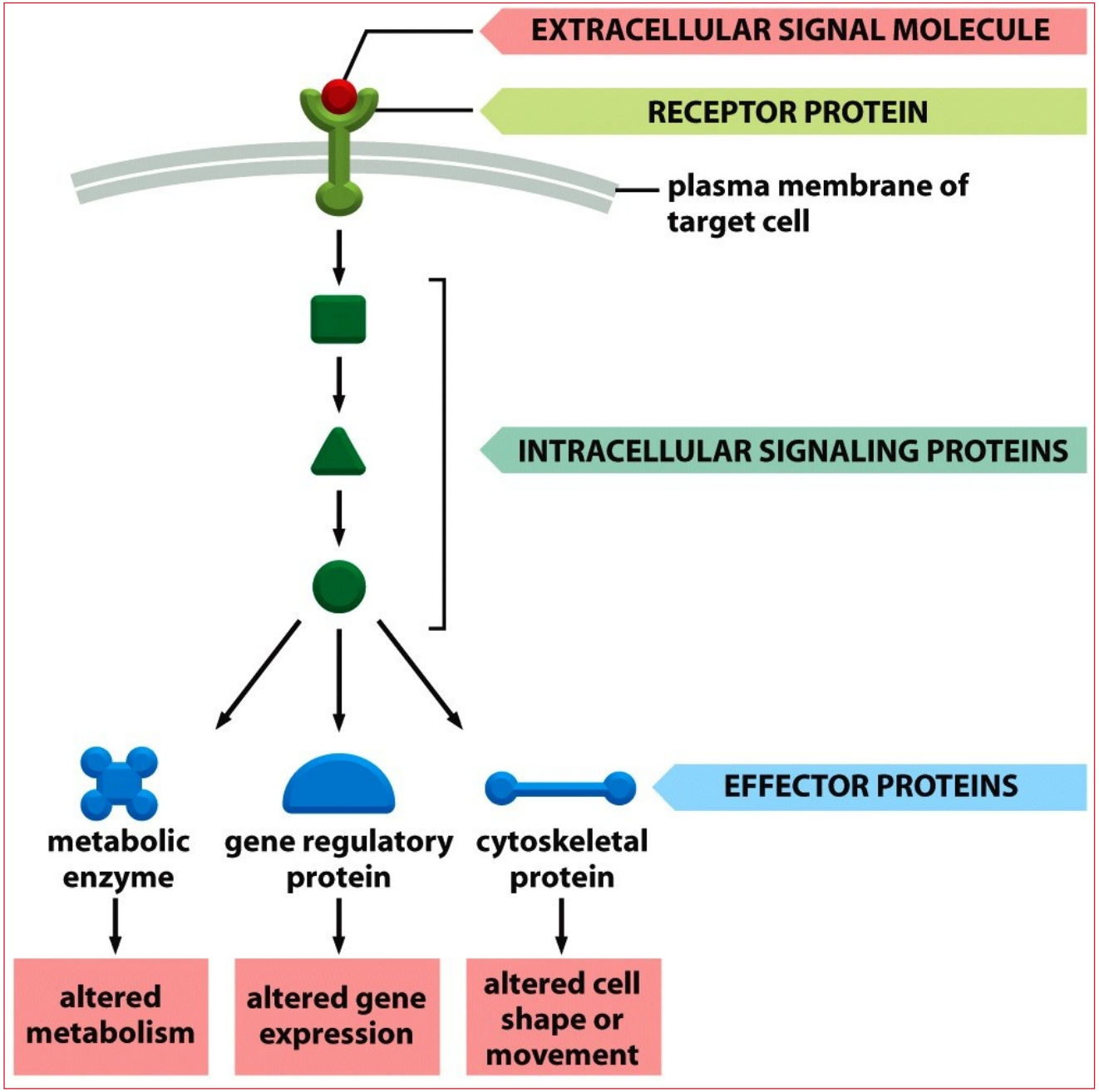
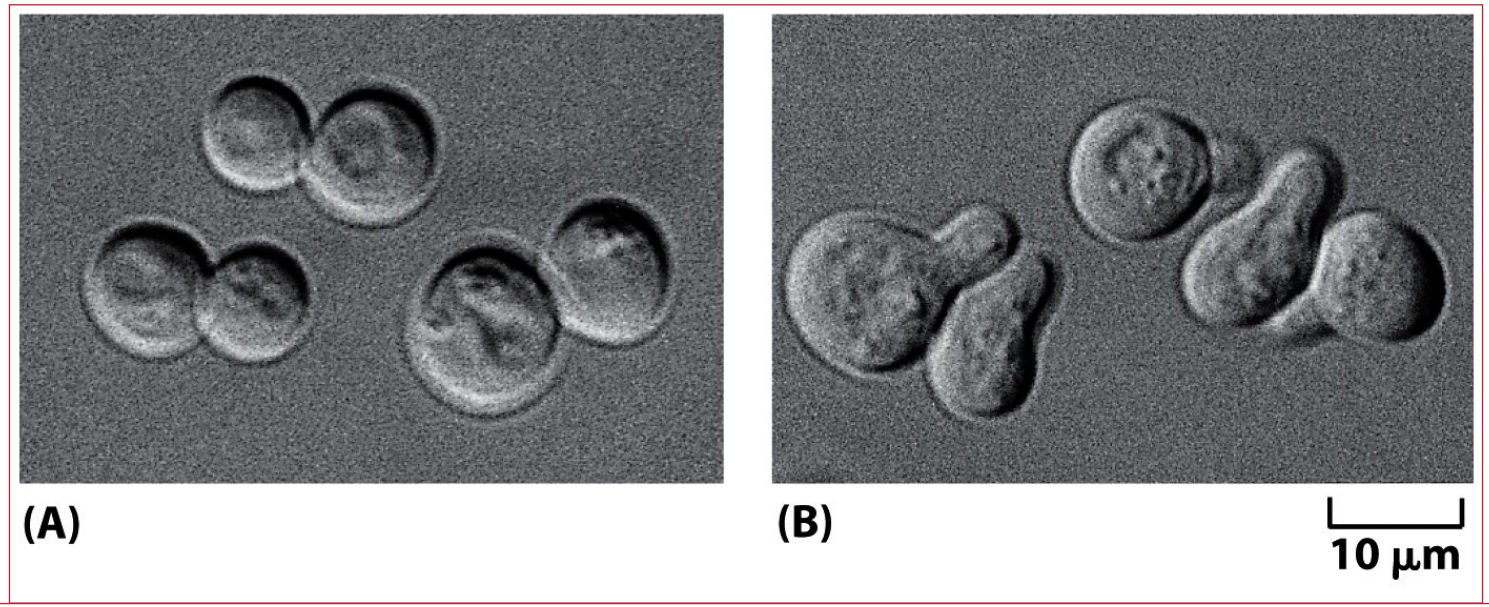
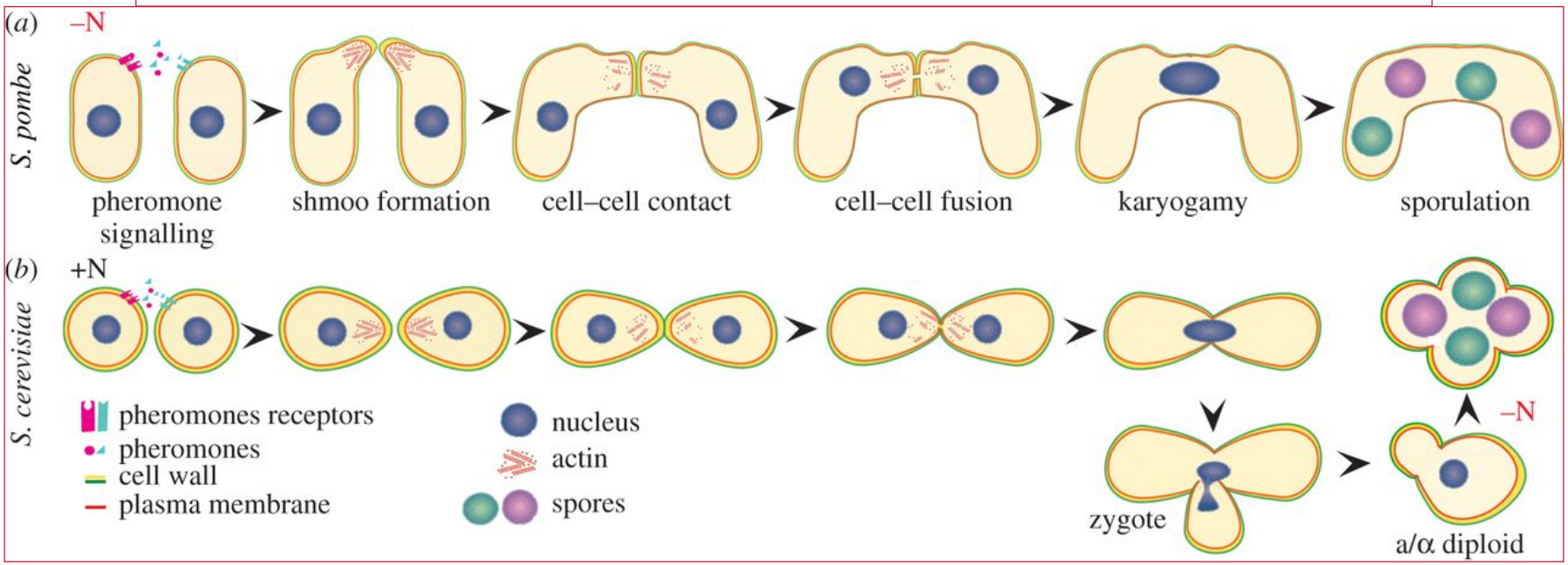
Hücre İletişim Mekanizmaları



Kinazlar, fosfatazlar, GTP bağlayan proteinler etkileştikleri diğer proteinler

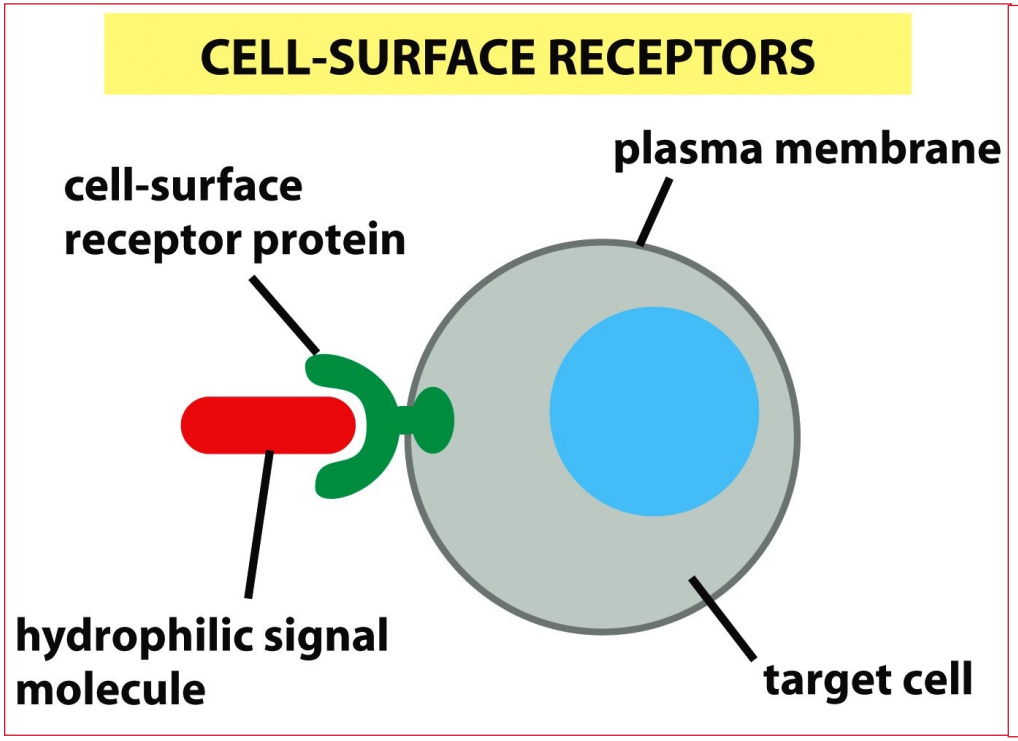
Figure 15-1 *Molecular Biology of the Cell* (© Garland Science 2008)

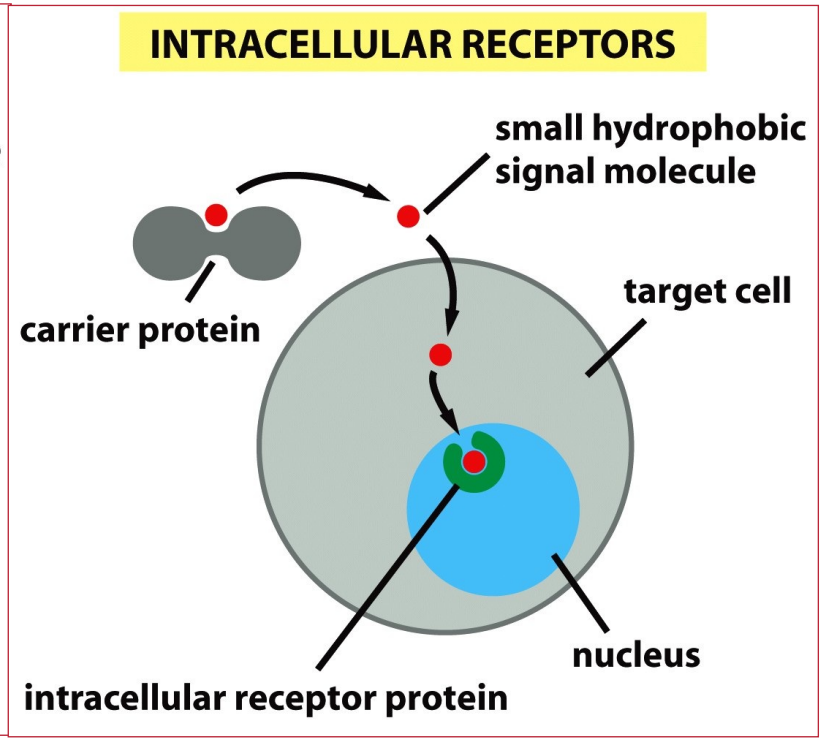




Alfa Mating Faktör: Haploid hücrelerin bölünmesini durdurur

Figure 15-2 *Molecular Biology of the Cell* (© Garland Science 2008)





proteinler, kısa peptidler, amino asitler, nükleotitler, nükleik asitler, steroidler, retinoidler, yağ asitleri, CO. NO…

Reseptörler bazen hücre yüzeyünde bazen hücre içinde olabilir.

Figure 15-3a *Molecular Biology of the Cell* (© Garland Science 2008)

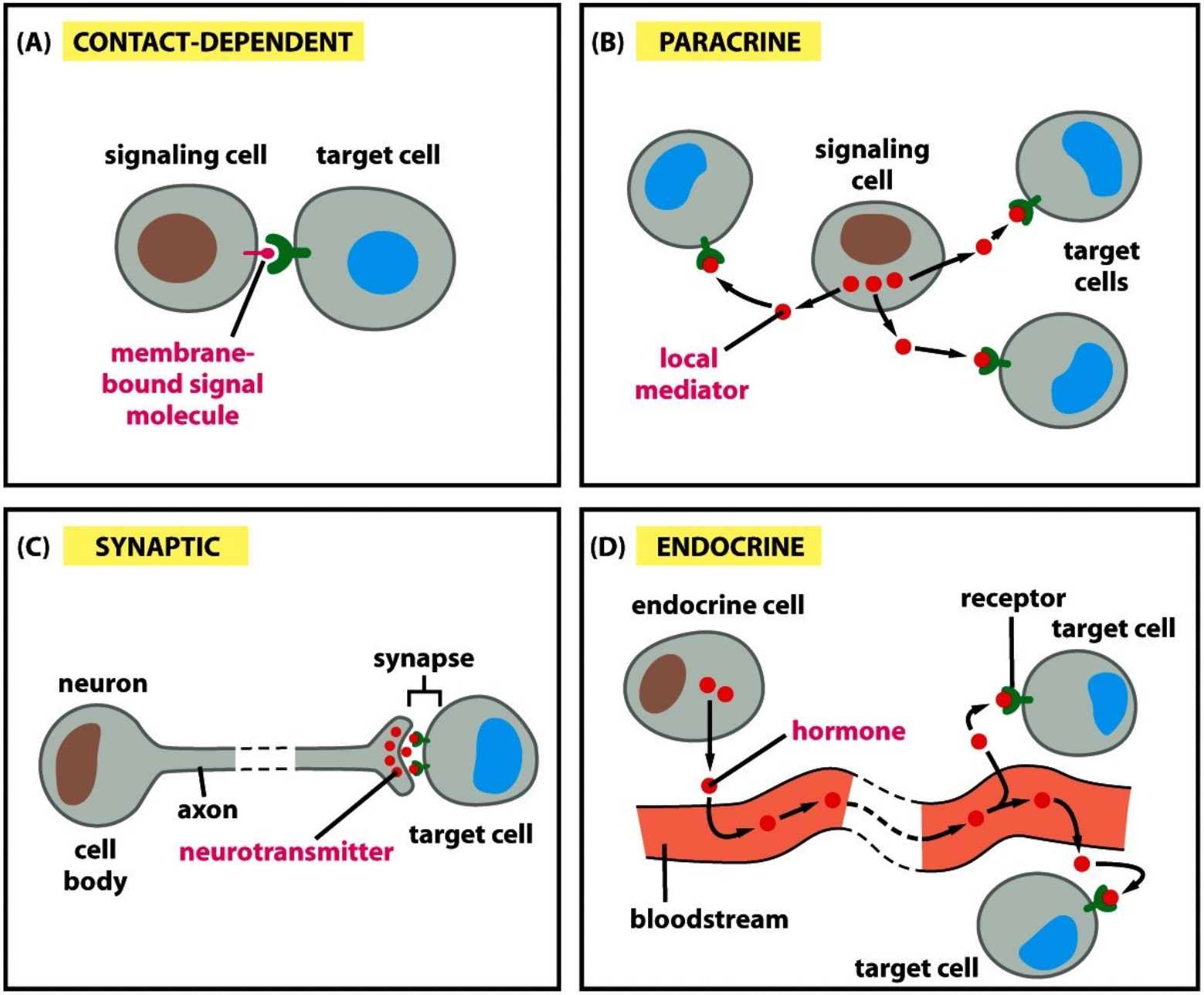
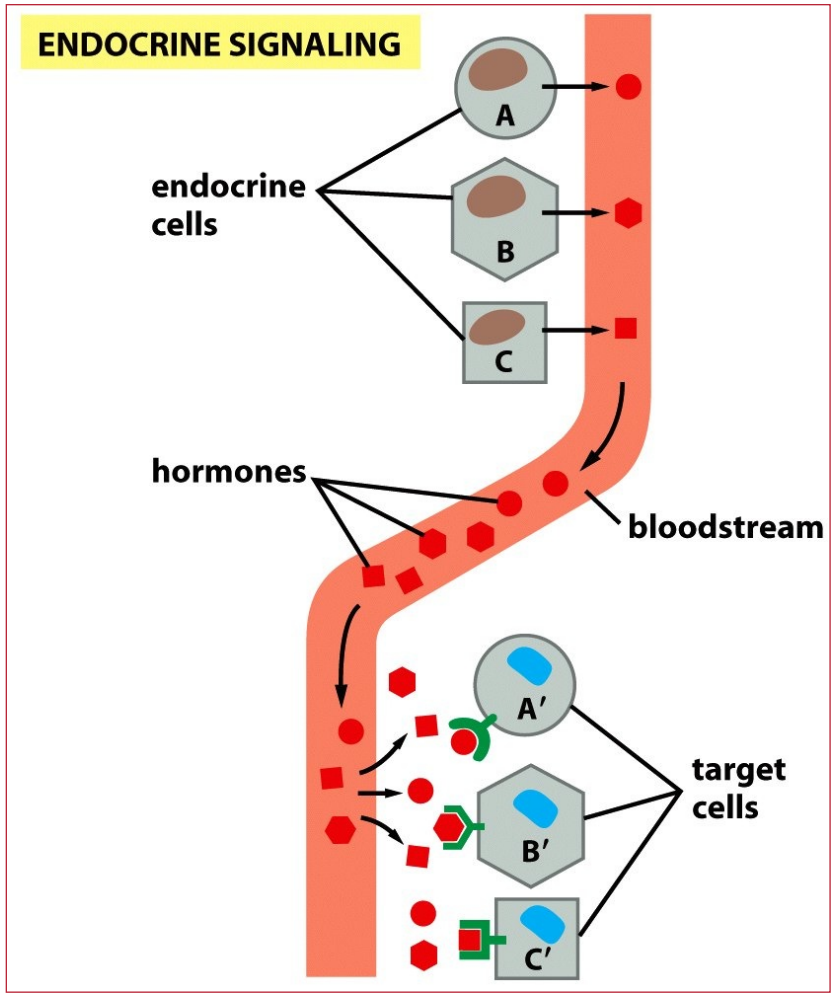
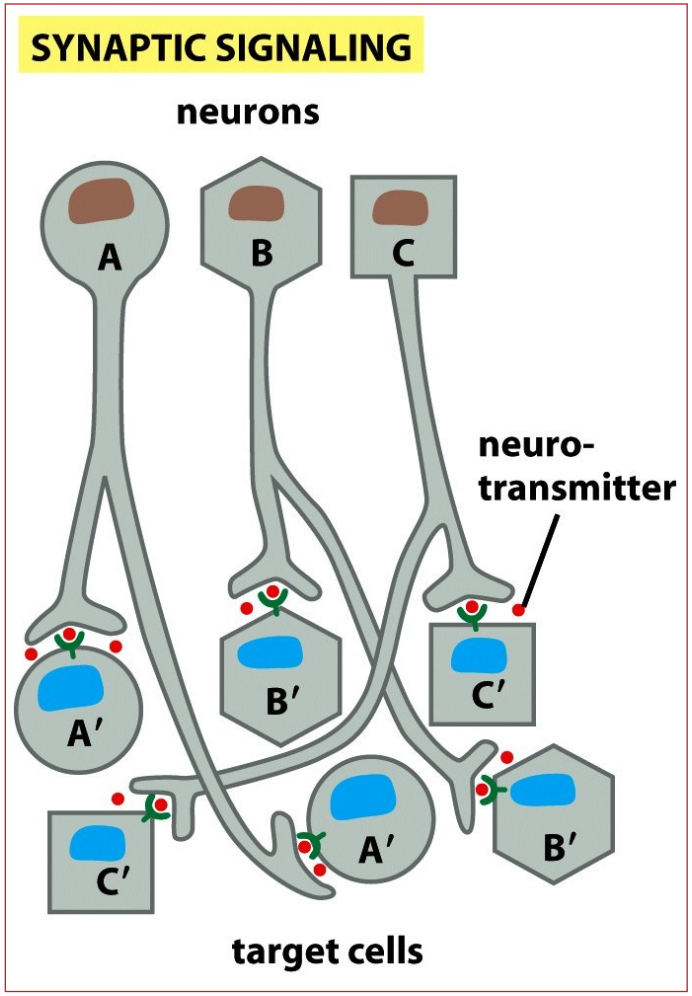


Figure 15-4 *Molecular Biology of the Cell* (© Garland Science 2008)





Sinaptik uyarı çok hızlı (100m/s) ve seyrelmiyor.

Figure 15-5a *Molecular Biology of the Cell* (© Garland Science 2008)

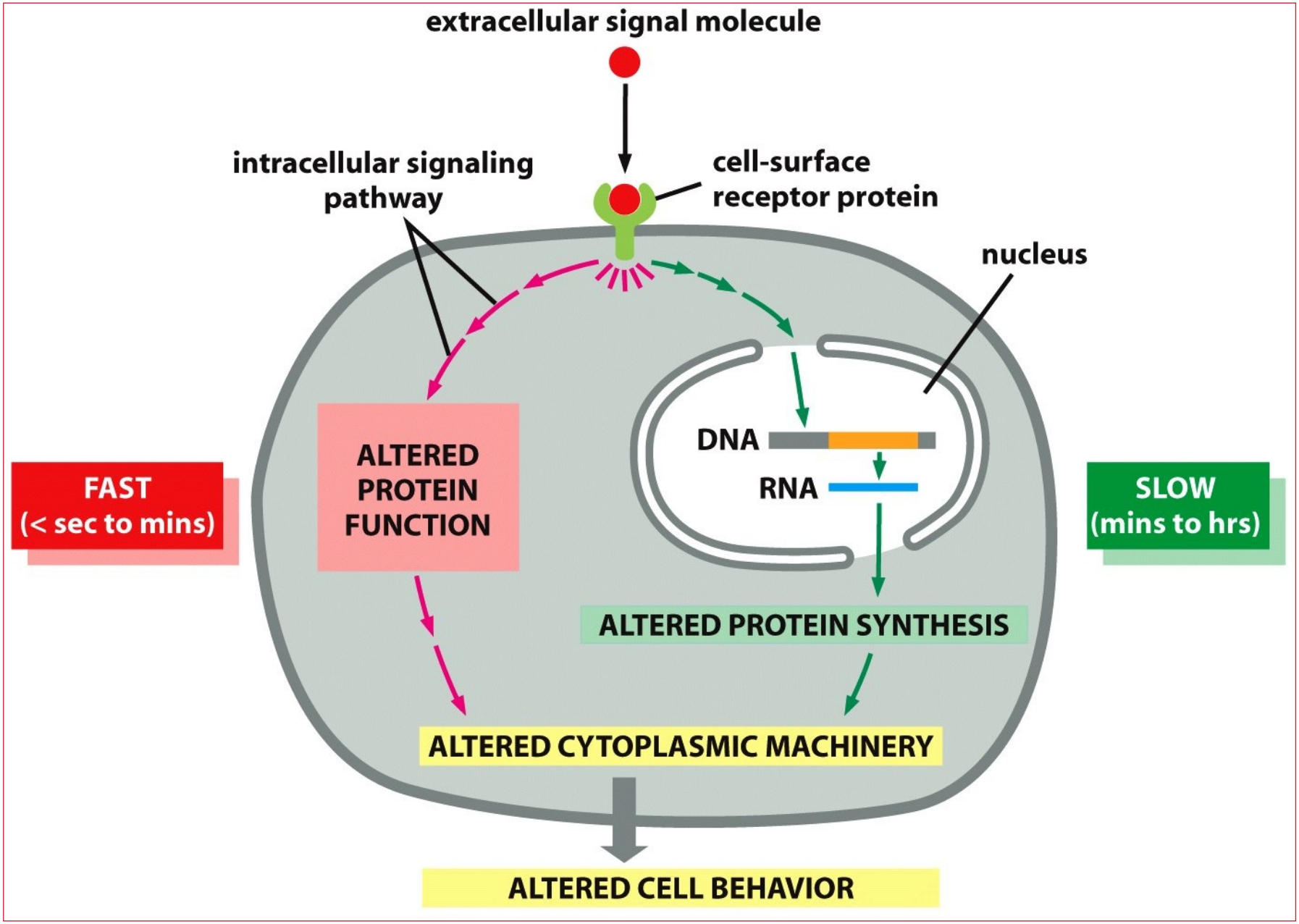
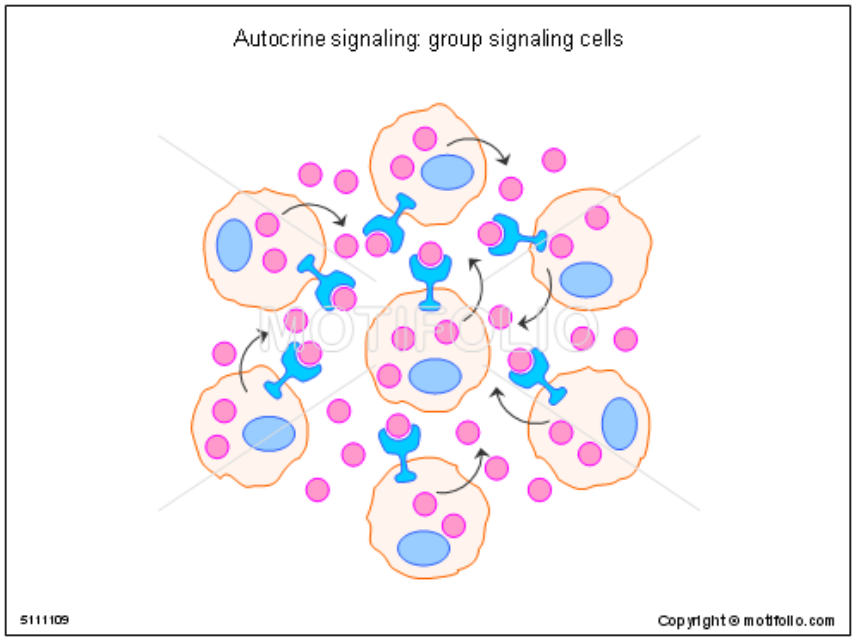
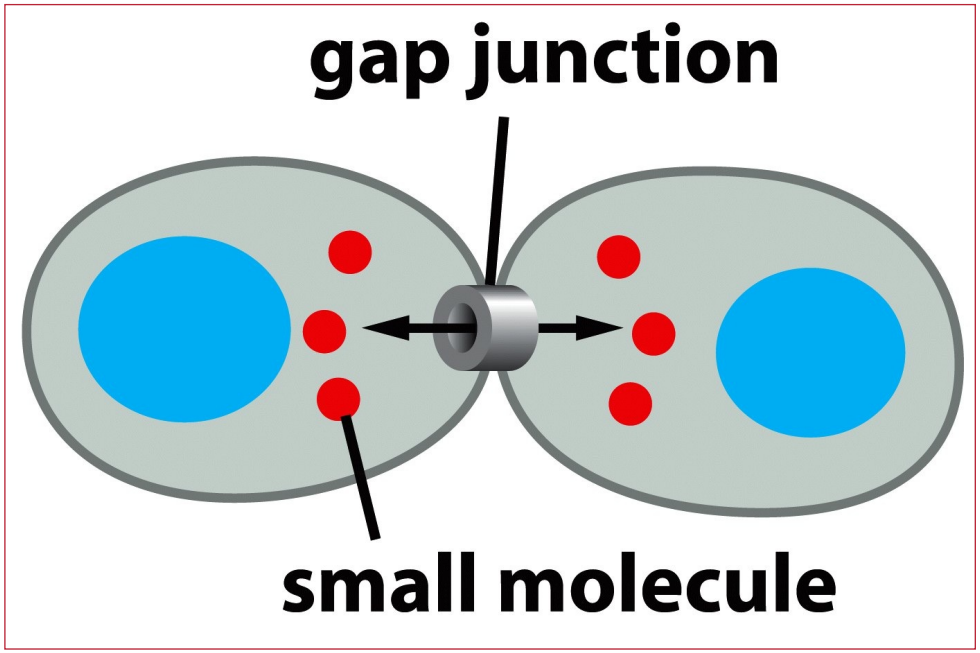


Figure 15-6 *Molecular Biology of the Cell* (© Garland Science 2008)





Su, Ca++, cAMP gibi küçük moleküller geçerken, DNA ve protein geçişine izin vermezler

Figure 15-7 *Molecular Biology of the Cell* (© Garland Science 2008)

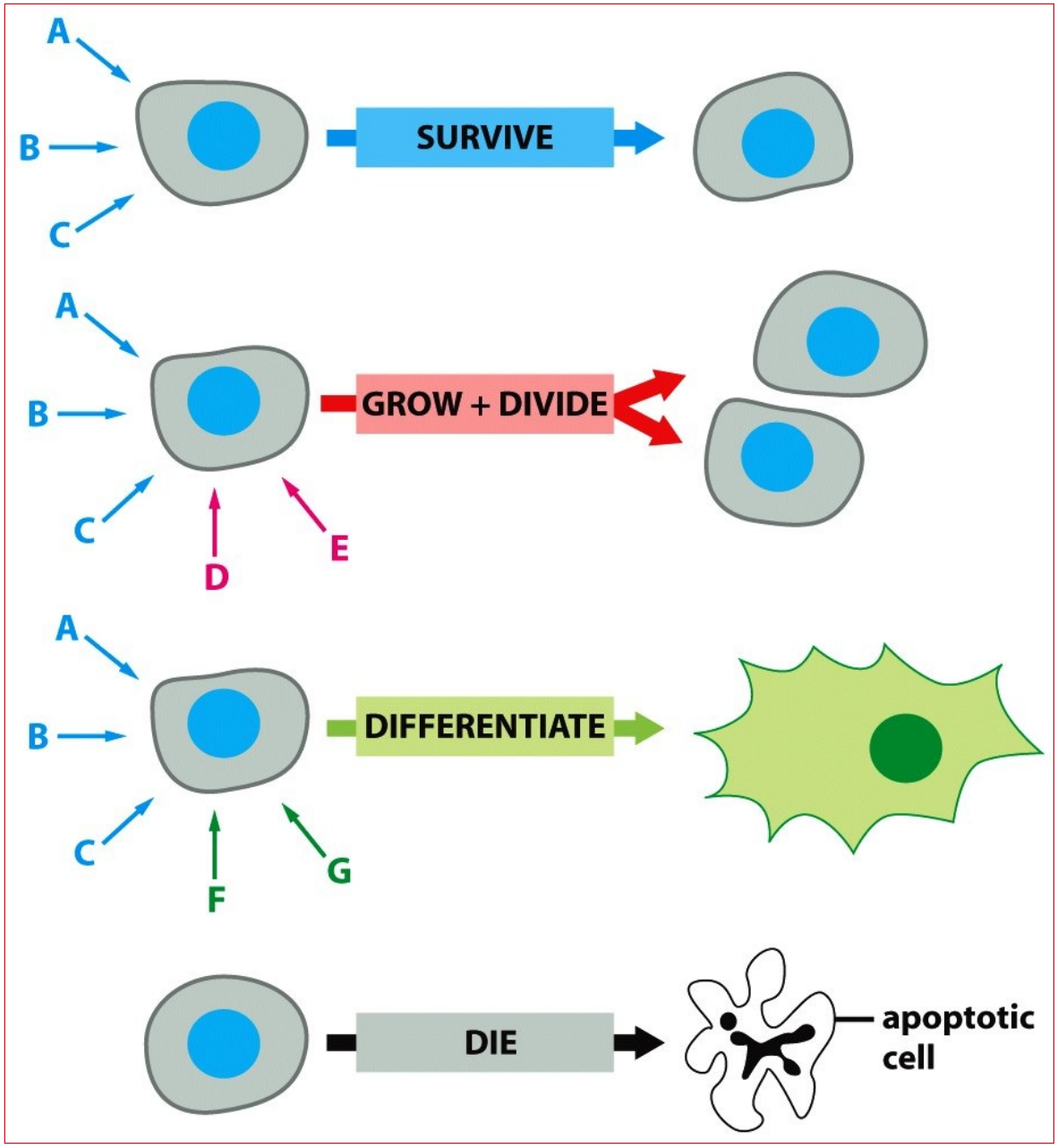
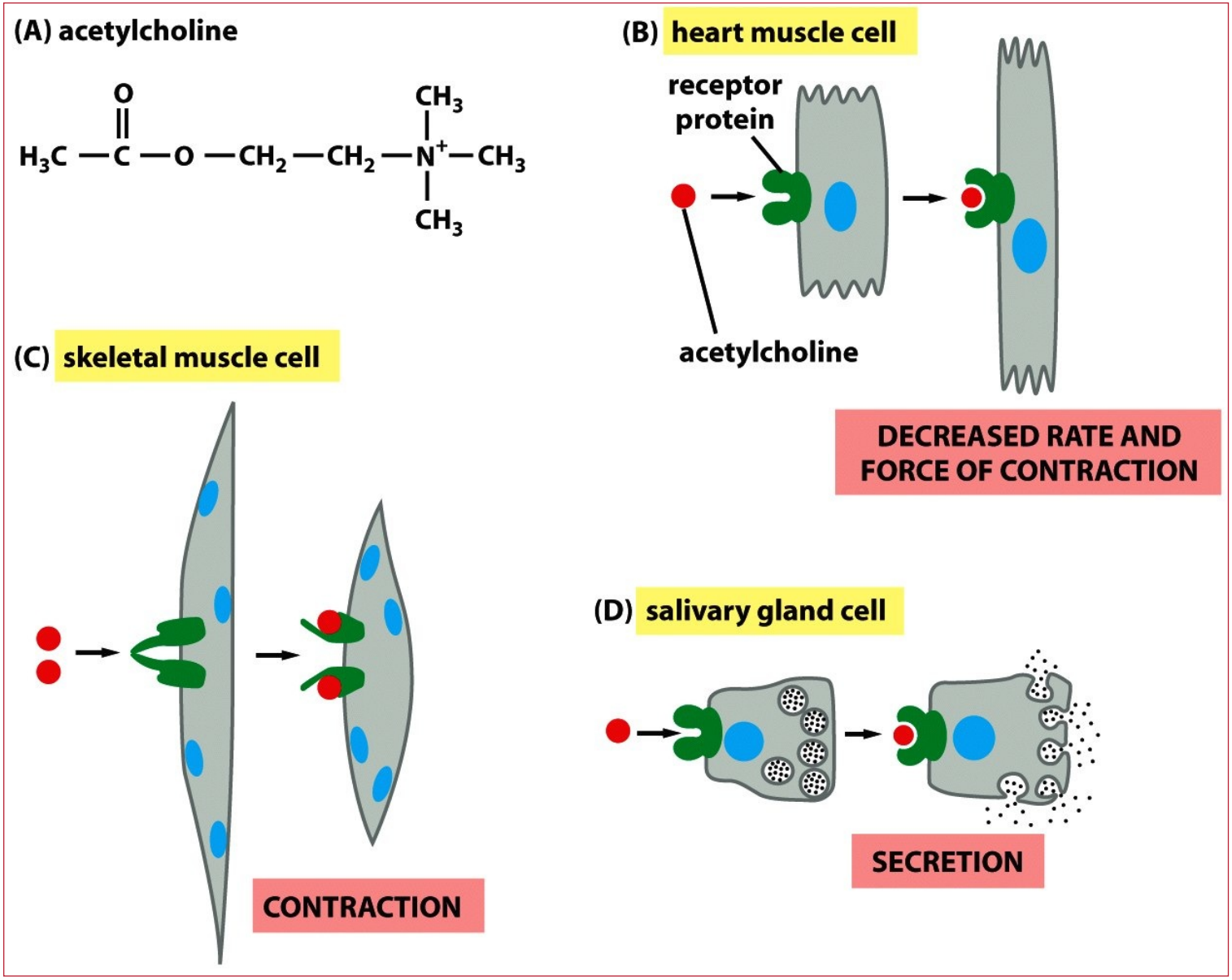
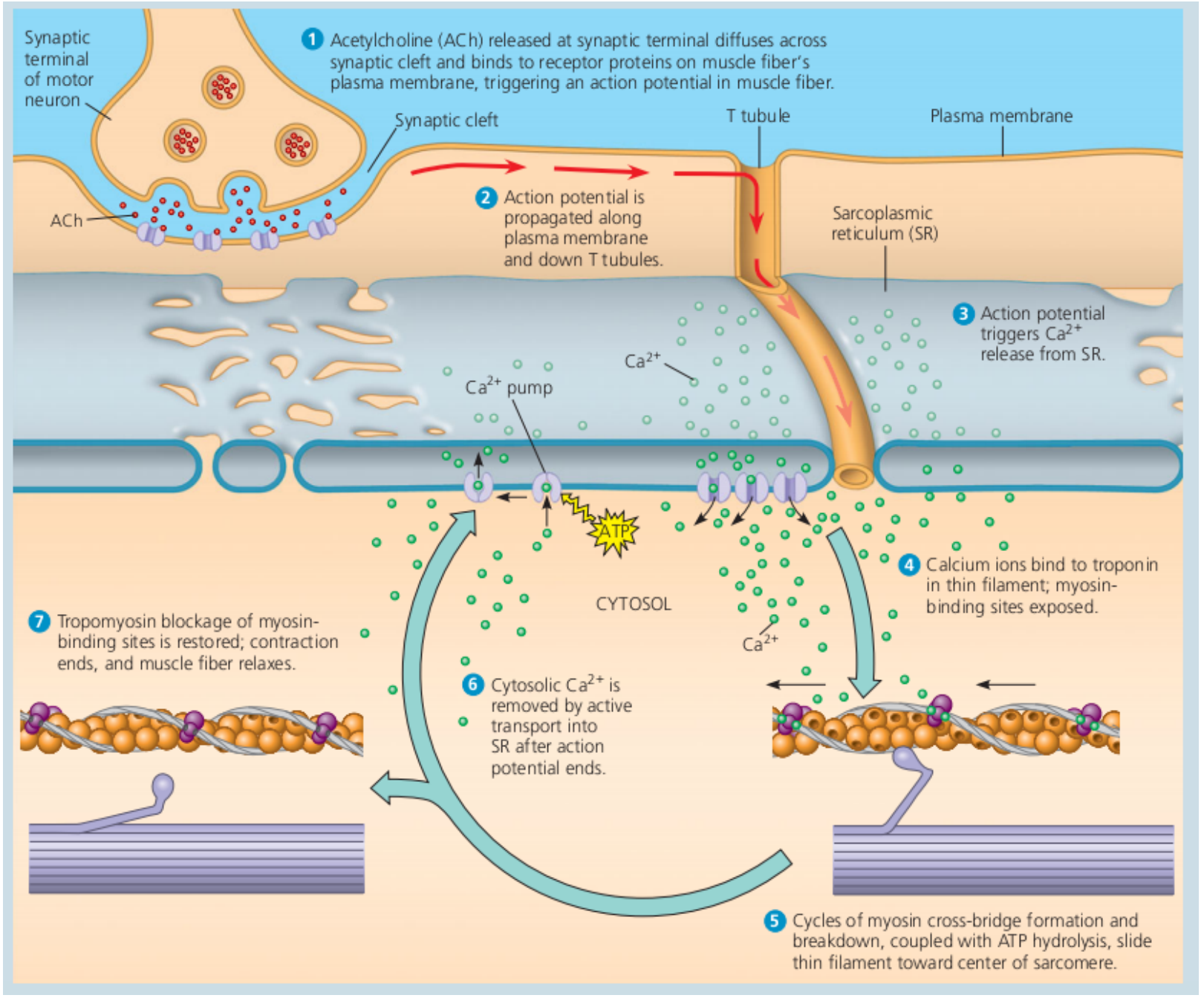


Figure 15-8 *Molecular Biology of the Cell* (© Garland Science 2008)

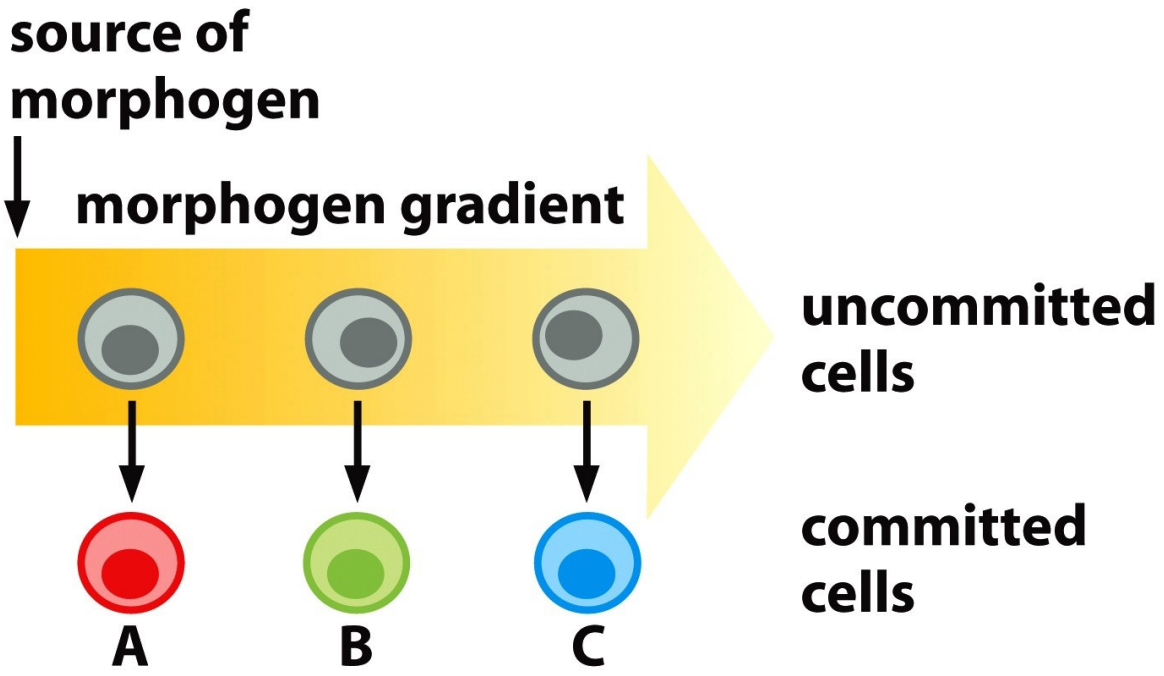


Asetilkolinin neden olduğu yanıtlar.

Figure 15-9 *Molecular Biology of the Cell* (© Garland Science 2008)

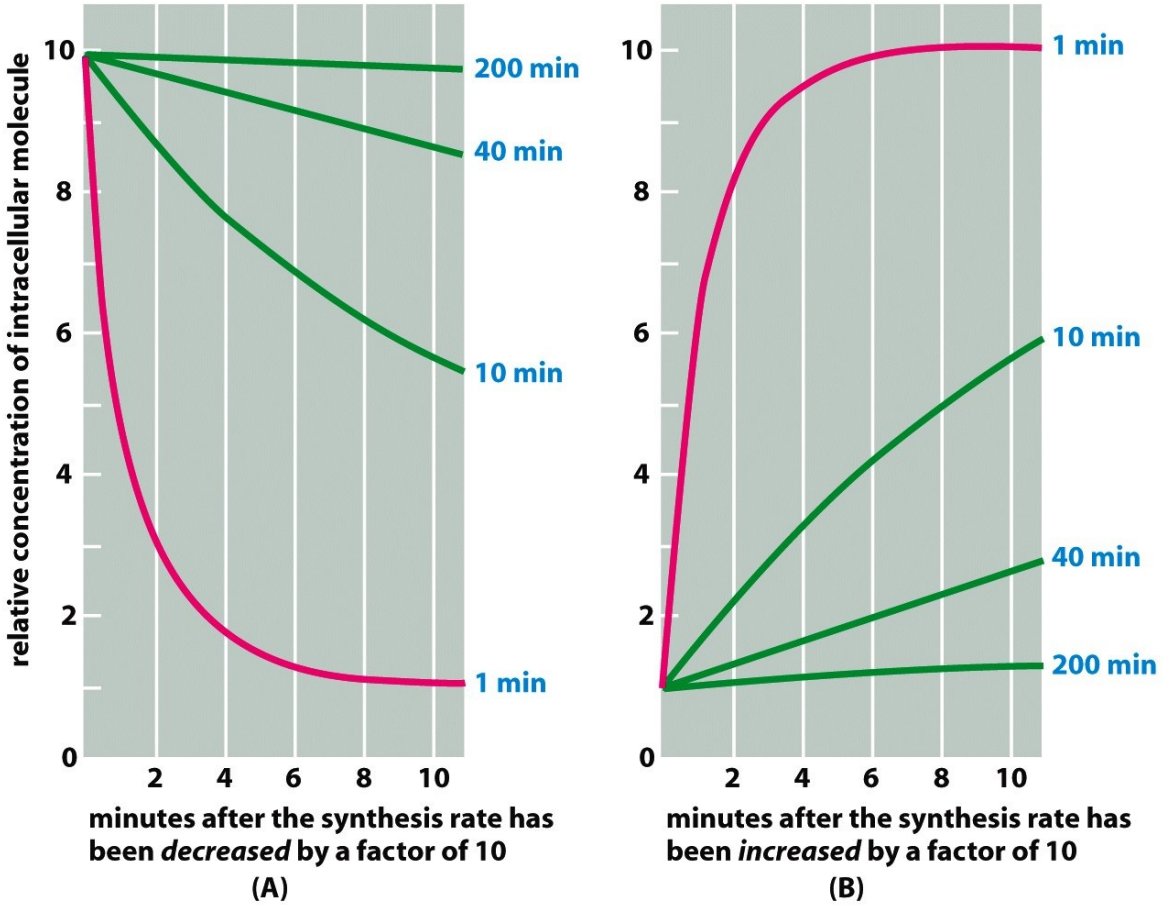


https://highered.mheducation.com/sites/9834092339/student_view0/chapter47/action_potentials_and_muscle_contraction.html



Gelişim sırasındaki değişimler kalıcıdır.

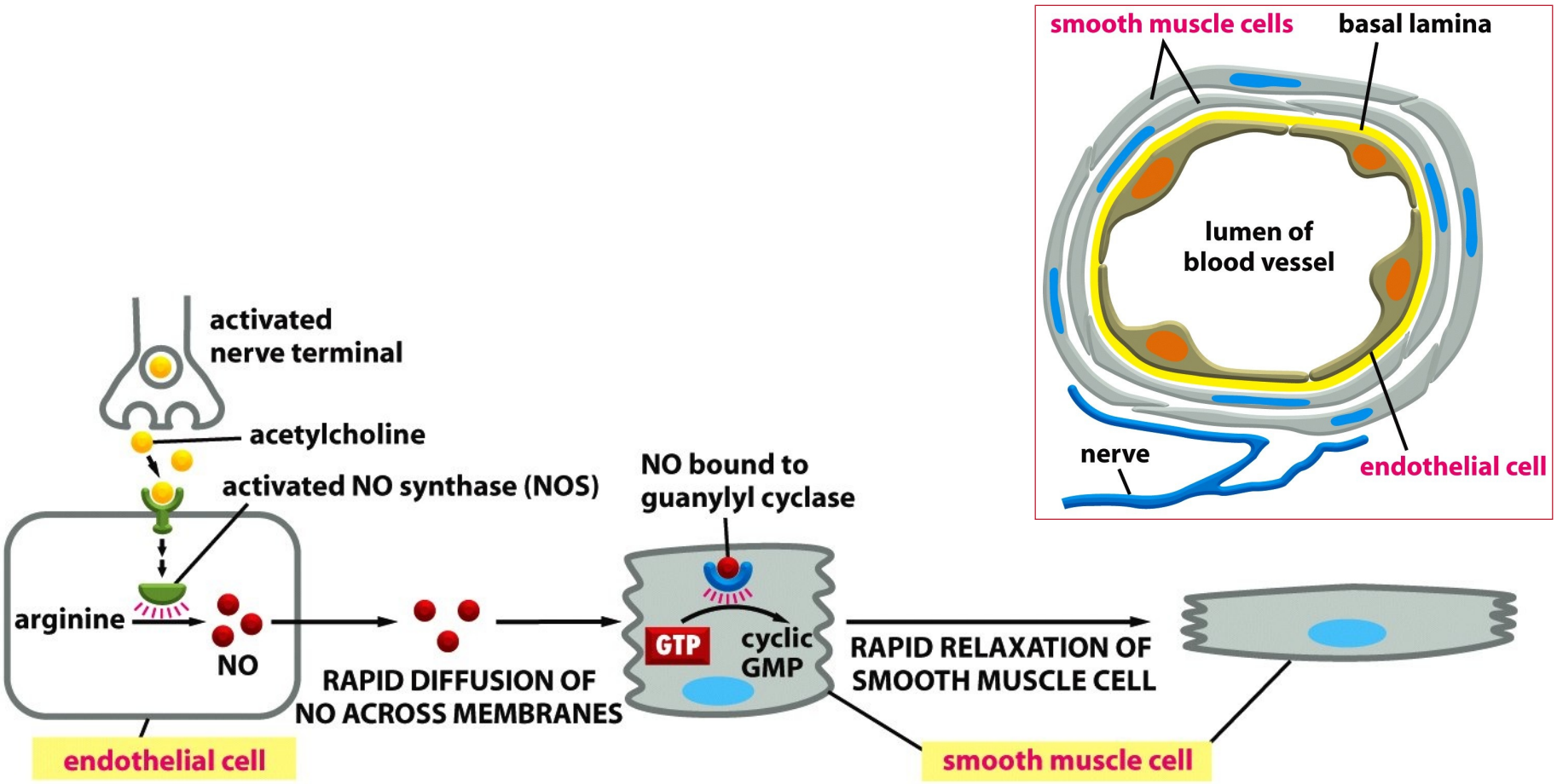
Figure 15-10 *Molecular Biology of the Cell* (© Garland Science 2008)



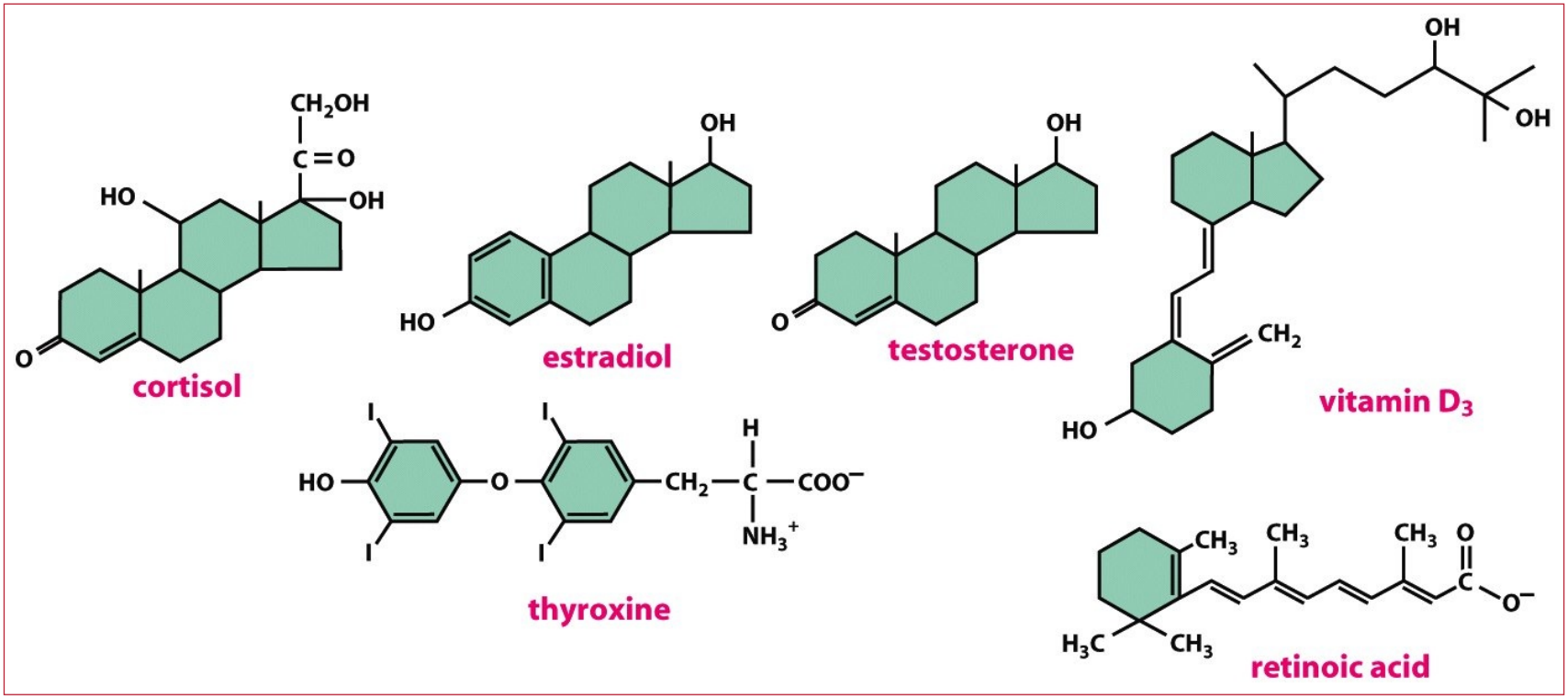
Y molekülü : 100 molekül/sn sentezleniyor/parçalanıyor
10 sn oft. ömür

X molekülü : 10 molekül/sn sentezleniyor/parçalanıyor
100 sn oft ömür.

Figure 15-11 *Molecular Biology of the Cell* (© Garland Science 2008)



NO, düz kaslara gevşeme sinyali sağlar. Anjina hastalarda 100 yıldır kullanılan nitrogliserin'in etki mekanizmasını açıklar. Nitrogliserin NO'ya çevrilerek kan damarlarını gevşetir ve kalp üzerideki iş gücünü azaltarak kalp kasının oksijen gereksinimini düşürür.



Bazı hidrofobik sinyal molekülleri plazma zarını aşarak reseptörlerine bağlanabilirler.

Figure 15-13 *Molecular Biology of the Cell* (© Garland Science 2008)

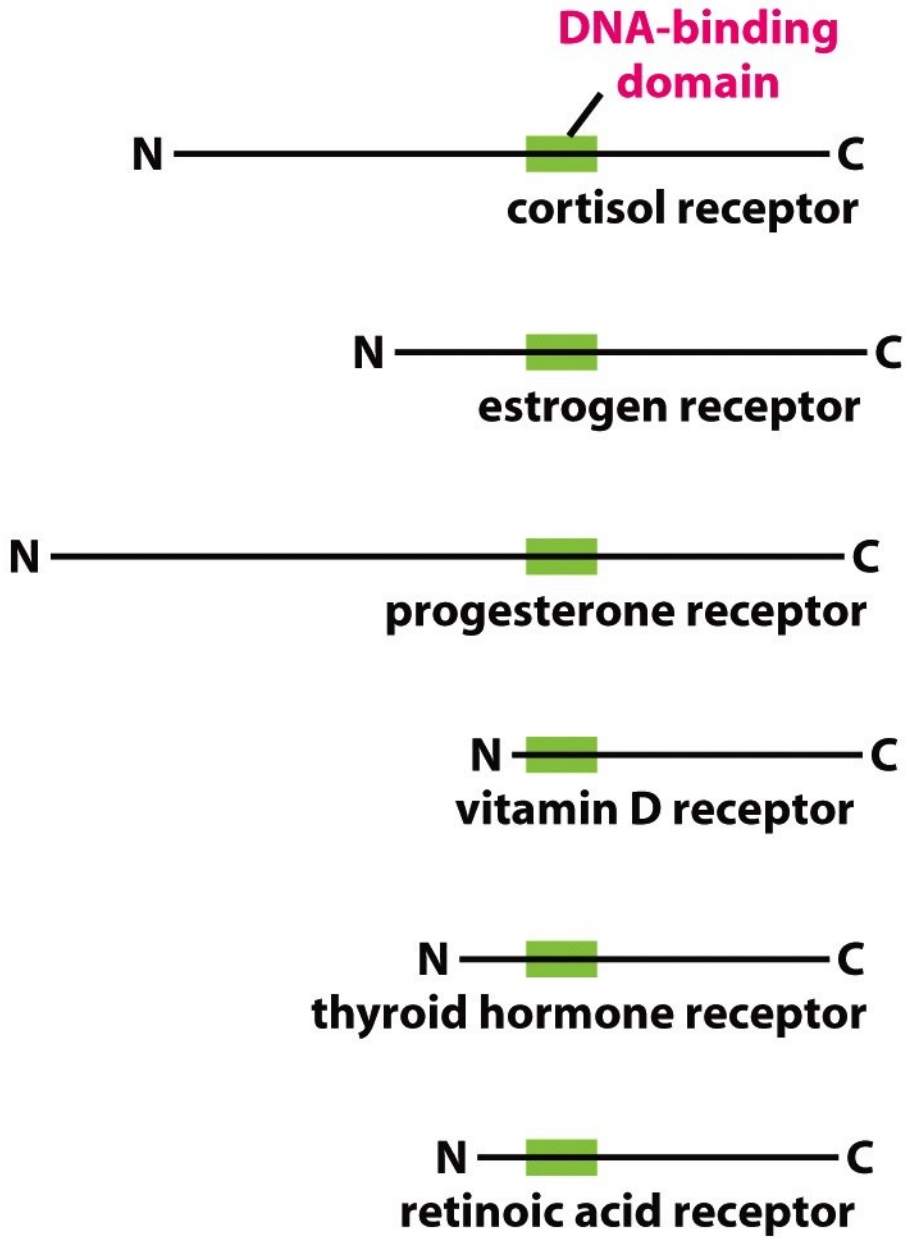
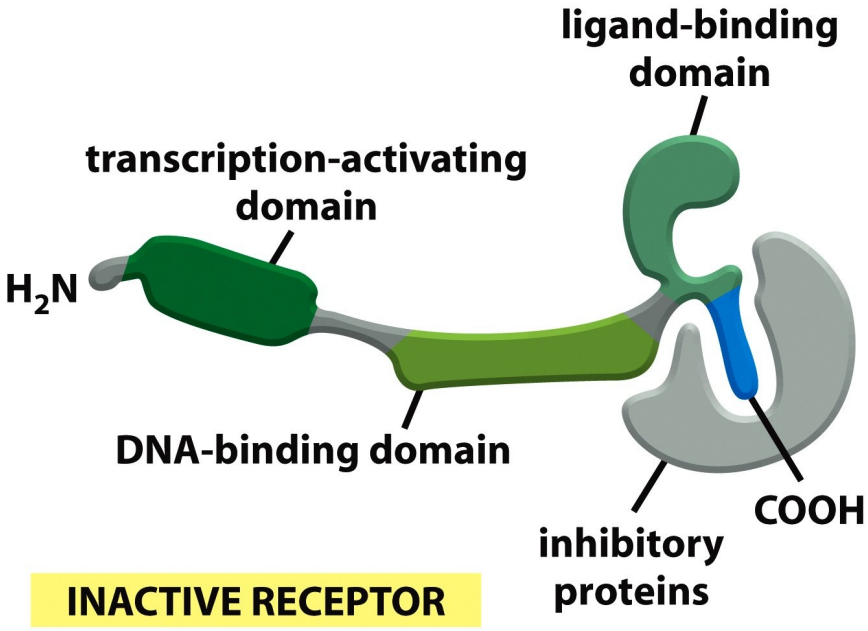
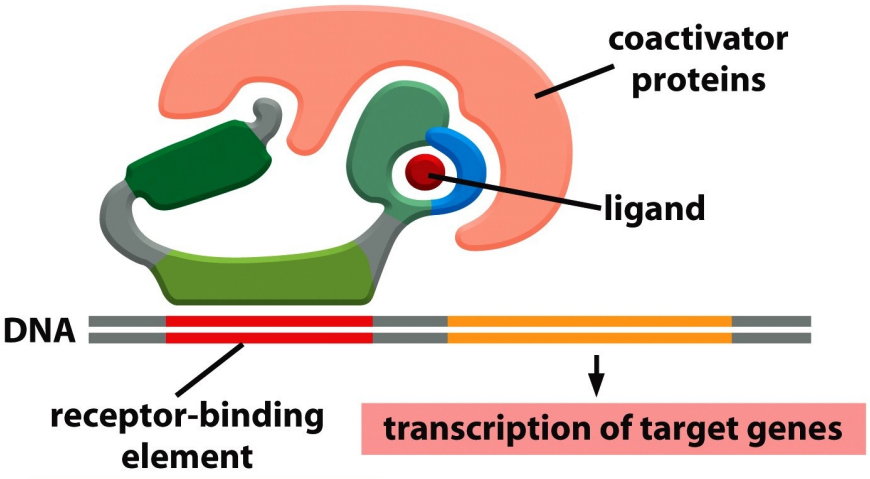
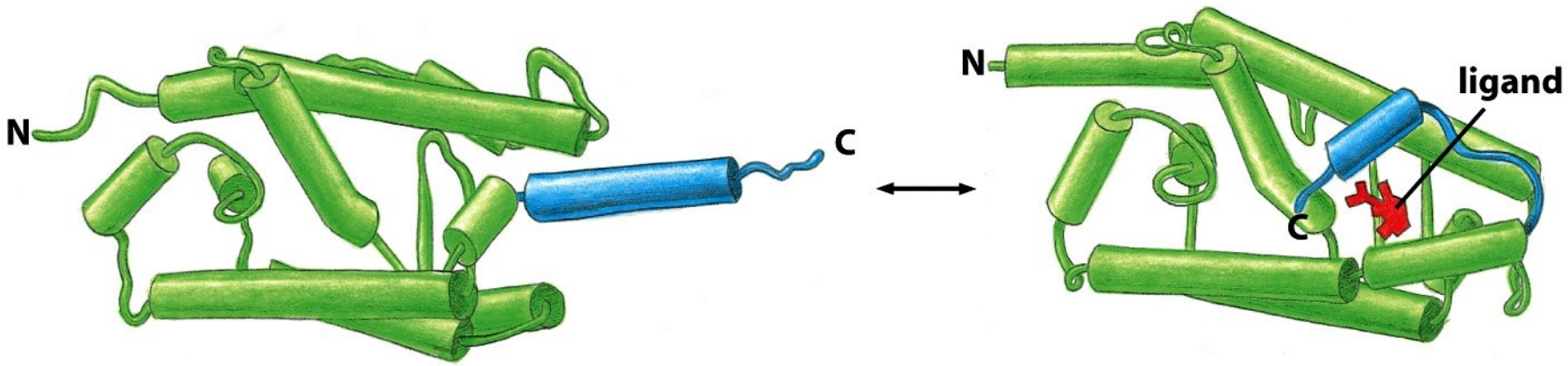


Figure 15-14a *Molecular Biology of the Cell* (© Garland Science 2008)


ligand-binding domain
transcription-activating domain
H_2N
DNA-binding domain
COOH
inhibitory proteins
INACTIVE RECEPTOR


coactivator proteins
ligand
DNA
receptor-binding element
transcription of target genes
ACTIVE RECEPTOR


N
C
N
ligand
C

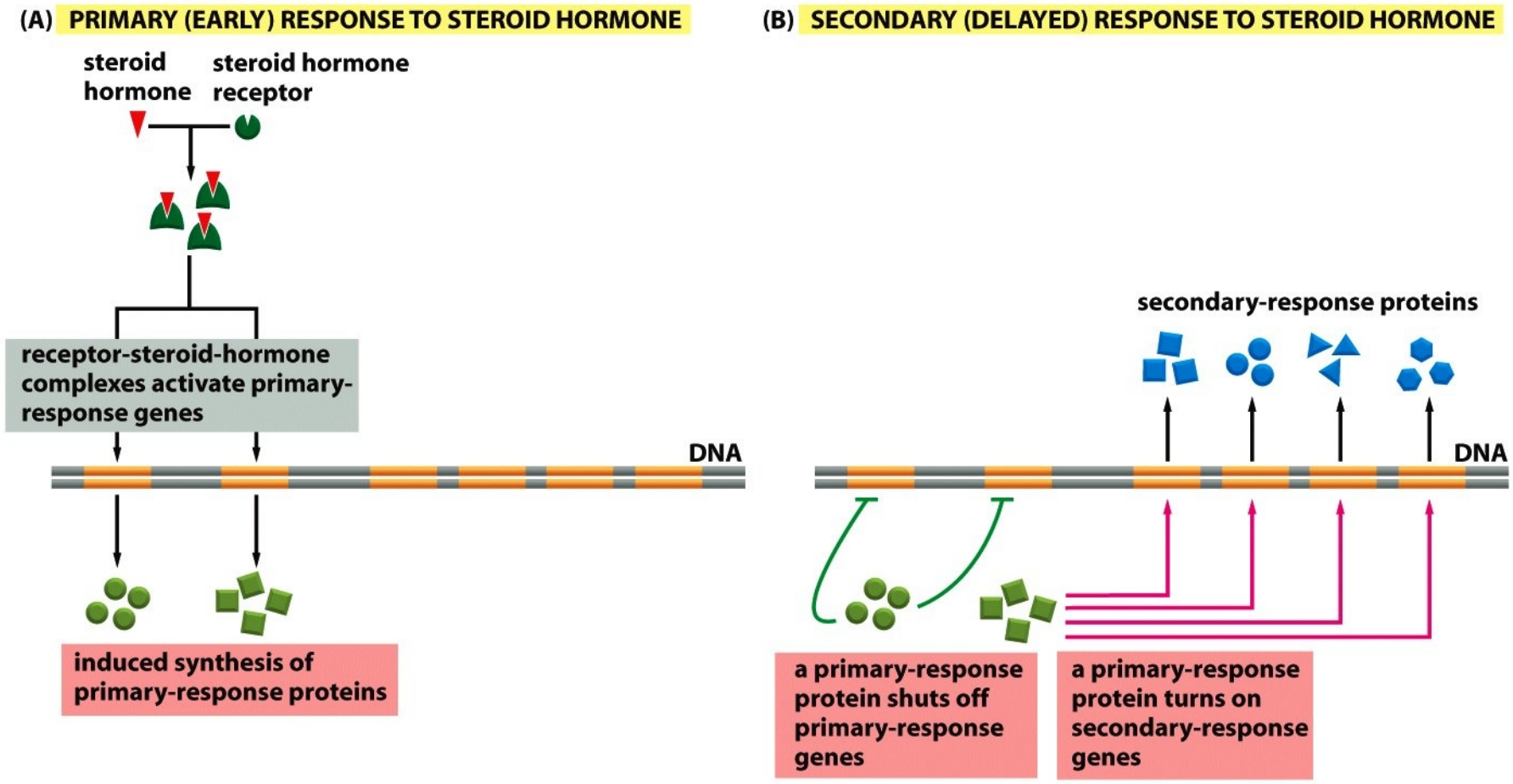
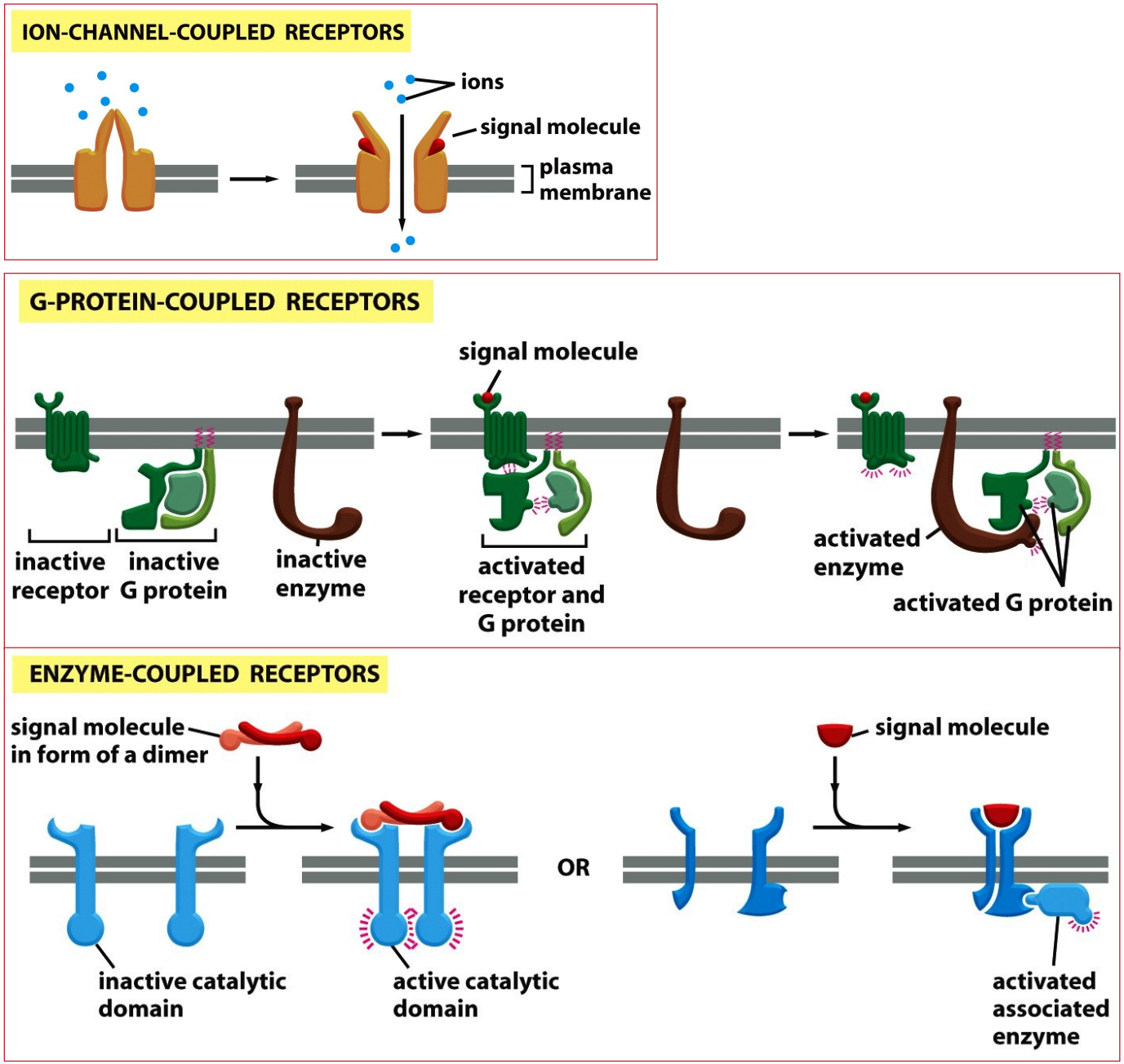
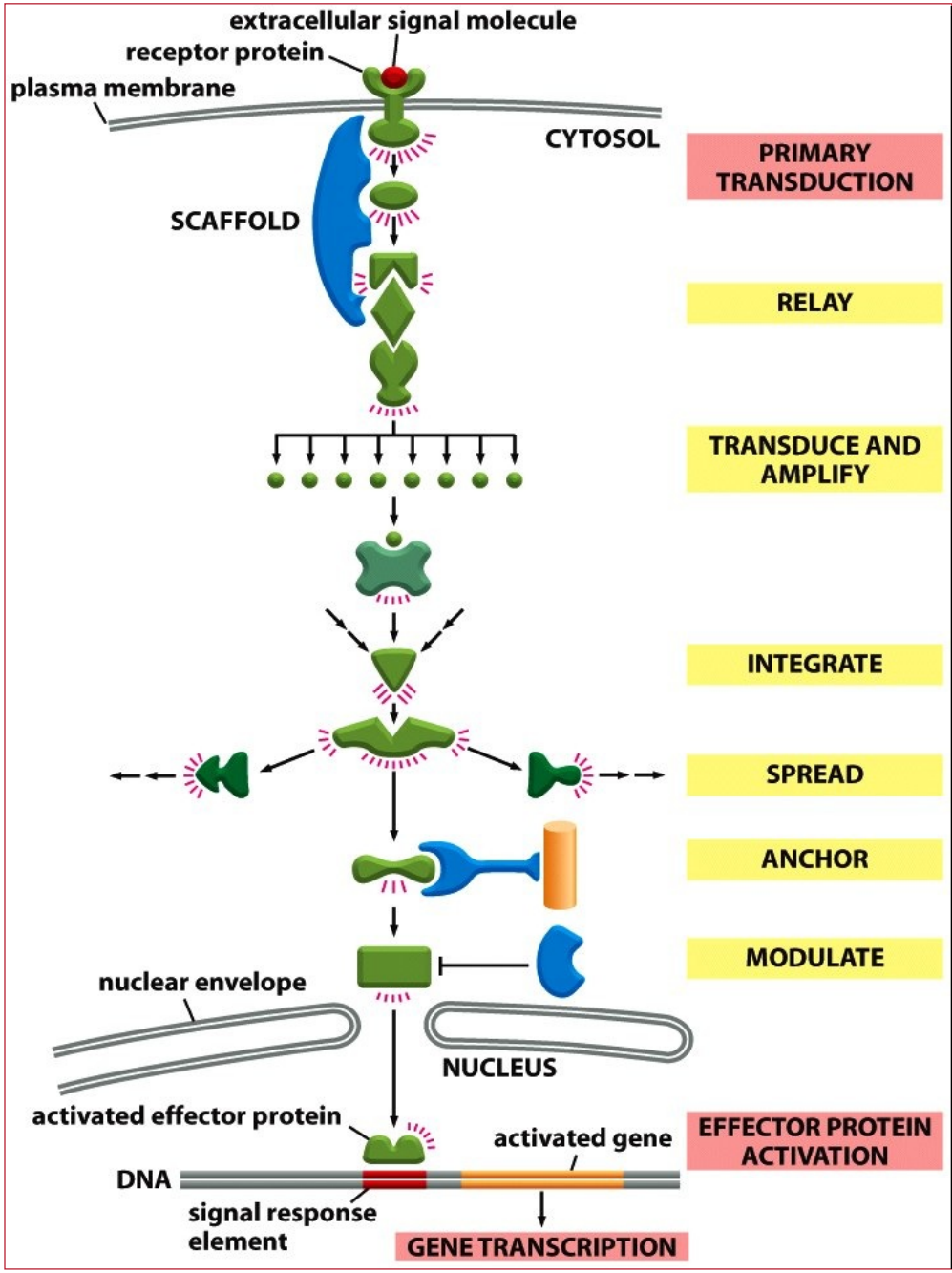


Figure 15-15 *Molecular Biology of the Cell* (© Garland Science 2008)





Küçük hücreiçi düzenleyiciler (ikincil mesajcılar)

Reseptörden gelen sinyalin hızla yayılmasını sağlarlar. cAMP ve Ca2+ suda çözünebildiklerinden sitozole. Diaçil gliserol gibi yağda çözünenler ise membrana doğru yönelir.

Hücreiçi sinyal proteinleri

İleti proteinleri:

Mesajcı proteinler:

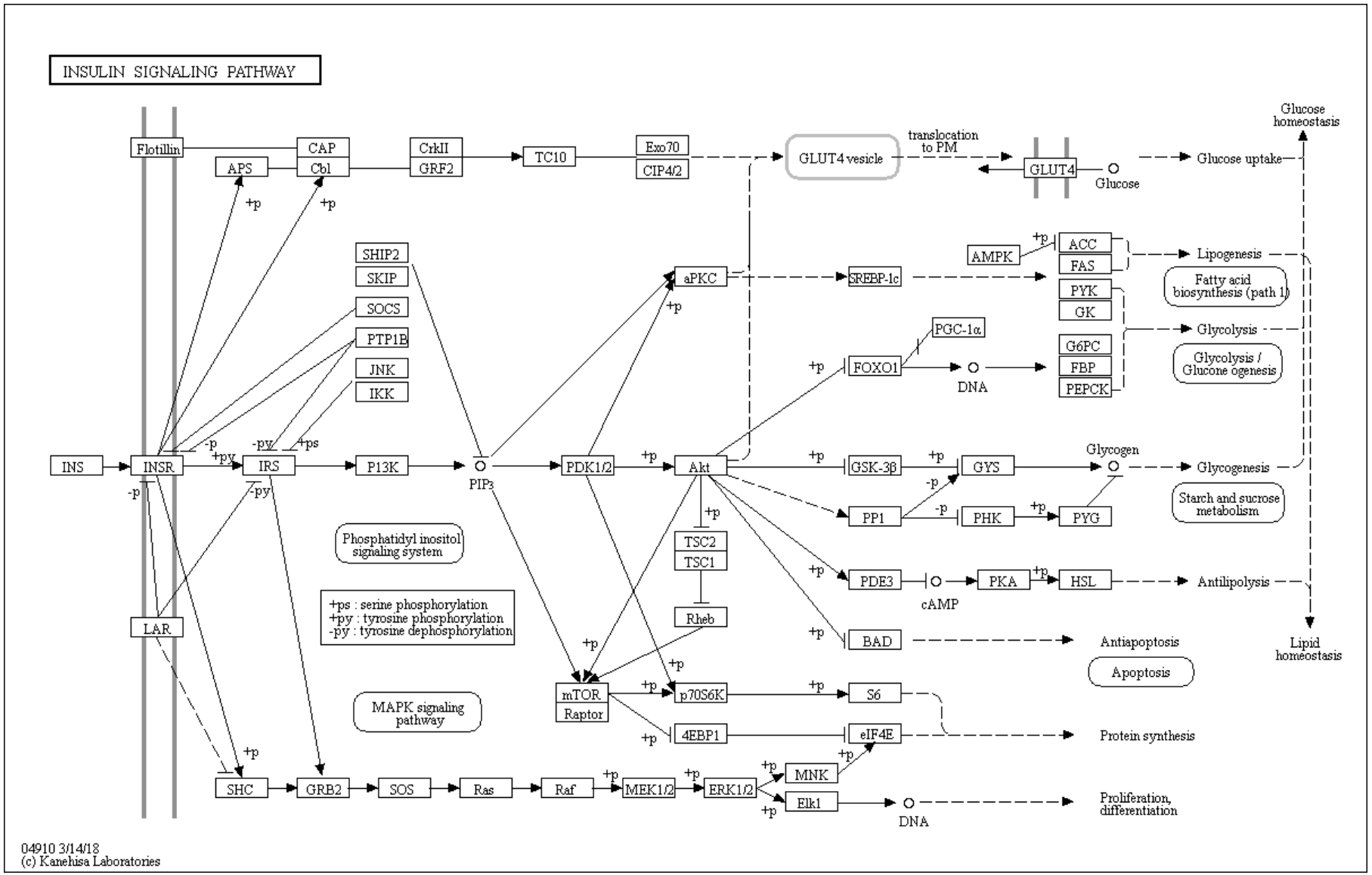
Amplifiye edici proteinler:

Dönüştürücü proteinler:

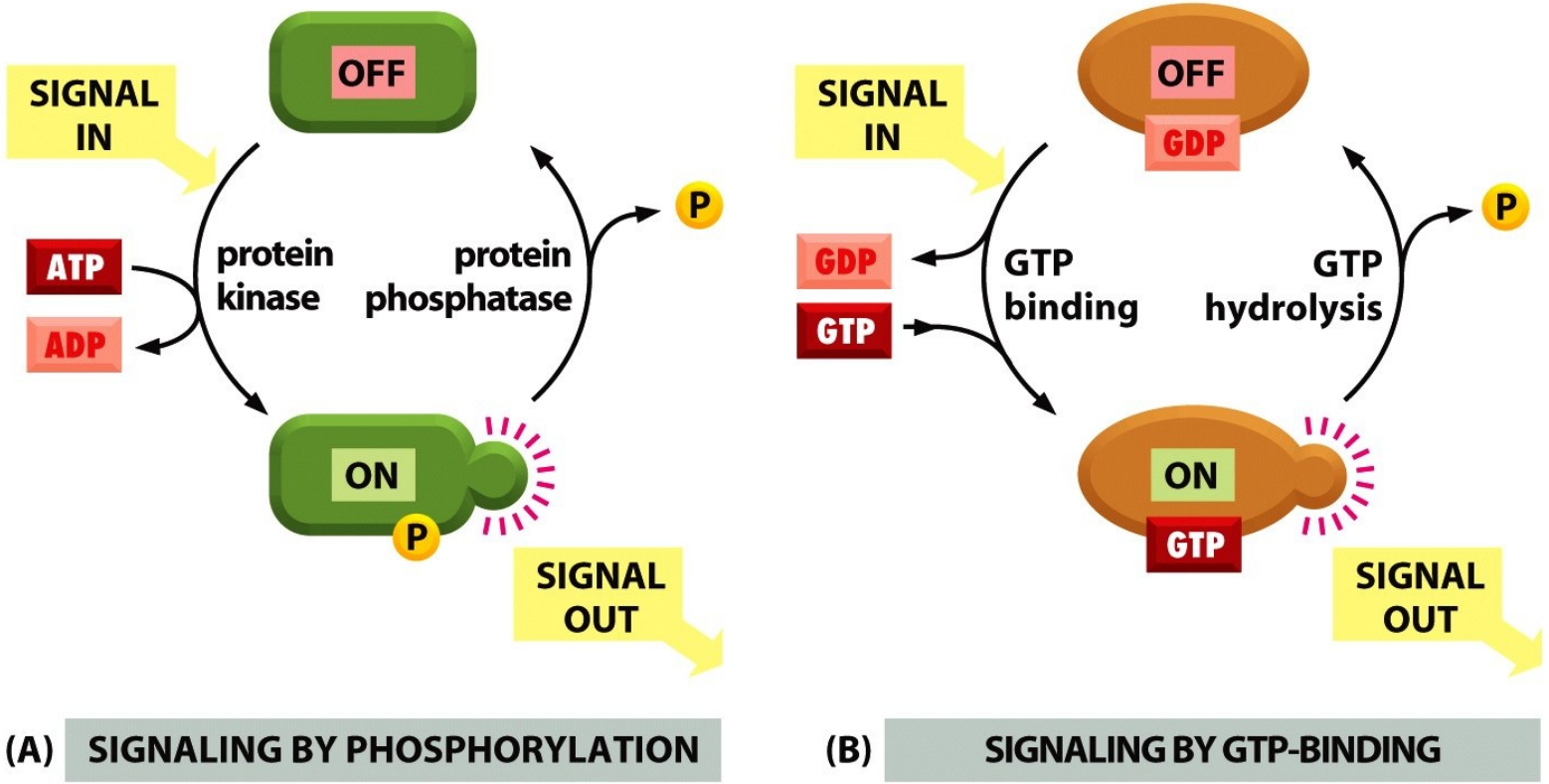
Çatallanma proteinleri:

Bütünleştirici proteinler

Genleri düzenleyen proteinler

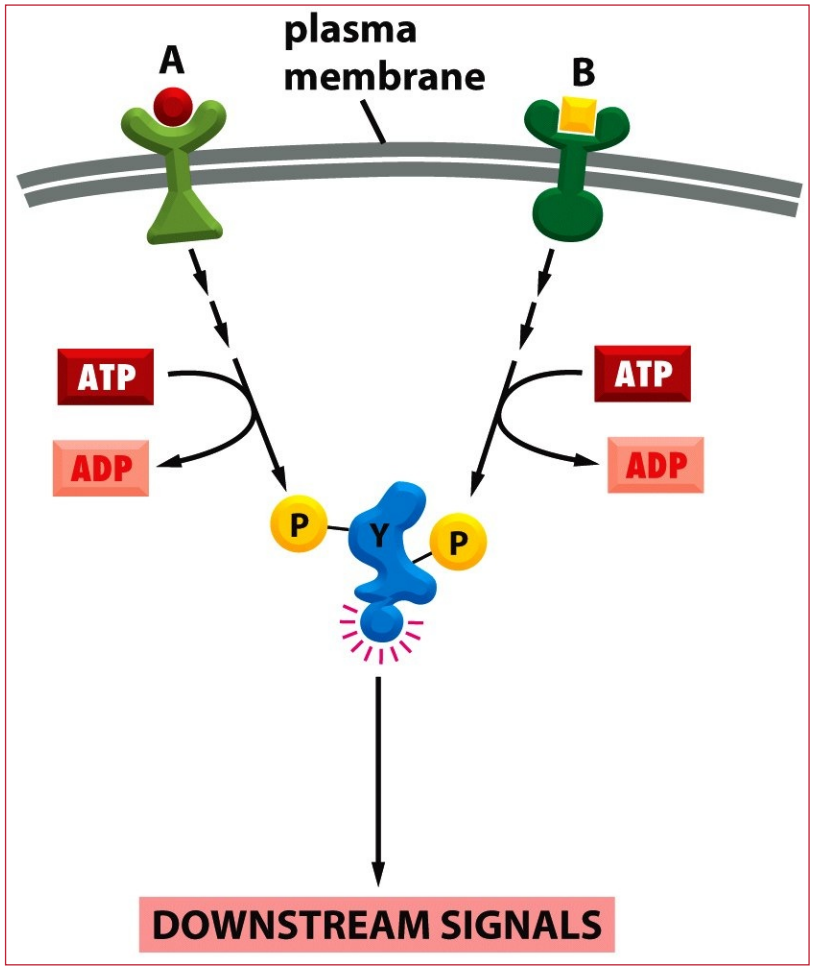

INSULIN SIGNALING PATHWAY
Flotillin
CAP
Cbl
APS
CrkII
GRF2
TC10
Exo70
CIP4/2
GLUT4 vesicle
translocation to PM
GLUT4
Glucose
Glucose uptake
Glucose homeostasis
SHIP2
SKIP
SOCS
PTP1B
JNK
IKK
aPKC
SREBP-1c
AMPK
ACC
FAS
Lipogenesis
Fatty acid biosynthesis (path 1)
PYK
GK
Glycolysis
Glycolysis / Glucone ogenesis
PGC-1α
FOXO1
DNA
G6PC
FBP
PEPCK
INS
INSR
IRS
P13K
PIP3
PDK1/2
Akt
GSK-3β
GYS
Glycogen
Glycogenesis
Starch and sucrose metabolism
PP1
PHK
PYG
TSC2
TSC1
Rheb
PDE3
cAMP
PKA
HSL
Antilipolysis
LAR
BAD
Antiapoptosis
Apoptosis
Lipid homeostasis
Phosphatidyl inositol signaling system
+ps : serine phosphorylation
+py : tyrosine phosphorylation
-py : tyrosine dephosphorylation
mTOR
Raptor
p70S6K
S6
4EBP1
eIF4E
Protein synthesis
MAPK signaling pathway
SHC
GRB2
SOS
Ras
Raf
MEK1/2
ERK1/2
MNK
Elk1
DNA
Proliferation, differentiation
04910 3/14/18
(c) Kanehisa Laboratories

KEGG



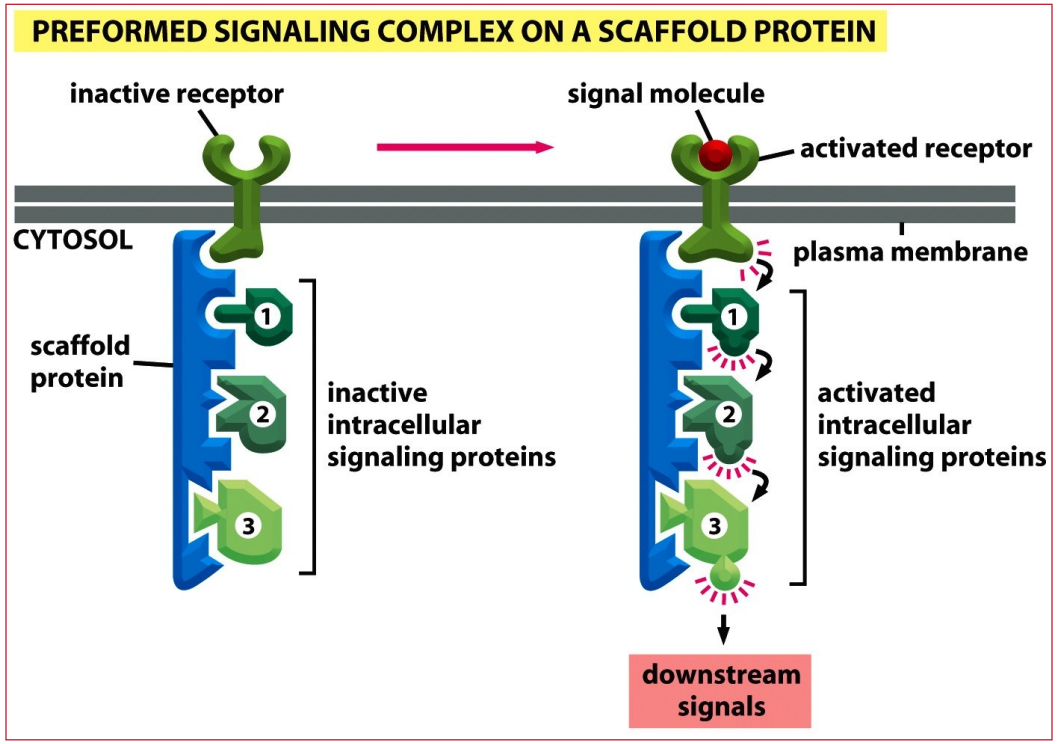
Moleküler Anahtarlar: Genellikle fosforillenme ile çalışır. Serin/Treonin kinazlar yada Tirozin kinazlarca gerçekleştirilir.

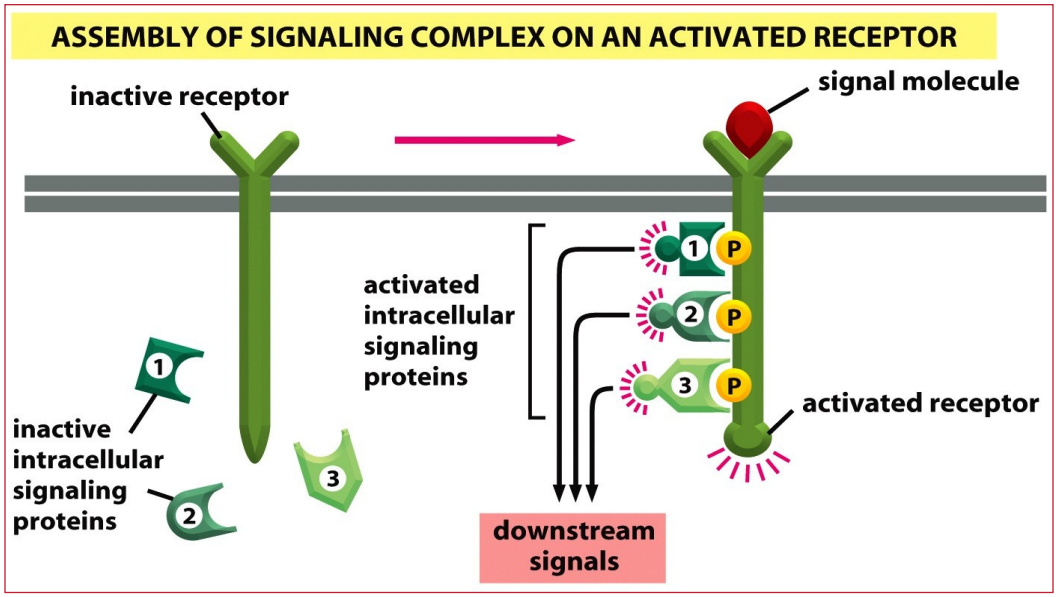
Diğer GTP Bağlayan proteinler. Hidrolaz aktivitesiyle GDP'ye dönüşüp inaktive ederler.



Farklı reseptörlerin sinyalleri bütünleşebilir.

Figure 15-20 *Molecular Biology of the Cell* (© Garland Science 2008)





Molecular Biology of the Cell (© Garland Science 2008)

İskele Proteinlerinin varlığında sinyal iletimi

Scaffold proteinlerinde ve reseptörlerde çok sayıda PDZ (postsynaptic density zone) alanlarından tutunarak etkili olurlar.

geçici

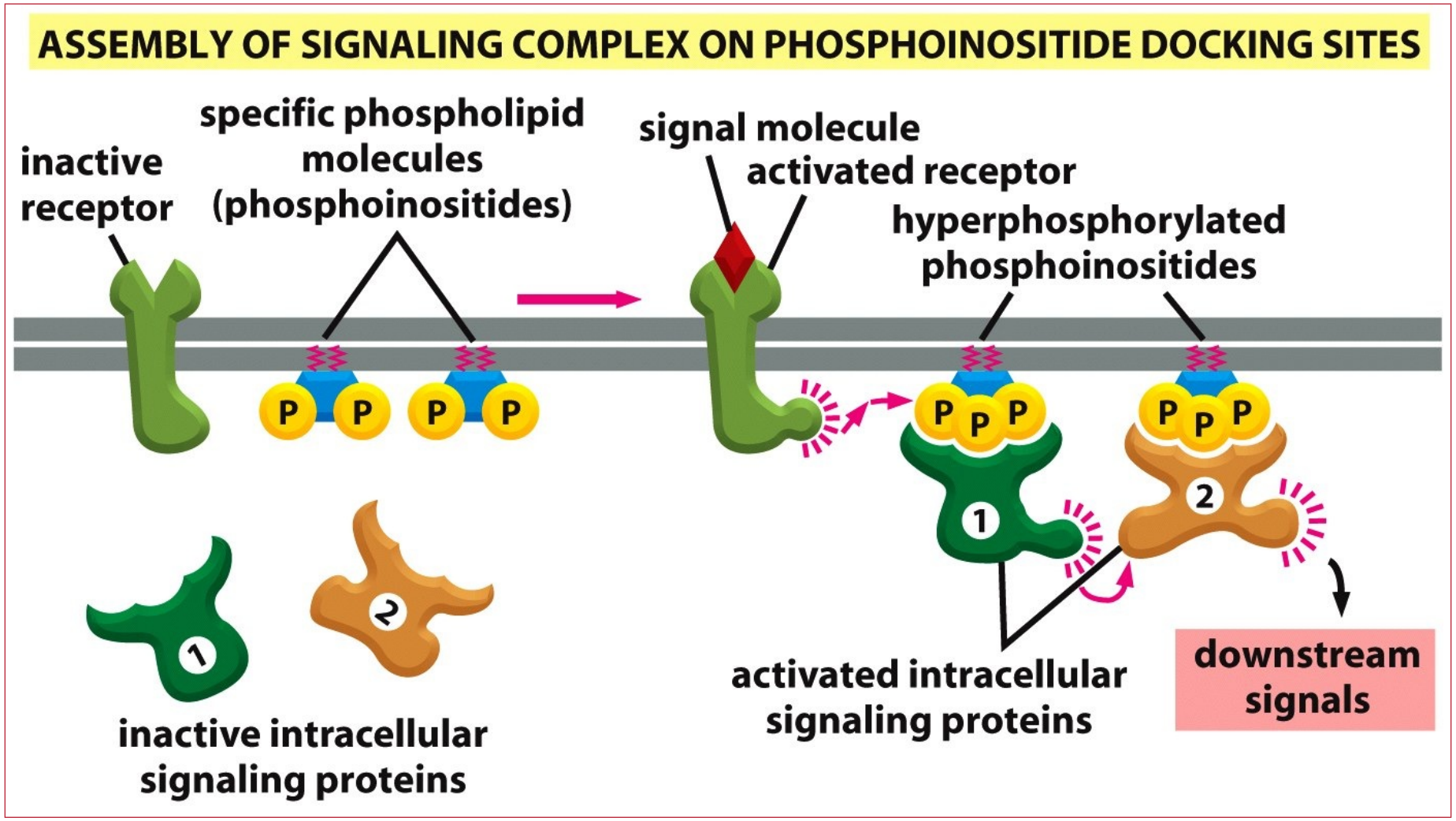
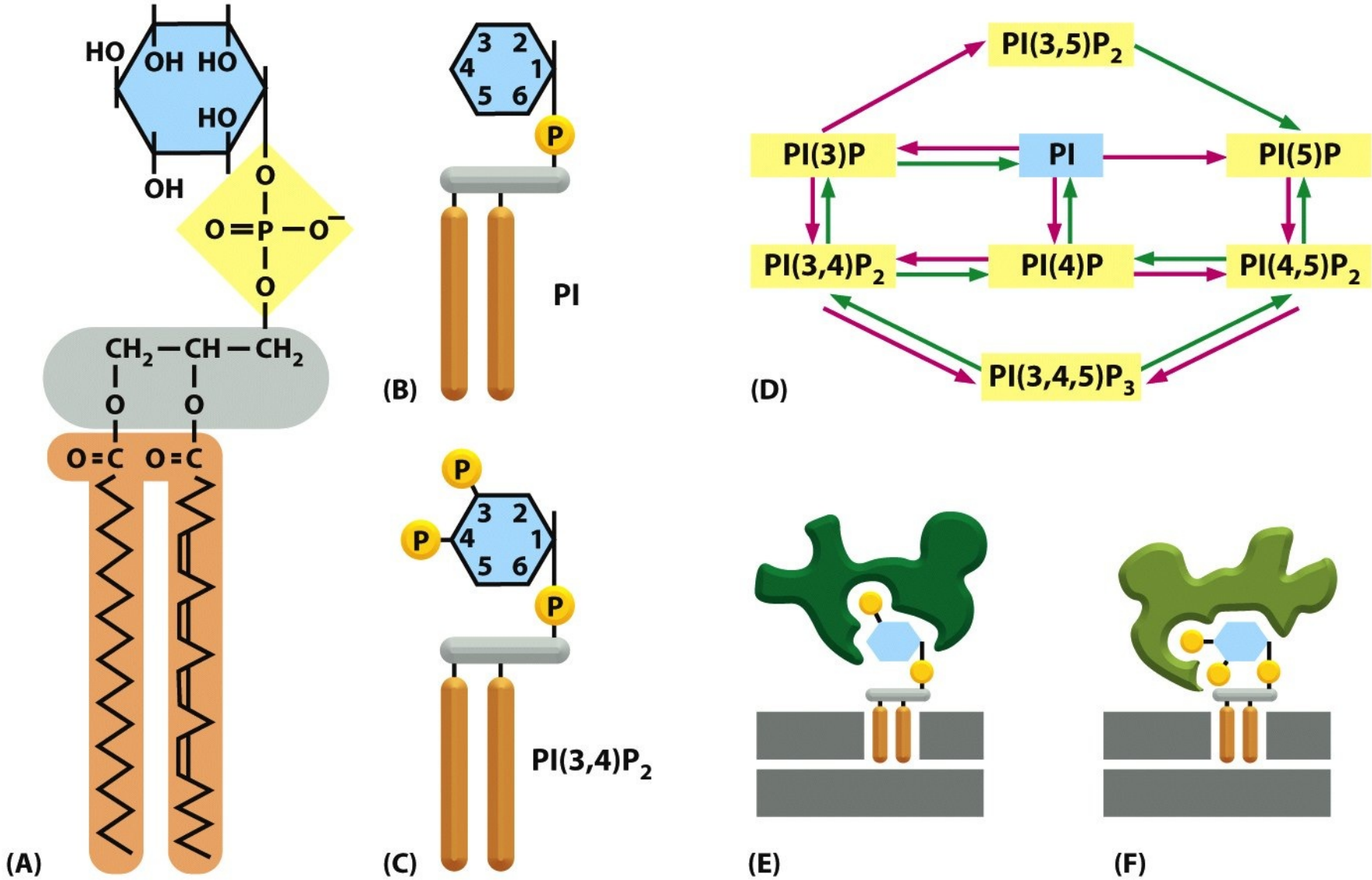
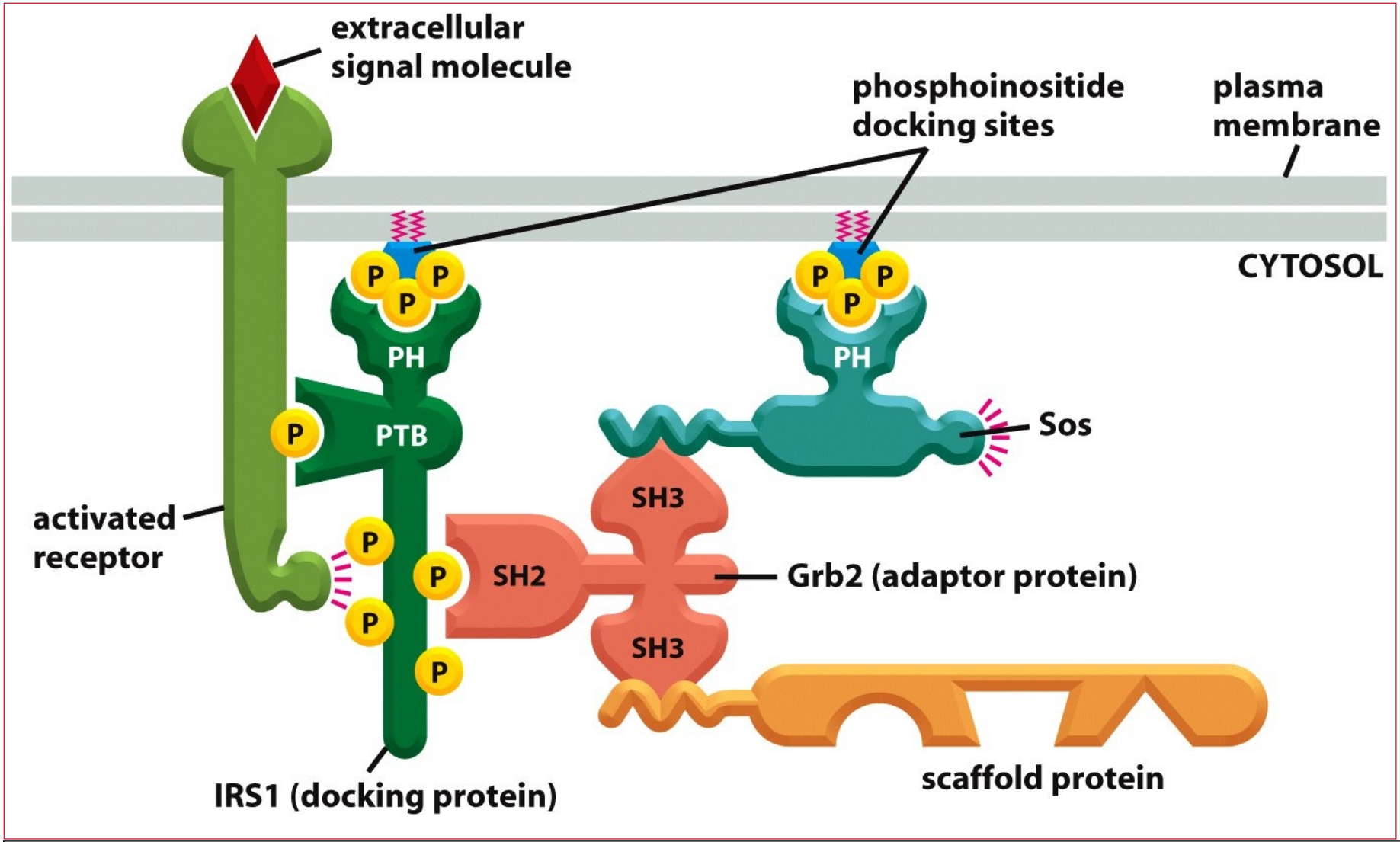


Figure 15-21c *Molecular Biology of the Cell* (© Garland Science 2008)

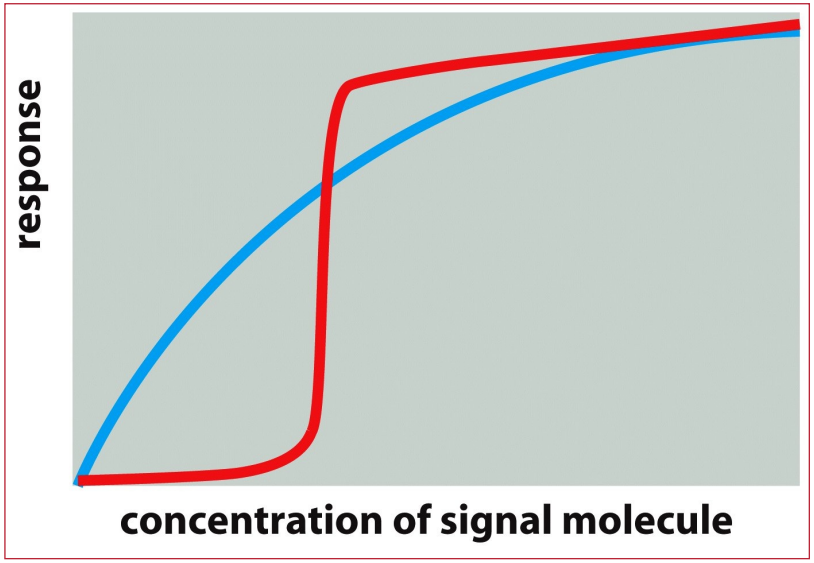




Bağlanma bölgelerinin kullanımı için özel modüler alanlar vardır. SH2 (Src2) ve PTB (Phosphotyrosine Binding domain) alanları genellikle fosforlanma için kullanılır.

Src homology 3 domain'i (SH3) kısa ve prolince zengin amino asit dizilerine bağlanır.

Pleckstrin homology domain'i (PH) ise Fosfoinositol fosfolipidlerinin yüklü başkısımlarına bağlanır.



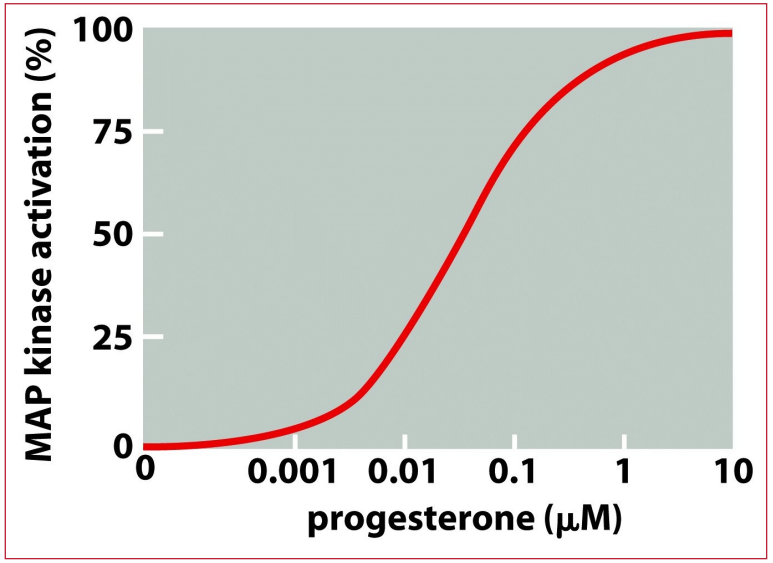


Figure 15-23 *Molecular Biology of the Cell* (© Garland Science 2008)

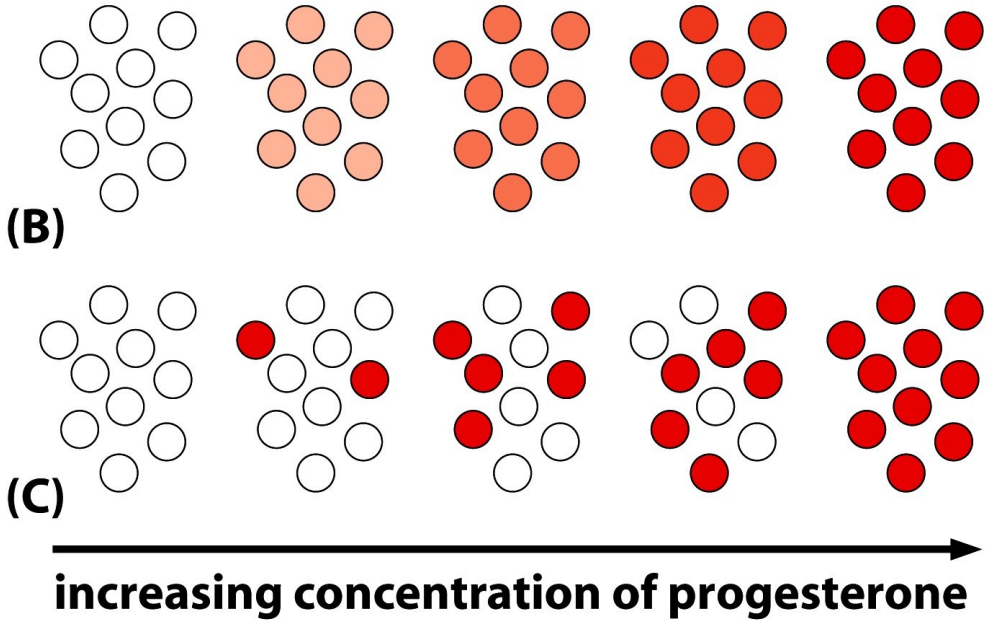


Figure 15-24b, c *Molecular Biology of the Cell* (© Garland Science 2008)

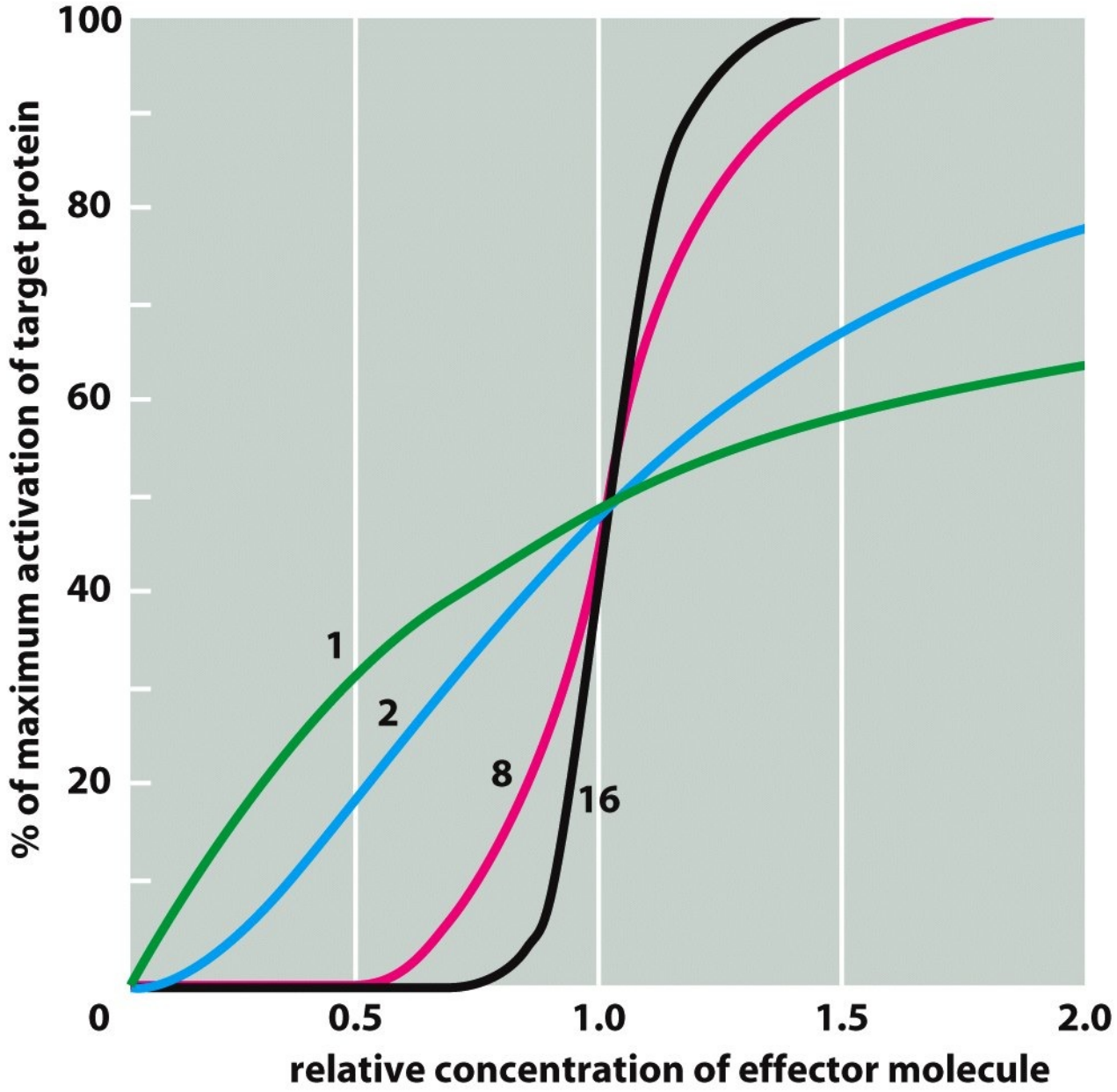


Figure 15-25 *Molecular Biology of the Cell* (© Garland Science 2008)

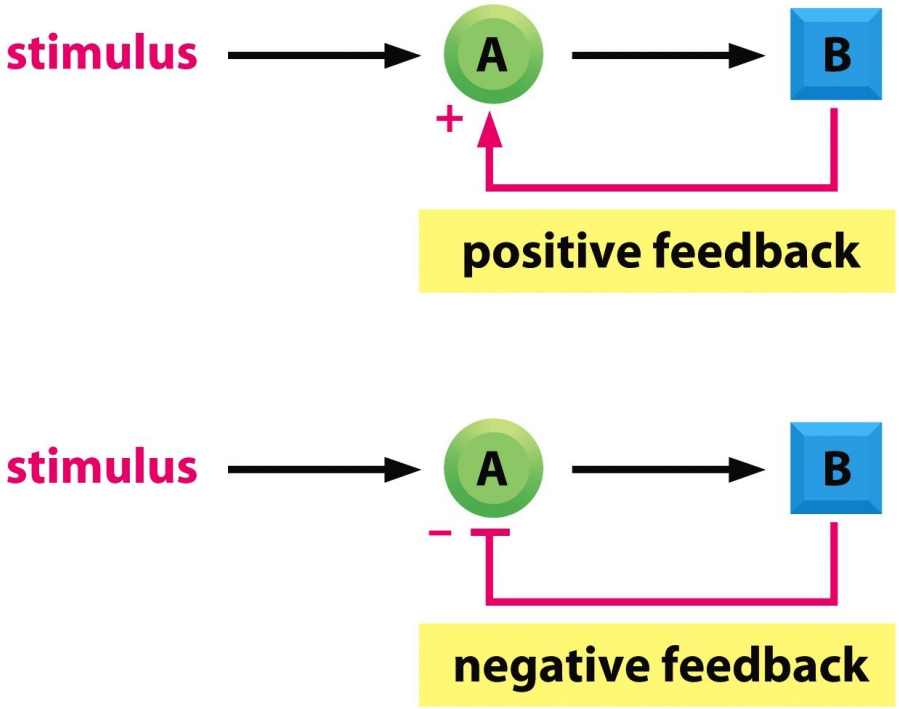


Figure 15-26 *Molecular Biology of the Cell* (© Garland Science 2008)

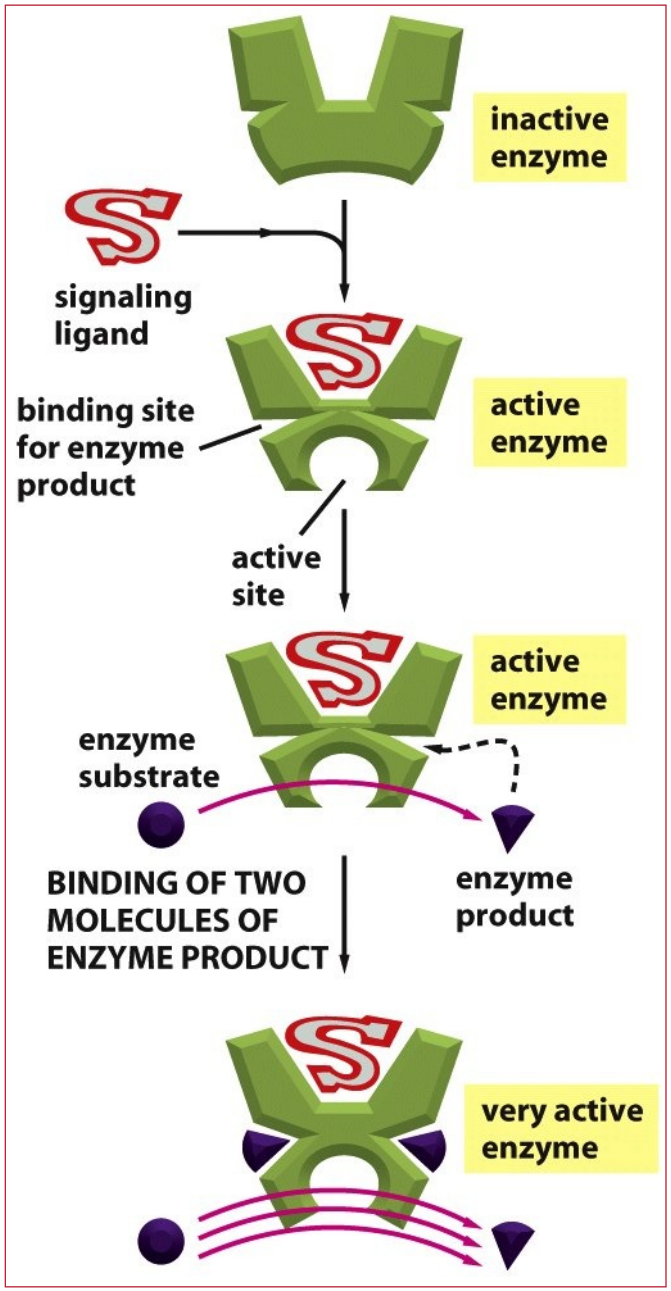


Figure 15-27 *Molecular Biology of the Cell* (© Garland Science 2008)

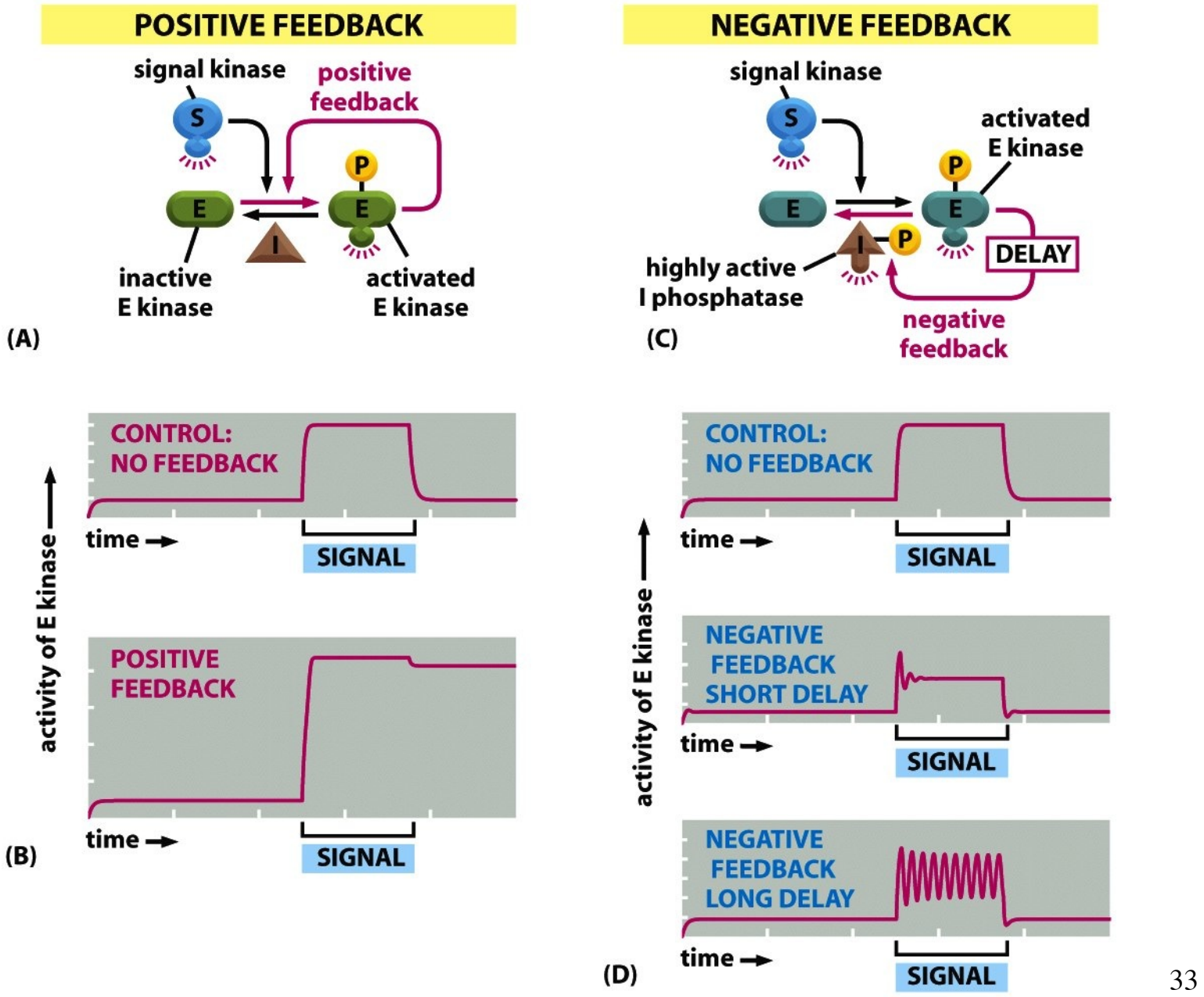
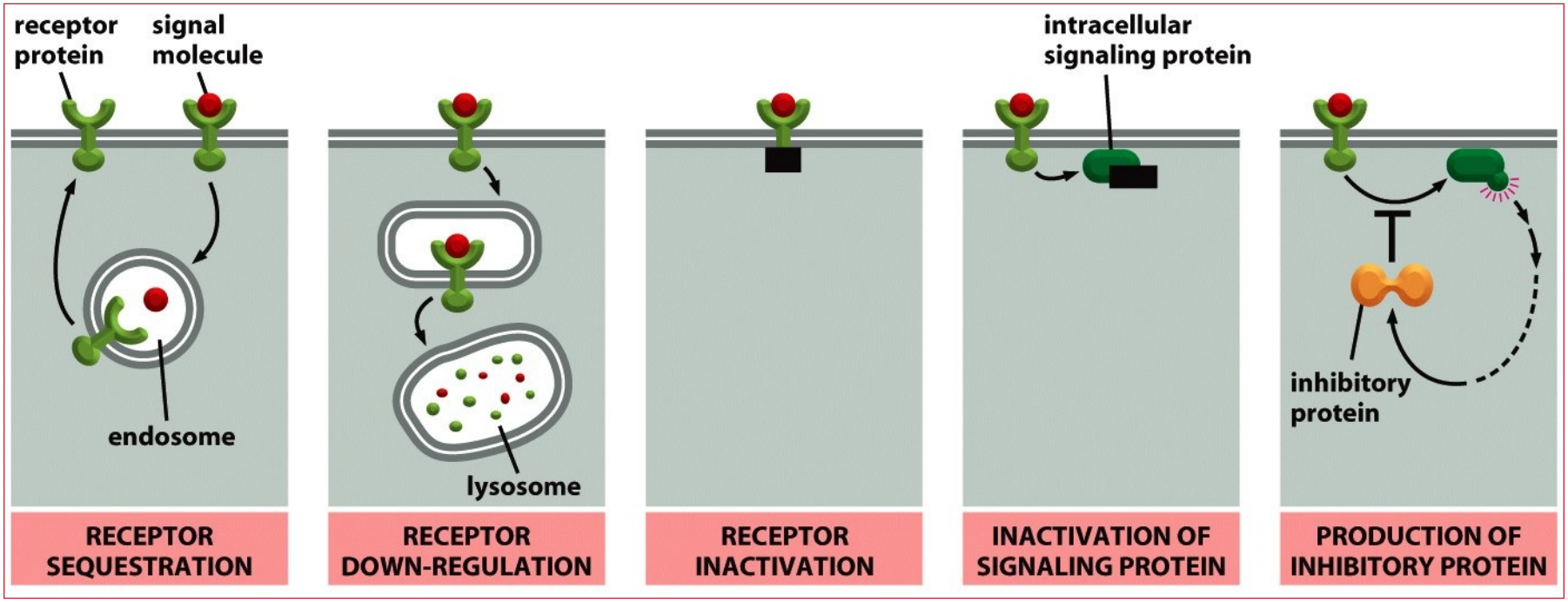
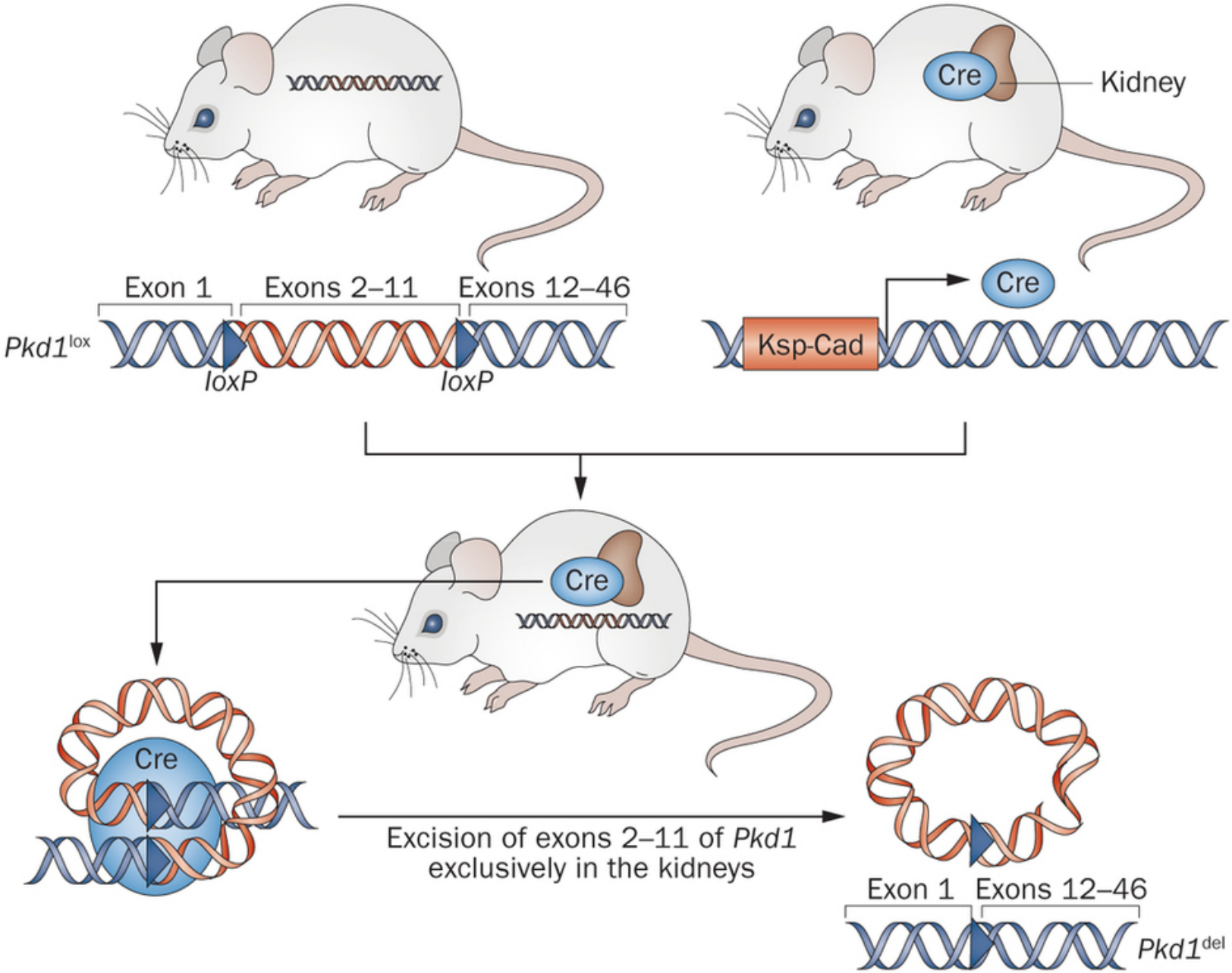


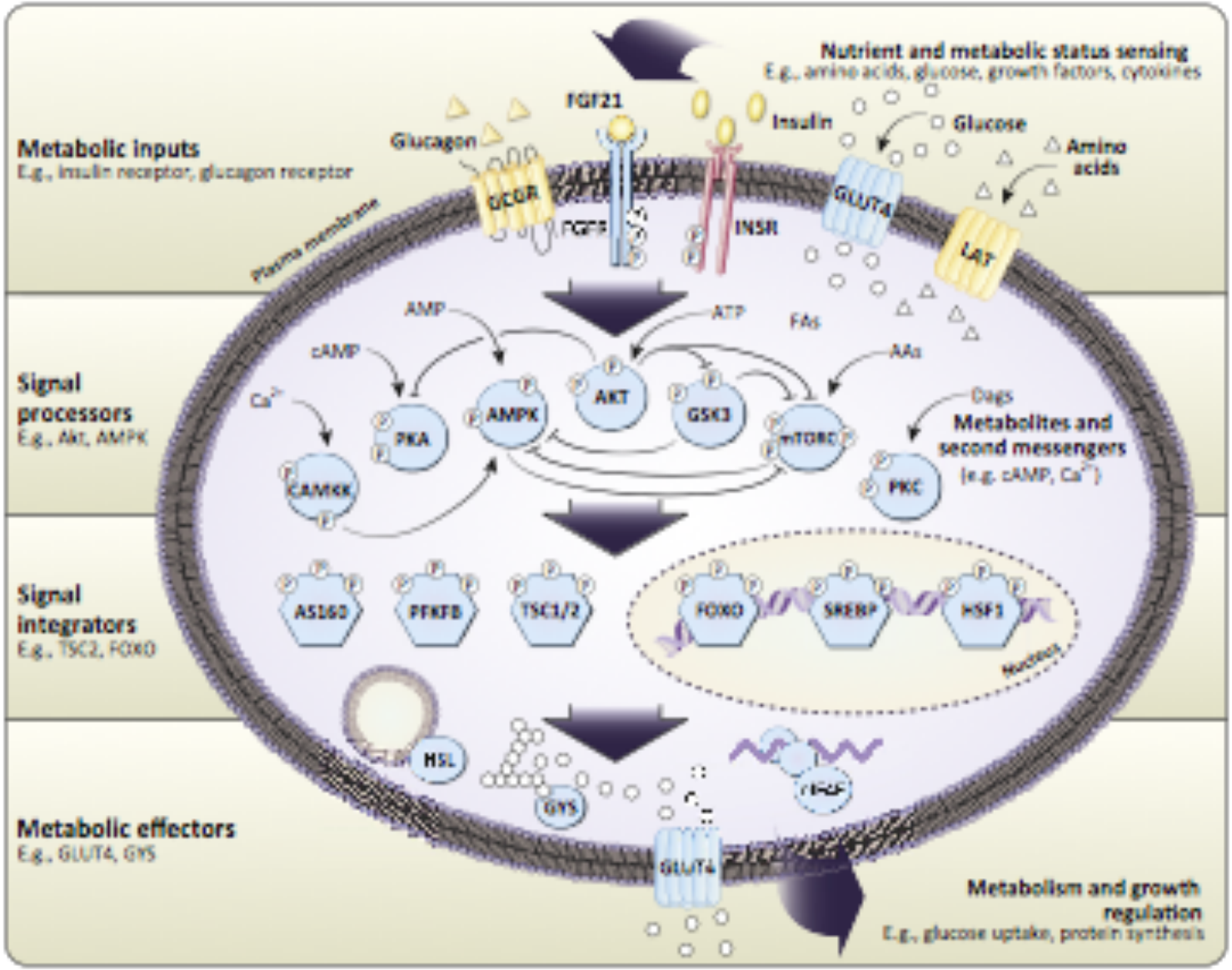
Figure 15-28 *Molecular Biology of the Cell* (© Garland Science 2008)



Uyum ve Duyarsızlaşma arasındaki dengenin korunması !!!



nrneph.2014.137



Trends Endocrinol Metab. 2015 Dec;26(12):676-87

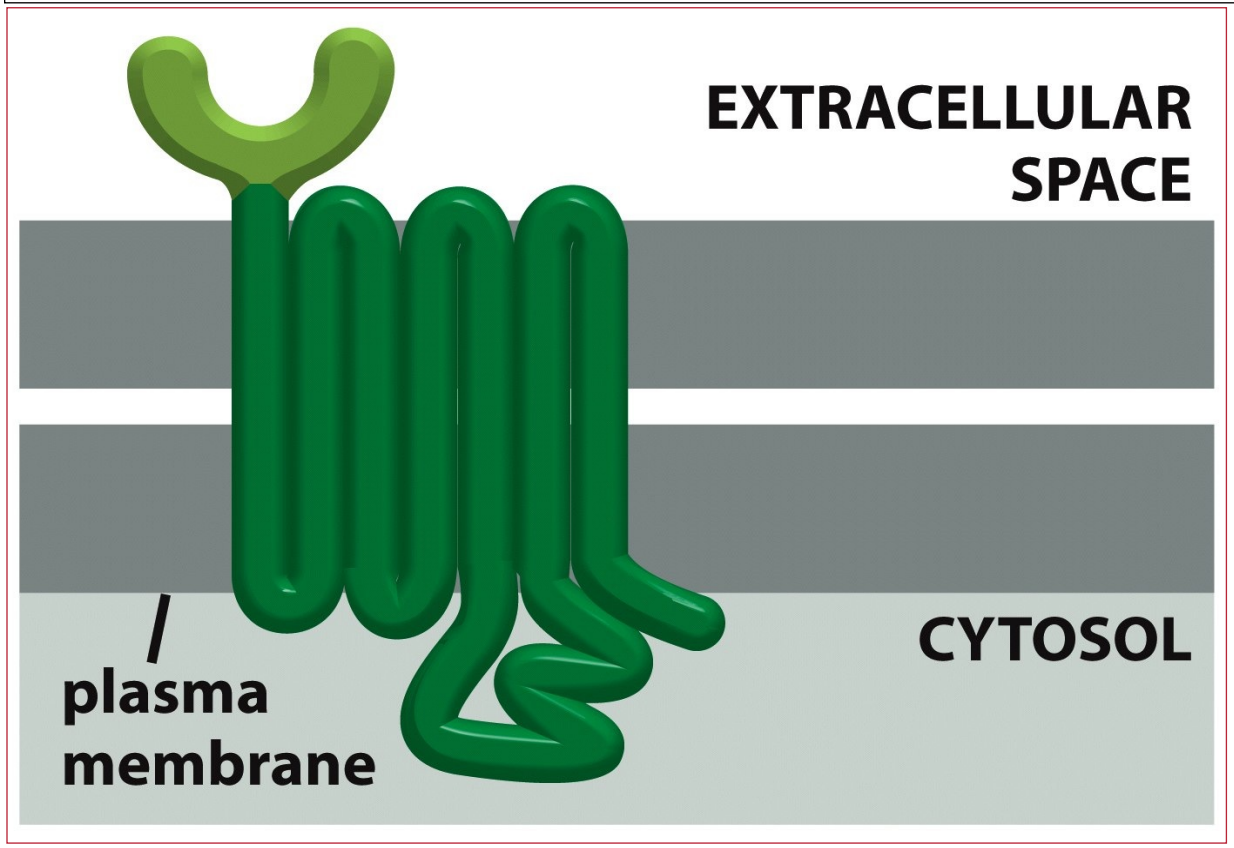
G Protein Bağlı Reseptörlerle Sinyal iletimi

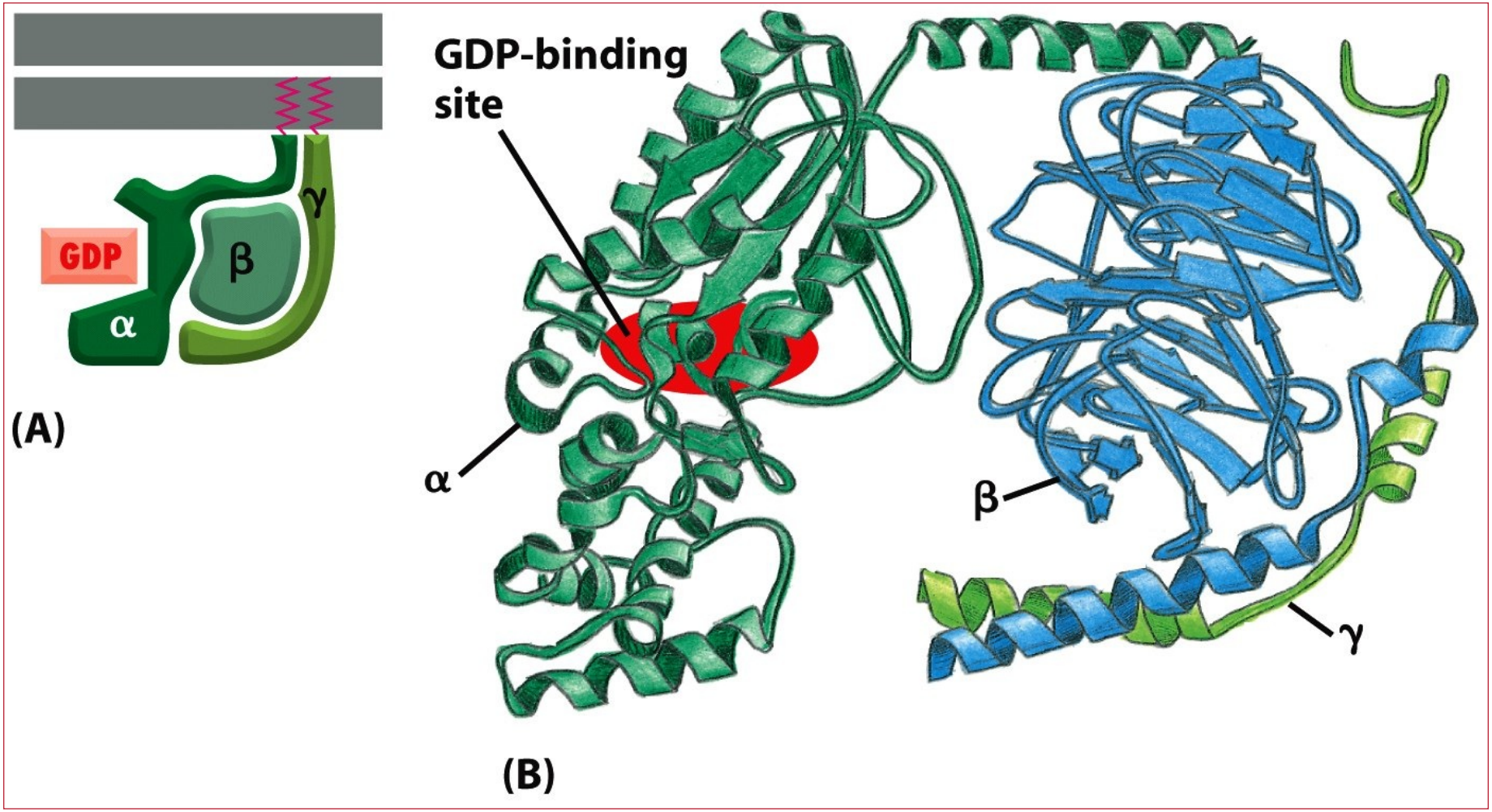
Bütün ökaryotlarda bulunur ve en geniş yüzey reseptör ailesidir. Çeşitleri tam olarak bilinmemektedir. Farede sadece koku almak için 1000 tane bulunduğu bilinmektedir.

Hormonlar, nörotransmitterler, bölgesel aracılar gibi çeşitli sinyal molekülüne cevap cevap sağlarlar. Değişik protein ve peptidler, amino asitler, yağ asitleri bunları etkinleştiren sinyal moleküllerdir.

yaklaşık 9 tane adrenalinle, 5'den fazlası asetilkolinle, 15'den fazlası da serotoninle aktifleşebilir.

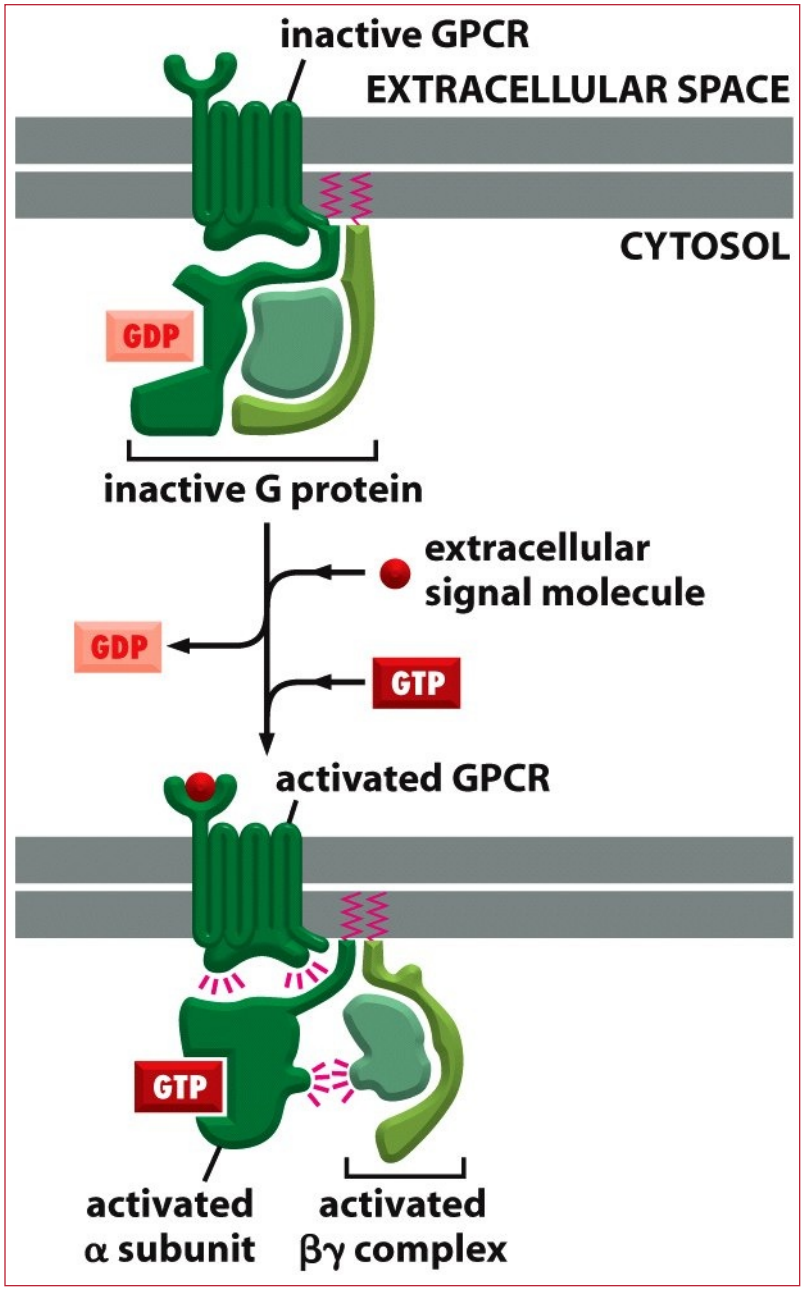
7 transmembran alan içerirler, İlaçların yarısı G-prot bağlı reseptörler üzerinden etkisini gösterir.





Uyarılmamış halinde alfa'ya GDP bağlıdır.

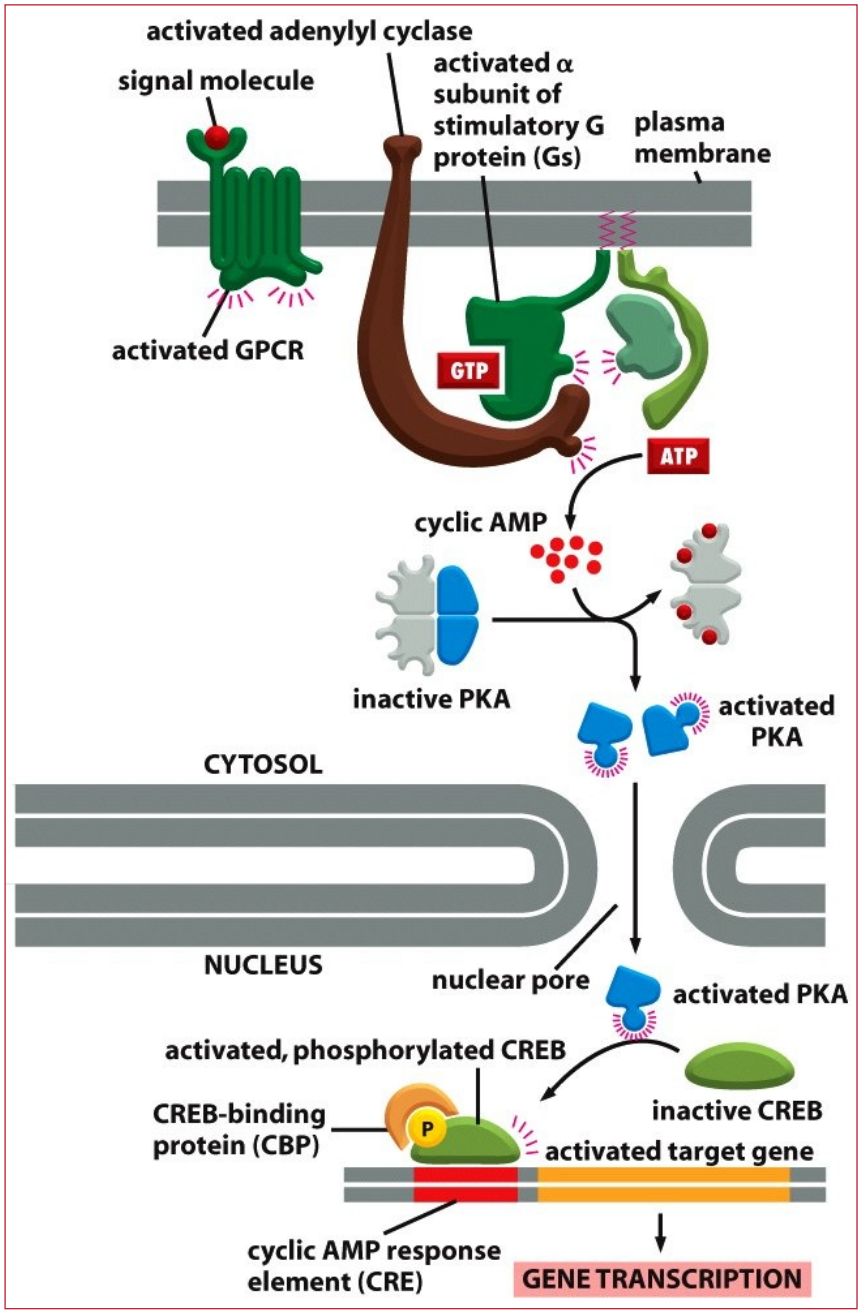
Figure 15-31 *Molecular Biology of the Cell* (© Garland Science 2008)



Uyarıldığında GDP'yi bırakıp GTP bağlar ve a ve B altbirimler aktifleşmiş olarak ayrılırlar.

a altbirimi bağlı olan GTP'yi hidrolizleyene kadar aktif kalır, bu altbirimin görevi GTPaz'dır.

cAMP Hücre içindeki derişimi 10^{-7}M, bir kaç sn'de 20 katına çıkabilir. Adenilil siklaz tarafından üretilir, cAMP fosfodiesterazlar tarafından 5'AMP'ye hidrolizlenir.



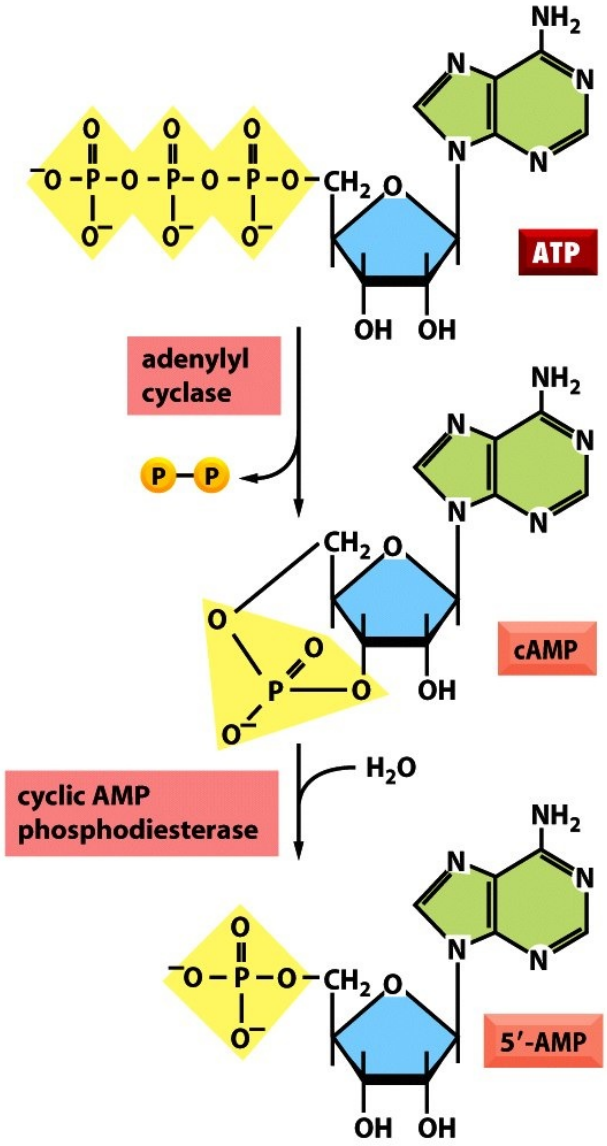


Figure 15-36 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 15–1 Some Hormone-induced Cell Responses Mediated by Cyclic AMP

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

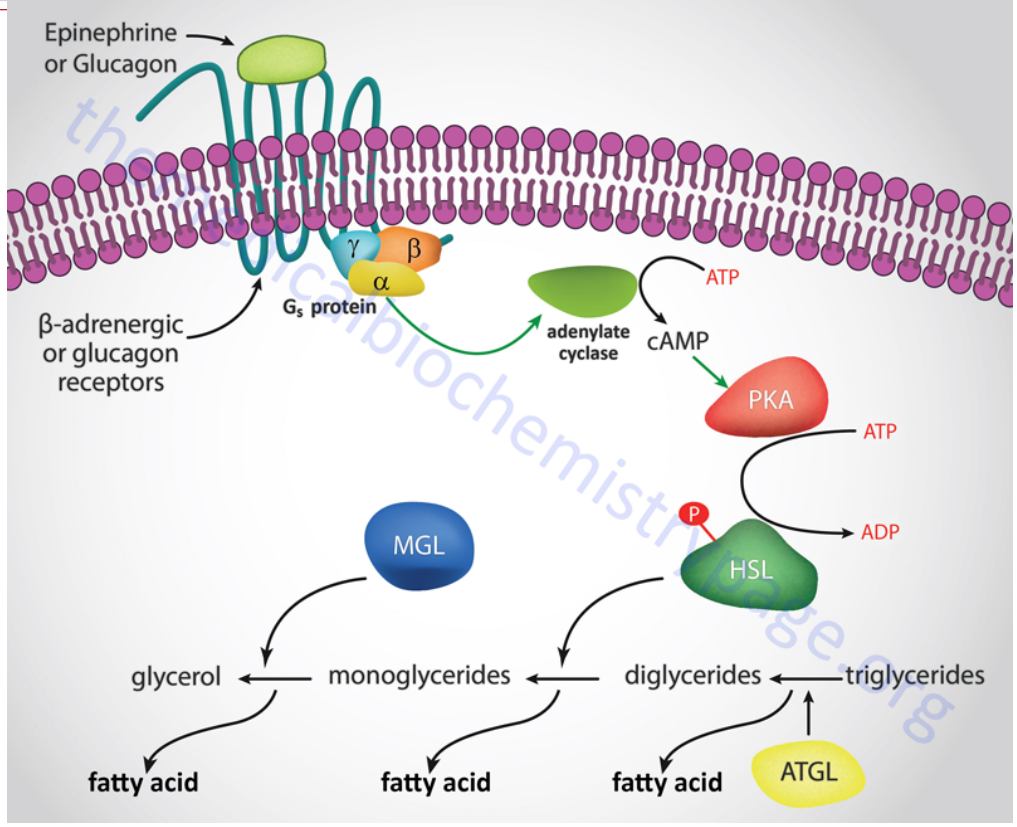


Table 15-1 *Molecular Biology of the Cell* (© Garland Science 2008)

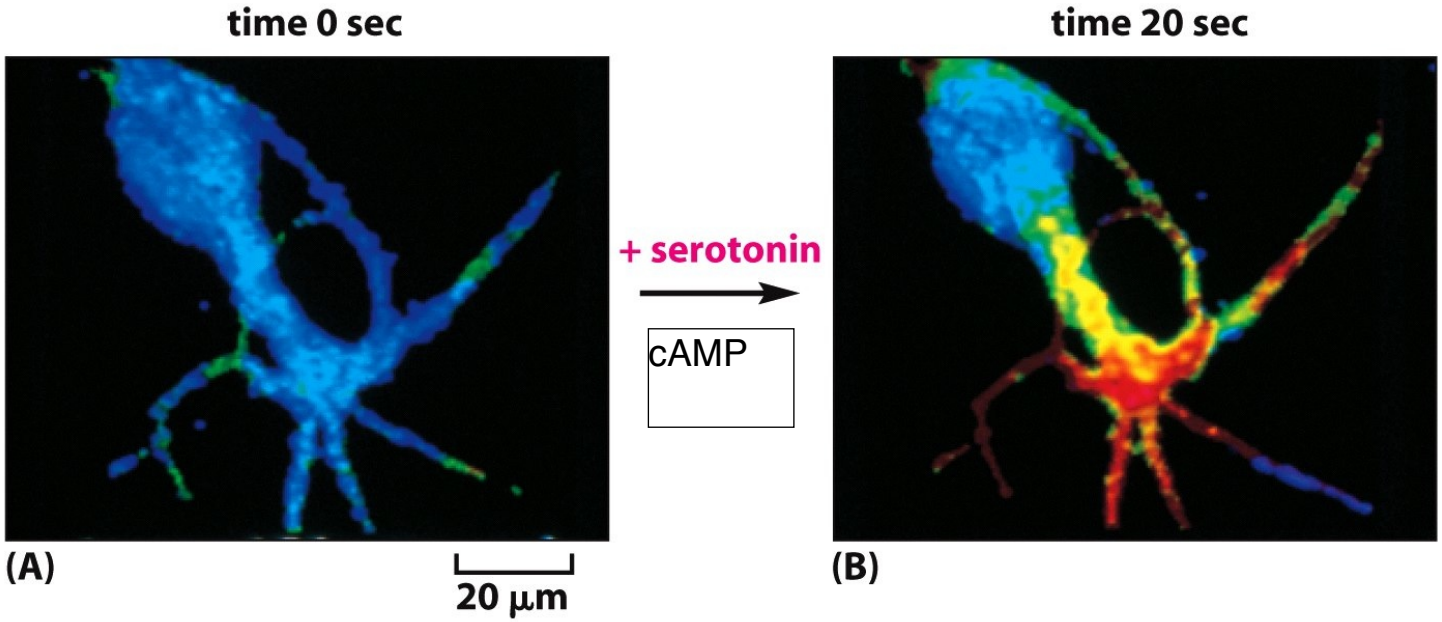
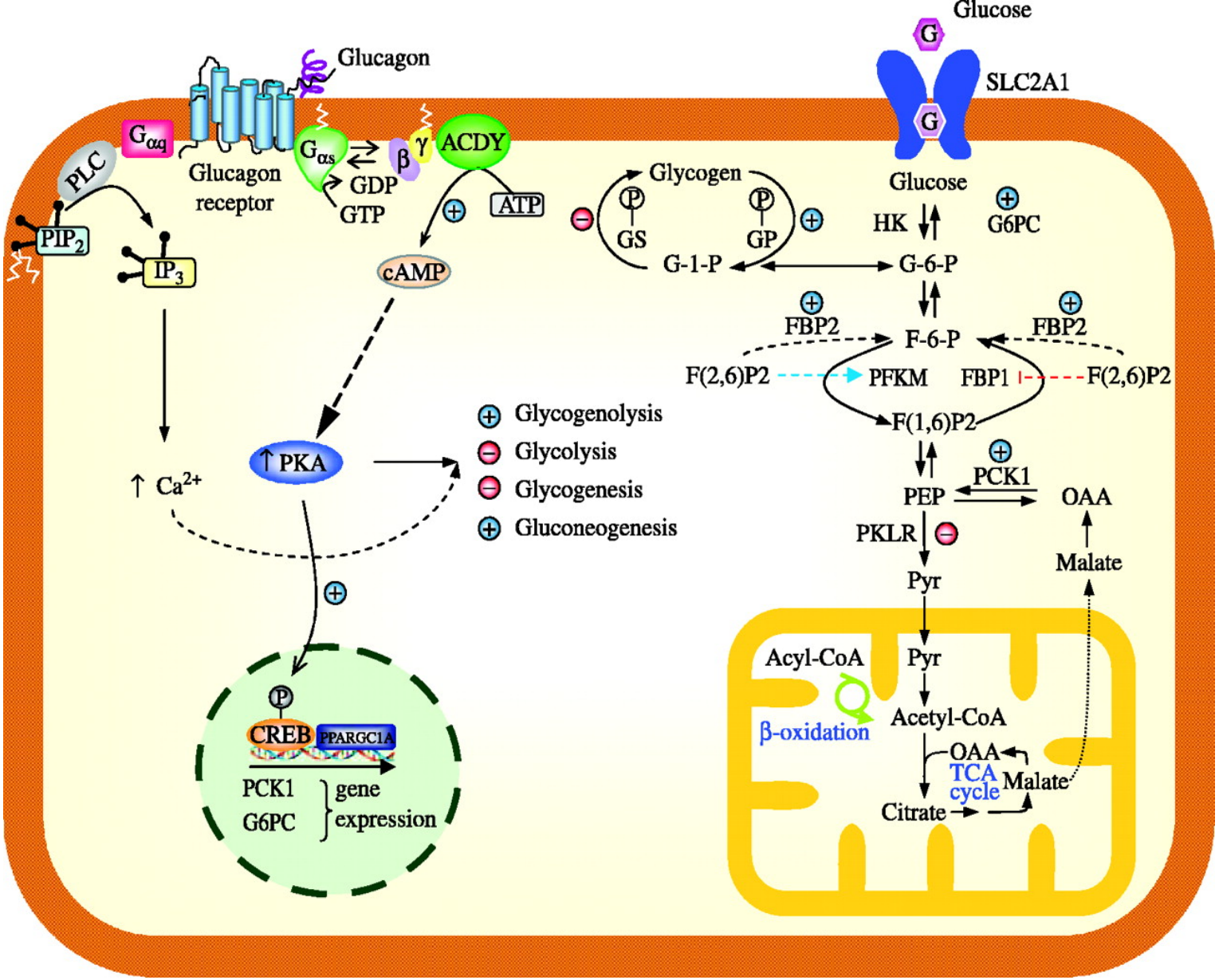


Figure 15-33 *Molecular Biology of the Cell* (© Garland Science 2008)



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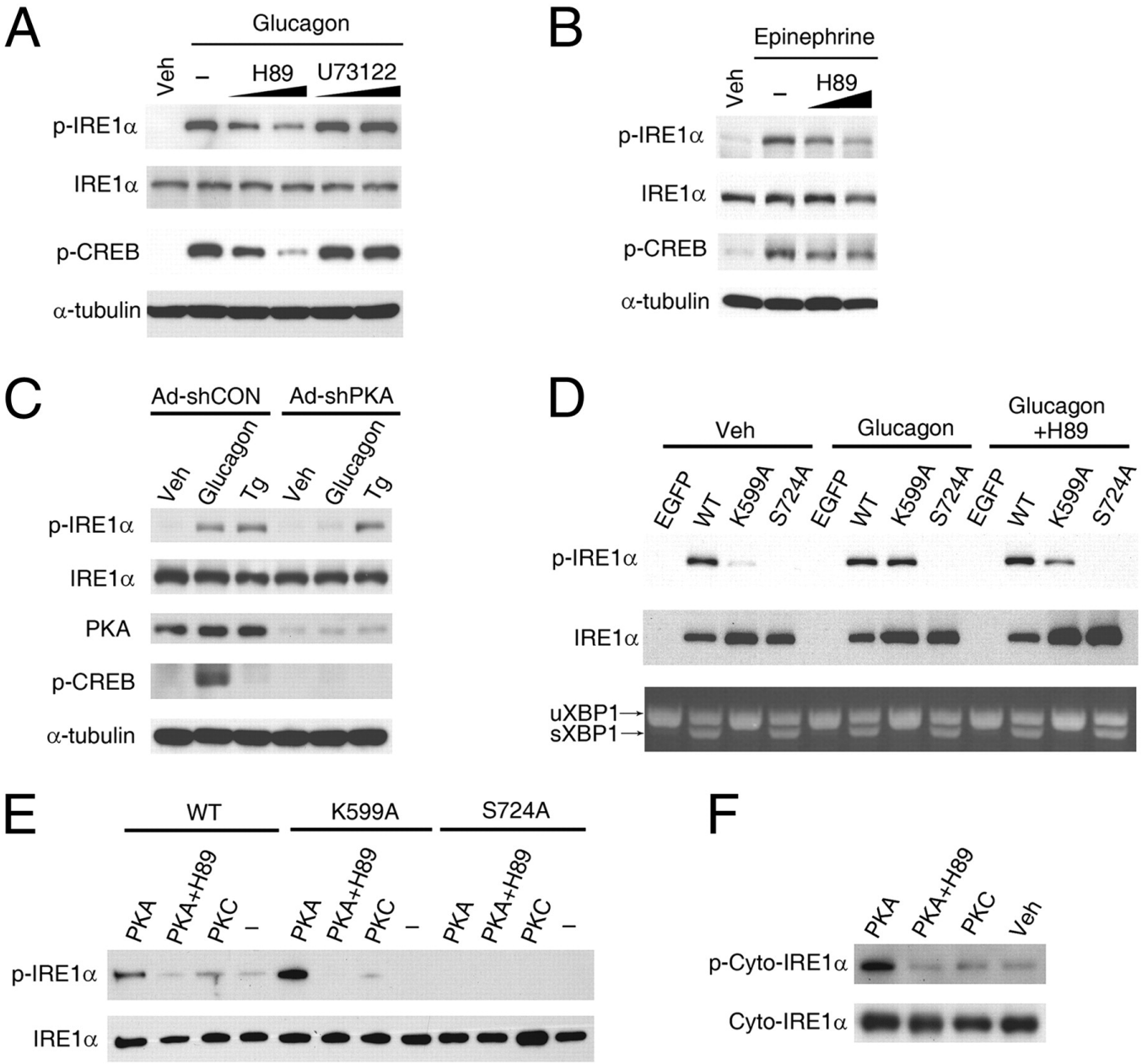

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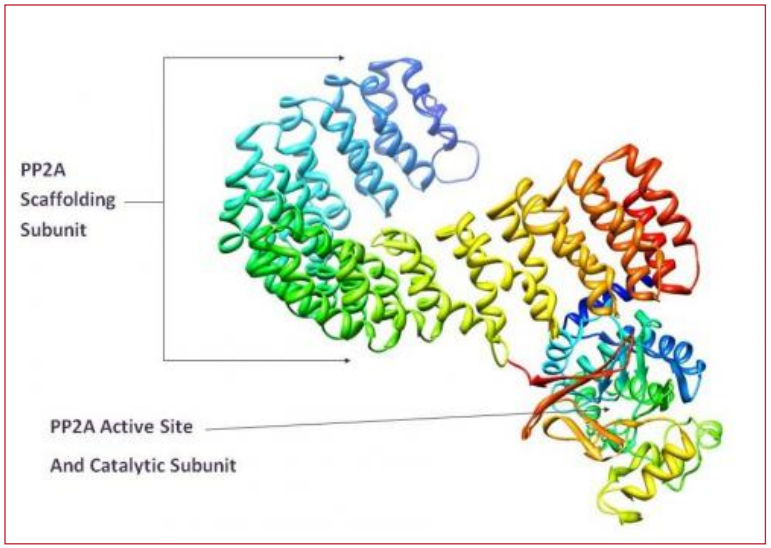

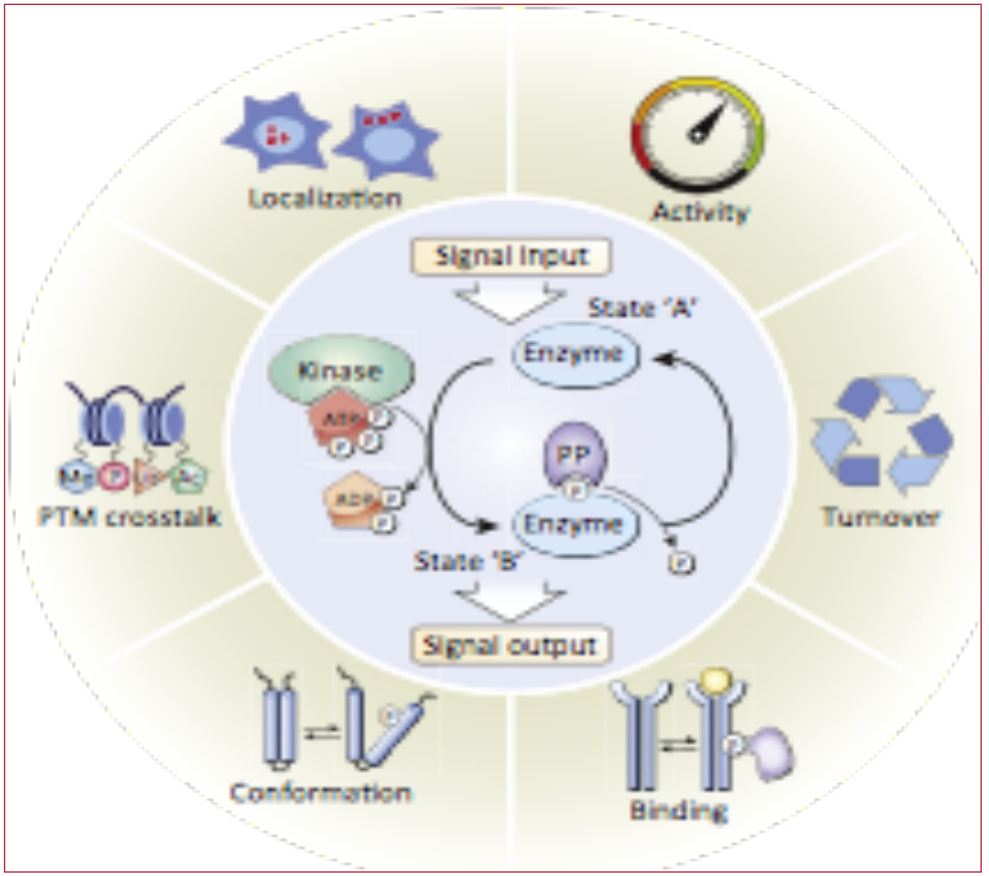

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4 tip Serin/treonin Fosfataz vardır.
Protein Fosfataz I, Protein Kinase A tarafından fosforlanmış bir çok proteinin defosforile eder.
Protein Fosfataz IIA, Ser/Thr Kinazların fosforladığı proteinlerin genel defosforile eder.
Protein Fosfataz IIB, Calcineurin Ca2+'la etkinleştirilir ve özellikle beyinde bulunur.
Protein Fosfataz IIC (Diğerlerinden alakasız bir yapısı vardır). Mn++ ve Mg++ bağımlıdır.

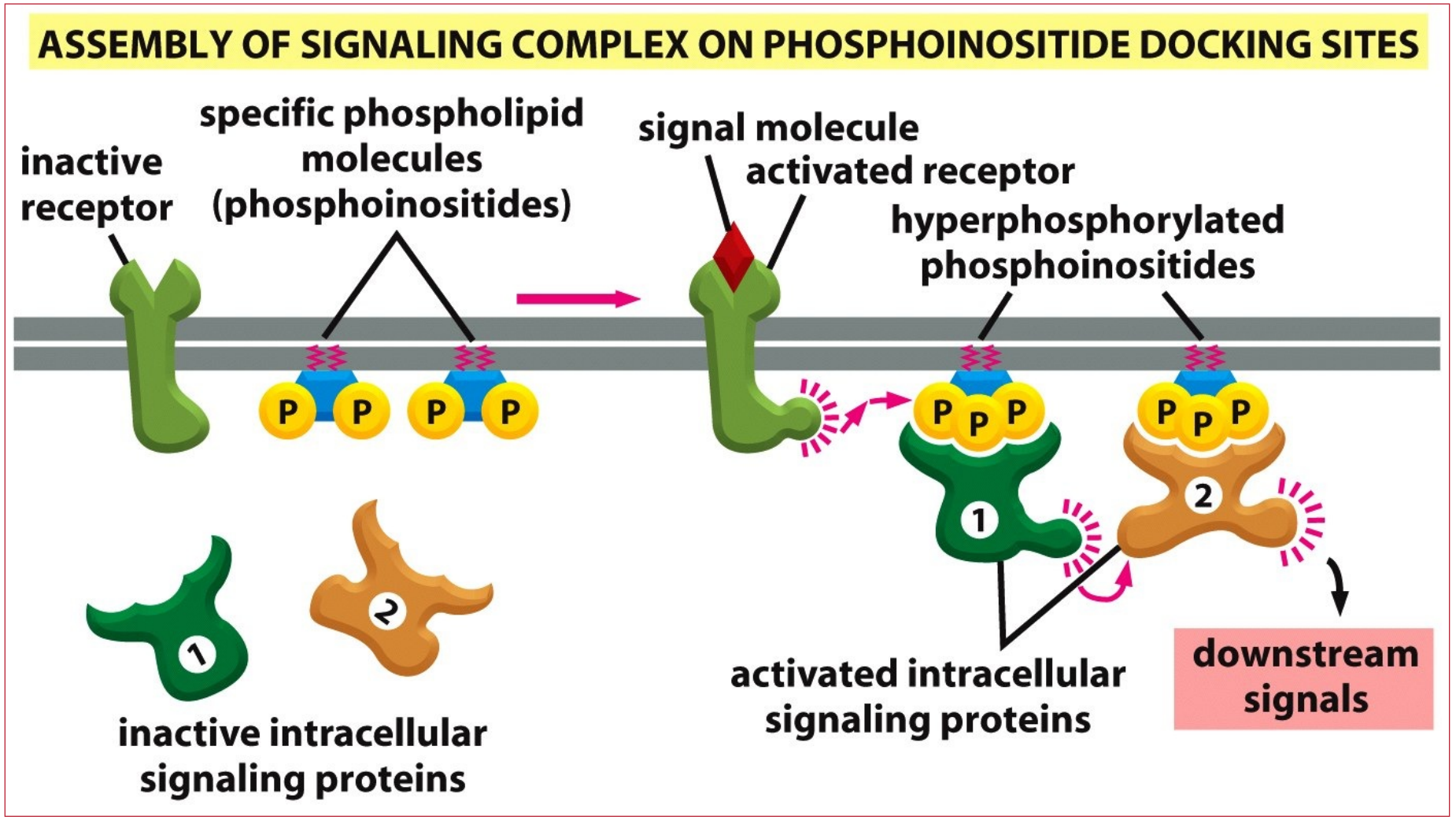
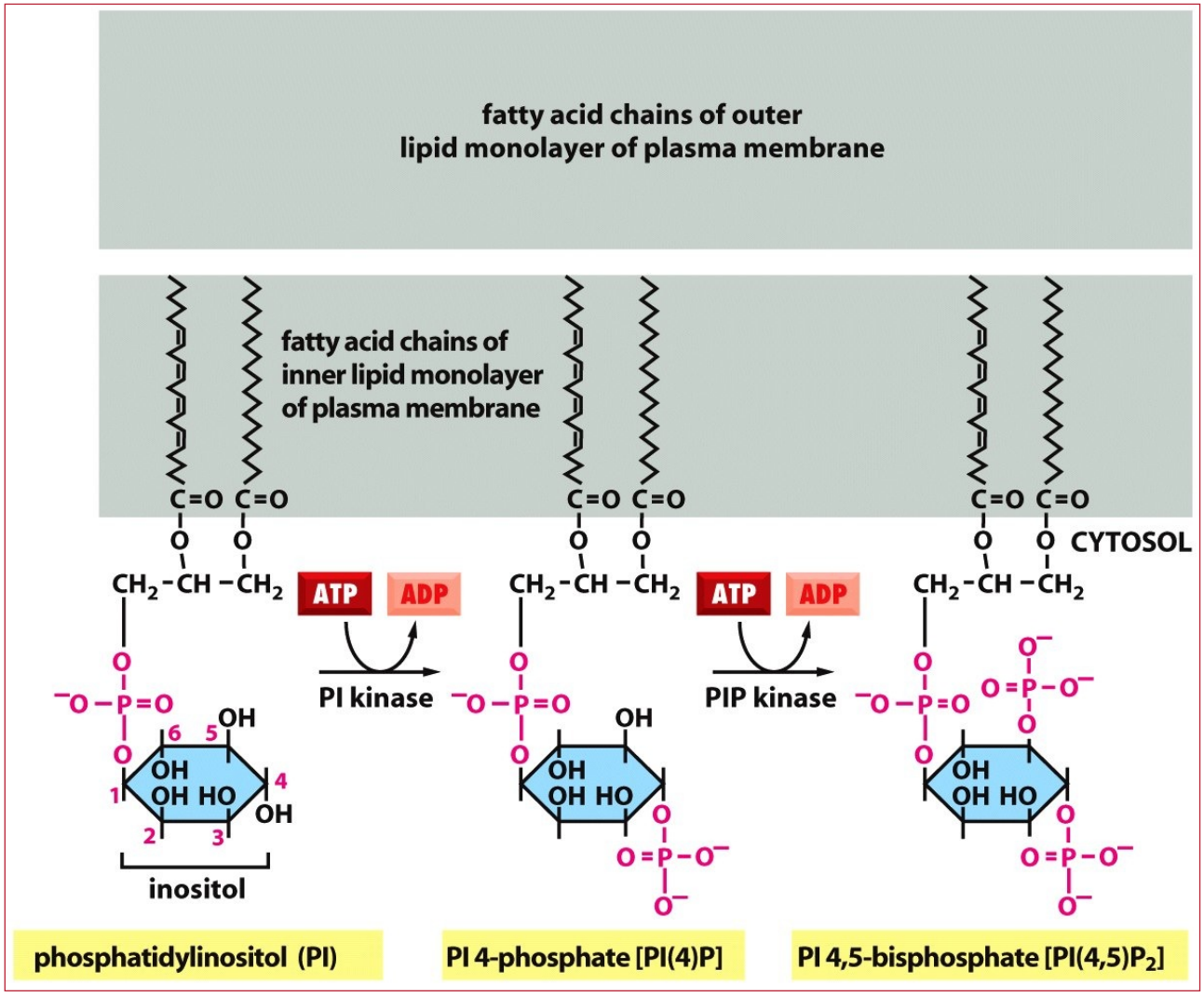


Figure 15-21c *Molecular Biology of the Cell* (© Garland Science 2008)



Bazı G Proteinleri, Fosfolipaz C'yi etkinleştirerek Inositol fosfolipit sinyal iletim yolağını etkinleştirirler

Figure 15-34 *Molecular Biology of the Cell* (© Garland Science 2008)

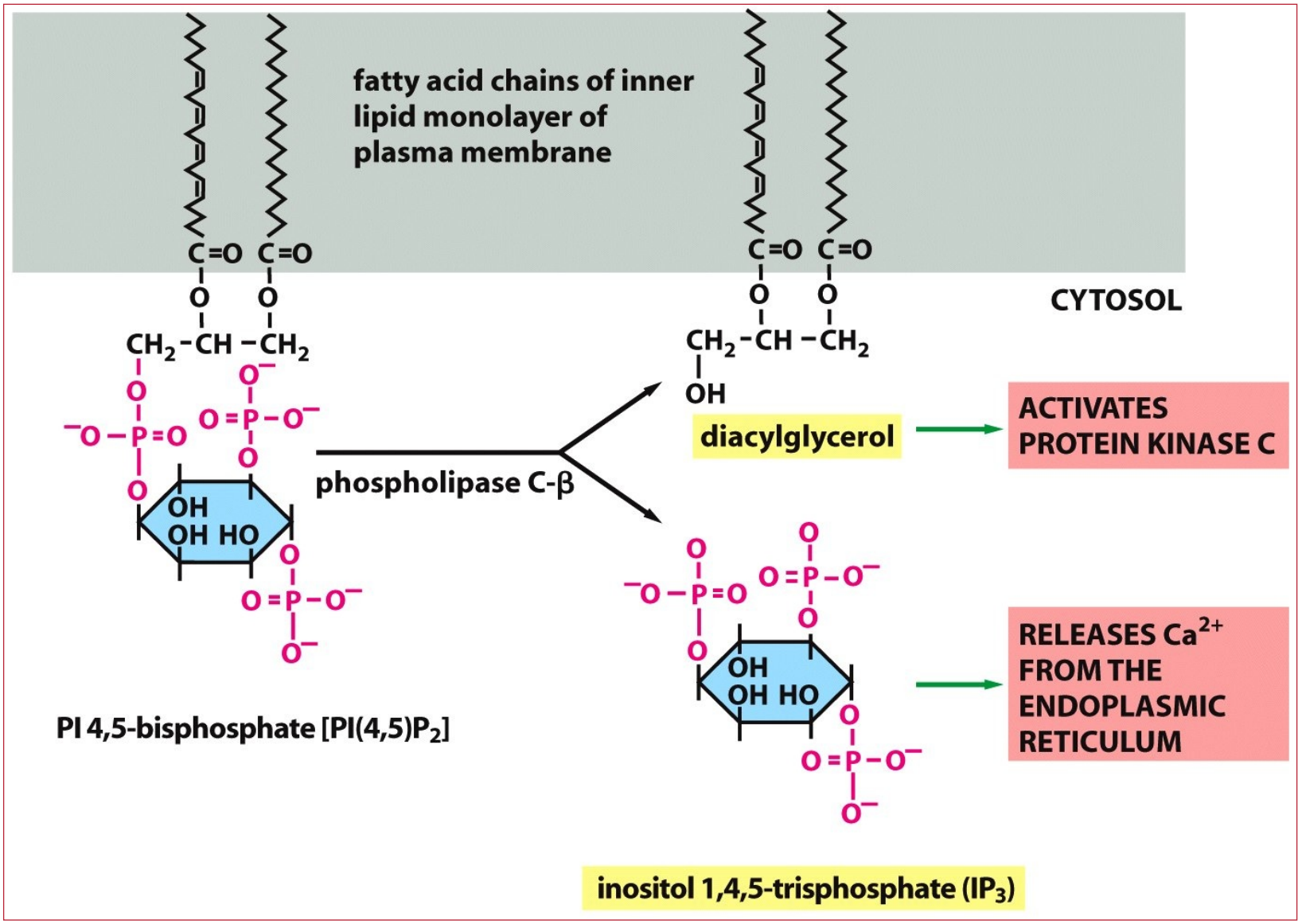


Figure 15-37 *Molecular Biology of the Cell* (© Garland Science 2008)

Table 15–2 Some Cell Responses in Which GPCRs Activate PLCβ

TARGET TISSUE	SIGNAL MOLECULE	MAJOR RESPONSE
Liver	vasopressin	glycogen breakdown
Pancreas	acetylcholine	amylase secretion
Smooth muscle	acetylcholine	muscle contraction
Blood platelets	thrombin	platelet aggregation