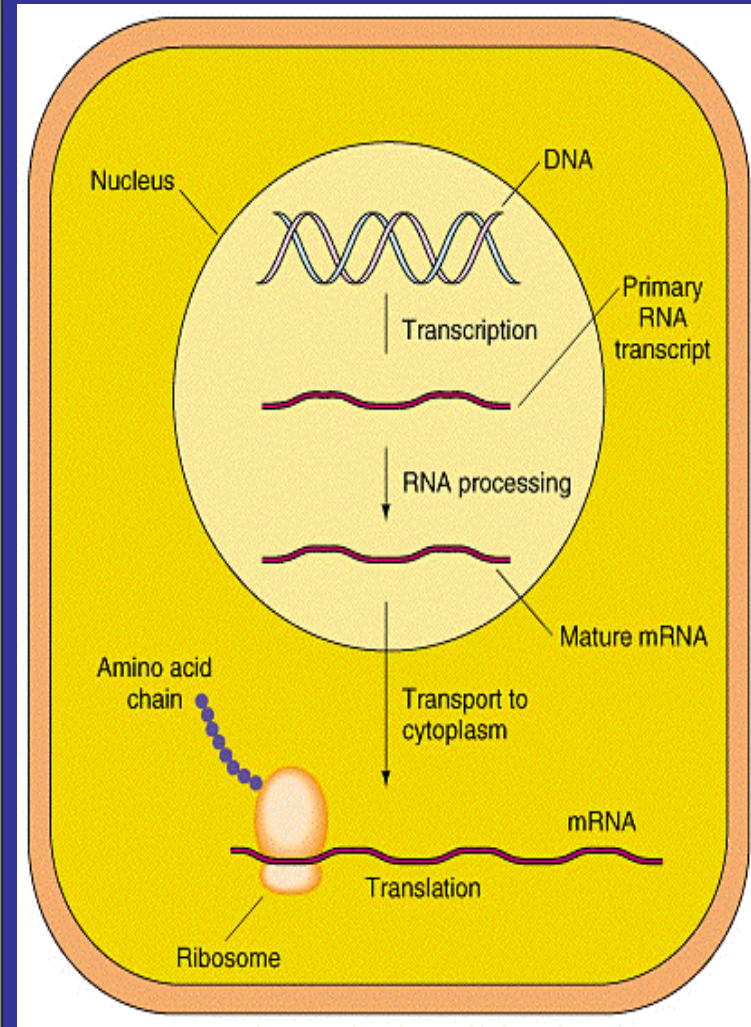
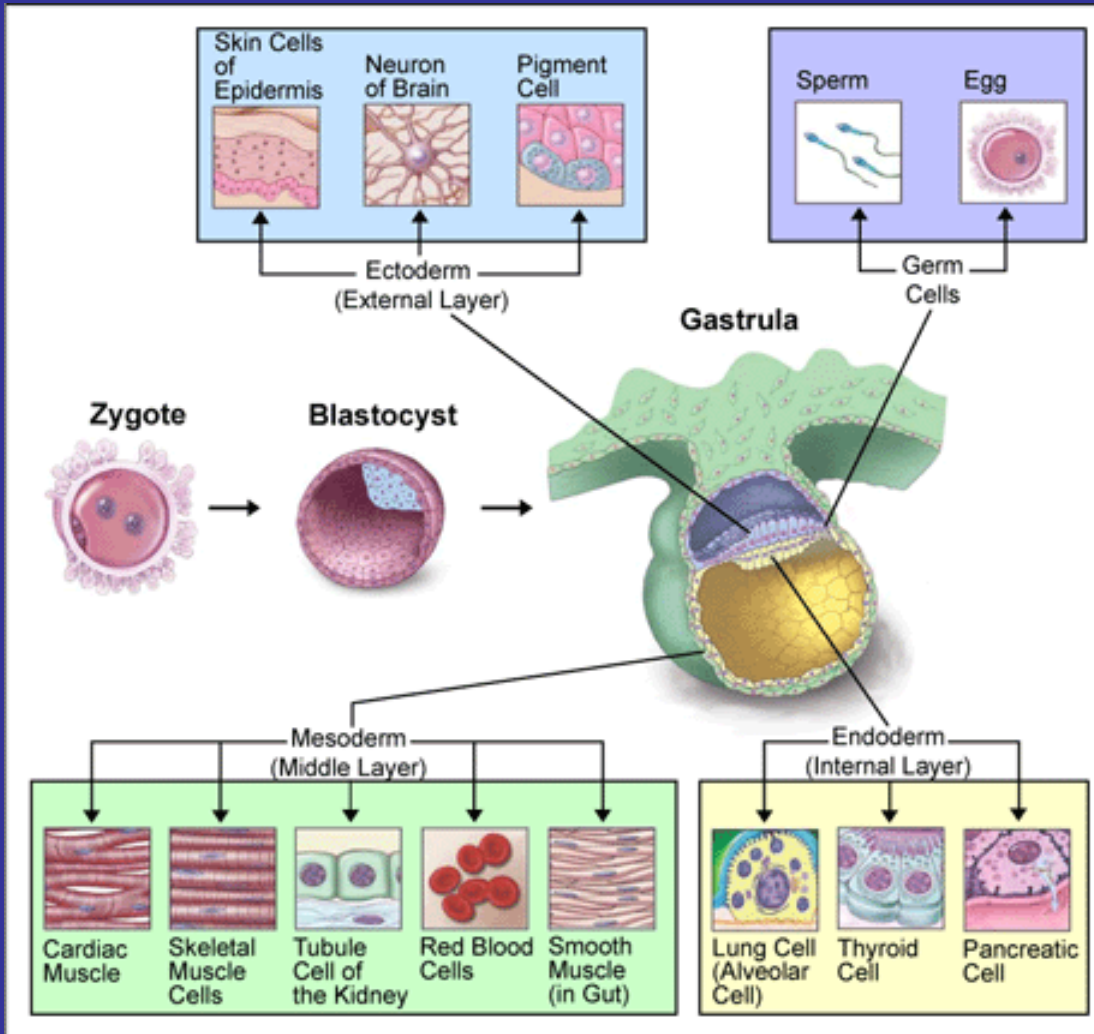


HÜCREDE SİNYAL İLETİM MEKANİZMALARI

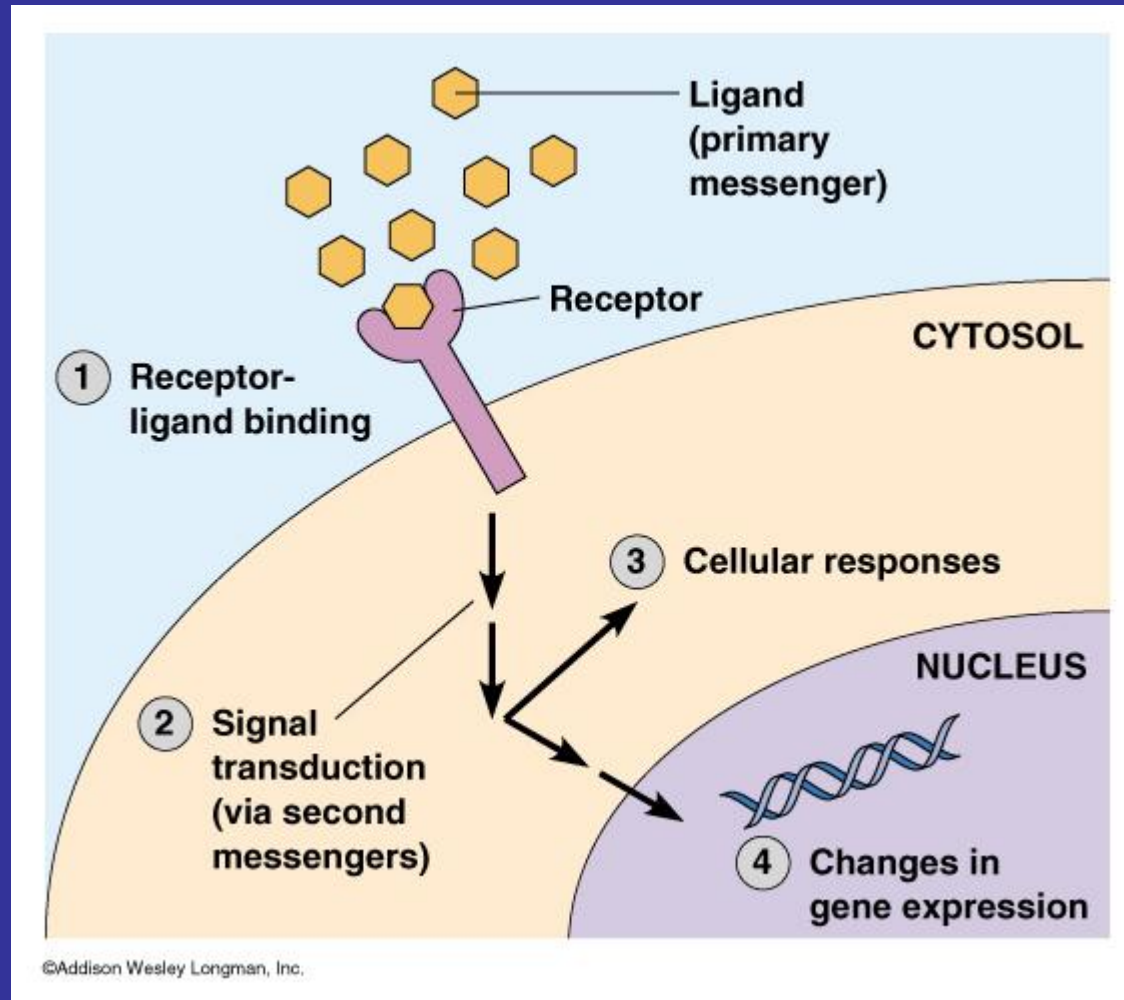
Ediz Demirpençe

HÜTF Biyokimya Anabilim Dalı

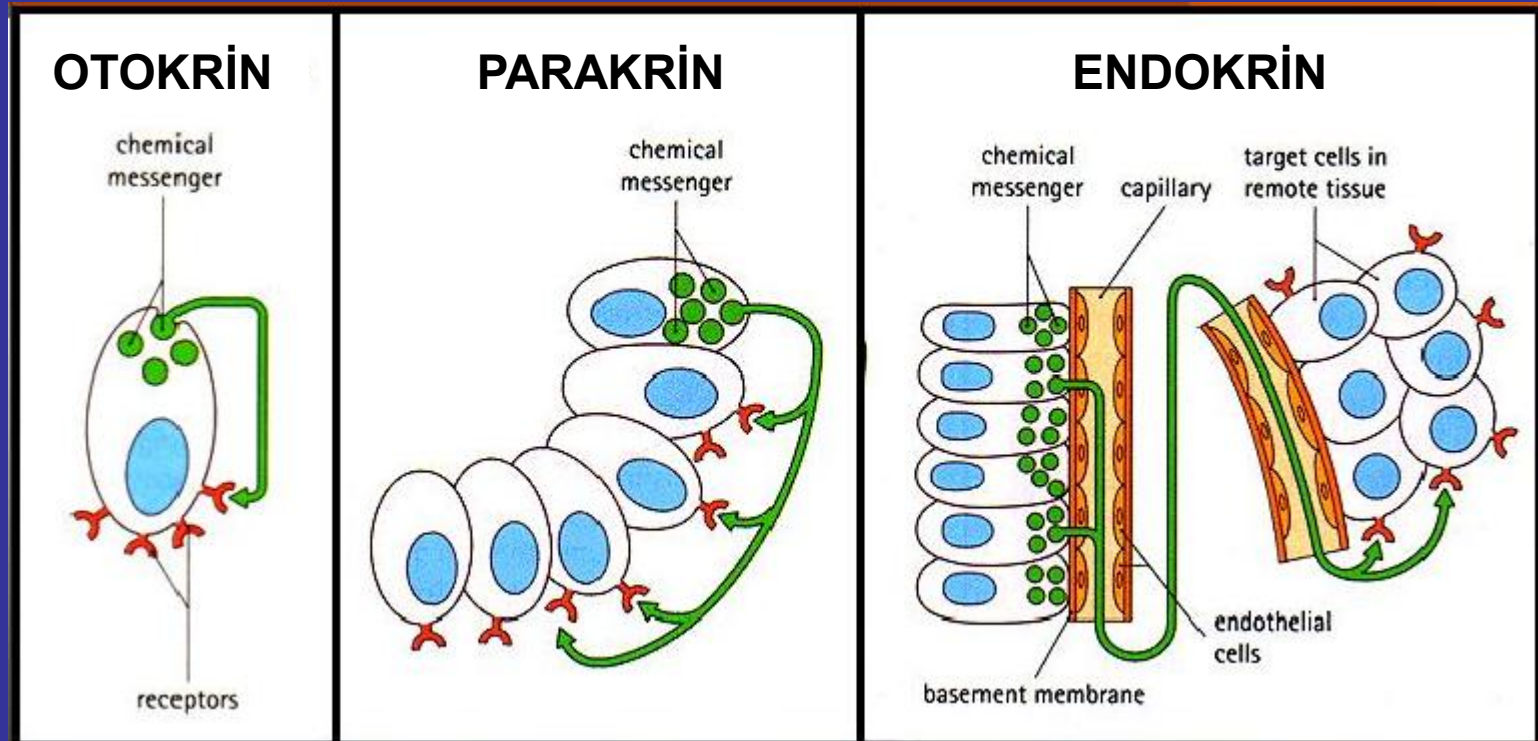
Neden iletişim gerekli?



Genel Kavramlar



Genel Kavramlar



Genel Kavramlar

- **Amplifikasyon**
- **Desensitizasyon-adaptasyon**
- **Entegrasyon**

- **Nükleer reseptörlerle sinyal iletimi**
- **Hücre zarına yerleşik reseptörlerle sinyal iletimi**

Nükleer Reseptörler

- Ökaryotlara özgü transkripsiyon faktörleridir
- Gelişim, farklılaşma ve metabolizma ile ilgili fonksiyonları düzenlerler

Steroid Hormon Reseptörleri

- GR: Glukokortikoid reseptörü (NR3C1)
- MR: Mineralokortikoid reseptörü (NR3C2)
- PR: Progesteron reseptörü (NR3C3)
- AR: Androjen reseptörü (NR3C3)
- ER: Östrojen reseptörü (NR3A1-2)

Ligandı Bilinen Diğer Reseptörler

T3R (NR1A1-2), VDR (NR1I1), RAR (NR1B1-2-3)

RXR (NR2B1-2-3), PPAR (NR1C1-2-3)

Ligandı Bilinmeyen “Orphan” Reseptörler

Nükleer Reseptörlerin Modüler Yapısı



C: DNA bağlama bölgesi (DBD)

E: Ligand bağlama bölgesi (LBD)



HRE: Hormone Responsive Element (enhancer)

Nasıl çalışır?

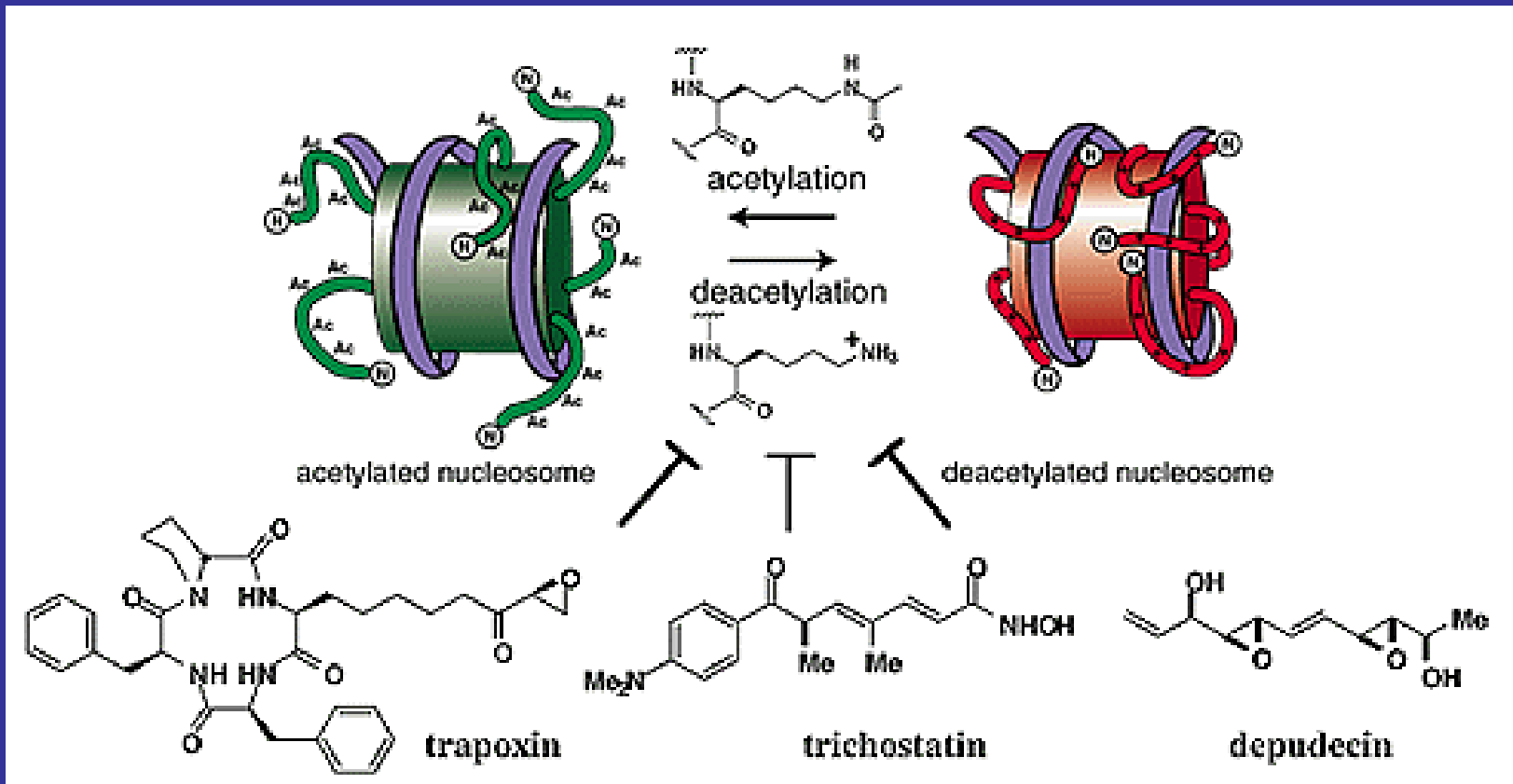


● Agonist



● Antagonist

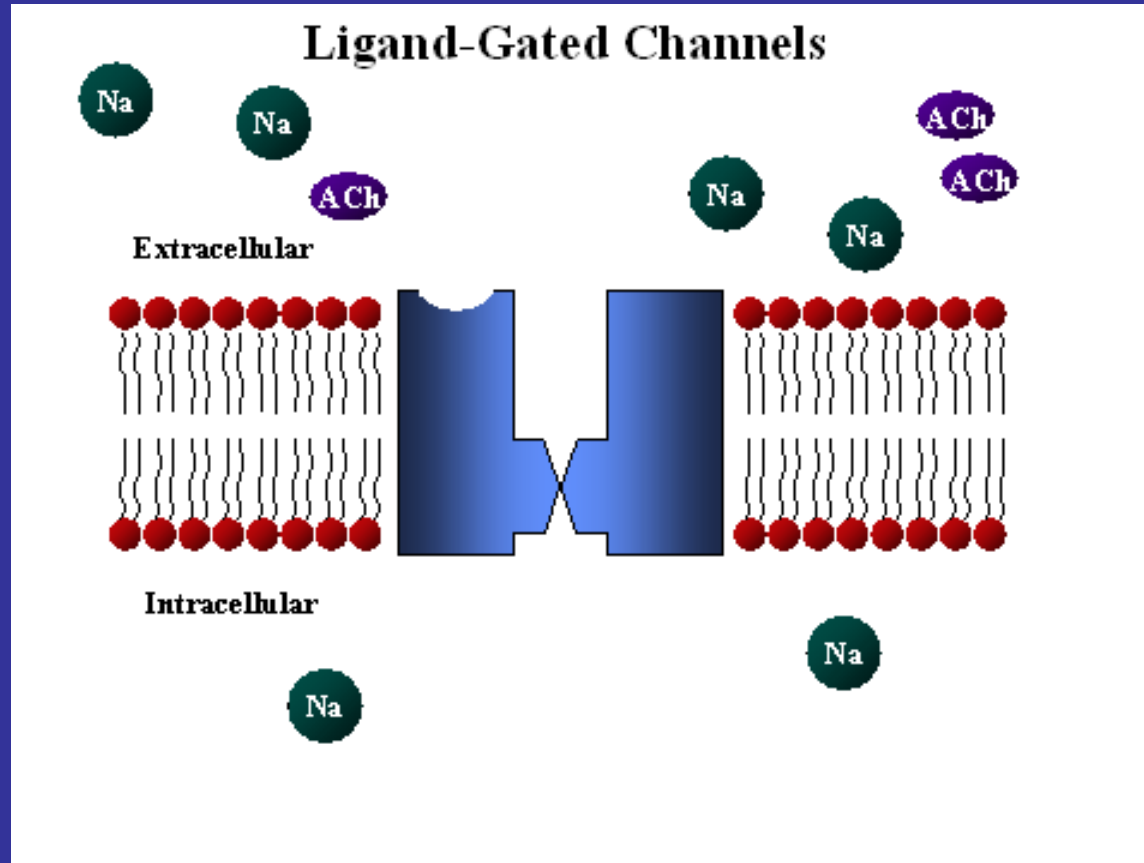
Histonların Asetilasyon ile Modifikasyonu



Hücre Zarına Yerleşik Reseptörlerle Sinyal İletimi

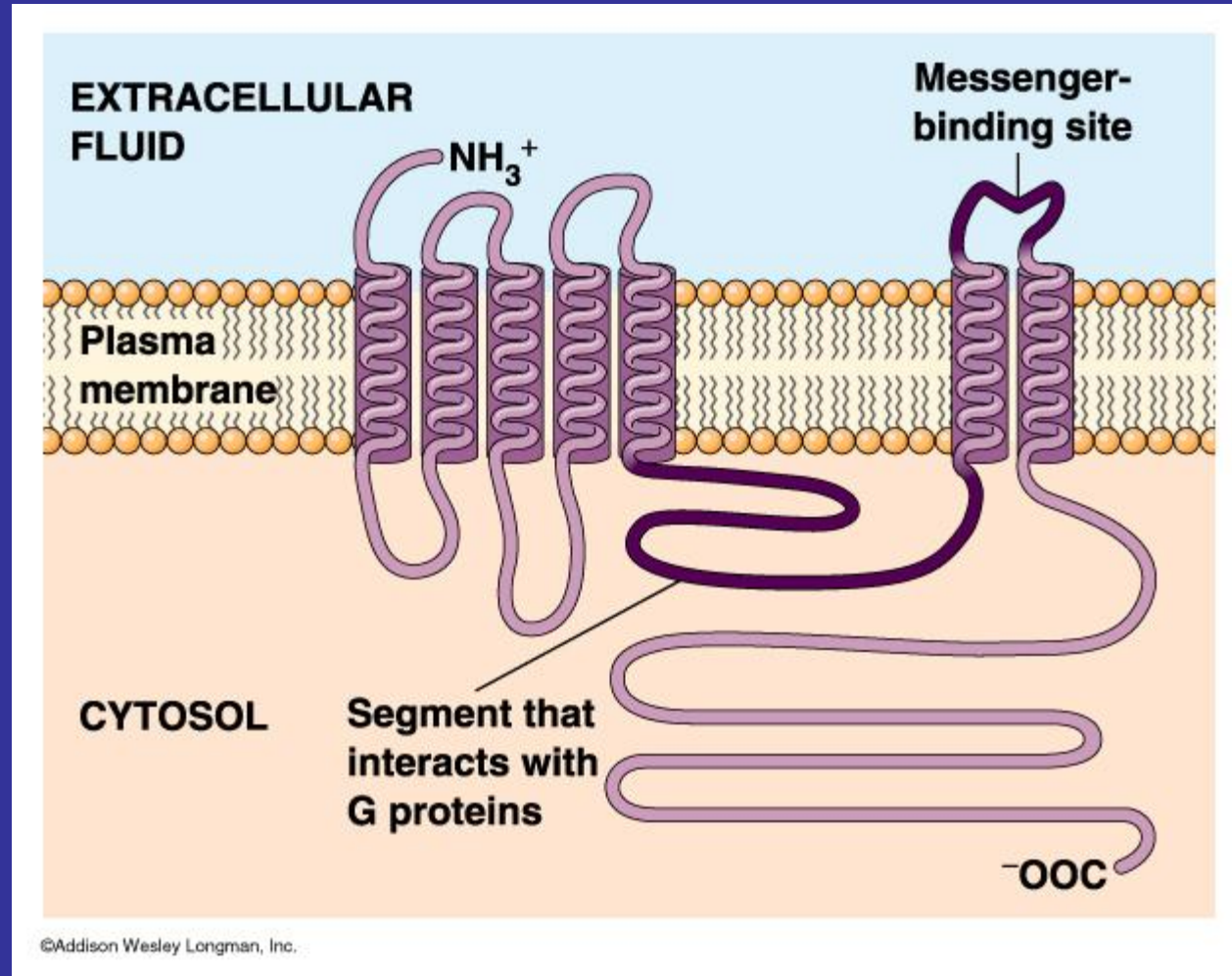
- İyon kanallarına birleşik reseptörler
- G-proteinlerine kenetlenmiş reseptörler
- Enzimatik aktivitesi olan reseptörler
- Sitoplazmadaki enzimleri aktive eden reseptörler

İyon Kanallarına Birleşik Reseptörler

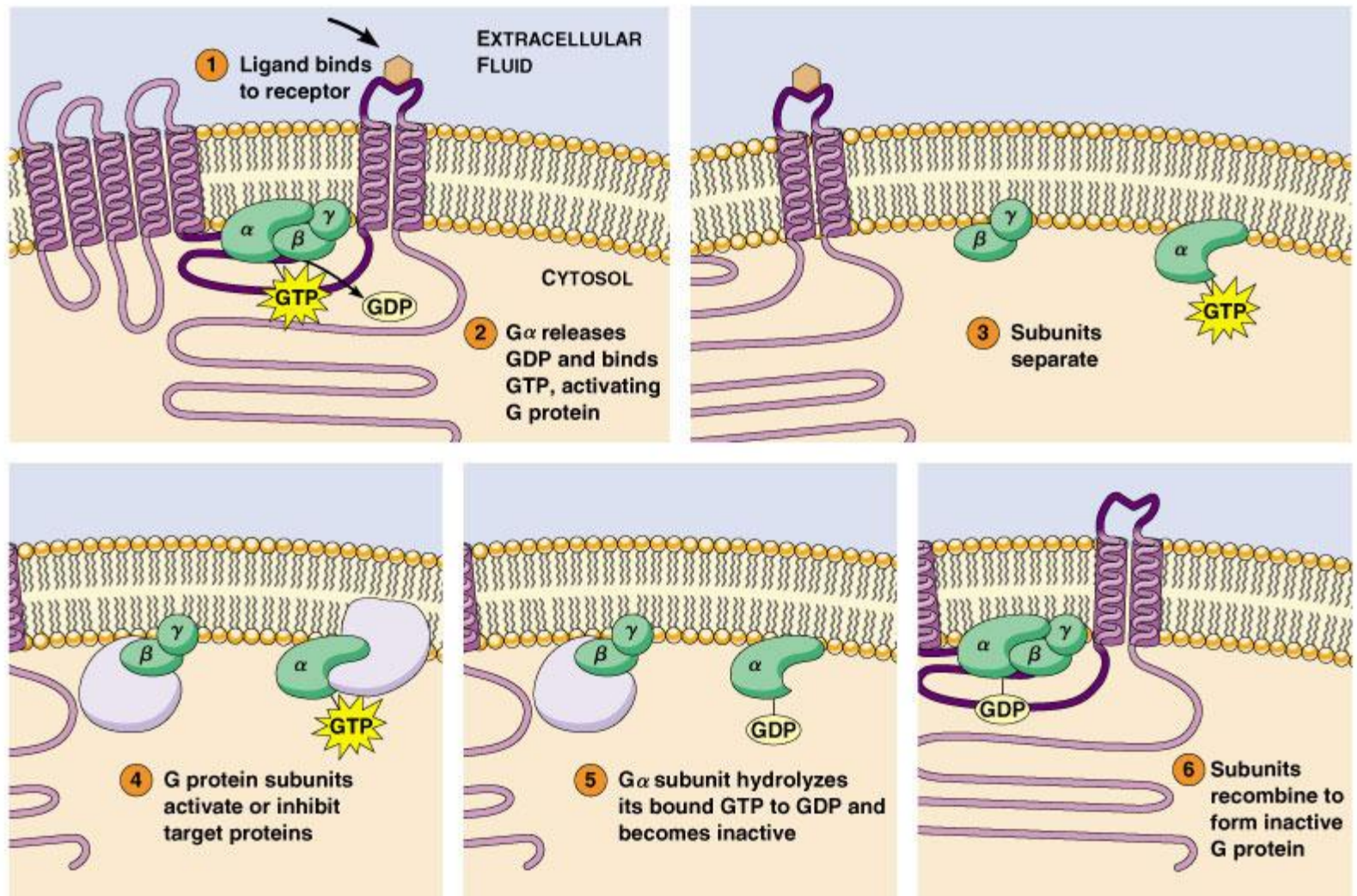


Örnek: Asetilkolin reseptörü- Na^+ kanalı

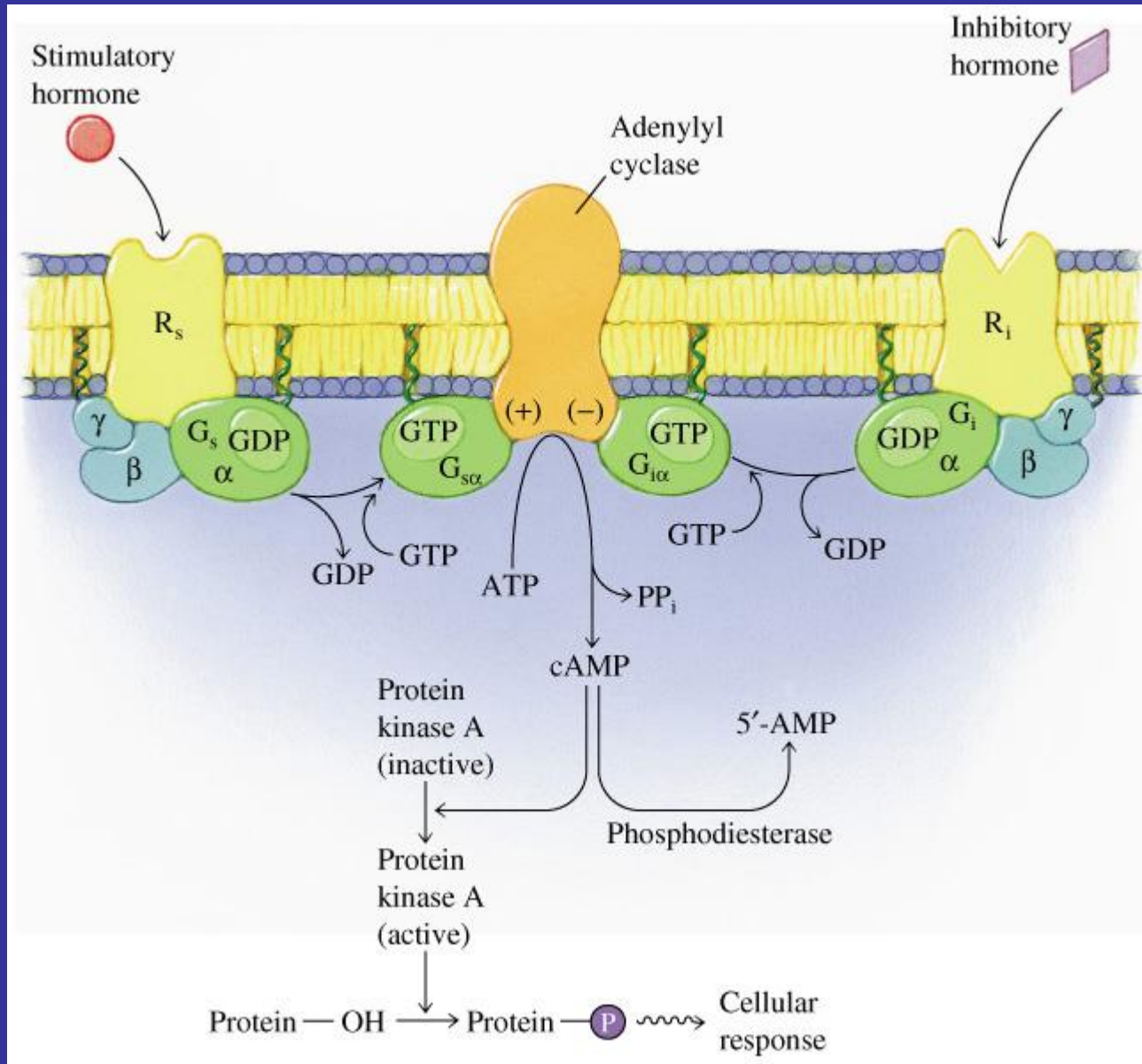
G-proteinlerine Kenetlenmiş Reseptörler



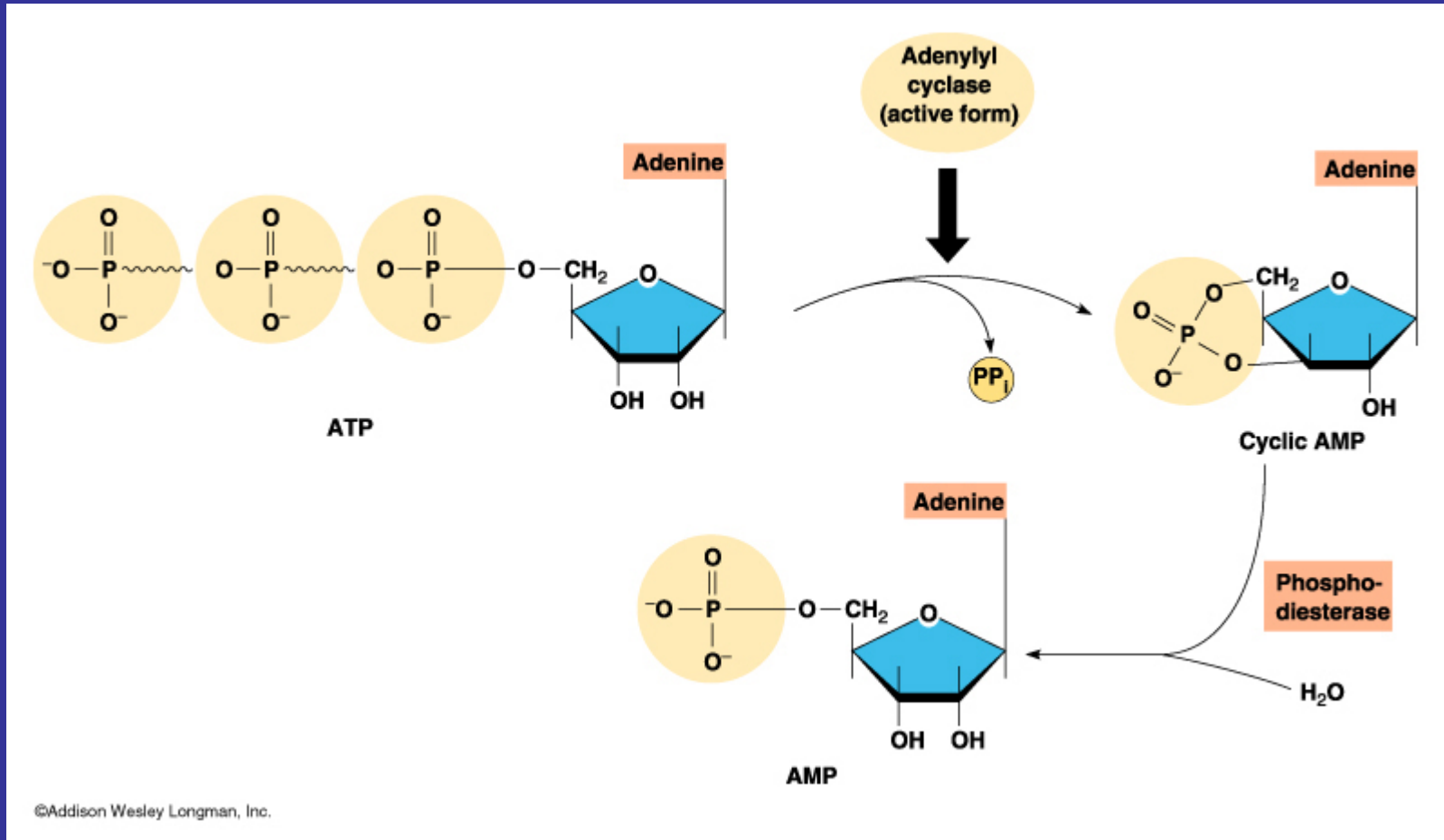
Nasıl çalışır?



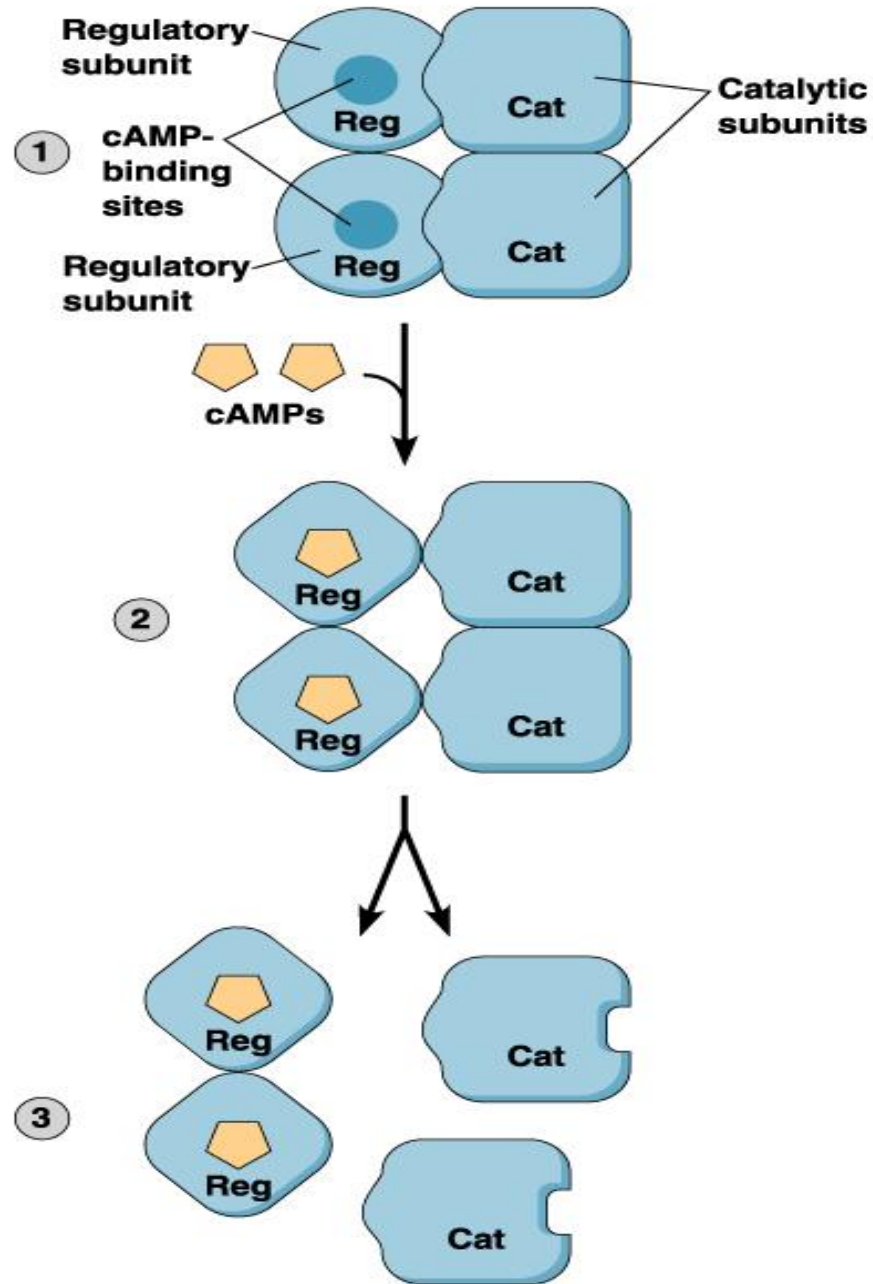
Adenilat siklaz üzerinden:

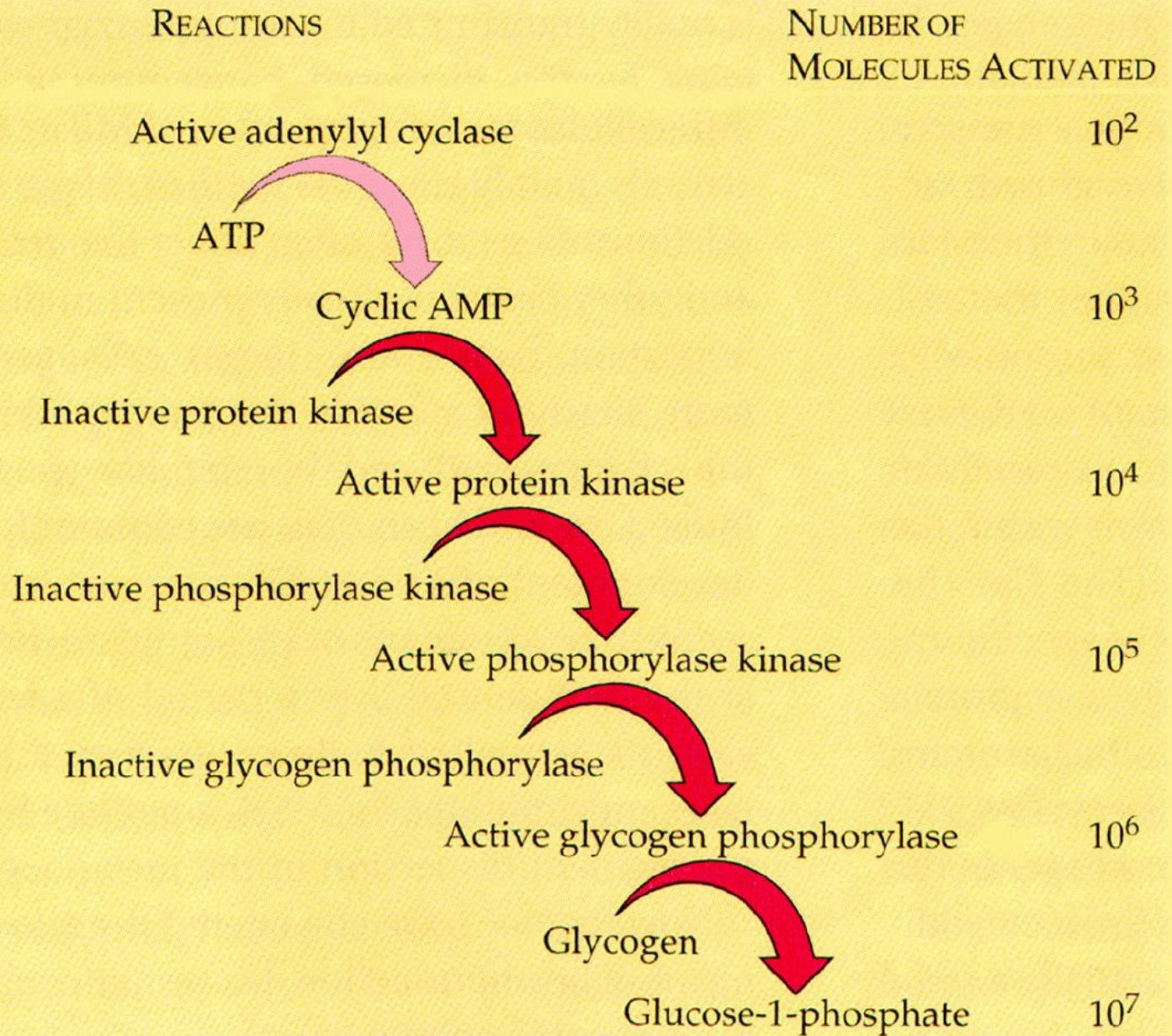


İkinci haberci: cAMP

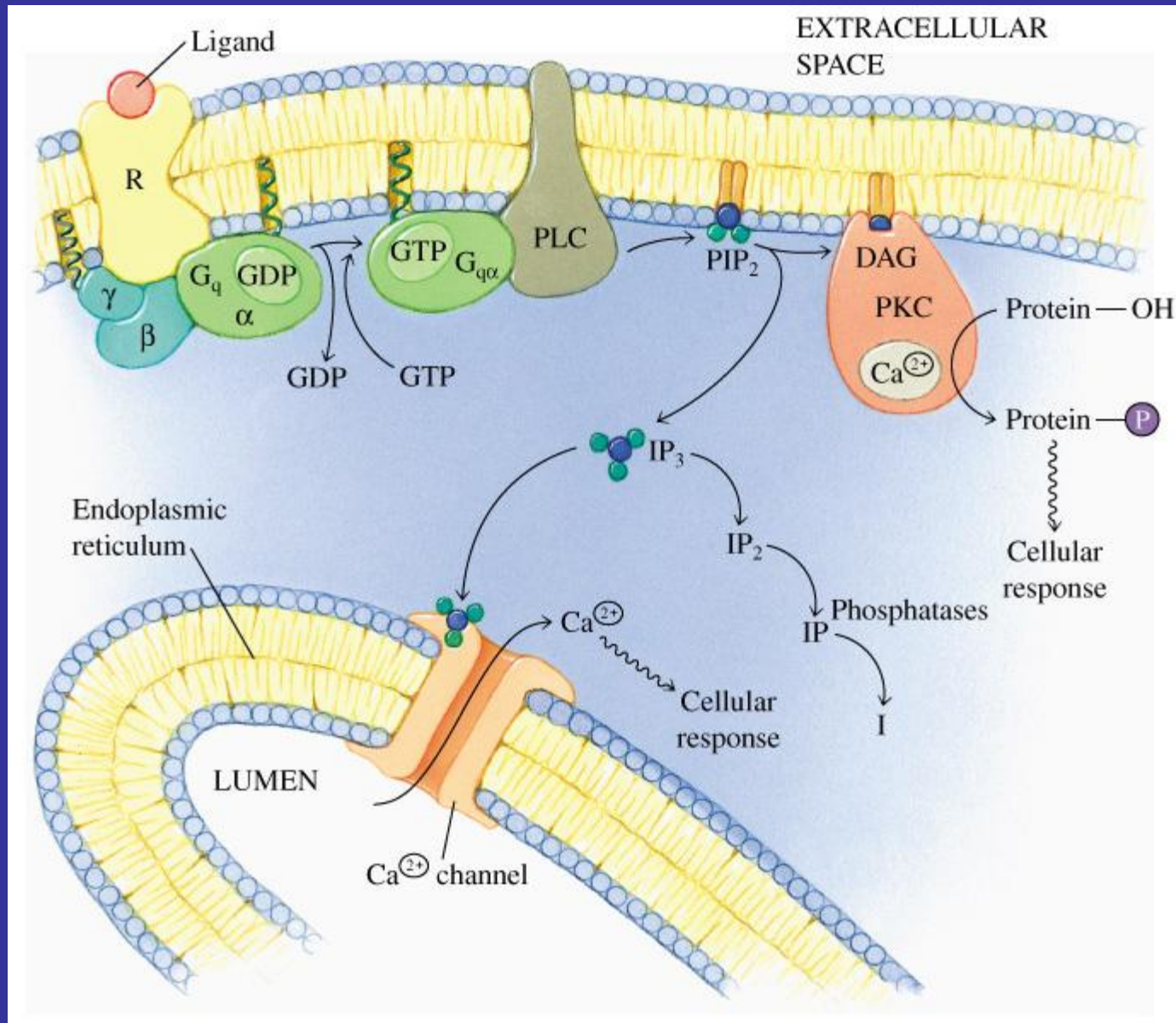


PKA

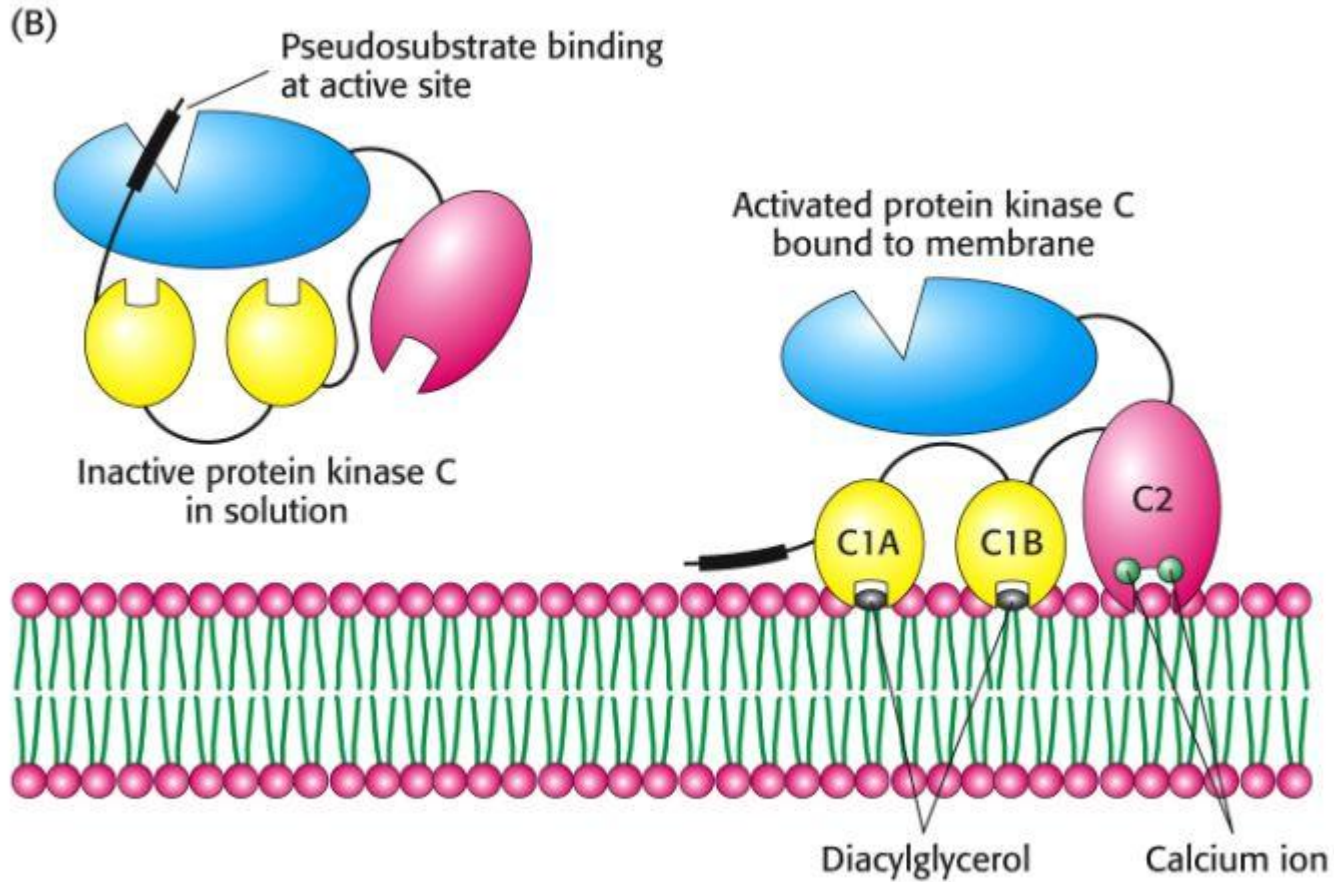




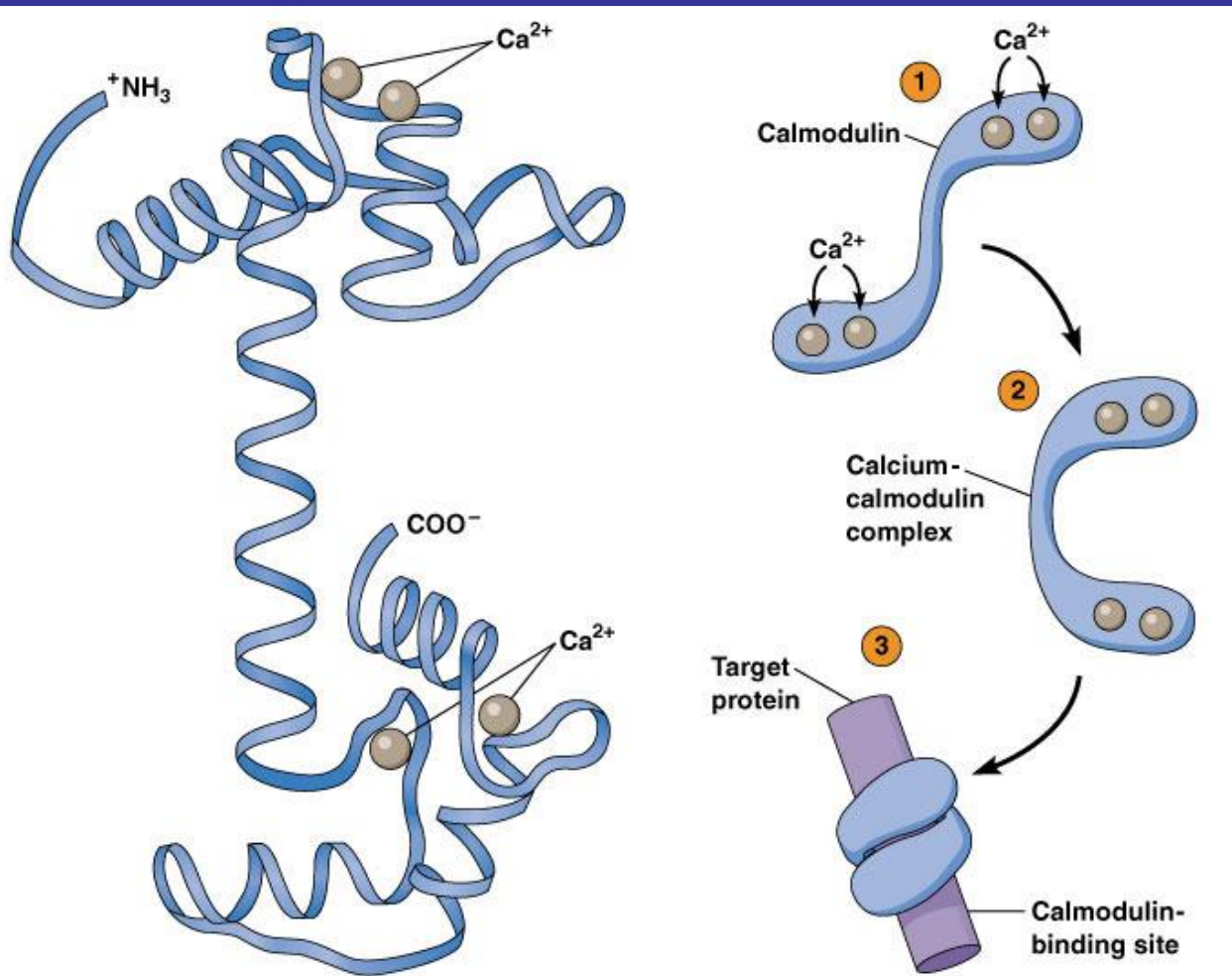
Fosfolipaz C üzerinden:



İkinci haberciler (Ca^{++} , DAG) ve PKC



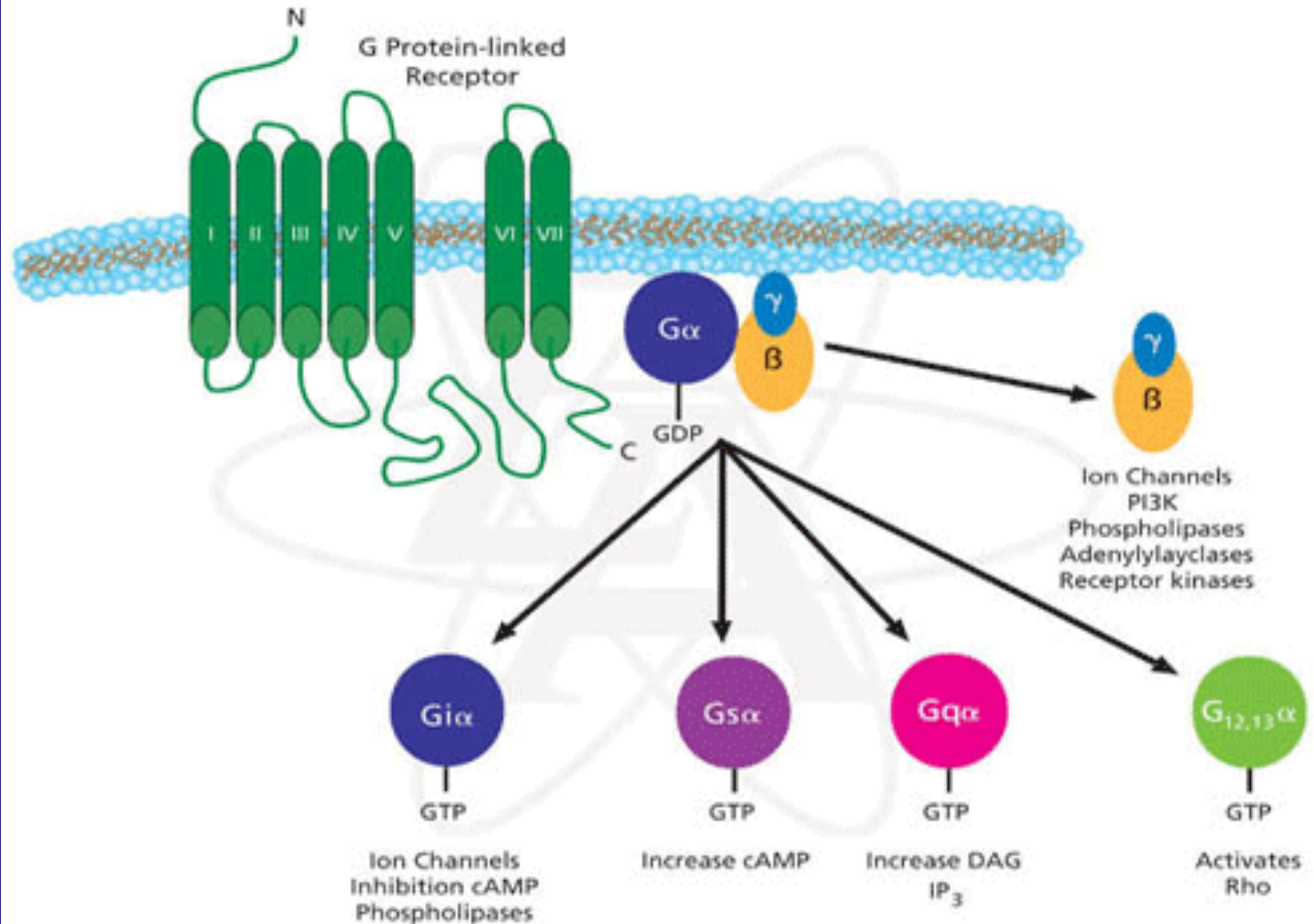
Calmodulin



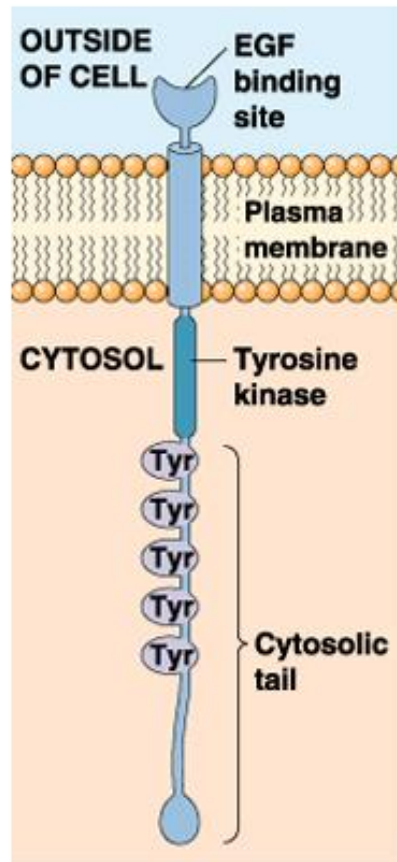
(a) Structure of Ca^{2+} -calmodulin complex

(b) Function of Ca^{2+} -calmodulin complex

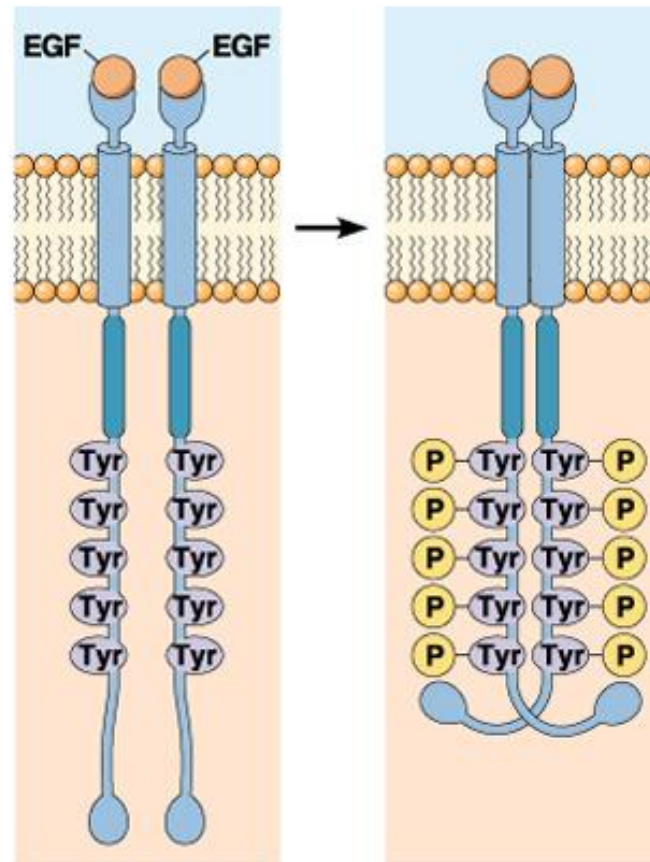
G_{α_s}	\uparrow Adenilat siklaz
$G_{\alpha_{olf}}$	RGS-PX1, Ca^{++} kanalları, Src tirozin kinaz
G_{α_T}	\uparrow cGMP fosfodiesteraz
$G_{\alpha_{gust}}$	Fosfodiesteraz
G_{α_i}	\downarrow Adenilat siklaz, \uparrow Src tirozin kinaz
$G_{\alpha_q}, G_{\alpha_{11,14,15,16}}$	\uparrow Fosfolipaz C
$G_{\alpha_{12,13}}$	Rho aktivasyonu, β -katenin salınımı
$G_{\beta\gamma}$	K^+ kanalları, \uparrow Adenilat siklaz (ACII, ACIV), Fosfolipazlar (PLC β 1-3), PI3K γ



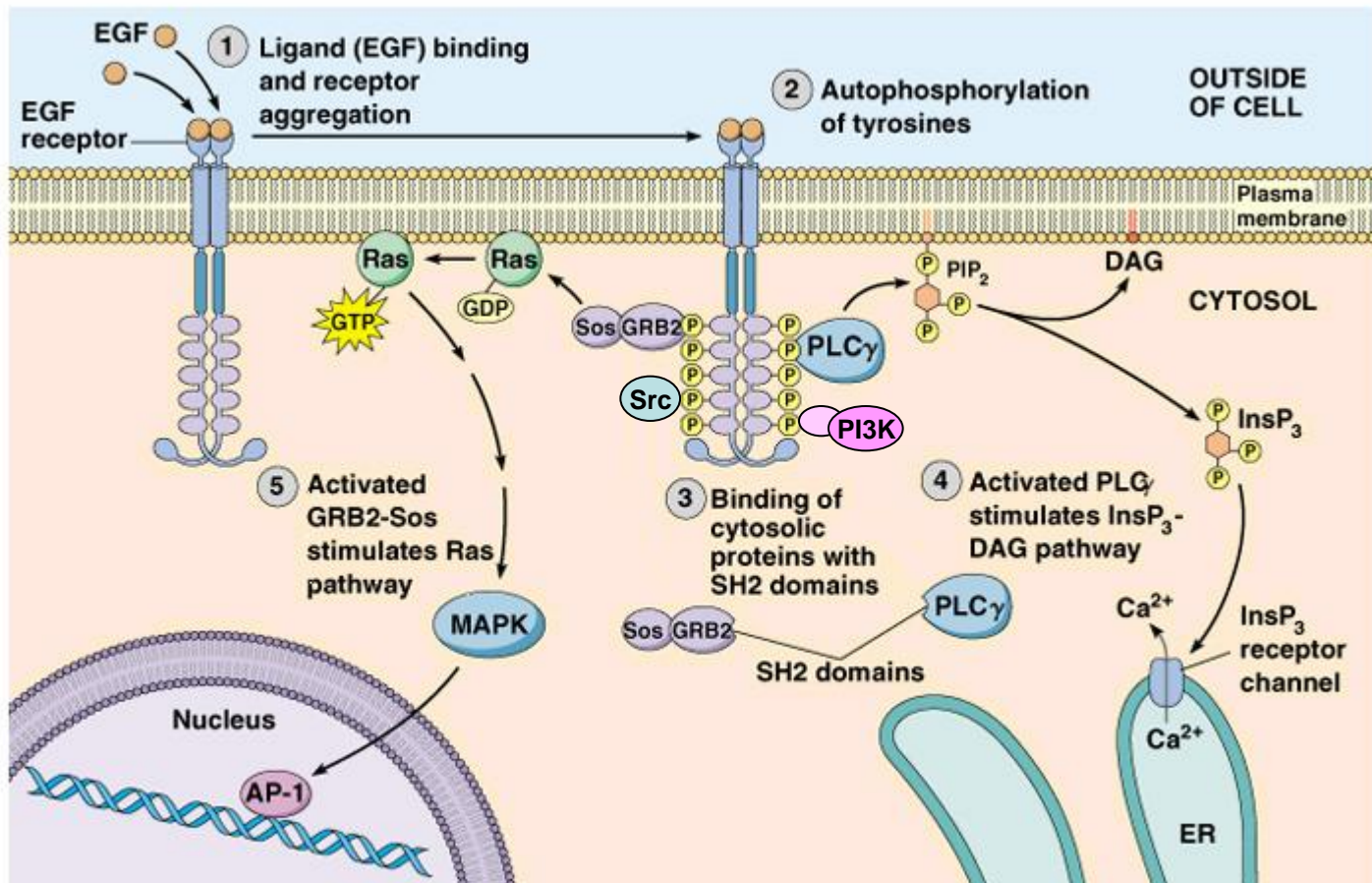
Enzimatik Aktivitesi Olan Reseptörler → RTK



(a) Structure of the epidermal growth factor (EGF) receptor

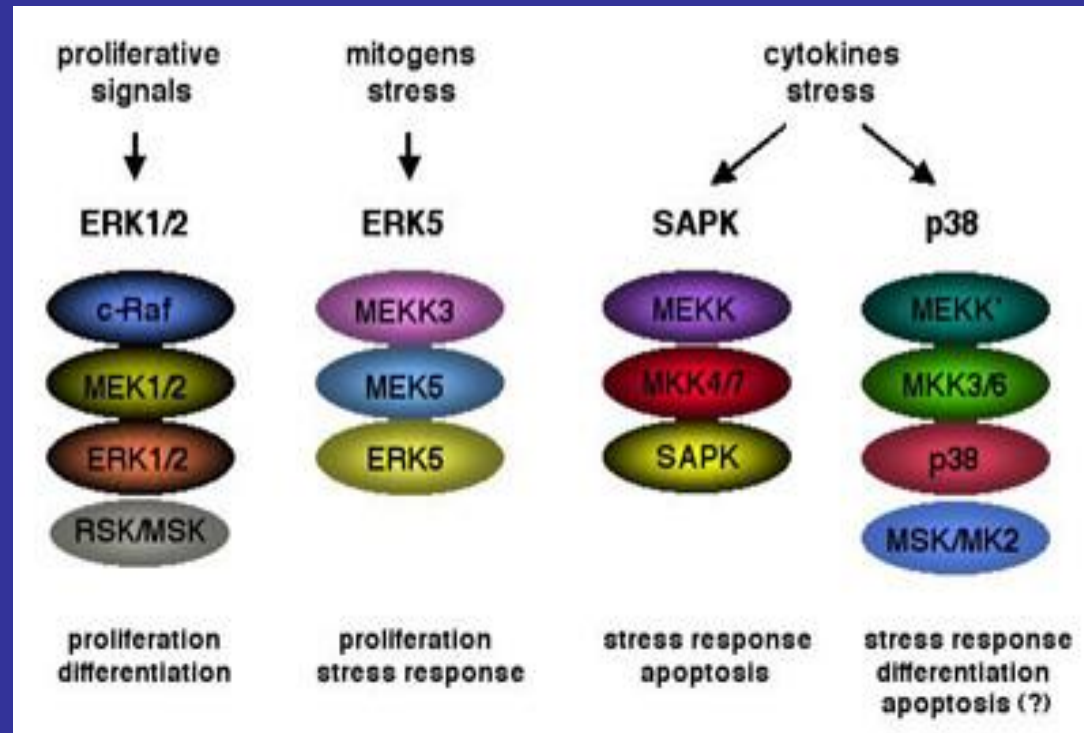
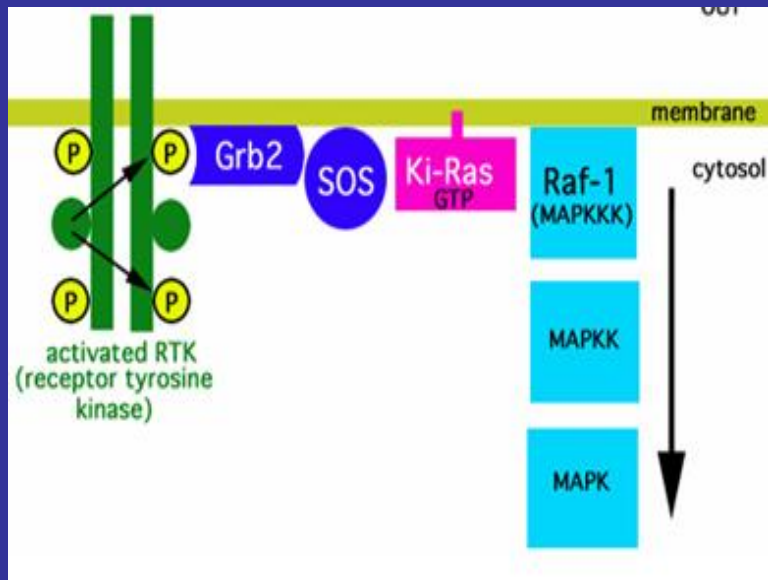


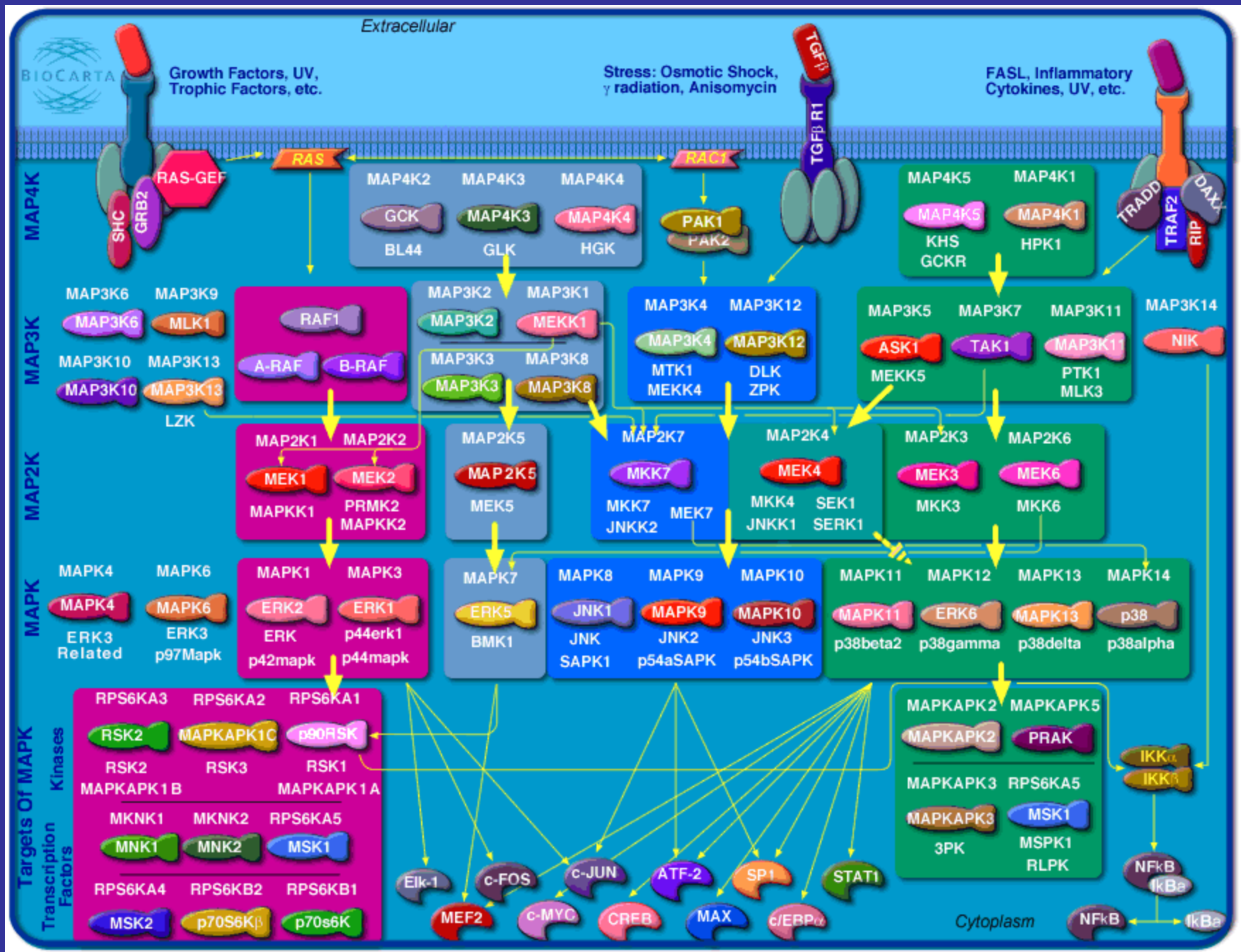
(b) Activation of the EGF receptor



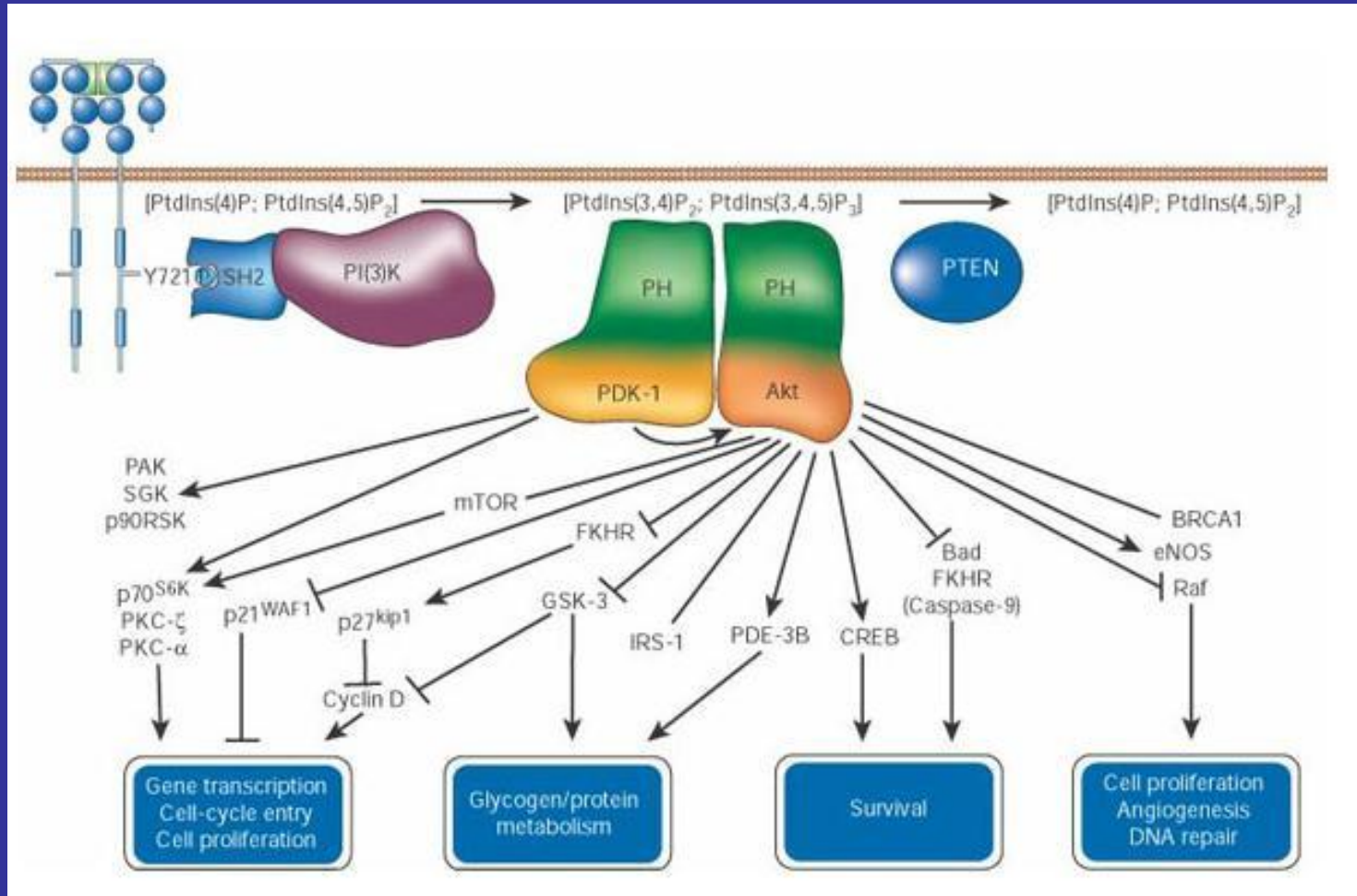
SH2 (Src homology) bölgesi içeren proteinler
 GRB2-Sos-Ras, PLC γ , p55-PI3K, Src

MAP Kinaz Aktivasyon Kaskadları

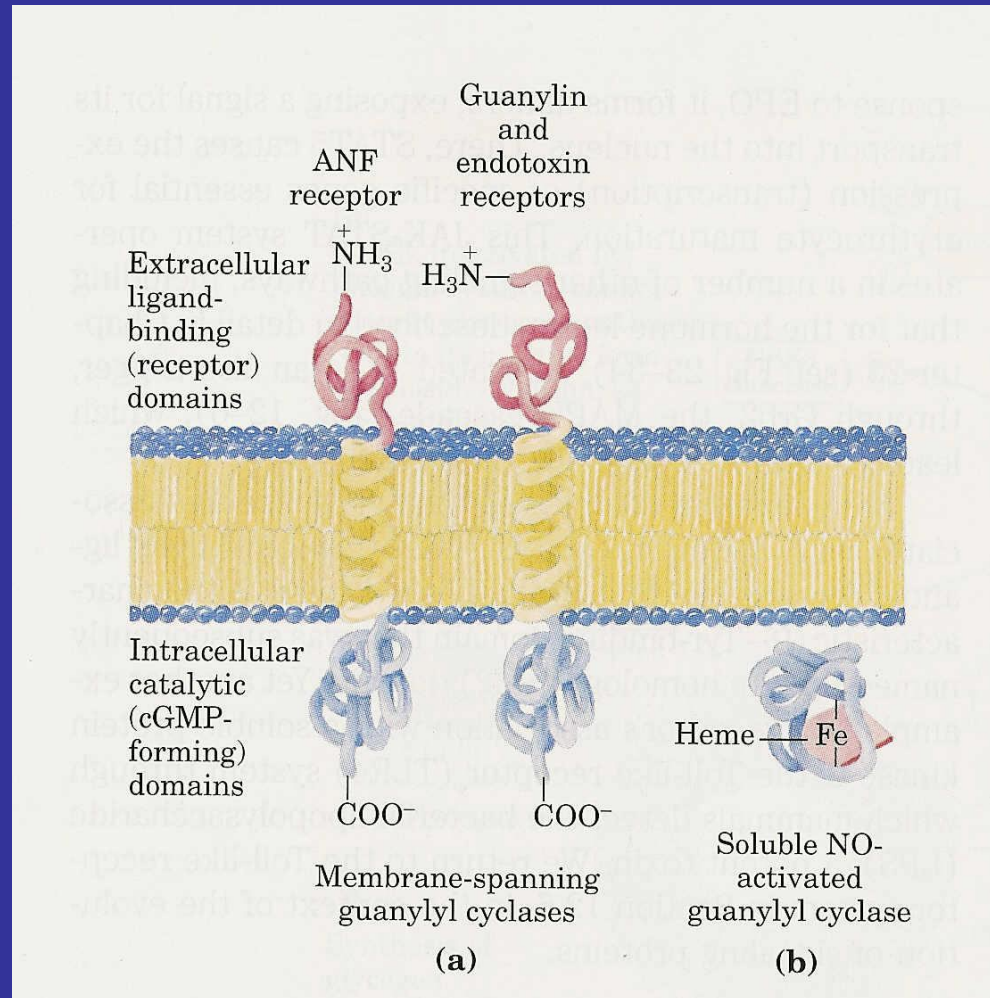




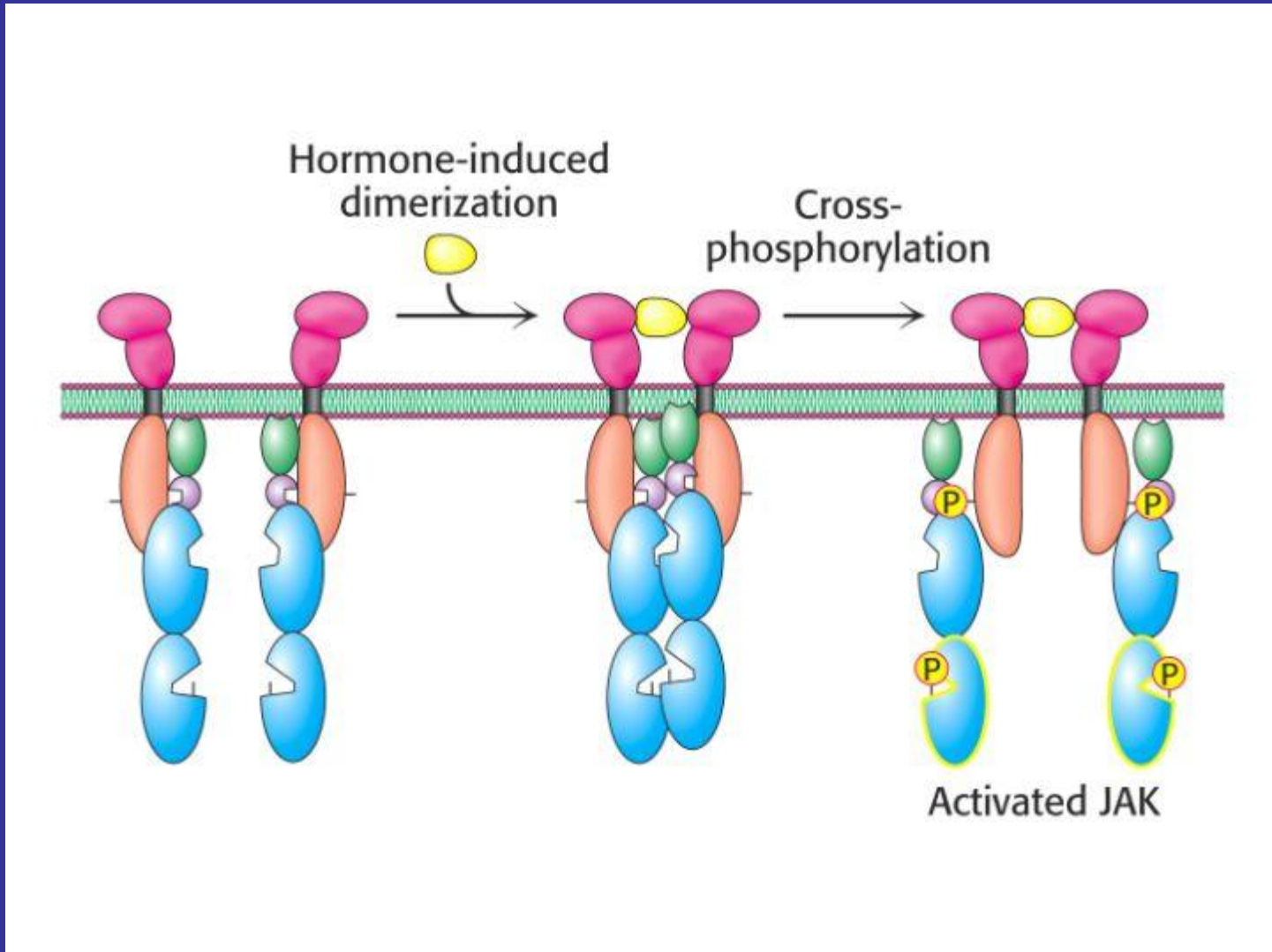
Protein Kinaz B (Akt) Aktivasyon Yolu

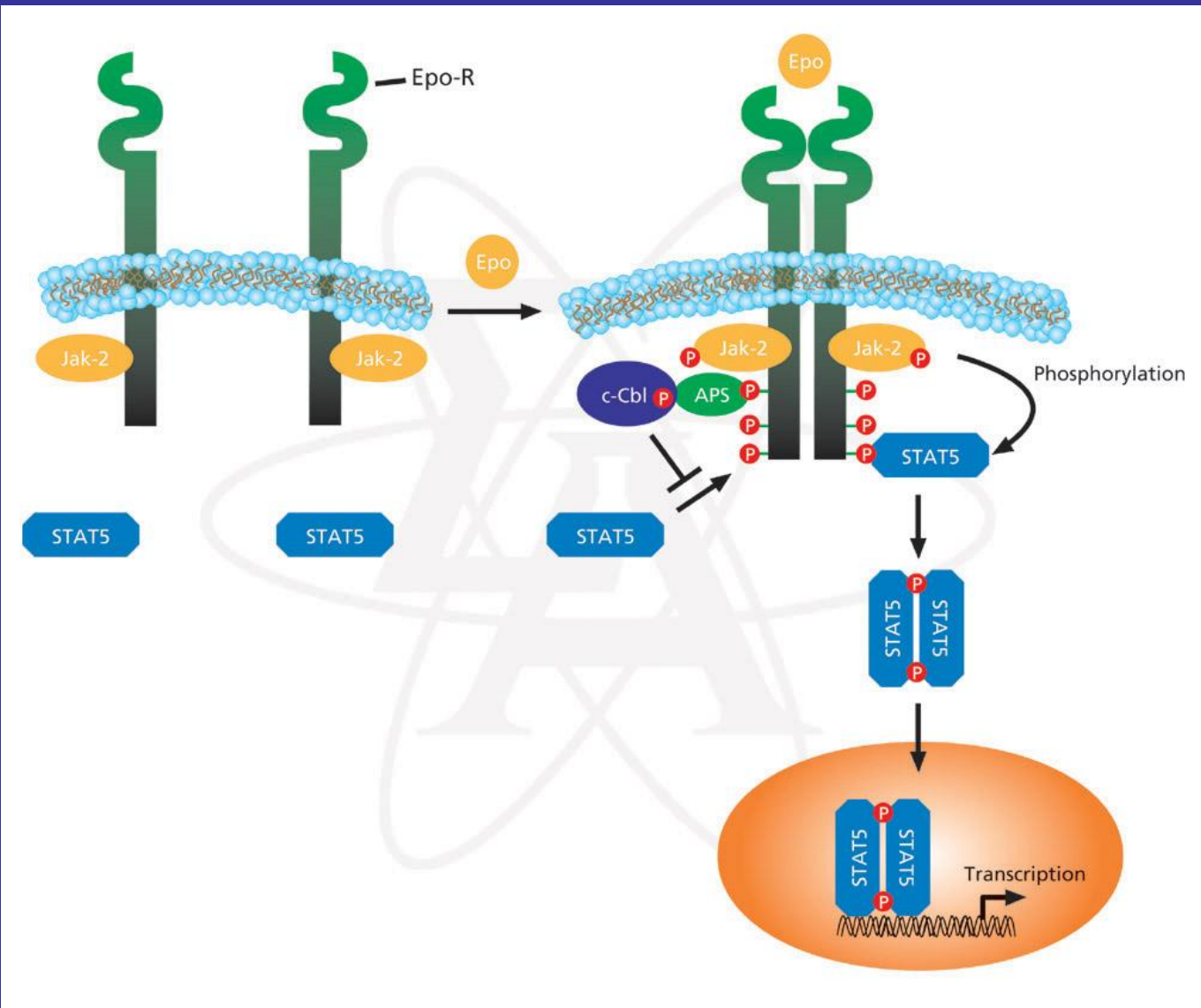


cGMP Oluşturan Reseptör Enzimler



Sitoplazmadaki Enzimleri Aktive Eden Reseptörler

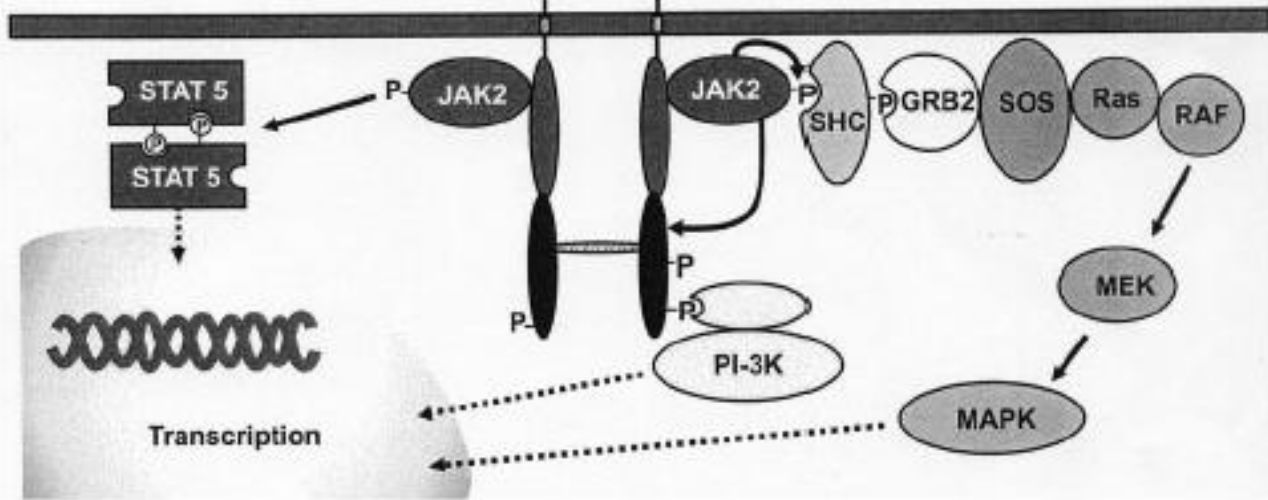




Cytokine receptor class I



- Homodimerization
- JAK2 phosphorylation
- Tyrosine phosphorylation of EPO receptor and cytosolic signal transducers
- Activation of transcription factors (STAT5) and enzymes (PI-3K, MAPK)
- Survival, proliferation, differentiation



Transcription

Sinyalin Sonlandırılması

- Reseptör düzeyinde inaktivasyon
 - Reseptör fosforilasyonu
 - Reseptörün endositozla hücre içine alınıp yıkılması
- Efektörler düzeyinde inaktivasyon
 - Efektörlerin defosforilasyonu

Hücre tipleri	200
Genler	~ 25000
Alternatif “splicing” yapılan genler	%40-60
Protein başına ortalama translasyon sonrası değişiklik	2,5
Transkripsiyon faktörü genleri	1850
Protein kinaz genleri	518
Protein fosfataz genleri	150
Reseptör genleri	1543

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[RNA sequence Databases](#)

[Protein sequence Databases](#)

[Structure Databases](#)

[Genomics Databases \(non-vertebrate\)](#)

[Metabolic and Signaling Pathways](#)

[Human and other Vertebrate Genomes](#)

[Human Genes and Diseases](#)

[Microarray Data and other Gene Expression Databases](#)

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