Cell Signaling and Regulation of Metabolism

By

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Objectives

- Different steps in signaling pathways
- The second messenger systems
- Function of signaling pathways for
  - Signal transmission
  - Amplification
- The role signaling pathways in regulation and integration of metabolism

No cell lives in isolation

- **Cells communicate with each other**
- **Cells send and receive information (signals)**
- **Information is relayed within cell to produce a response**

Signaling Process

- **Recognition of signal**
  - **Receptors**
- **Transduction**
  - **Change of external signal into intracellular message with amplification and formation of second messenger**
- **Effect**
  - **Modification of cell metabolism and function**

Signaling Process

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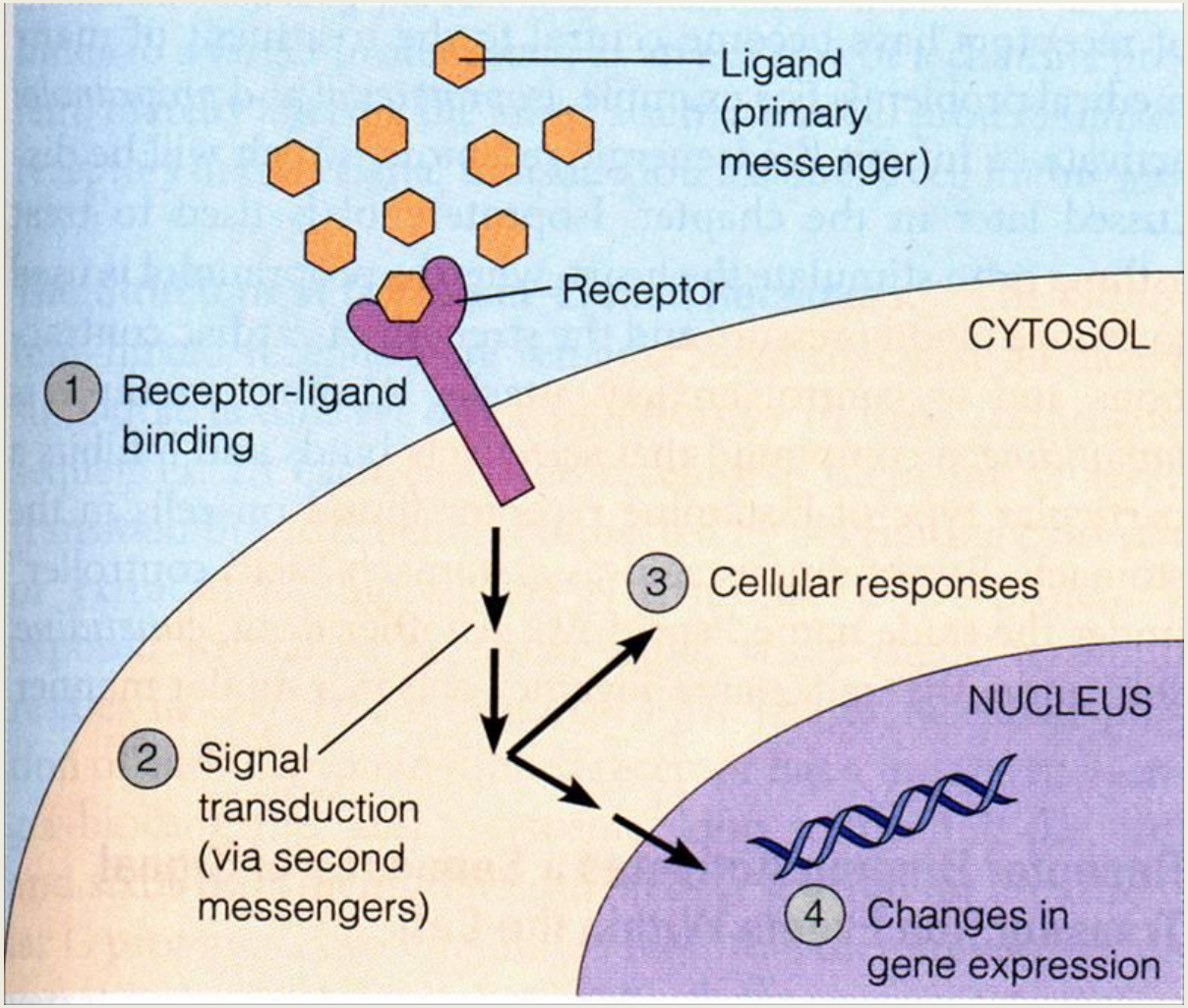
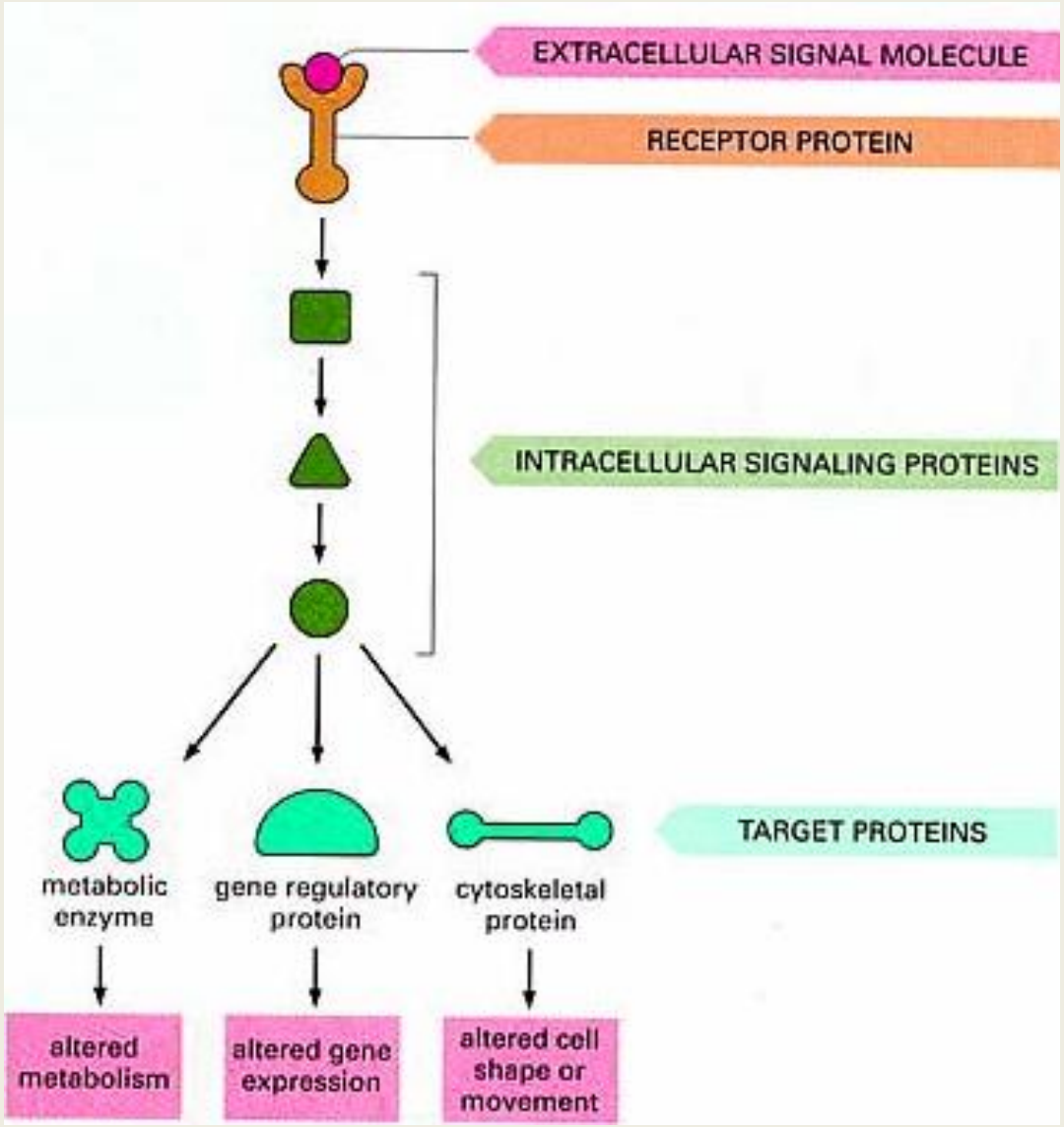
General Signaling Pathway



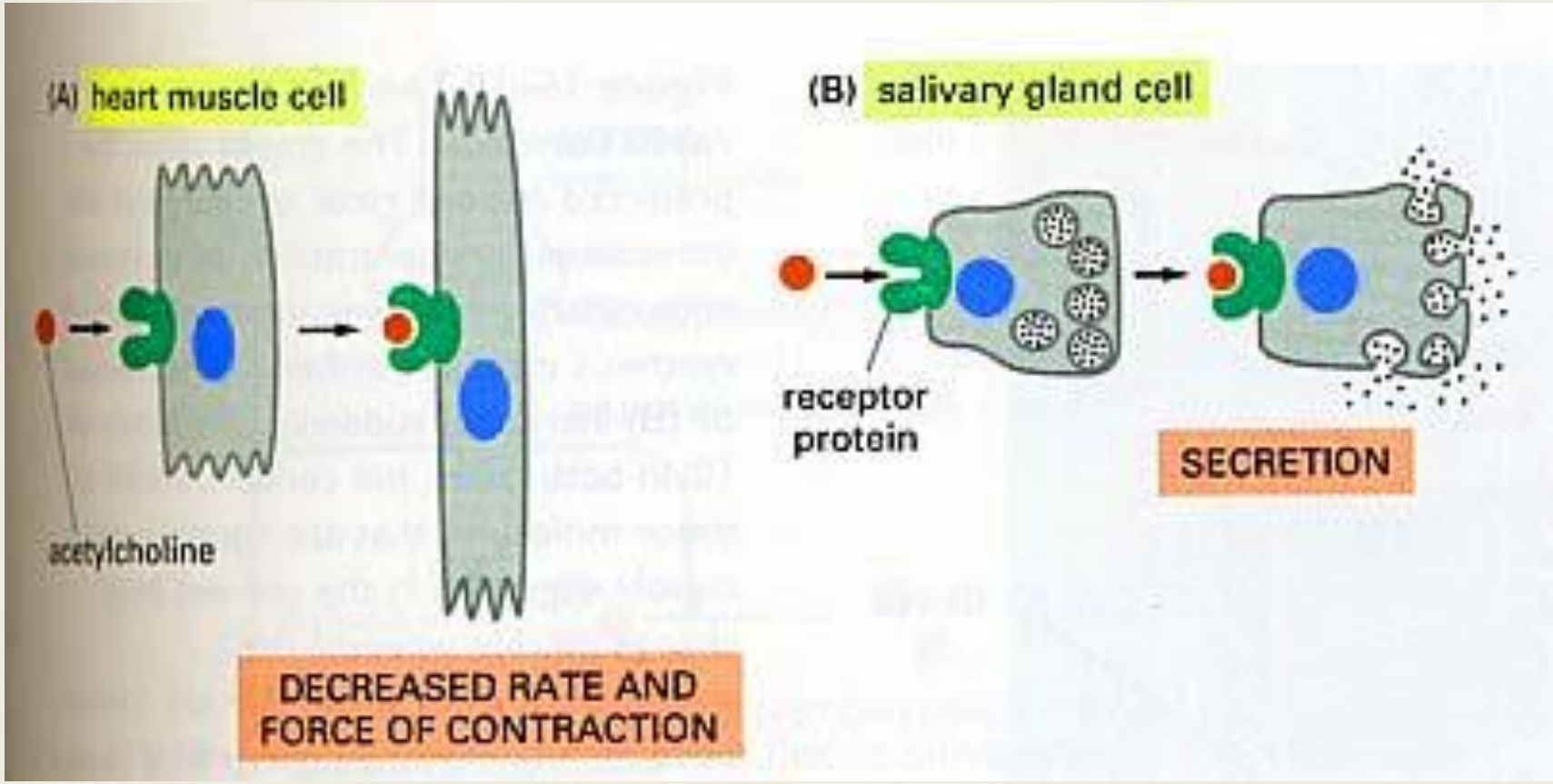
Signaling Cascades



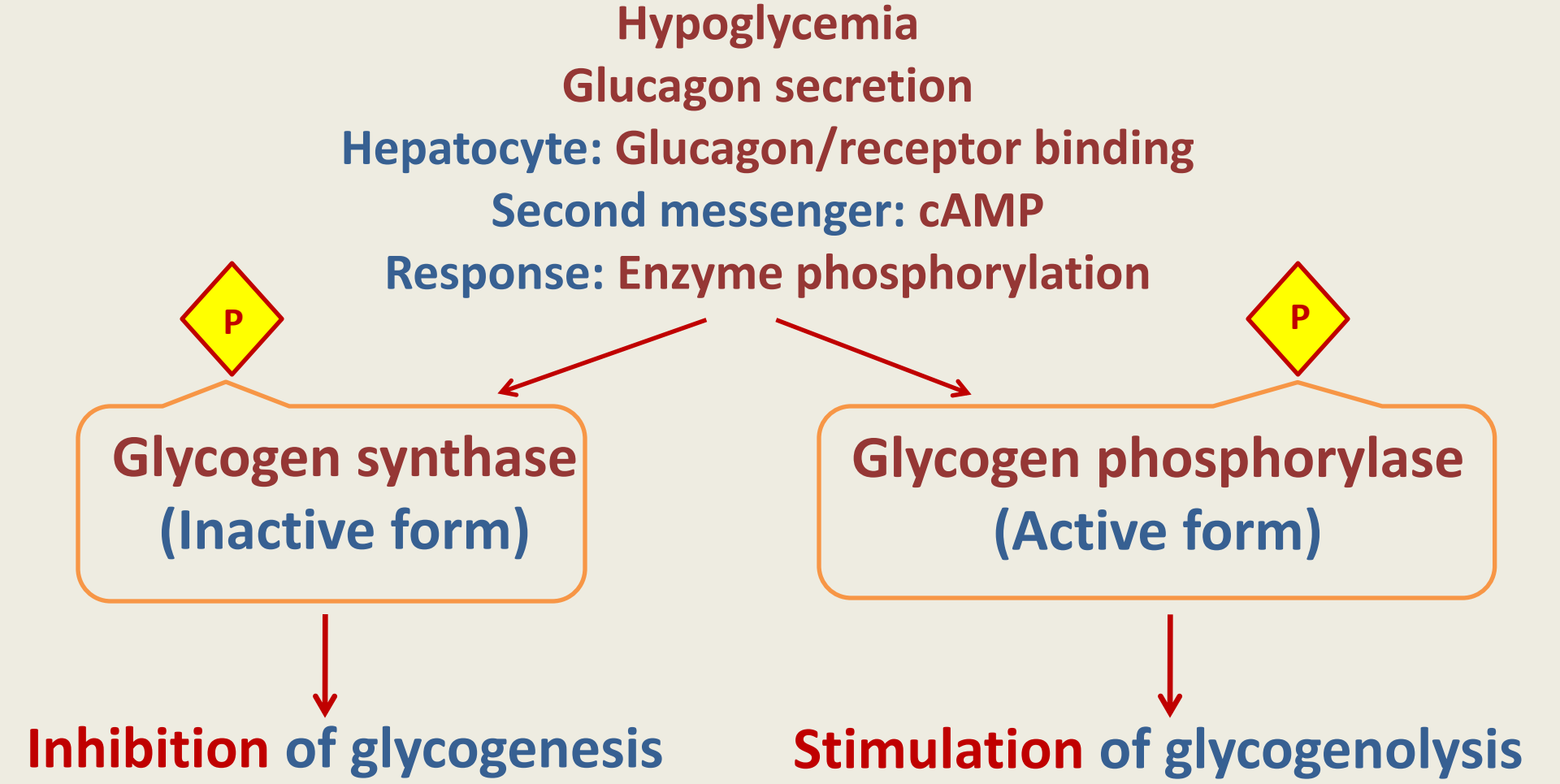
Recognition

- **Performed by receptors**
- **Ligand will produce response only in cells that have receptors for this particular ligand**
- **Each cell has a specific set of receptors**

Different Responses to the Same Signaling Molecule
(A) Different Cells



Different Responses to the Same Signaling Molecule
(B) One Cell but, Different Pathways



GTP-Dependant Regulatory Proteins (G-Proteins)

G-Proteins: Trimeric membrane proteins (αβγ)
G-stimulatory (G_s) and G-inhibitory (G_i)
Binds to GTP/GDP

Forms of G-Proteins

Inactive form
Trimeric –bound GDP
(αβγ/GDP)

Active form
α-bound GTP
(α/GTP)

The α-subunit has intrinsic GTPase activity, resulting in hydrolysis of GTP into GDP and inactivation of G-proteins

Signaling Pathways for Regulation of Metabolism

Two important second messenger systems:

Adenylyl cyclase system

Calcium/phosphatidylinositol system

Adenylyl cyclase

Adenylyl cyclase: Membrane-bound enzyme
Converts ATP to cAMP

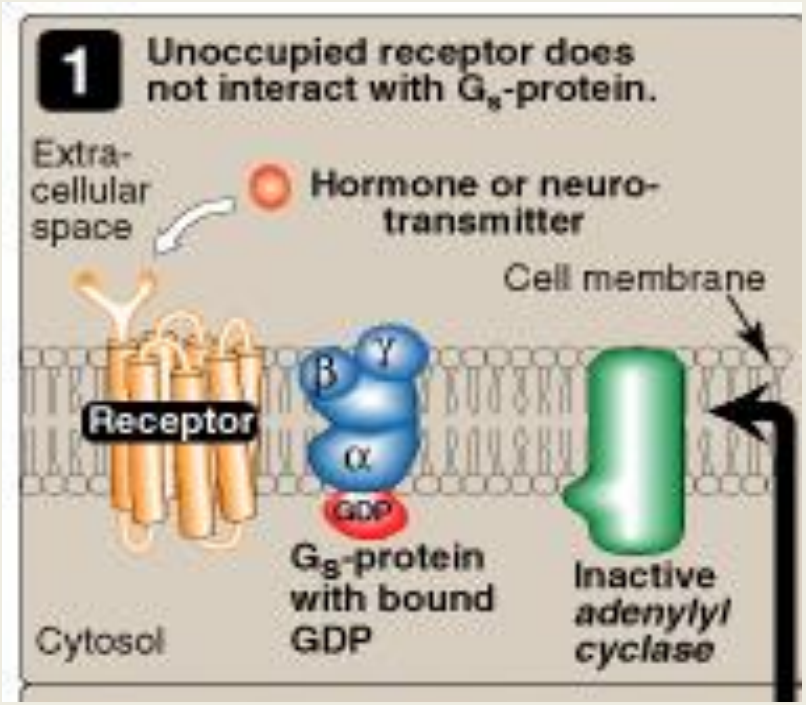
Activation/Inhibition:

Signal: Hormones or neurotransmitters
(e.g., Glucagon and epinephrine)
or Toxins
(e.g., Cholera and pertussis toxins)

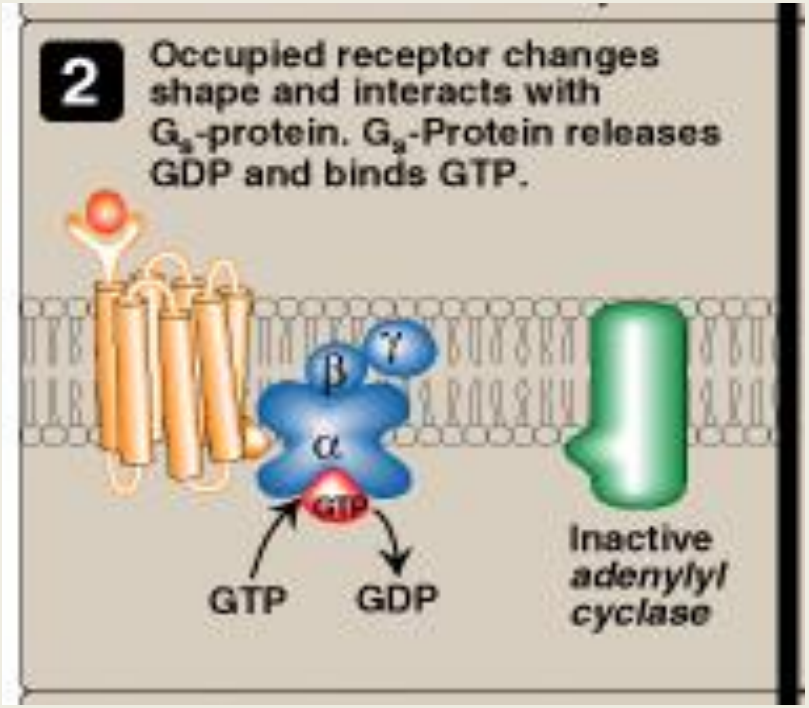
Receptor: G-protein coupled receptor

Response: Activation/inhibition of protein kinase A
(cAMP-dependent protein kinase)

Signal Transduction: Adenylyl Cyclase System



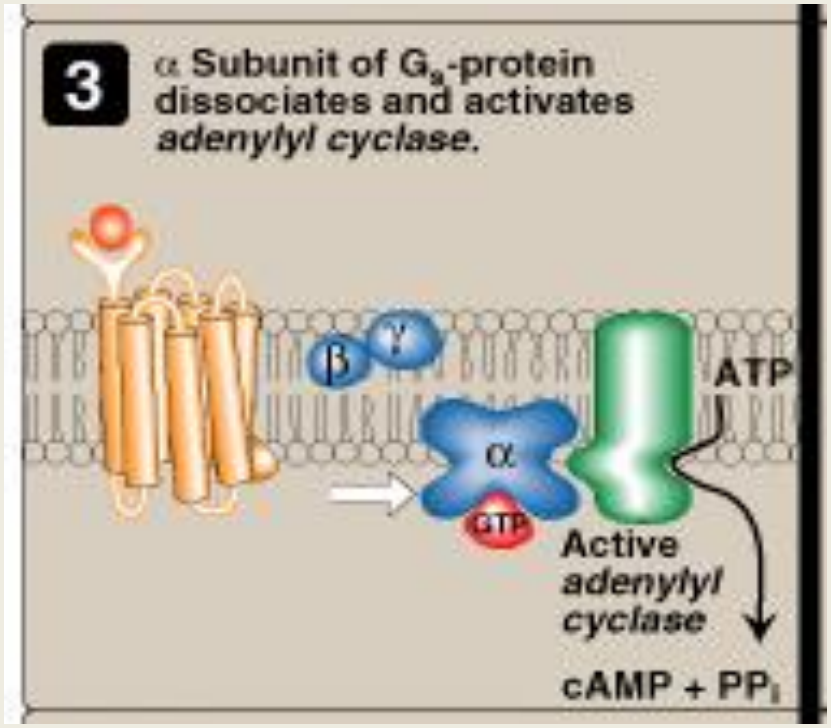
Resting state: No Signal



Ligand/Receptor Binding

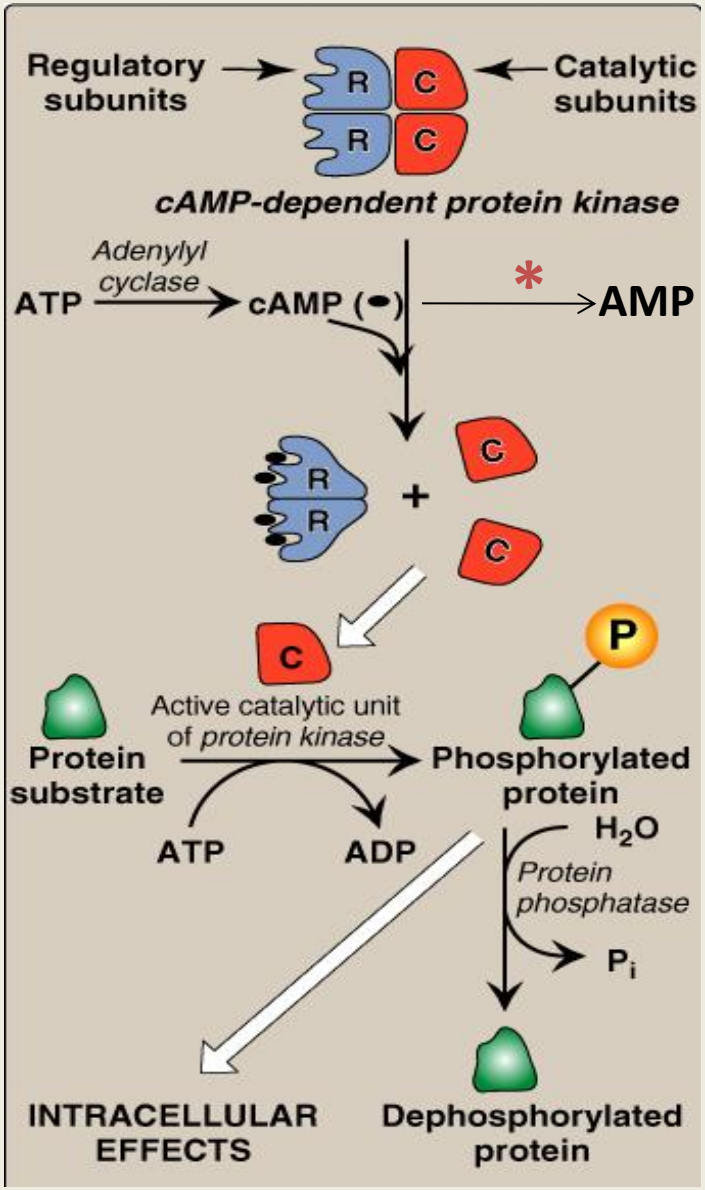
Activation of G_s-protein

Signal Transduction: Adenylyl Cyclase System



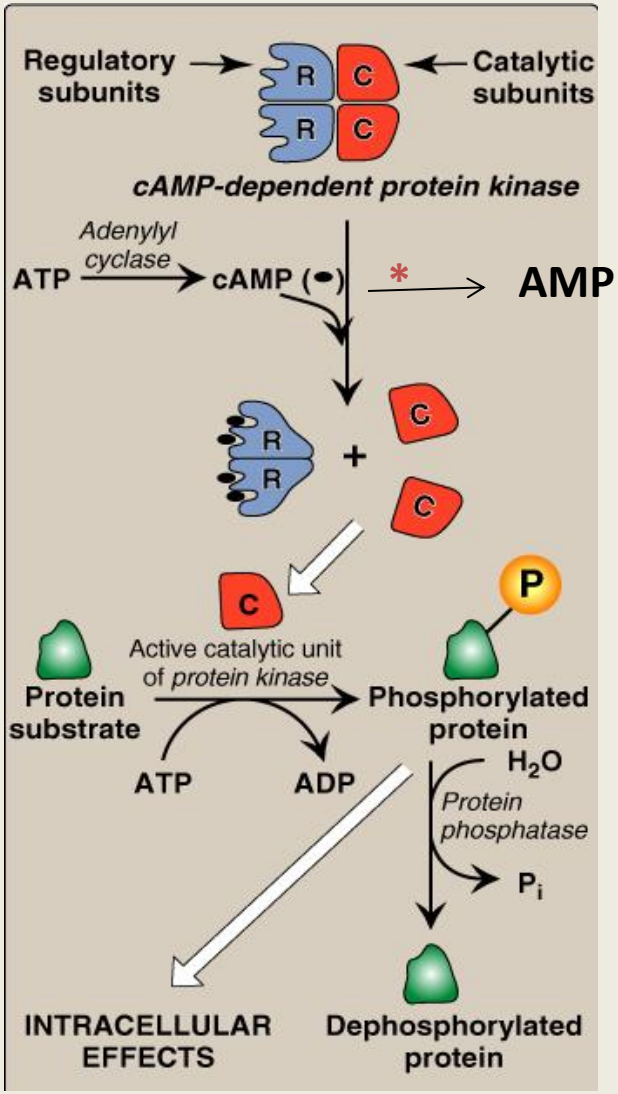
Activation of adenylyl cyclase

Adenylyl Cyclase System: cAMP-Dependent Protein Kinase (Protein Kinase A)



*Phosphodiesterase

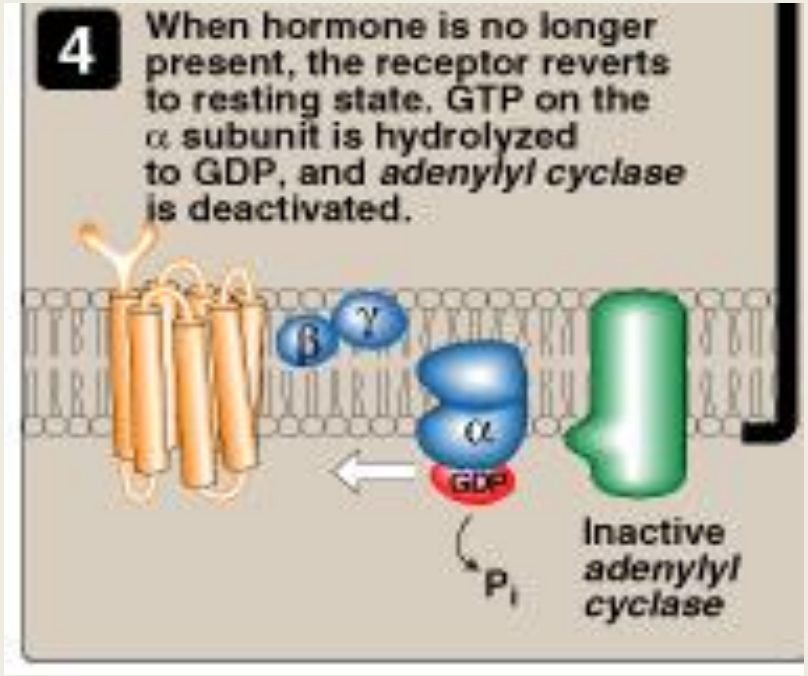
Termination of Signal (A)



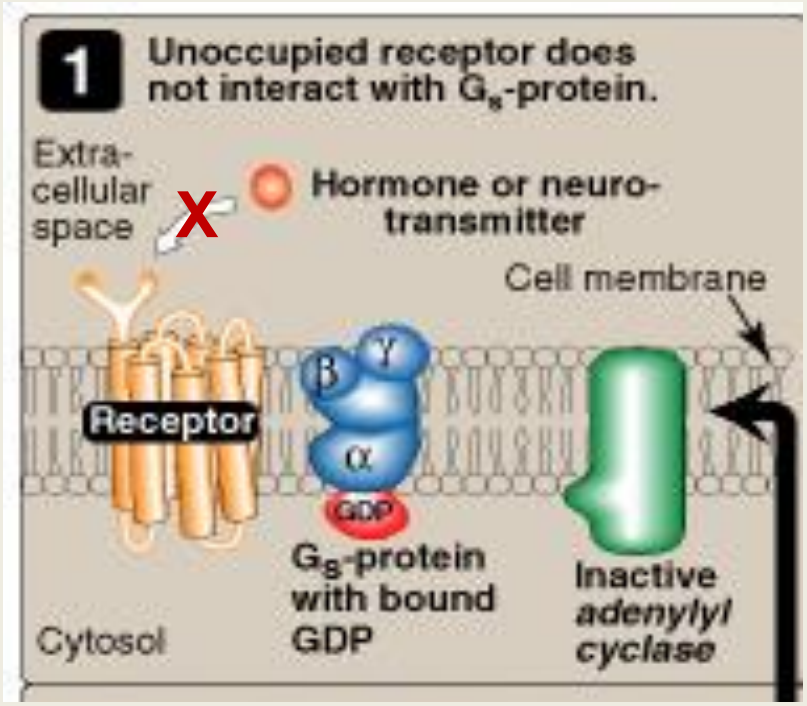
*Phosphodiesterase

- Protein phosphatase
- Phosphodiesterase → ↓cAMP → Inactive protein kinase

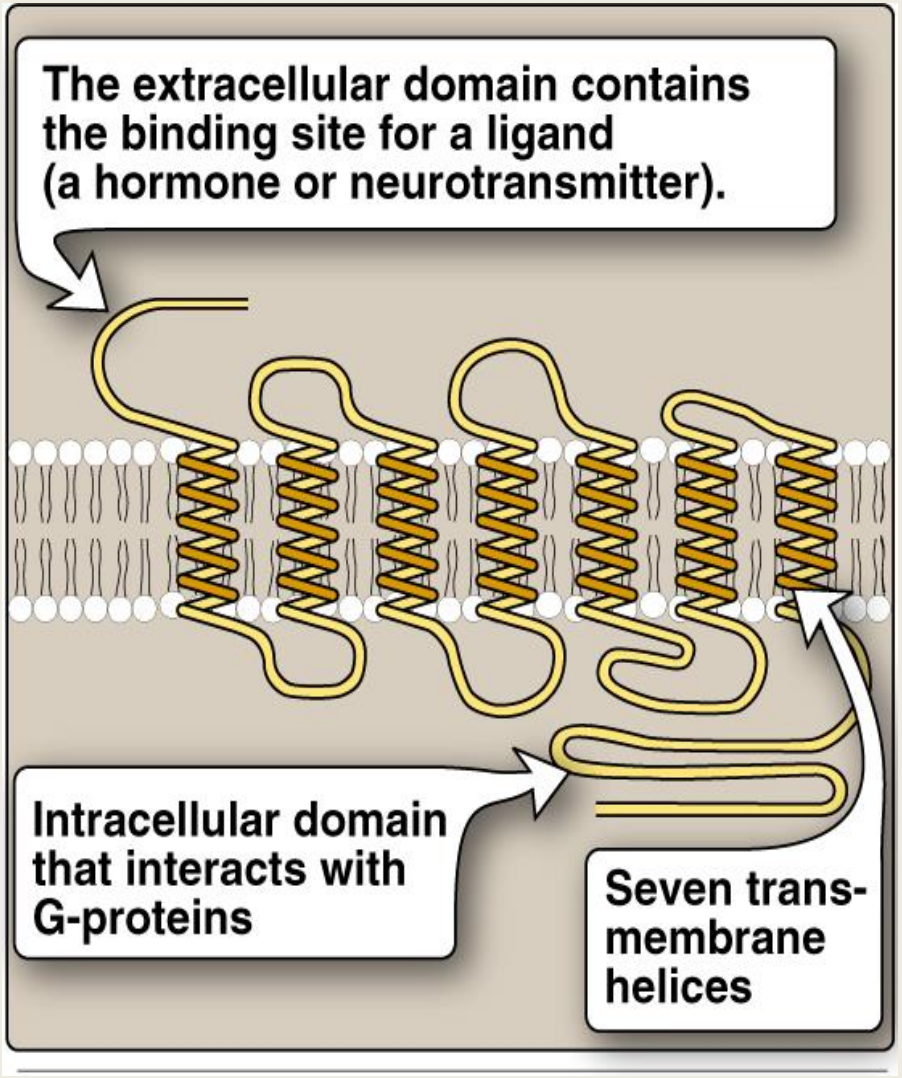
Termination of Signal (B)



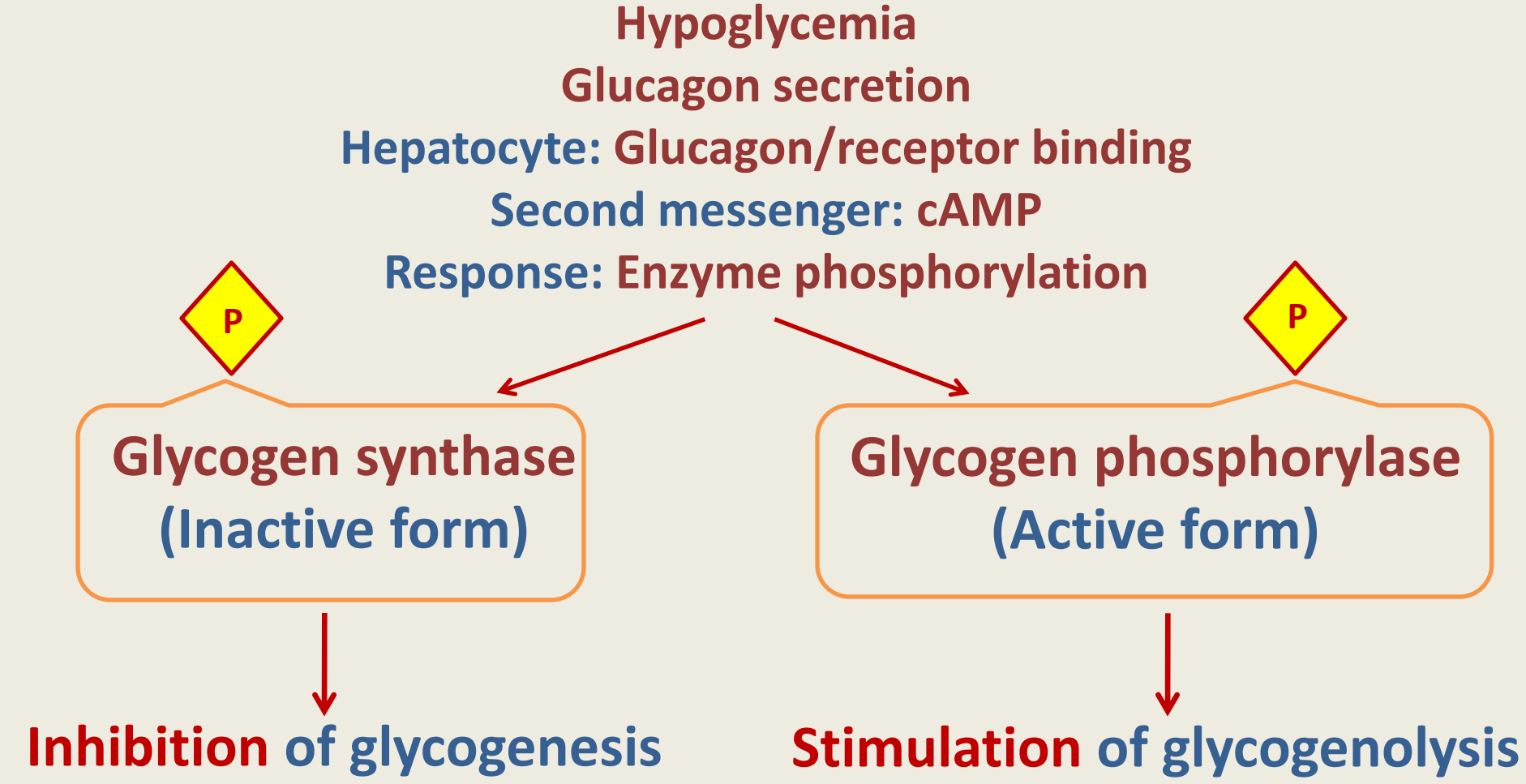
Termination of Signal (C)



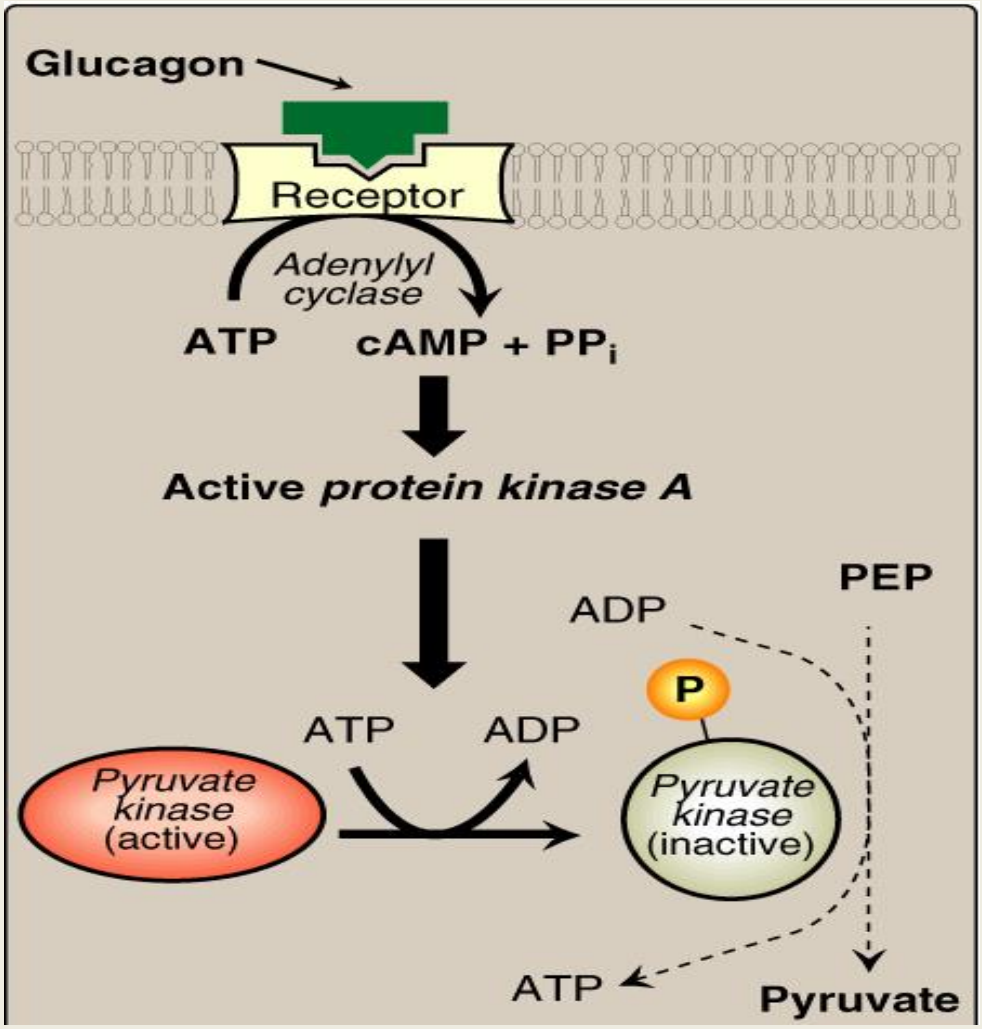
G-Protein Coupled Membrane Receptor



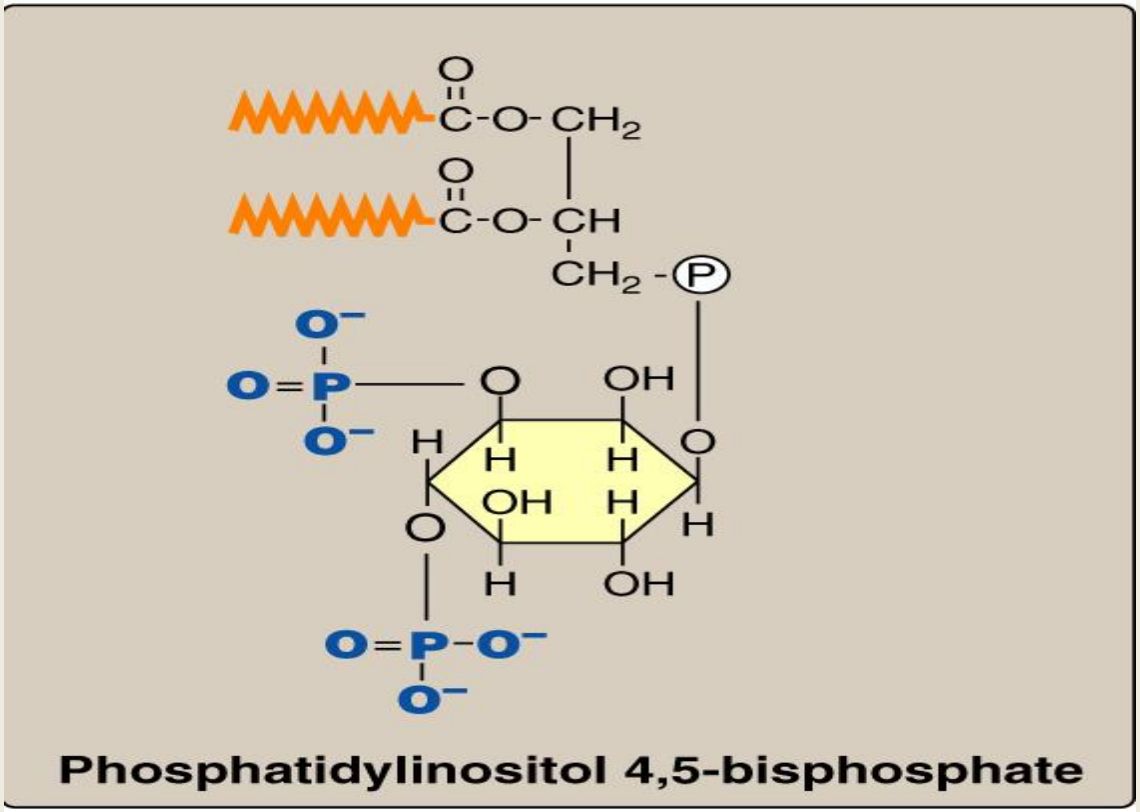
Regulation of Glycogen Metabolism by Glucagon: Effects on Glycogen Synthase and Phosphorylase



Pyruvate Kinase Regulation: Covalent Modification



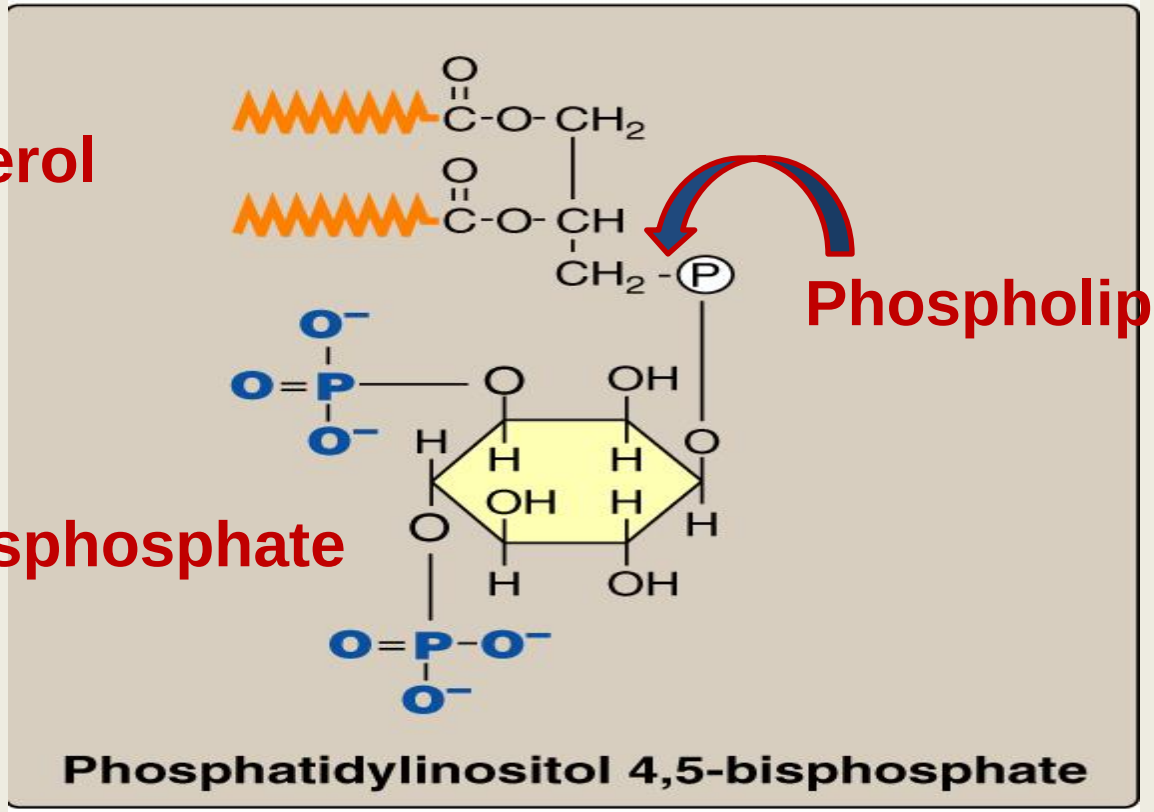
Calcium/Phosphatidylinositol System

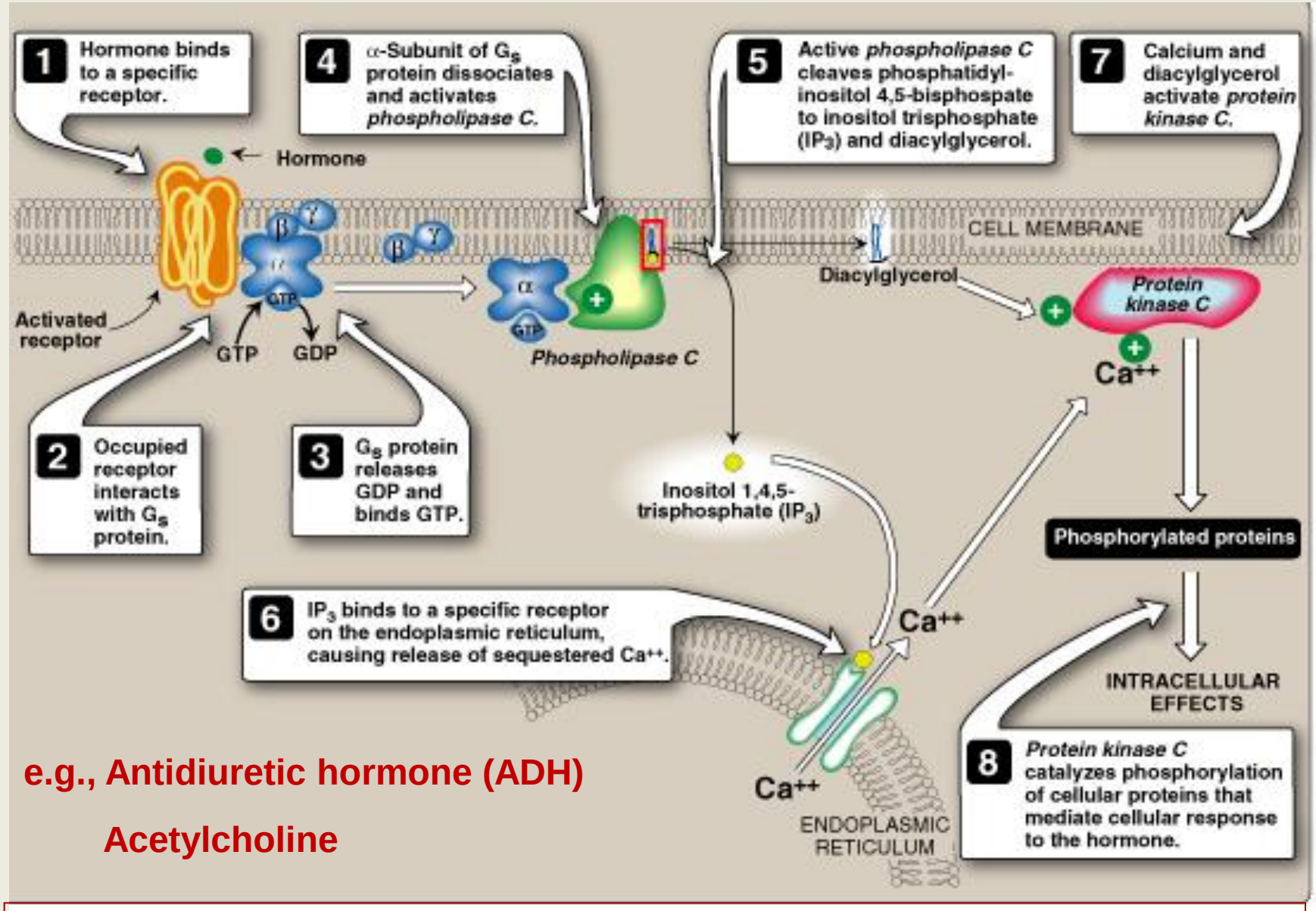


Calcium/Phosphatidylinositol System

Diacylglycerol (DAG)

Inositol Trisphosphate (IP_3)



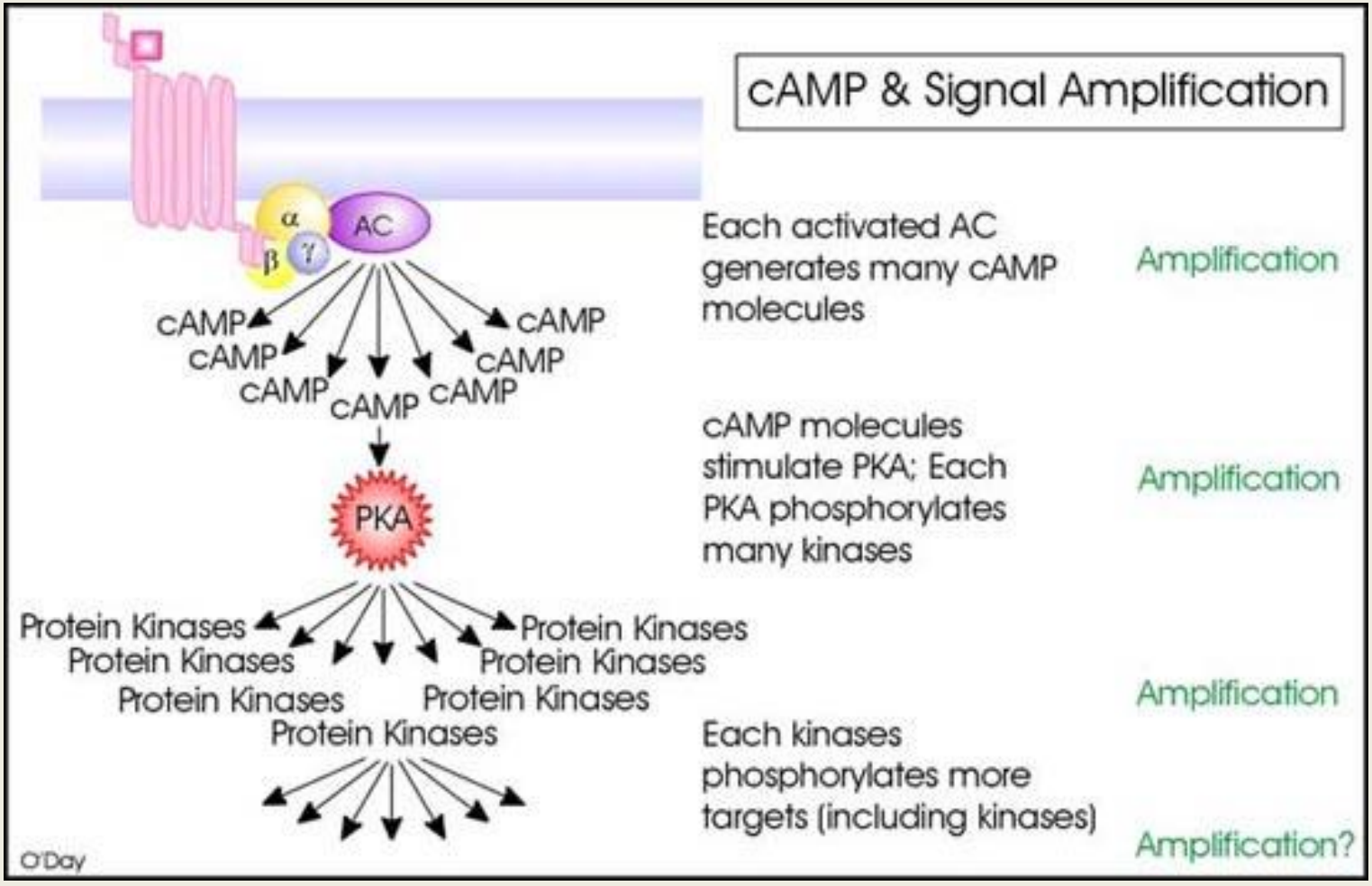


e.g., Antidiuretic hormone (ADH)

Acetylcholine

Intracellular Signaling by Inositol trisphosphate

Signal Amplification



Take Home Message

Cell signaling allows

- Signal transmission and amplification
- Regulation of metabolism
- Intercellular communications & coordination of complex biologic functions