

Cell Signaling and Regulation of Metabolism

By

Dr. Reem M. Sallam, *MD, PhD*

**Clinical Chemistry Unit
Department of Pathology**

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**



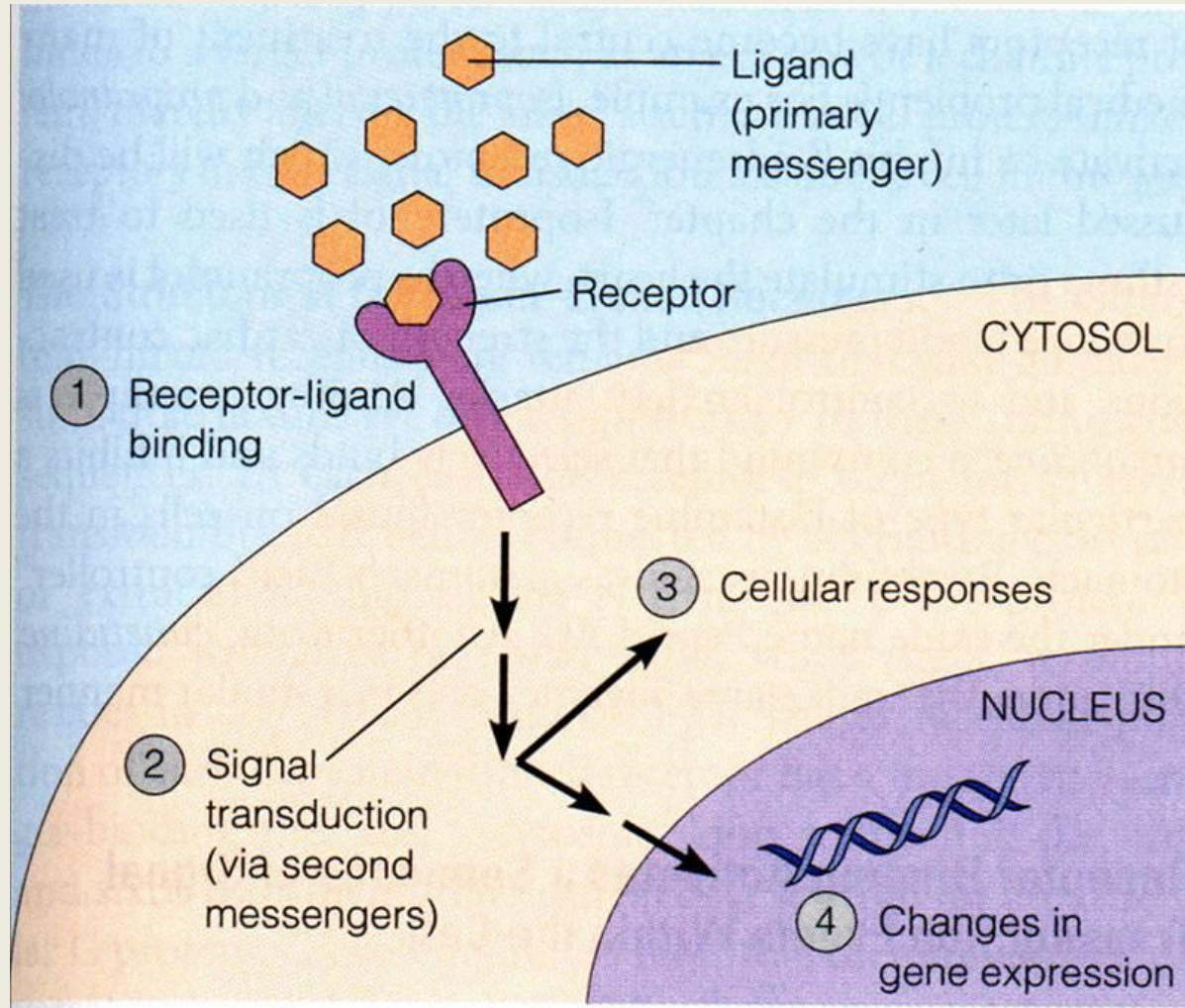
Signaling Process

- **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**

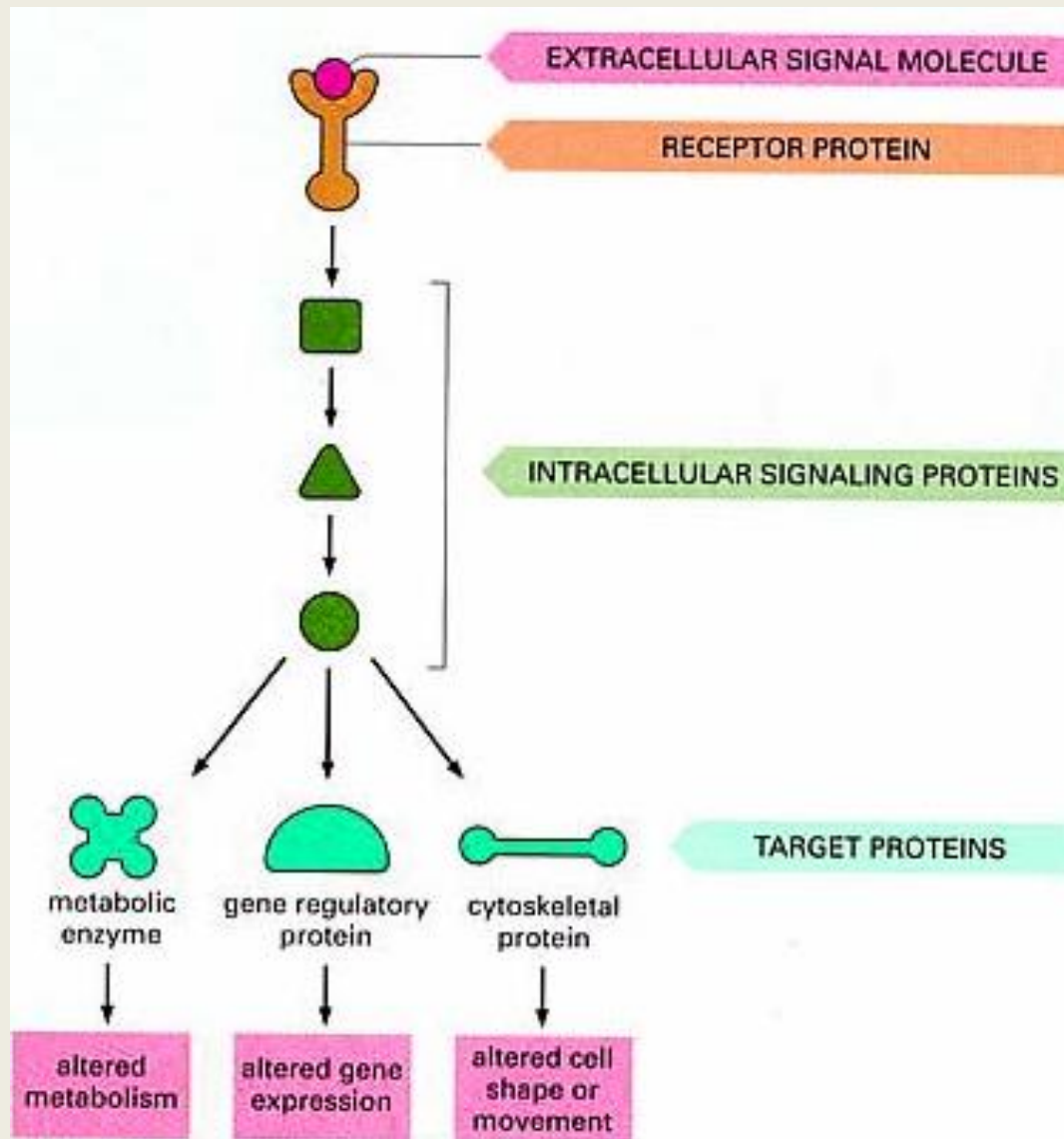
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General Signaling Pathway



Signaling Cascades

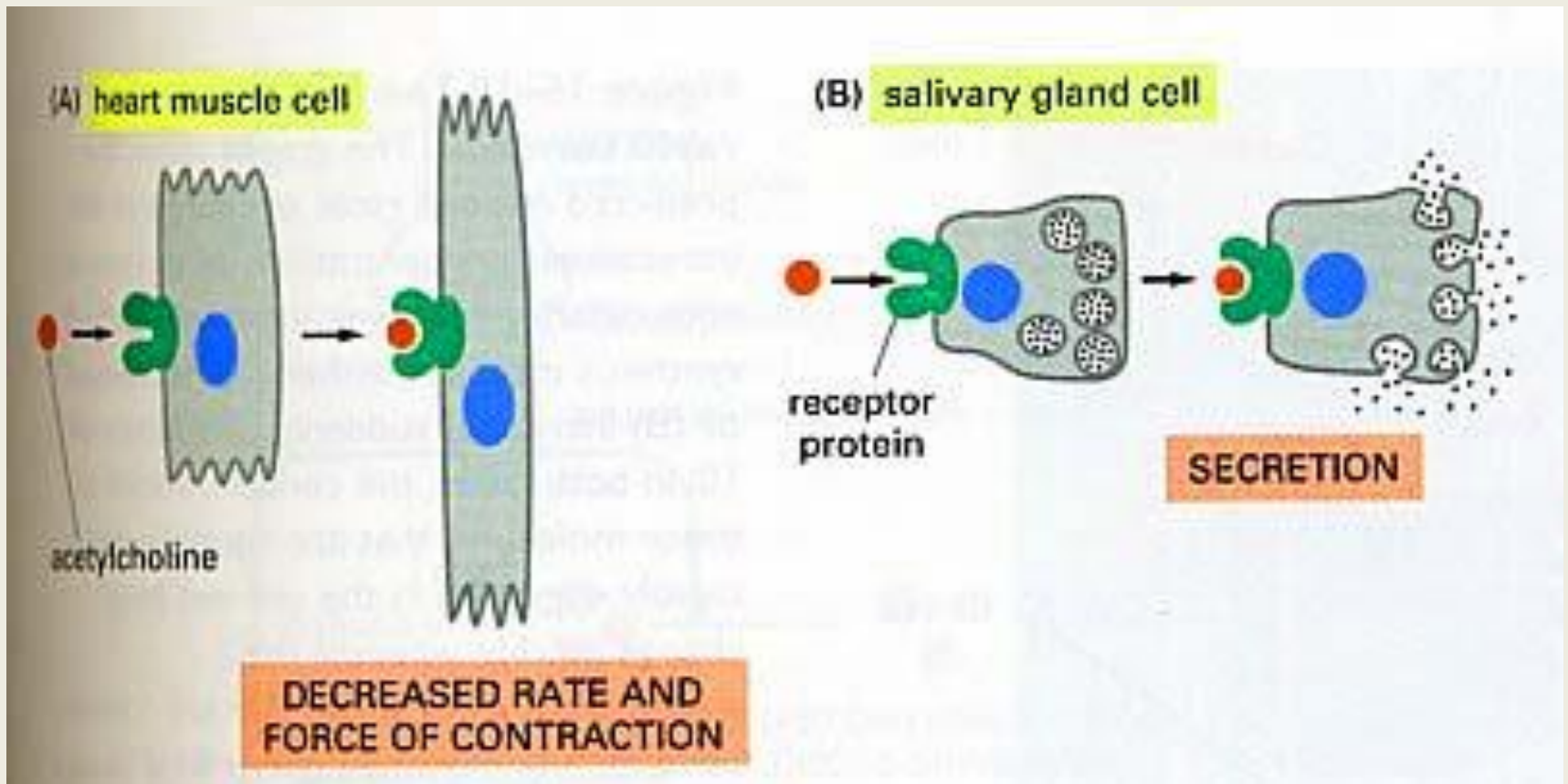


Recognition

- **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**

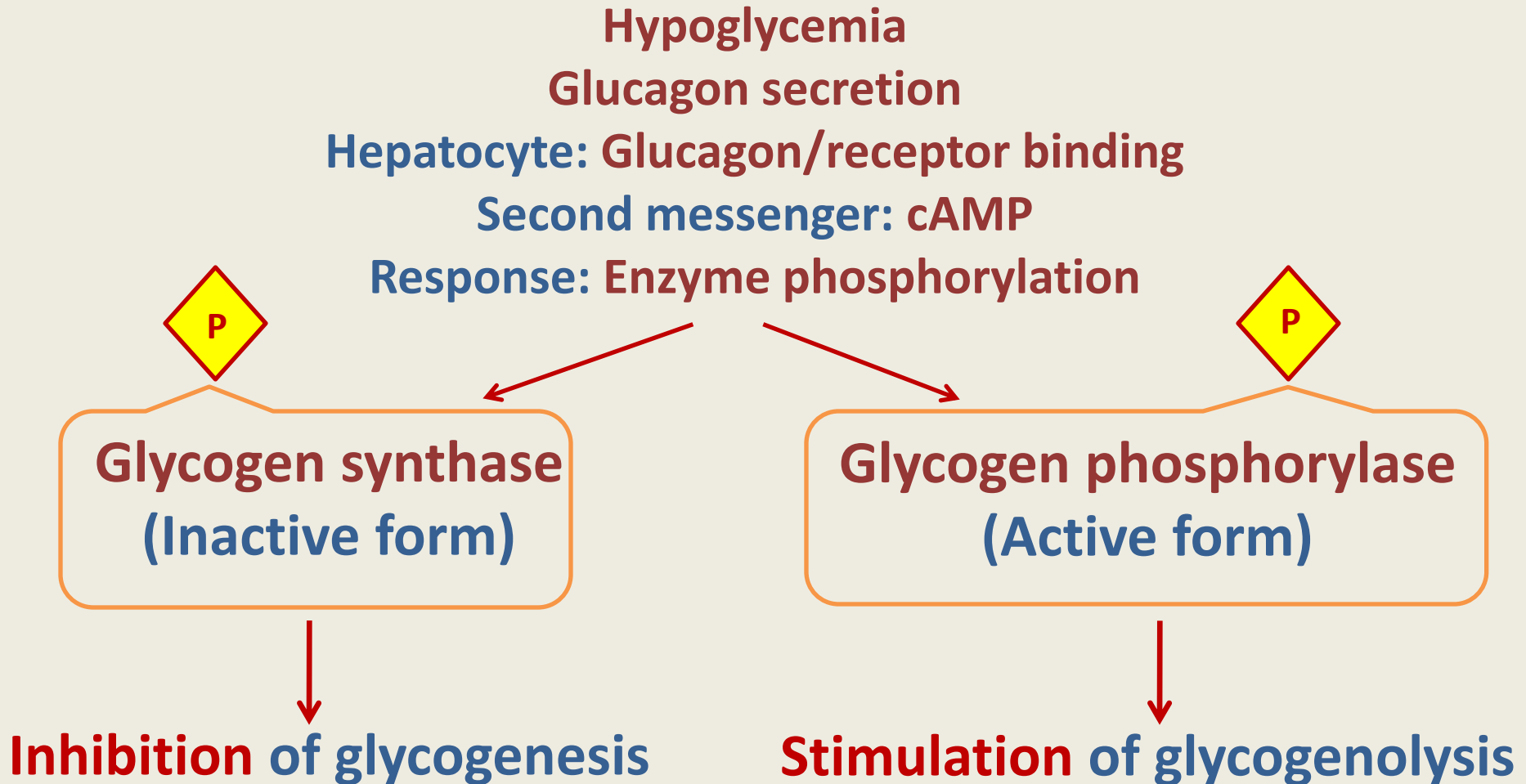
Different Responses to the Same Signaling Molecule

(A) Different Cells



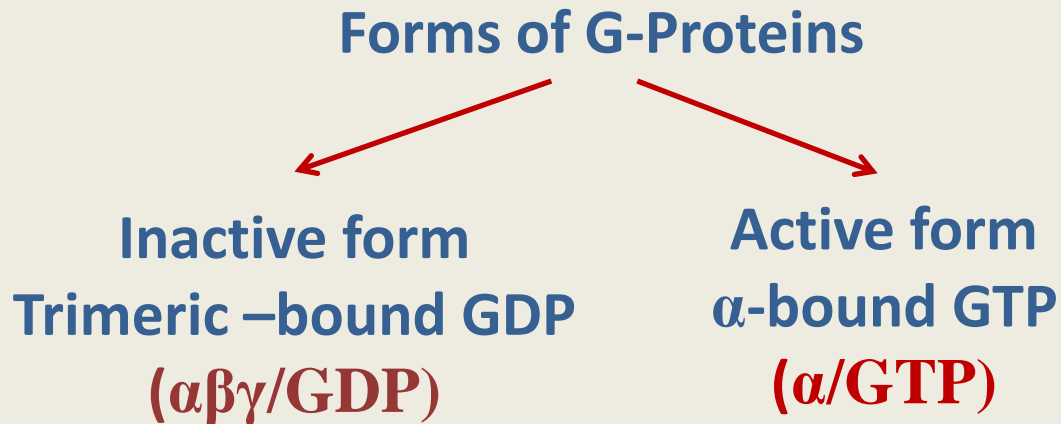
Different Responses to the Same Signaling Molecule

(B) One Cell but, Different Pathways



GTP-Dependant Regulatory Proteins (G-Proteins)

G-Proteins: Trimeric membrane proteins ($\alpha\beta\gamma$)
G-stimulatory (G_s) and G-inhibitory (G_i)
Binds to GTP/GDP



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

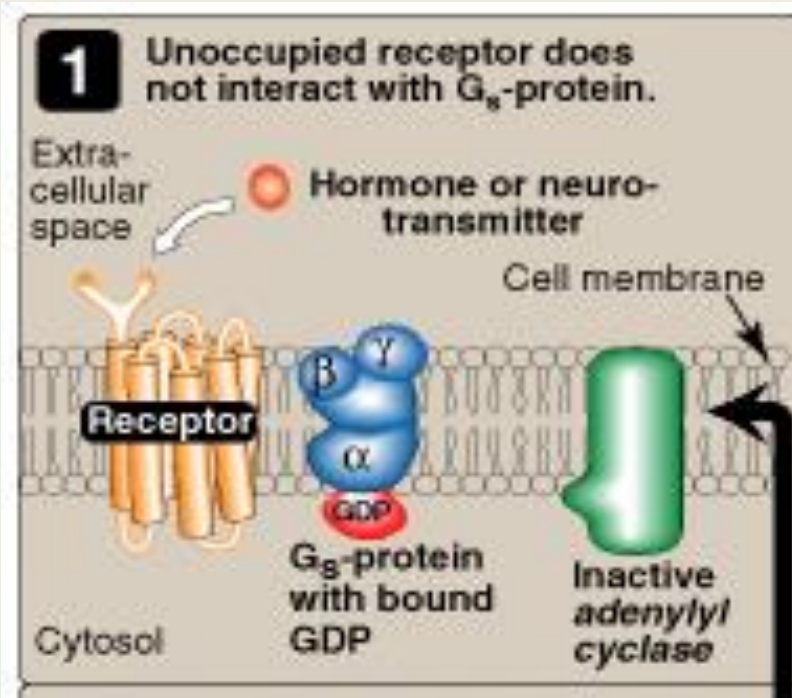
Activation/Inhibition:

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

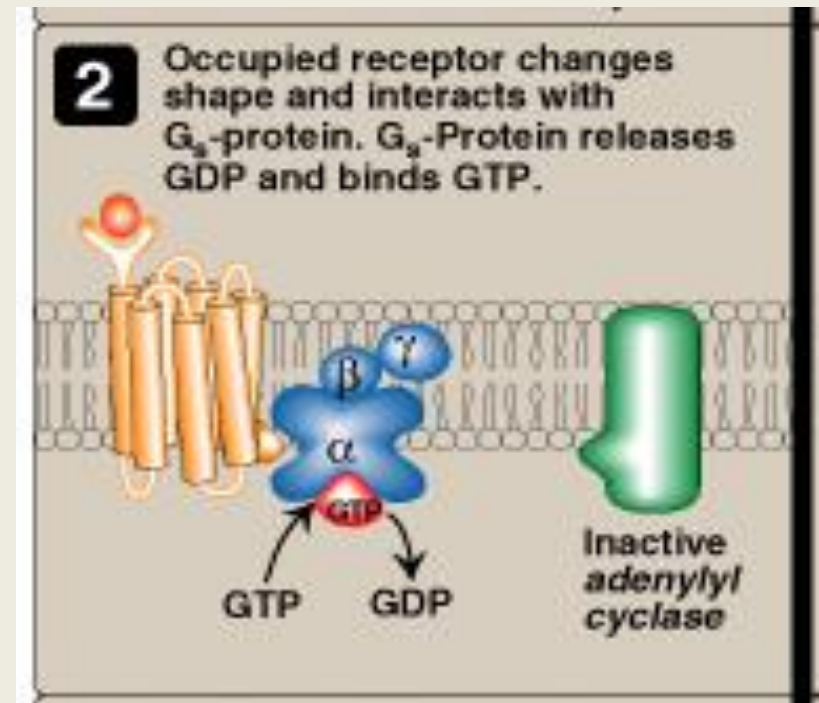
Receptor: G-protein coupled receptor

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

Signal Transduction: Adenylyl Cyclase System

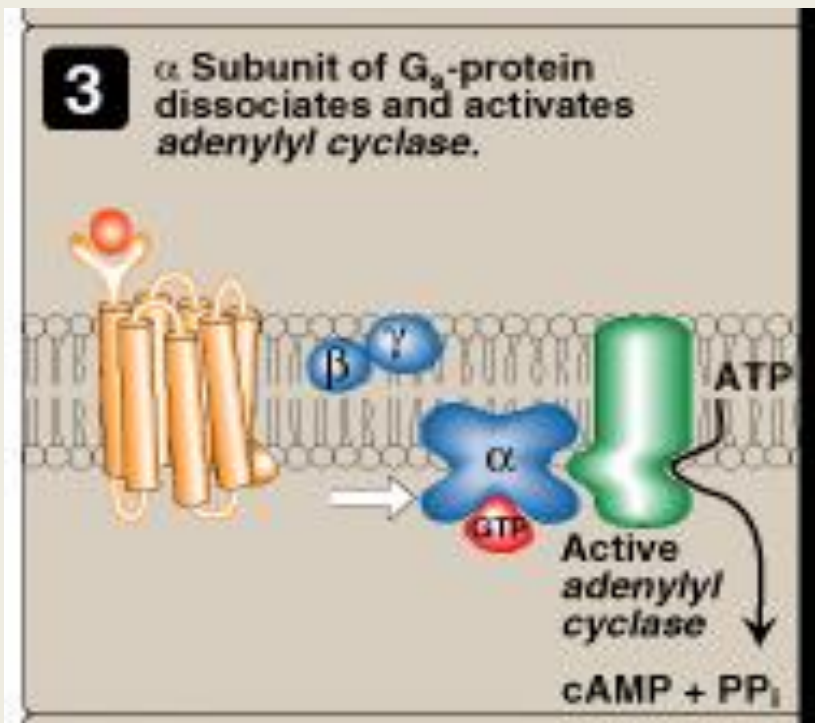


Resting state: No Signal



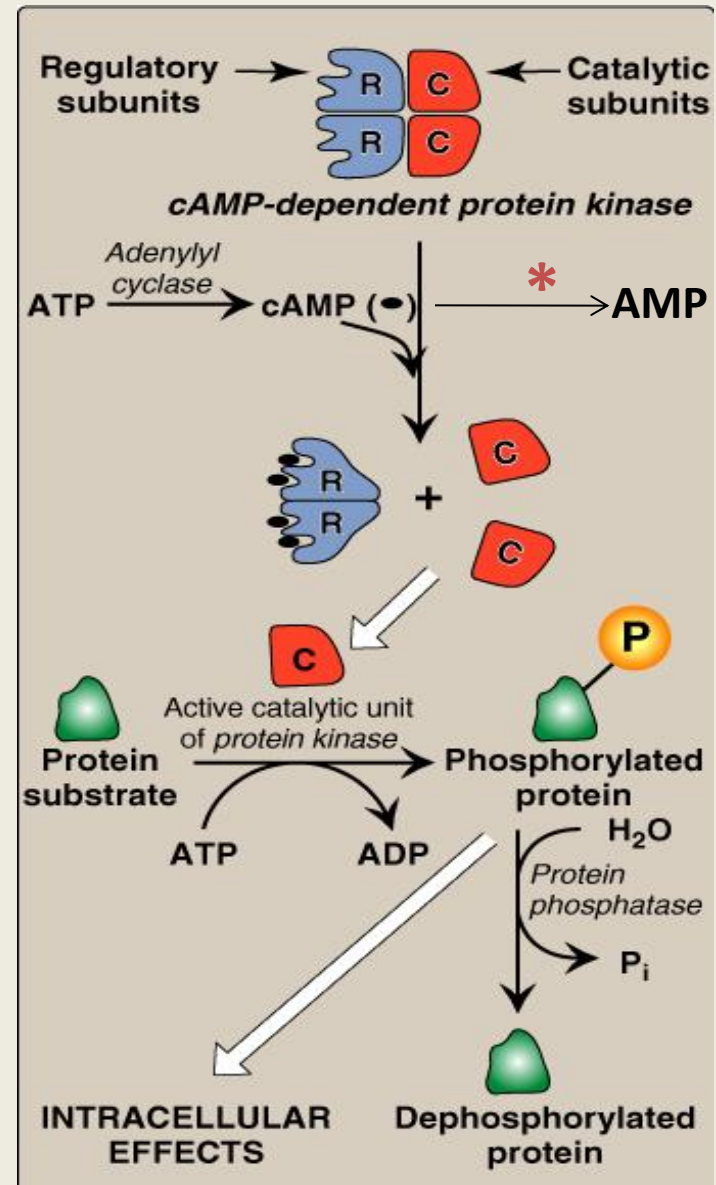
**Ligand/Receptor Binding
Activation of G_s -protein**

Signal Transduction: Adenylyl Cyclase System



Activation of adenylyl cyclase

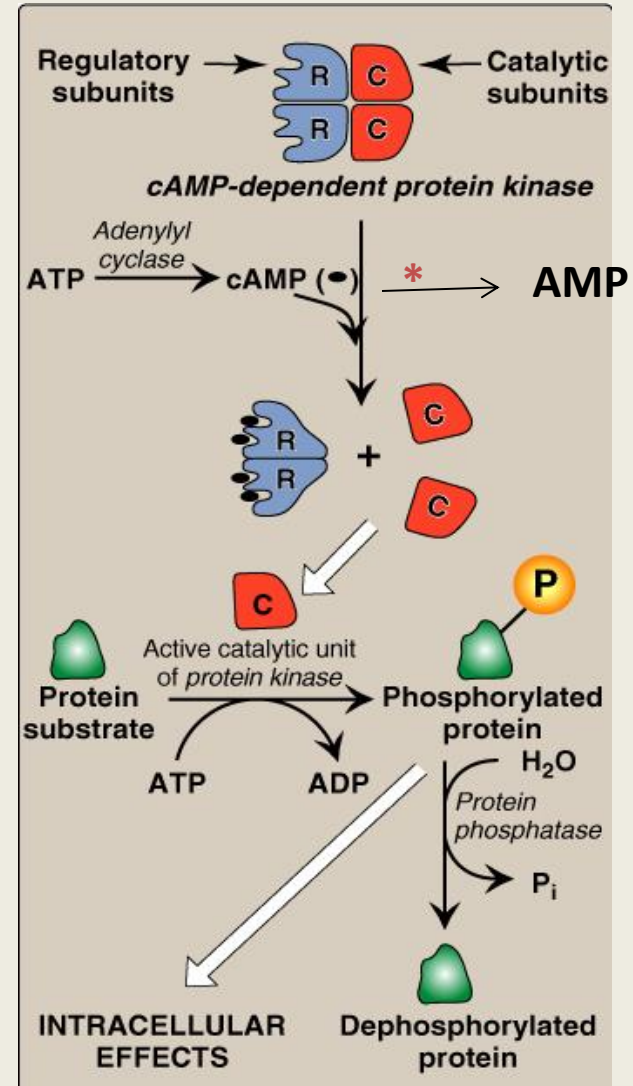
Adenylyl Cyclase System: cAMP-Dependent Protein Kinase (Protein Kinase A)



***Phosphodiesterase**

Termination of Signal (A)

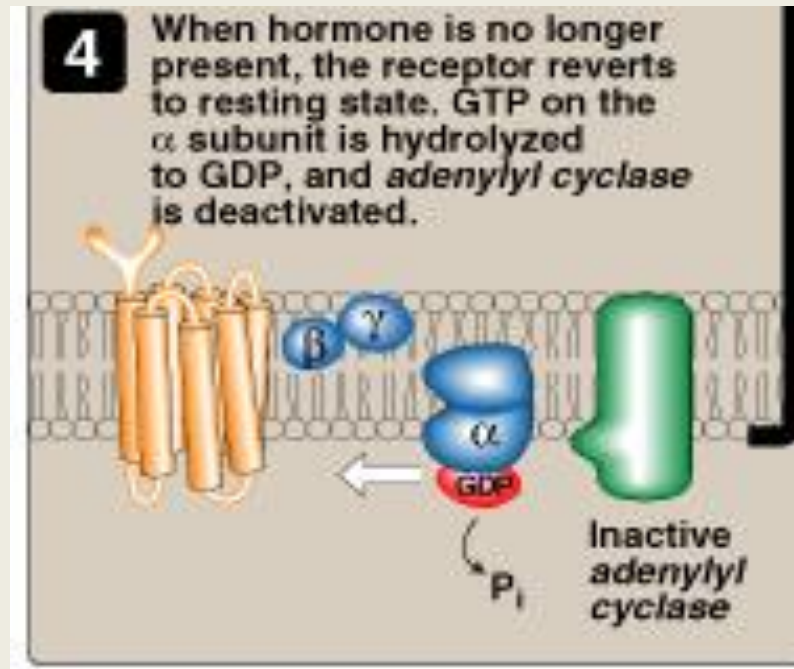
*Phosphodiesterase



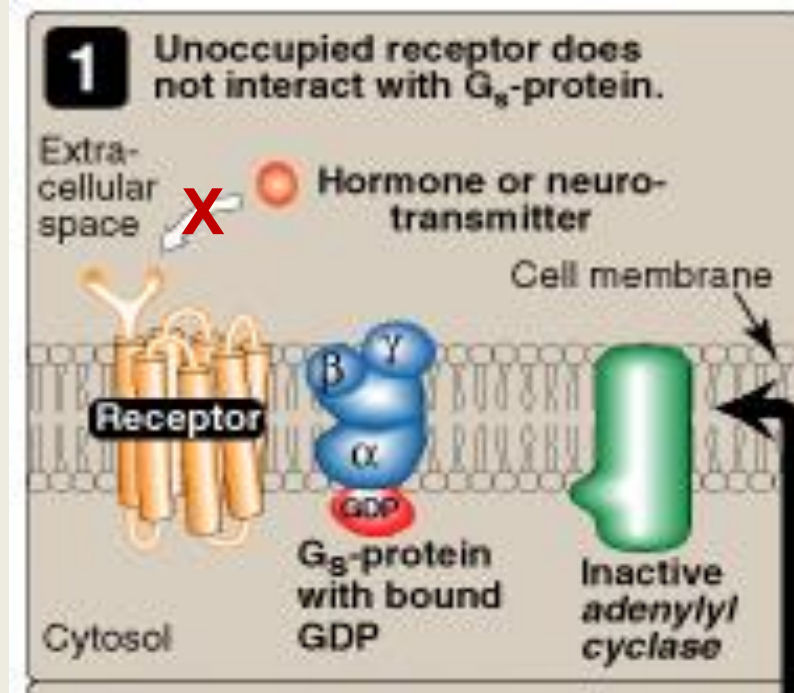
•Protein phosphatase

•Phosphodiesterase → ↓cAMP → Inactive protein kinase

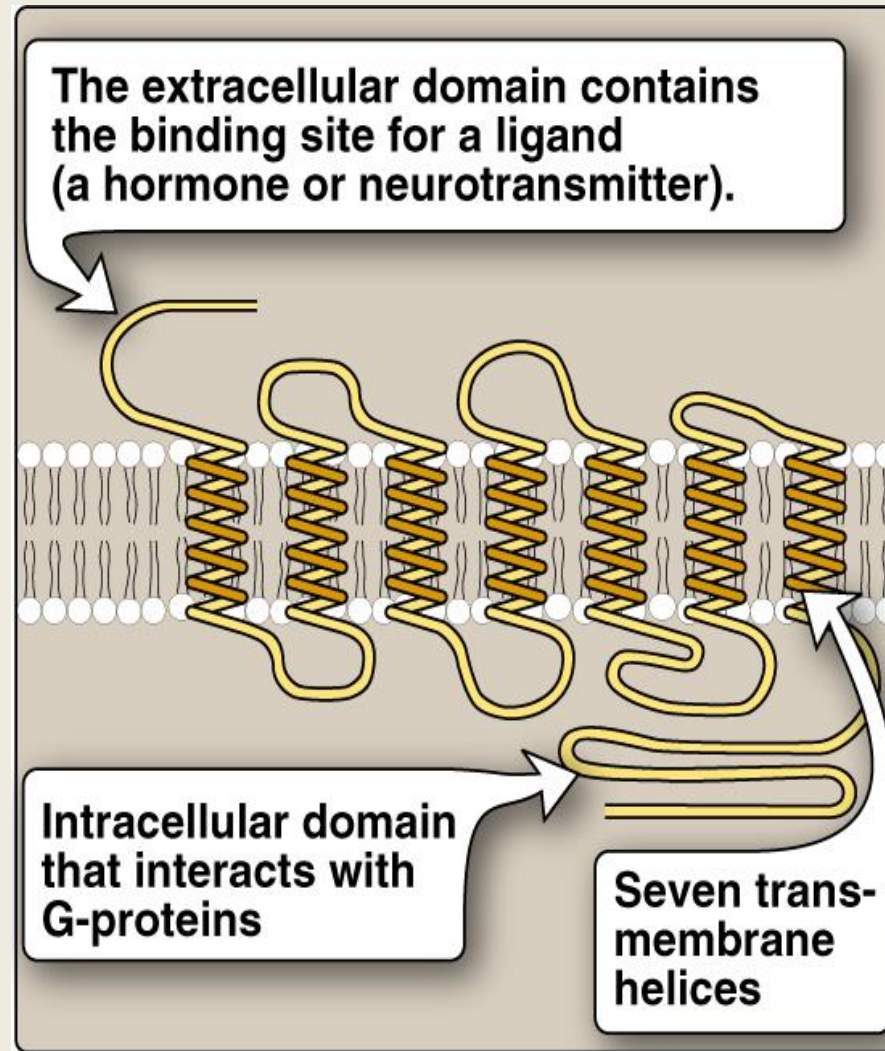
Termination of Signal (B)



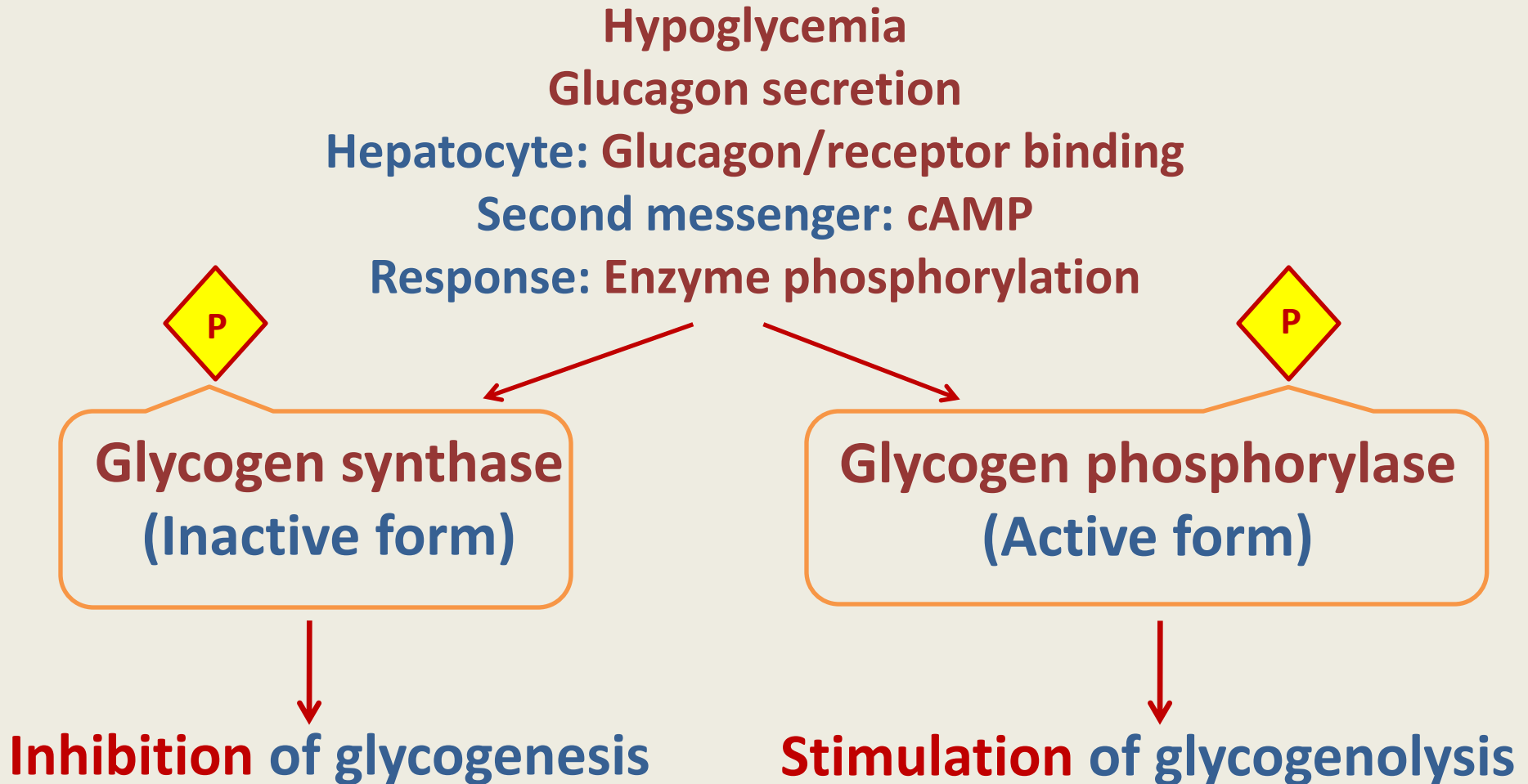
Termination of Signal (C)



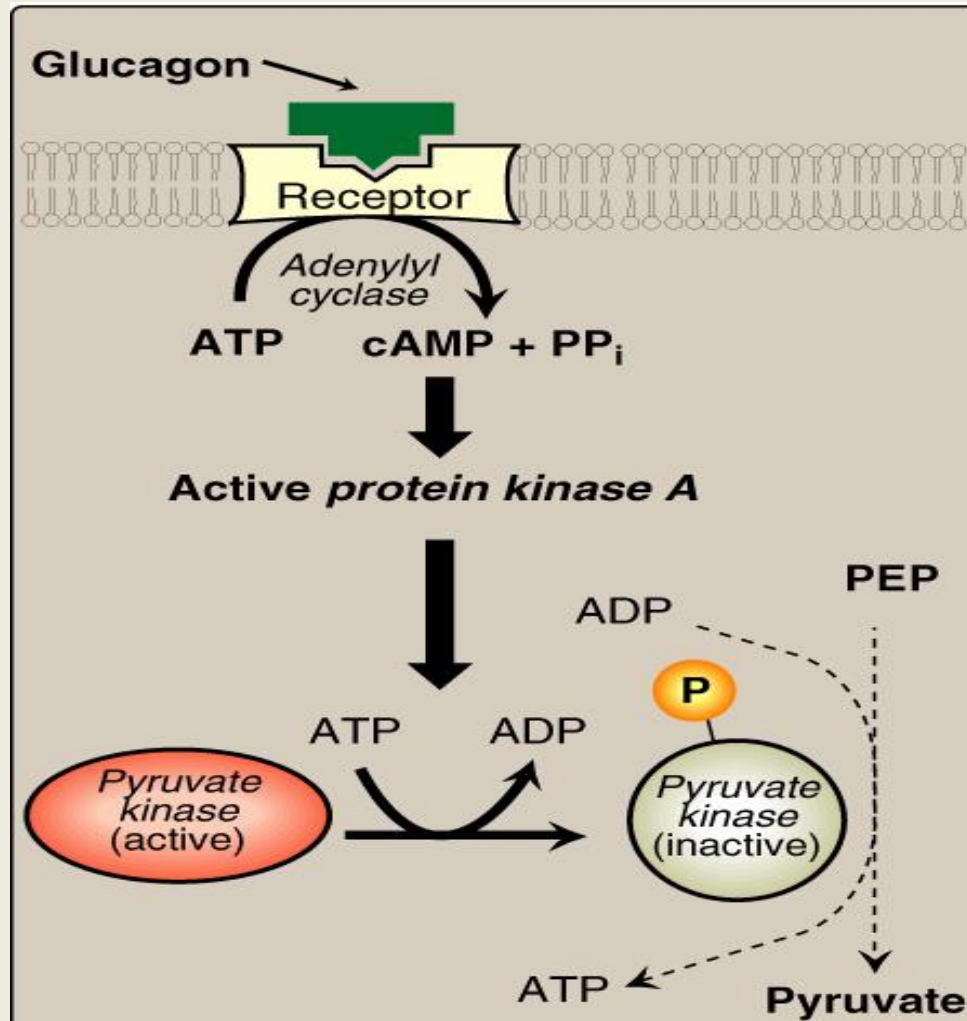
G-Protein Coupled Membrane Receptor



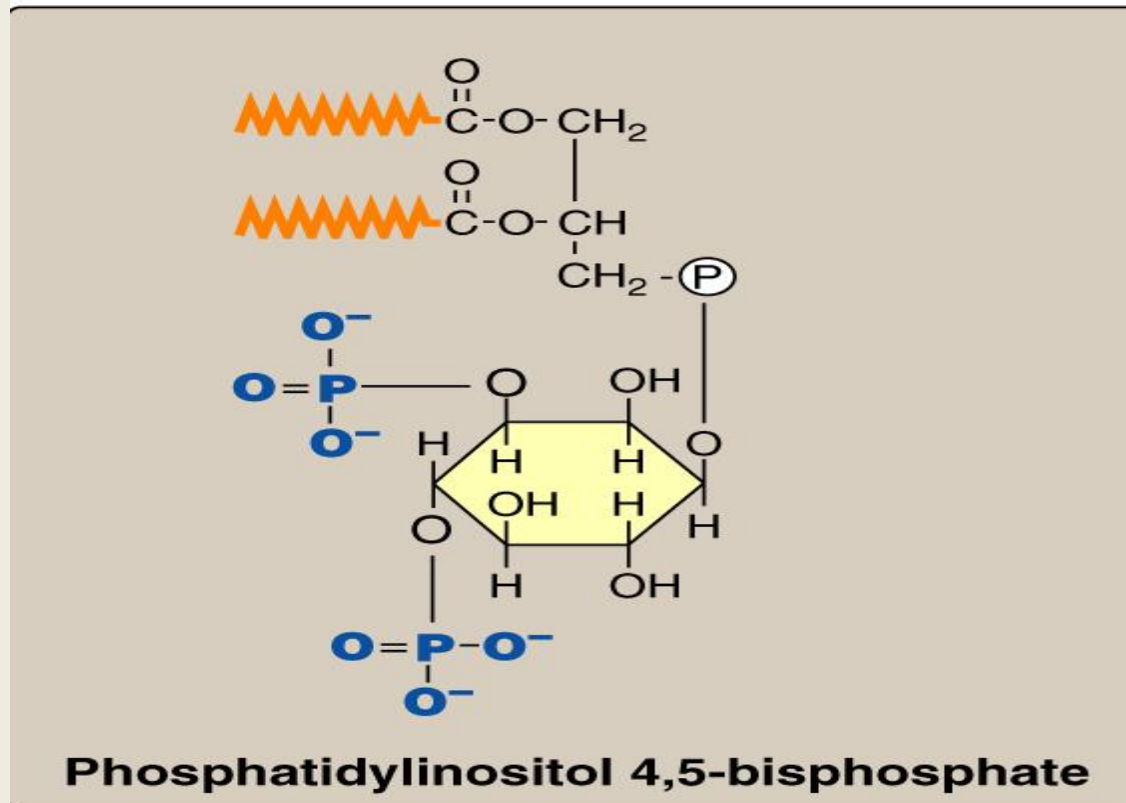
Regulation of Glycogen Metabolism by Glucagon: Effects on Glycogen Synthase and Phosphorylase



Pyruvate Kinase Regulation: Covalent Modification



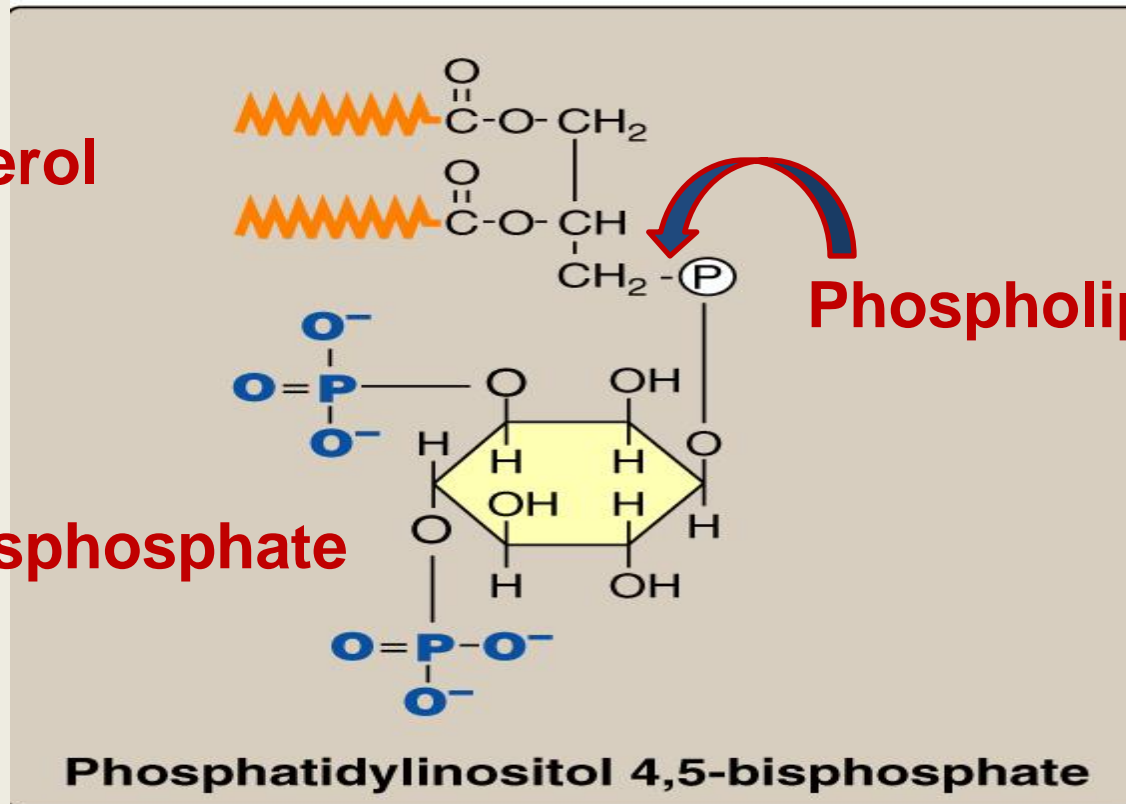
Calcium/Phosphatidylinositol System



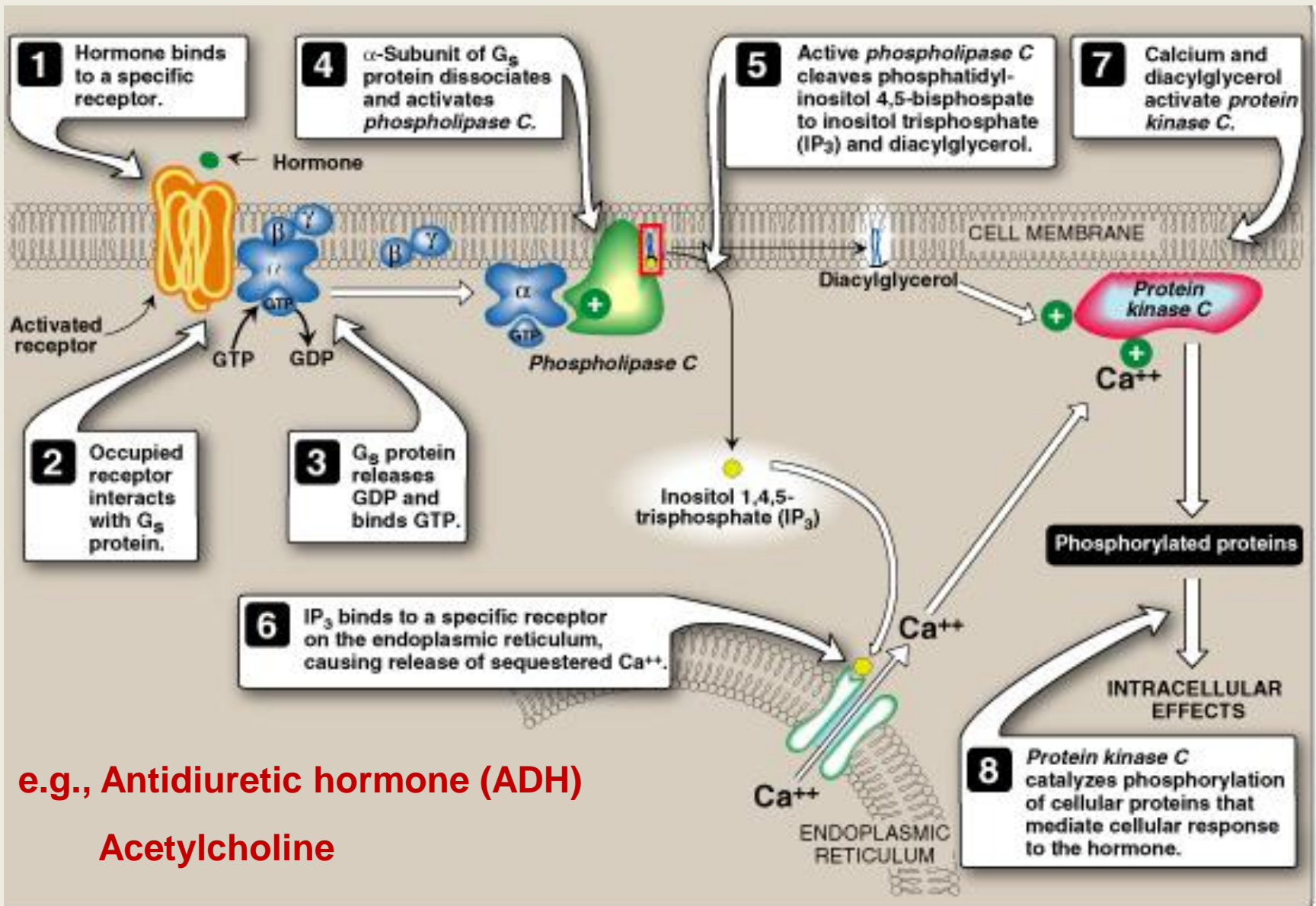
Calcium/Phosphatidylinositol System

Diacylglycerol (DAG)

Inositol Trisphosphate (IP₃)



Phospholipase C

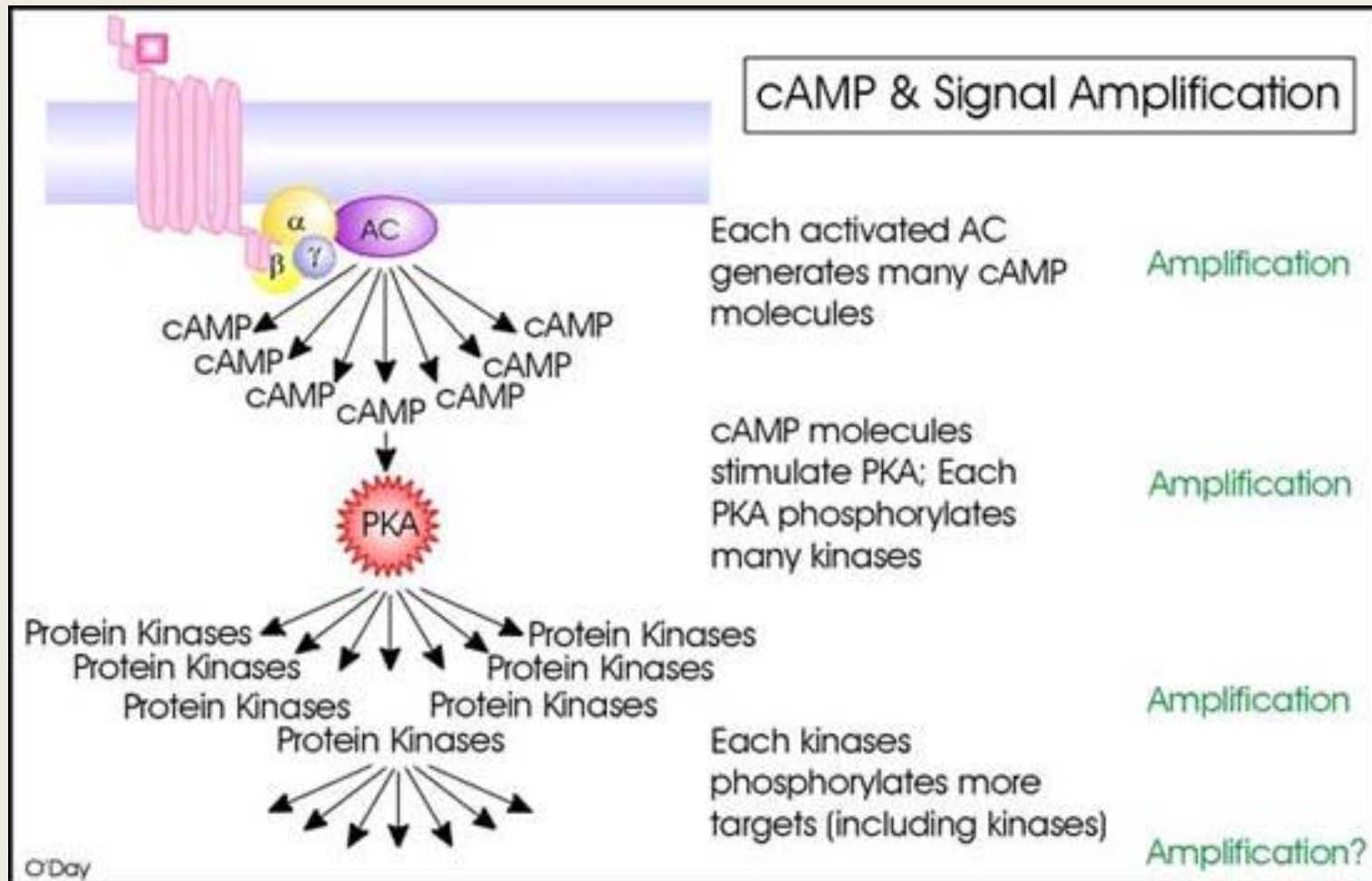


e.g., Antidiuretic hormone (ADH)

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