Cell Signaling and Regulation of Metabolism

BIOCHEMISTRY TEAM

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

لاتوجد خلية تعمل لوحدها
في الإنسان

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

اذا عملت اي تغير في الخليه ،سيكون للخلية القدره على العوده من جديد لاستقبال تغير اخر

Relayed=passed from One messenger to the Other

Signaling Process

A ligand can effect on one specific receptor

Recognition of signal

Receptors

Transduction

From outside to inside the cell

Change of external signal into intracellular message with amplification and formation of second messenger

Effect

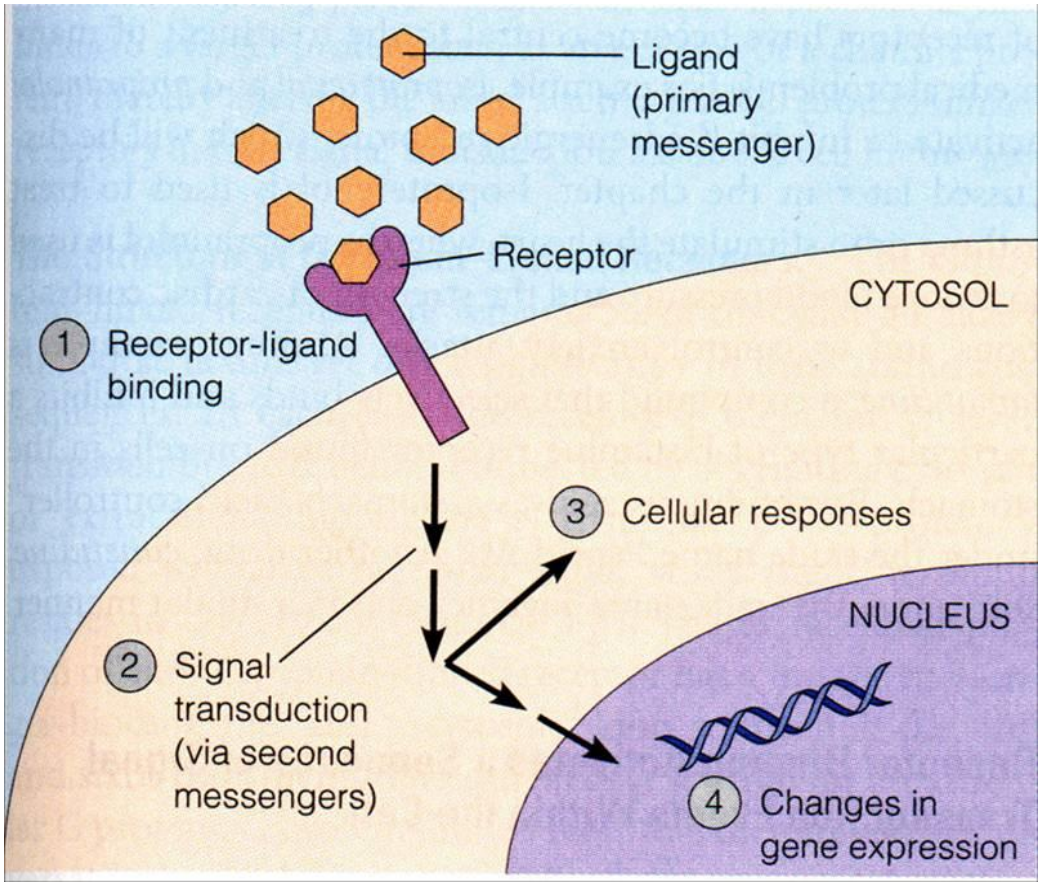
Modification of cell metabolism and function

Note

First messenger ---> OUTSIDE the cell
Second messenger ---> INSIDE the cell

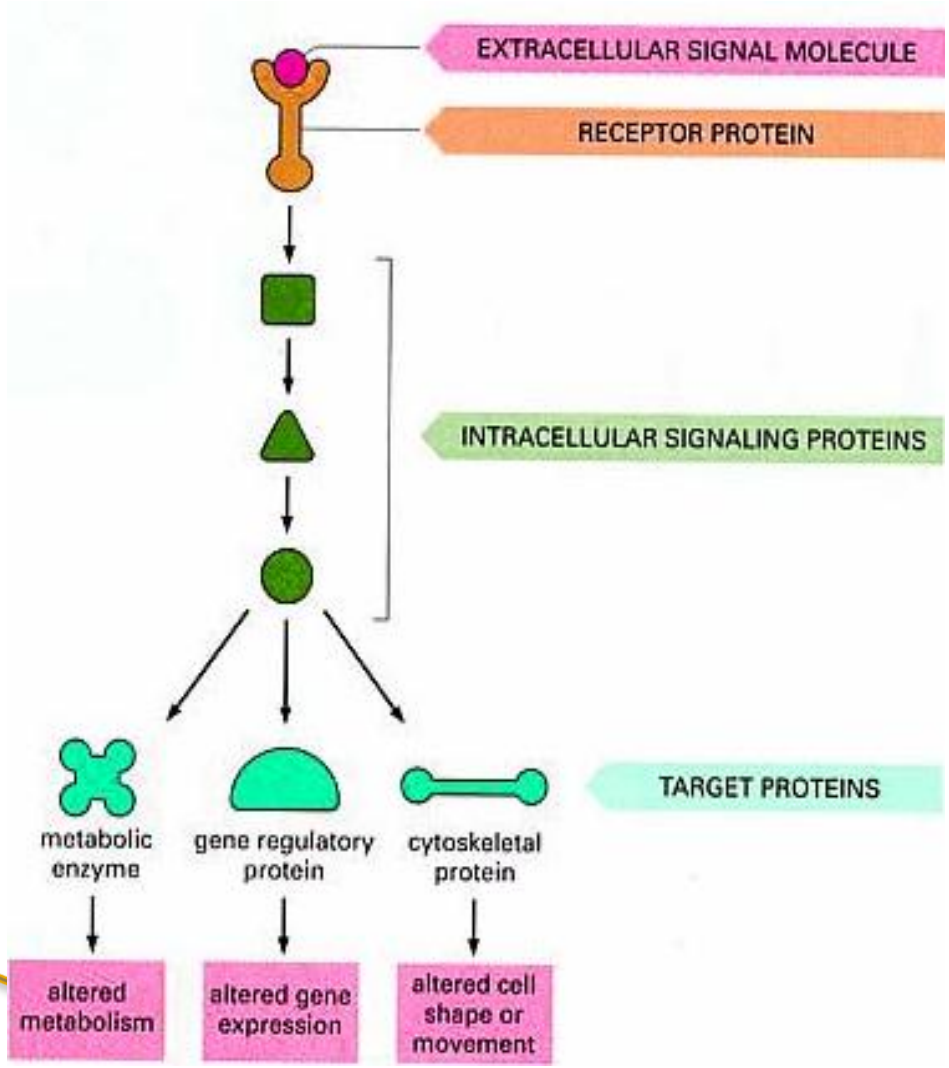
General Signaling Pathway

Any signaling pathway
Starts with a signal
And end with an effect



Signaling Cascades

Singling is a process in which one ligand being recognized by a receptor (e.g. G-protein coupled receptors) could lead to a series of magnified steps. (ending with an effect)



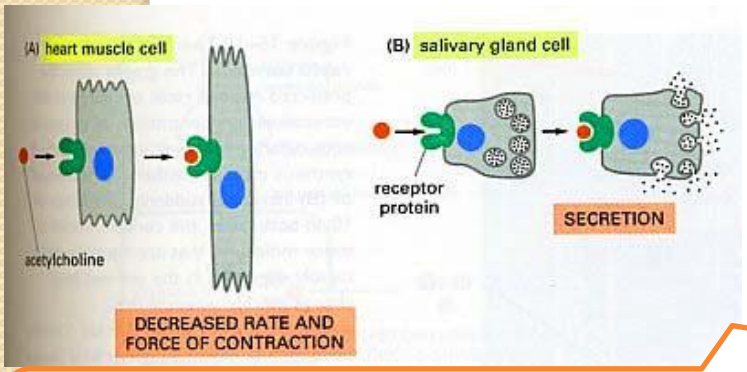
Effect

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**

Recognition could involve different responses to the same Signaling Molecule

Acting on Different Cells



E.g. Ach acts on both myocytes (in heart) & salivary cells (for parasympathetic "rest & digest" action)

Action on one Cell but in Different Pathways

Causing different (or opposite) effects

e.g. Glucagon
Further details next slide

"One Cell but, Different Pathways"

Glucagon:

Effects on **Glycogen Synthase** and **Phosphorylase** → enzymes

How does it regulate the blood sugar with two opposite pathways?

Low sugar in blood ←

1) Hypoglycemia
2) Glucagon secretion → From pancreas

Recognized by "liver cells" ←

3) Hepatocyte: Glucagon/receptor
4) binding
5) Second messenger: cAMP → Released inside the cell by the cell
6) Response: Enzyme phosphorylation

In two ways

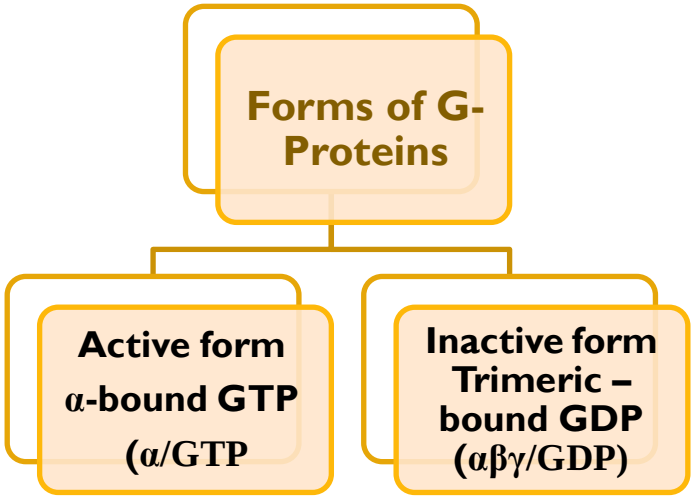
Enzyme phosphorylation

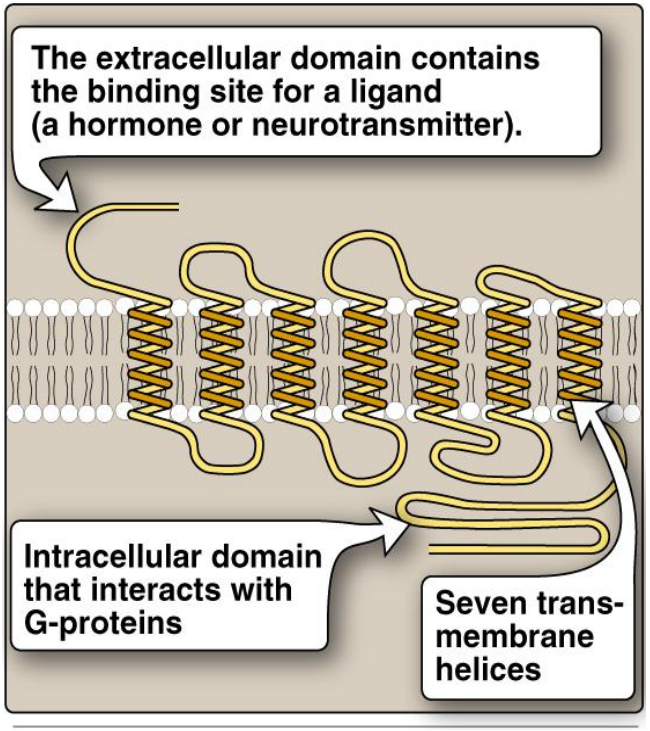
- **turn Glycogen into synthase Inactive form** — result → **Inhibition of glycogenesis** → ايسوي بلوك لعملية التخزين بحيث يحافظ على الجلكوز في الدم
- **Turn Glycogen phosphorylase into Active form** — result → **Stimulation of glycogenolysis** → يسوي تسريع للهدم من السكر المخزن في الكبد

Some receptors are coupled with G-proteins. What are they?

GTP-Dependant Regulatory Proteins (G-Proteins)

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





The α-subunit has intrinsic GTPase activity, resulting in hydrolysis of GTP into GDP (leading to inactivation of G-proteins)

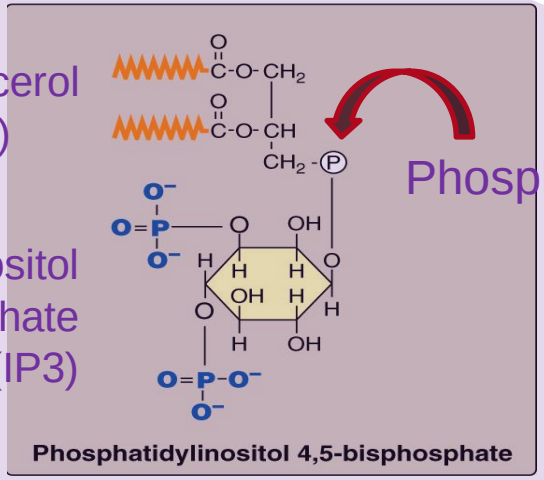
G-proteins on the other hand activate an effecter that sends a 2nd messenger to complete the singling pathway

Two important second messenger systems

Calcium/phosphatidyl inositol system

Diacylglycerol (DAG)

Inositol Trisphosphate (IP3)



Phospholipase C

معلومات اضافية

Adenylyl cyclase system

It's a membrane-bound enzyme that converts ATP to cAMP

Signal

Hormones or neurotransmitters

Signal Transduction

Response

Activation/inhibition of protein kinase A

cAMP-dependent protein kinase

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

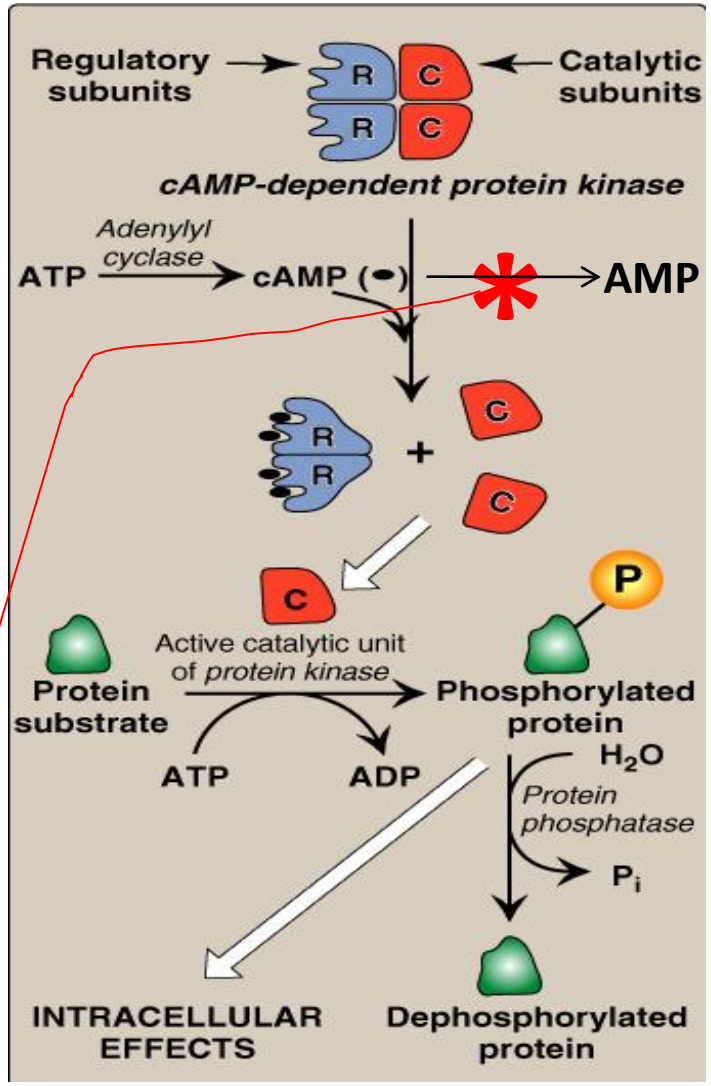
After the G-protein has activated the effecter to release the 2nd messenger:

1.ATP is converted to cAMP.

2.cAMP activates protein kinase and is left with AMP.

3.Protein kinase phosphorylates some proteins in the cell

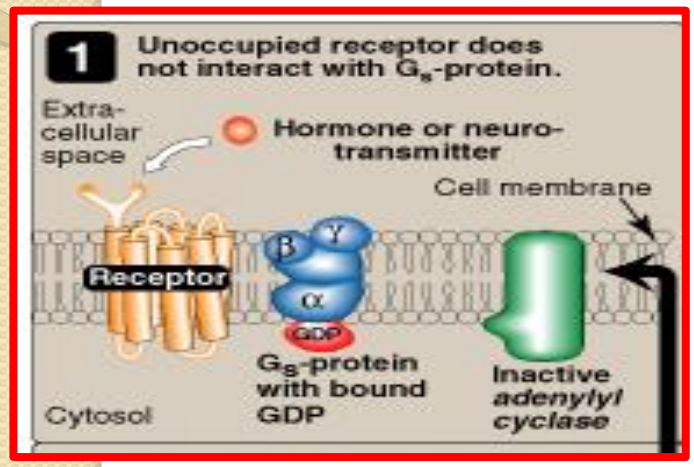
Phosphorylation does not mean activation
It could cause inhabitation too



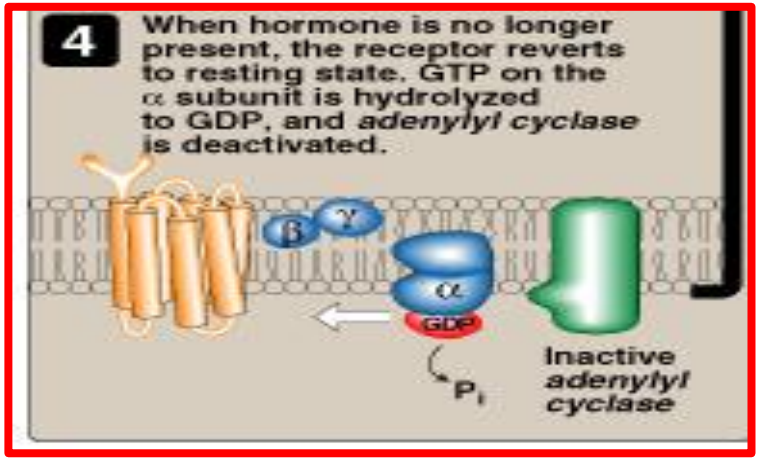
* **By phosphodiesterase**

Termination of Signal

Termination of Signal (C)



Termination of Signal (B)



Termination of Signal (A)

One of the three:

Protein phosphatase, dephosphorylates proteins

Or phosphodiesterase

Will decrease cAMP by converting it into AMP

↓

Leads to inactive protien kinase

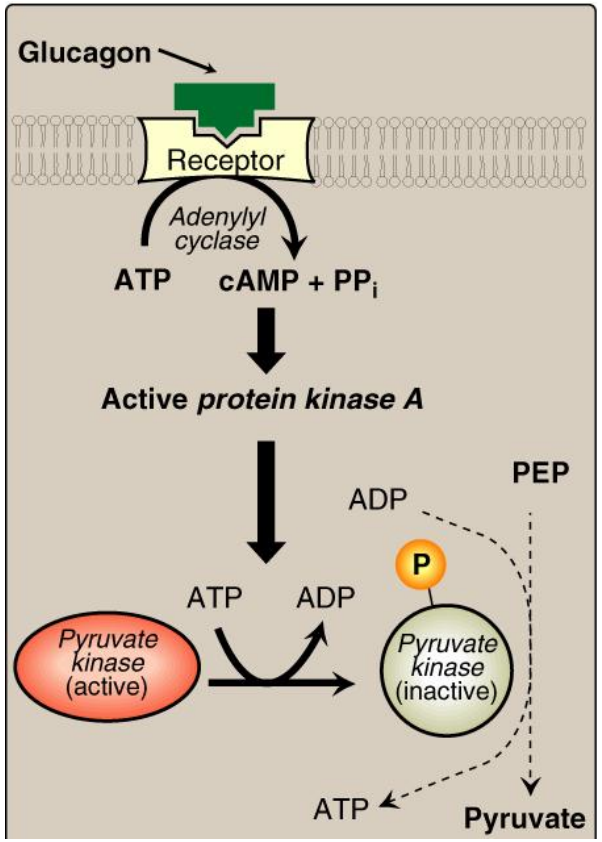
↓

Response stops

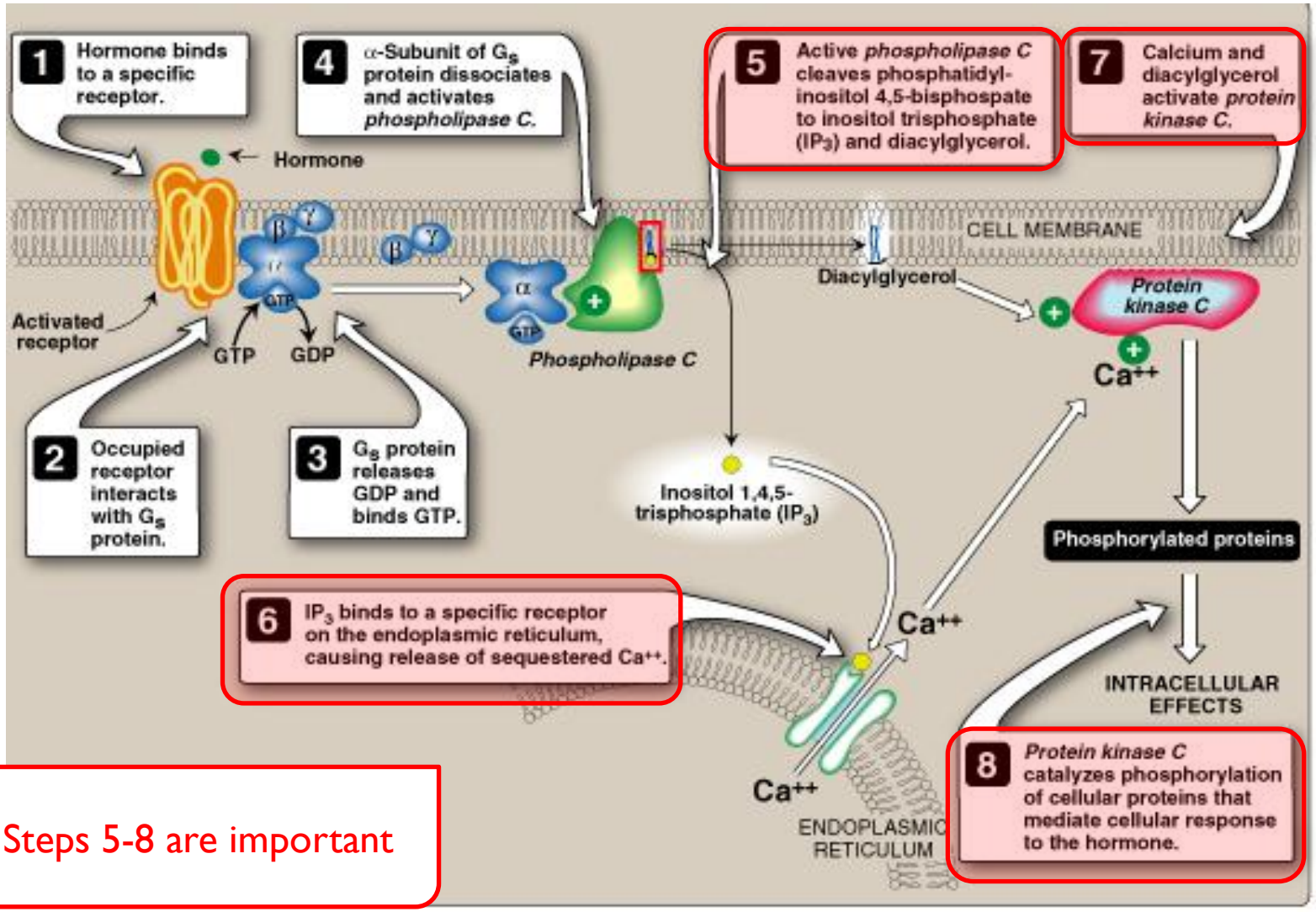
Example of termination: In Glycolysis

Pyruvate Kinase Regulation: Covalent Modification

Protein kinase A phosphrylates pyruvate kinase to inactivate it



2) Calcium/Phosphatidylinositol System



Steps 5-8 are important

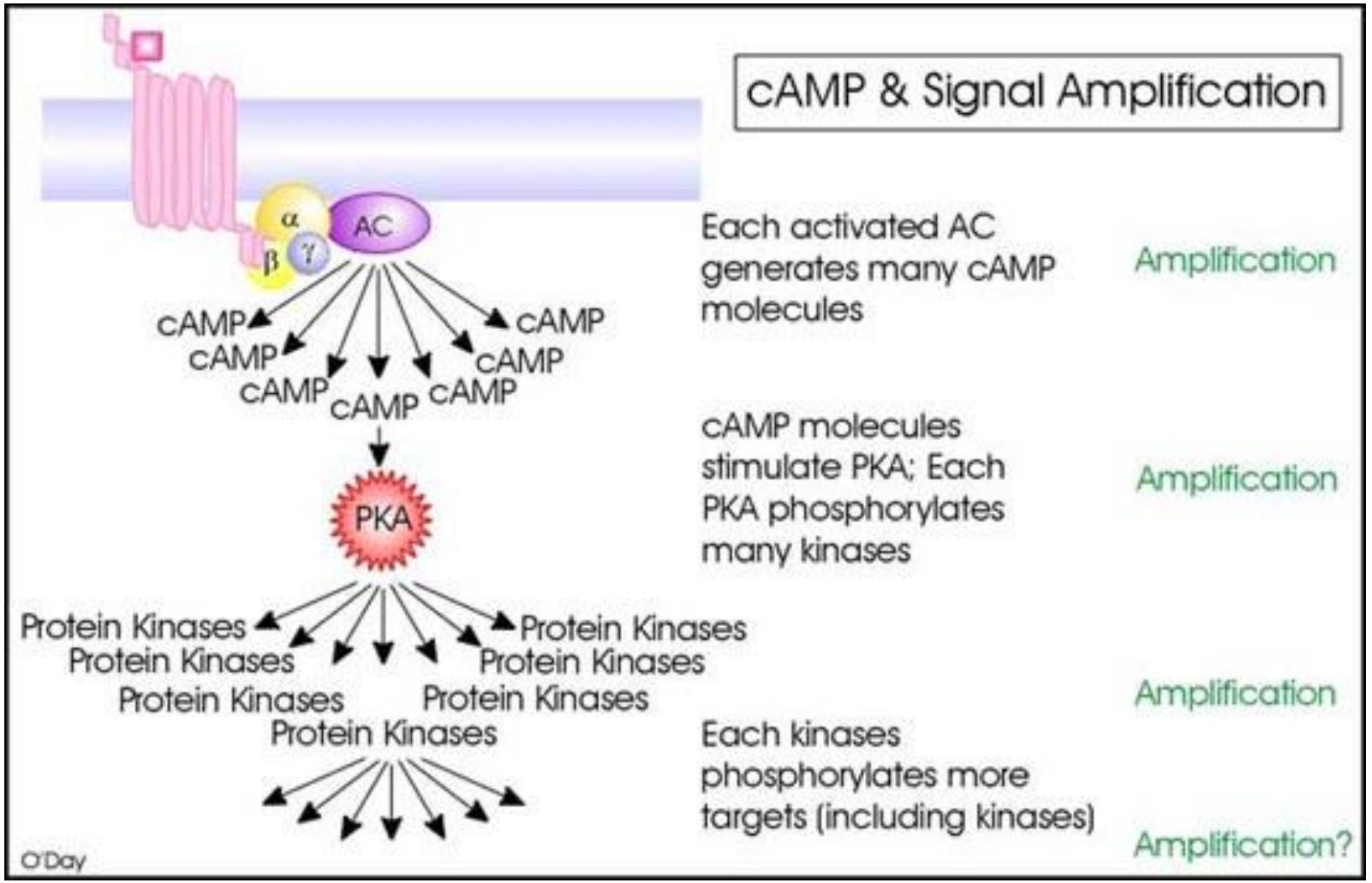
Intracellular Signaling by Inositol trisphosphate

↓

Second messenger

Signal Amplification

هرمون (على سبيل المثال) قد يقوم بالتأثير على خلية لإنتاج استجابة ما، حيث "يتضاعف" الأثر في كل خطوة من خطوات الاستجابة



Thank you O.o