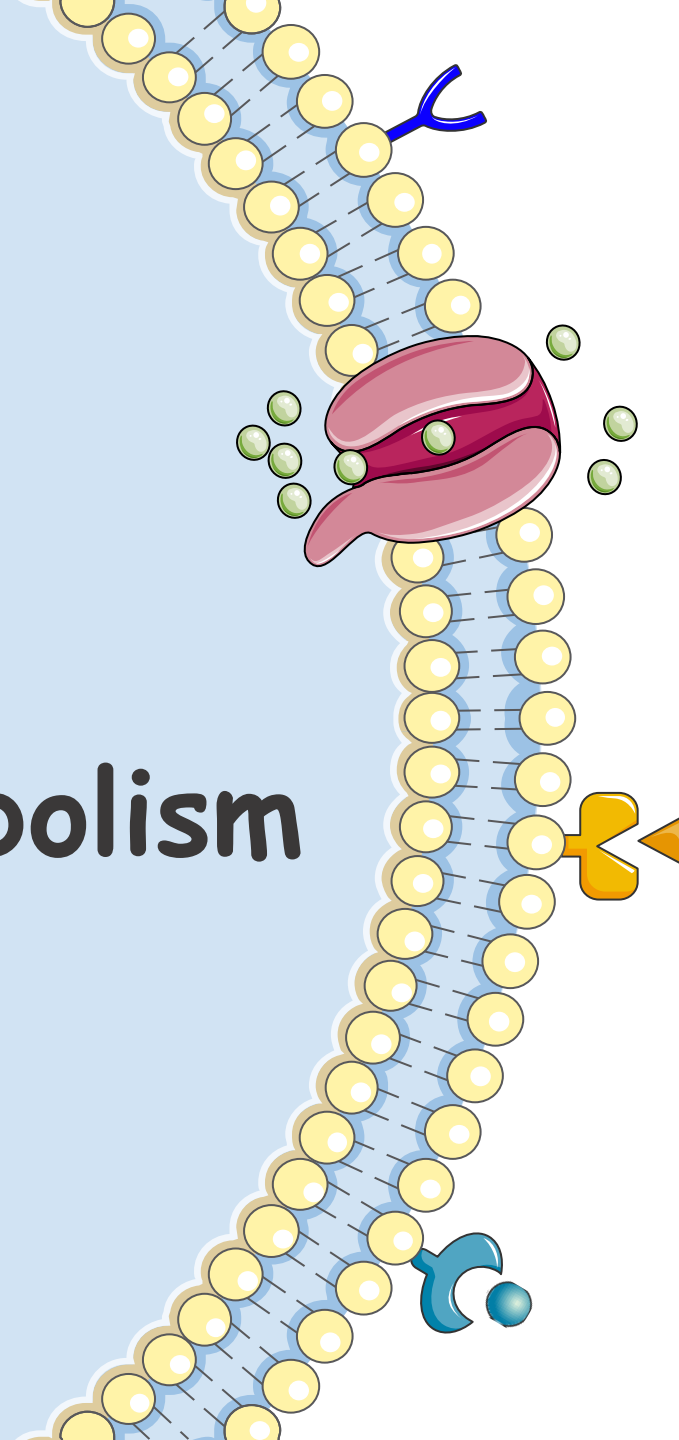
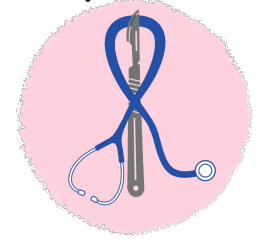


Cell Signaling & Regulation of Metabolism



MED441
KING SAUD UNIVERSITY

Revised & Reviewed
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Faye Wael Sendi



14

V1

Foundation
Block - KSU

Color Index:

- Main text
- Important
- Notes
- Boys slides'
- Girls slides'
- Extra

[Editing File](#)

Objectives

1

Differentiate different steps in signaling pathways.

2

Describe the second messenger systems.

3

Recognize the function of signaling pathways for:



Signal transmission



Amplification

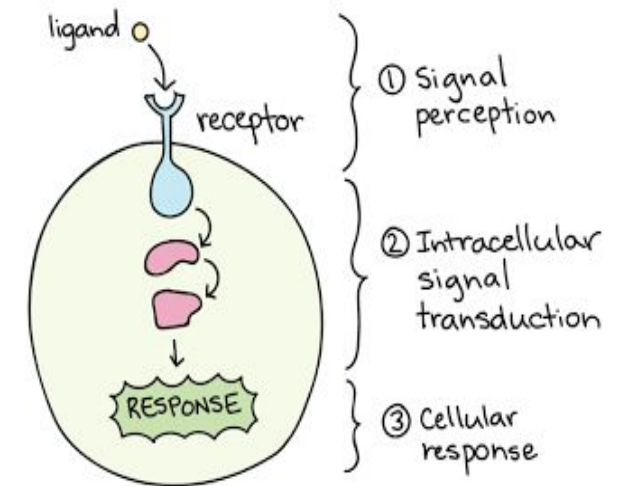
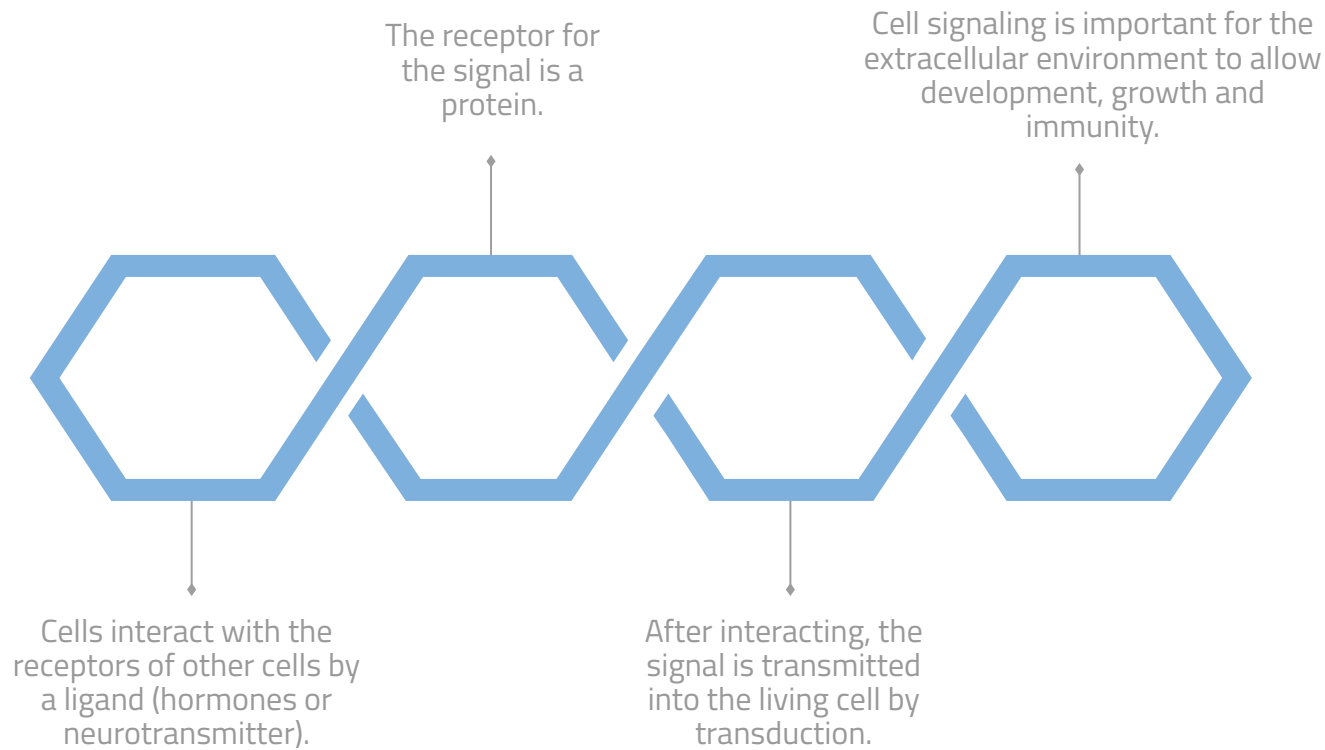
4

Discuss the role of signaling pathways in regulation and integration of metabolism.

Introduction

This is an **extra slide** just to help you to understand the lecture

- **Cell signaling:** the fundamental process by which specific information is transferred from the cell surface to the cytosol and ultimately to the nucleus, leading to changes in gene expression.



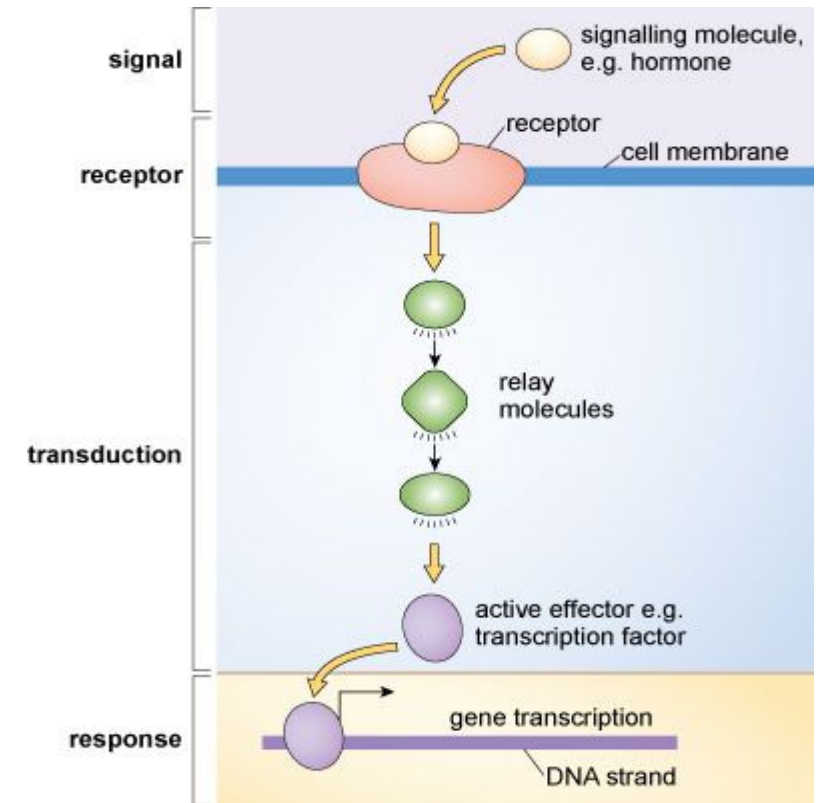
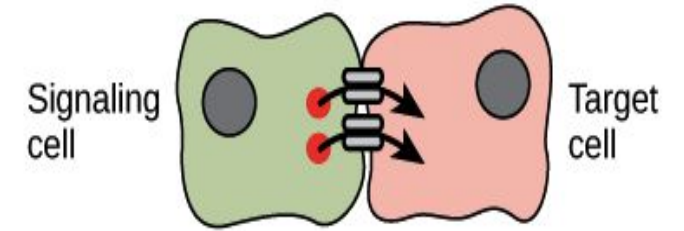
Cell Signaling

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.
 - (The response is necessary in maintain homeostasis)

Signaling Process

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



General Signaling Pathway

1

The ligand binds to the receptor

The ligand is the primary messenger and it could be hormones or neurotransmitters.

2

Signal transduction

The change of the primary messenger into an intracellular second messenger

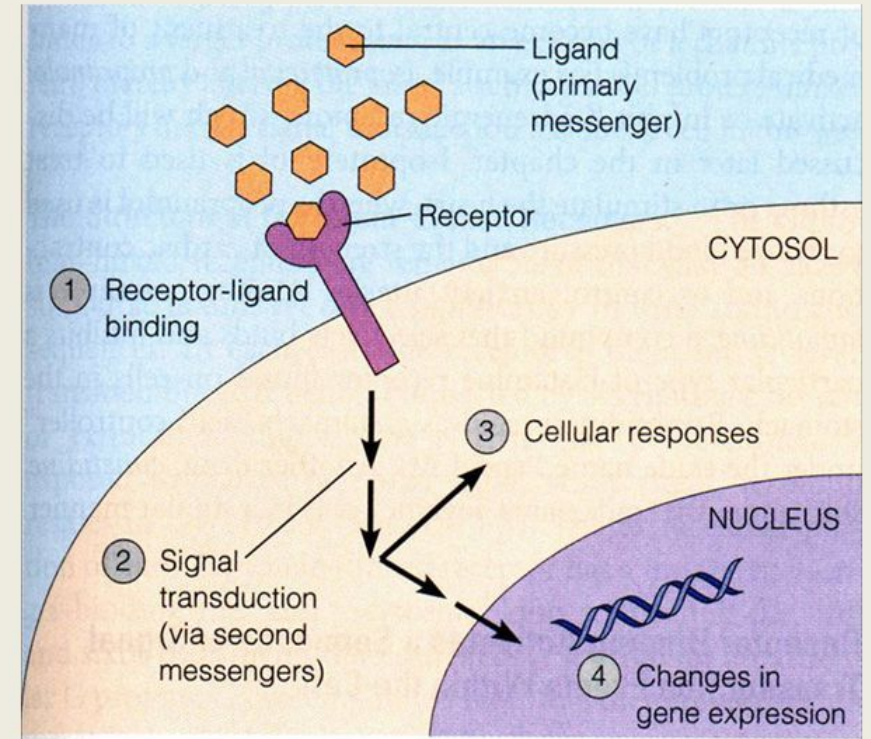
3

Cellular response or changes in gene expression

The second messenger modifies the cell's function and metabolism.

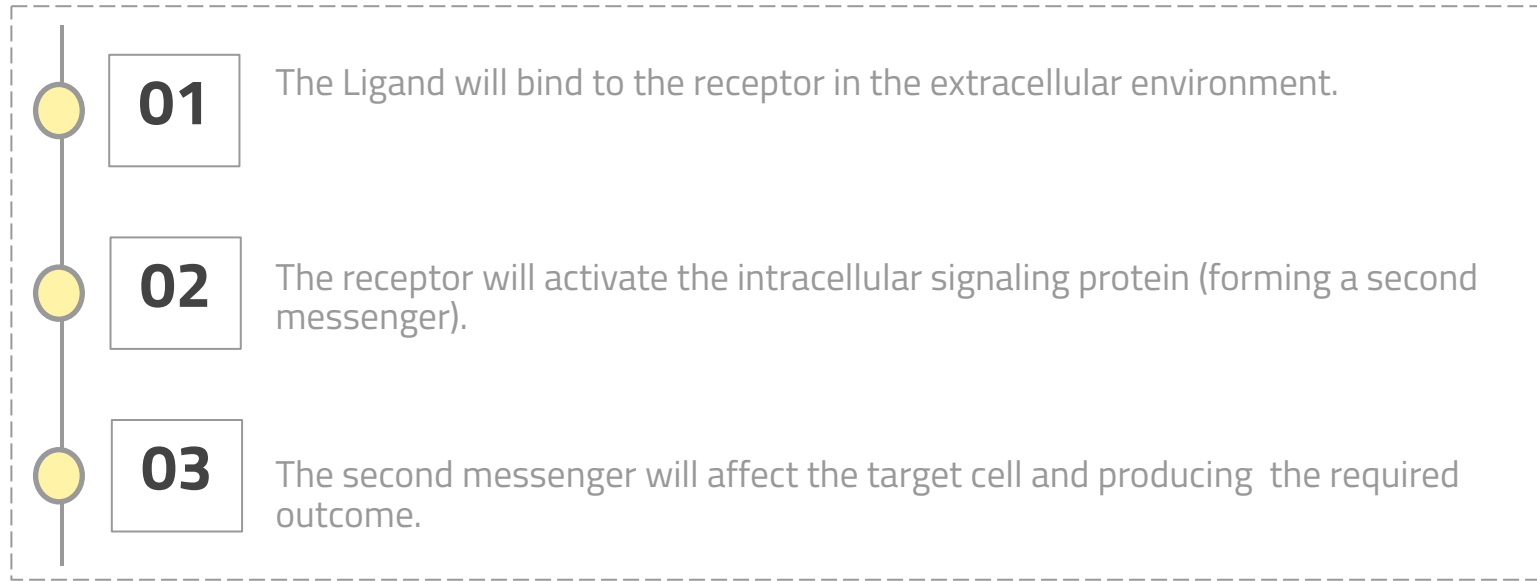
Note that any disruption or error found in this process gives rise to various diseases and cancers.

General Signaling Pathway

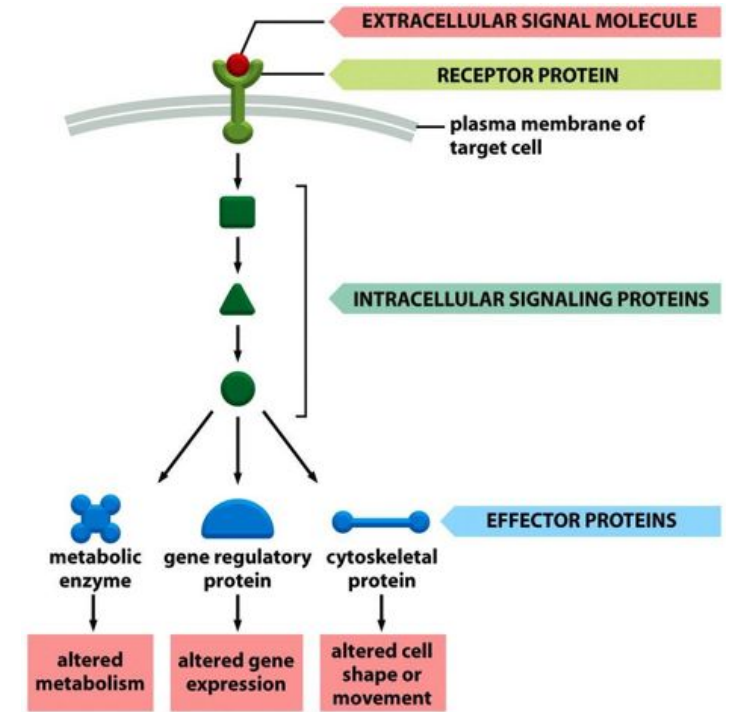




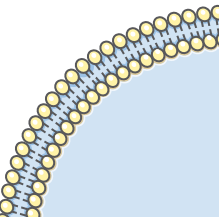
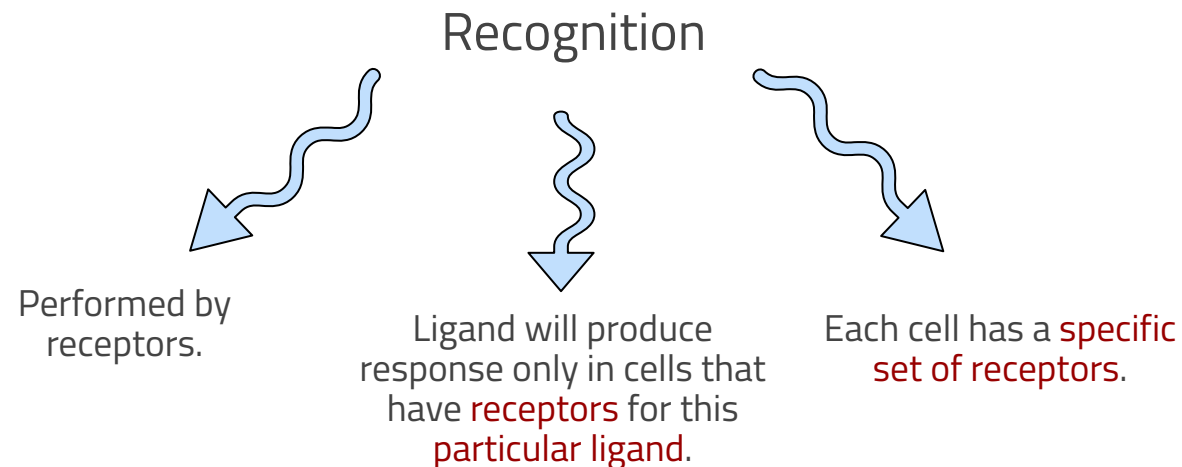
Signaling Cascades



This is a brief explanation of the image, the image is on the original presentation and thus it should be well understood.



Recognition



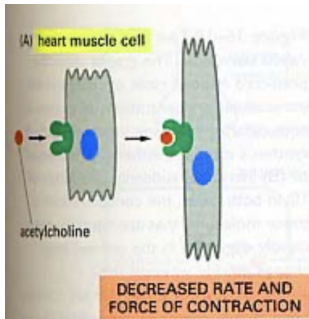
Different Responses to the Same Signaling Molecule

Different Responses to the Same Signaling Molecule

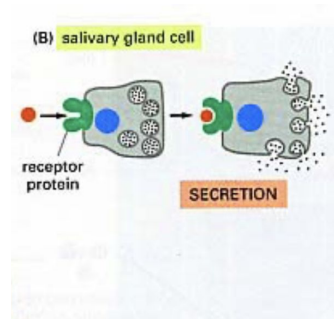
Different Cells

A single ligand (in this case, acetylcholine) has **different effects** according to the target **cell**.

If acetylcholine binds to receptors at the heart muscle cells, the effect is: decreased rate and force of contraction.



If acetylcholine binds to receptors at the salivary gland cells, the effect is: secretion.



Different Pathways (One Cell)

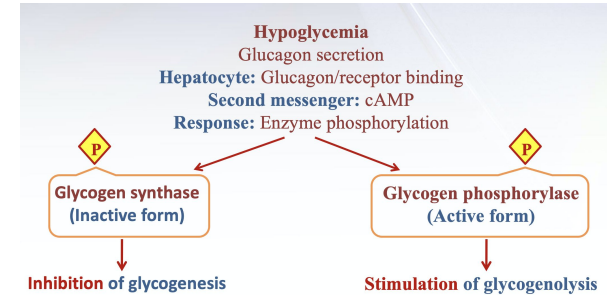
(eg; hypoglycemia) A single ligand (in this case; glucagon) binds to receptors of the **same cell** (in this case; hepatocytes) and has **different effects** according to the **pathway**.

If glucagon binds to receptors at hepatocytes, cAMP is produced resulting in the **phosphorylation of glycogen synthase**, the effect is: **inhibition** of glycogenesis.

The **phosphorylation of glycogen synthase** inactivates it.

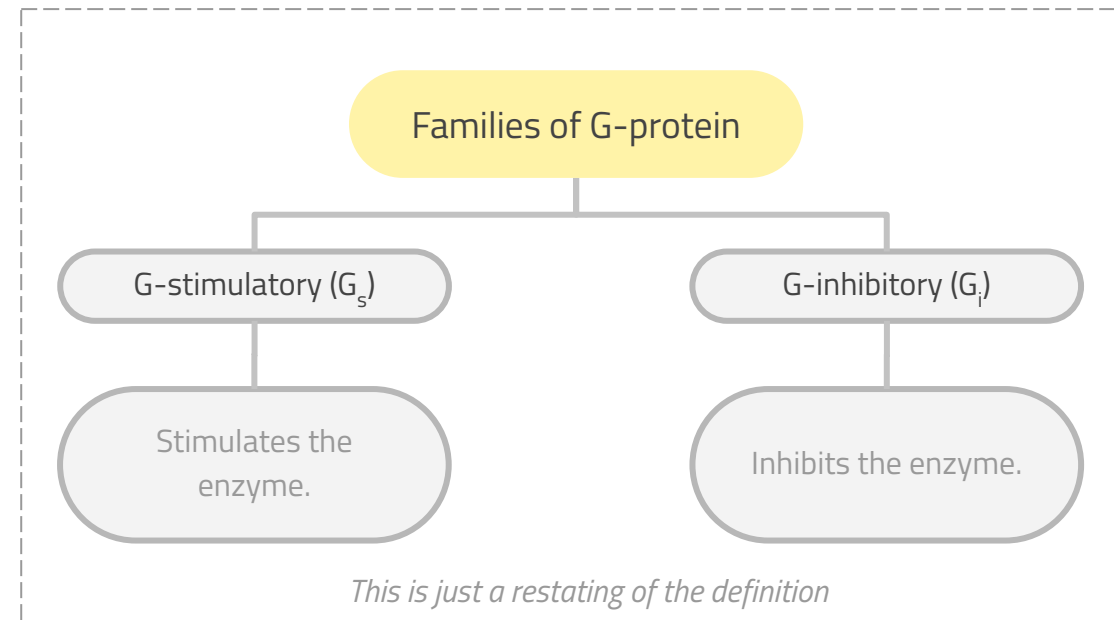
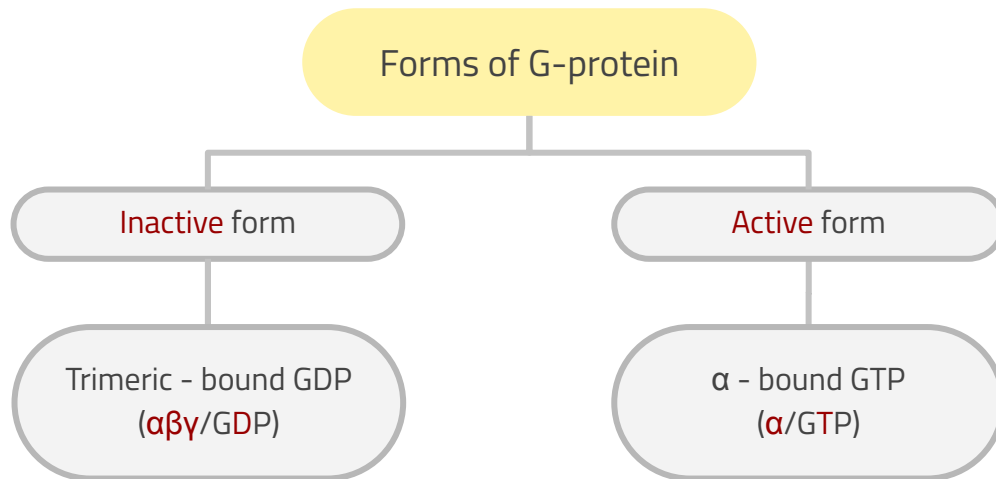
If glucagon binds to receptors at hepatocytes, cAMP is produced resulting in the **phosphorylation of glycogen phosphorylase**, the effect is: **stimulation** of glycogenolysis.

The **phosphorylation of glycogen phosphorylase** activates it.



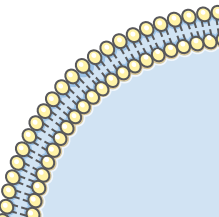
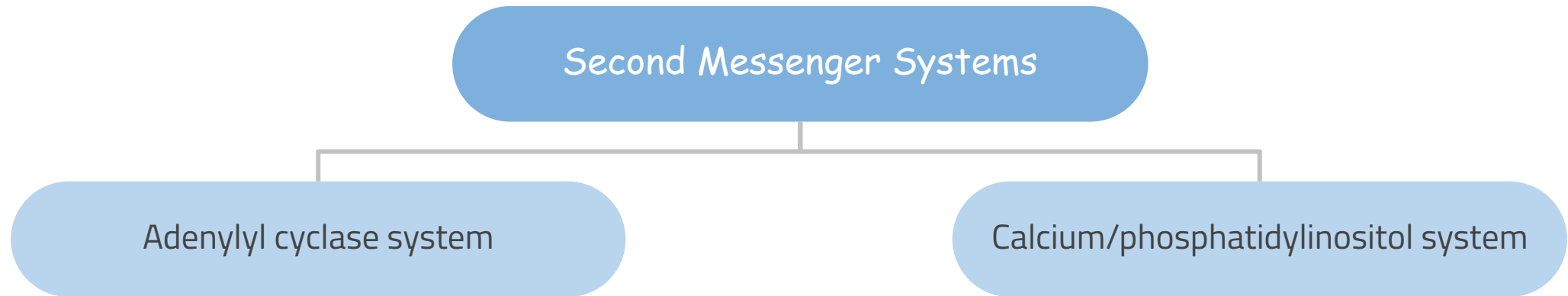
GTP-Dependant Regulatory Proteins (G-Proteins)

- **G-Proteins:** trimeric membrane proteins ($\alpha\beta\gamma$) G-stimulatory (G_s) and G-inhibitory (G_i) binds to GTP/GDP.
 - G-proteins have three subunits: α , β , and γ .
 - G-proteins bind to guanosine nucleotides: GTP or 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

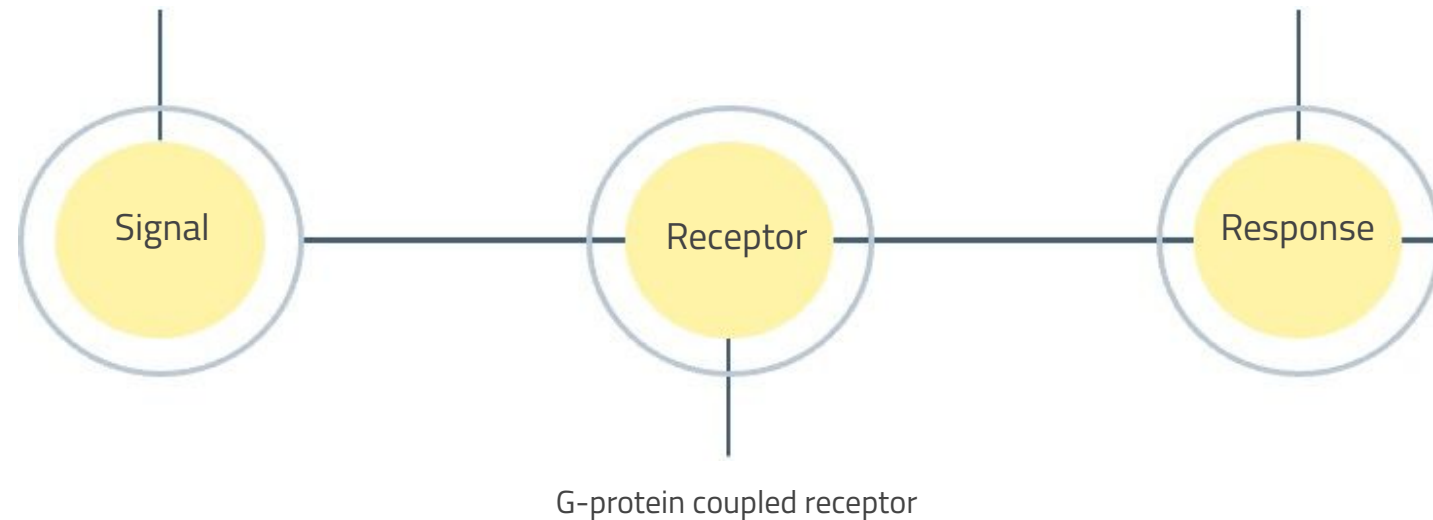


Adenylyl Cyclase System

- **Adenylyl cyclase:** membrane-bound enzyme, converts ATP to cAMP.
- Activation/Inhibition:

- Hormones or neurotransmitters (Glucagon and epinephrine).
- Toxins (Cholera and pertussis السعال الديكي toxins).

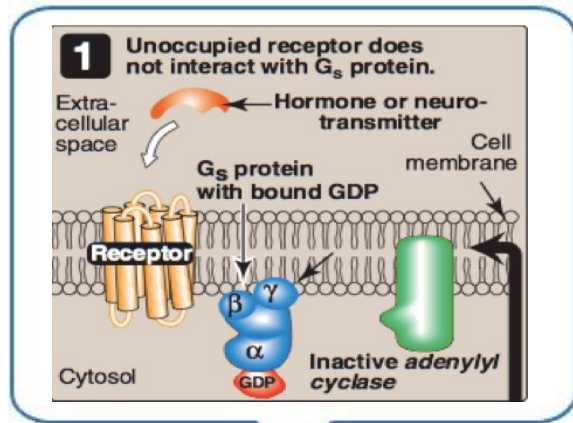
- Activation/inhibition of protein kinase A (cAMP-dependent protein kinase)
- Kinase A cause phosphorylation



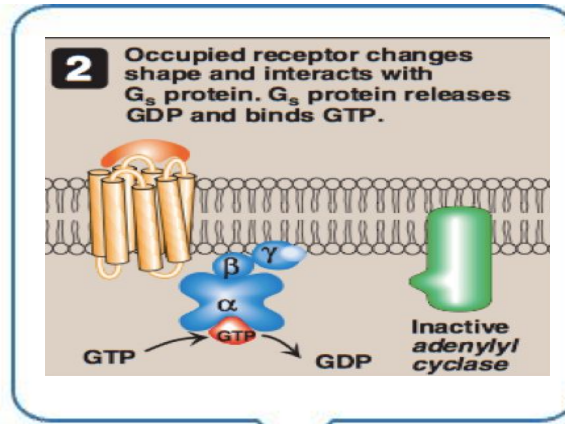
The receptor starts coupling with G-protein only when there is Signal.

- The signal won't affect the enzyme (Adenylyl cyclase) directly. It will affect the receptor (G-protein couple Receptor) first.
 - Then the receptor will activate G-protein which will activate the system

Signal Transduction: Adenylyl Cyclase System

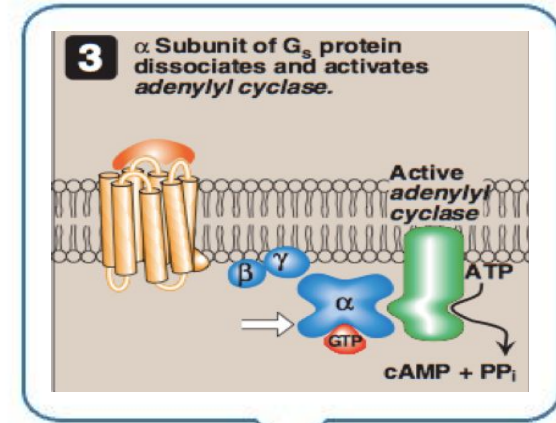


Resting state: No Signal



Ligand/Receptor Binding

Activation of G_s-protein



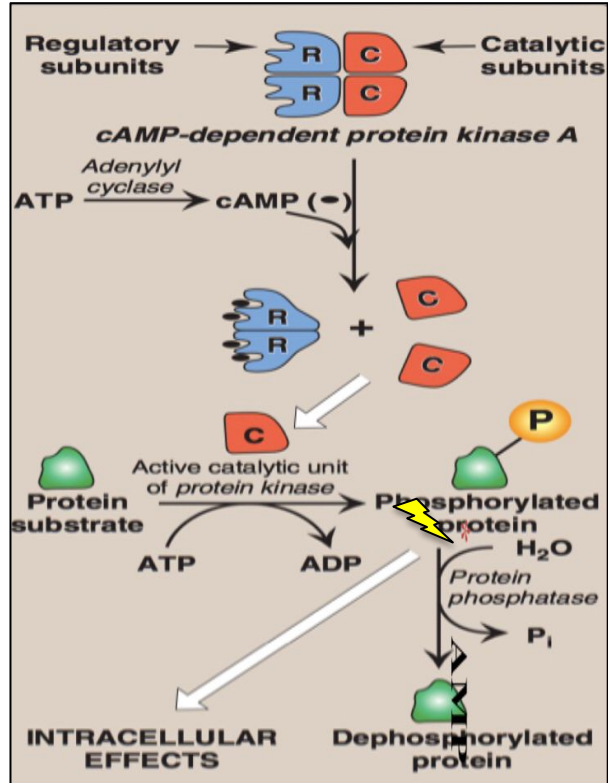
Activation of adenylyl cyclase

Actions of cAMP

A summary here



1. cAMP binds with the regulatory subunits of kinase A leading to activation of the catalytic unit of protein kinase.
1. Activated catalytic unit will phosphorylate a protein giving us a phosphorylated protein.
1. The phosphorylated protein will do its intra-Cellular effect.



Signal Termination

There are 3 ways for signal termination

1. Protein phosphatase:



Protein phosphatase removes the phosphate group from the phosphorylated protein which gives us dephosphorylated protein

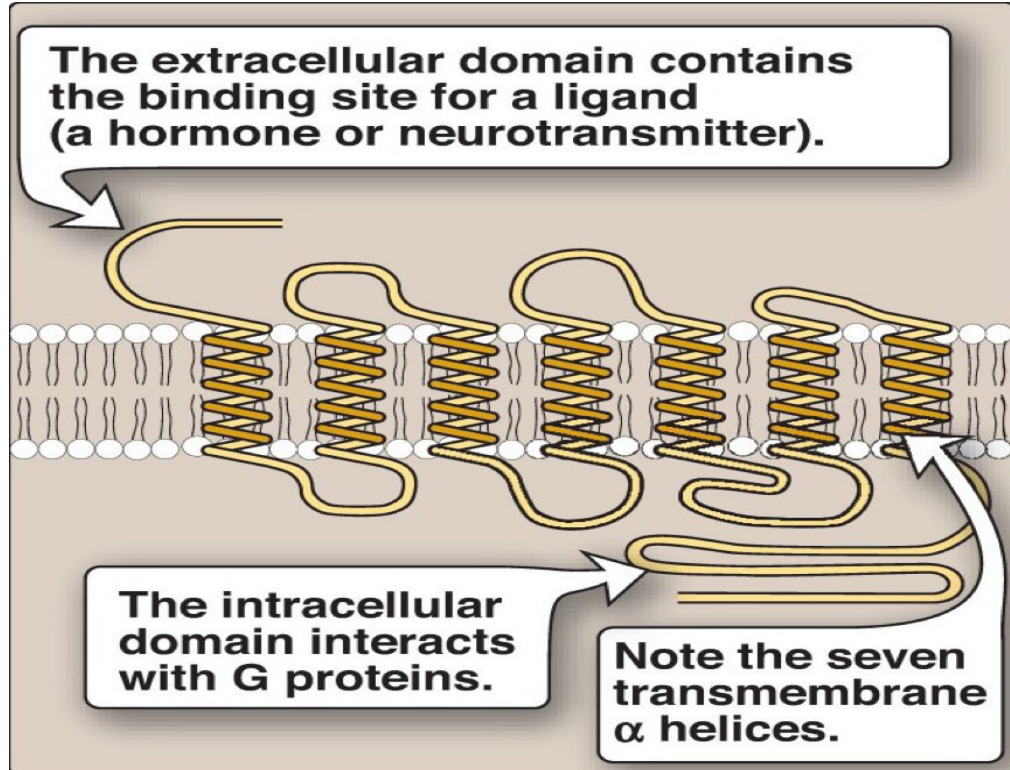
2. Phosphodiesterase:

Using phosphodiesterase to decrease cAMP which give us an inactive protein kinase

3. hormone is no longer present

- Receptor back to resting state
- GTP On alpha subunits is hydrolyzed into GDP
- Adenylyl cyclase is deactivated

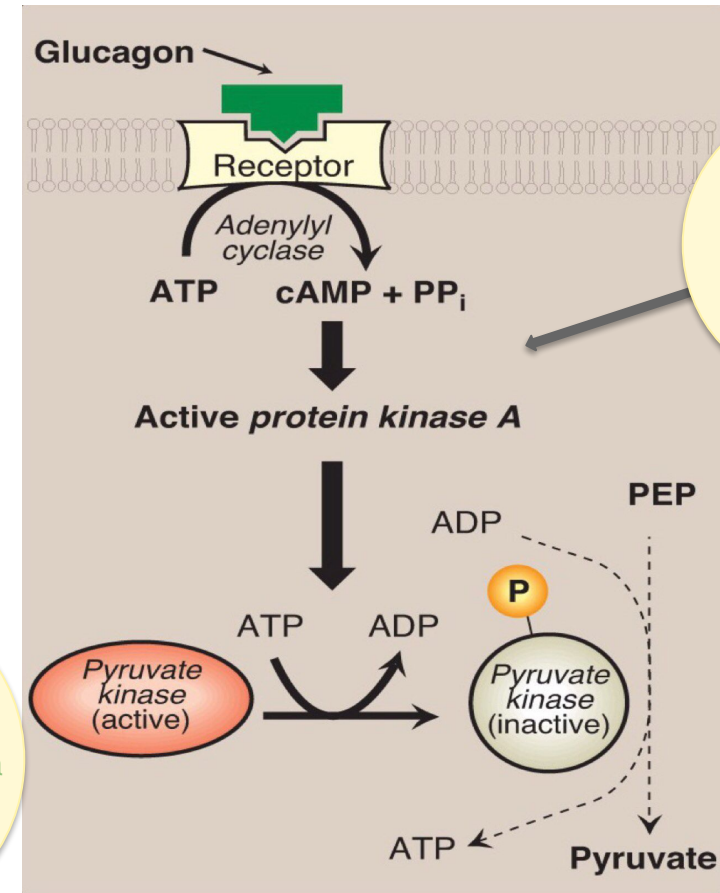
G-Protein Coupled Membrane Receptor



Pyruvate Kinase Regulation:

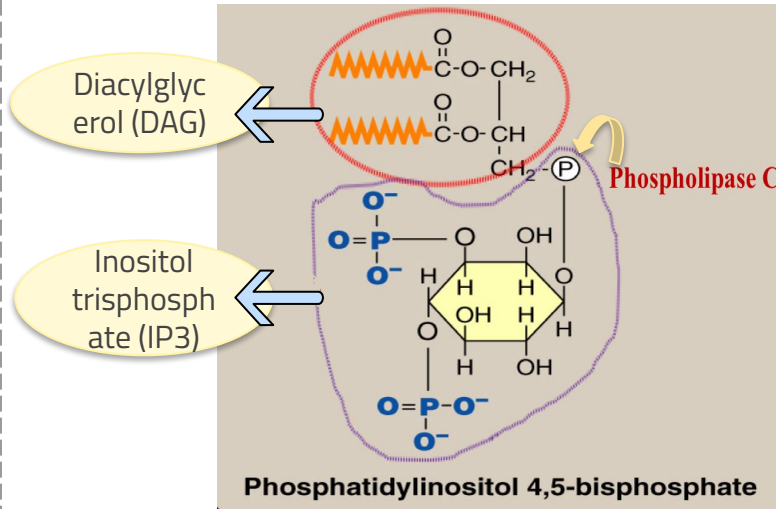
Covalent Modification

- This is an example of Adenylyl cyclase system



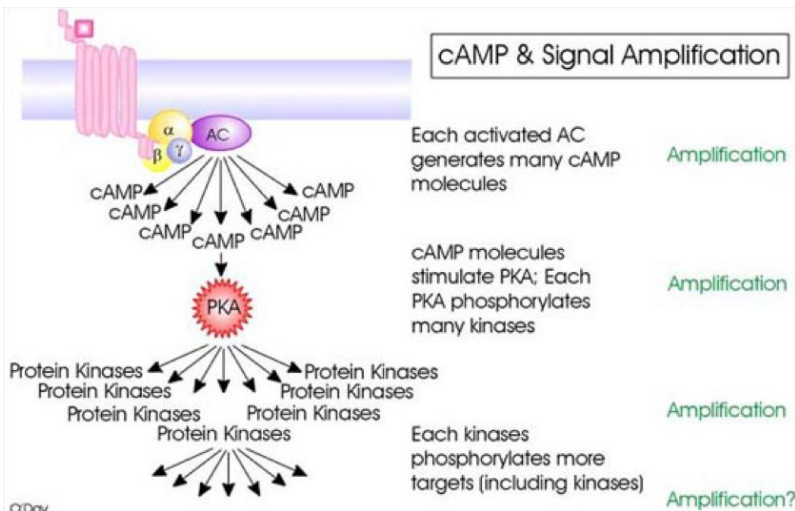
- Target: pyruvate kinase
- This occurs due to hypoglycemia

Calcium/Phosphatidylinositol System

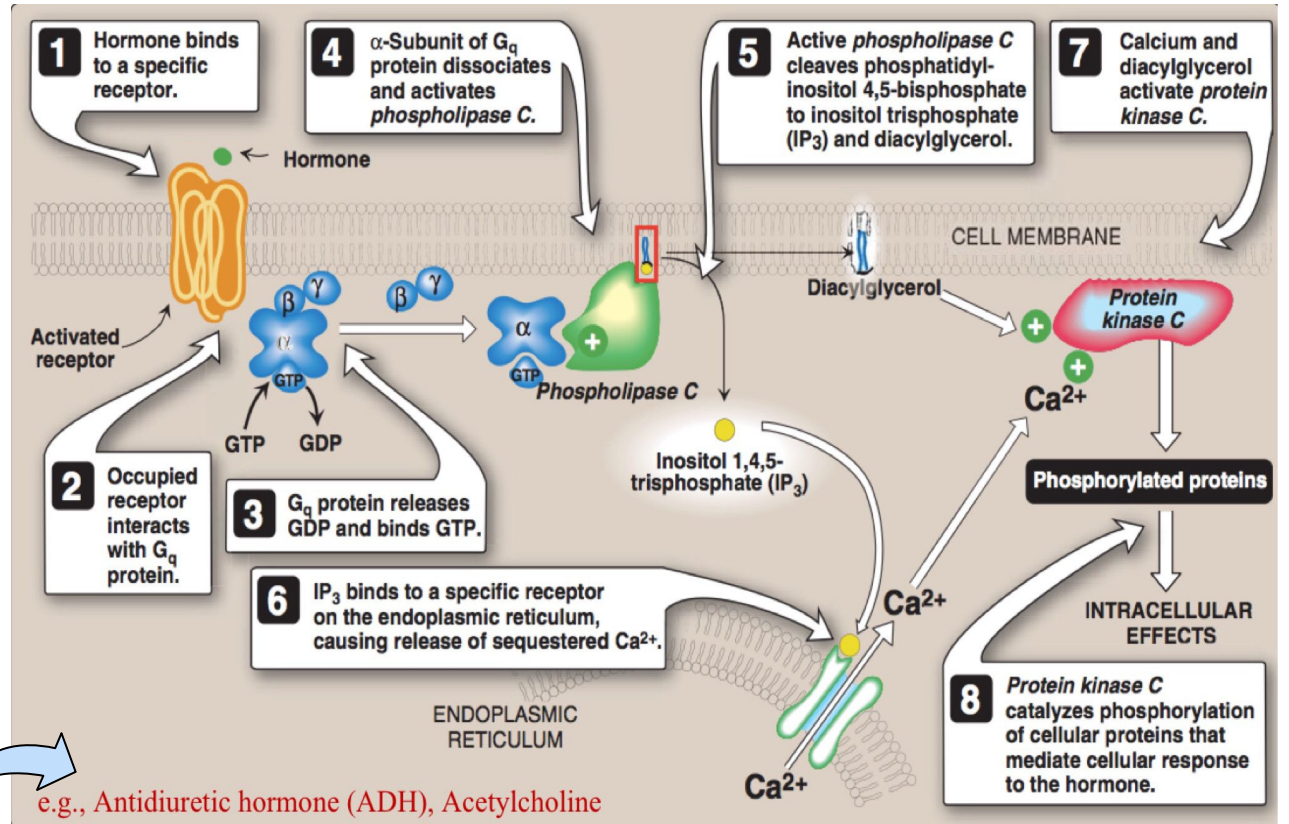


There are Different type of phospholipase
The difference between them is the target bond they are going to break

Signal Amplification




Intracellular Signaling by Inositol trisphosphate

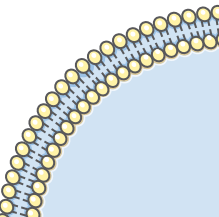


Protein kinase C depend on Ca for activation.



Take Home Messages

- 
- 01** Signal transmission and amplification.
 - 02** Regulation of metabolism.
 - 03** Intercellular communications & coordination of complex biologic functions.



Quiz

Q1: Change of external signal into intracellular message with amplification and formation of second messenger is called:

- A Recognition B Effect C None D Transduction

Q2: The recognition process is done by:

- A Receptors B Neurotransmitter C Hormones D DNA

Q3: The inactive form of G-protein is:

- A $\alpha\beta\gamma/GTP$ B $\alpha\beta\gamma/GDP$ C α/GTP D α/GDP

Q4: cAMP activates:

- A Kinase B B Kinase A C Kinase C D Both C&B

Q5: An enzyme that can terminate signal:

- A Phospholipase C B Kinase A C Phosphatase D cAMP

Q6: Explain how a single ligand can cause different effects.

Q7: List the three main steps of the signaling process.

Q8: Kinase C is activated by

Q9: Phospholipase C can break phosphatidylinositol into

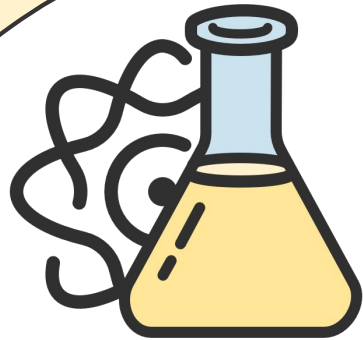
Q6:
Slide 7

Q7:
Recognition → transduction → effect

Q8:
Diacylglycerol & calcium

Q9:
Diacylglycerol (DAG)
Inositol 1 trisphosphate (IP3)

Answer Key: C (5) B (4) B (3) A (2) D (1)



Biochemistry 441

Girls



★ **Ghadah Alarify - Leader**

Yara Almufleh
Reema Alrashedi
Wareef Almousa
Joud Alangari
Fay Alluhaidan
Sarah Alhamlan
Arwa Almobeirek
Jumana AL-qahtani

Latifa Alkhdiri
Alanoud Alhaider
Futoon Almotairi
Manal Aldhirgham
Raaoum Jabor
Norah alawlah
Shahad Helmi
Rand Aldajani

Boys



★ **Khalid Alhamdi - Leader**

Ahmed Alayban
Sultan Alosaimi
Abdullah Alomran
Bassam Alghizzi
Ibrahim Aljurayyan
Mohammed Almutairi
Turki Alkhalifa
Malik Alshaya

Faisal Alhmoud
Abdulrahman Alnoshan
Ahmed Alqahtani
Hamad Alshaalan
Anas Alharbi
Mohammed Alwahibi
Saad Alghadir



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