Cell Signaling and Regulation of Metabolism

Lecture 14

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- Girls' slides
- Boys' slides
- Doctors' notes
- Important
- Extra info

Editing File

Biochemistry
442

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Objectives

By the end of this lecture, students are expected to:

- Differentiate different steps in signaling pathways
- Describe the second messenger systems
- Recognize the function of signaling pathways for
- Signal transmission
- Amplification
- Discuss the role of 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

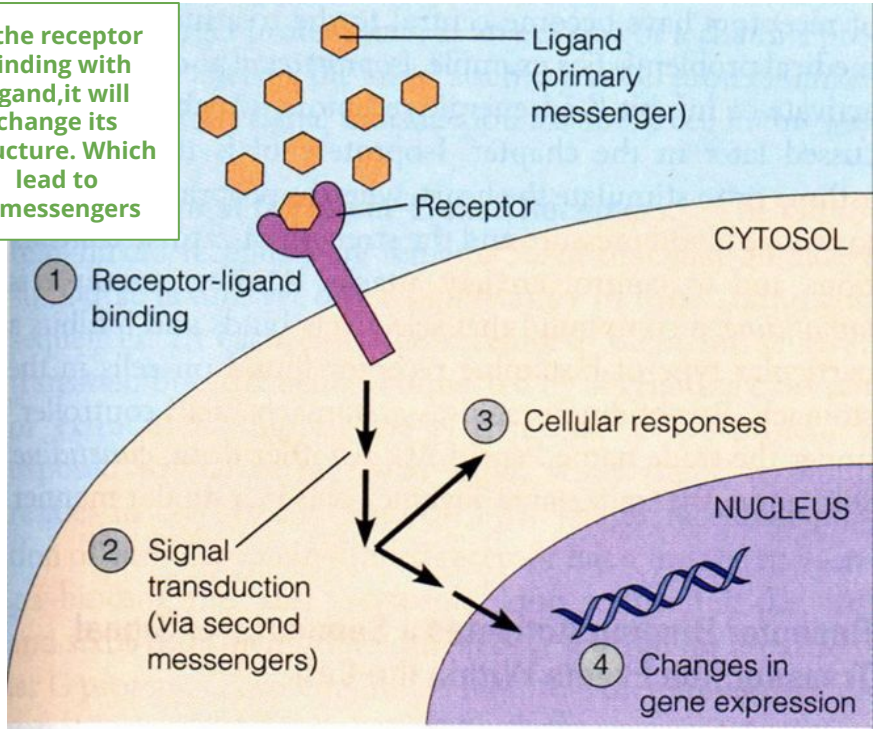
Signaling Process

1. Recognition :of signal (done by)- Receptors-
2. Transduction:Change of external signal into intracellular message with amplification and formation of second messenger
3. Effect :Modification of cell metabolism and function

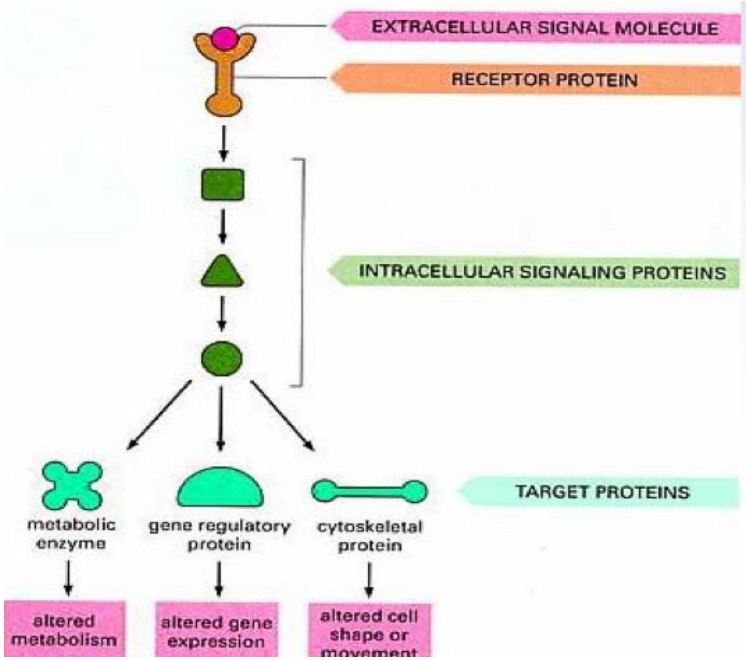
تبدأ singnaling process من الrecognition
وليس من release of molucule or hormone

General Signaling Pathway

If the receptor binding with ligand,it will change its structure. Which lead to 2*messengers



Signaling cascades

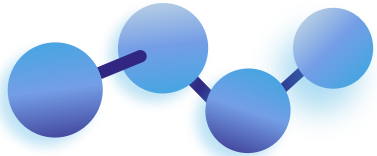


Recognition

Performed by receptors

Ligand will produce response only in cells that have receptors for this particular ligand.

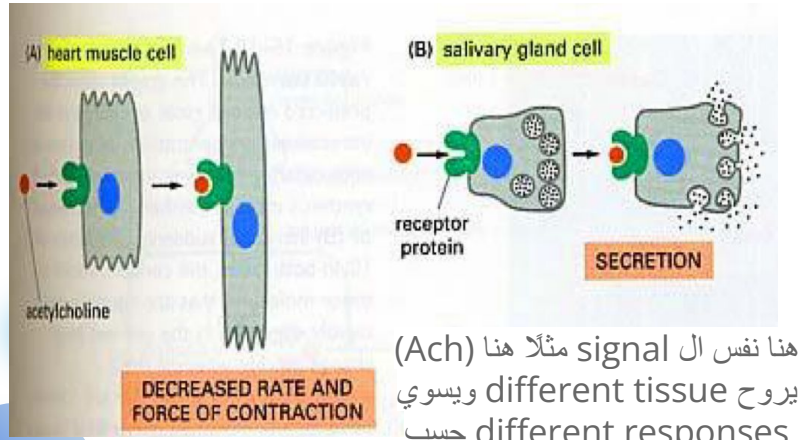
Each cell has a specific set of receptors



Different Responses to the Same Signaling Molecule

A

Different Cells

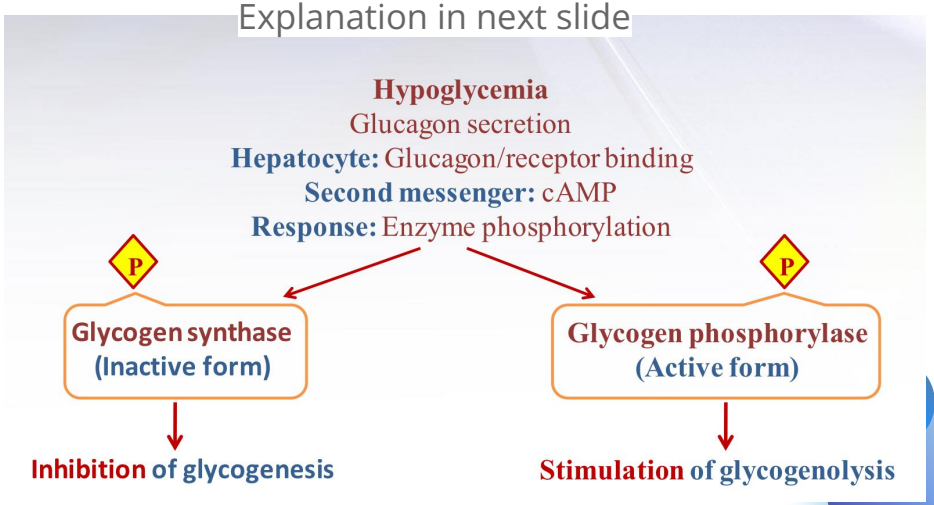


هنا نفس ال signal مثلًا هنا (Ach) يروح different tissue ويسوي different responses حسب وظيفته

B

One Cell but, Different Pathways

Explanation in next slide



Hypoglycemia

Glucagon secretion (the single ligand)

Hepatocyte:Glucagon/receptor binding

إضافة P يا بيسوي activation ولا inhibition حسب نوع الانزيم

بيحفز بروتينات تقدر تسوي phosphorylation

Second messenger**: cAMP**

Response: Enzyme phosphorylation

عندي نقص بالجلوكوز لذلك بزيد تكسير الجليكوجين (عشان احصل على الجلوكوز)

واقلل تصنيع الجليكوجين لأن مو وقته انا محتاجة جلوكووز

Glycogen synthase (Inactive form)

Glycogen phosphorylase (active form)

Inhibition of glycogenesis

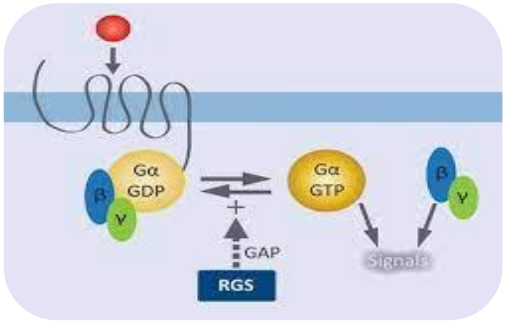
Stimulation of glycogenolysis

GTP-Dependant Regulatory Proteins (G-Proteins)

G-Proteins: Trimeric (3 subunits) membrane proteins (αβγ)
G-stimulatory(Gs) and G-inhibitory (Gi) binds to GTP/GDP

Forms of G-protein

Inactive form
Trimeric –bound GDP
(αβγ/GDP)



Active form
α-bound GTP
(α/GTP)

يروح ويتحرك

The **α-subunit** has intrinsic(by own) **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**

Example of second messenger system: is Adenylyl cyclase system
Example of second messenger:is CAMP

Adenylyl Cyclase System

Adenylyl cyclase: membrane-bound enzyme, converts ATP to cAMP.

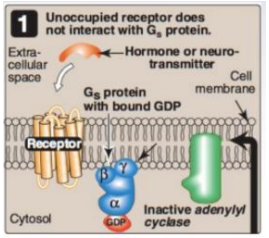
Activation/Inhibition:

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

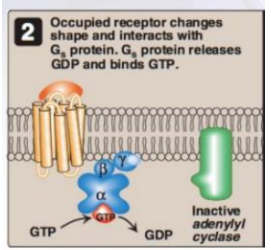
- Receptor:
G-protein coupled receptor

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

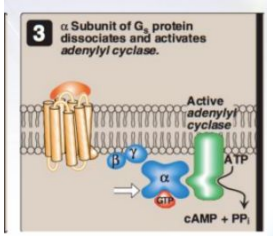
441 notes:
The receptor starts coupling with G-protein only when there is Signal.
• The signal won't affect the enzyme (Adenylyl cyclase) directly. It will affect the receptor (G-protein coupled Receptor) first.
• Then the receptor will activate G-protein which will activate the system



Resting state: No Signal



Ligand/Receptor Binding
Activation of G_s-protein



Activation of adenylyl cyclase

Actions of cAMP & Signal Termination

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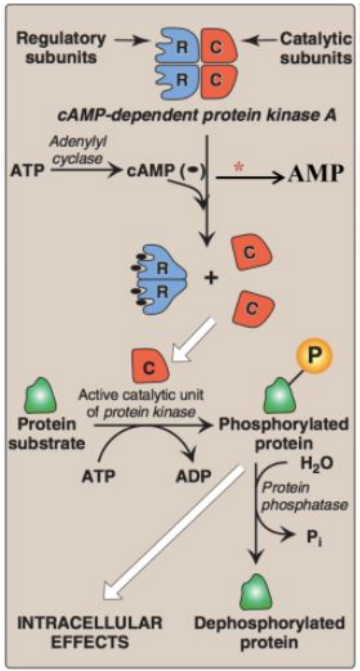
1. cAMP binds with the regulatory subunits of kinase A leading to activation of the catalytic unit of protein kinase.

2. Activated catalytic unit will phosphorylate a protein giving us a Phosphorylated protein.

3. The phosphorylated protein will do its intra-Cellular effect.

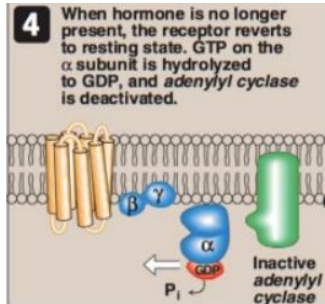


There are 3 ways for signal termination

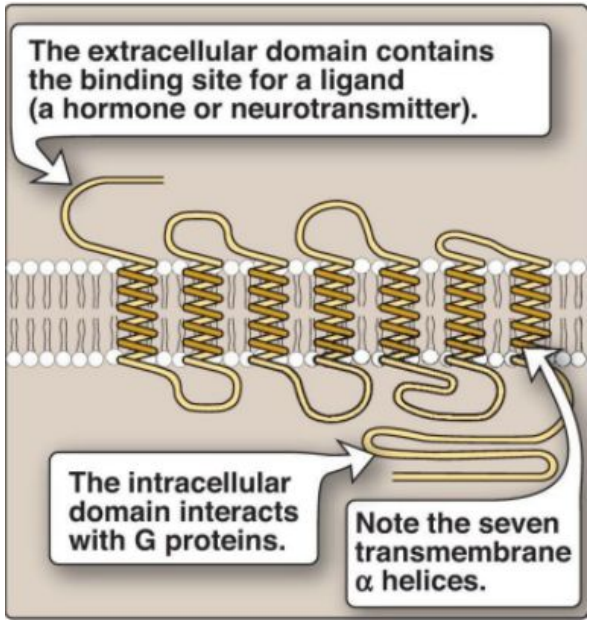
1. Protein phosphatase:
Protein phosphatase removes the phosphate group from the phosphorylated protein which gives us dephosphorylated Protein

2. Phosphodiesterase:
Using phosphodiesterase to decrease cAMP which give us an inactive protein kinase

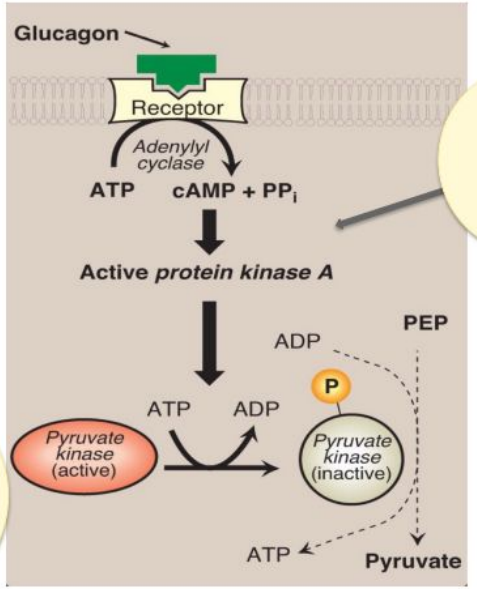
3. hormone is no longer present:
- Receptor back to resting state
- GTP On alpha subunits is hydrolyzed into GDP
- Adenylyl cyclase is deactivated



G-Protein Coupled Membrane Receptor



Pyruvate Kinase Regulation: Covalent Modification

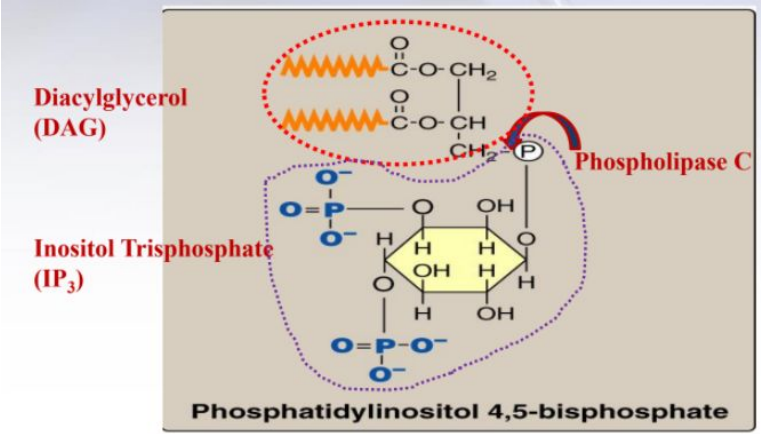


Here, it is the same as the previous

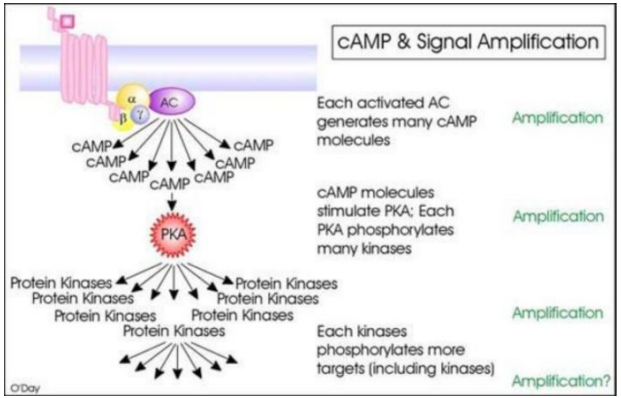
- Target: pyruvate kinase
- This occurs due to hypoglycemia

Calcium/Phosphatidylinositol System

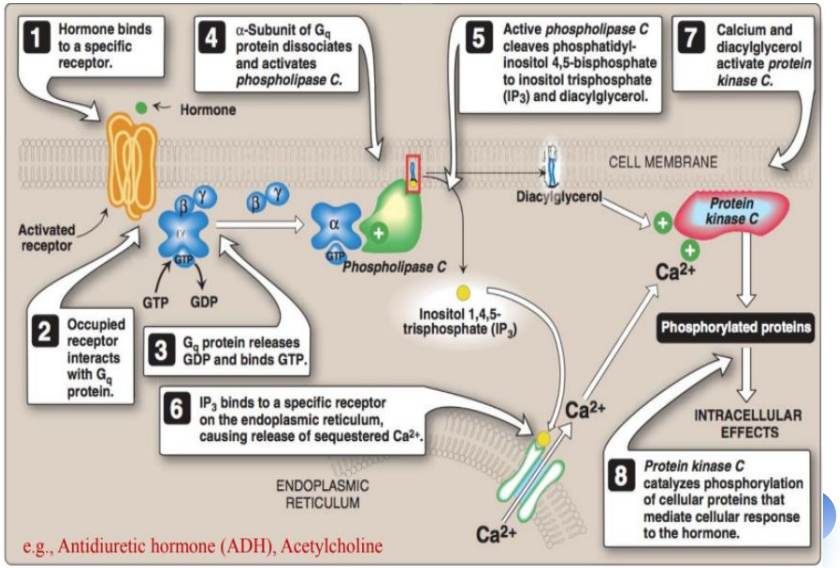
There are Different type of Phospholipase The difference between them is the target bond they are going to break



Signal Amplification



Intracellular Signaling by Inositol trisphosphate



Quiz

Q1: Change of external signal into intracellular message with amplification and formation of second messenger is called:			
Recognition	Effect	None	Transduction
Q2: The recognition process is done by			
A-Receptor	B-Neurotransmitter	C-Hormones	D-DNA
Q3: The inactive form of G-protein is:			
A- αβγ/GTP	B- αβγ/GDP	C - α/GTP	D - α/GDP
Q4:cAMP activates			
A-kinase B	B-kinase A	C-kinase c	D-both B&C

5)C
4)B
3)B
2)A
1)D

Our Team

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