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Special thanks to :

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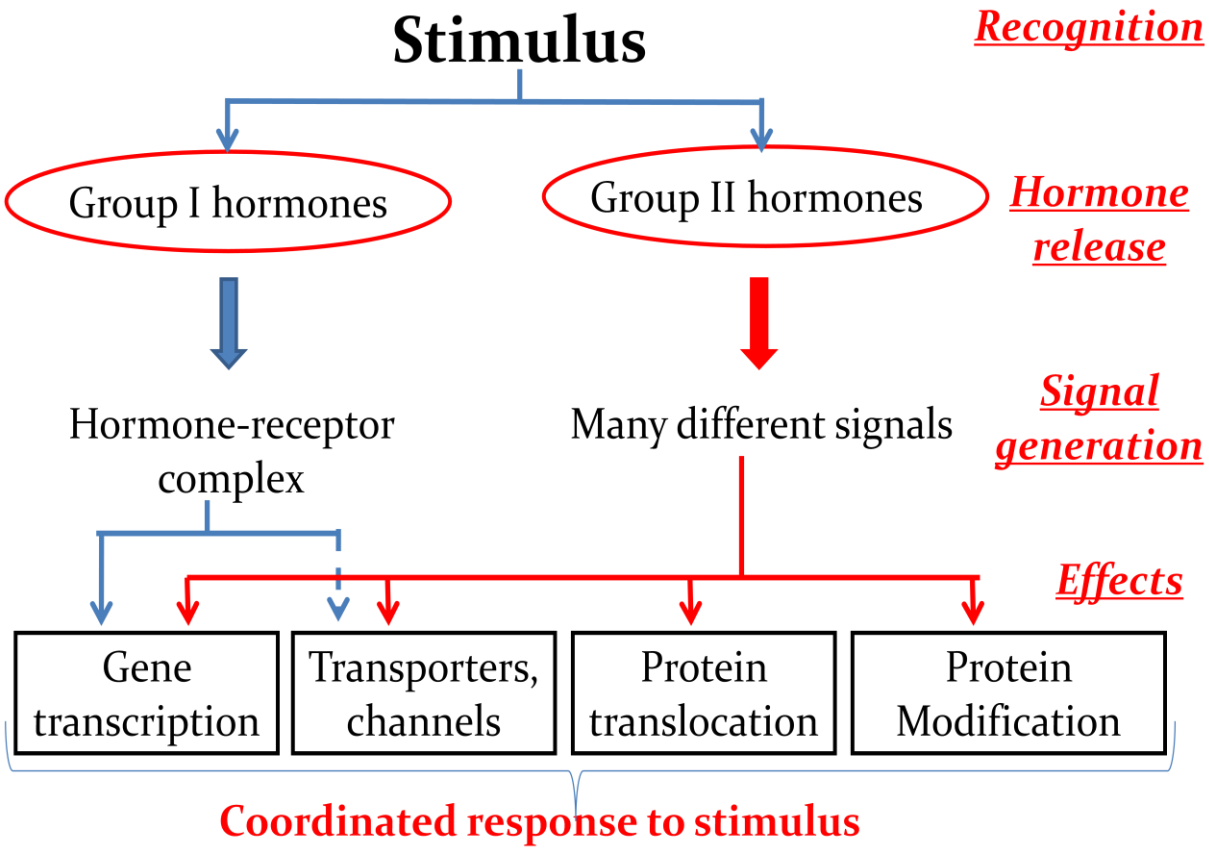
Background:

- Multicellular organisms depend in their survival on their adaptation to a constantly changing environment
- Intercellular communication is necessary for this adaptation to take place
- Human body synthesizes many hormones that can act specifically on different cells of the body
- More than one hormone can affect a given cell type
- Hormones can exert many different effects in one cell or in different cells
- A target is any cell in which the hormone (ligand) binds to its receptor

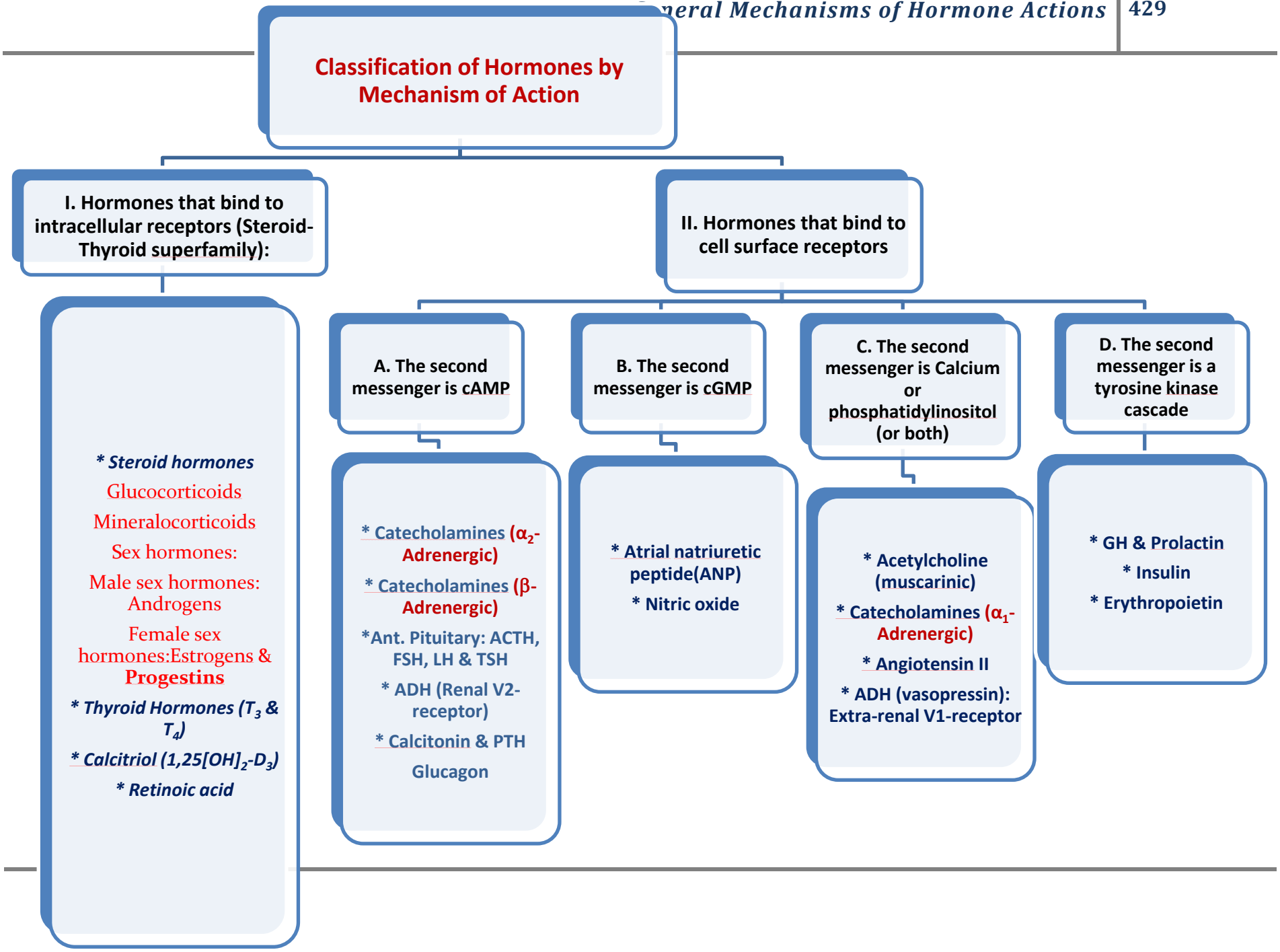
Factors determining the response of a target cell to a hormone:

- The rate of synthesis & secretion of the hormones
- The conversion of inactive forms of the hormone into the fully active form
    - The target tissue will exert physiological action of hormones are in fully active form and inversely it will exert no action if the hormones are inactive form
- The rate of hormone clearance from plasma (half-life & excretion)
    - The more the hormone is bound to a plasma protein (i.e. albumin) the more its action will last in the body
- The number, relative activity, and state of occupancy of the specific receptors
- Post-receptor factors


Stimulus
Recognition
Group I hormones
Group II hormones
Hormone release
Hormone-receptor complex
Many different signals
Signal generation
Effects
Gene transcription
Transporters, channels
Protein translocation
Protein Modification
Coordinated response to stimulus

General Features of Hormone Classes：

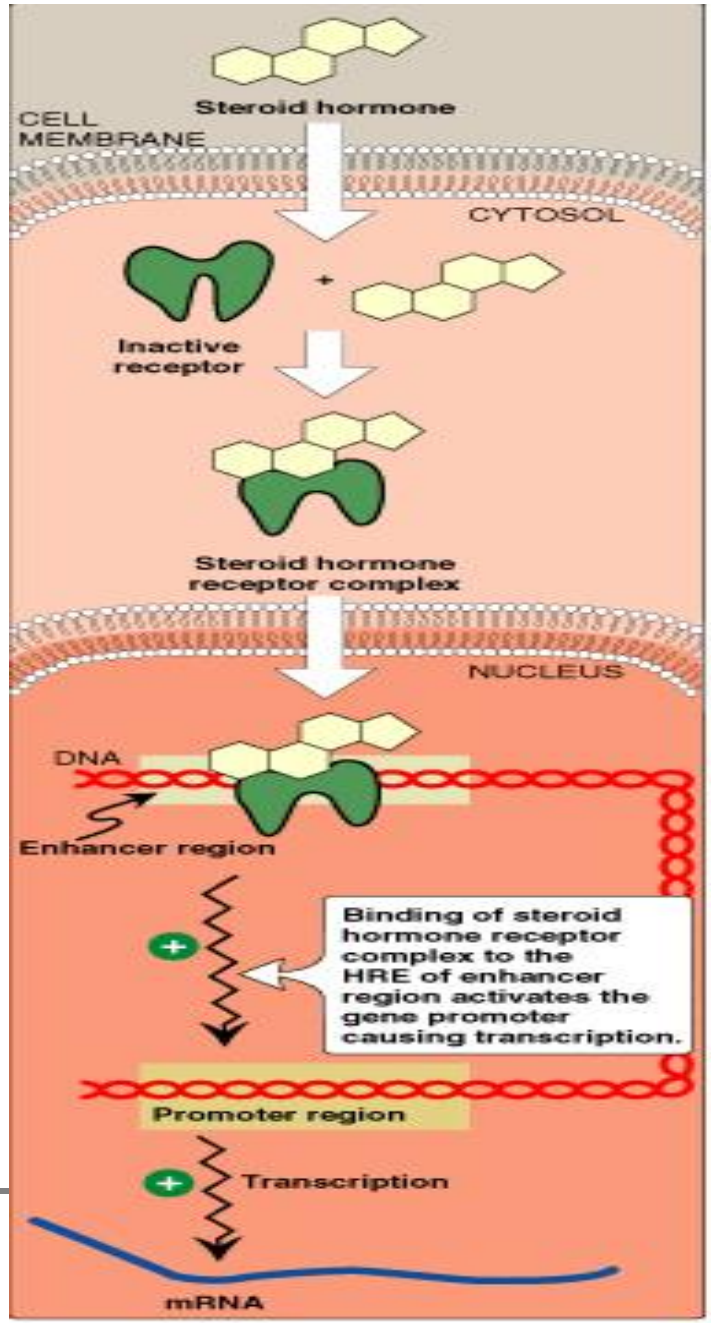
	Group I	Group II
Types	**Steroids, iodothyronines, calcitriol (active form of Vitamine D), retinoids**	Polypeptides, glycoproteins, catecholamines
Solubility	**Lipophilic**	Hydrophilic
Transport proteins	**Yes**	No
Plasma half-life	**Long (hours – days)**	Short (minutes)
Receptor	**Intracellular**	Plasma membrane
Mediator	**Receptor-hormone complex**	cAMP, cGMP, Ca^{2+}, metabolites of complex phosphoinositols, tyrosine kinase cascades


Classification of Hormones by Mechanism of Action
I. Hormones that bind to intracellular receptors (Steroid-Thyroid superfamily):
* Steroid hormones
Glucocorticoids
Mineralocorticoids
Sex hormones:
Male sex hormones: Androgens
Female sex hormones:Estrogens & Progestins
* Thyroid Hormones (T_3 & T_4)
* Calcitriol ($1,25[OH]_2$-D_3)
* Retinoic acid
II. Hormones that bind to cell surface receptors
A. The second messenger is cAMP
* Catecholamines (α_2-Adrenergic)
* Catecholamines (β-Adrenergic)
*Ant. Pituitary: ACTH, FSH, LH & TSH
* ADH (Renal V2-receptor)
* Calcitonin & PTH
Glucagon
B. The second messenger is cGMP
* Atrial natriuretic peptide(ANP)
* Nitric oxide
C. The second messenger is Calcium or phosphatidylinositol (or both)
* Acetylcholine (muscarinic)
* Catecholamines (α_1-Adrenergic)
* Angiotensin II
* ADH (vasopressin): Extra-renal V1-receptor
D. The second messenger is a tyrosine kinase cascade
* GH & Prolactin
* Insulin
* Erythropoietin

Group I : hormones binds to intracellular receptor

Mechanism of Action of Steroid-Thyroid Hormones:

1- Hormone across the cell membrane due to it solubility
2- Bind to a specific cytosolic OR nuclear receptor (hormone-receptor complex is formed)
3- This hormone receptor complex go to the nucleus , dimerize and binds to DNA sequence
(called: hormone receptor element HRE)
4- The effect is produced :
- transcription (mRNA) → ribosome in the cytoplasm → protein is formed
- inhibits transcription



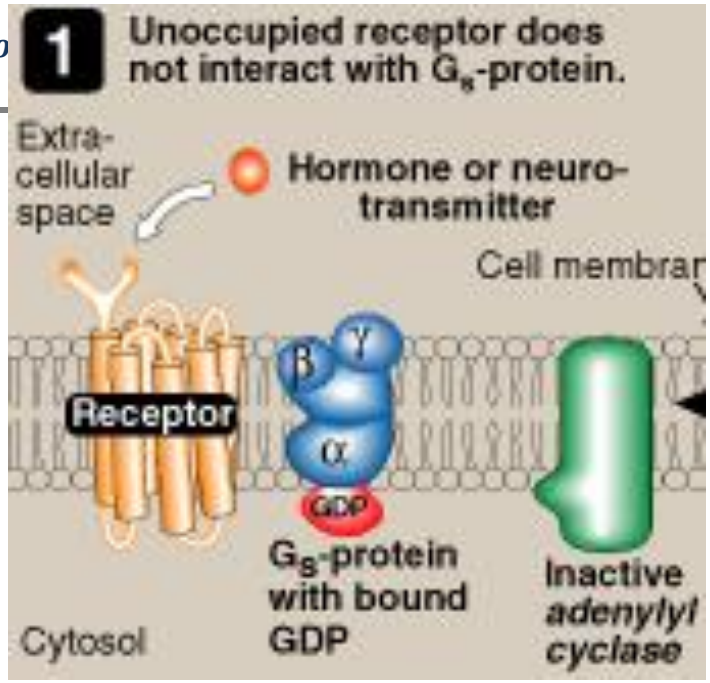
Group II. Hormones that bind to cell surface receptors

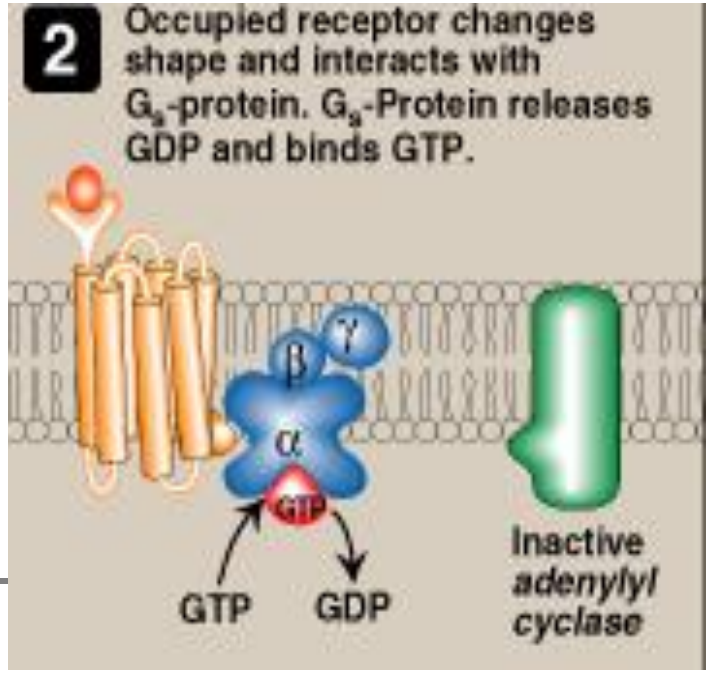
A. The second messenger is cAMP

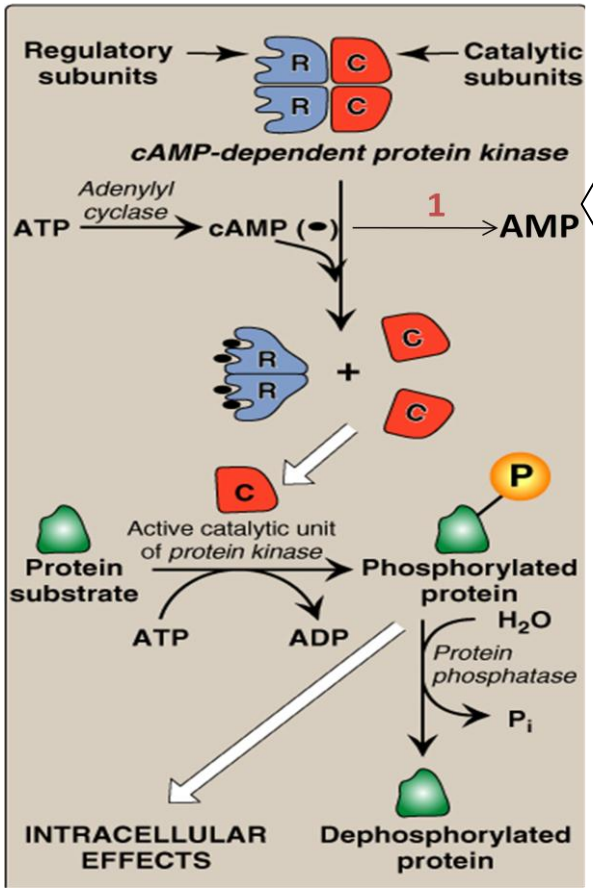
- **Glucagon**
- **Catecholamines (β- Adrenergic)**
- **ADH (Renal V2-receptor**

Mechanism of action :

1. **These hormones are lipophobic so they cannot cross the plasma membrane**
2. **Hormones bind to the receptor and causes conformational change**
3. **This changed(activated) receptor then interacts with G protein and**
4. **When G proteins are inactivated they are interact with GDP and once they are activated by the activated receptor the GDP is changed to GTP**
5. **After the G protein is coupled with GTP it loses the beta and gamma subunits and keeps the alpha this complex of GTP and alpha subunit then activates adenylylcylase**
6. **As a result adenylylcylase changes ATP to cAMP**

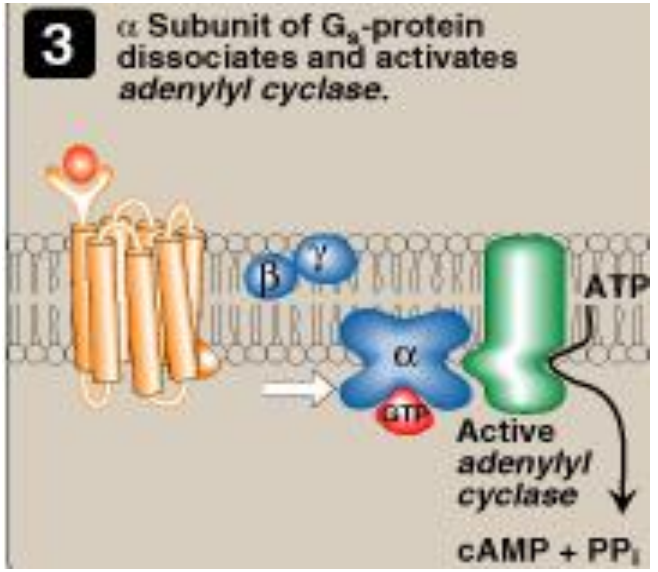






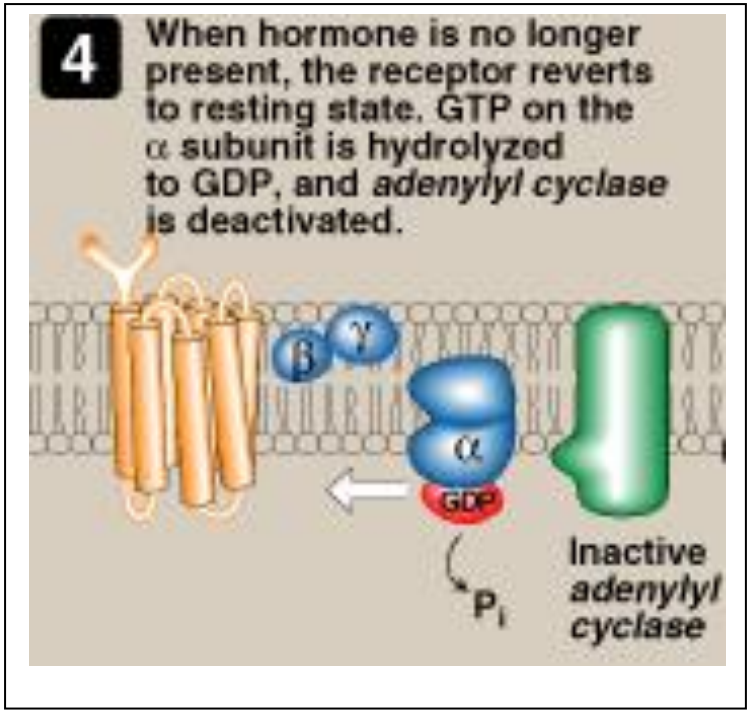
cAMP is converted to AMP by :

phosphodiesterase



cAMP then activates protein kinase A by binding to its regulatory subunits and causing the release of its 2 catalytic subunits

Then these 2 catalytic subunits of protein kinase A causes phosphorylation of proteins leading to activation or inactivation thus regulating cellular function.



When the hormone is not present any more

The GTP is hydrolyzed to GDP and all the system will be off : 1- NO activation to adenyl cyclase

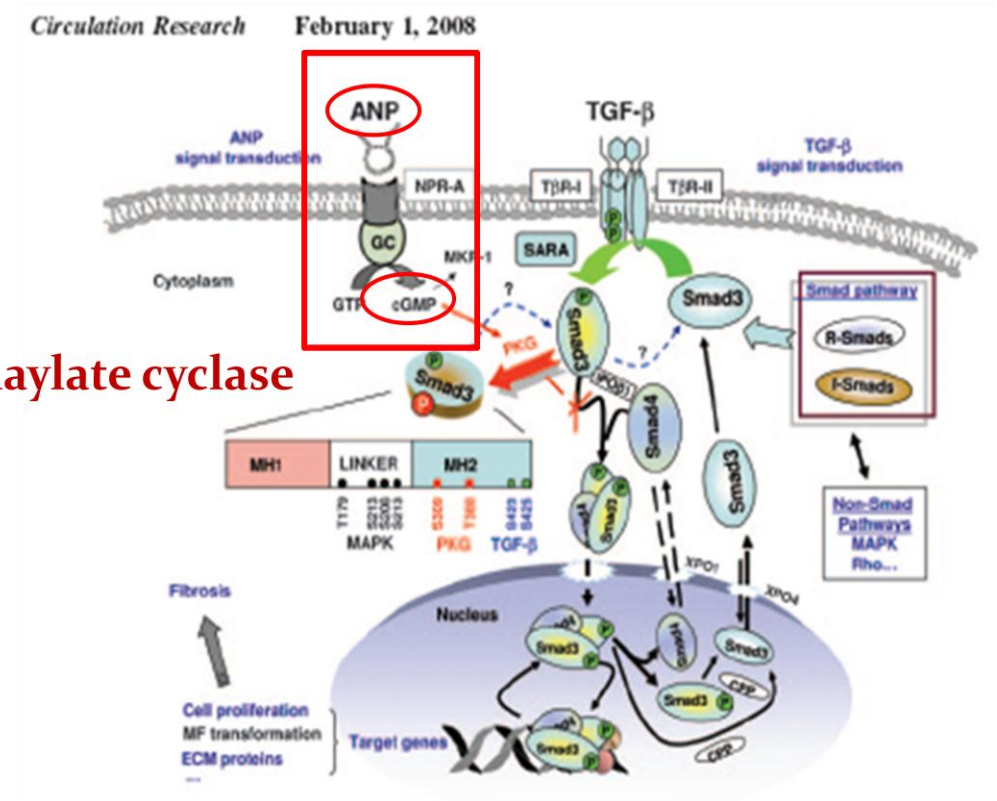
2 –NO ATP will be converted to cAmp

3- NO activation of protein kinase

B. The second messenger is cGMP

The activated enzyme is guanylate cyclise

For Example: ANP and NO



GC: Gunaylate cyclase

The difference between this reaction and the one before is : ANP and NO the mechanism involves cGMP not cAMP

Adenylyl cyclase:(the previous mechanism) *: which its action is remove p from ATP to form CAMP*

But here the Enzyme is

Gunaylate cyclase *: which its action is remove p from GTP to form cGTP*

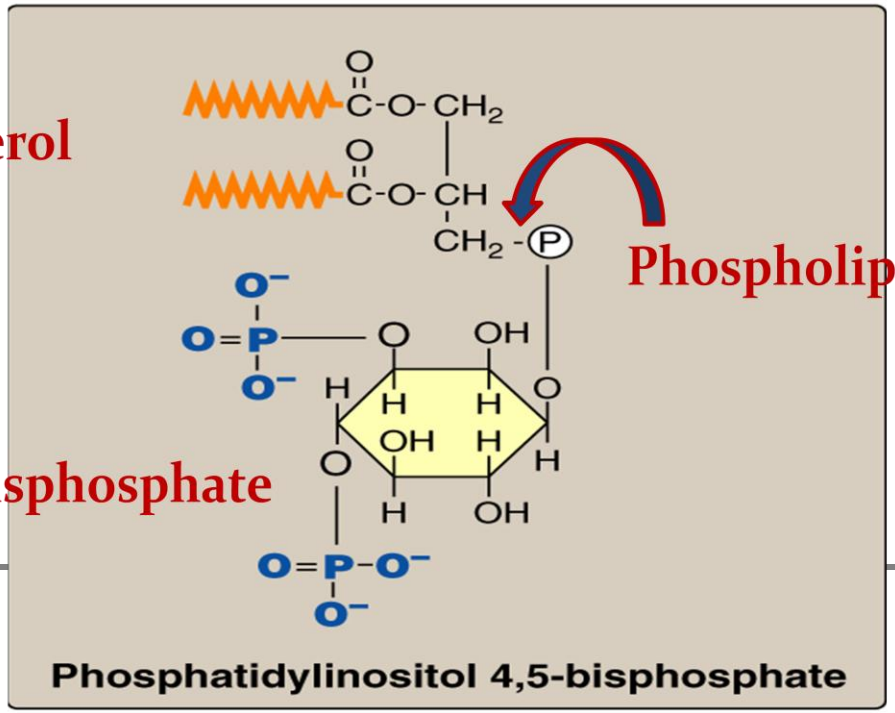
C. The second messenger is calcium or phosphatidylinositol (or both)

- *Catecholamines (α_1-Adrenergic)*
- *ADH (vasopressin): Extra-renal V1-receptor*

Calcium/Phosphatidylinositol System

Diacylglycerol (DAG)

Inositol Trisphosphate (IP_3)

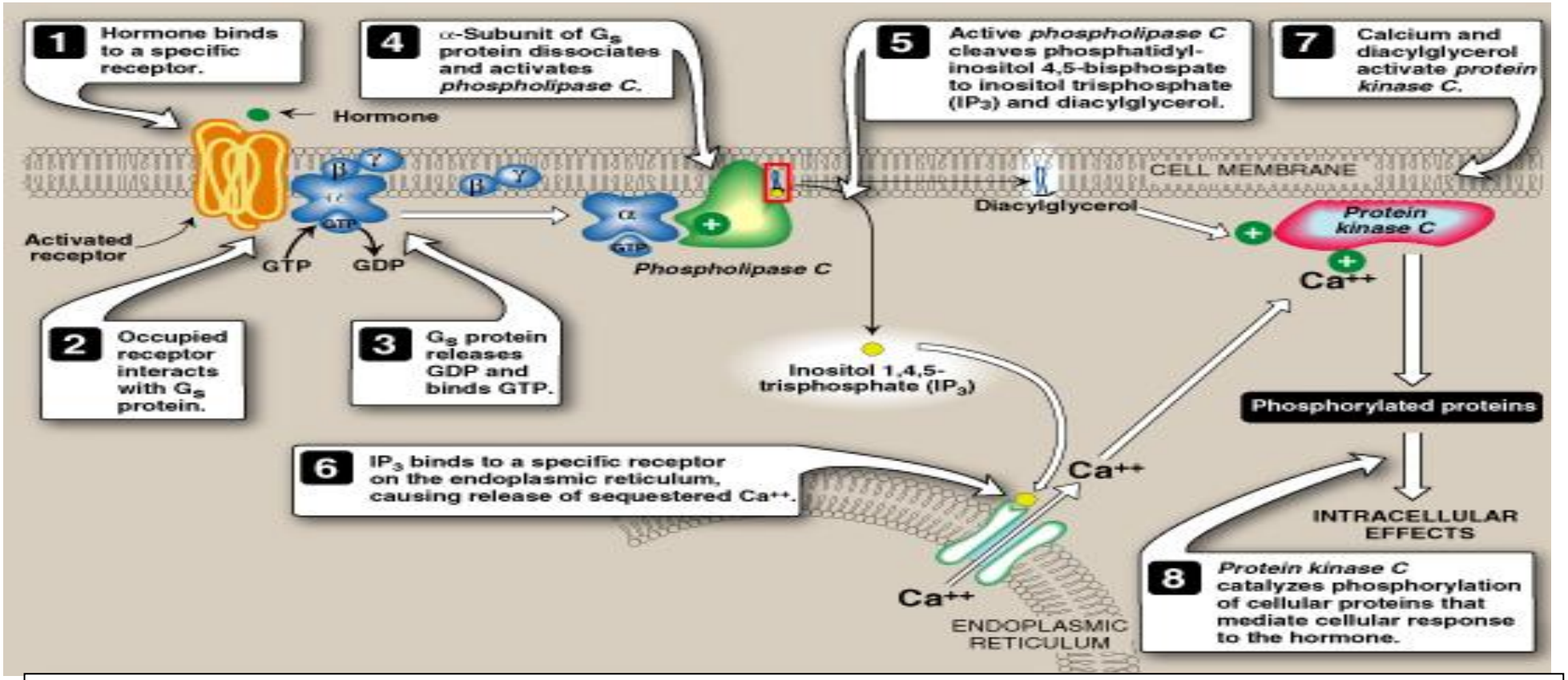


Phospholipase C

Phospholipase c is an enzyme that cleavage the

(phosphatidylinositol 4-5 bisphosphate)

into (DAG) and (IP3)→ which work as



MOA : **1- The hormone binds to receptor > activate Gs protein > G protein activates phospholipase C**

2-Phospholipase C then cleaves part phosphatidyl-inositol 4,5 bisphosphate to

a. Inositol triphosphate (IP3) which binds to the endoplasmic reticulum and cause increase of intracellular Ca++ (that is the only function of IP3)

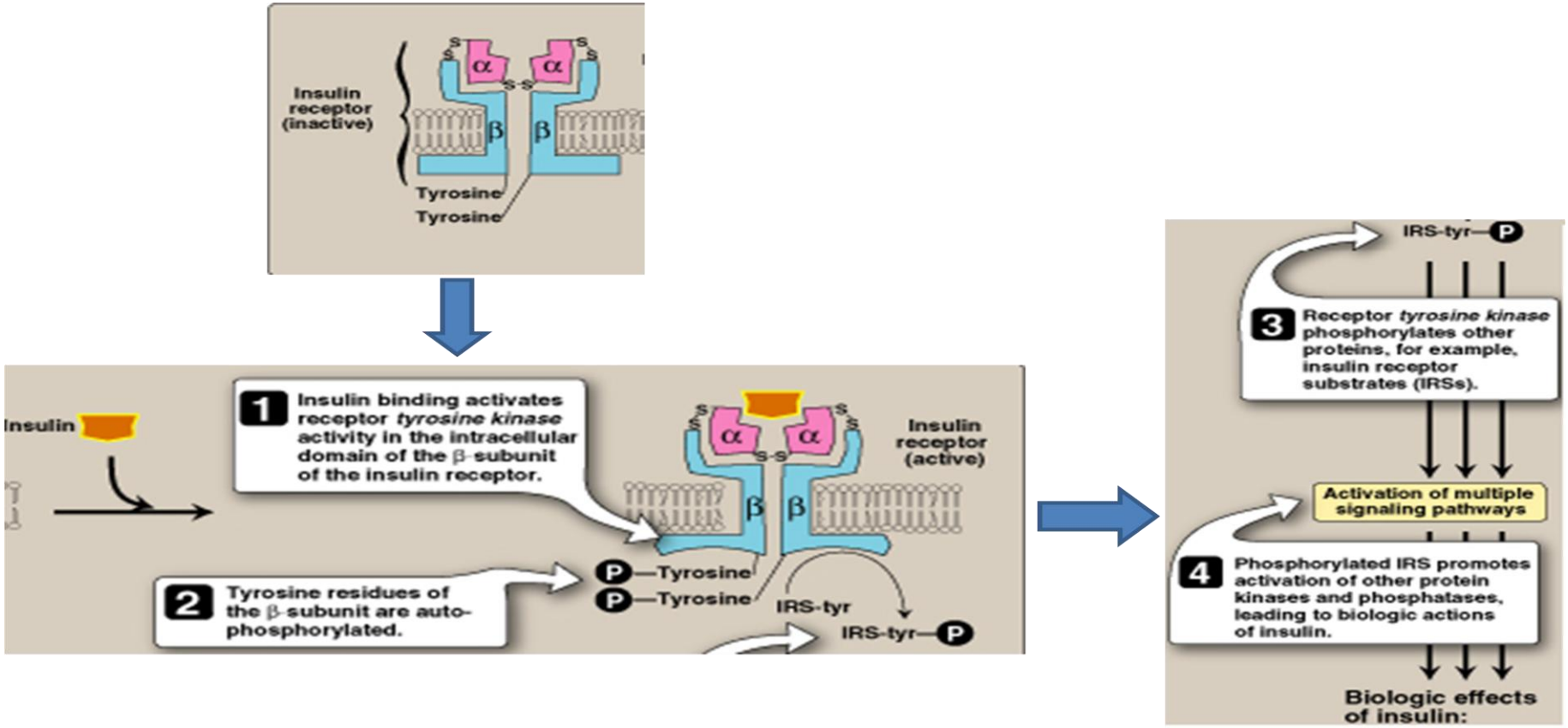
b. Diacyelglycerol (DAG)

3-Then both DAG and Ca++ activate protein kinase C which gives cellular responses

Remember in the cAMP mechanism the protein kinase was protein kinase A

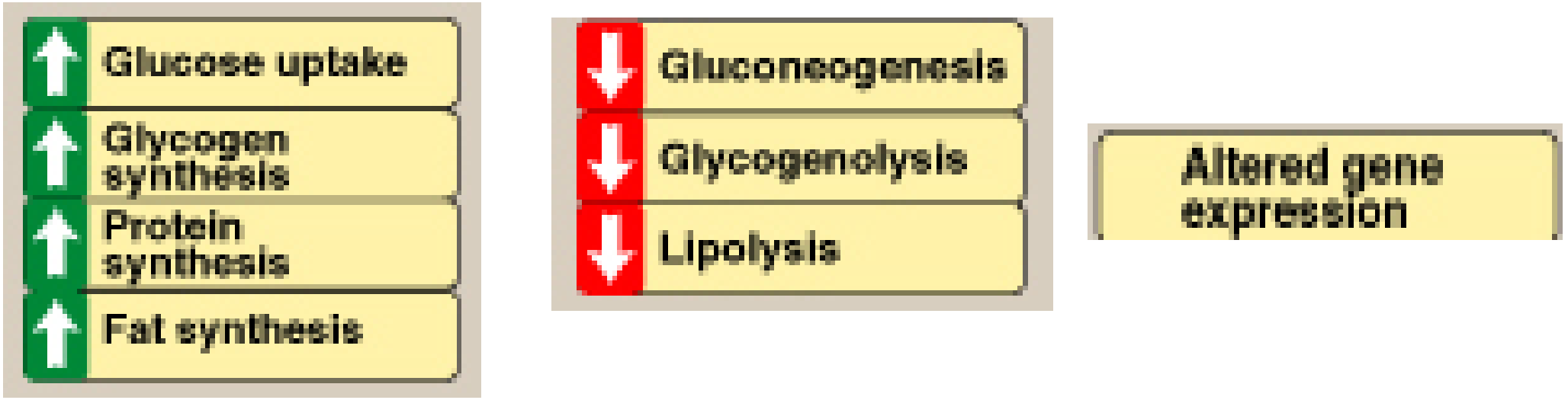
In the calcium or phosphatidylinositol mechanism the protein kinase is protein kinase C

D. The second messenger is a tyrosine kinase cascade: *1- Insulin 2-Growth hormone*



1. Insulin receptor has two subunits
    a. Subunit alpha which lies outside the cell membrane and this is where insulin binds
    b. Subunit beta which lies within the cell and this is a tyrosine kinase protein that is activated when insulin binds to alpha subunit
2. After the binding of insulin to the receptor the tyrosine residues are AUTOPHOSPORYLATED
3. This phosphorelated receptor then phosphorolates other proteins like IRS (insulin receptor substrates)
4. IRS causes physiological effects of insulin

Biologic Effects of Insulin:



Biomedical Importance :

— ***Excessive, deficient, or inappropriate production /release of hormones are major causes of diseases***

— ***Many drugs act through influencing the pathways of hormones***