

# General Mechanisms of Hormone Actions

*Endocrine Block*

# OBJECTIVES

**By the end of this lecture, students should be able to:**

- **Acquire the knowledge for general consequence of hormone-receptor interaction**
- **Understand different mechanisms of action of hormones**
- **Recognize the biomedical importance due to disturbance in the normal mechanisms of hormonal action**

# Lecture Outlines

- **Background**
- **Factors determining the response of a target cell to a hormone**
- **Hormone-receptor interaction**
- **General features of hormone classes**
- **Classification of hormones by mechanism of action**
- **Biomedical importance**

# 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**

# Background

- **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 rate of hormone clearance from plasma (half-life & excretion)**
- **The number, relative activity, and state of occupancy of the specific receptors**
- **Post-receptor factors**

# Stimulus

Group I hormones

Group II hormones

Hormone release

Hormone/receptor binding at the target cells

Recognition

Hormone-receptor complex

Second messengers

Signal generation

Gene transcription

Transporters, channels

Protein translocation

Protein Modification

Effects

**Coordinated response to stimulus**

# General Features of Hormone Classes

	Group I	Group II
Types	Steroids Thyroid Hs (T <sub>3</sub> & T <sub>4</sub> ) Calcitriol, 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 <sup>2+</sup> , 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**

**Thyroid Hormones ( $T_3$  &  $T_4$ )**

**Calcitriol (active form of vitamin D,  $1,25[OH]_2-D_3$ )**

**Retinoic acid**

# Mechanism of Action of Steroid-Thyroid Hormones

**Steroid Hormones:**

Glucocorticoids

Mineralocorticoids

Sex hormones:

Male sex hormones: Androgens

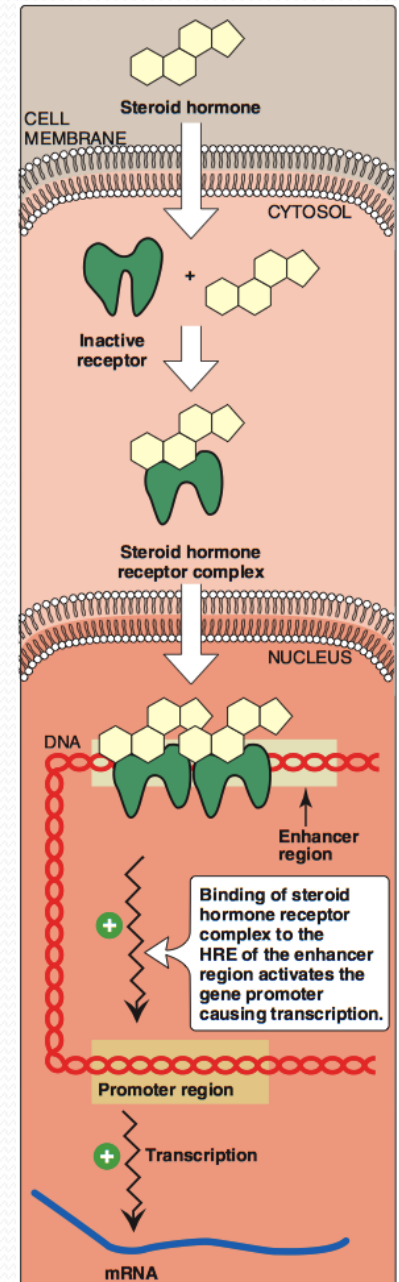
Female sex hormones: Estrogens &

Progestins

**Thyroid Hormones ( $T_3$  &  $T_4$ )**

**Calcitriol ( $1,25[\text{OH}]_2\text{-D}_3$ )**

**Retinoic acid**



# Classification of Hormones by Mechanism of Action

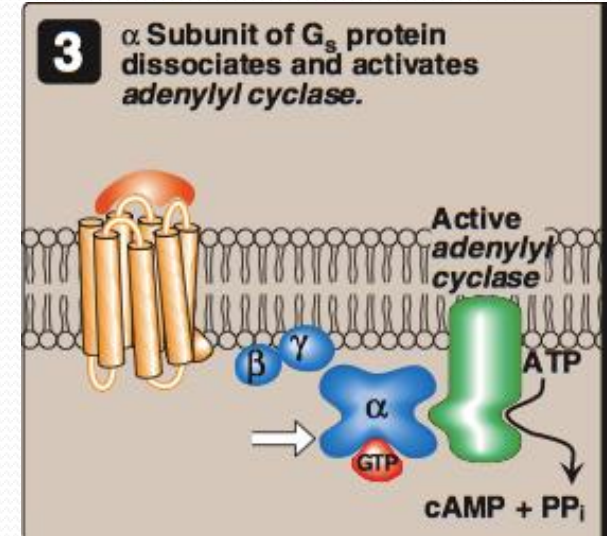
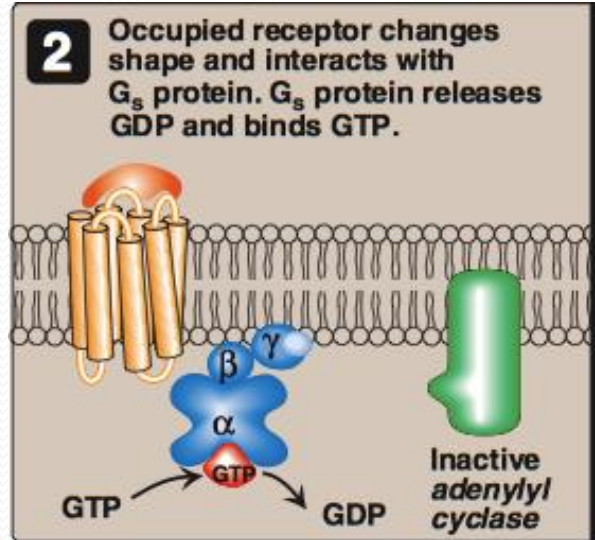
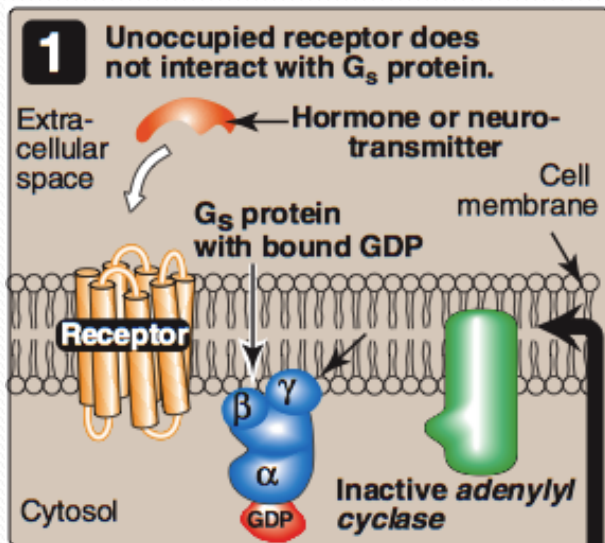
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## II. Hormones that bind to cell surface receptors

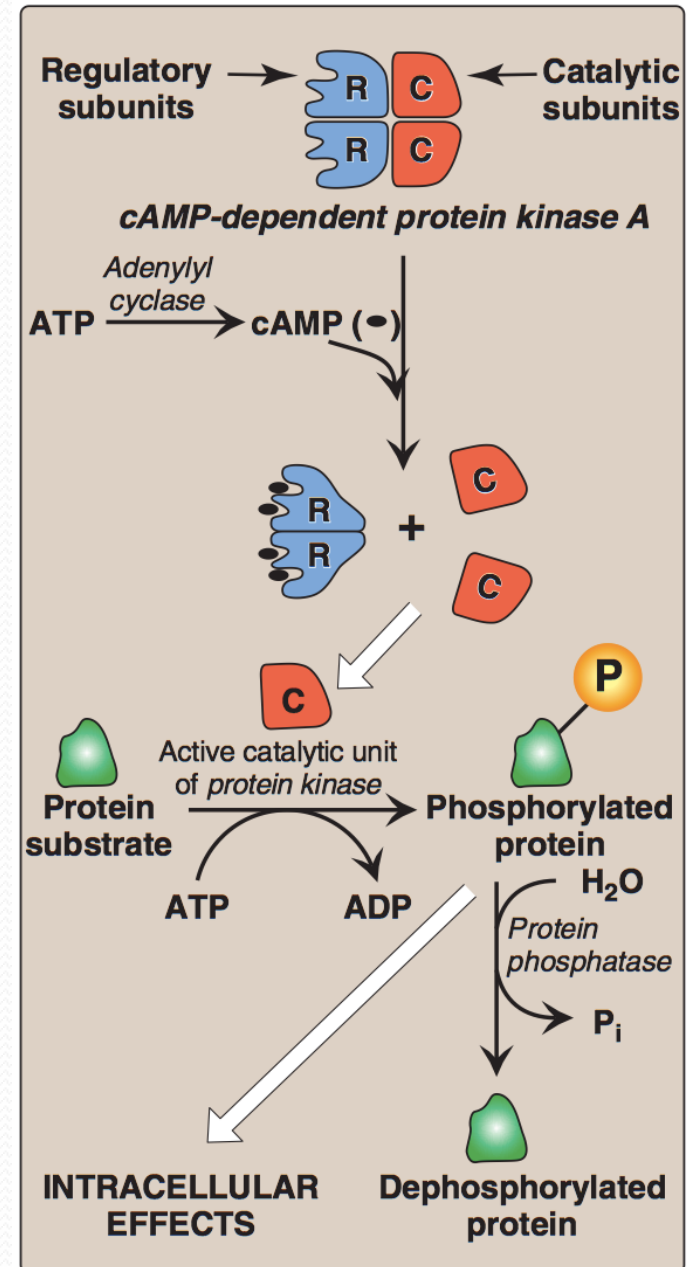
### A. The second messenger is cAMP

- Catecholamines ( $\alpha_2$ - Adrenergic)
- Catecholamines ( $\beta$ - Adrenergic)
- Ant. Pituitary: ACTH, FSH, LH & TSH
- ADH (Renal V<sub>2</sub>-receptor)
- Calcitonin & PTH
- Glucagon

# Cascade for formation of cAMP by cell-surface hormones

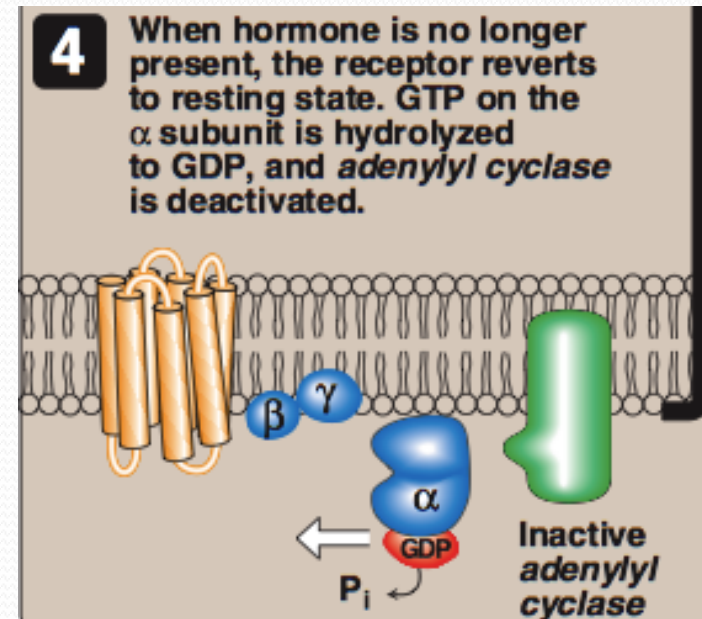
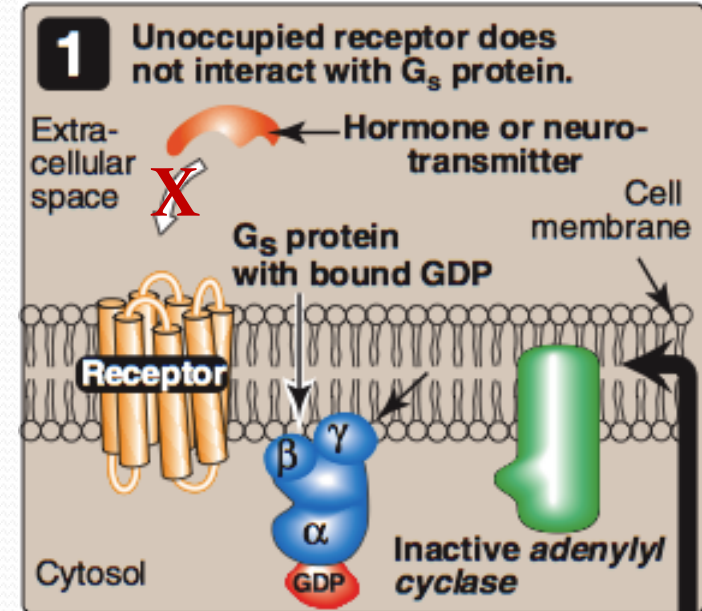


# Actions of cAMP



# Abortion of Hormonal Stimulus

1. Release of hormone from its receptor (unbound receptor)
2. Dephosphorylation of protein substrate by phosphatase
3. Degradation of cAMP into AMP by phosphodiesterase
4. Inactivation of protein kinase A by a decrease of cAMP
5. Hydrolysis of GTP into GDP
6. Binding of  $\alpha$ -subunit to  $\beta\gamma$ -subunits
7. Inactivation of adenylyl cyclase



# Classification of Hormones by Mechanism of Action

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## II. Hormones that bind to cell surface receptors B. The second messenger is cGMP

**Atrial natriuretic peptide (ANP)**

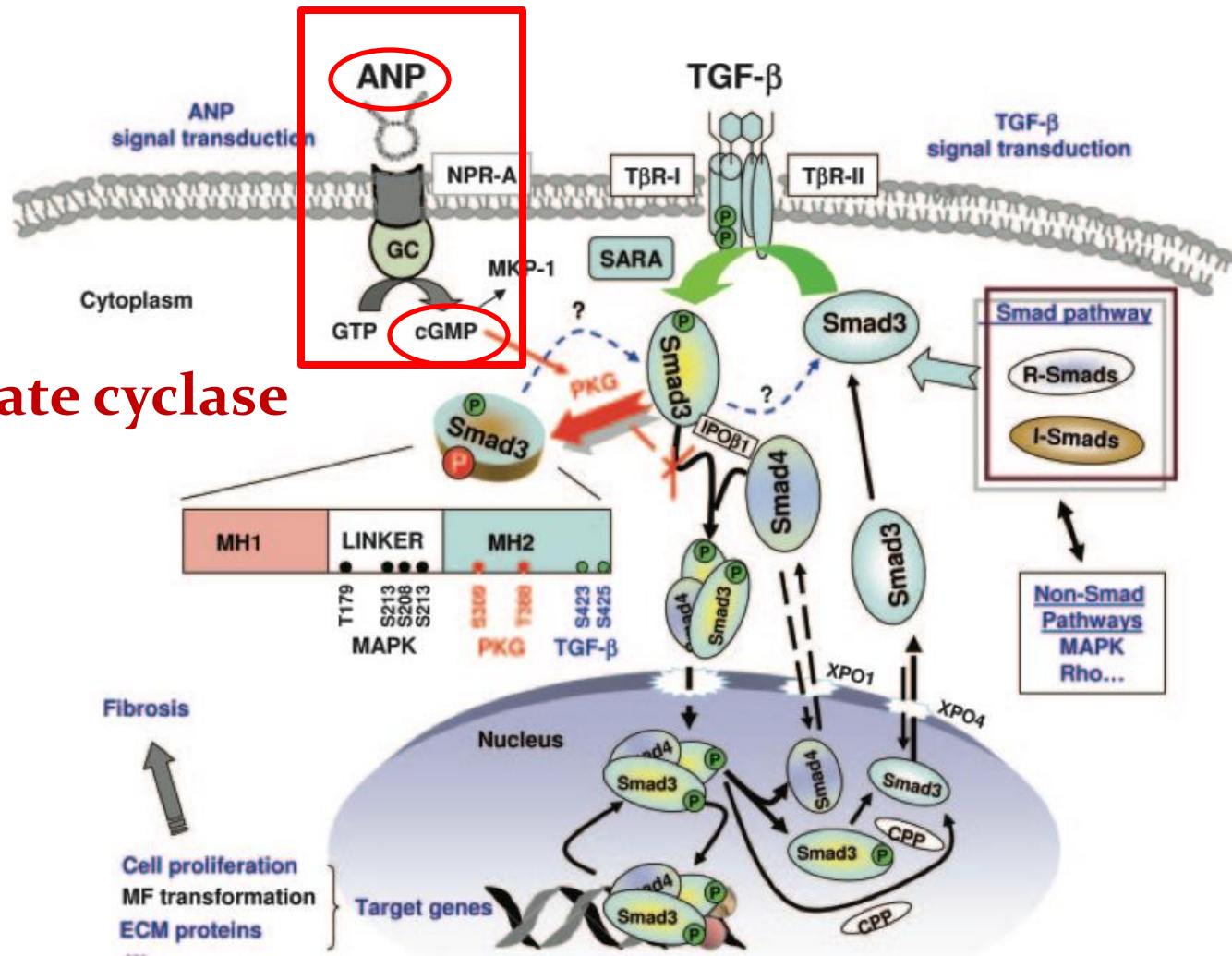
**Nitric oxide**



# Atrial Natriuretic Peptide (ANP)

*Circulation Research*

February 1, 2008



GC: Guanylate cyclase

Fibrosis



Cell proliferation  
MF transformation  
ECM proteins

Target genes



# Classification of Hormones by Mechanism of Action

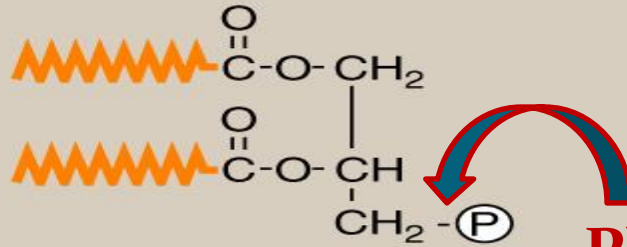
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## II. Hormones that bind to cell surface receptors C. The second messenger is calcium or phosphatidylinositol (or both)

- Acetylcholine (muscarinic)
- Catecholamines ( $\alpha_1$ -Adrenergic)
- Angiotensin II
- ADH (vasopressin): Extra-renal  $V_1$ -receptor

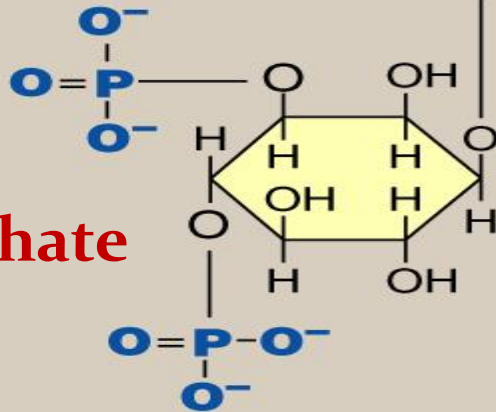
# Calcium/Phosphatidylinositol System

Diacylglycerol (DAG)

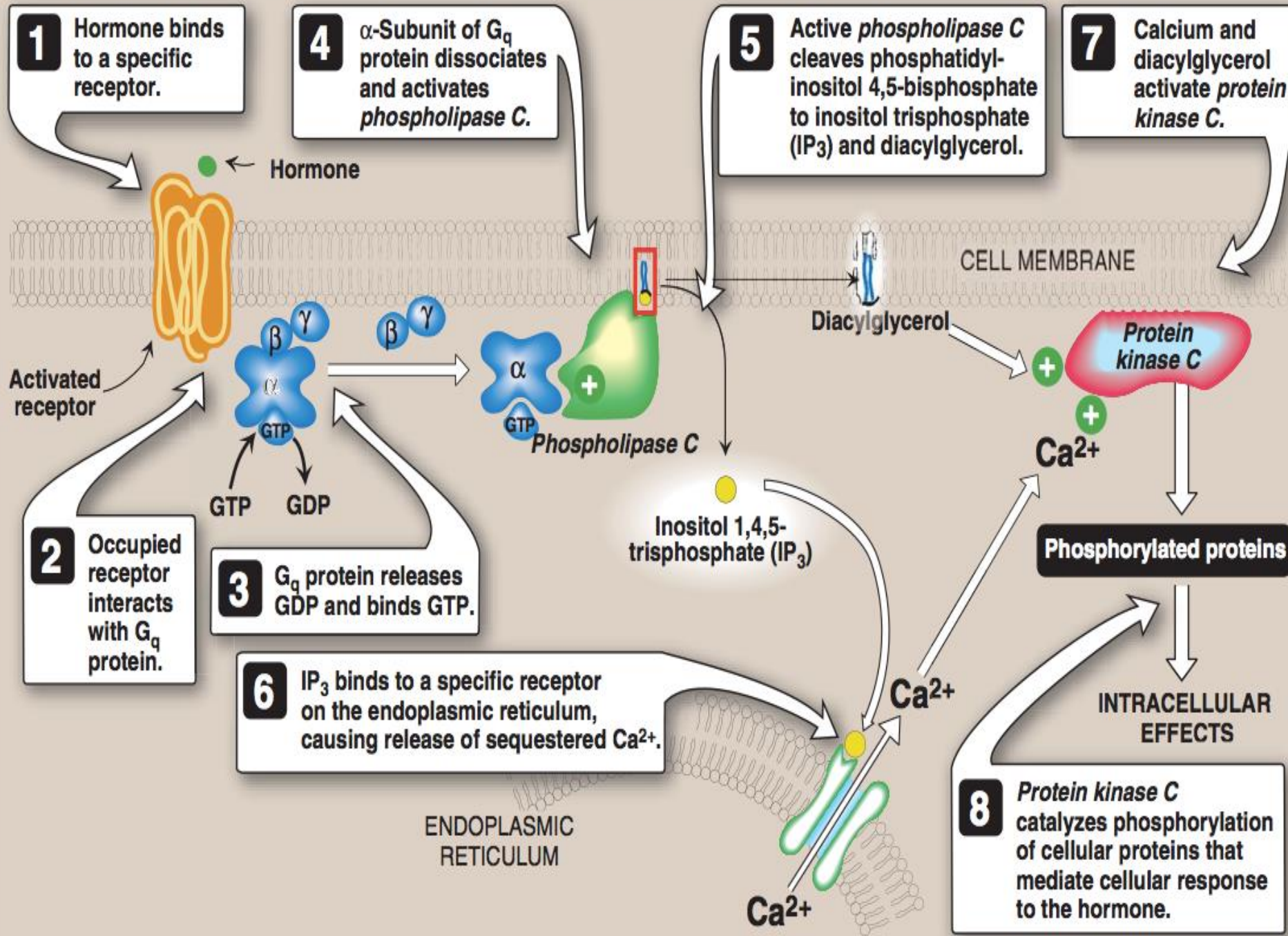


Phospholipase C

Inositol Trisphosphate (IP<sub>3</sub>)



Phosphatidylinositol 4,5-bisphosphate



# Classification of Hormones by Mechanism of Action

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II. Hormones that bind to cell surface receptors

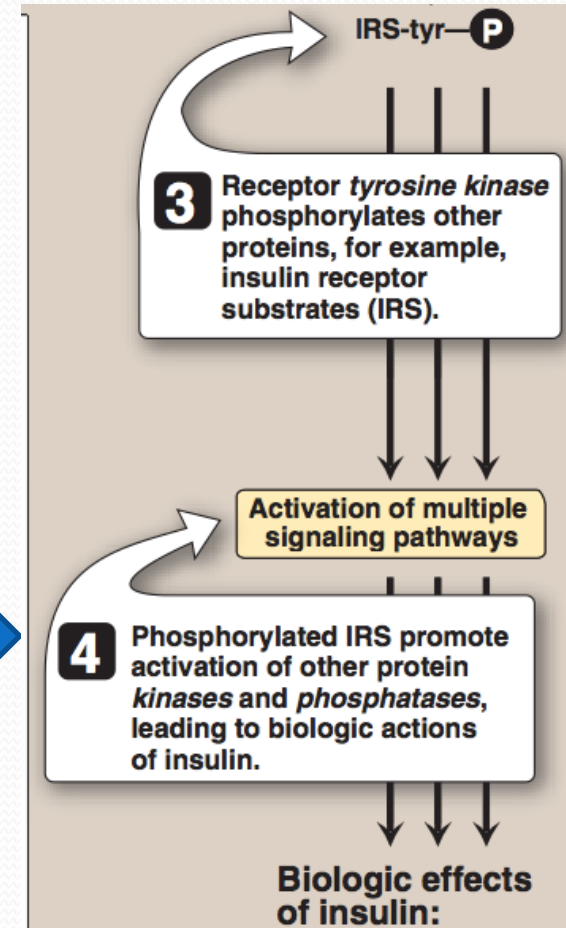
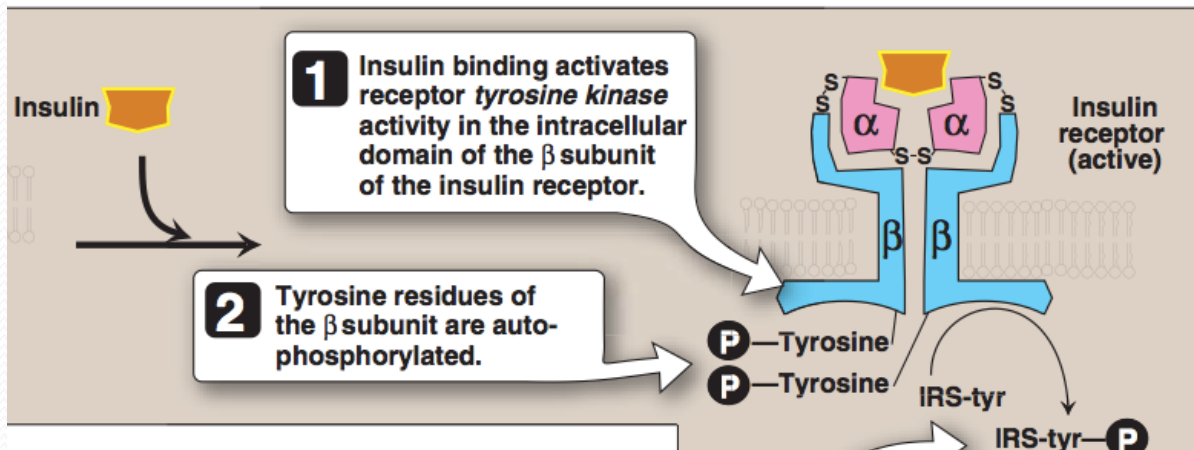
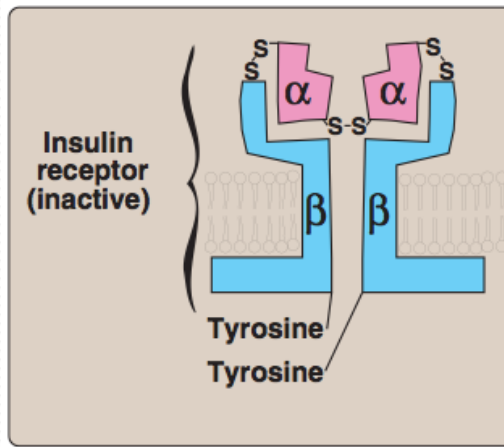
D. The second messenger is a tyrosine kinase cascade

**GH & Prolactin**

**Insulin**

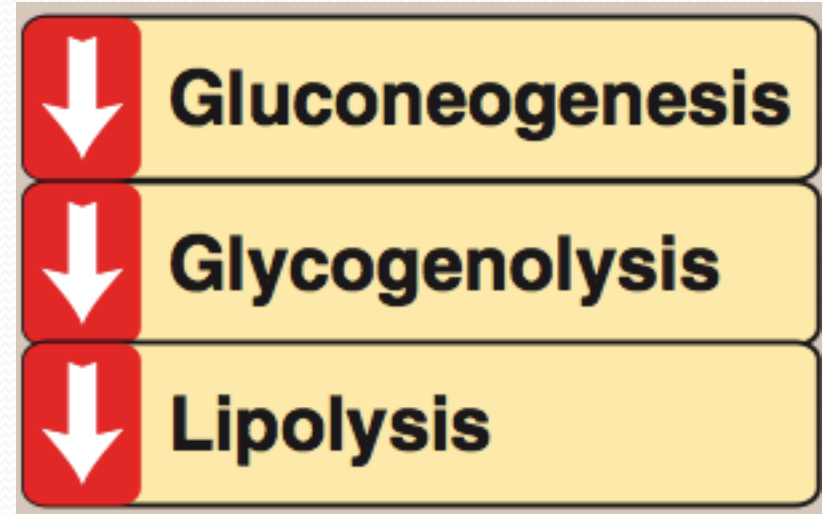
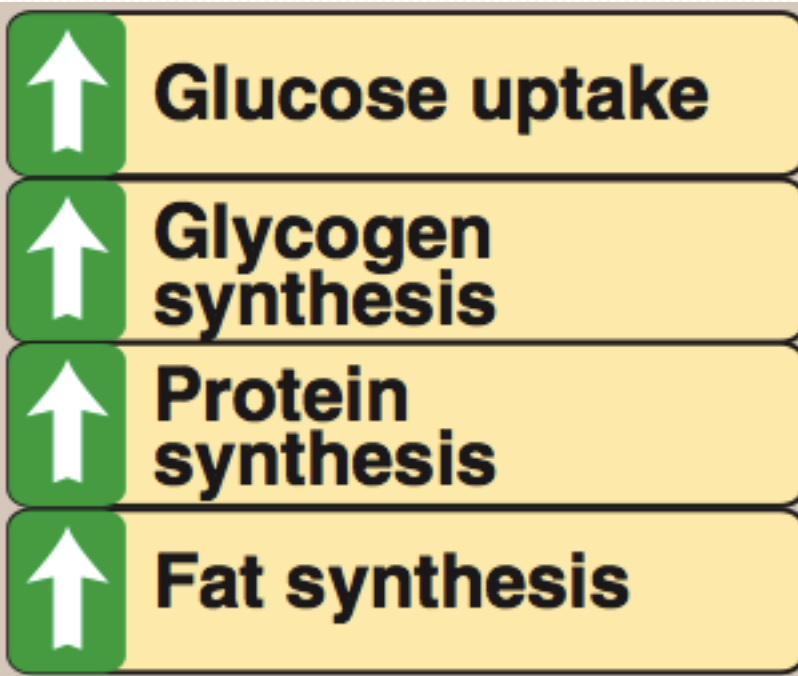
**Erythropoietin**

# Mechanism of Insulin action





# Biologic Effects of Insulin



Altered gene expression

# Biomedical Importance

- **Excessive** (e.g., hyperthyroidism, Cushing), **deficient** (e.g., hypothyroidism, Addison), or **inappropriate secretion** (e.g., syndrome of inappropriate secretion of ADH “SIADH”) of hormones are major causes of diseases
- Pharmacological treatment of these diseases depends on replacement of deficient hormone (*hypo-*) or use of drugs that interfere with the mechanism of action of the hormones (*hyper- or inappropriate*)

# Take home message

- **Hormones are involved in responses to a stimulus, using a variety of signaling mechanisms to facilitate cellular adaptive responses.**
- **Group I hormones are lipophilic, while group II are hydrophilic. Other differences exist between both groups.**
- **Hormones can be classified according to their mechanism of action (*specific examples of each category were discussed*)**
- **Biomedically, studying hormones' actions in details helps to:**
  - **understand consequences of abnormal hormone release-related diseases (excessive, deficient or inappropriate)**
  - **design therapeutic approach for such diseases.**



# References

- Lippincott's Illustrated Reviews Biochemistry: 6<sup>th</sup> edition, Chapters 8, 17 and 23.
- Buxton, Iain LO, and Dayue Duan. "Cyclic GMP/Protein Kinase G Phosphorylation of Smad3 Blocks Transforming Growth Factor- $\beta$ -Induced Nuclear Smad Translocation." (2008): 151-153.



THANK YOU