

ENDOCRINE SYSTEM



LECTURE 1 :

General Mechanisms of actions of hormones

Objectives:

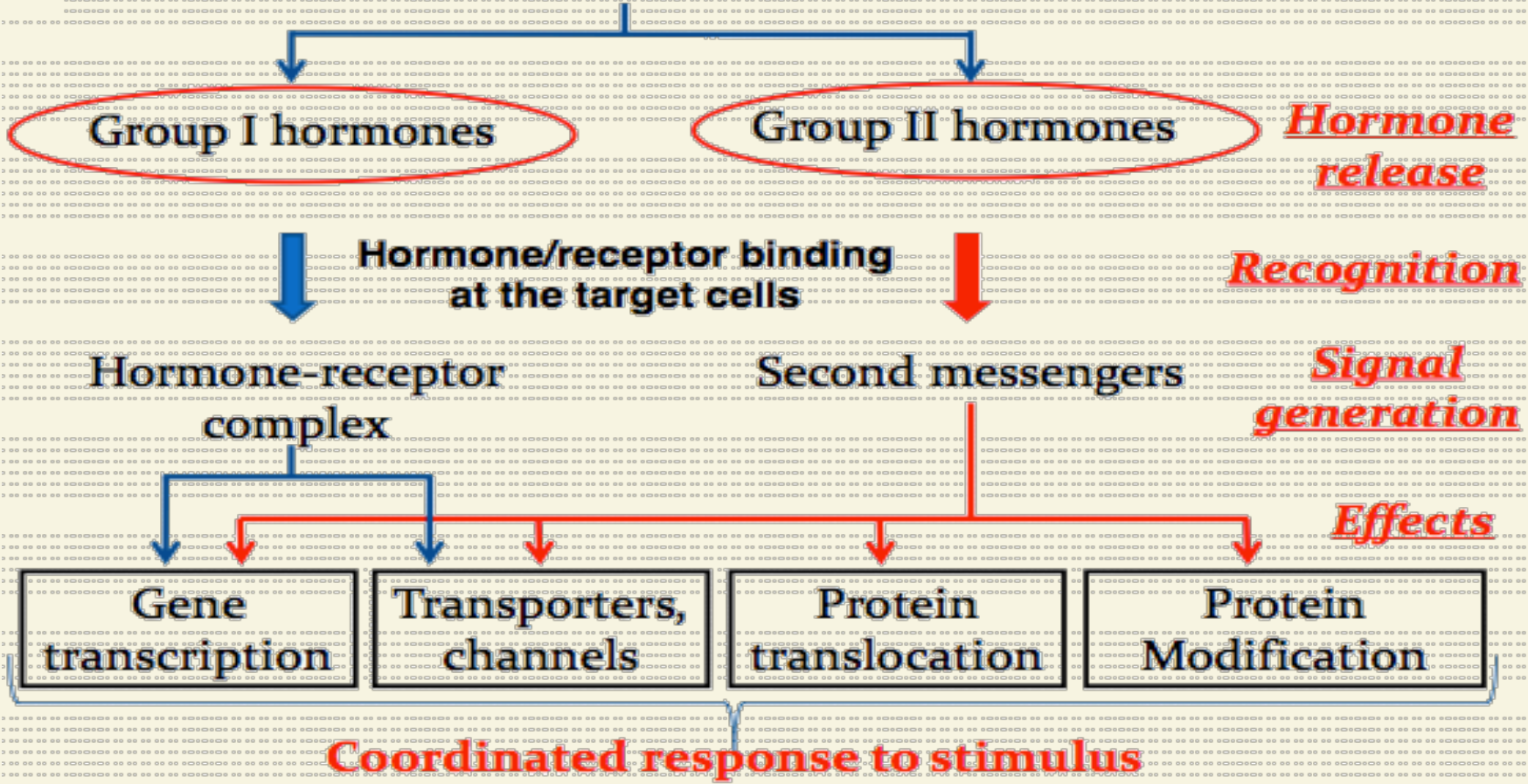
- Acquire the knowledge for general consequence of hormone-receptor interaction
- Understand different mechanisms of action of hormones
- Recognize the biomedical importance due to disturbance in the normal mechanisms of hormonal action

- 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 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: Lipid-soluble hormones
Group II hormones: Water-soluble hormones

Classification of Hormones based on their features

Hormone class	Group I	Group II
Types	<ul style="list-style-type: none"> <input type="checkbox"/> Steroids <input type="checkbox"/> Thyroid Hormones (T₃ & T₄) <input type="checkbox"/> Calcitriol <input type="checkbox"/> Retinoids 	<ul style="list-style-type: none"> <input type="checkbox"/> Polypeptides <input type="checkbox"/> Glycoproteins <input type="checkbox"/> Catecholamines
Solubility	Lipophilic	Hydrophilic
Transport proteins	Yes	No
Plasma half-life	Long (hours – days)	Short (minutes)
Receptor	Intracellular	Plasma membrane
Mediator	Receptor-hormone complex	<ul style="list-style-type: none"> ✓ cAMP, cGMP, Ca₂₊ ✓ metabolites of complex phosphoinositols ✓ tyrosine kinase cascades

Classification of Hormones based on their mechanism of action

II. Hormones that bind to cell surface receptors

I. Hormones that bind to intracellular receptors

A. The second messenger is cAMP

B. The second messenger is cGMP

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

D. The second messenger is tyrosine kinase cascade

I. Hormones that bind to intracellular receptors (Steroid-Thyroid superfamily):

❑ **Steroid Hormones:** including

- ✓ Glucocorticoids
- ✓ Mineralocorticoids
- ✓ Sex hormones

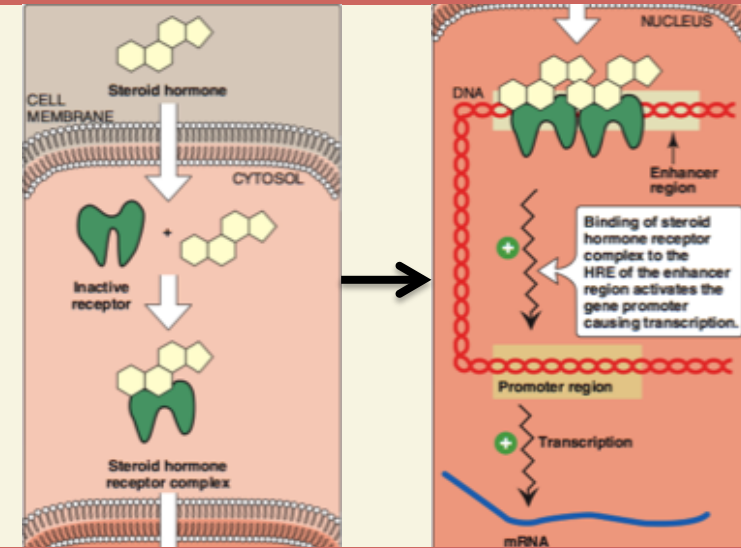
Male sex hormones: Androgens

Female sex hormones: Estrogens & Progestins

❑ **Thyroid Hormones** (T_3 & T_4)

❑ Calcitriol (1,25[OH] $_2$ -D $_3$)

❑ Retinoic acid

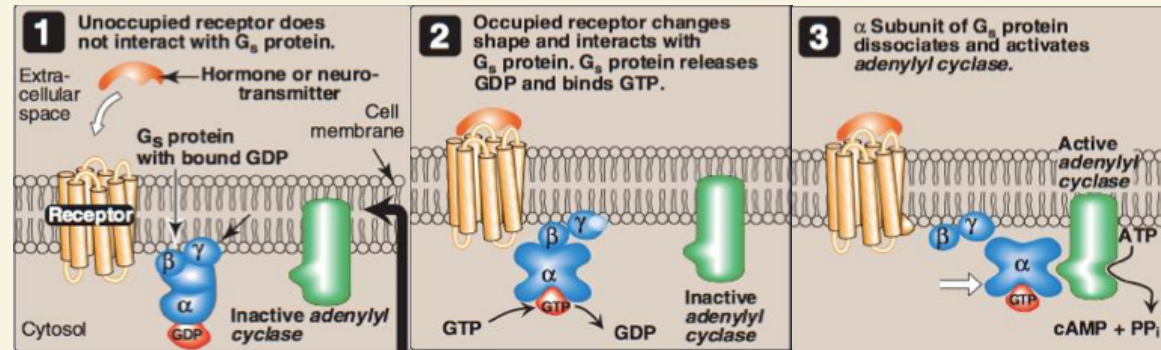


II. Hormones that bind to cell surface receptors

A. The second messenger is cAMP

- Catecholamines (α 2- Adrenergic)
- Catecholamines (β - Adrenergic)
- Ant. Pituitary: ACTH, FSH, LH & TSH
- ADH (Renal V $_2$ -receptor)
- Calcitonin & PTH
- Glucagon

Cascade for formation of cAMP by cell-surface hormones



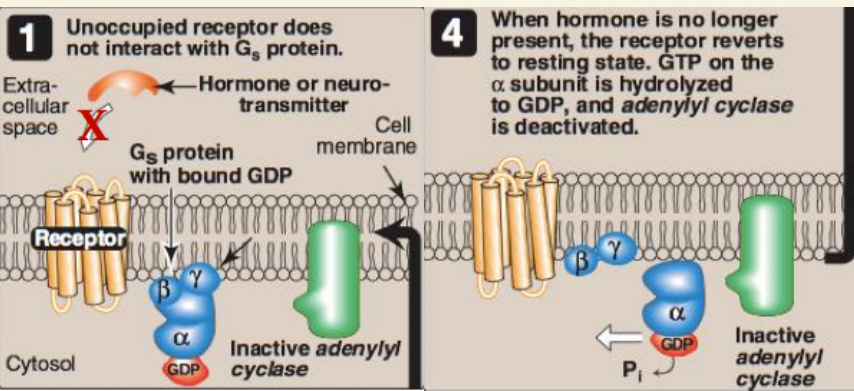
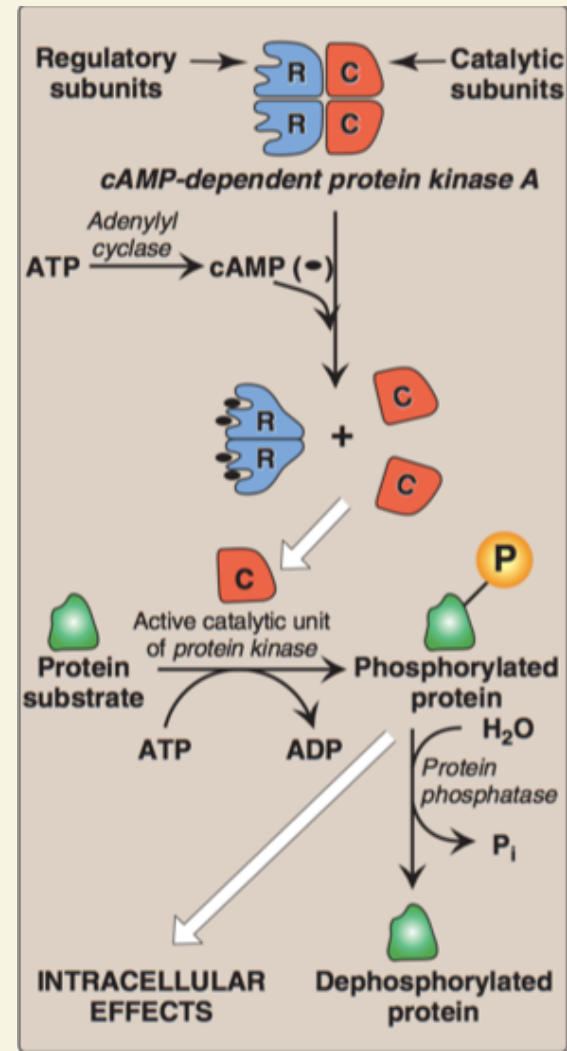
II. Hormones that bind to cell surface receptors

Continued... A. The second messenger is 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 phosphodiesteras
4. Inactivation of protein kinase A by a decrease of cAMP
5. Hydrolysis of GTP into GDP
6. Binding of α -subunit to $\beta \gamma$ -subunits
7. Inactivation of adenylyl cyclase

Actions of cAMP

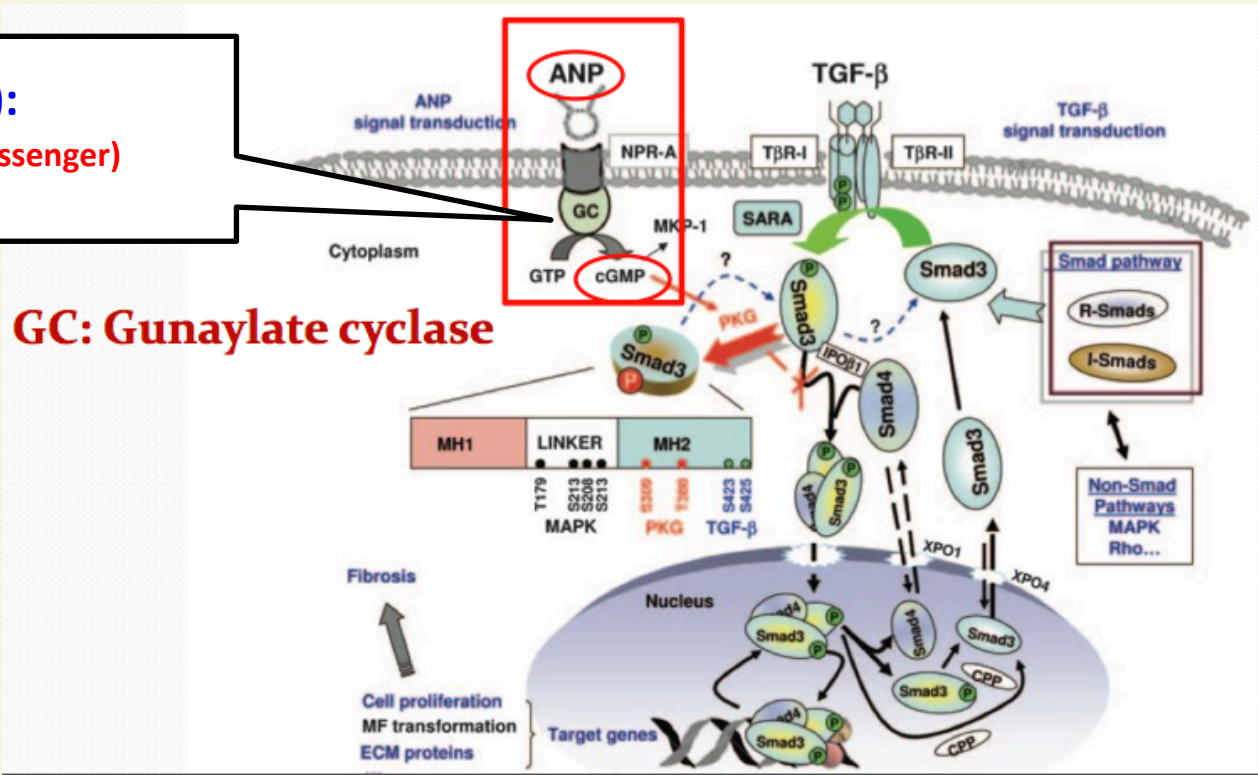


II. Hormones that bind to cell surface receptors

B. The second messenger is cGMP

- Atrial natriuretic peptide (ANP)
- Nitric oxide

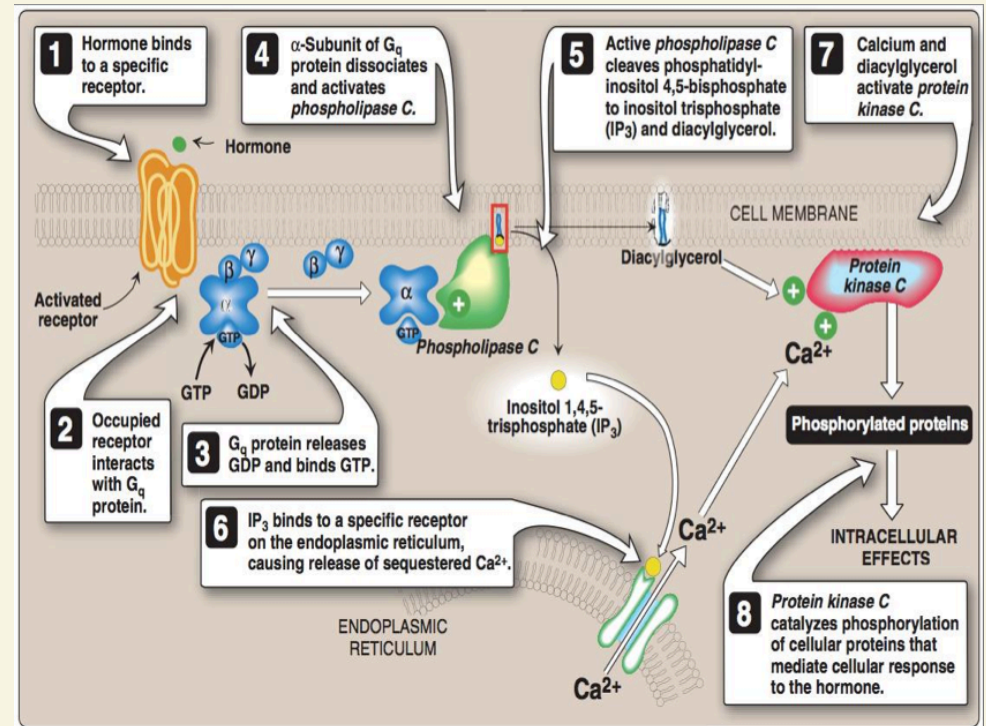
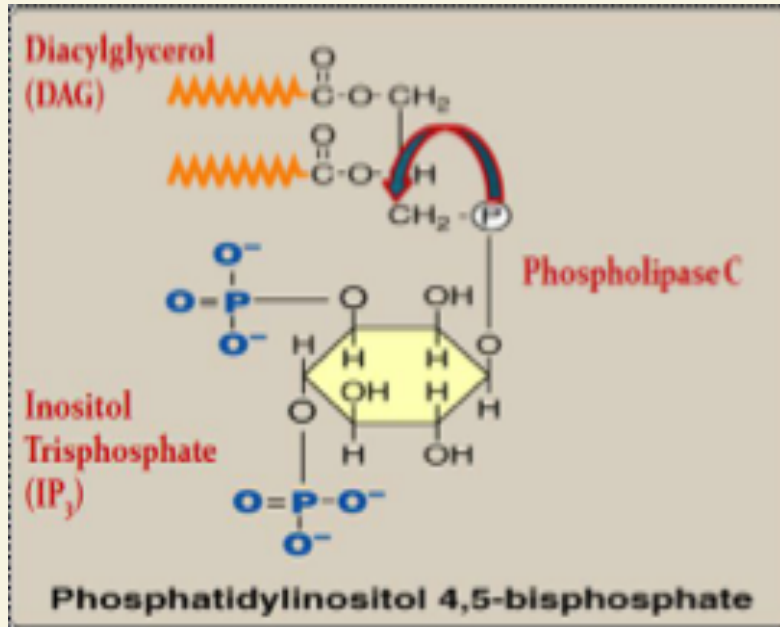
Gunaylate cyclase (GC):
Converts GTP to cGMP (2nd messenger)



II. Hormones that bind to cell surface receptors

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

- ❑ Acetylcholine (muscarinic)
- ❑ Catecholamines (α 1- Adrenergic)
- ❑ Angiotensin II
- ❑ ADH (vasopressin): Extra-renal V1-receptor



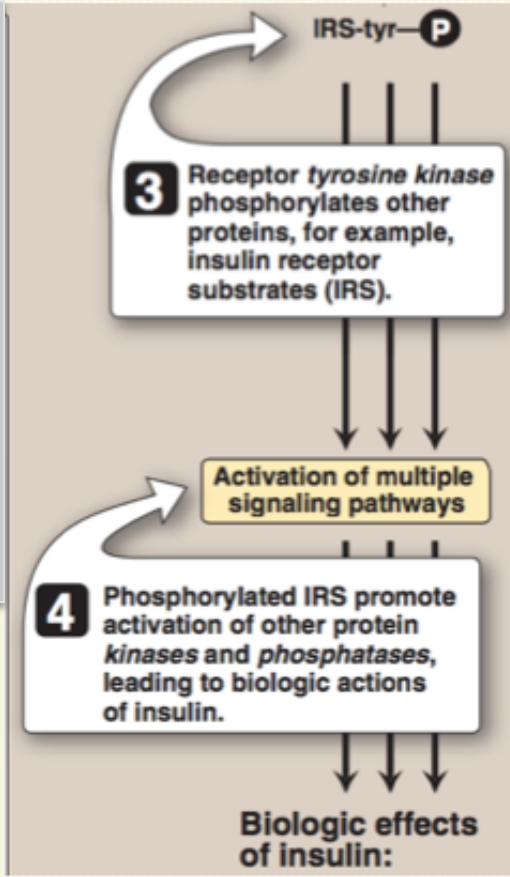
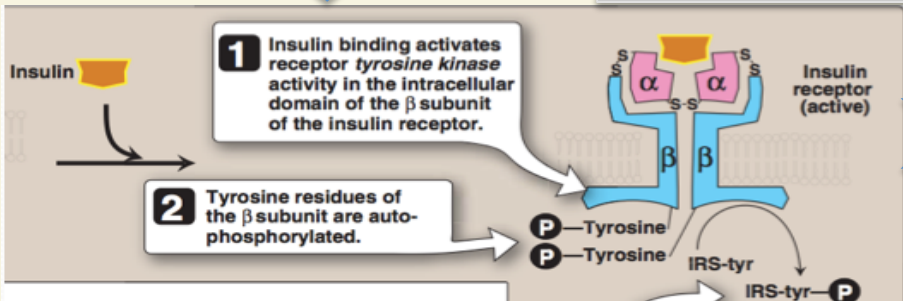
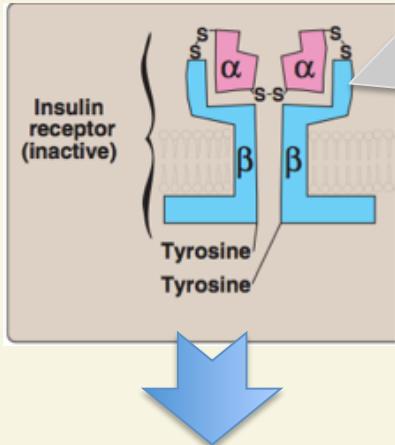
II. Hormones that bind to cell surface receptors

- D. The second messenger is Tyrosine kinase cascade :**
- GH & Prolactin
 - Insulin**
 - Erythropoietin

Mechanism of insulin action

- Alpha subunit :** responsible for recognizing and binding to insulin (contains insulin binding domain),
- Beta subunit:** responsible for intracellular effect (contains the tyrosine residue that will be phosphorylated after binding to the insulin) => receptor will be active and undergo conformational changes.
- Receptor itself is phosphorylated (autophosphorylation) and gets activated as an enzyme.

It phosphorylates IRS- tyrosine (insulin receptor substrate).



Biologic Effects of Insulin

↑ Glycogen synthesis
↑ Glucose uptake
↑ Protein synthesis
↑ Fat synthesis
↓ lipolysis

↓ Gluconeogenesis
↓ Glycogenolysis

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)

Summary

	Group I	Group II			
Receptor	intracellular	Binds to the surface			
2 nd messenger	Receptor intracellular	cAMB	cGMP	Ca ⁺ & phosphatidylinositol	Tyrosine kinase
Examples	1. Steroids (Sex hormones) 2. Thyroid hormones T3 ,T4 & calcitriol	1. Catecholamine 2. Anterior pituitary hormones (ACTH, FSH, LH, TSH)	1. Atrial natriuretic peptide 2. nitric oxide	1. Acetylcholine 2. α 1-adrenergic 3. angiotensin II	1. GH, prolactin 2. insulin 3. erythropoietin

TEST YOURSELF!

1. The action of inositol triphosphate (IP3) is :

- A. To activate protein kinase C
- B. To activate Adenylyl cyclase
- C. To release Ca from endoplasmic reticulum
- D. To activate protein kinase A

2. When ADH binds to its extra renal V1 receptor , its second messenger will be

- A. CA/phosphatidylinositol (Ca/PIP)
- B. cAMP
- C. cGMP
- D. Tyrosine kinase

3. Which one of the following hormones uses tyrosine kinase cascade as a second messenger :

- A. Prolactin
- B. ADH
- C. Acetylcholine
- D. Androgens

4. Which one of the following is a biological effect of insulin :

- A. Increase gluconeogenesis
- B. Decrease lypolysis
- C. Increase glycogenolysis
- D. Decrease glucose uptake

5. In CA/phosphatidylinositol system , the function of diacylglycerol is :

- A. To activate protein kinase A
- B. To activate protein kinase C
- C. To activate protein kinase G
- D. To release calcium from endoplasmic reticulum

6. Which one of the following is hydrophilic :

- A. glucocorticoids
- B. progestin
- C. epinephrine
- D. Retinoic acid

7. In cGMP pathway , protein kinase G activated by :

- A. Adenylyl cyclase
- B. phospholipase
- C. Protein kinase A
- D. Gunaylate cyclase

8. Which one of the following has the longest plasma half life :

- A. Thyroxin
- B. epinephrine
- C. ADH
- D. PTH

9. The second messenger for atrial natriuretic peptide is :

- A. cAMP
- B. cGMP
- C. Tyrosine kinase
- D. Ca

10. Which one of the following hormones does NOT need second messenger to do its action :

- A. FSH
- B. Estrogen
- C. LH
- D. Insulin

ANSWERS: 1-C 2-A 3-A 4-B 5- B 6-C 7-D 8-A 9-B 10- B

THANK YOU ...

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