Biochemistry of hormones-1. General endocrinology

Lecture #26

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Hormones

- **Hormones** are organic substances, produced in small amounts by specific tissues (endocrine gland), secreted into the blood stream to control the metabolic and biological activities in the target cells.

Functions of hormones and their regulation

- The word hormone is derived from the Greek [*hormao*] meaning ***'I excite or arouse'***.
  - Hormones communicate this effect by their unique chemical structures recognized by specific receptors on their target cells, by their patterns of secretion and their concentrations in the general or localized circulation.

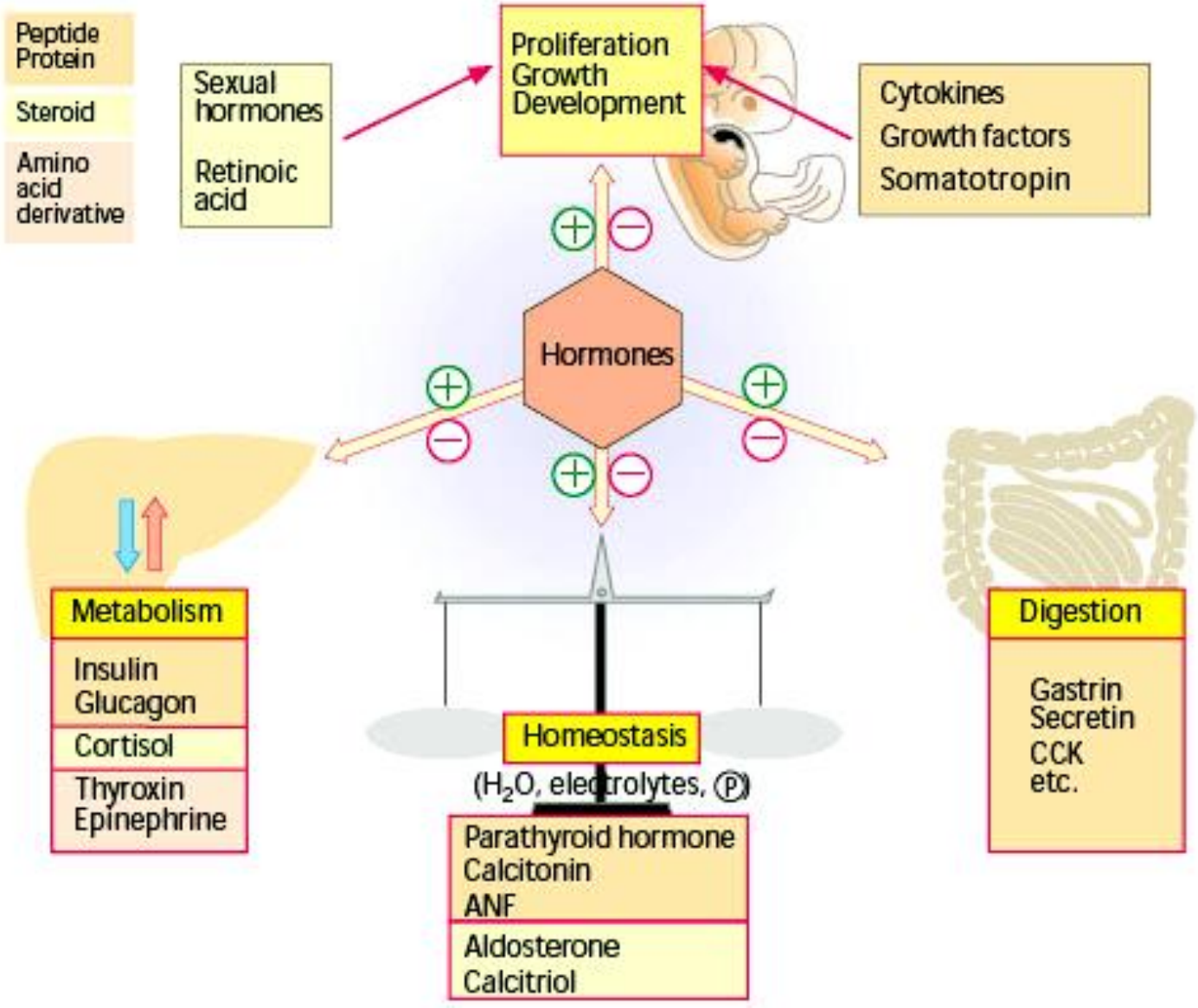
Role of Endocrine System

- The **integration** of body functions in humans and other higher organisms is carried out by the nervous system, the immune system, and the endocrine system.
  - The **endocrine system** is composed of a number of tissues that secrete their products, called endocrine hormones, into the circulatory system;
    - from there they are disseminated throughout the body, regulating the function of distant tissues and maintaining homeostasis.

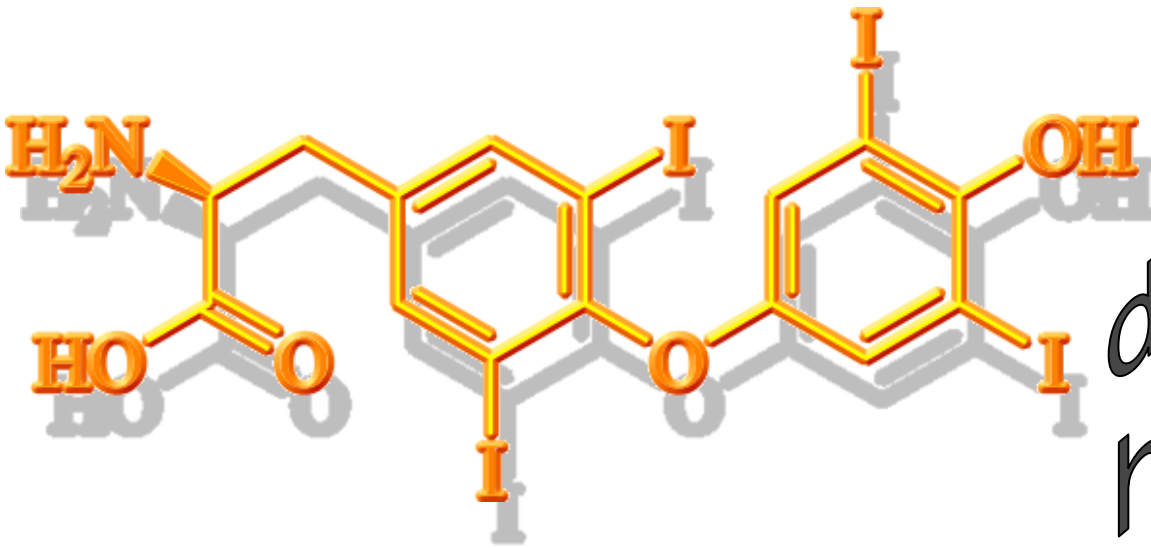
Functions

- Reproduction and sexual differentiation;
- Development and growth;
- Maintenance of the internal environment; and
- Regulation of metabolism and nutrient supply.
  - A single hormone may affect more than one of these functions and each function may be controlled by several hormones.

Hormones: Overview



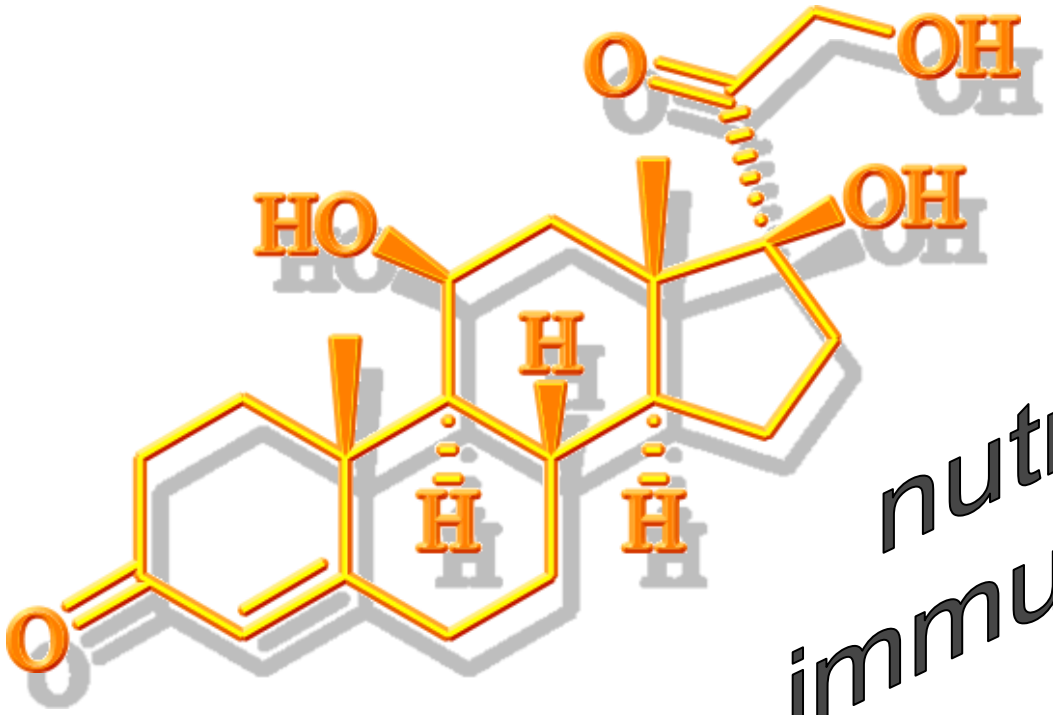
Example 1 : Thyroid hormones



development
homeostasis
metabolism

- **Thyroid hormone** is essential in development as well as many aspects of homeostasis and metabolism,

Example 3: Cortisol



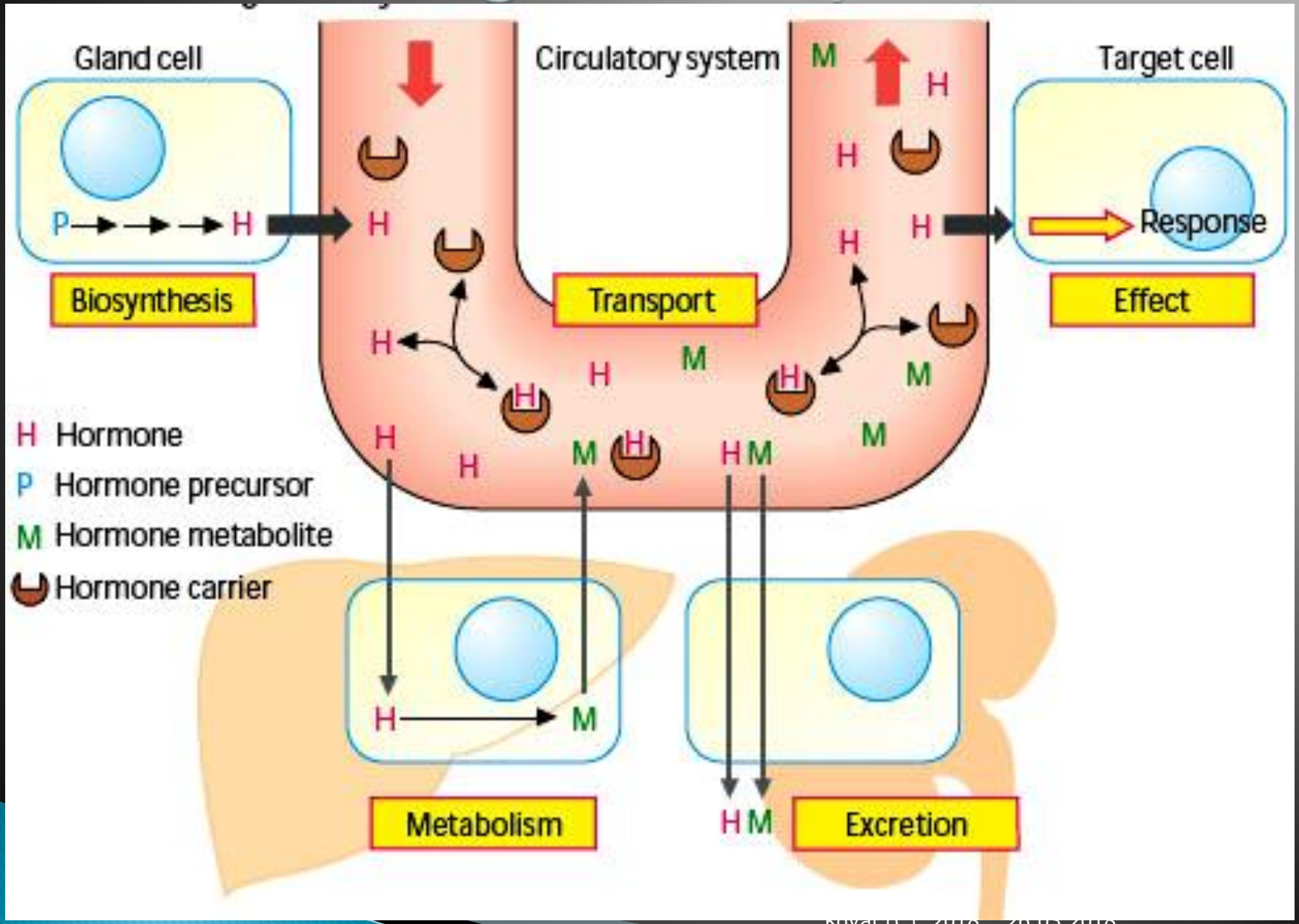
growth
nutrient supply
immunomodulator

- …whilst **glucocorticoids**, such as *cortisol*, are important both in growth and nutrient supply and are also modulators of immune function.

Example 3: Insulin, Glucagon, Cortisol, Epinephrine in Control of Blood Glucose

- The roles several hormones play in one function is exemplified by the control of blood glucose which involves the pancreatic peptide **insulin** and its counter regulatory hormone, glucagon, as well as **cortisol**, **growth hormone** and **epinephrine**.
- Hormones act in concert and thus, an abnormality in a controlled variable, such as blood glucose concentration may result from defects in the control of any one of several hormones.

Hormonal Regulation System



The Properties of Hormones

- Hormones act
  - At very low concentrations
  - Distantly
  - Reversibly
  - With certain specificity

Very Low Concentrations of Hormones

- Hormones are normally present in the plasma and interstitial tissue at concentrations in the range of 10^{-7} M to 10^{-10} M.
  - Because of these very low physiological concentrations, sensitive protein **receptors** have evolved in target tissues to sense the presence of very weak signals.
  - **Signal transduction** is always coupled with **signal amplification** (*by cascade mechanism*).
  - In addition, systemic **feedback mechanisms** have evolved to regulate the production of endocrine hormones.

Distant Action of Hormones

- Classically, endocrine hormones are considered to be derived from **amino acids**, **peptides**, or **sterols** and to act at sites distant from their tissue of origin.
- However, some hormons are paracrinic, or autocrinic.
  - Insulin-like growth factor-I (IGF-I), which behaves as **endocrine**, **paracrine**, and **autocrine**.

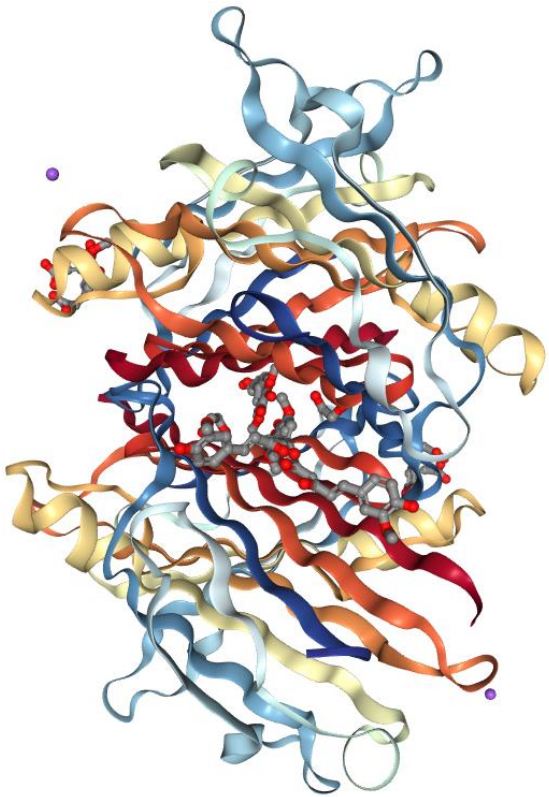
Reversibility of Hormone Action

- After end of signaling, the hormone concentration is dropped, and the action is stopped.

Specificity

- Every hormone has specific receptor.
  - It provides specific action of hormone.
- Some hormones has specific transporters in blood.
- Hormones perform specific action to the target cells.

Specific Plasma Protein Carriers



Human transthyretin (TTR) complexed with ferulic acid and curcumin
http://www.rcsb.org/structure/4PME

- Once a hormone is secreted by an endocrine tissue, it generally binds to a specific plasma protein carrier, with the complex being disseminated to distant tissues.
- Plasma carrier proteins exist for all classes of endocrine hormones.

Carrier proteins

- Carrier proteins for peptide hormones prevent hormone destruction by plasma proteases.
  - Carriers for steroid and thyroid hormones allow these very hydrophobic substances to be present in the plasma at concentrations several hundred-fold greater than their solubility in water would permit.
  - Carriers for small, hydrophilic amino acid--derived hormones prevent their filtration through the renal glomerulus, greatly prolonging their circulating half-life.

Receptors

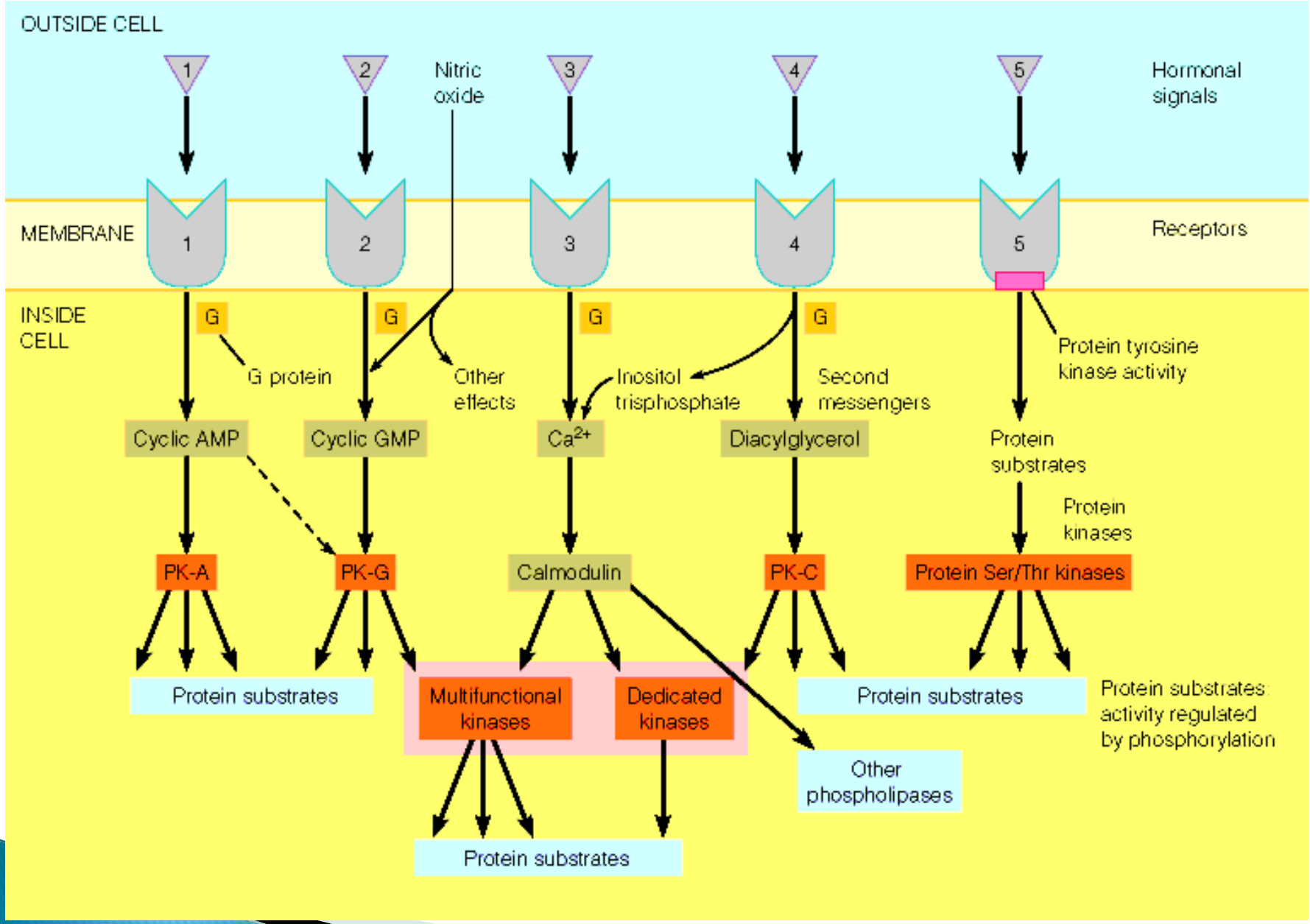
- Tissues capable of responding to endocrines have 2 properties in common:
  - they posses a receptor having very high affinity for hormone,
  - and the receptor is coupled to a process that regulates metabolism of the target cells.

The final effects of hormones

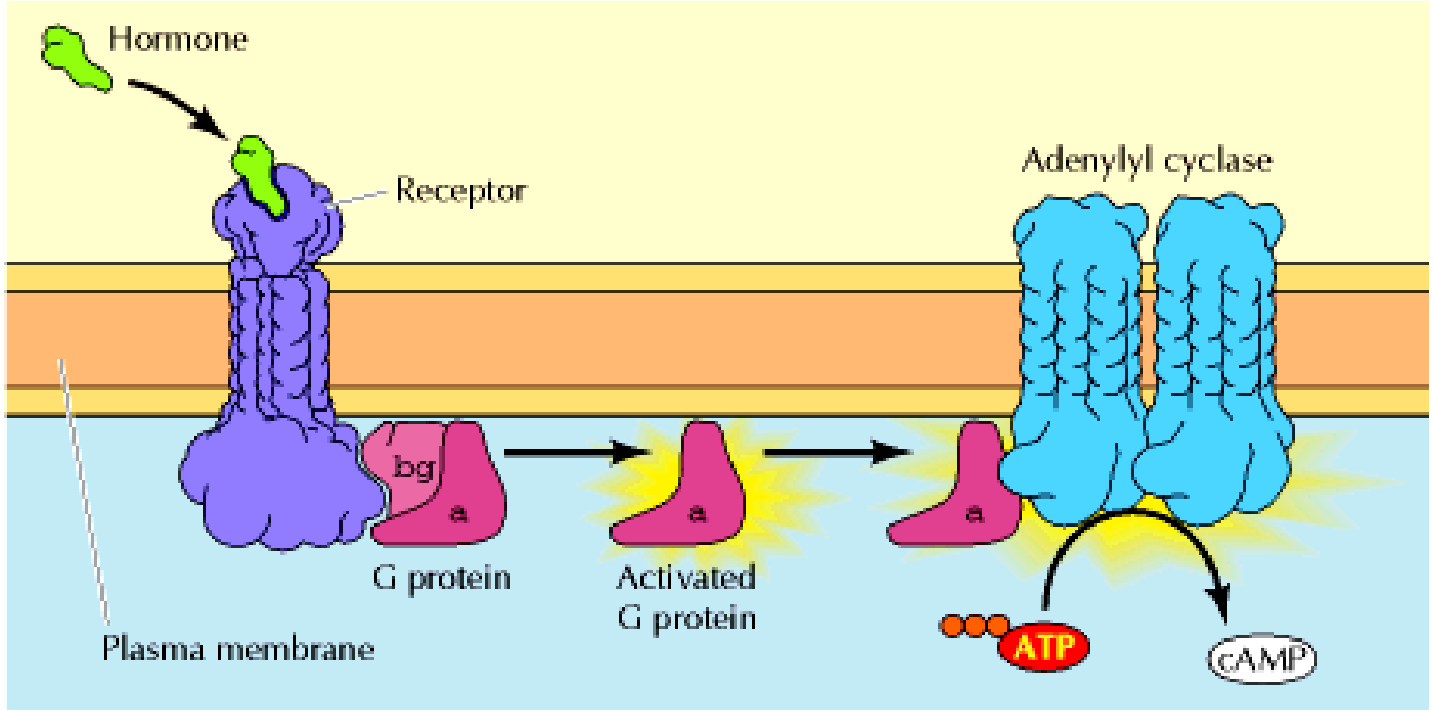
- The basis of the action of all hormones is **the change in metabolism**
  - **Metabolic** – metabolic changes.
  - **Kinetic (trigger)** – changes in the activity of organs (adrenaline rush heart rate).
  - **Correcting (adapting)** – changing the intensity of the functions of organs and tissues.
  - **Morphogenetic** – differentiation of organs and tissues, growth effects, stimulation of morphogenesis.
  - **Behavioral** – formation of motivations, behavior change.

Receptors for Peptide Hormones

- Receptors for most amino acid-derived hormones and all peptide hormones are located on the plasma membrane.
- Activation of these receptors by hormones (the first messenger) leads to the intracellular production of a second messenger, such as cAMP, which is responsible for initiating the intracellular biological response.

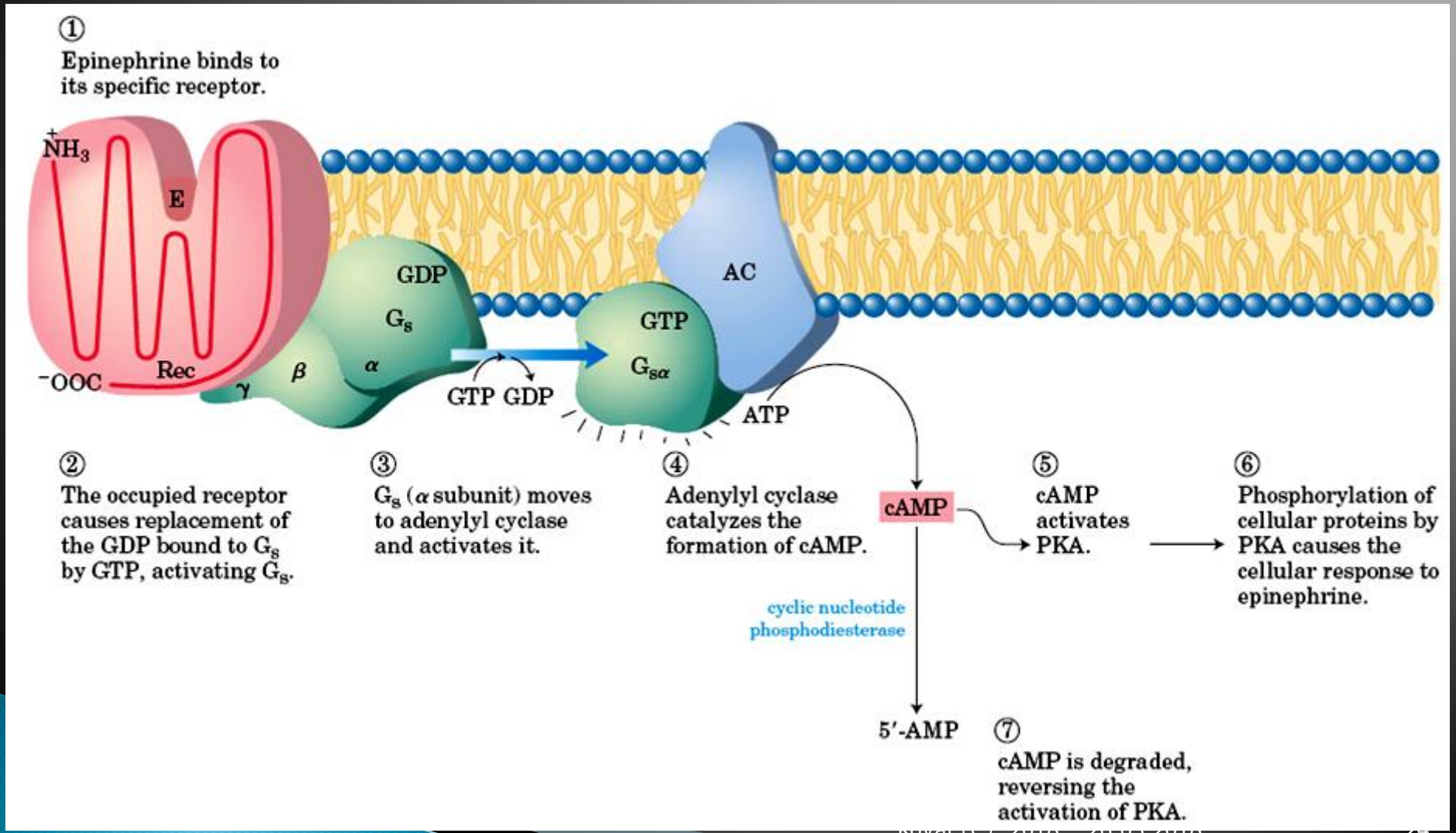

OUTSIDE CELL
1
2
Nitric oxide
3
4
5
Hormonal signals
MEMBRANE
1
2
3
4
5
Receptors
INSIDE CELL
G
G
G
G
G protein
Other effects
Inositol trisphosphate
Second messengers
Protein tyrosine kinase activity
Cyclic AMP
Cyclic GMP
Ca2+
Diacylglycerol
Protein substrates
Protein kinases
PK-A
PK-G
Calmodulin
PK-C
Protein Ser/Thr kinases
Protein substrates
Multifunctional kinases
Dedicated kinases
Protein substrates
Other phospholipases
Protein substrates
Protein substrates: activity regulated by phosphorylation

Hormonal Activation of Adenylyl Cyclase

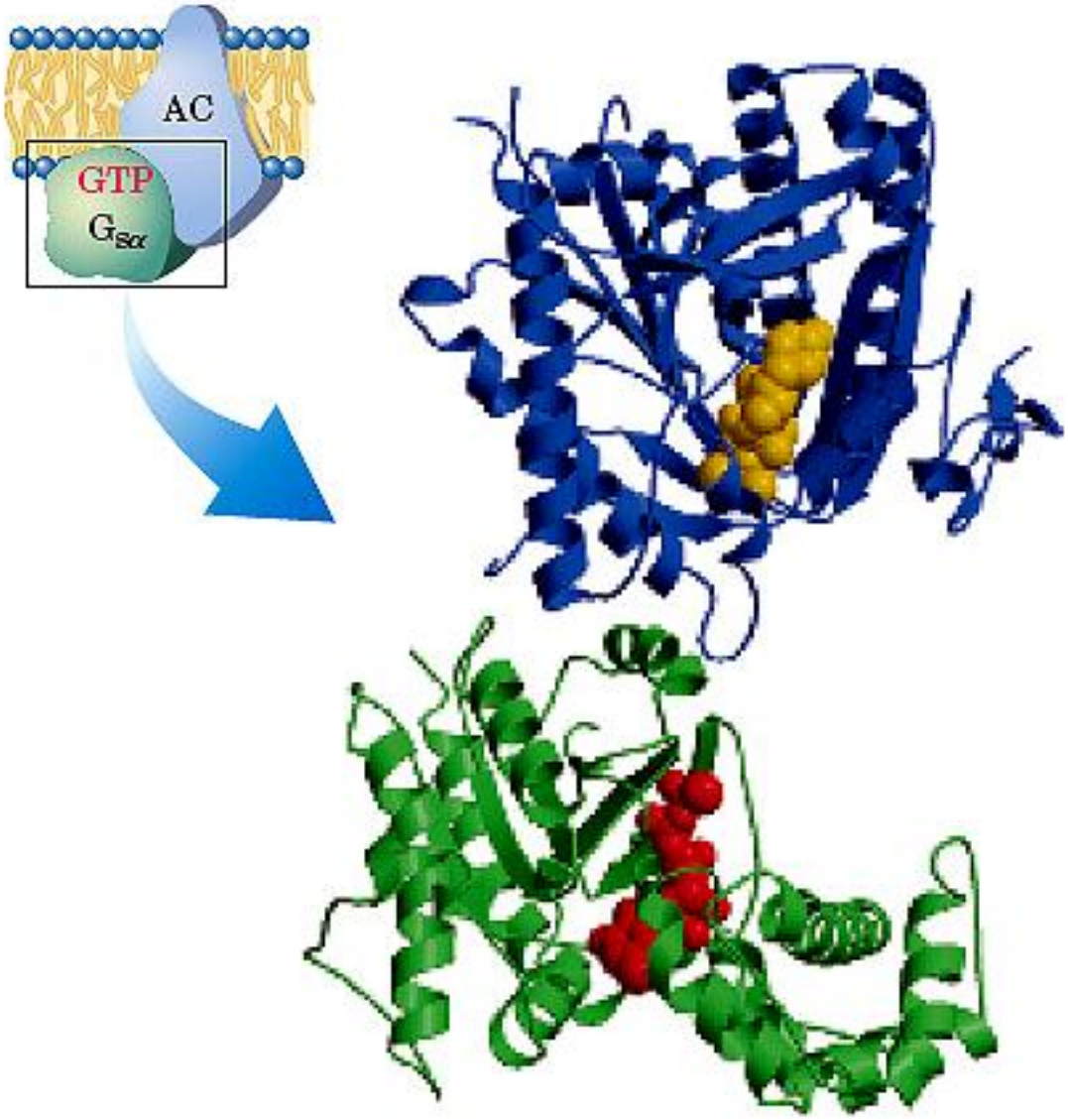


- Binding of hormone promotes the interaction of the receptor with a G protein.
- The activated G protein a subunit then dissociates from the receptor and stimulates **adenylyl cyclase**, which catalyzes the conversion of ATP to cAMP.

β-adrenergic Pathway via cAMP

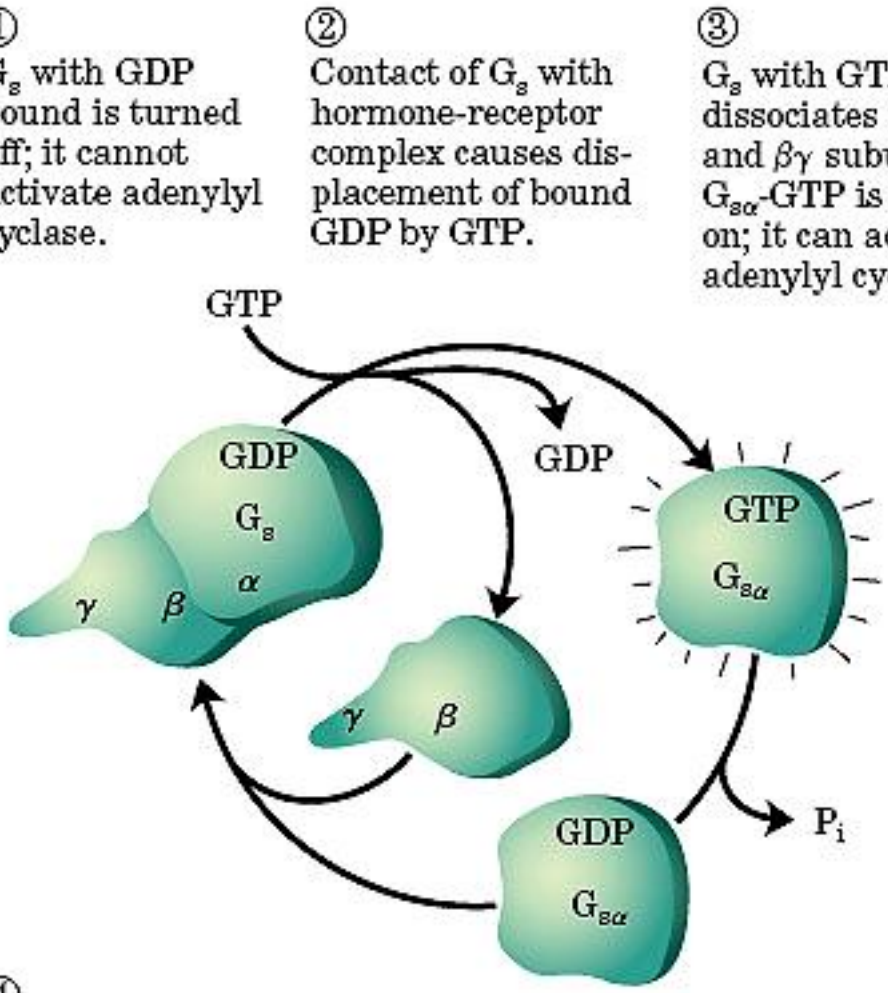


Interaction of Gsα with adenylyl cyclase



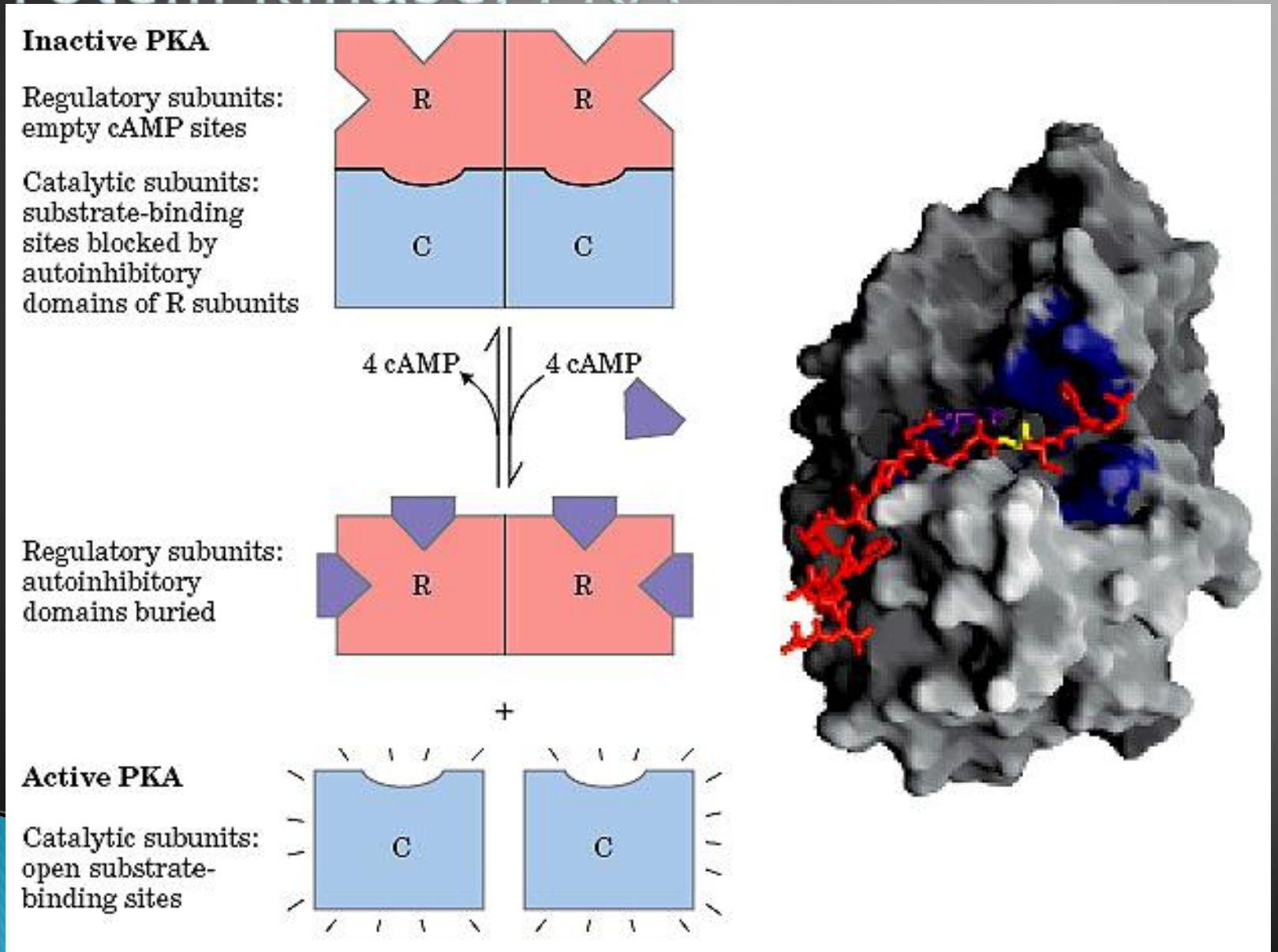
- The soluble catalytic core of the adenylyl cyclase (AC, blue), severed from its membrane anchor, was cocrystallized with Gs (green) to give this crystal structure.
- The plant terpene forskolin (yellow) is a drug that strongly stimulates the enzyme, and GTP (red) bound to Gs triggers interaction of Gs with adenylyl cyclase.

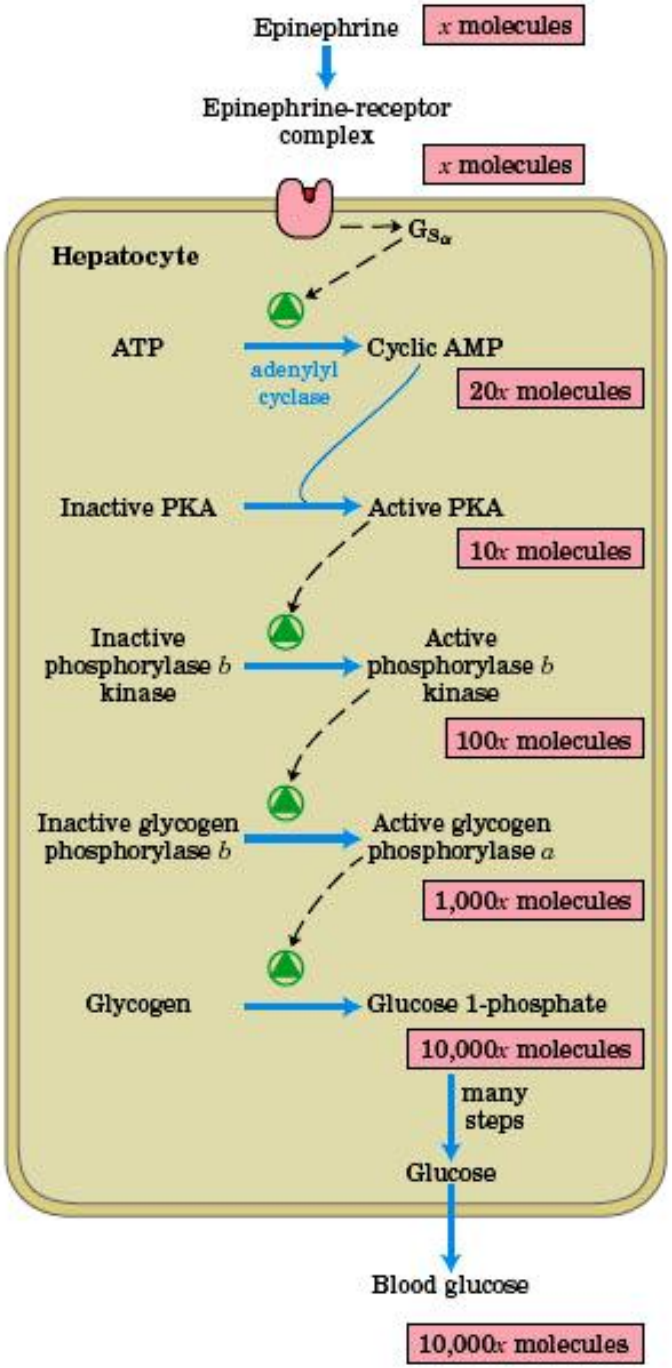
Self-inactivation of Gs



- The protein's intrinsic GTPase activity, in many cases stimulated by RGS proteins (*r*egulators of *G* protein *s*ignaling), determines how quickly bound GTP is hydrolyzed to GDP and thus how long the G protein remains active.

Activation of cAMP-dependent protein kinase, PKA

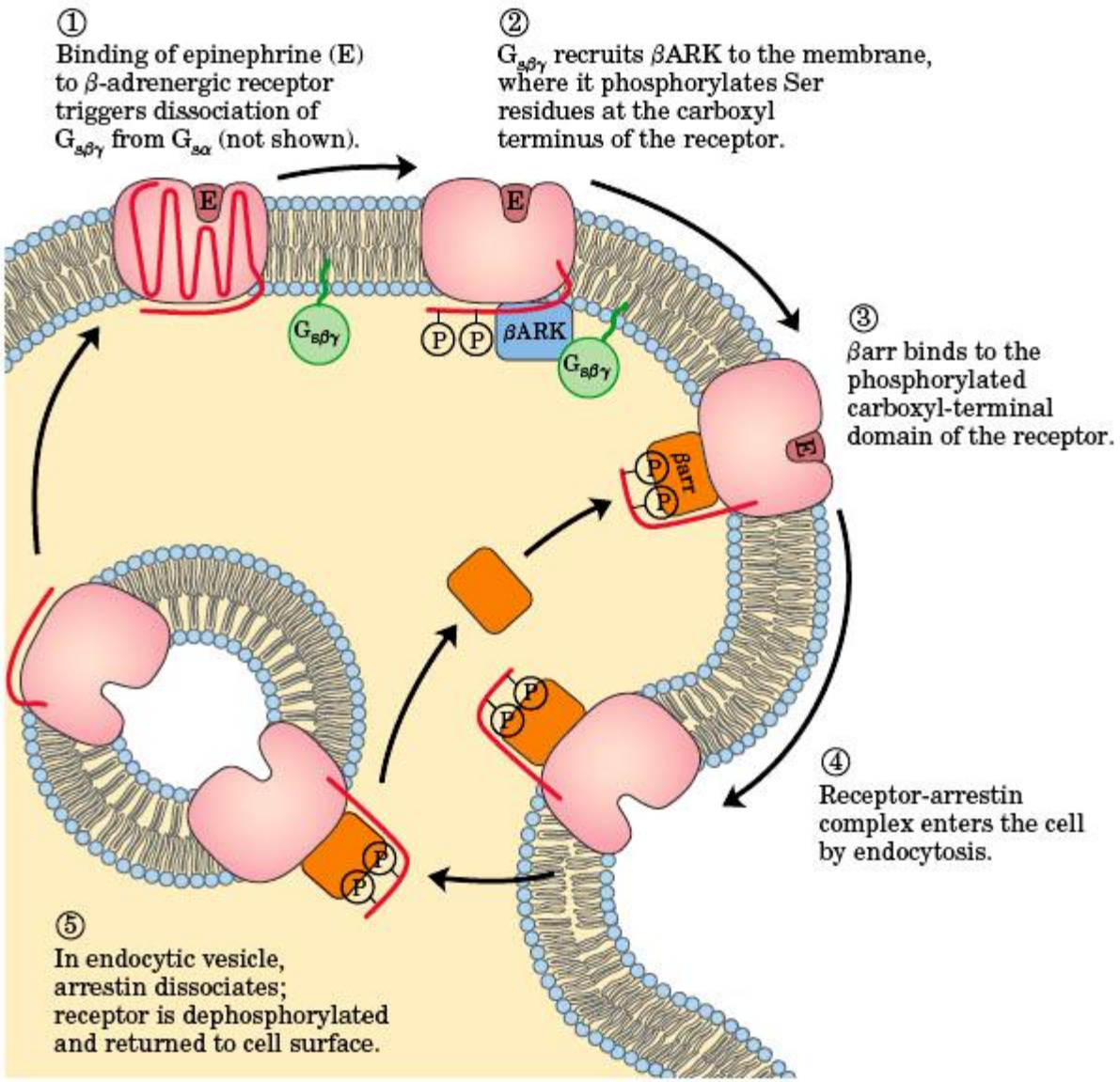




Epinephrine cascade

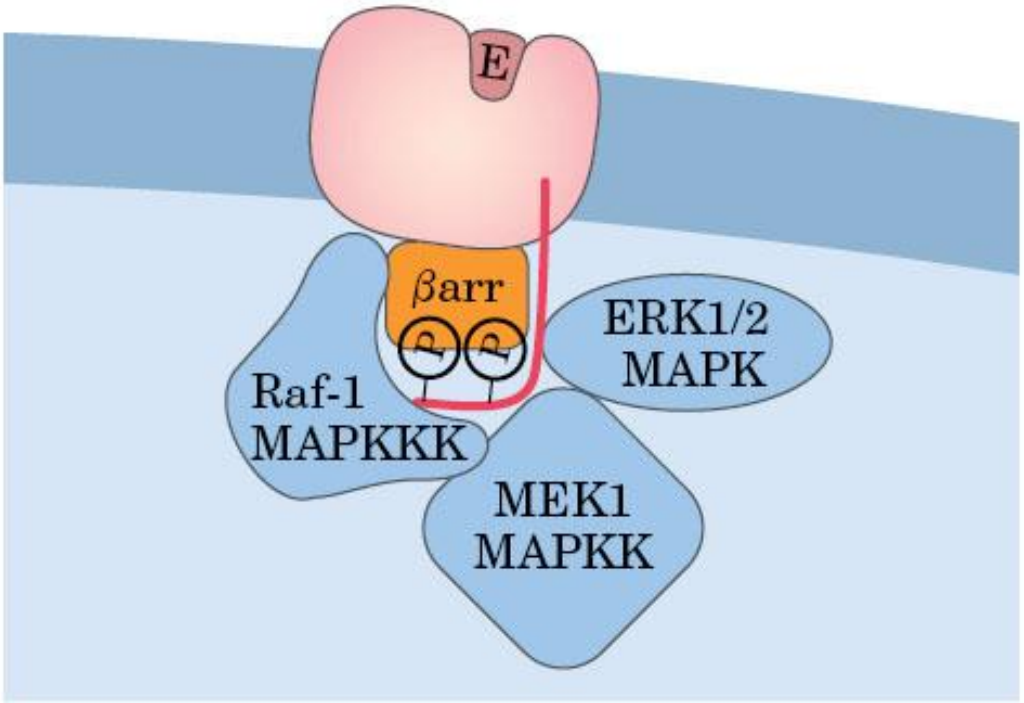
- Epinephrine triggers a series of reactions in hepatocytes in which catalysts activate catalysts, resulting in great amplification of the signal.
- Binding of a small number of molecules of epinephrine to specific β-adrenergic receptors on the cell surface activates adenylyl cyclase.
- To illustrate amplification, we show 20 molecules of cAMP produced by each molecule of adenylyl cyclase, the 20 cAMP molecules activating 10 molecules of PKA, each PKA molecule activating 10 molecules of the next enzyme (a total of 100), and so forth. These amplifications are probably gross underestimates.

Desensitization of the β-adrenergic receptor in the continued presence of epinephrine



- This process is mediated by two proteins:
- β-adrenergic protein kinase (βARK) and
- β-arrestin (βarr; arrestin 2).

β-Arrestin uncouples the serpentine receptor from its G protein…



- …and brings together the three enzymes of the MAPK cascade.
- The effect is that one stimulus triggers two distinct response pathways:
  - the path activated by the G protein and
  - the MAPK cascade

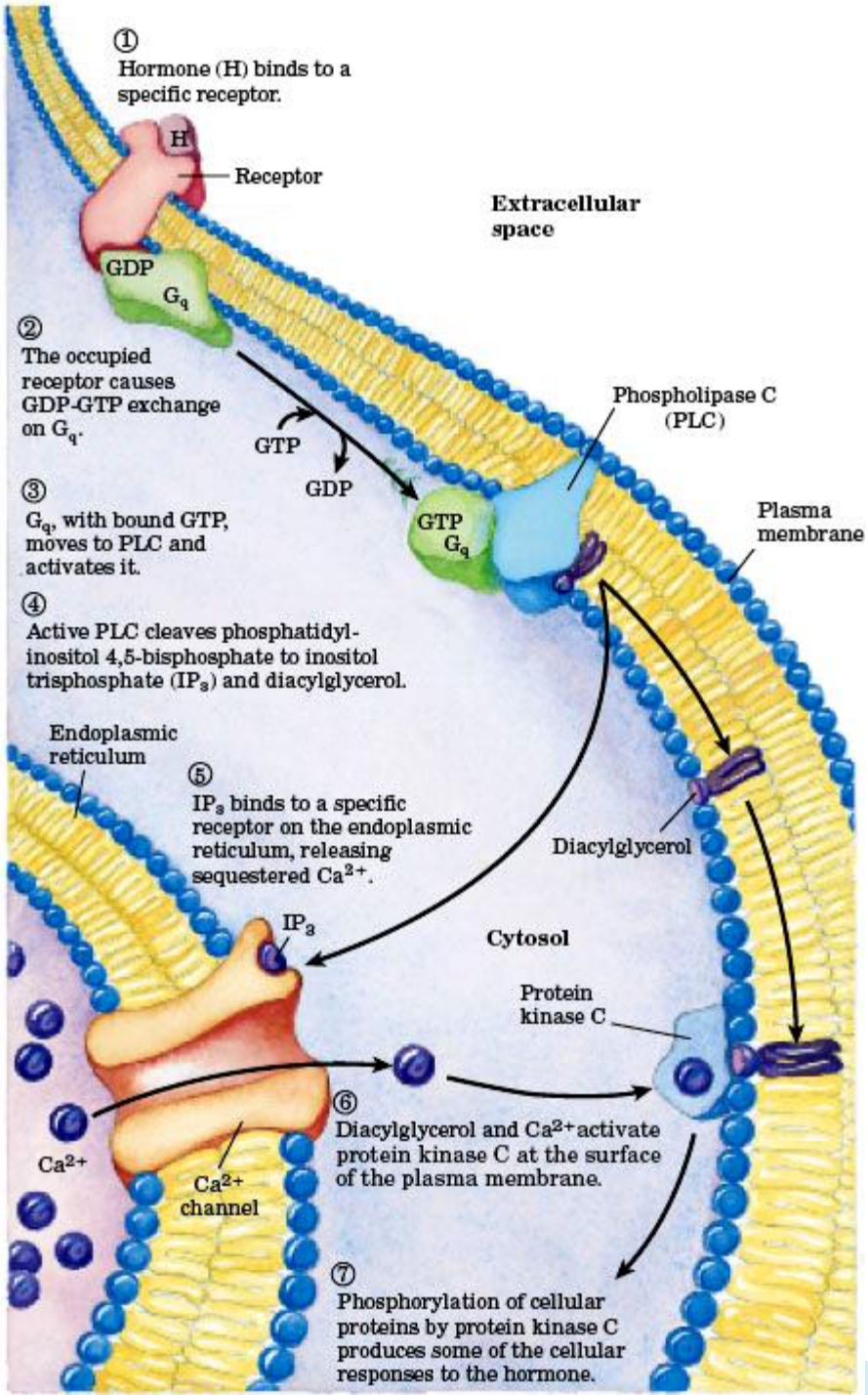
Some Signals That Use cAMP as Second Messenger

- Corticotropin (ACTH)
- Corticotropin-releasing hormone (CRH)
- Dopamine [D1, D2]*
- Epinephrine (β-adrenergic)
- Follicle-stimulating hormone (FSH)
- Glucagon
- Histamine [H_2]*
- Luteinizing hormone (LH)
- Melanocyte-stimulating hormone (MSH)
- Odorants (many)
- Parathyroid hormone
- Prostaglandins E_1, E_2 (PGE_1, PGE_2)
- Serotonin [5-HT-1a, 5-HT-2]*
- Somatostatin
- Tastants (sweet, bitter)
- Thyroid-stimulating hormone (TSH)

** Receptor subtypes in square brackets. Subtypes may have different transduction mechanisms. For example, serotonin is detected in some tissues by receptor subtypes 5-HT-1a and 5-HT-1b, which act through adenylyl cyclase and cAMP, and in other tissues by receptor subtype 5-HT-1c, acting through the phospholipase C-IP3 mechanism*

Hormone-activated phospholipase C and IP_3

- Two intracellular second messengers are produced in the hormone-sensitive phosphatidylinositol system: inositol 1,4,5-trisphosphate (IP_3) and diacylglycerol. Both contribute to the activation of protein kinase C.
- By raising cytosolic [Ca^{2+}], IP_3 also activates other Ca^{2+}-dependent enzymes; thus Ca^{2+} also acts as a second messenger.



Some Signals That Act through Phospholipase C and IP_3

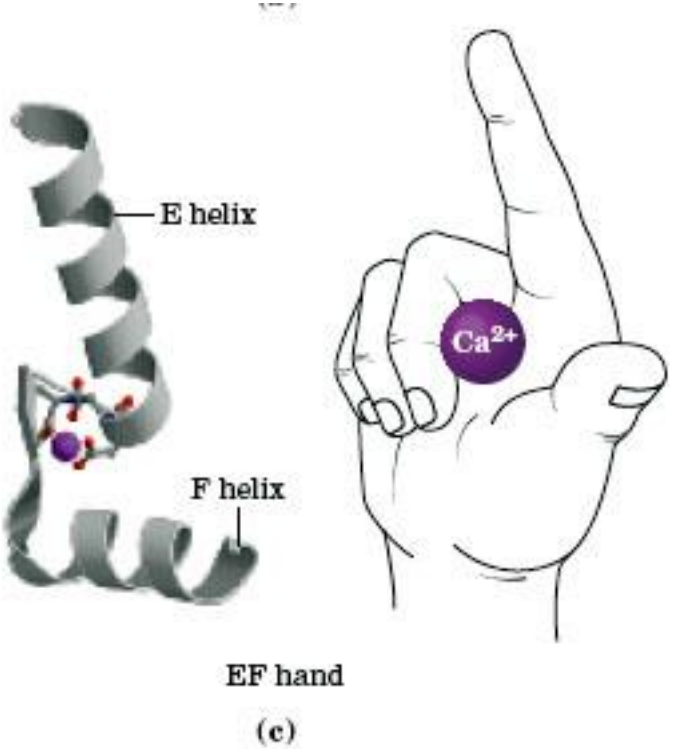
Acetylcholine [muscarinic M_1]	Histamine [H_1]*
α1-Adrenergic agonists	Light (*Drosophila*)
Angiogenin	Oxytocin
Angiotensin II	Platelet-derived growth factor (PDGF)
ATP [P_{2x} and P_{2y}]*	Serotonin [5-HT-1c]*
Auxin	Thyrotropin-releasing hormone (TRH)
Gastrin-releasing peptide	Vasopressin
Glutamate	
Gonadotropin-releasing hormone (GRH)	

Some Proteins Regulated by Ca^{2+} and Calmodulin

Adenylyl cyclase (brain) Ca^{2+}/calmodulin-dependent protein kinases (CaM kinases I to IV) Ca^{2+}-dependent Na channel (*Paramecium*) Ca^{2+}-release channel of sarcoplasmic reticulum Calcineurin (phosphoprotein phosphatase 2B) cAMP phosphodiesterase	cAMP-gated olfactory channel cGMP-gated Na, Ca^{2+} channels (rod and cone cells) Glutamate decarboxylase Myosin light chain kinases NAD kinase Nitric oxide synthase Phosphoinositide 3-kinase Plasma membrane Ca^{2+} ATPase (Ca^{2+} pump) RNA helicase (p68)

Calmodulin

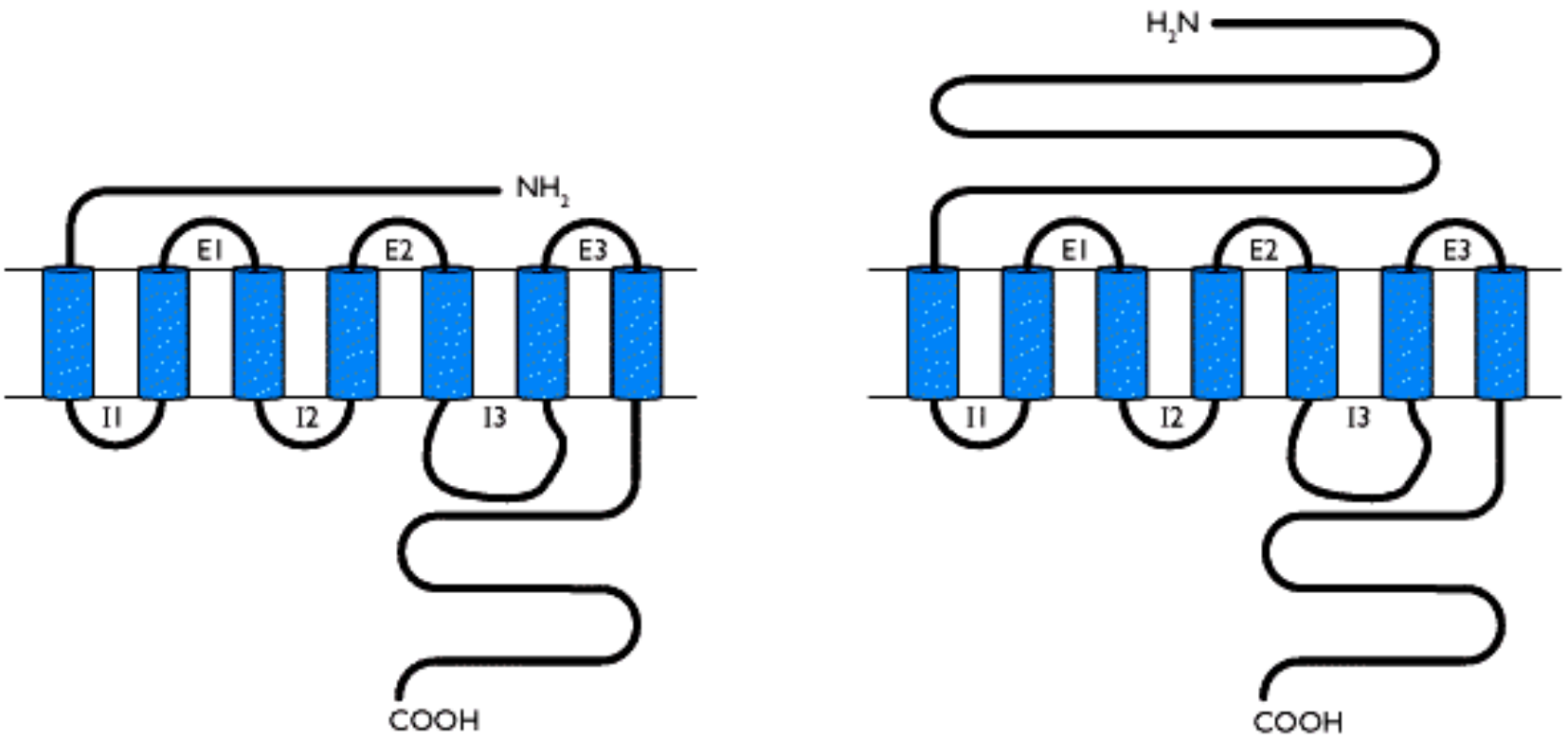
- This is the protein mediator of many Ca^{2+}-stimulated enzymatic reactions. Calmodulin has four high-affinity Ca^{2+}-binding sites.
- **(a)** A ribbon model of the crystal structure of calmodulin. The four Ca^{2+}-binding sites are occupied by Ca^{2+} (purple). The amino-terminal domain is on the left; the carboxyl-terminal domain on the right.
- **(b)** Calmodulin associated with a helical domain (red) of one of the many enzymes it regulates, calmodulin-dependent protein kinase II. Notice that the long central helix visible in **(a)** has bent back on itself in binding to the helical substrate domain. The central helix is clearly more flexible in solution than in the crystal.
- **(c)** Each of the four Ca^{2+}-binding sites occurs in a helix-loop-helix motif called the EF hand, also found in many other Ca^{2+}-binding proteins.




(a)

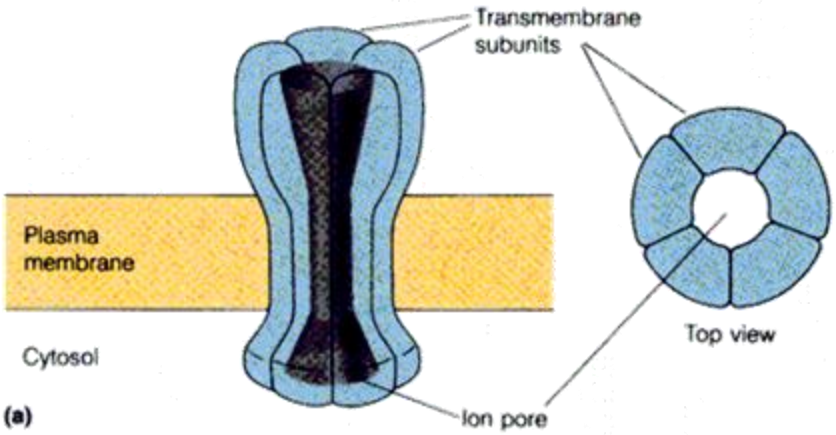

(b)

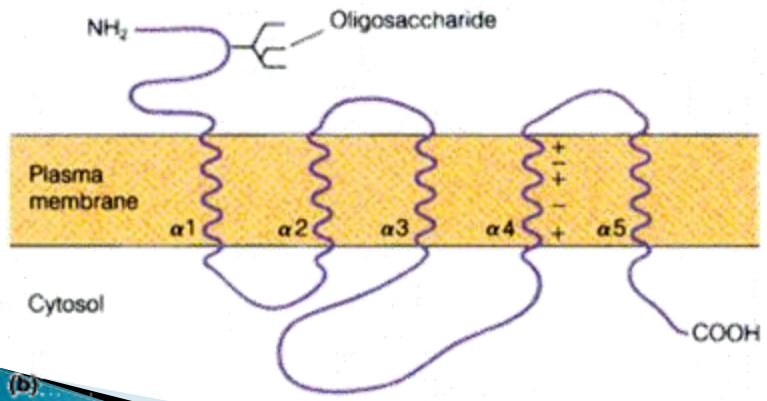
G-protein Linked Receptors



- These receptors frequently activate serine/threonine kinases through **second messengers** such as *cAMP, diacylglycerol, calmodulin*.

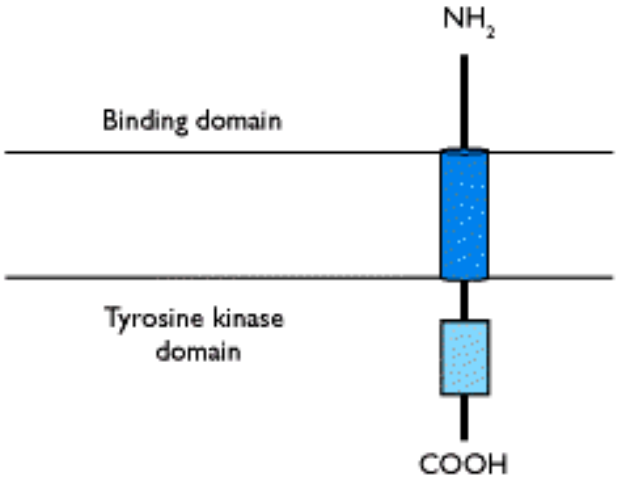
Nicotinic Acetylcholine Receptor

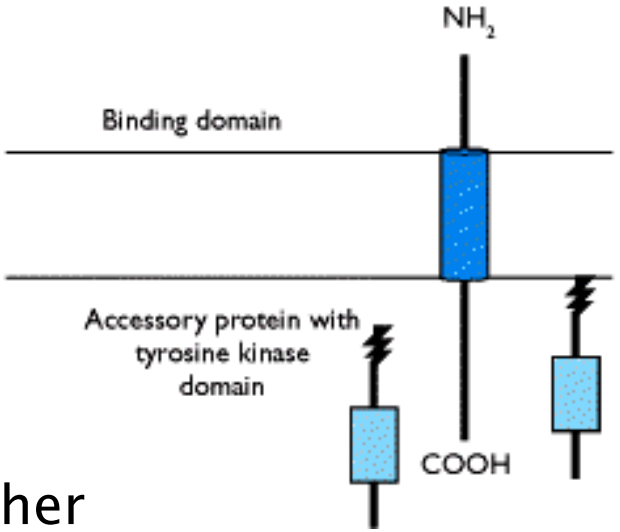




- Receptors that form ion channels – comparable to the nicotinic acetylcholine receptor.
  - Peptide hormones and epinephrine interact with this type of receptor.

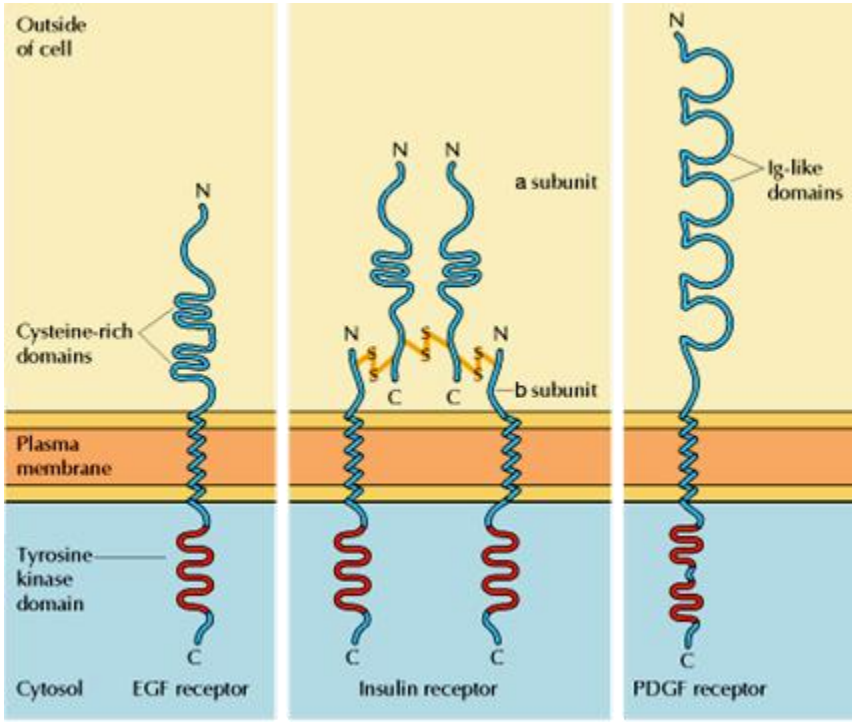
Receptors with Inherent Tyrosine Kinase Activity





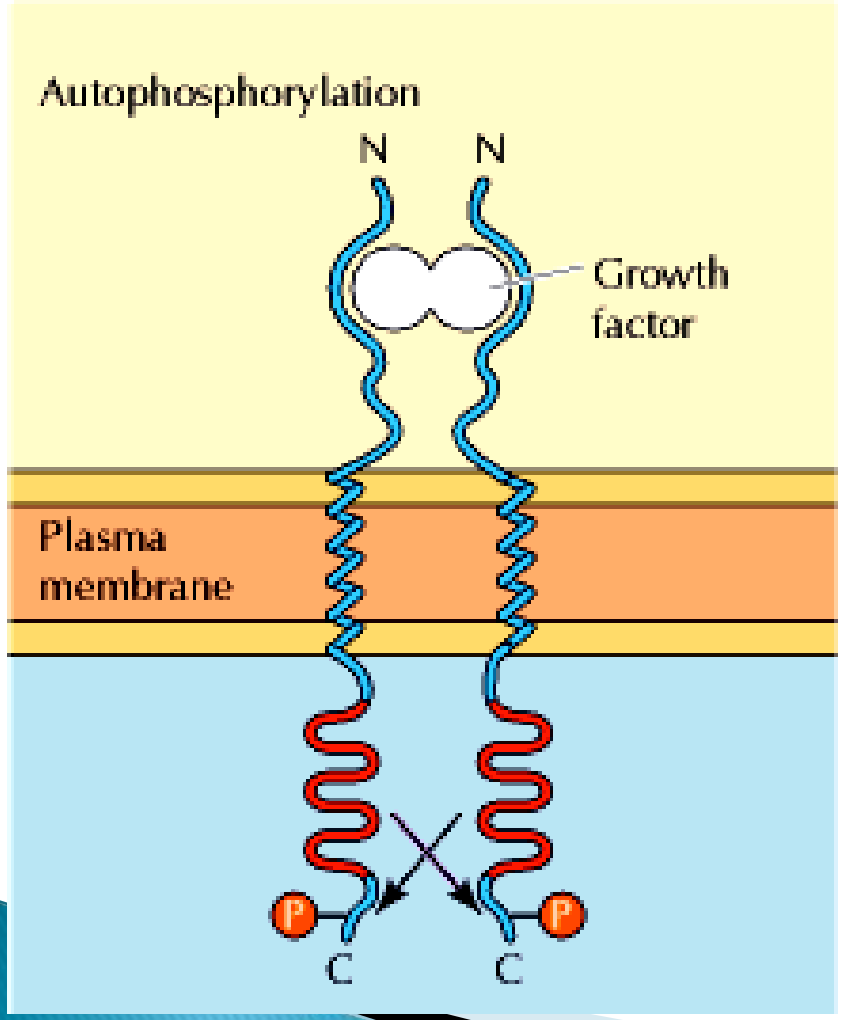
- Transmembrane receptor with either
  - inherent protein tyrosine kinase activity on the intracellular domain (e.g. **insulin** and **growth factor** receptors) or
  - associated intracellular molecules that have this activity (e.g. receptors for **growth hormone**, **prolactin** and **cytokines**).
- Binding of the hormone results in receptor dimerization initiating either **autophosphosphorylation** or **phosphorylation** of an associated enzyme.
- Signal transduction involve both cytoplasmic and nuclear events.

Organization of Receptor Protein-Tyrosine Kinases



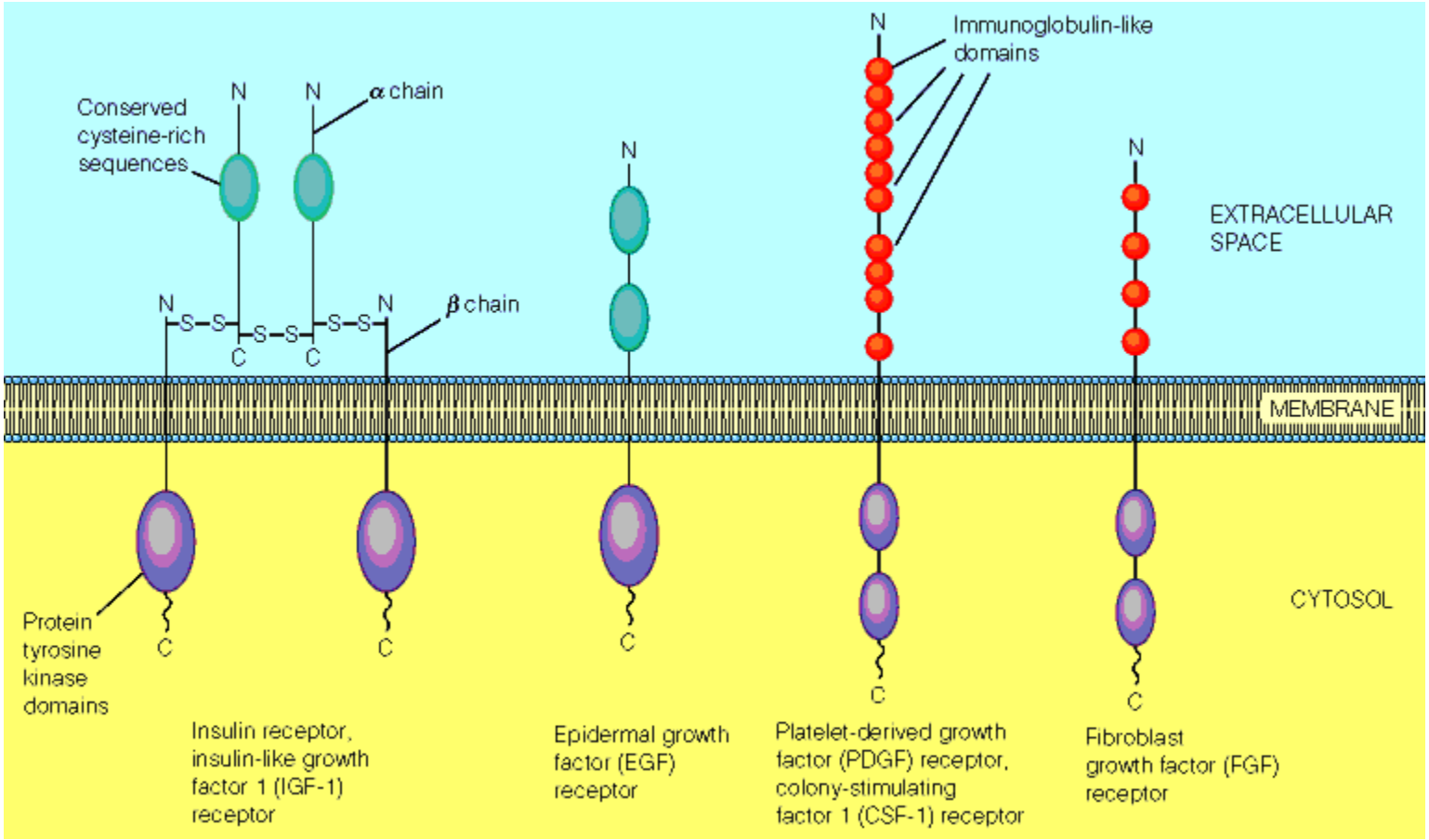
- The receptors consist of an
  - N-terminal extracellular ligand-binding domain,
  - transmembrane α-helix,
  - cytosolic C-terminal domain with protein-tyrosine kinase activity.
- The EGF receptor and insulin receptor both have cysteine-rich extracellular domains, whereas the PDGF receptor has immunoglobulin (Ig)-like domains.
- The PDGF receptor: its kinase domain is interrupted by an insert of ~100 amino acids.
- The insulin receptor is a dimer of two pairs of polypeptide chains (α and β).

Dimerization and Autophosphorylation of Receptor Protein-Tyrosine Kinases

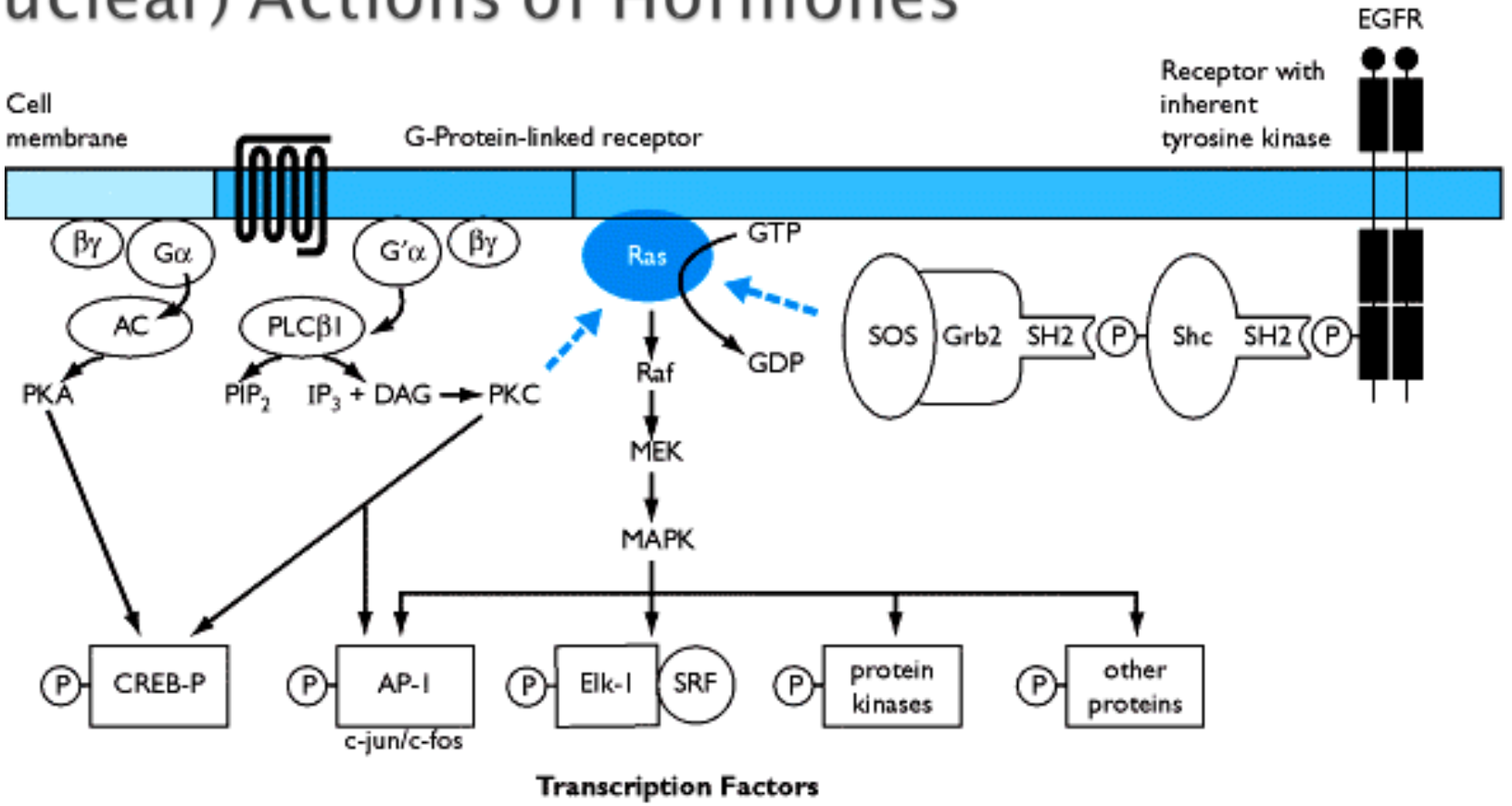


- Growth factor binding induces receptor **dimerization**, which results in receptor autophosphorylation as the two polypeptide chains phosphorylate one another

Insulin Receptor and its Relationship to Other Transmembrane Receptors with Protein Tyrosine Kinase Activity



Signal Transduction Pathways and Transcriptional (Nuclear) Actions of Hormones

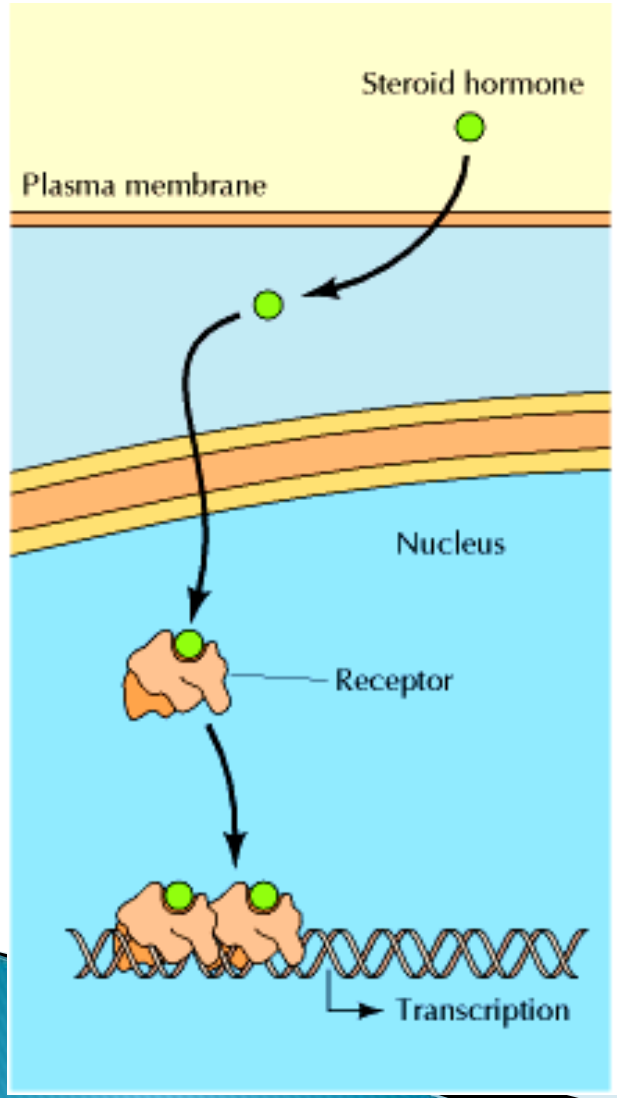


- Protein and peptide hormones can activate a number of transcriptional factors by **phosphorylation**.
- This may involve the **MEK-MAP pathway** (serine-threonine kinases) or direct activation of transcription factors by **protein kinase** (PK) A, PKC or the Ca^{2+}-calmodulin activated CaM protein kinase (not shown).

Receptors for Steroid and Thyroid Hormones

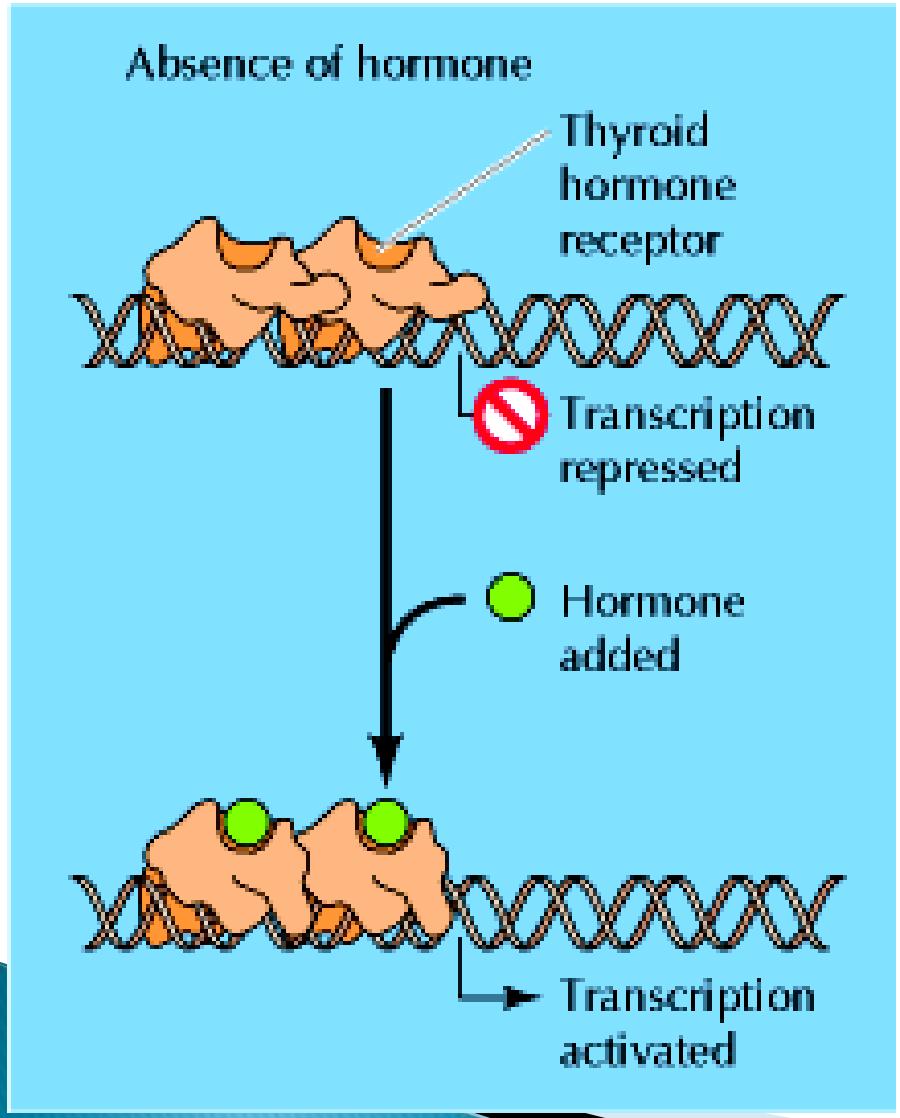
- Steroid and thyroid hormones are hydrophobic and diffuse from their binding proteins in the plasma, across the plasma membrane to intracellularly localized receptors.
- The resultant complex of steroid and receptor bind to response elements of nuclear DNA, regulating the production of mRNA for specific proteins.

Action of Steroid Hormones



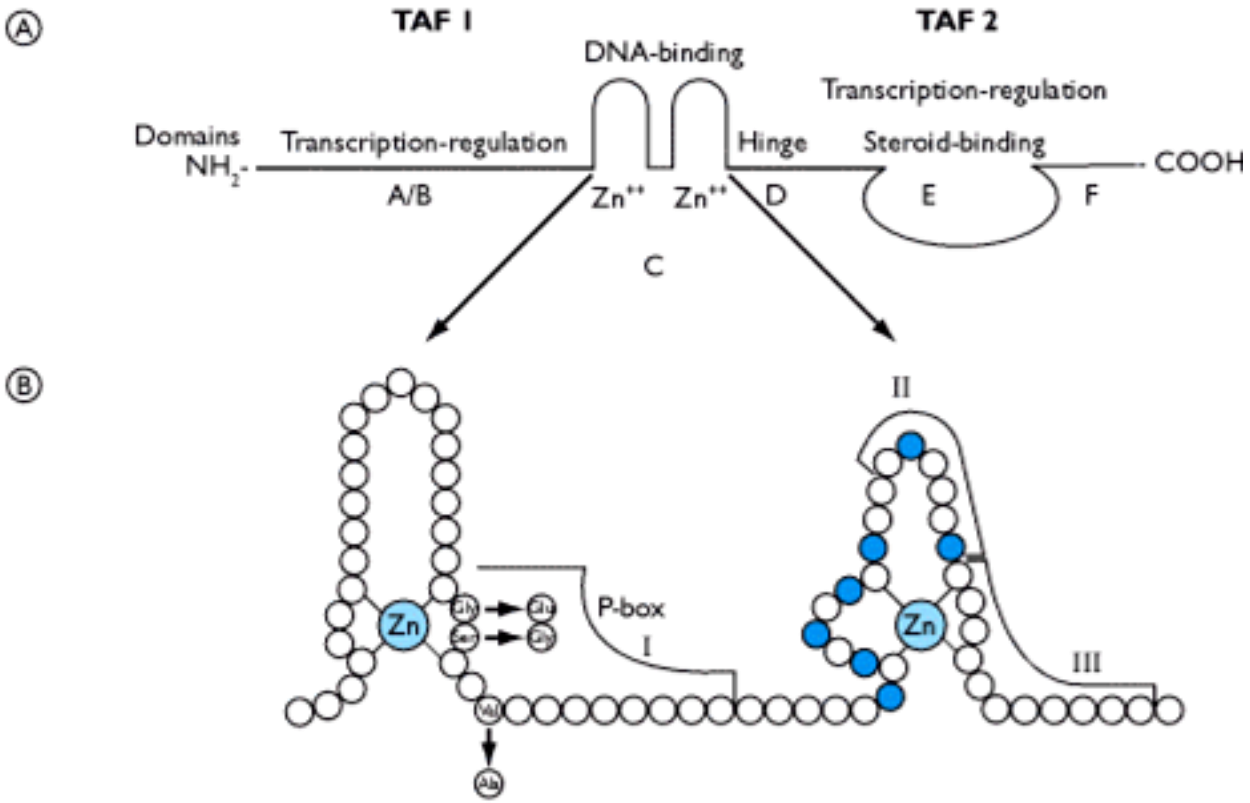
- The steroid hormones diffuse across the plasma membrane and bind to nuclear receptors, which directly stimulate transcription of their target genes.
- The steroid hormone receptors bind DNA as dimers.

Gene Regulation by the Thyroid Hormone Receptor



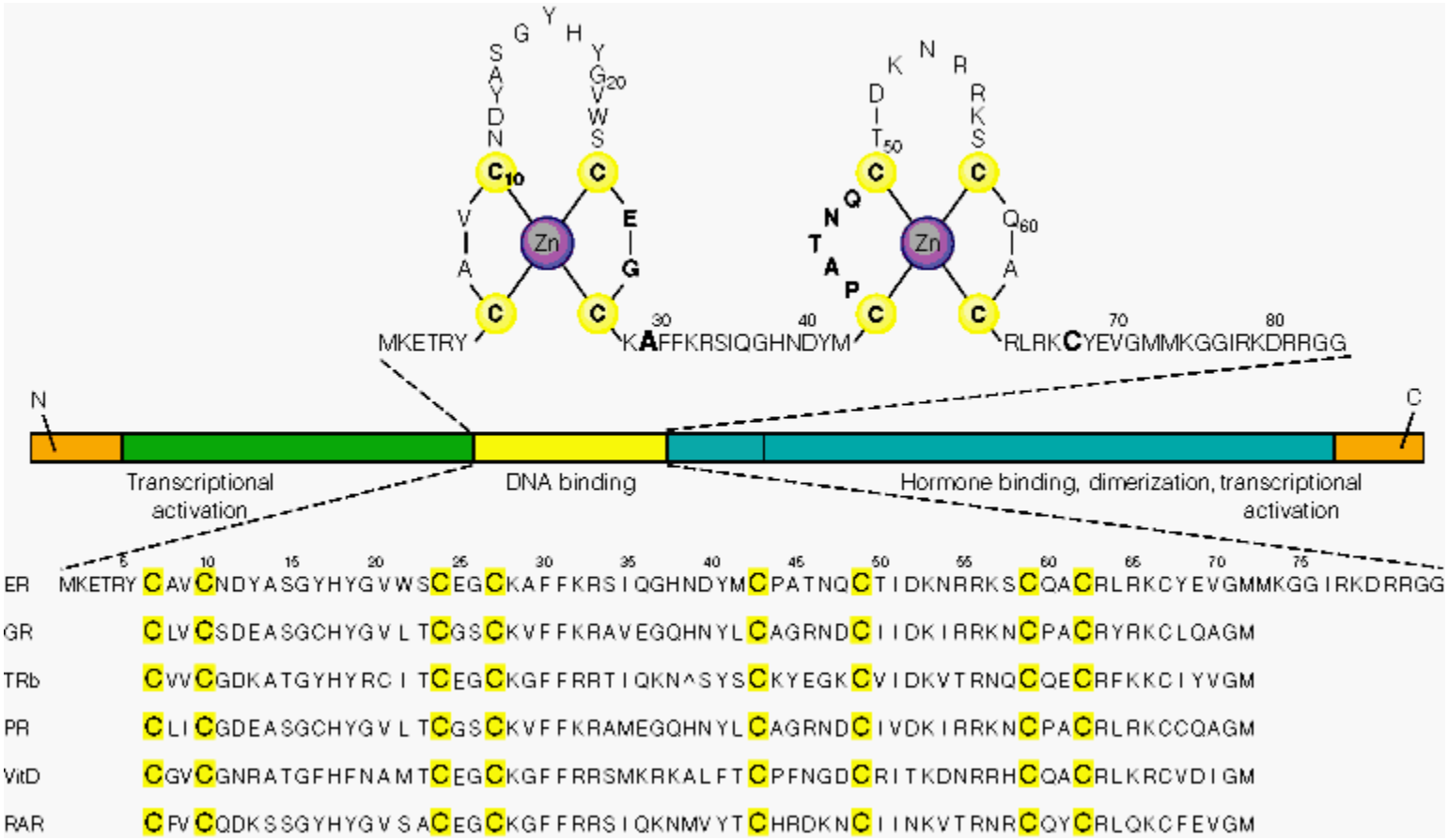
- Thyroid hormone receptor binds DNA in <u>either the presence or absence of hormone</u>.
  - However, hormone binding changes the function of the receptor from a **repressor** to an **activator** of target gene transcription.

Steroid Receptors, Zinc Fingers

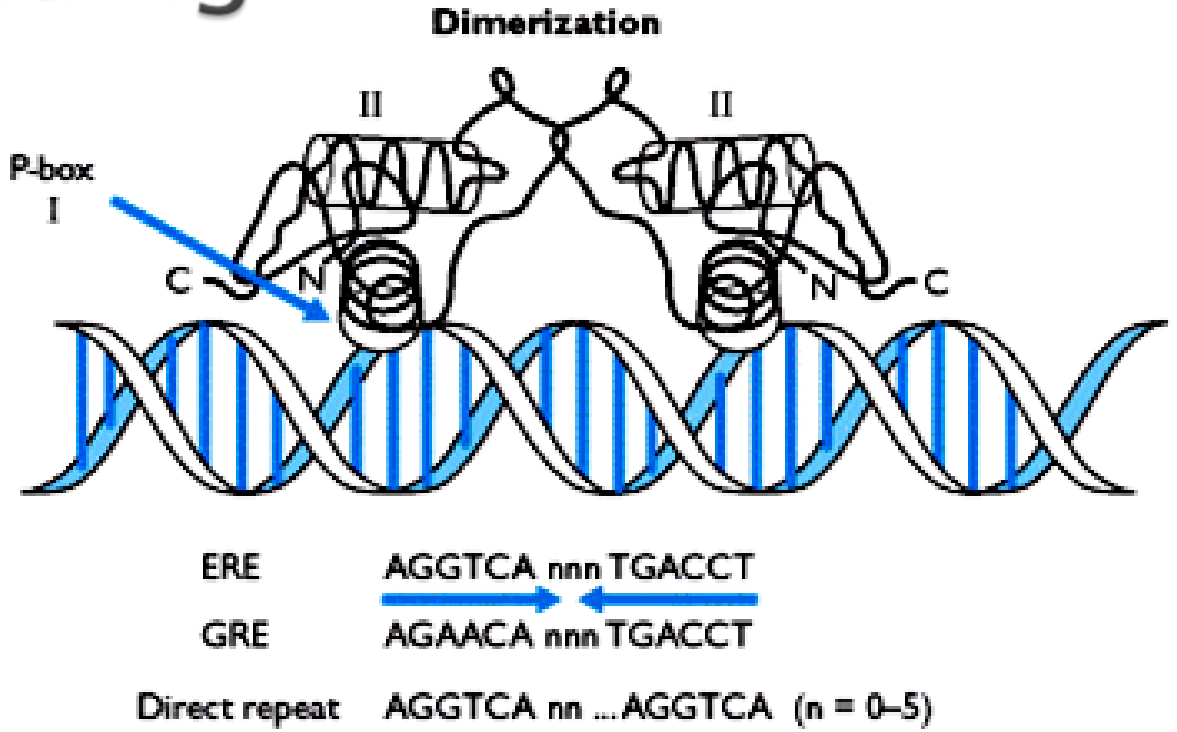


- Generalized structure of all steroid hormone receptors showing the different domains, location of the zinc fingers and the regions of the receptor responsible for transcriptional activity (TAF).

The Conserved DNA-Binding Domain in Steroid Receptors

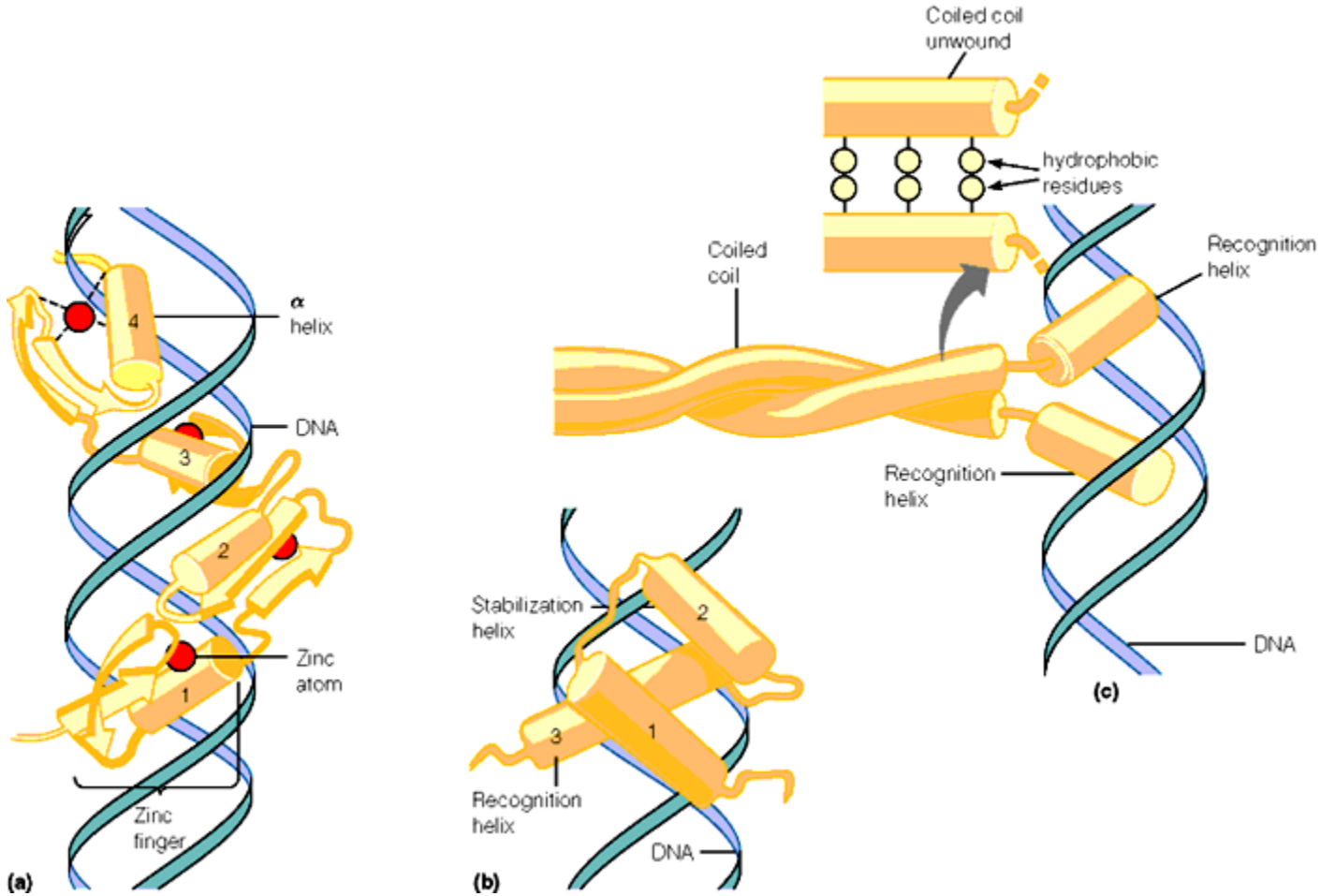


DNA Binding

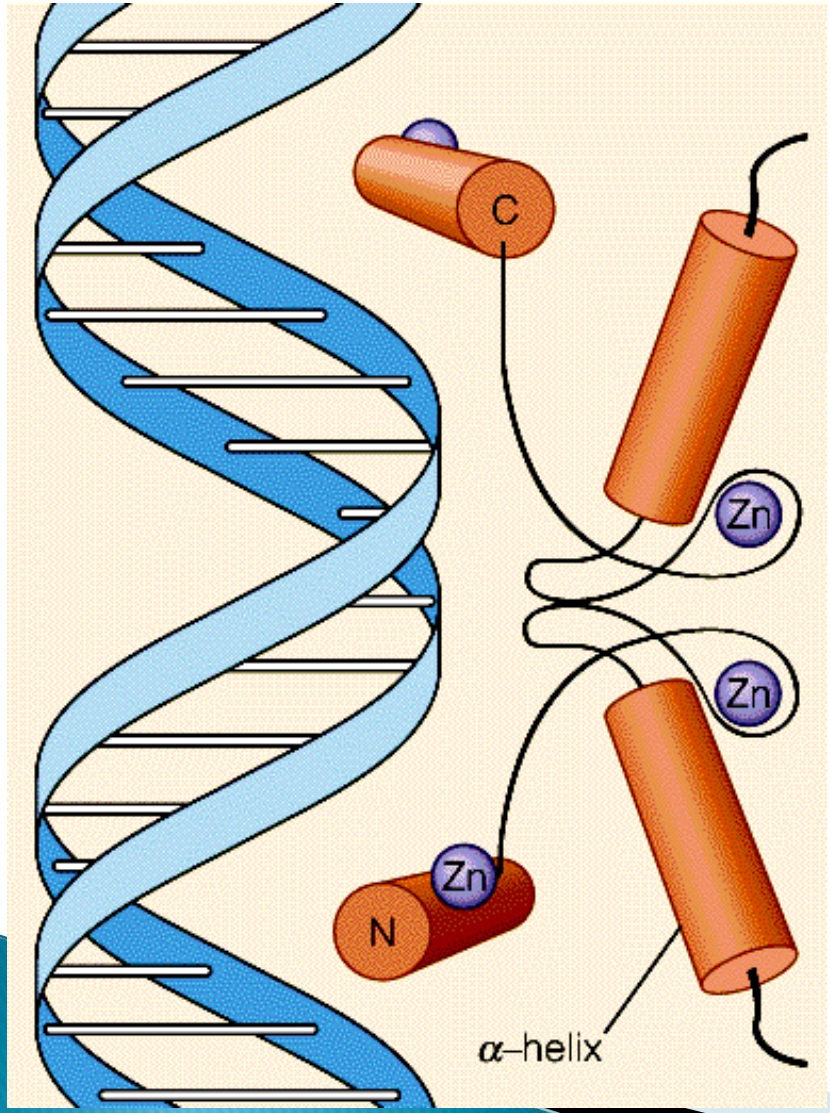


- Diagram showing dimerization of two receptors and helix I of each receptor slotting into the helix of the DNA.
- The base sequences of the ERE and GRE are shown plus the palindromic sequence.
- An example of a direct repeat sequence is also shown.

Structures of Three Common Types of DNA-Binding Motifs From Eukaryotic Transcription Factors

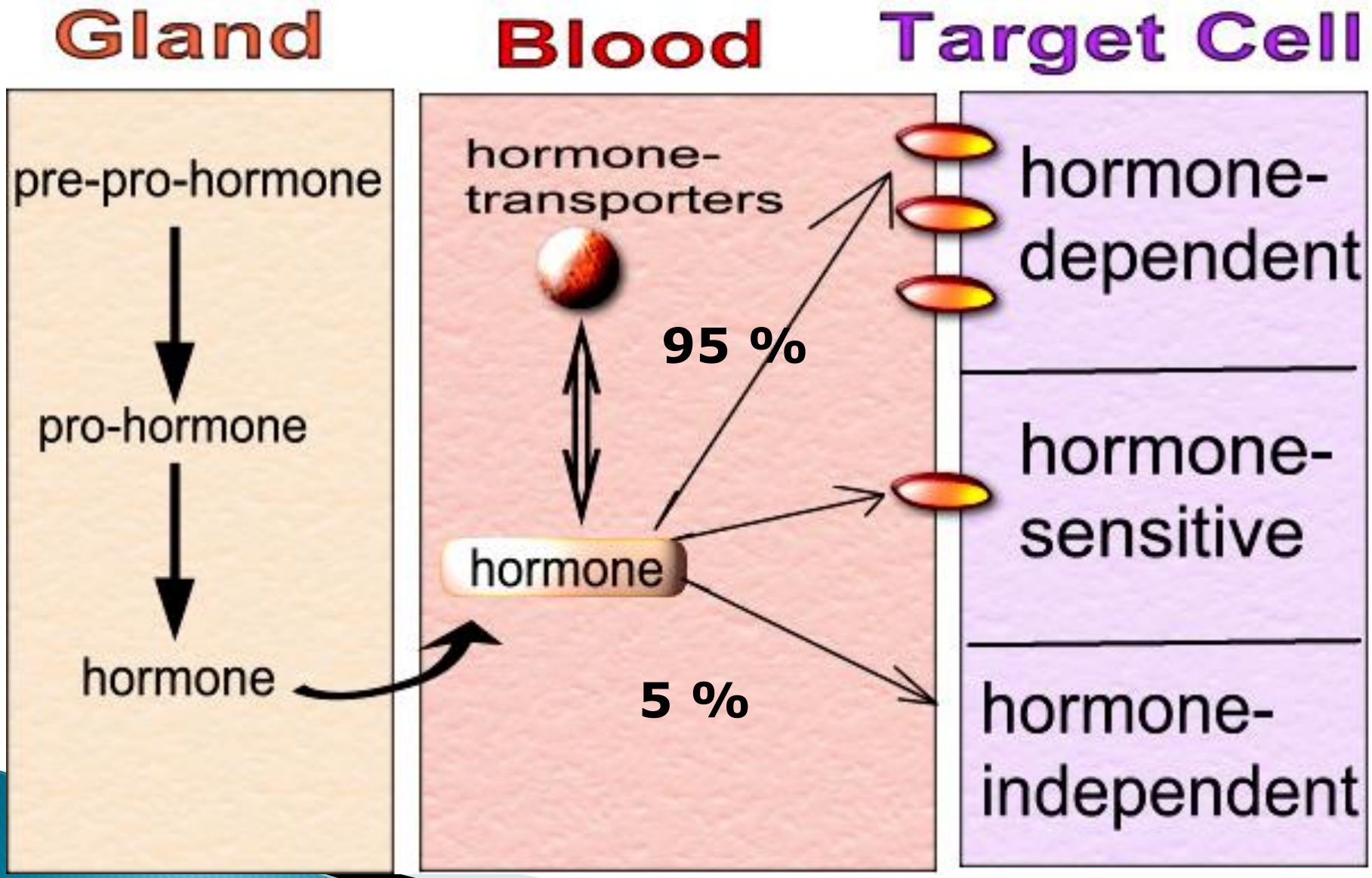


Binding of the Estrogen Receptor to DNA

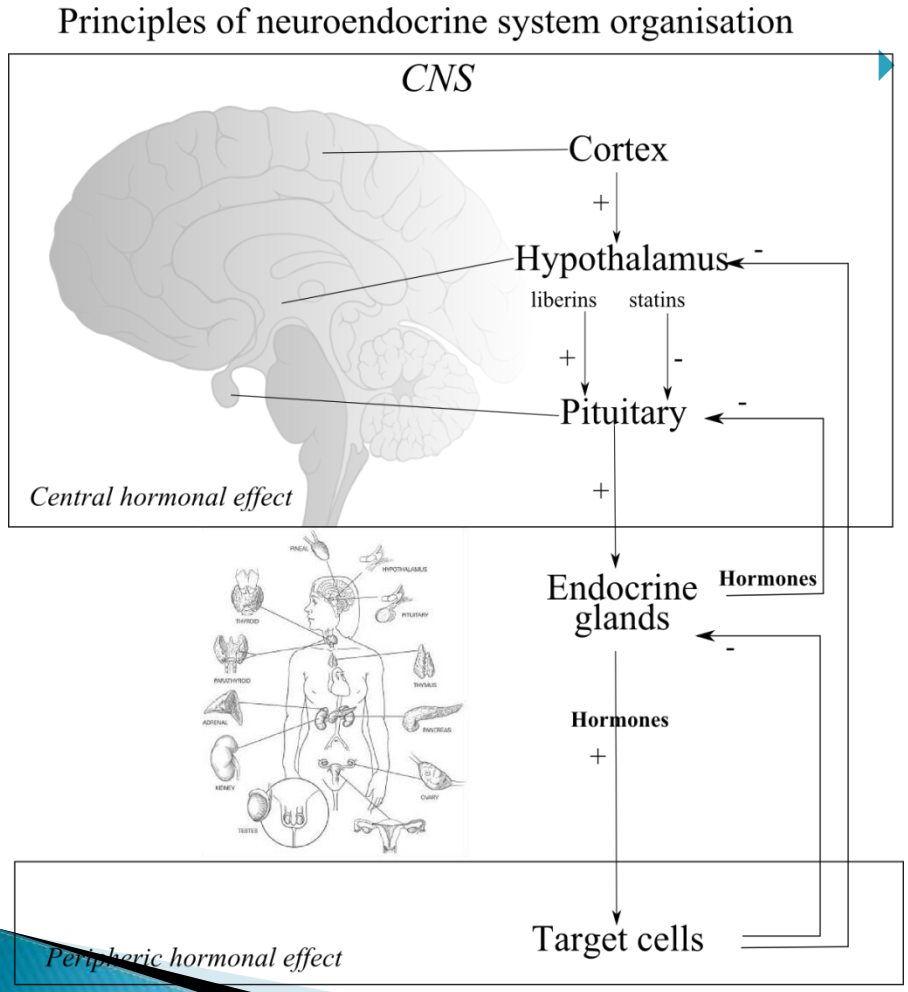


- Zinc atoms are probably complexed by the cysteine sulfurs in a pattern akin to the "zinc finger" structural motif of other eukaryotic transcriptional regulatory proteins

Hormone response factors

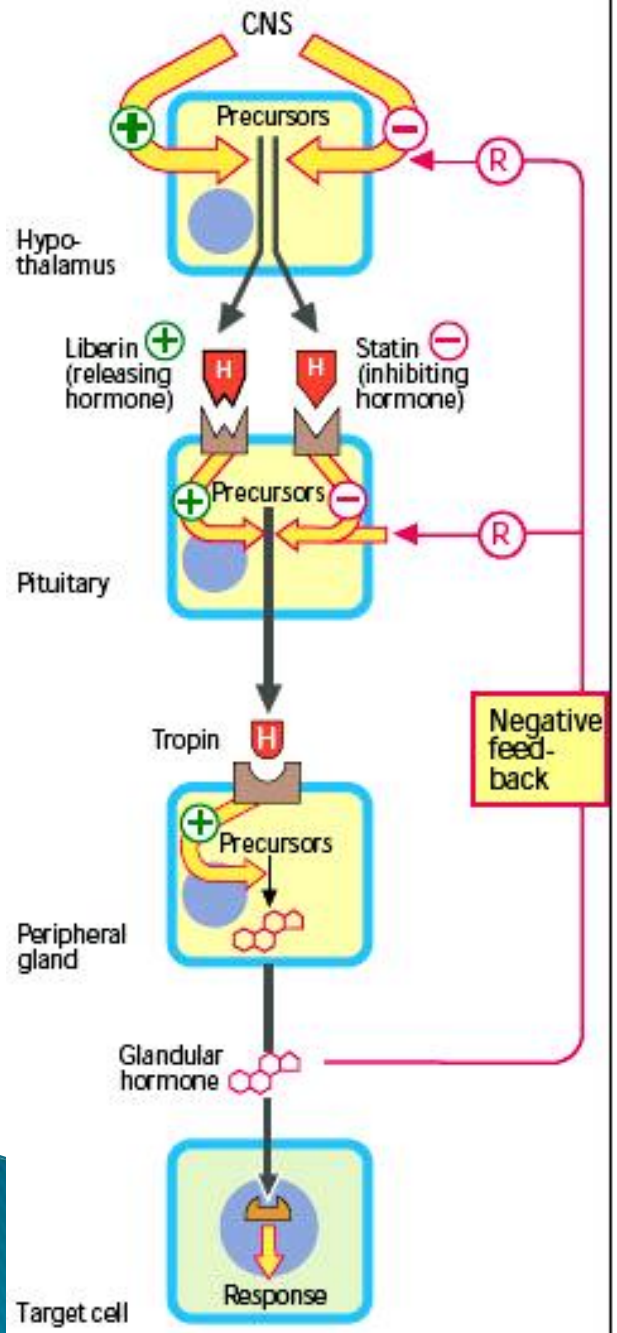


Principles of Organization of Neuroendocrine System



4 Principles of the organization of neuroendocrine system:

- Hierarchy
- Direct and feedback positive and negative communications (+, – interactions)
- Central and peripheral effect of hormones
- Threshold of sensitivity of hypothalamus.

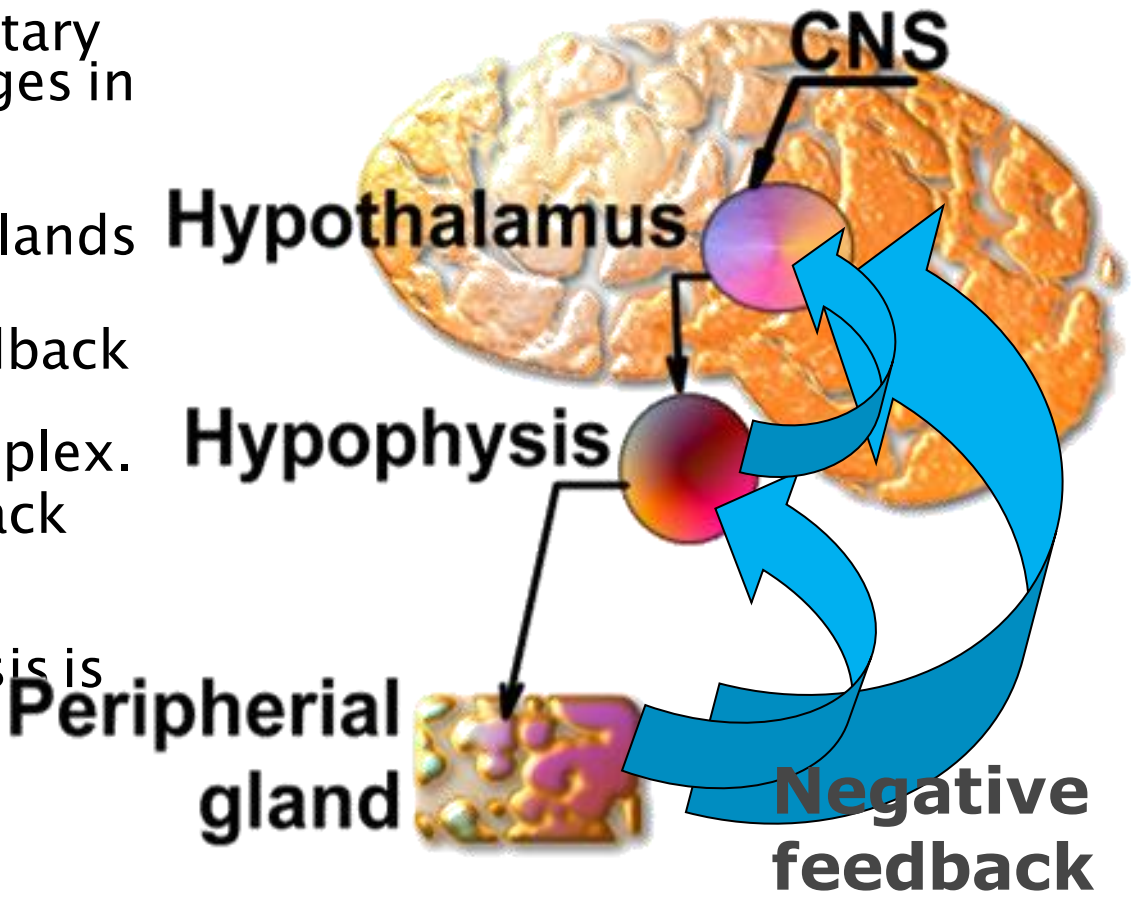


Hierarchy Principle

- level of intracellular hormones:
  - cAMP
  - cGMP.
  - (PG, LT, Tx) as metabolites of arachidonic acid, ($C_{20:4}$).
  - Inositolphosphates, Ca^{2+}
  - NO etc.
- level of hormones of peripheric glands;
- level of stimulating hormones of hypophysis;
- level of hypothalamus neurohormones.
- central nervous system.

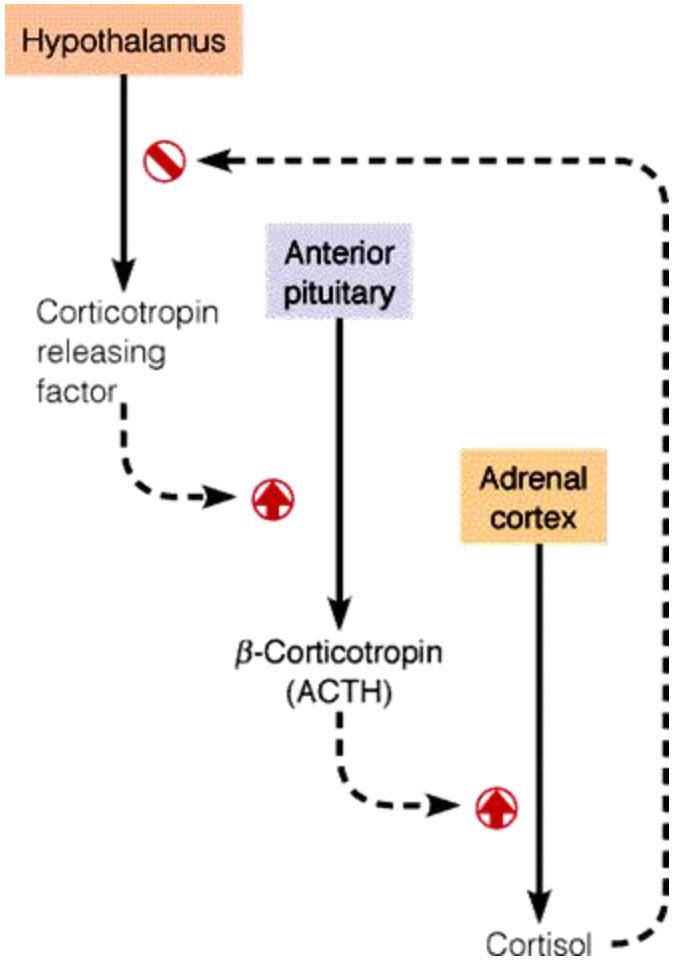
Direct and Feedback Communications

- Feedback loops may involve the hypothalamo-pituitary axis that detects changes in the concentration of hormones secreted by peripheral endocrine glands or a single gland.
- The integration of feedback loops involving several hormones may be complex.
- Disturbances in feedback loops are clinically important and their significance in diagnosis is pivotal.



Negative Feedback Control

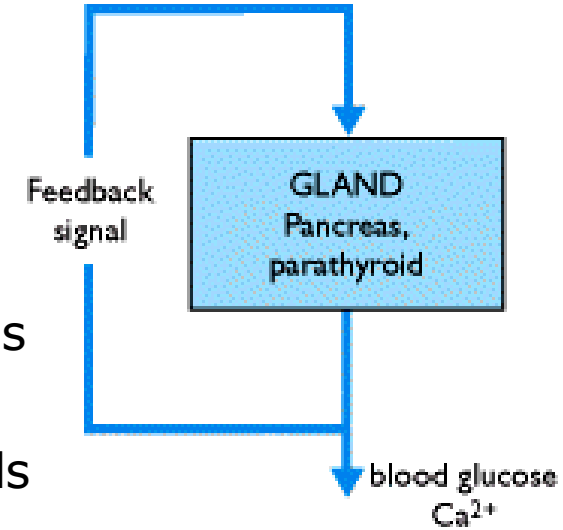
- The secretion of hormones is subject to **negative feedback control**, and there are several ways by which this is achieved.

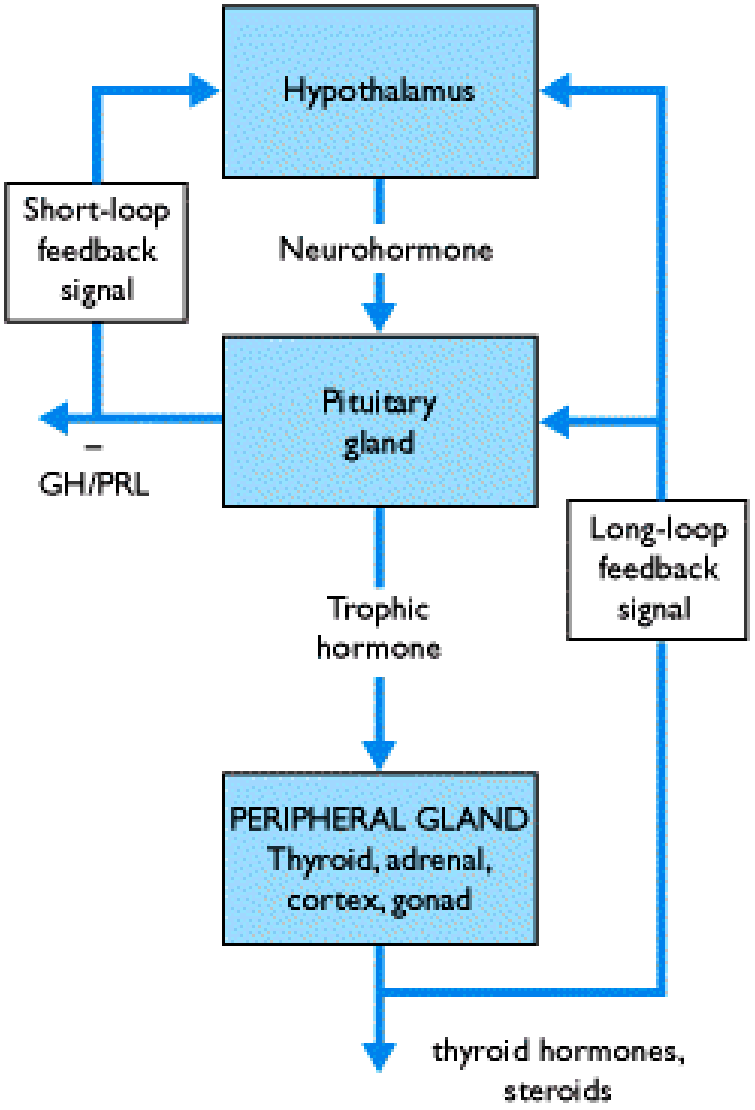


Principles of feedback control in the endocrine system

- The activity of the thyroid gland, adrenal cortex and gonads is controlled by the feedback effects of their circulating hormones on the hypothalamic–pituitary axis.

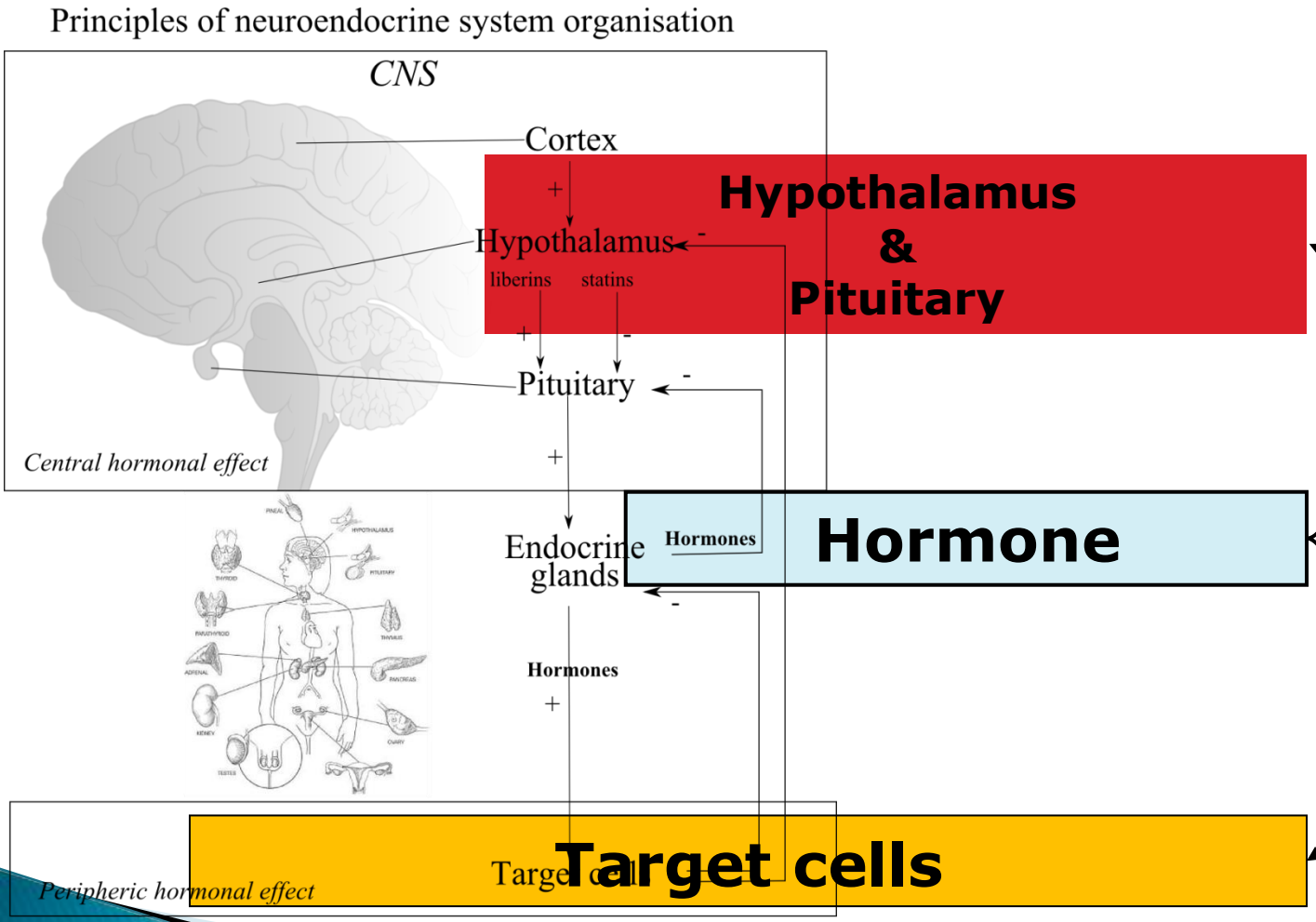
The secretory activity of glands not under direct control of the hypothalamic-pituitary axis i.e. endocrine pancreas and parathyroid gland is controlled by feedback signals of the regulated variable they control blood glucose and calcium





Abbreviations: GH, growth hormone; PRL, prolactin

Central and Peripheral Effect of Hormones

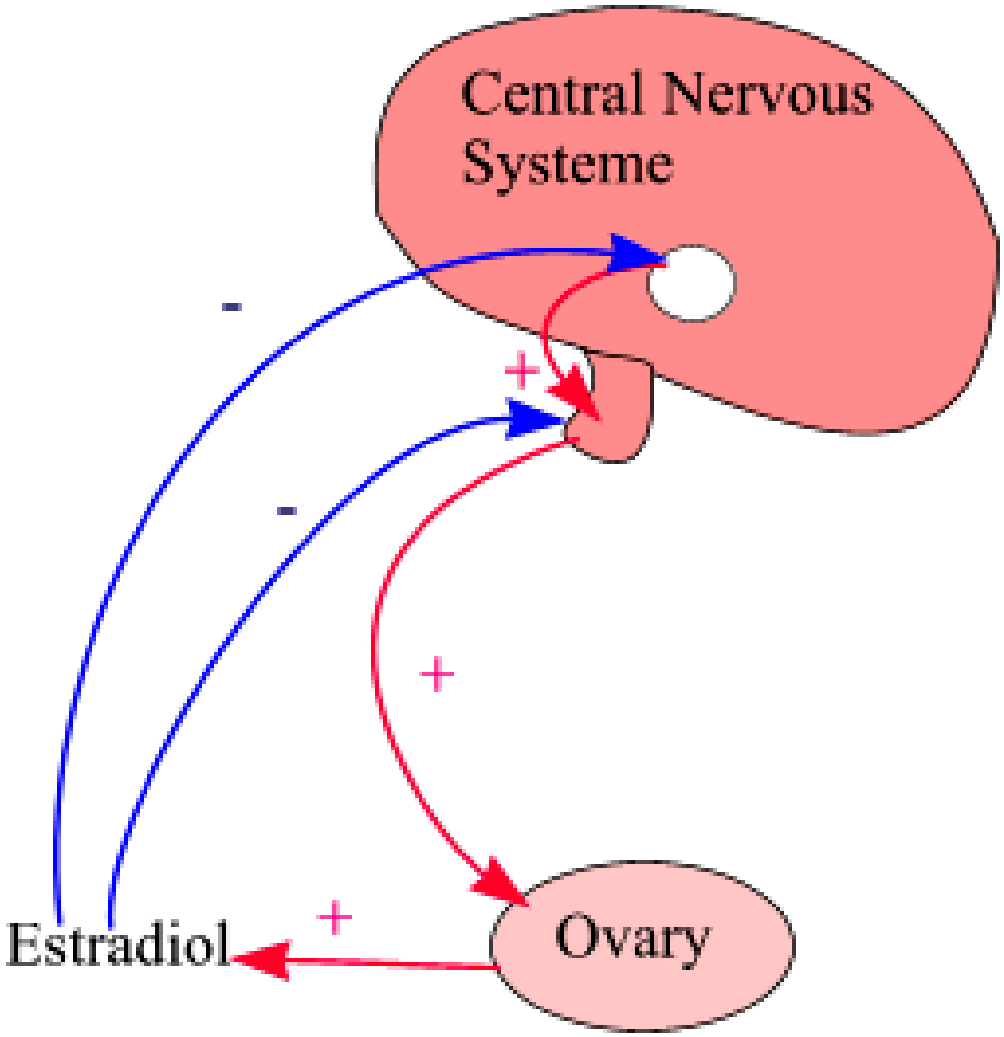


Central effect
Often only "-" (feedback inhibition)

Peripheral Effect
(+ or -)

Threshold of Sensitivity of Hypothalamus

- **Threshold of sensitivity of hypothalamus** is the minimal concentration of hormone which might inhibit the production of corresponding releasing factor.



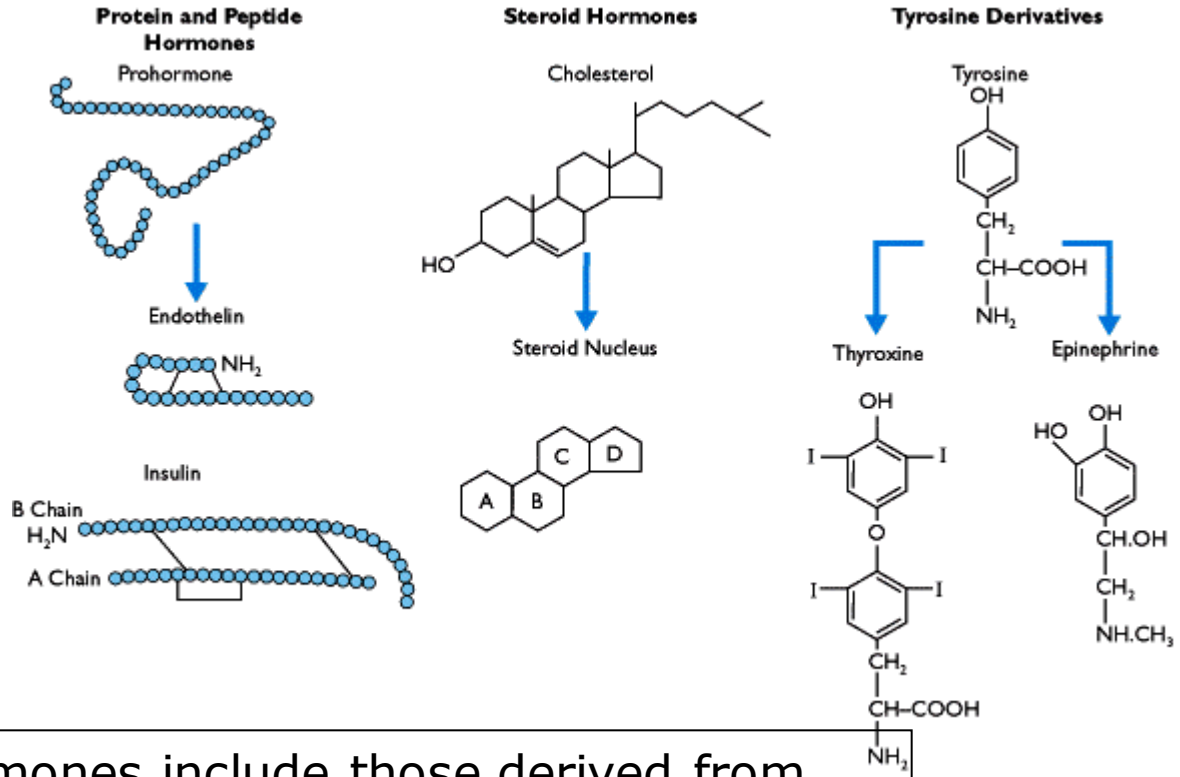
Ontogenetic (Elevation) Mechanism of Developement

- In newborn girl the threshold of hypothalamus to estrogen is low – i.e. feedback inhibition is significant.
- Minimal weight of organism 48–50 kg – action of STH. Increasing of body weight. The threshold of hypothalamus is also increasing (less receptors and their affinity).
- Hypothalamus produces more GnL →FSH → Estrogen.
- 12–14 years – secondary sexual characters (puberty age).
- 18–25–40 years – childbearing age. Hormonal status is stabilized. The threshold of hypothalamus is steady increasing. Also the body weight.
- After 45–50 years: stimulation of production of estrogens – defective hormones – peripheral effect is increased, central effect is decreased.
- Increased risk for neoplasy in target tissues.

Chemical Classification of Hormones

- Hormones are derived from:
  - **Amino acids,**
  - **Cholesterol,**
  - **Phospholipids.**
- By far the most numerous are the **protein** or **peptide** hormones, ranging in size from just three to over 200 amino acids.
- Some hormones, such as *insulin*, are made up of two sub-units joined by disulfide bonds between two cysteine molecules
- whilst the glycoprotein hormones of the anterior pituitary gland are not only made up of two protein sub-units but also have complex sugar moieties attached.

Chemical structures of the three major classes of human hormones



Other hormones include those derived from **tryptophan** (*serotonin* and *melatonin*) and those derived from **fatty acids** (*eicosanoids*).

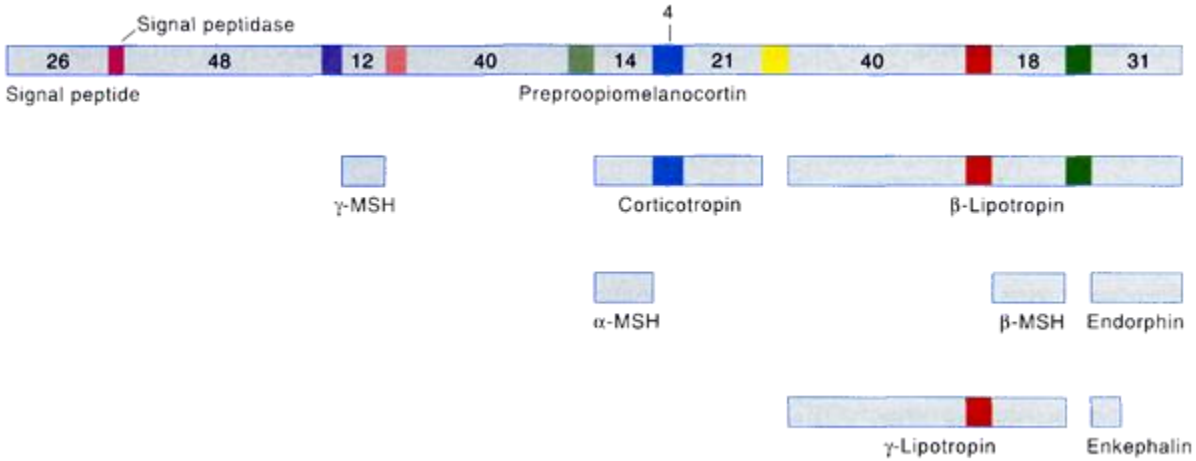
Chemical Classification of Hormones (cont'd)

- The steroid hormones (vitamin D and hormones of adrenal cortex and gonads) are derived from **cholesterol**.
- The third group of hormones are derived either from **tyrosine** or from **tryptophan**.
  - A single **tyrosine** molecule yields the **catecholamines, epinephrine** and **norepinephrine** (a neurotransmitter and a hormone).
  - The **thyroid** hormones are formed by the conjugation of two tyrosine molecules and resemble steroid hormones in binding to serum proteins and in the mechanism of action.
  - **Tryptophan** is the precursor of **serotonin** (5-hydroxytryptamine) and **melatonin** synthesis.
  - Finally, hormones derived from lipids and phospholipids include the major classes of **eicosanoids** including **prostaglandins, prostacyclins, thromboxanes** and **leukotrienes**.

Hormone Synthesis: Protein and Peptide Hormones

- Protein and peptide hormone synthesis requires
  - transcription of gene,
  - post-transcriptional modification by exision of the introns,
  - translation of the mRNA and
  - post-translational modifications of the original amino acid sequence.
- As a result, more than one pro-hormone may be derived from a single gene (e.g. *calcitonin* and *calcitonin-gene related peptide*).

Structure and Properties of Pro-Opiomelanocortin

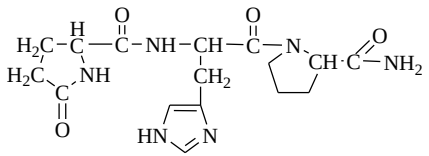


- **post-translational processing** of a pro-hormone may result in the formation of different biologically active peptide fragments (e.g. *pro-opiomelanocortin*).

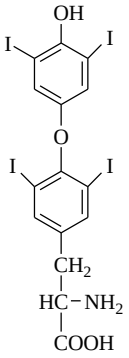
Hormone Synthesis: Steroid Hormones

- The synthesis of **steroid hormones** that occurs in the mitochondria and rough endoplasmic reticulum does not require immediate gene expression.
  - It requires the presence of specific enzymes that convert cholesterol into the appropriate steroid.
  - Different enzymes are expressed in different steroid secreting cells and their expression is controlled by trophic hormones and/or other factors.

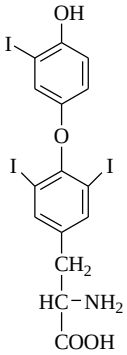
Structure of Some Hormones



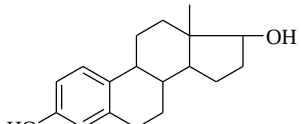
Thyrotropin-releasing hormone (TRH)



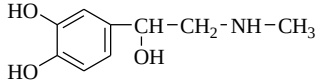
Tetraiodothyronine (thyroxine; T_4)



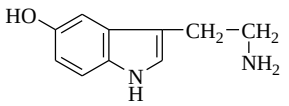
triiodothyronine (T_3)



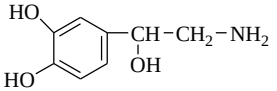
Estradiol



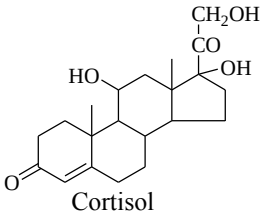
Epinephrine (adrenaline)



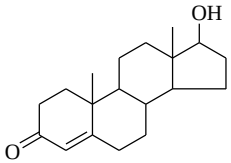
Serotonin



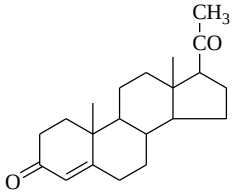
Norepinephrine (noradrenaline)



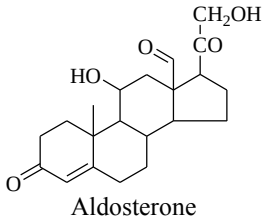
Cortisol



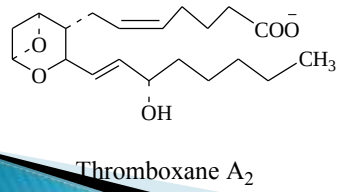
Testosterone



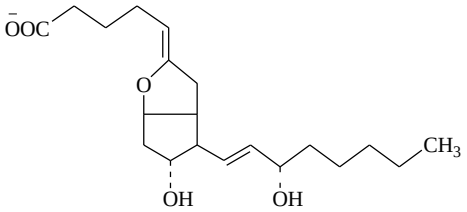
Progesterone



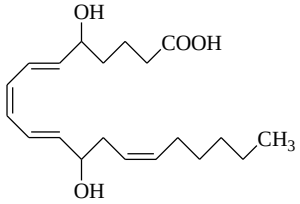
Aldosterone



Thromboxane A_2

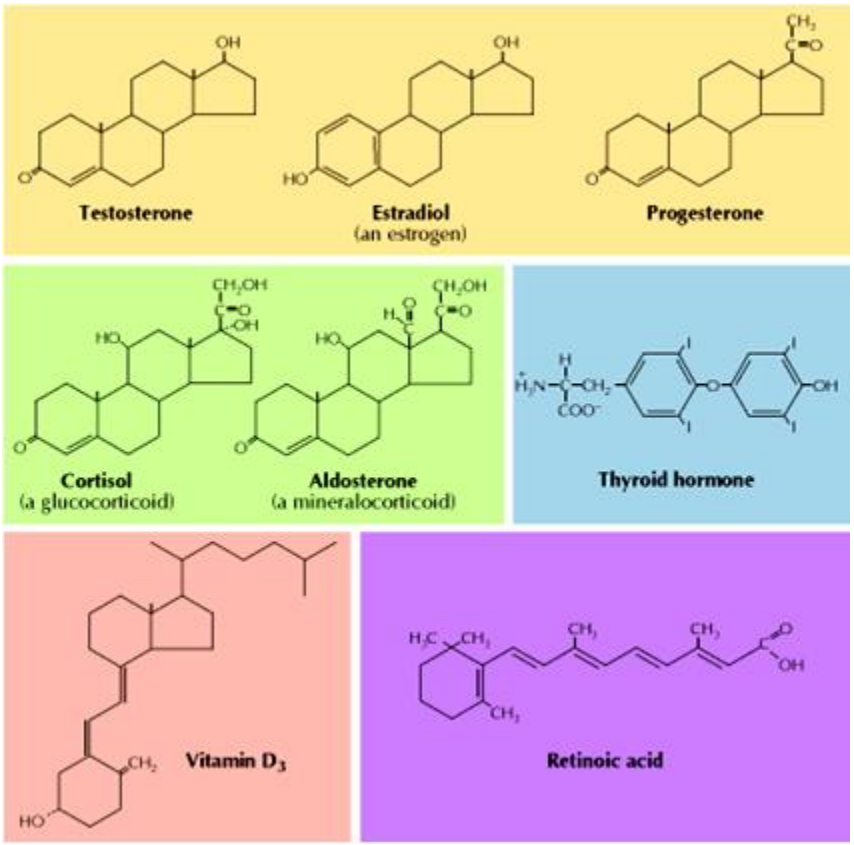


Prostacycline (PGI_2)



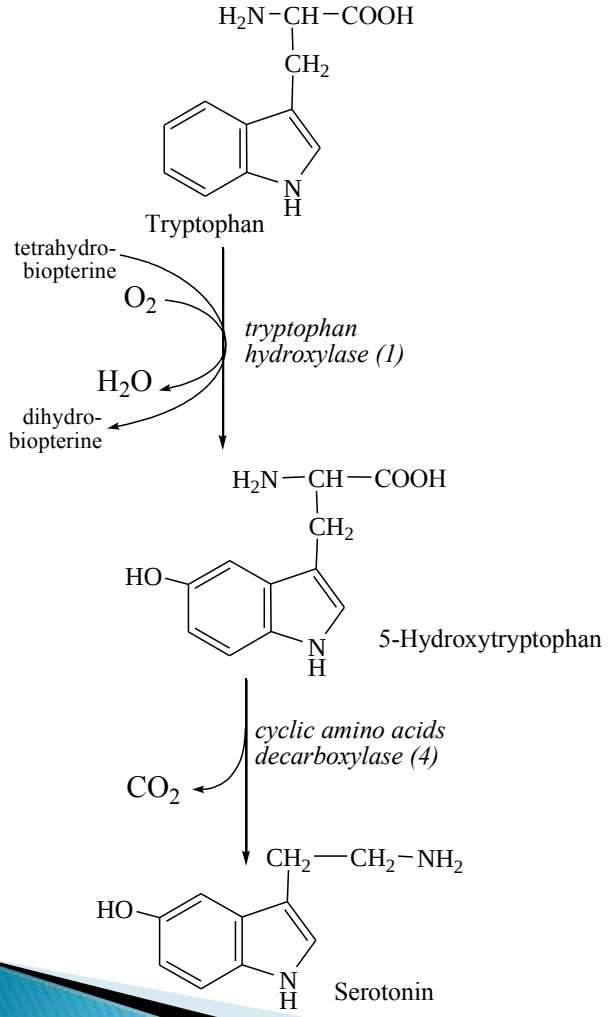
Leukotriene B

Structure of Steroid Hormones, Thyroid Hormone, Vitamin D_3, and Retinoic Acid



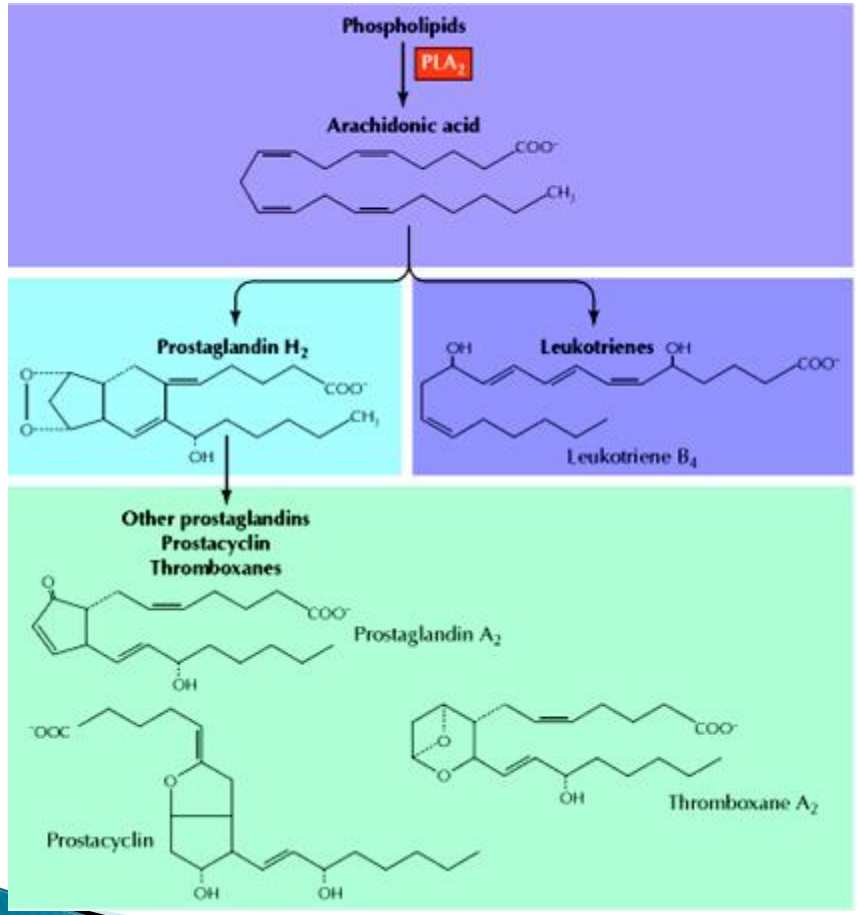
- The steroids include the sex hormones (testosterone, estrogen, and progesterone), glucocorticoids, and mineralocorticoids.

Hormone Synthesis: Amine Hormones



- The **amine hormones** such as the **catecholamines**, **melatonin** and **serotonin** are formed by side-chain modifications of either a single *tyrosine* or *tryptophan* molecule while the **eicosanoid** family of hormones are formed from *lipids*.

Hormone Synthesis: Eicosanoids



- The <u>eicosanoids</u> include the **prostaglandins**, **prostacyclin**, **thromboxanes**, and **leukotrienes**.
  - synthesized from **arachidonic acid**, by the hydrolysis of phospholipids catalyzed by **phospholipase A_2** (PLA_2).
- **Arachidonic acid** can then be metabolized via two alternative pathways;
  - one pathway leads to synthesis of prostaglandins, prostacyclin, and thromboxanes,
  - the other pathway leads to synthesis of leukotrienes.

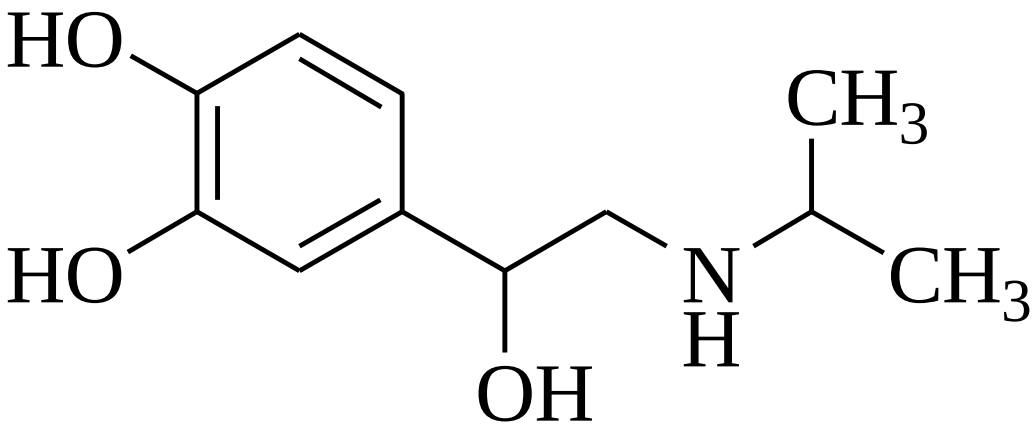
The Role and Medical Significance of Eicosanoids

- The eicosanoids are rapidly broken down and therefore act locally in **autocrine** or **paracrine** signaling pathways.
- They stimulate a variety of responses in their target cells, including **blood platelet aggregation**, **inflammation**, and **smooth-muscle contraction.**
- The enzyme *cyclooxygenase* is the target of **aspirin** and other **nonsteroidal anti-inflammatory drugs.**
  - By inhibiting synthesis of the prostaglandins, aspirin reduces inflammation and pain.
  - By inhibiting synthesis of thromboxane, aspirin also reduces platelet aggregation and blood clotting.
  - Because of this activity, small daily doses of aspirin are frequently prescribed for prevention of strokes.
- In addition, aspirin and nonsteroidal anti-inflammatory drugs have been found to reduce the frequency of colon cancer, apparently by inhibiting the synthesis of prostaglandins that act to stimulate cell proliferation and promote cancer development.

Hormone Agonists and Antagonists

- A hormone **agonist** is an analog of the hormone that binds productively to a receptor and mimics the action of the endogenous hormone.
  - An **agonist** is comparable to an alternative substrate for an enzyme.
  - Because its binding to a receptor is productive; that is, it evokes a metabolic response comparable to that of binding the hormone.
- By contrast, a hormone **antagonist** binds to receptors but does not provoke the normal biological response.
  - An **antagonist** is to a receptor as a competitive inhibitor is to an enzyme;
  - that is, both **antagonists** and competitive inhibitors compete with a normal ligand (hormone or substrate, respectively) for binding to a specific site on a protein and, by so binding, inhibit a normal biological process.

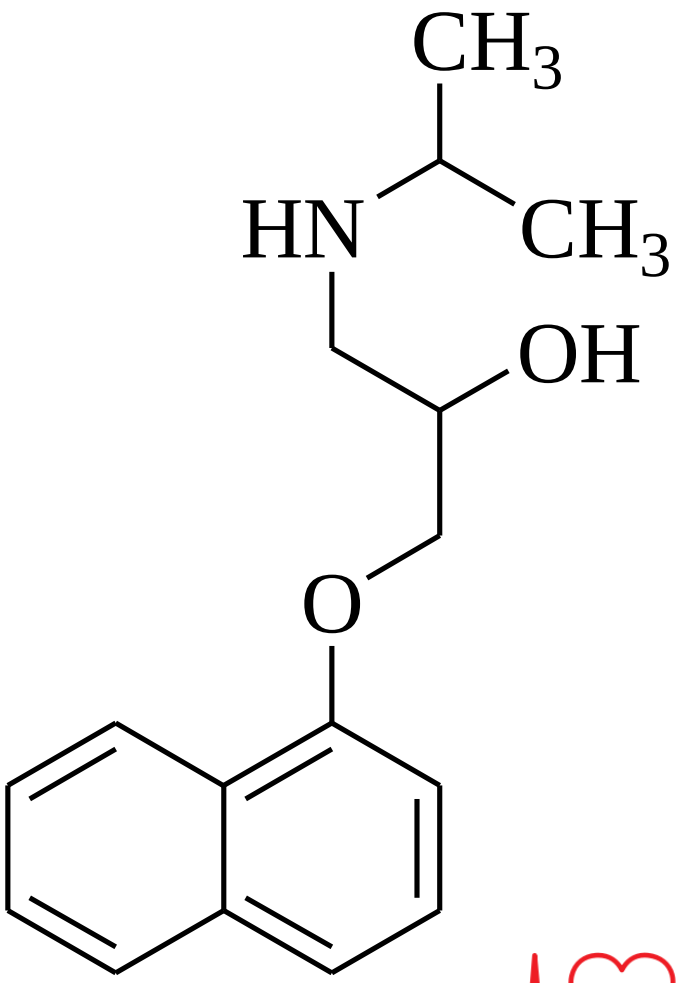
Hormone Agonist: Isoproterenol



Isoproterenol

- The agonist is used to treat asthma, because it mimics the effects of **catecholamines** in relaxing bronchial muscles in the lung;
- it does so by interacting with one specific class of **adrenergic receptors** (so-called because they bind adrenaline).

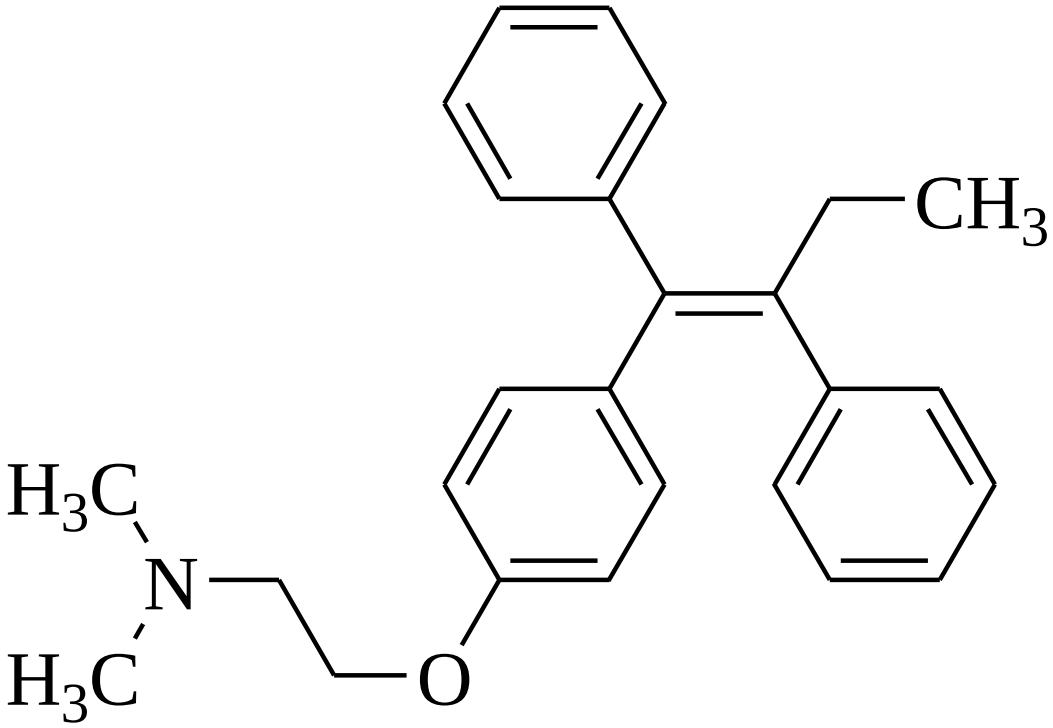
Hormone Antagonist: Propranolol



Propranolol

- Another important drug, used to control blood pressure and pulse rate in cardiac patients, is **propranolol**, an antagonist of another class of adrenergic receptors, which control blood pressure and heartbeat rate.

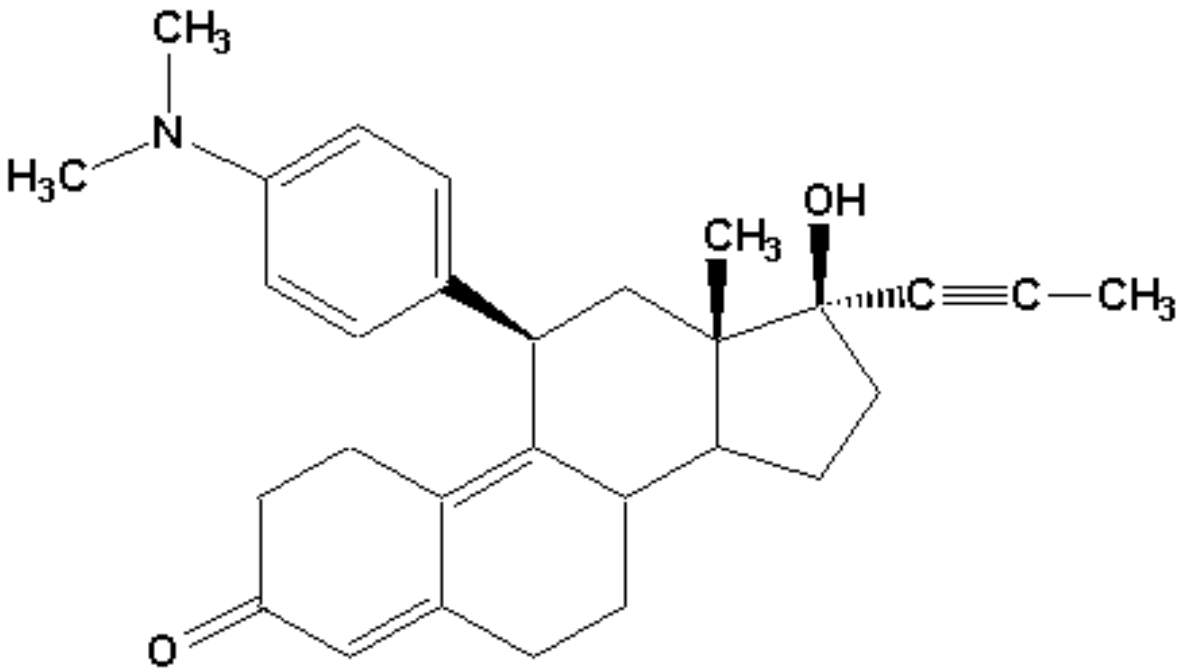
Hormone Antagonist: Tamoxifen



tamoxifen

- The growth of some breast tumor cells is activated by estrogen.
- The drug, **tamoxifen** binds to estrogen receptors without activating estrogen-responsive genes.
- Tamoxifen treatment of patients with such tumors after surgery or chemotherapy often antagonizes estrogen binding in residual tumor cells and retards their growth.

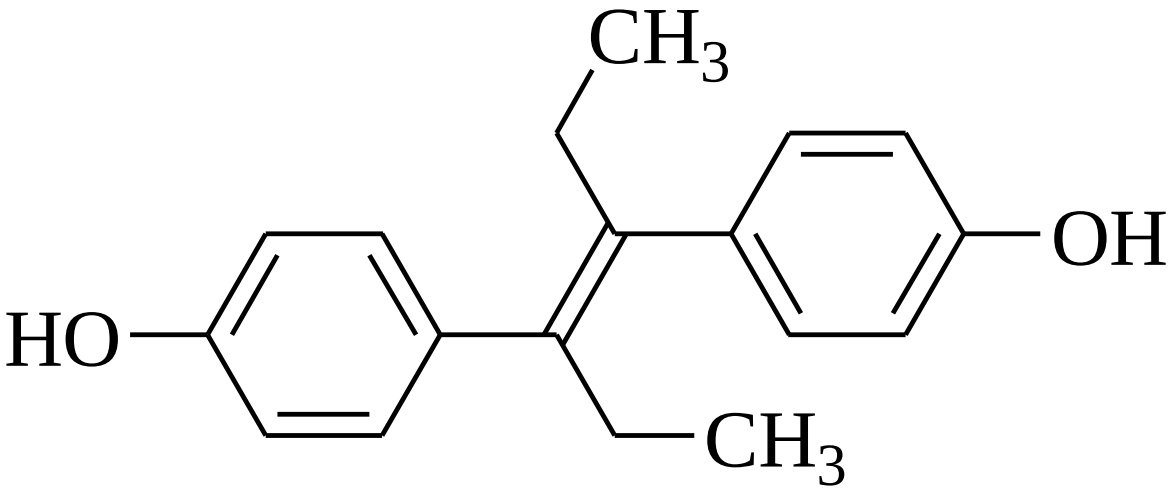
Hormone Antagonist: RU486



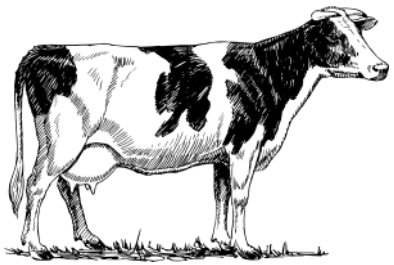
RU486

- The drug, **RU486**, binds to progesterone receptors and blocks the events essential to implantation of a fertilized ovum in the uterus.
- Hence, RU486 is an effective contraceptive agent, even when taken after intercourse.

Diethylstilbestrol



Diethylstilbestrol



- **Diethylstilbestrol** is a synthetic estrogen previously used to promote growth of beef cattle, until it was found to be potentially **carcinogenic** at the levels found in meat from treated cattle.


Thank you
for your attention