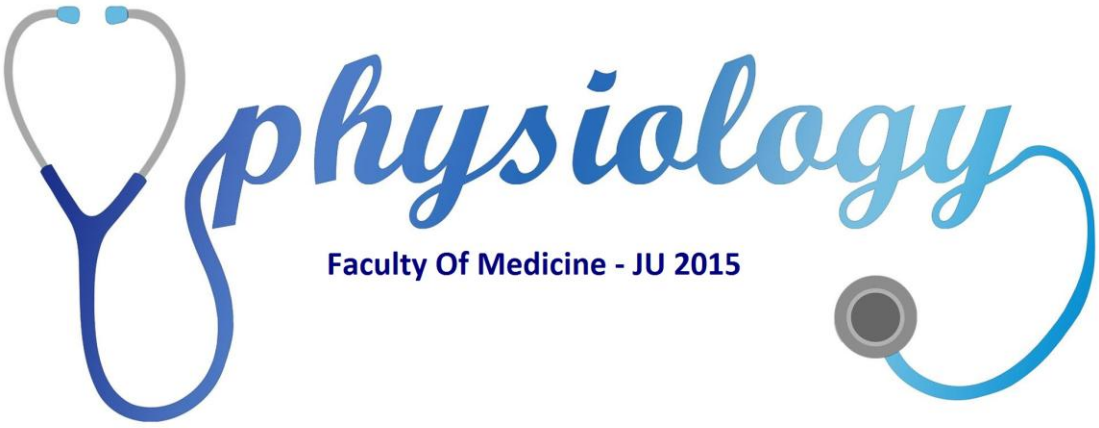


Done by : Rossul Al-Bahadli

Corrected by : Dr. Ebaa Alzayadneh

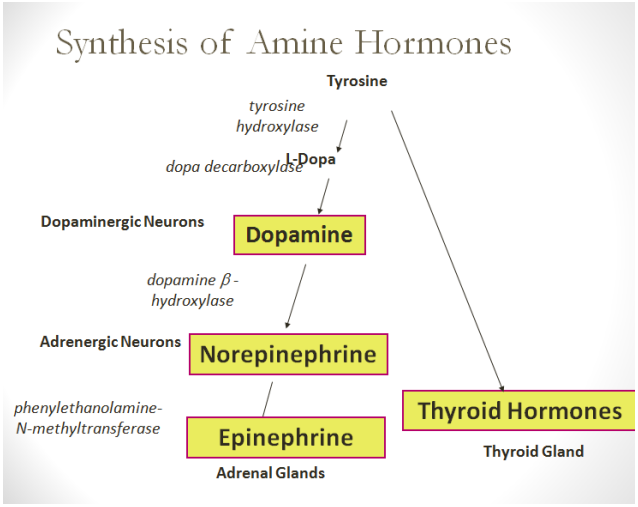
Chemical classification of hormones:

Endocrine hormones are classified into:

- Amino acid derivatives: epinephrine, norepinephrine, and thyroid hormones (T3,T4). These are all derived from the amino acid tyrosine.
- Peptides: antidiuretic hormone (vasopressin) and hypothalamus hormones. The hypothalamus hormones are called releasing factors since they stimulate other endocrine glands to release their hormones.
- Proteins or (glycoproteins): anterior pituitary hormones.
- Steroids: sex hormones, estrogen, progesterone, cortisol and corticosteroids.

Paracrine hormones are classified into:

- Amino acid derivative: histamine.
  Histamine can be a neurotransmitter or a paracrine hormone depending on the secreting cell and the affected cell.
- Arachidonic acid derivatives: prostaglandins (inflammatory mediators).



Synthesis of amine hormones:

One amino acid can be a precursor for the synthesis of several hormones, for example tyrosine.

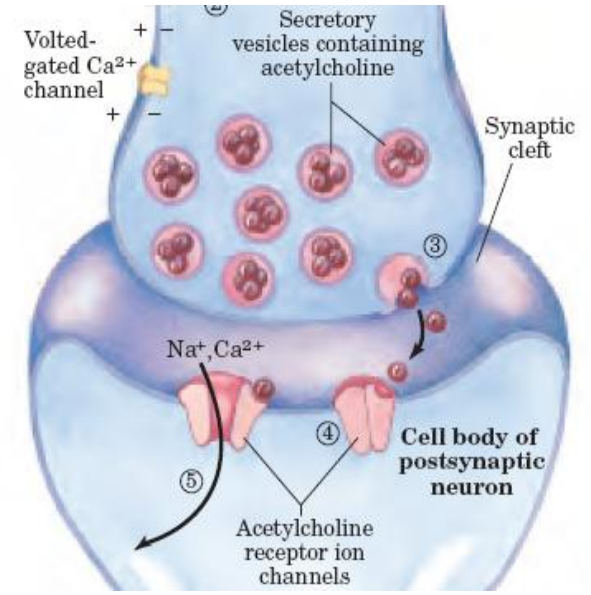
In the presence of a certain enzyme, tyrosine is converted to L-Dopa. L-Dopa is later converted to Dopamine which is converted to norepinephrine if the enzyme betahydroxylase is present in the cell. (Norepinephrine is a neurotransmitter released from neurons in the sympethatic nervous system). Lastly, norepinephrine is converted to epinephrine in the adrenal gland because it expresses the enzyme that is able to convert NE to EP. Production of these hormones

depend on the presence of the specific producing enzymes. Thyroid hormones are synthesized from the same precursor (tyrosine) through a different pathway in the thyroid gland.

Hormone receptors:

Hormones affect target tissues by first binding to their specific receptors, these receptors include:

- **Ion channel-linked receptors**: binding of the ligand (hormone) to its receptor causes conformational changes in the channel protein allowing flow of ions inside or outside the cell, which means channels are activated and opened. Example: sodium ion channels.



-In the synaptic cleft, acetylcholine binds to its receptor on the postsynaptic membrane, causing the activation of ion channels and allowing sodium and calcium ions in the cell, by this way action potential is generated in the postsynaptic neuron.

- **G protein coupled receptors**: these are very important and diverse, they are distributed in all parts of the body and share similar characteristics that include:
  7 trans-membrane helix receptor with an extracellular domain that binds to ligand, and an intracellular domain that binds to alpha subunit of G protein. GPCR can bind to neurotransmitters or hormones. but also some types can be stimulated by light for example and not a ligand.

  <u>Mechanism:</u>

  a. Binding of ligand to extracellular domain of GPR induces conformational change that allows intracellular domain of the receptor to bind to inactive G protein at inner face of plasma mebrane.

  b. This interaction activates the G protein, which dissociates from the receptor.

  c. Activated G protein α subunit can now bind GTP (guanine triphosphate) instead of GDP (guanine diphosphate), causing dissociation of activated α from$\beta\gamma$ subunits.

* An activated **receptor** (GPCR) normally serves as **GEF** for a heterotrimeric G-protein (guanine nucleotide exchange factor)**d.** The activated α and βγ subunits target plasma membrane bound enzymes, or ion channels, or intracellular proteins, which induces cellular response.

Inactivation of G protein: GTPase enzyme exchange GDP for GTP, the G protein α binds βγ inactive subunits and the cycle is terminated.

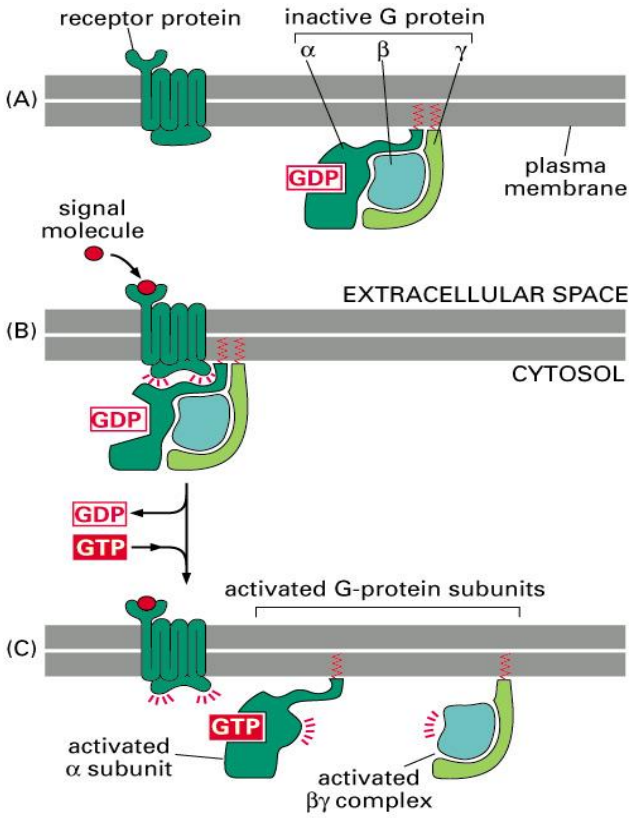
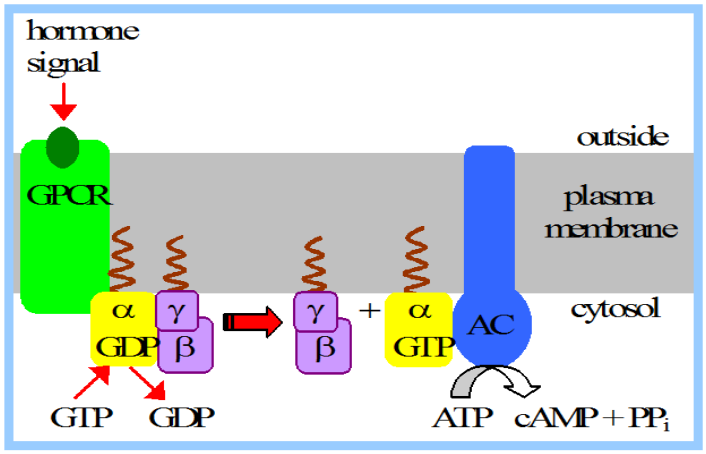


Figure 15–28. Molecular Biology of the Cell, 4th Edition.

- Rodhopsin is a light sensitive G protein coupled receptor in the eye retina, it was the first of these receptors to have its 7-helix structure confirmed by X-ray crystallography. It is responsible for low light vision.
- Other examples for GPCR: β-adrenergic receptor that is activated by epinephrine and norepinephrine, opioid receptor, glucagon receptor.
- G protein coupled receptors mechanism is important in pharmacology, some drugs are agonists (stimulate the receptor's activity and reinforce it), other drugs are antagonists (inhibit receptor's activity).
- Various **GPCR-interacting proteins** (**GIPs**) modulate receptor function and affects its activity. Effects of GIPs may include:
    1. altered ligand affinity
    2. receptor dimerization (when two receptors attach) or oligomerization (more than two)
    3. control of receptor **localization**, including transfer to or removal from the plasma membrane
    4. promoting close **association** with other signal proteins
- **G-proteins** are **heterotrimeric**, with 3 subunits α, β, γ.

- A G-protein that activates cyclic-AMP (second messenger) formation within a cell is called a **stimulatory G-protein**, designated $\mathbf{G_s}$ with alpha subunit $\mathbf{G_{sa}}$, examples: epinephrine receptor(adrenergic receptor) and glucagon receptor. Other G proteins cause inhibitory to cAMP and are called inhibitory G proteins.
- There two kinds of adrenergic receptors: α 1 and 2, β 1 and 2.
- G protein is inactive when bound to GDP, it is activated when bound to GTP and the α subunit dissociates from the β, γ subunits that are inhibitory to it.
- The active α subunit binds to membrane bound enzyme adenylate cyclase that forms the second messenger cAMP.



- Summary:
  - Conformational changes in protein shapes trigger each step.
  - The main concept of activation is binding of GTP to the α subunit.
  - the G protein then dissociates into α and β γ subunits, the α binds to adenylate cyclase and further cellular responses are triggered.
  - Finally, termination occurs when the GTP phosphorylates the adenylate cyclase and ADP is exchanged for GTP, the α subunit becomes inactive and reassembles with the other two β γ subunits units .