MECHANISM OF HORMONE ACTION

Classification of hormone action

- Which involve second messenger
  - Receptors are located on PM
    - This action is discovered by Sutherland in 1972.
- Activating or supressing gene
  - Receptor either in cytoplasm or on nucleus.
  - Discoved by Karlsson (1965)

Receptors:

Signal Transjunction – At end of which second messenger is achieved.

→ Receptors are generally glycoprotein. They have very high affinity to hormone.

→ When they bind with hormone they undergo certain confirmational changes. this change triggers the biological action.

+ **Substances like hormones:**

Agonist – Which can bind with receptor and after binding the receptor produced the biological action ie. triggers the biological action.

Antagonist – Substances like hormone which can bind to receptor. It doesn't trigger the biological action

Regulation of receptors:

No. of receptors is always changing. When receptor no. is high then tissue is said to be more responsive.

– Receptor is regulated by certain factor. These factor may be same hormone or different hormone.

Homospecific – If same hormone increases it's same receptor. eg. Insulin.

Heterospecific – If other hormone Tes it's receptor.
eg. – FSH.

LH decreases → LH-R ↓] Homospecific regulation
GnRH decreases → GnRH-R ↓] Down.

FSH increases → FSH-R ↑] Homospecific regulation up.

Heterospecific < Down / Up

Mechanism of hormone action:-

— Receptor —

Particular tissue respond for particular hormone due to presence of receptor on them. When no. of receptors is increased for a particular hormone, then responsiveness increases.

H (Hormone) + R (receptor) $\rightleftharpoons$ HR complex
at equilibrium

Hormone and receptors are combined by the law of mass action.

$$H + R \underset{K^{-1}}{\overset{K^{+1}}{\rightleftharpoons}} HR \quad (\text{Hormone-receptor complex})$$

$$\frac{H+R}{HR} = \frac{K^{+1}}{K^{-1}} = K_D \quad (\text{Dissociation constant})$$

K_D - The conc^n of hormone at which 50% of receptor binds with it to produce hormone-receptor complex. It also gives value of hormone conc^n at which maximum biological effect is seen.

→ Orphan receptor - Recombinant DNA technology had lead to discovery of a no. of hormone receptors whose ligands are not known. These are k/a orphan receptors.

eg, PPAR α, PPAR γ

[PPAR - Peroxisome Proliferator Activator Receptor.]

The scientist have prepared agonist for this receptor and that has been used as drug Rosiglitazone, Troglitazone. This drug is mainly used in curing Type II diabetes.

→ Spare receptor - Most of the receptors ($\simeq$ 90-95%) are free and not used to produce hormone-receptor complex. These are c/a spare receptor. Only a minute numbes (1-5%) of receptors are occupied by hormone molecule to produce maximum biological response.

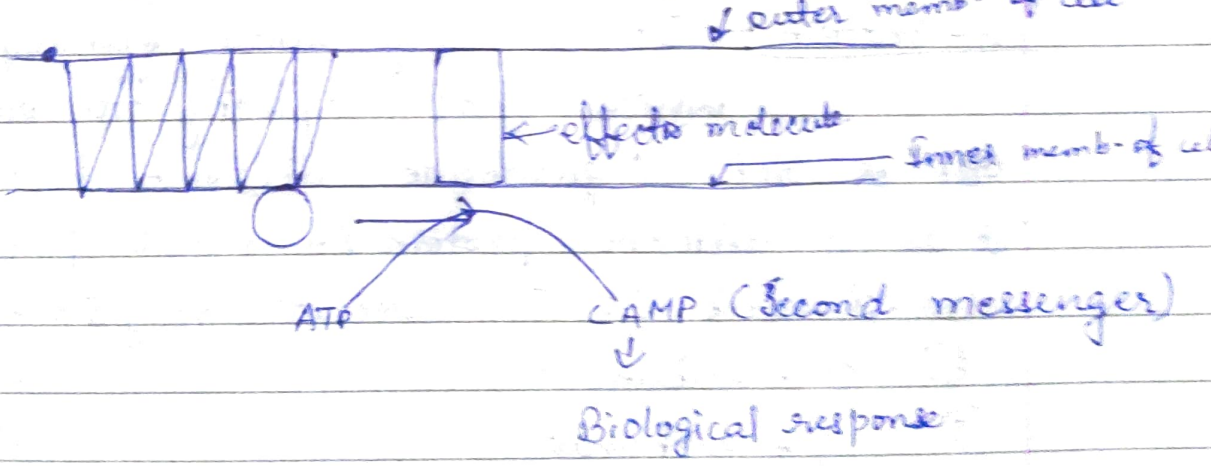
- Hormone action through cell surface receptor -

Receptors are of following type

1. Receptors associated with G- proteins - most common type of receptor (cell surface receptor)
2. Ion channel receptor
3. Enzyme linked receptors - where receptor itself is an enzyme or associated with enzyme.

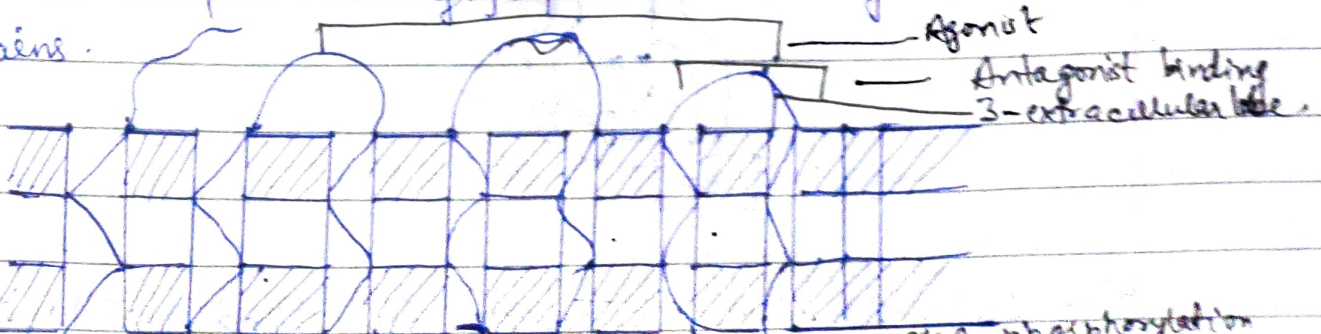
1. Receptor associated with G- protein -

These are multitransmembrane receptor and they are associated with very small protein c/a G- protein. With help of G- protein they relay the information received by receptor (~~intracellular~~) to a intracellular ~~effector~~ effector molecule which is responsible for communication with intracellular effector molecule. Effector molecule is an enzyme in inactive stage which is associated with G- protein.



These are more than 1000 receptors.

- G protein receptor is glycoprotein having 7 transmembrane domains.



phosphorylated. To decrease in number is c/a receptor down regulation.

- Receptor up regulation - No. of receptor is increased. It is achieved by synthesis of new protein by transcription and translation.

G-protein - It is very small family of protein which has capacity to bind with GDP or GTP (guanosine di/tri - phosphate)

It is a trimeric protein i.e. made up of 3-subunits.

1. α - subunit - Molecular weight = 42,000
2. β - subunit - 35,000
3. γ - subunit - 10,000