
◉Sheet ○Slides

Number

21

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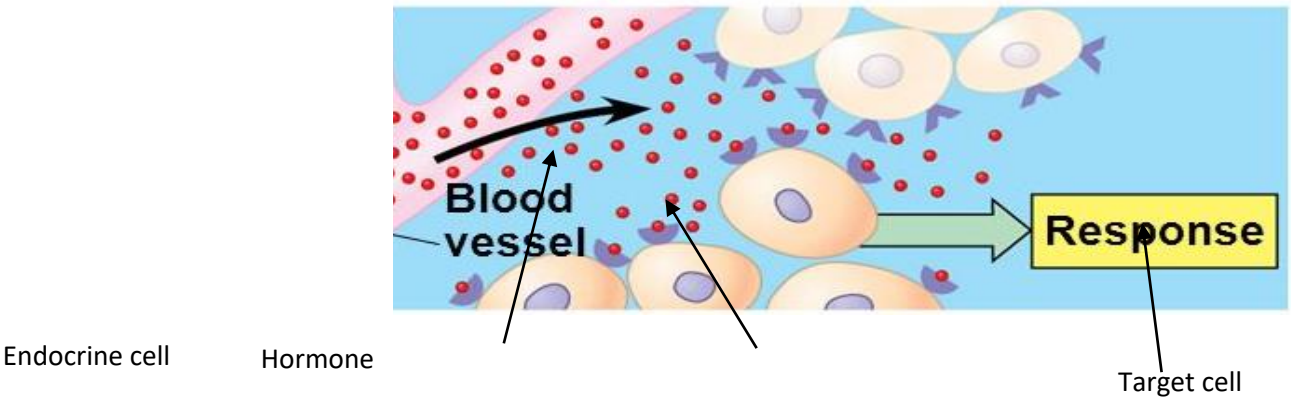
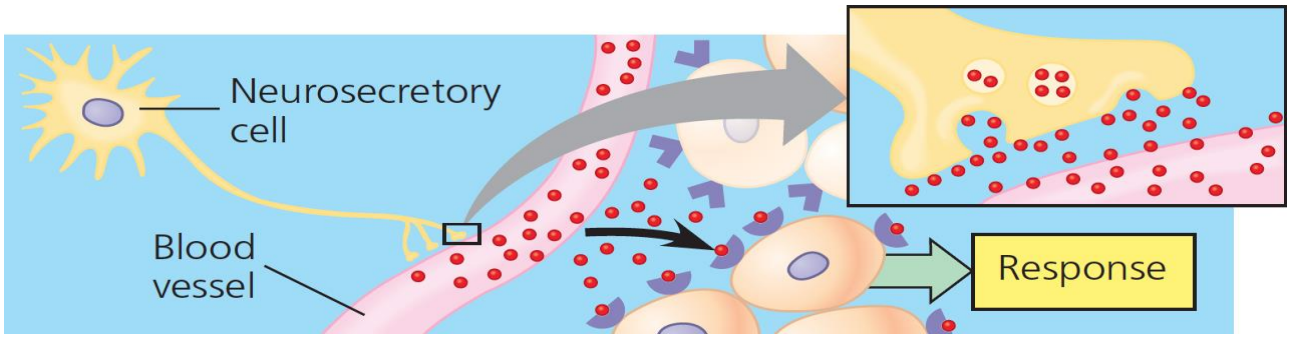
**Recap:**

**Intercellular Communication** could be:

1)Endocrine: Releases hormones into the blood stream to the target cell (The target cell is far from the endocrine cell).

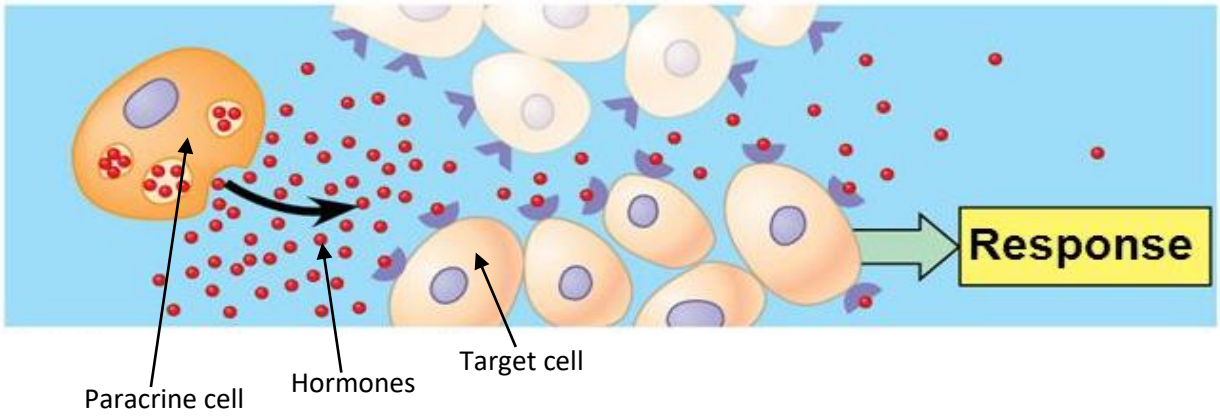



2)Neuroendocrine: Releases Neurohormones into the blood stream and triggers responses in target cells anywhere in the body.



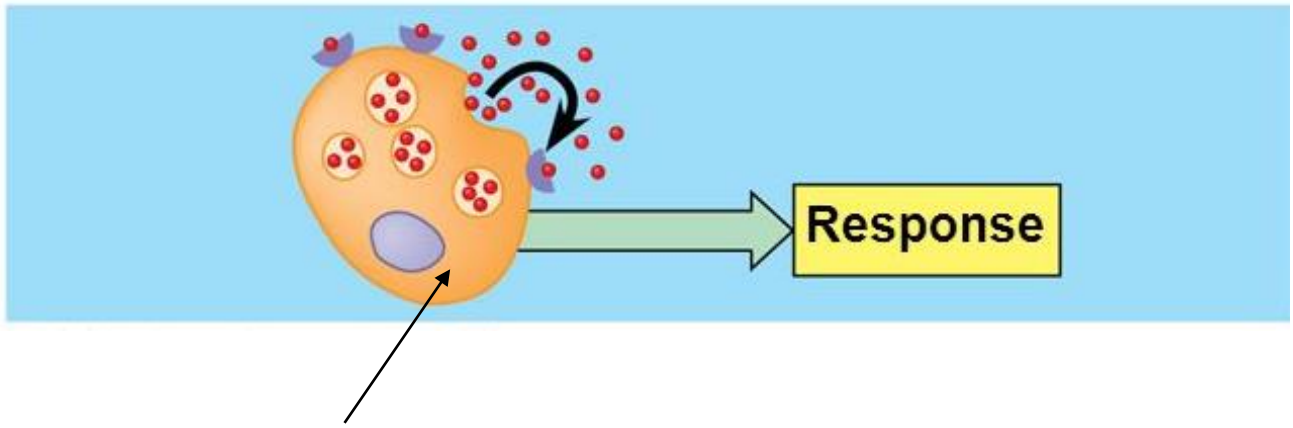

3)Paracrine: Releases Hormones that Binds to its neighboring cells (the target cell is close to the Paracrine cell).

-The hormone is called local hormone since it does not travel a long distance from the paracrine cell.




4)Autocrine: Releases hormones that target the Secreting cell itself.

-Releases local hormones as well.




**Classes of Hormones:**

1) Peptide &ProteinHormones:

-They are water soluble (Hydrophilic).

-If it consists of 100 or less amino acids it is considered as peptide hormone (For example; ADH).

-if it consists of more than 100 amino acids then it is considered as Protein Hormones. (For example; Growth Hormones).

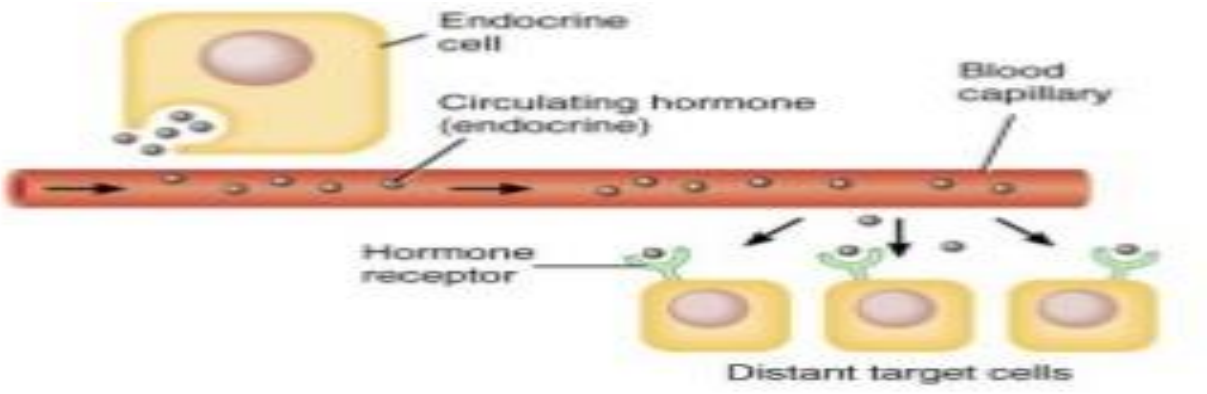
2)Steroids:

-Derived from Cholesterol.
-They are Lipid Soluble (Lipophilic).
-For example: Testosterone, Estradiol, Cortisol and Progesterone.

3)Amine Hormones:
-Single Amino Acid Molecule.
-They are Hydrophilic.
-Derived from tyrosine and tryptophan
-For example: Catechol Amine, Thyroxine(T4-lipophilic), Epinephrine(Epi), and Norepinephrine(NE)

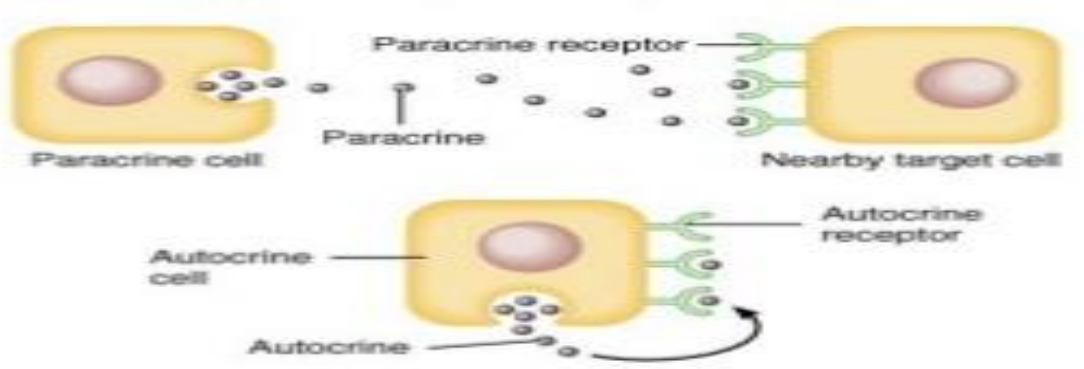
4) Gasses:
-Lipid soluble.
-Diffuses into the cells easily.
-For example: Nitric oxide(NO) and Carbon monoxide(CO).

**Hormone Types:**
1)Circulating Hormone:
-Circulates in blood throughout the body.
-Acts on distant targets.
-Secreted by endocrine and Neuroendocrine cells.



2)Local Hormones:

-Act locally on either neighboring cells (Paracrine) or the same cell (Autocrine) that secreted the hormone.




**Chemical classification of Hormones:**

1)Lipid Soluble (Lipophilic):

a) Steroids:

-Secreted from adrenal Cortex

-For example: Cortisone, Aldosterone, Androgen, Progestin, and Estrogen.

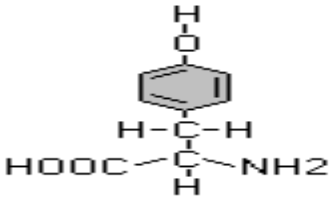
b) Thyroids:

-T3 or T4

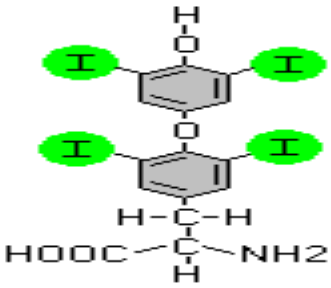
-The numbers next to the “T” refer to the number of iodine atoms that are bound to the tyrosine.

-one tyrosine molecule can bind to two Iodine atoms at Once, which means that more than one molecule of tyrosine

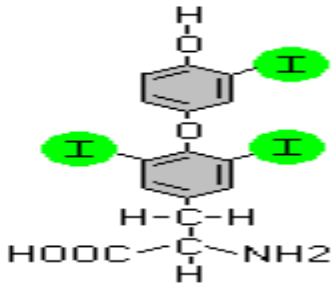
Is required for the formation of T4.



Tyrosine



Thyroxine (T4)



Triiodothyronine (T3)

c) Nitric Oxide (Gases)

-Lipid soluble hormones do not dissolve in the plasma, so they need transporters that are usually proteins.

-the transporters can either be specific carriers or non-specific.

2)Water Soluble:

a) Amines

b) Polypeptides and proteins

c)Eicosanoid (Prostaglandins):

-Derived from fatty acids (arachidonic acid)

-Arachidonic acid composes of 20 carbon atoms with 4 Double bonds in its structure, it is found in the membrane Is converted by enzymes into Eicosanoid.

d)Glycoproteins:

-Long polypeptides (over 100 amino acids) that are Covalently bonded to one or more carbohydrate group.

-For example: FSH, LH, TSH, and hCG (human chorionic

Gonadotropin) which is related to pregnancy.

- They consist of 2 Alpha chains and 2 Beta chains
- Alpha chains are identical between all glycoprotein Hormones, while the Beta chains are more specific One hormone to another.

Thus, testing the quantity of any of these hormones Means that we are testing for beta chains, even in Testing for pregnancy, we test for the presence of hCG according to its beta Chains.

- In some cases where the alpha exceeds the amount of Beta in tremendous folds, the test can interact with the Alpha chain instead. For example: if FSH alpha chains Exist in a much higher concentration than the hCG beta Chains, pregnancy testing may come out as positive, when It didn't detect any hCG (False Positive).

**Hormones can also be divided into:**

1)Polar (Water soluble)

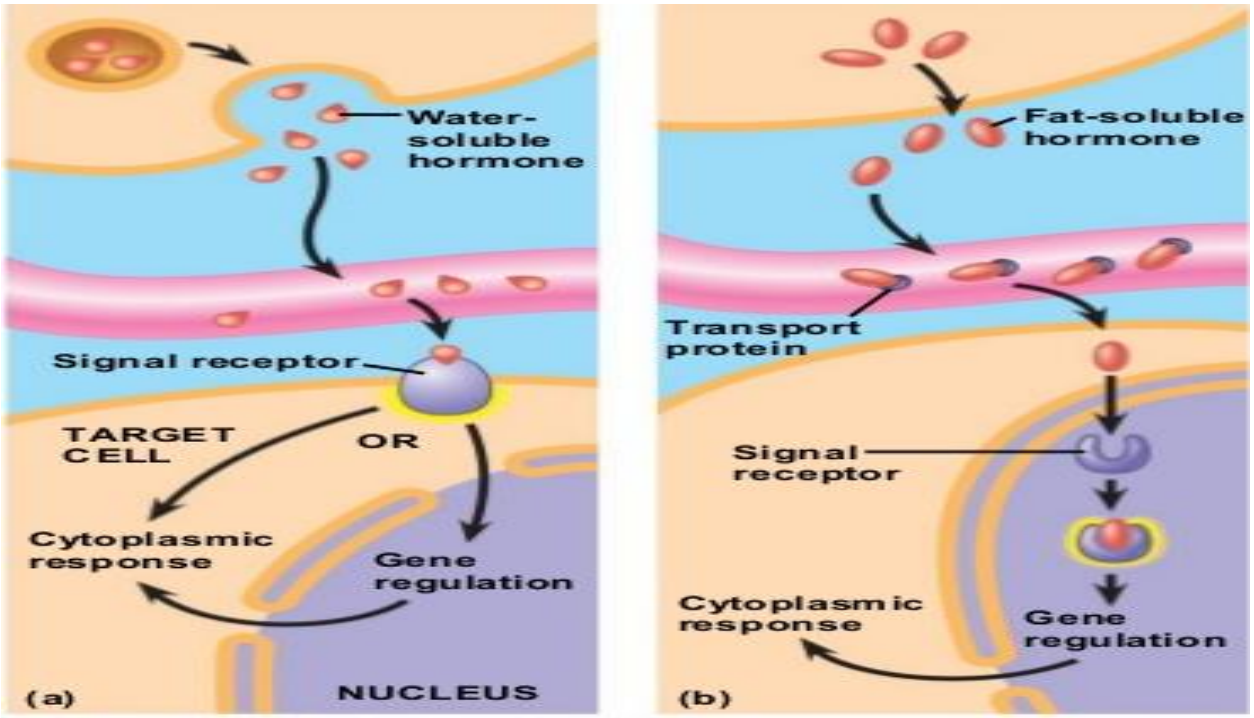
2)Nonpolar (Lipid Soluble)

**Why it is important to tell if the hormone is lipid soluble or not:**

-Knowing if the hormone is lipid soluble or not helps us determine where its receptor on the target cell is going to be located.

-if it's lipid soluble, then its receptor can exist on the inner parts of the cell (on the nucleus for example), since it can easily cross the phospholipid bilayer of the cell. (see figure b)

-if it's water soluble, then its receptor will exist on the outer surface of the membrane since it cannot pass the phospholipid bilayer of the cell if it does not contain channel proteins. (see figure a)




**Prohormones and Prehormones:**

-The hormones are synthesized in the Nucleus then packaged in the ER, then into the Golgi apparatus for post-translational modification, packaged then released by exocytosis.

-Before the modification (precursor) = Prohormones

-Prohormones: Precursor is a longer chained polypeptide that is cut and spliced together to make the hormone.

For example: Proinsulin

-Preprohormones: Larger precursor molecule that prehormones are derived from.

For example: Preproinsulin

*Long story short*:

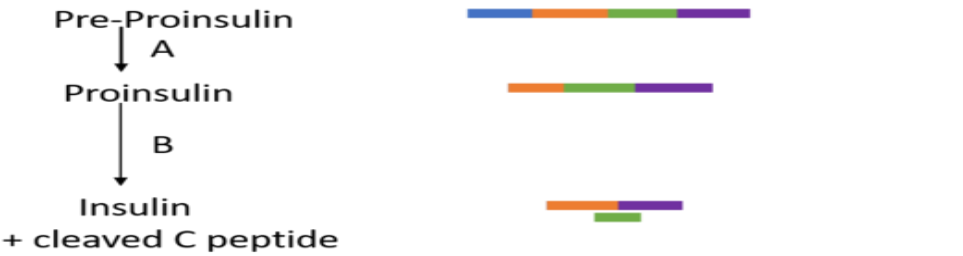



Figure 1: Progression of Insulin-like structures. A. The signal peptide of pre-proinsulin is cleaved, forming proinsulin. B) Proinsulin is folded in the ER, then transported to the Golgi apparatus where the C-peptide is cleaved using type I and type II endoproteases to form free C peptide and mature insulin.

-Prehormones: Molecules secreted by endocrine glands that are inactive until changed into hormones by target cells. Like the conversion of T4(which is the less active form of thyroxine) into T3.

-in this case, T4 is the prehormone.

## Peptide & Protein hormones:

| Gland/Tissue | Hormones | Gland/Tissue | Hormones |
|---|---|---|---|
| Hypothalamus | ▪ TRH, GnRH, CRH GHRH, Somatostatin, | Placenta | ▪ HCG, HCS or HPL |
| Anterior pituitary | ▪ ACTH, TSH, FSH, LH, PRL, GH | Kidney | ▪ Renin |
| Posterior pituitary | ▪ Oxytocin, ADH | Heart | ▪ ANP |
| Thyroid | ▪ Calcitonin | G.I. tract | ▪ Gastrin, CCK, Secretin, GIP, Somatostatin |
| Pancreas | ▪ Insulin,Glucagon, Somatostatin | | |
| Liver | ▪ Somatomedin C (IGF-1) | Adipocyte | ▪ Leptin |
| Parathyroid | ▪ PTH | Adrenal medulla | ▪ Norepinephrine, epinephrine |

**Amine Hormones:**

| Gland/Tissue | Hormones |
|---|---|
| Hypothalamus | Dopamine |
| Thyroid | $T_3$, $T_4$ |
| Adrenal medulla | NE, EPI |

**Steroid Hormones:**

| Gland/Tissue | Hormones |
|---|---|
| Adrenal Cortex | Cortisol, Aldosterone, Androgens |
| Testes | Testosterone |
| Ovaries | Estrogens, Progesterone |
| Corpus Luteum | Estrogens, Progesterone |
| Placenta | Estrogens, Progesterone |
| Kidney | 1,25-Dihydroxycholecalciferol (calcitriol) |

**Hormone Activity:**

-Hormones only affect specific target tissues with specific receptors.

-Receptors are dynamic and can be either broken down or synthesized in the membrane.

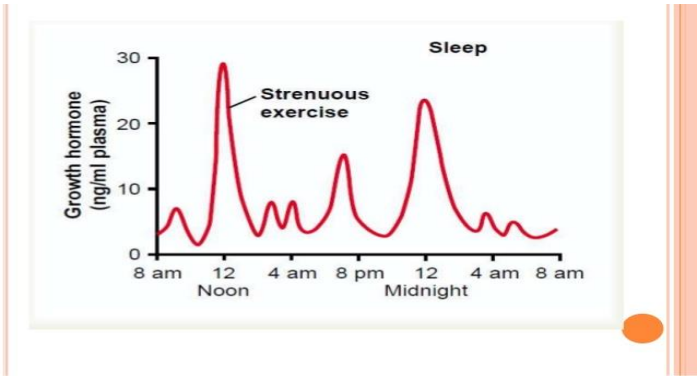
-Upregulation: increase in the number of receptors.

Upregulation Increases the sensitivity and activity of the hormone which leads to a greater response, this is called the priming effect.

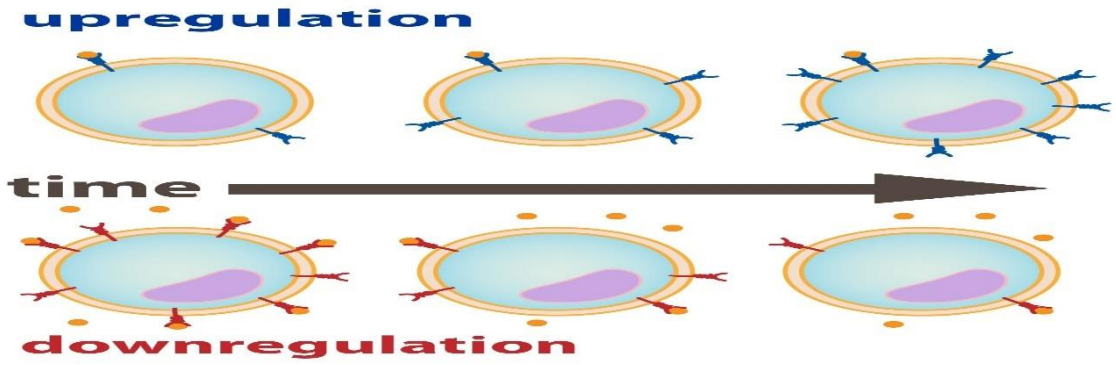
-Downregulation: decrease in the number of receptors.

Downregulation decreases the activity of the hormone and causes desensitization caused from prolonged exposure to hormones, especially the polypeptide hormones. For example, insensitivity of insulin does not mean that the insulin is not there, it just means that it exists in high levels, so the cells are not sensitive to it anymore.

- our body prevents downregulation from occurring by secreting hormones in a pulsatile form.




For example: the growth hormone (while sleeping (rapid eye movement stage)) and the cortisol (reaches its peak at the morning, thus u feel alerted and energetic when you wake up).




**Half-life of the hormone:**

Time required for the concentration of the hormone to reduce to half its reference(original) value.

Like when we say that we started with 60 molecules of a hormone, how much time is required for the molecules to become 30.

The half-life of a hormone determines how many times can a patient ingest the hormone in a certain period.

For example: the half life of insulin is about 20 minutes, so it must be taken at least once every 20-30 minutes for diabetes patients.

-We can prolong the half-life of insulin to a day by binding it with other molecules.

- The responds of the tissue will remain normal if the hormone is present with normal Physiological range.

**Mechanism of hormones:**

-Knowing the chemical structure of the hormone you can suspect what is the mechanism of action.

-hormones have the same chemical structure, have almost the same mechanism of action. These similarities include:

a) Location of cellular receptor proteins.

b) events that occur in the target cells.

-Receptor on the membrane → acts on IP3/G- protein

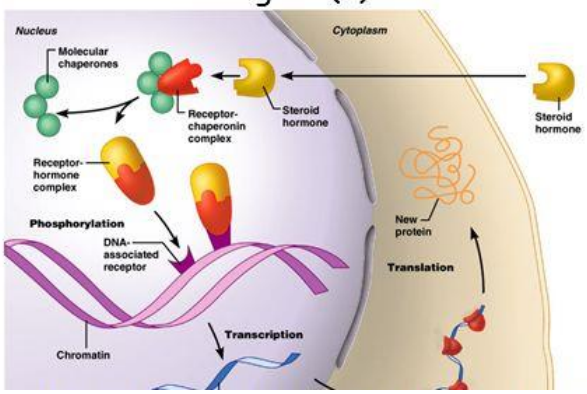
-Receptor in the nucleus → acts on Genes, etc.

- to respond to a hormone, the target cell must have specific receptors for that hormone.

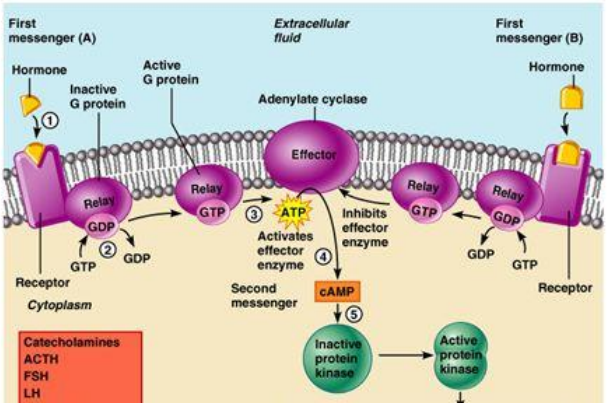
Hormones Show,Affinity (Binding to the receptor with high strength) and Saturation (because of low capacity of receptors) towards their receptors.

# Mechanisms of Hormone Action

- Lipid-soluble steroids & thyroid hormones
  - Diffuse through plasma membrane
  - Enter nucleus
  - Forms "hormone-receptor complex", binds as TFs to chromosome to activate/ inactivate gene(s)




- Peptides & water-soluble amines
  - Hormone (A) binds to receptor on cell surface
  - Activates G- protein
  - Activates adenylate cyclase
    - Converts ATP to cAMP
  - cAMP activates protein kinases, which produce final effect.




(Same thing as before, nothing new).

Activates Second messenger system which causes amplification the original small signal.

Responsiveness of Target cell depends on:

a) Hormone's concentration

b) Abundance of target cell receptors

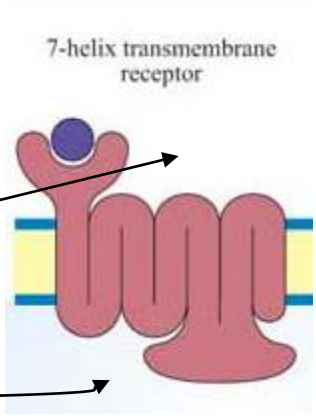
If we increase the hormone's concentration but there are little to no receptors, the responsiveness won't be high, if we increase receptors but decrease hormone concentration, the responsiveness won't be high as well, both factors depend on each other.

**Membrane Receptors:**

1) Ionotropic receptors:

The ligand binds to the receptor which in turn opens the ion channel or closes it and changes the affinity of the hormone

2)Metabotropic:



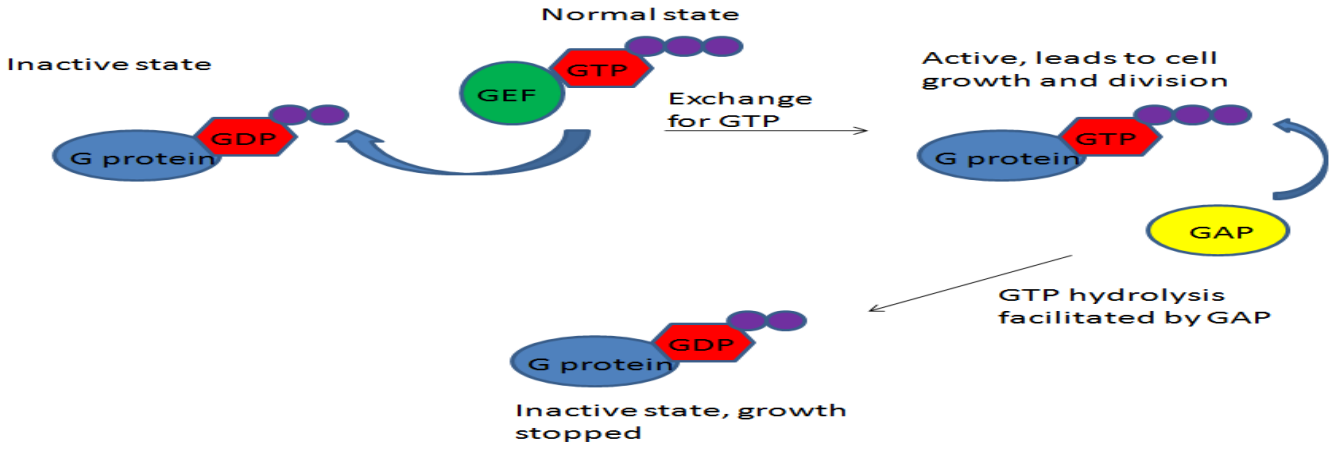

Coupled with G-protein

-Consists of Hepta-helical transmembrane receptors.

-Has two sides, extracellular and cytosolic site.

-G protein binds to GDP and GTP and acts as signal transduction.

-At the resting state (Bound to GDP), it consists of alpha, beta and gamma subunits, when exchanged with GTP, the alpha unit is disassociated and activated.




**Good Luck ☺..**