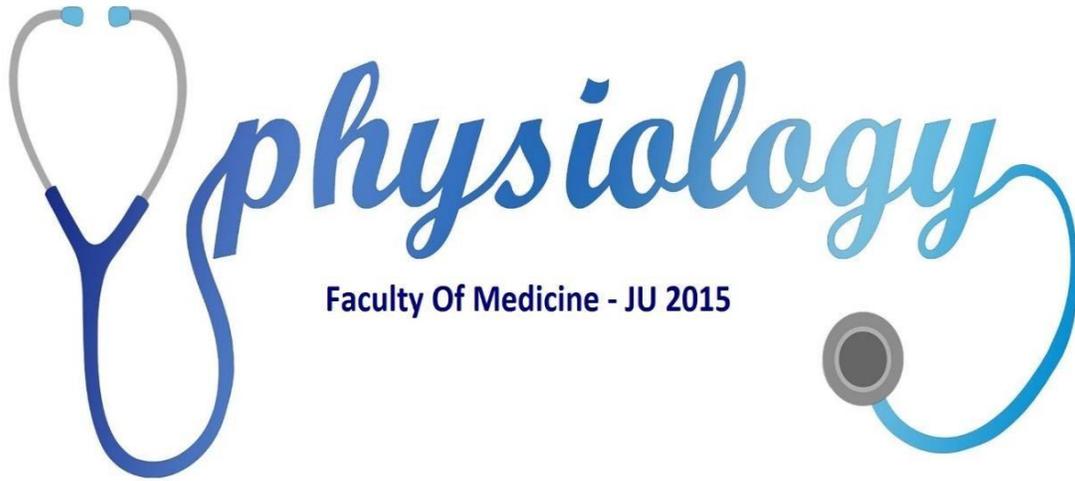




University of Jordan
Faculty of Medicine



Lecture number 12

Signal transduction

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Signal Transduction

-what does cellular signaling mean?

It is a way of communication between the cells to affect each other's function(cell-cell communication)

Note* A lot of aspects of cellular functions can be altered by cellular signaling.

What does signaling transduction mean?

Similar to cellular signaling but it focuses on Conveying an external stimulus to a change in intracellular function.

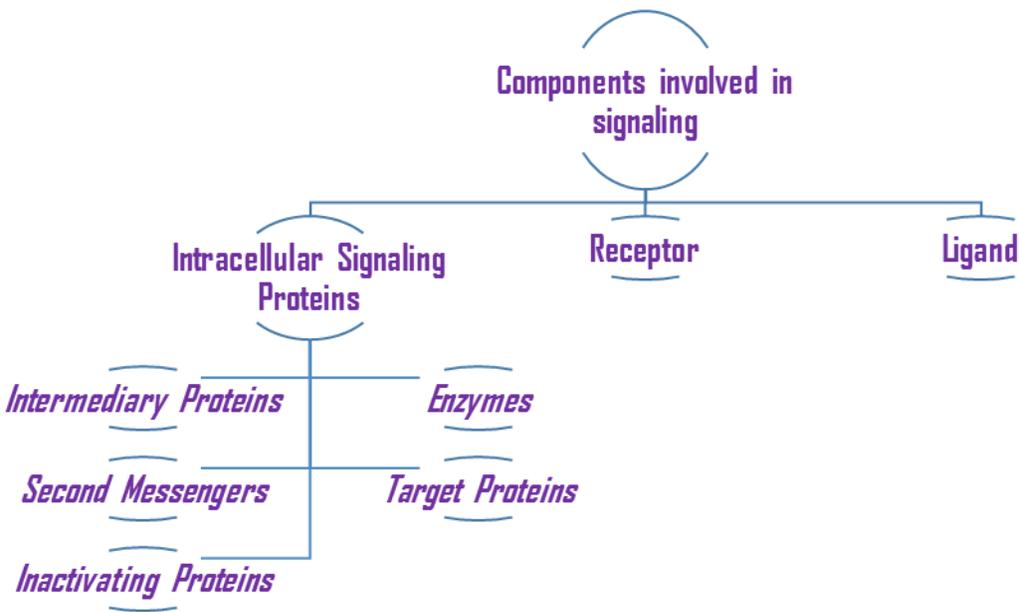
Note* it is usually across the plasma membrane so it is called transduction, it is like if we have a barrier between ICF & ECF and we need something to transduce the signal across the membrane.

Ligand: the signaling molecule, or any molecule that can bind to its specific receptor in order to transfer a signal.

Receptor: Binds to specific ligands and Transmits signals to intracellular targets. Different receptors can respond differently to the same ligand. (usually a protein or a glycoprotein that could be found in the plasma membrane or cytosolic or on the nuclear membrane or even inside the nucleus).

Ligand binds to its receptor (key and lock)

This binding should affect something in the receptor, it could be a conformational change of the receptor and this change will be the first step of transduction and this change will be transduced from the receptor into another protein to propagate the signal into the target that we want.



The main function of the receptor is to transport the signal from **ECF** to **ICF** (but it may present on the intracellular side and the ligand can cross the plasma membrane and bind to the receptor).

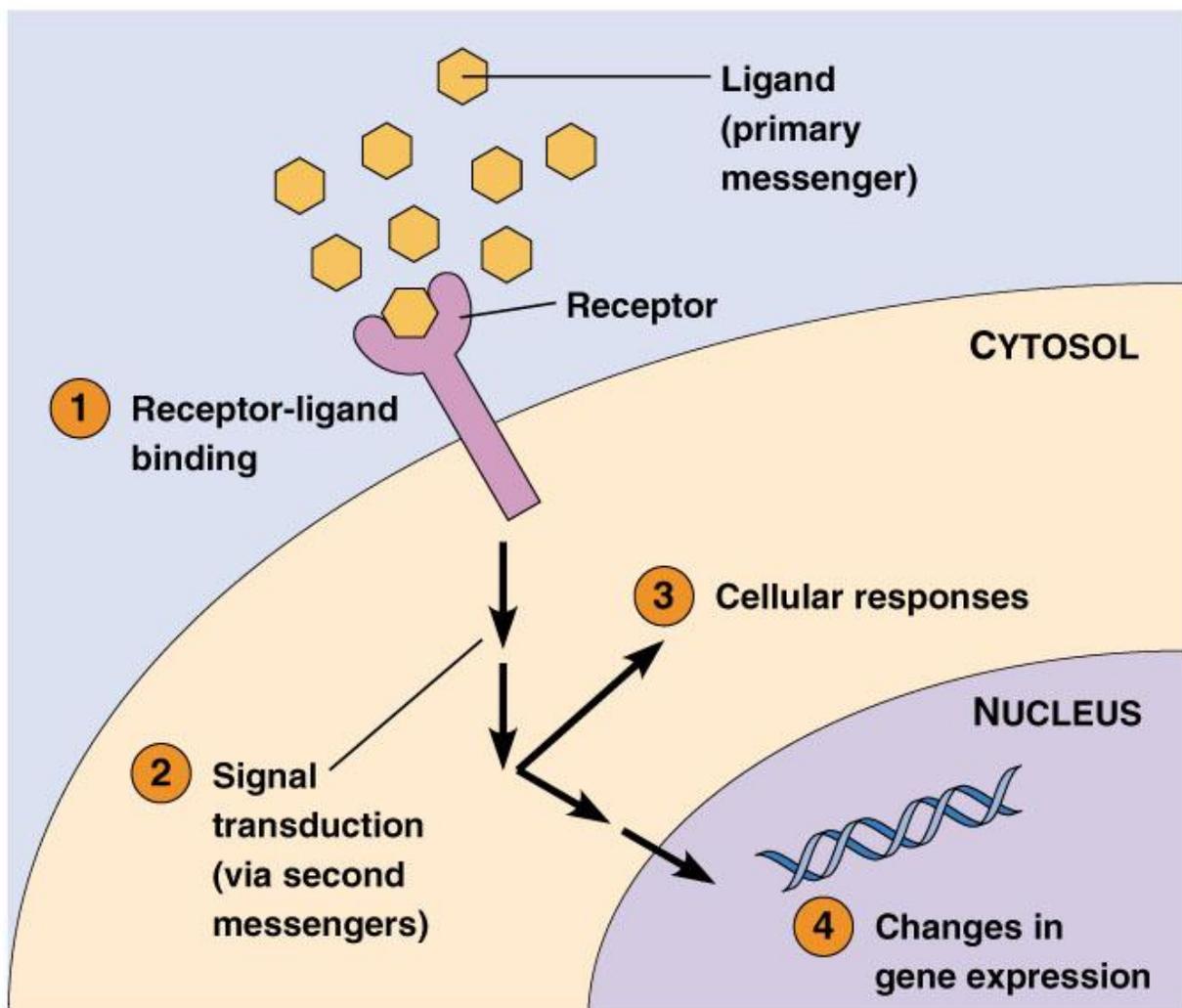
Note* The receptor is **NOT** always on the plasma membrane

Changes are various (phosphorylation, dephosphorylation, chemical changes that change the function or moves the protein to bind to

another protein) the change may cause alteration of activity of enzymes (might be excited or inhibited)

Note* the signal is not always excitatory; it may be inhibitory.

Note* It may affect the gene expression.



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-The external stimulus could be a rise or decrease in temperature, light or pressure.

-sometimes only light can cause conformation of the receptor so the ligand is not always required.

-signaling can help the cell to differentiate and can tell them what type of cells this should specify.

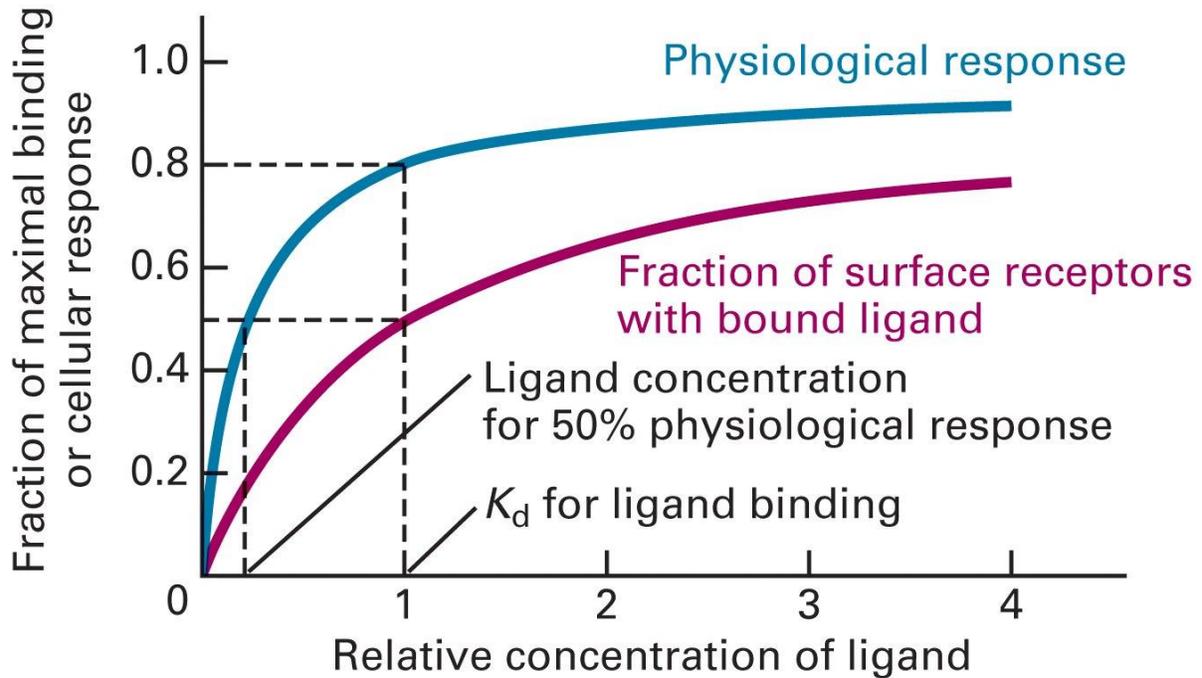
For example: Red Blood Cells and White Blood Cells are from the same origin (hematopoietic cells) but certain signals decide the type of the differentiated cell.

Note* it's not always a single signal but it could be more than one signal that integrate to get a net signal.

-Not all receptors should be bound to their ligands to cause a physiological response.

Example: insulin, we don't need insulin to saturate all of its receptors to make a change.

Note* It is NOT all or none principle.



Notice: to reach half of the maximum response we need one fourth of the relative concentration of ligand.

-small amount of ligand may be able to induce a big response.

Types of signaling between cells:

-cell signaling starts with ligand secretion.

- 1.-ligand can bind to a nearby cell via interstitial fluid.

This is called (paracrine)

2. If it binds to a receptor on the same cell it is called **(autocrine)**

Autocrine and paracrine are (local mediated).

3. Autocrine is mainly for positive or negative feedback.

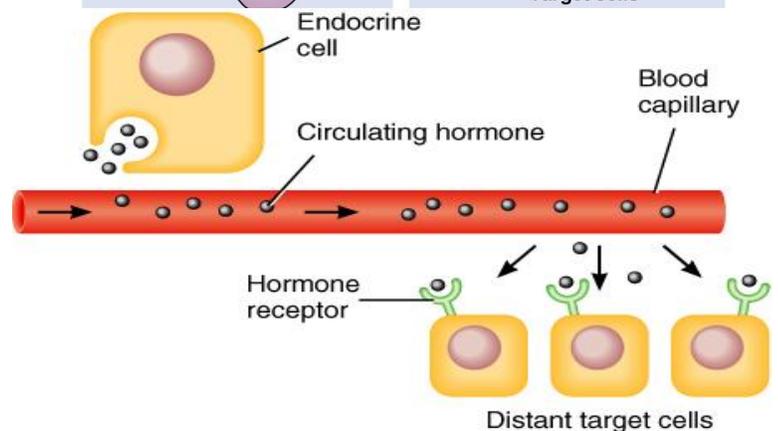
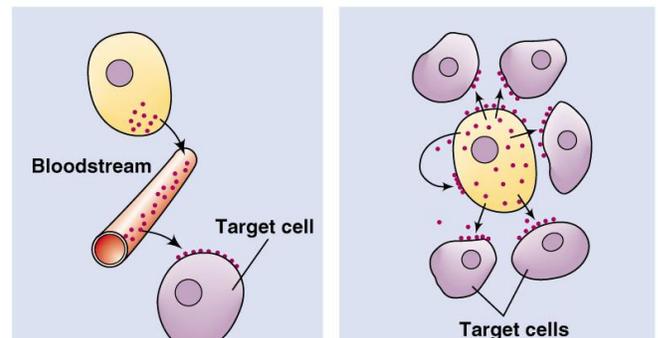
-if the ligand is secreted into blood and then transported into another location it is **endocrine**.

4. Synaptic and neurocrine

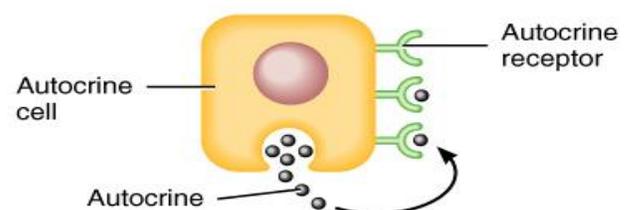
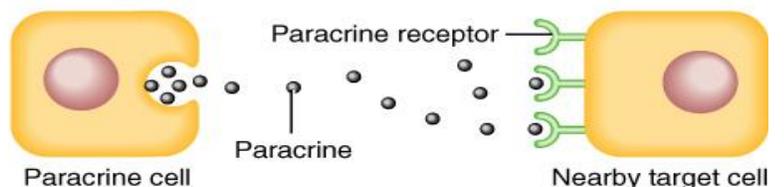
The changes may be very fast or slow

If we need to change the genetic expression, it will take a long time.

If we changed the

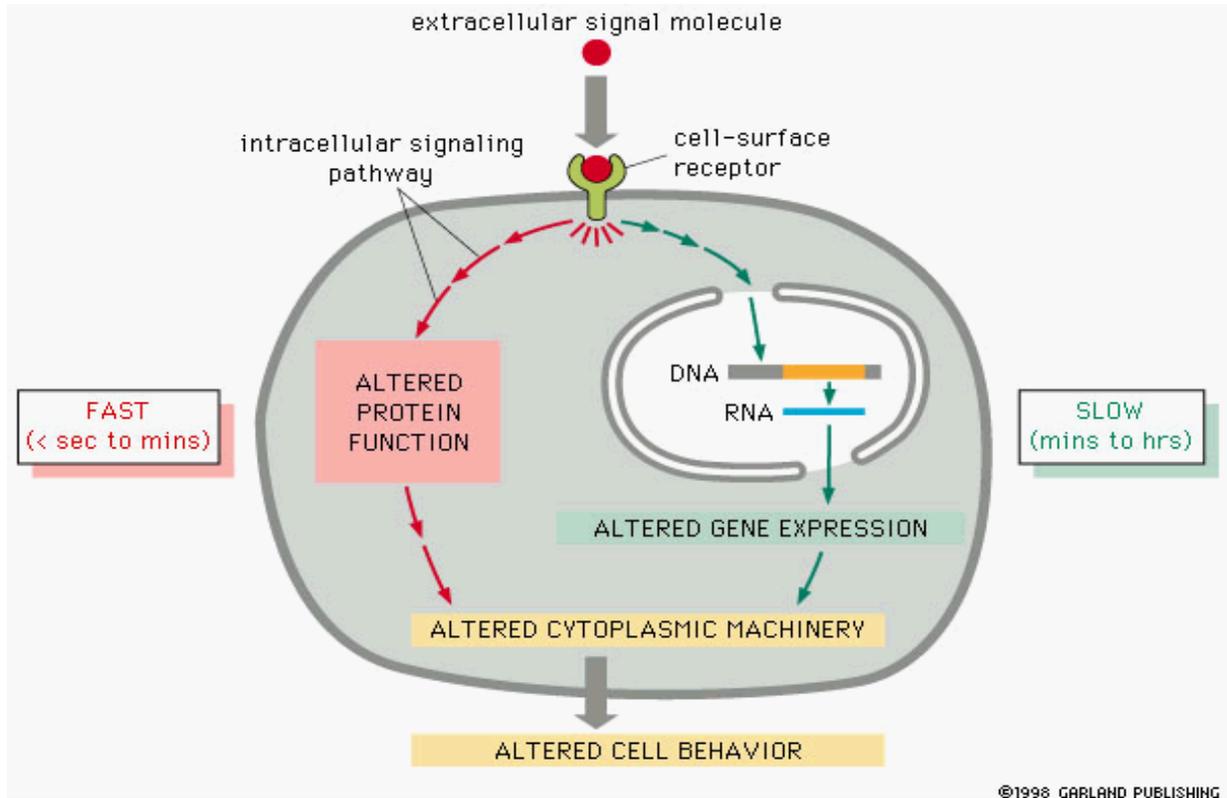


(a) Circulating hormones



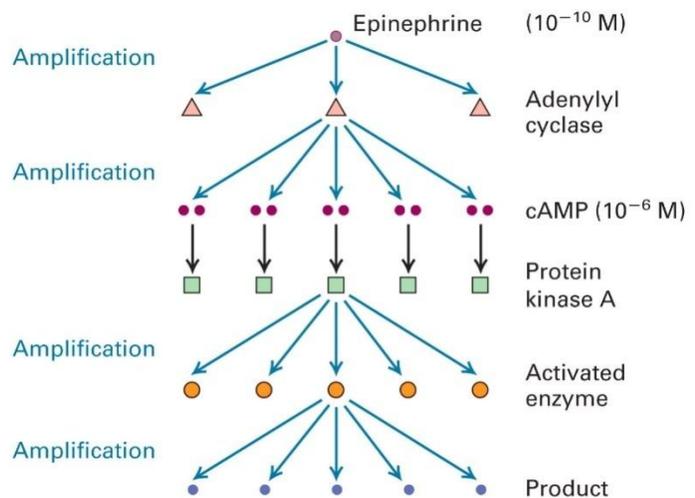
(b) Local hormones (paracrines and autocrines)

function of a protein, enzymatic activity or membrane potential, it might be very fast.



Amplification of signal: A huge number of proteins will be affected and they will affect other proteins.

Amplification of signal



When a neuron secretes neurotransmitters from the bulb of axon terminal, these neurotransmitters affect other cells (it is like paracrine but if it is in neurons we call it synaptic secretion) it can happen between neural cell and muscle cell.

Endocrine	Paracrine	Autocrine	Synaptic
Ligand is secreted into blood	Ligand is secreted into interstitial fluid	Ligand is secreted into interstitial fluid	Ligand is secreted into interstitial fluid
Receptors are on distant target cells	Receptors are on nearby cells	Receptors are on the same cell	Receptors are on nearby cells and action on post-synaptic cell in response to electrical stimuli

Note* neurotransmitters can be secreted into blood to other organs. For example: Epinephrine from adrenal medulla. Antidiuretic hormone also is synthesized from hypothalamic neurons and then transported through neuron axons into the

posterior pituitary gland and then secreted after a stimulus, this is a type of neurocrine signaling which affect water reabsorption in the tubules of kidney.

*Another classification (chemically):

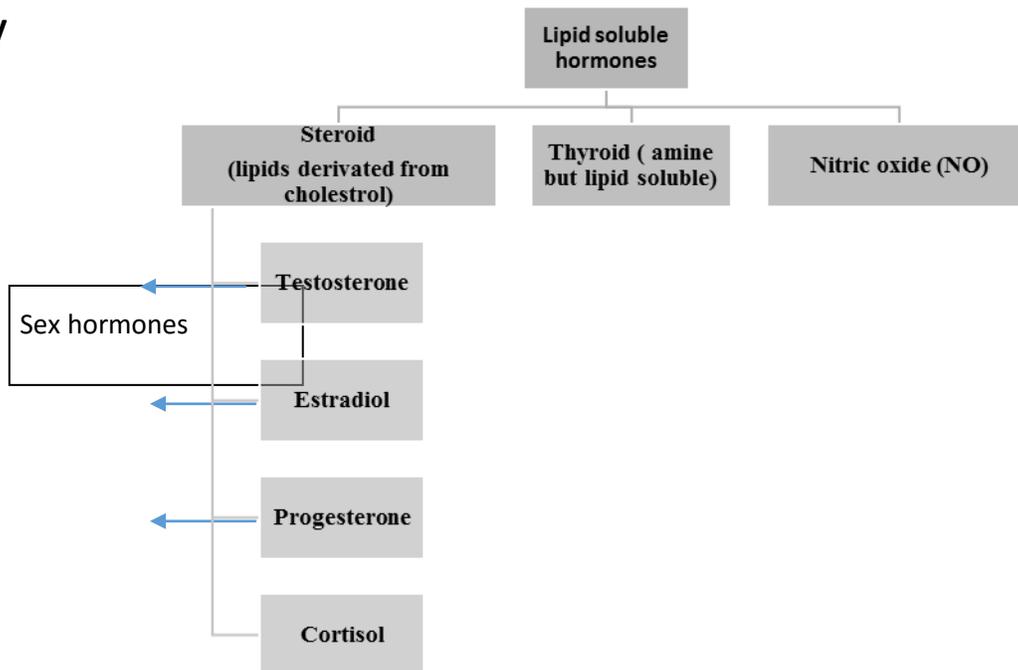
Ligands can be classified into:

A-lipophilic (lipid soluble-hormone):

*90% bound to a protein in plasma, 1-10 % free,

why
?

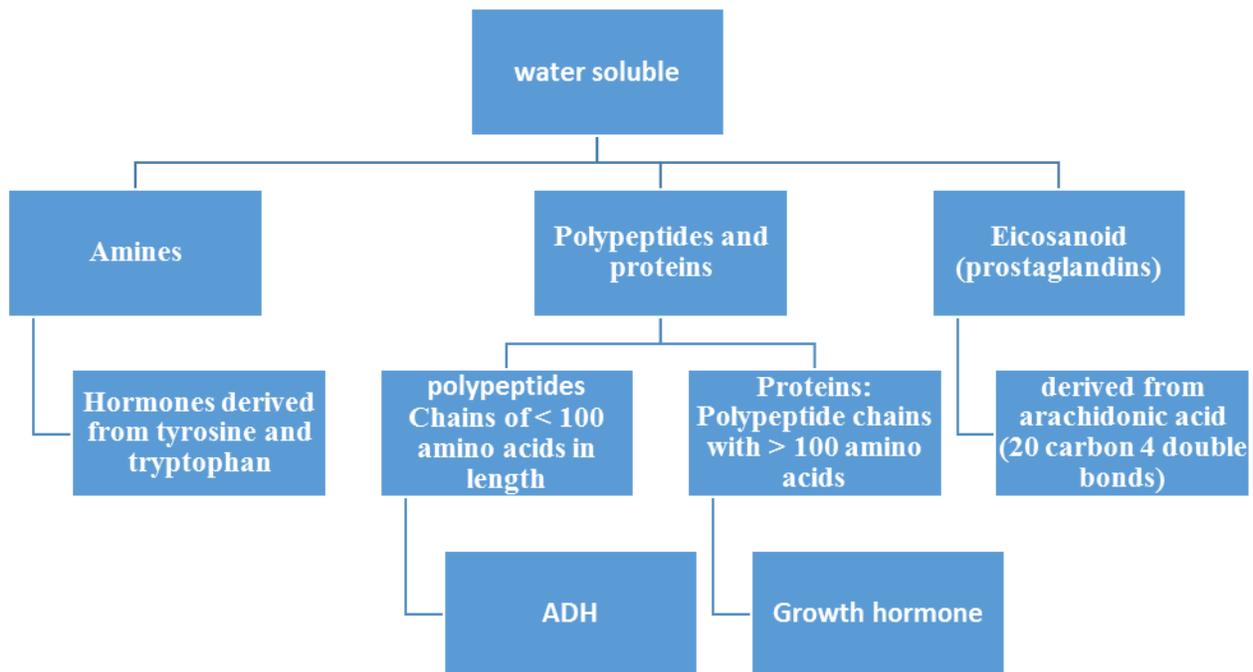
Bin
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considered as reservoirs for the hormones to protect them and prevent them from being lost through kidney filtration. Bound hormones should be freed from binding proteins in order to be

considered active and to be able to bind to their receptors. ex: T4 is bound to Thyroglobulin.

B-water soluble hormones (they don't need to bind to a protein in blood, they circulate in free form in the plasma):



***Glycoprotein hormones:** Long polypeptides (>100) bound to 1 or more carbohydrate (CHO) groups.

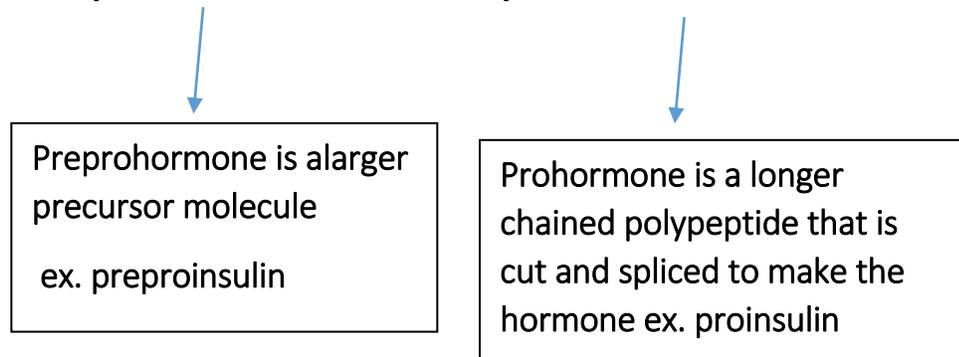
Examples: FSH and LH, TSH and hCG (human chorionic gonadotropin), They have α and β subunits (α is common and β is specific).

- Hormones can also be divided into:

- Polar: H_2O soluble.
- Nonpolar (lipophilic): H_2O insoluble.
 - Can gain entry into target cells.
 - Steroid hormones and T_4 (thyroxine –tetra iodothyronine)

Note* usually when the mRNA is translated to produce peptide as a hormone, it is not in the final form.

Preprohormone ---> prohormone -----> hormone



- Prehormone:
 - Molecules secreted by endocrine glands that are inactive until changed into hormones by target cells.
 - T_4 converted to T_3 (tri-iodothyronine).

Prohormone: proinsulin(inactive until spliced)