ENDOCRINE

Biochemistry

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??

Sheet no. ?

Normal كلام الدكتور

SLIDES

Extra info كلام خارجي

V2 !

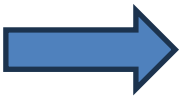
In pg:5

GH is the biggest 

GHRH is the biggest among hypothalamus hormones.

In pg:12

Fibroblast growth factor 23

Is an extremely big protein 

Fibroblast growth factor 23 is the biggest protein hormone.

In pg:16

This reaction is dependent on NADPH , **so is considered a reduction reaction**

(the underlined sentence was added)

In this lecture many slides will be covered , but lots of them will be discussed later and found here only for exposing them to you

So focus just on what doctor mentions and explains

المحاضرة بإذن الله سهلة و بسيطة ولا يغرنكم كثرة الصفحات و لا كثرة الكلام ، فأغلب المعلومات مكررة مما أخذناه سابقا كما و قمنا بإضافة القليل من المعلومات الخارجية بهدف تحسين الفهم ، و بالنهاية و نقلا عن الدكتور نافذ الفهم هو الأساس في هذه المادة

"ومن يتوكل على الله فهو حسبه"

CLASSIFICATION OF HORMONES BASED ON THE MECHANISM OF ACTION:

The mechanism of action is related to the location of the receptor (intracellular or extracellular)

1. **Extracellular: the hormone binds the receptor, then the receptor activates second messengers to produce the desired action of the hormone.**
2. **Intracellular: the hormone binds to the receptor inside the cell then it acts directly on the DNA affect gene transcription.**

HORMONES THAT BIND TO INTRACELLULAR RECEPTORS:

An example of them are :

- **Steroids**
- **Thyroid hormones**
- **Calcitriol, retinoic acid**

They have a long half-life (hrs.-days) and require transport proteins.

These hormones make a hormone-receptor complex that acts directly on the regulation of certain genes to upregulate the synthesis of certain proteins (enzymes, channels, etc.) which takes long time to start and prolonged action, or make a rapid response by directly affecting some components of the cell.

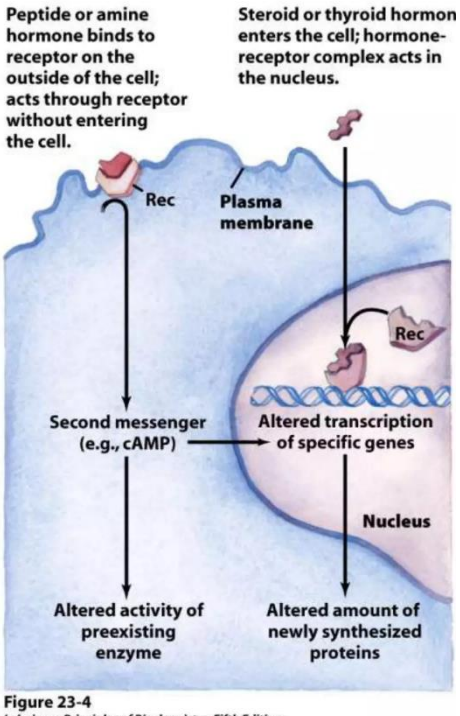


Figure 23-4
Lehninger Principles of Biochemistry, Fifth Edition

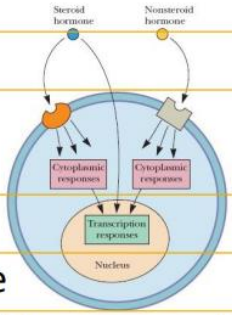
HORMONES THAT BIND TO CELL SURFACE RECEPTORS:

They are classified according to the second messenger:

- **cAMP (β adrenergic factor, glucagon, ACTH)**
- **cGMP (atrial natriuretic factor, nitric oxide)**
- **calcium or phosphatidyl inositol (oxytocin, TRH)**
- **kinase of phosphatase cascade (insulin, GH)**

General features of hormone classes

	Group I	Group II
Types	Steroids, iodothyronines, calcitriol, retinoids	Polypeptides, proteins, glycoproteins, catecholamines
Action	Slow	Fast
Solubility	Lipophilic	Hydrophilic
Transport proteins	Yes	No
Plasma $t_{1/2}$	Long (hrs - days)	Short (minutes)
Receptor	Intracellular	Plasma membrane
Mediator	Receptor- hormone complex	cAMP, cGMP, Ca^{2+}, kinase cascades, metabolites of phosphoinositols



water soluble hormones still bind to transport proteins but not as a requirement, unlike lipid soluble hormones.

Genomic responses vs. rapid responses

TABLE 1-1 Nuclear Receptors and Involvement in Genomic and/or Rapid Biological Responses

(Steroid receptor) & ligand	# aa Receptor	Steroid nuclear receptors & gene transcription generate genomic responses (GR)	Steroid membrane receptors generates rapid responses (RR)
(Thyroid β) T_3	461	T_3 binding to its nuclear receptor, in target cells stimulates dissociation of co-repressors, recruitment of co-activators, etc. to complete a GR.	T_3 activates PI3kinases and MAP kinase **RR** pathways which can result in glucose uptake, Ca^{2+}-ATPase, Na^+/H^+ antiporter.
(Vitamin D receptor) 1α,25$(OH)_2$- vitamin D_3	427	Both intestinal Ca^{2+} absorption & kidney Ca^{2+} reabsorption requires **GR** for production of new calcium binding proteins (CaBP).	**RR** opening of Cl^- channels in osteoblasts & keratinocytes in 20 min; insulin secretion from β-cells, MAP kinase activation in NB4 cells.
(Estrogen receptor α) Estradiol	595	ERα **GR** are required for normal ovarian function.	ERα activates PI3K and then AKt **RR** stimulates nitric oxide NO.
(Estrogen receptor β) Estradiol	530	ERβ **GR** are required for ovulation & pregnancy.	The cell membrane ERβ bound to caveola has been implicated in RR.
(Glucocorticoid receptor) Cortisol	777	Knockout (KO) of the mouse GC receptor is lethal at time of birth.	Cortisol stimulates PI3-kinase/Akt to activate in seconds NO release.
(Mineralocorticoid receptor) Aldosterone	919	MR **KO** mice die of Na^+ and H_2O deprivation.	Aldosterone activates in 3–15 minutes the **RR** of Na^+/H^+ exchange in renal cells.
(Progesterone receptor) Progesterone	933	The progesterone receptor participates in **GR** sexual differentiation determination.	Progesterone stimulates **RR** within seconds to minutes, the acrosome reaction in spermatozoa.
(Androgen receptor) Testosterone	919	**KO** of the AR male mouse causes development of female genitalia.	Activation of MAP kinase then activates the ERK pathway via **RR**.

GR = genomic responses; RR = rapid responses. RR are not dependent on genomic responses. KO = Knock-out renders affected genes inactive.

<u>This table is not for memorization, it's just to know that lipid soluble hormones' receptors have two sites initiating two different responses, there are genomic responses (from a nuclear receptor) and rapid responses that controls metabolism (from a cell surface receptor) .</u>

STRUCTURE OF HORMONES BY LOCATION : know we will go over each gland mentioning its hormones and their structure , it is not required to know all of the structures as some are included here only to get you exposed on them, what will be discussed about the structure is the only required .

1.HYPOTHALAMUS

Hypothalamus

Hormone	Composition
Growth hormone releasing hormone (GHRH)	Two forms: polypeptides (40 & 44 amino acids)
Somatostatin	Two forms: polypeptides (14 & 28 amino acids)
Dopamine	Catecholamine (amino acid derivative)
Corticotropin releasing hormone (CRH)	Polypeptide (41 amino acids)
Gonadotropin releasing hormone (GnRH)	Polypeptide (10 amino acids)
Thyrotropin releasing hormone (TRH)	Polypeptide containing 3 amino acids

You need to know a few important things about these hormones :

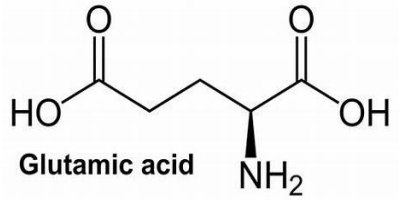
- **dopamine is the only one of them that is not a polypeptide but an amino acid derivative.**
- **TRH is the smallest peptide hormone consisting of 3 amino acids, while GHRH is the biggest among hypothalamus hormones.**
- **The special feature in somatostatin is that it has a sulfur bridge .As you will notice, many proteins have disulfide bonds , why ?**

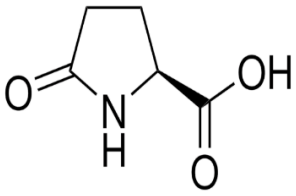
After protein folds to its 3D structure , disulfide bonds are formed to stabilize the structure.

- **Growth hormone and somatostatin have two forms**

- **TRH is composed of a modified form of glutamic acid called pyroglutamic acid + histidine + proline:**

Extra images + extra info.

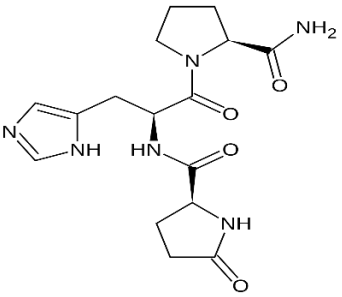


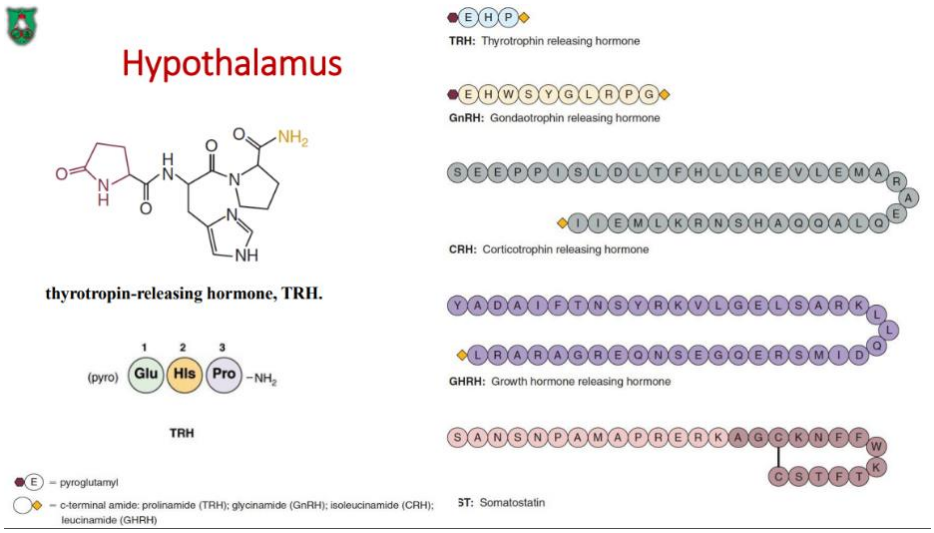


Pyroglutamic acid

Pyroglutamic acid is used to synthesize glutathione, if a person who have glutathione synthatase difficiency ingested a dose of paracetamol this will cuase depletion of glutathione triggering the body to activate its synthesis pathway, but due to enzyme difficiency pyroglutamic acid accumulates in the serum which may cause metabolic acidosis (too much acid in blood)

Thyrotropin releasing hormone





Pic. From the slides

2. ANTERIOR PITUITARY

Anterior Pituitary

Hormone	Composition
Growth hormone (somatotropin, GH)	Straight-chain protein: two forms (191 aa) and (176 aa)
Prolactin (PRL)	Straight-chain protein (198 aa)
Adrenocorticotropic hormone (ACTH)	Small polypeptide (39 aa)
Follicle-stimulating hormone (FSH)	2-chain glycoprotein: (α, 92 aa; β, 111 aa)
Luteinizing hormone (LH)	2-chain glycoprotein: (α, 92 aa; β, 116 aa)
Thyrotropic hormone (TSH)	2-chain glycoprotein: (α, 92 aa; β, 112 aa)

- **all anterior pituitary gland hormones are glycoproteins, (except prolactin).**
- **The glycosylation of the proteins gives them a greater binding ability.**

Why are carbohydrates added?

لتفهم الفكرة تذكر عملية صنع قطر الحلويات ، إضافة السكر للماء أكسبه صفتين :

Viscous & Sticky, and that is why it is added to hormones -to make it more sticky- which enhances their binding ability to the receptor, it is important to understand that adding carbs have no role on targeting the hormone to the receptor (making hormone specific or higher in affinity to certain receptor) it just makes hormones sticky.

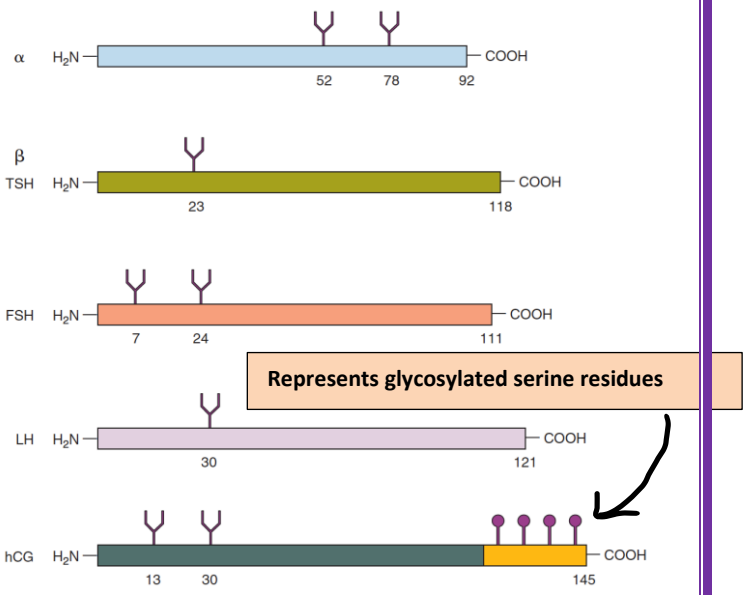
And that process isn't only used on hormones, cells put glycosylated proteins on their surface to be cohesive with adjacent cells , another example is glycosylating the Fc portion of IgM to make it stick on B-cell surface or of IgE to stick it on mast cells

الأمثلة السابقة ليست للحفظ، بل فقط لتفهم ما أهمية إضافة الكربوهيدرات للهرمونات

- **FSH, LH, and TSH are 2 subunit proteins consisting of α and β subuints connected together by a disulfide bridge.**

- **The α subunit in these proteins are identical indicating that it has only a structural role , while the β subunits are different indicating that it has a functional role.**

In this image, the forks represent sites for binding carbs ,There are two types of glygosylation : N on aspargine(adding them to amine groub) and O on serine, therionine and tyrosine (adding them to oxygen of hydroxyl groub) , all anterior pituitary hormones are N-glycosylated.

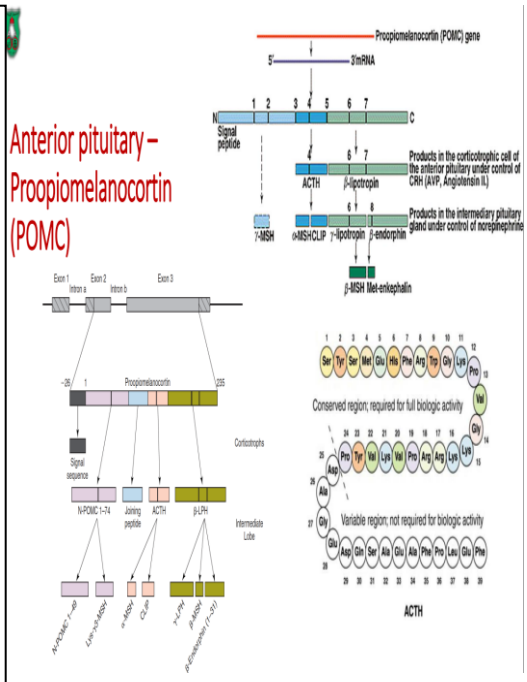


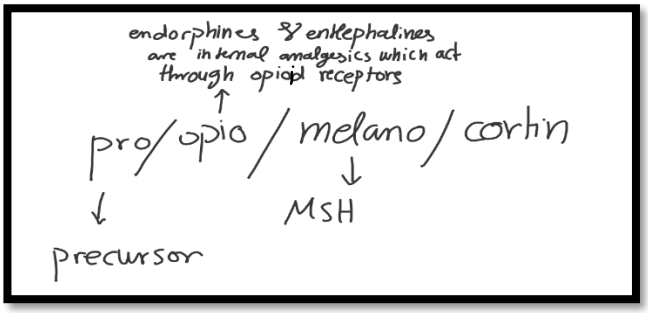
***hCg (human chorionic gonadotropin) has O-glycosylated region, this hormone is produced by placenta during pregnancy, it shares the alpha subunit with anterior pituitary hormones.**

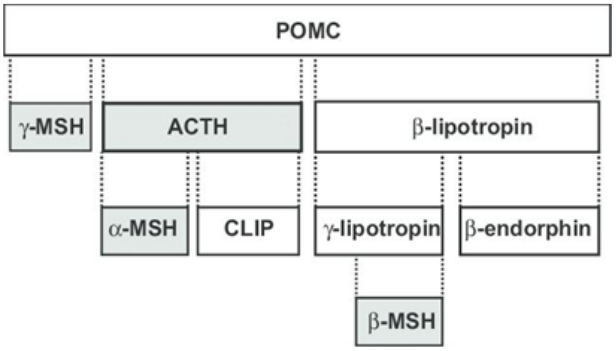
Proopiomelanocortin (POMC) is a pro-hormone synthesised in corticotrophs and it's a <u>precursor for ACTH</u> alongside many other hormones like :

- **<u>Melanotrophins (melanocyte stimulating hormone)</u>** so secretion of ATCH is associated with pigmentation
- **<u>Endorphins</u> (analgesics)**
- **<u>Enkephalin</u>** penta-peptide, are of two types methionine and leucine enkephalins , have analgesic effect.

إفرازهم مع ال(ACTH) منطقي، لأنه يحفز إفراء الكورتيزول و الذي يفرز بعد تأثير ال (fight or flight) ليبقى الجسم متحفزا فتقوم ال (analgesics) بتهدئته







This pro-hormone gives different other hormones by [alternative splicing] and giving different exons

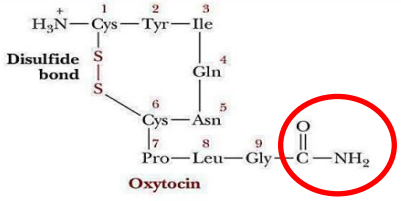
ACTH can also be further sipliced to [MSH & CLIP]

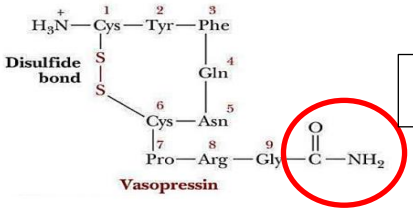
CLIP: a protein that binds to MHCII receptor to prevent its degradation if not bound to antigen

3. POSTERIOR PITUITARY

Posterior pituitary

Hormone	Composition
Oxytocin	Polypeptide containing 9 amino acids
Antidiuretic hormone (ADH; vasopressin)	Polypeptide containing 9 amino acids; two forms: arginine-ADH (most common in humans) and lysine-ADH



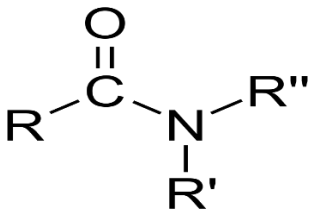


c-terminal

- **Posterior pituitary gland secretes two hormones both of them contain 9 amino acids with one disulfide bridge, they are identical in 7 of these amino acids, they differ in amino acid number 3 and 8.**
- **Amino acid number 8 in vasopressin (ADH) could be either arginine or lysine, but in humans it's mostly arginine.**
- **These two hormones have two different functions, but the similarity in structure could make an overlap in their function.**

- **In regular cases , carboxyl group is found at the C-terminal ,but here there is an amide groub , the process of amidation at the C-terminal protects the hromone from degradation**

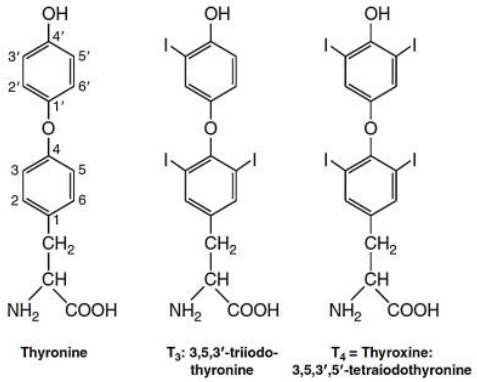
Extra image & info : Amide group= carbonyl attached to nitrogen

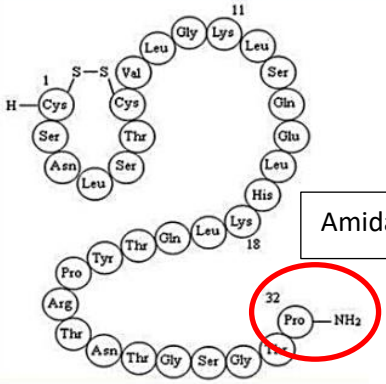


4. THYROID

Thyroid

Hormone	Composition
Thyroxine (tetraiodothyronine, T4)and triiodothyronine (T3)	Amino acid derivative
Calcitonin (thyrocalcitonin)	Polypeptide containing 32 amino acids





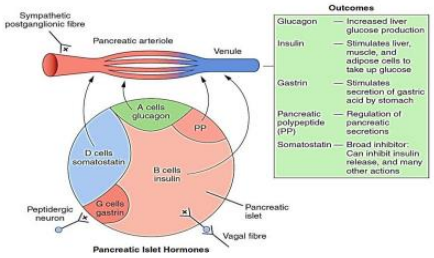
Amidation on C-termina

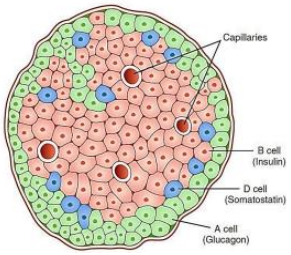
- **Thyroid hormone is a derivative of tyrosine, it's made by connecting two tyrosine molecules together.**
- **Calcitonin has an amide linkage in its C terminal (the last amino acid)**
- **Calcitonin contributes to Ca++ homeostasis in the body**

5. PANCREAS

Pancreas

Hormone	Composition (amino acids)
Insulin	51
Glucagon	29
Somatostatin	37
Pancreatic polypeptide (PP)	14
Gastrins	34, 17, 14

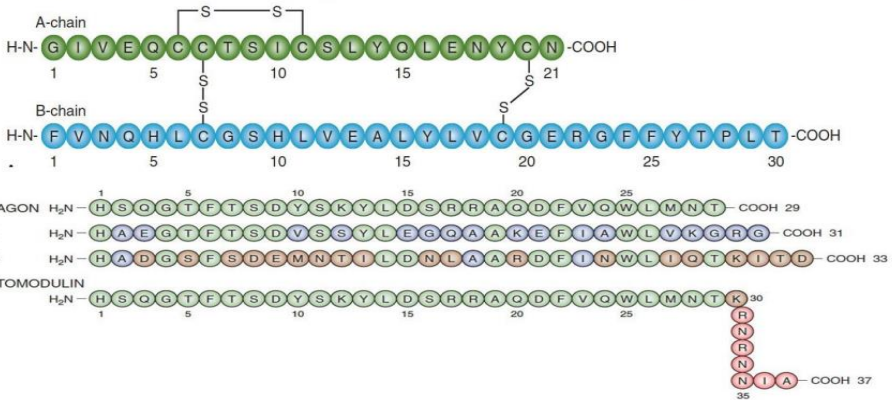




- **Insulin is a much bigger hormone than glucagon.**
- **Insulin has only one form while glucagon has multiple, the first is pancreatic glucagon (29 aa) and the other is glucagon like peptides (GLPs) (31, 33 aa) and oxyntomodulin (37aa) which are secreted by the intestinal cells, they are differentiated by alternative splicing.**
- **Insulin consists of two subunits (A&B subunits) connected with 3 disulfide bridges: 2 disulfide bridges between A&B subunits + 1 disulfide bridge internal in A subunit**

Pancreas

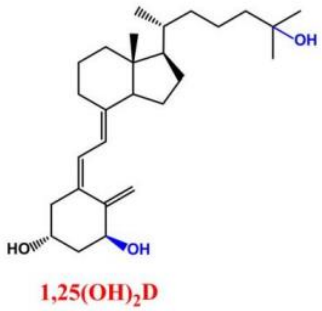
Primary structure of insulin: Amino acid sequence of the A-chain and B-chain of one insulin molecule.

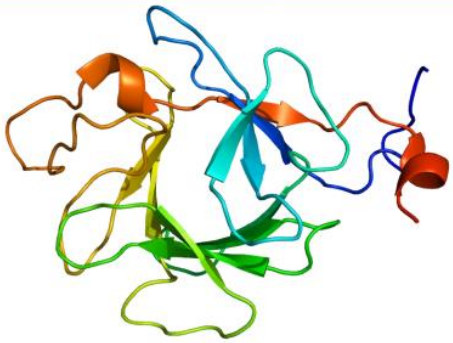


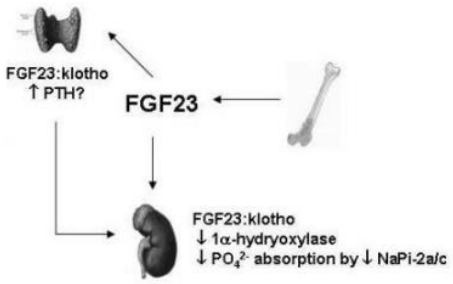
6. CALCIUM REGULATING HORMONES

Calcium Regulating Hormones

Hormone	Composition
Parathyroid hormone (PTH)	Polypeptide 84 amino acids
Vitamin D	Steroid
Calcitonin	Polypeptide 32 amino acids
Fibroblast Growth Factor 23	Protein 251 amino acids

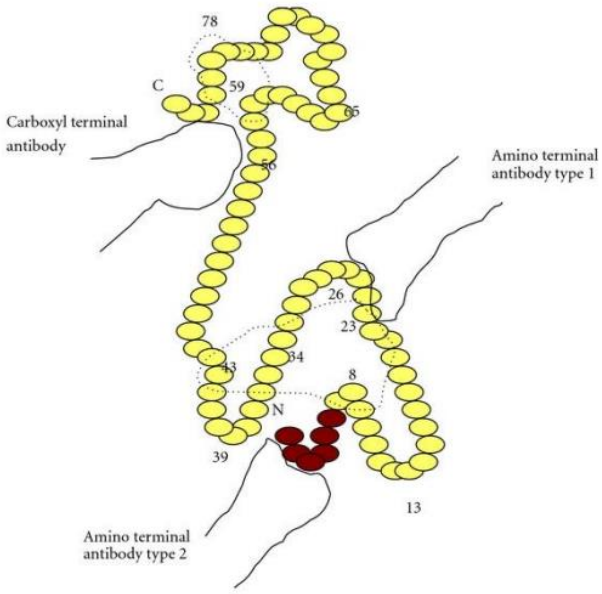


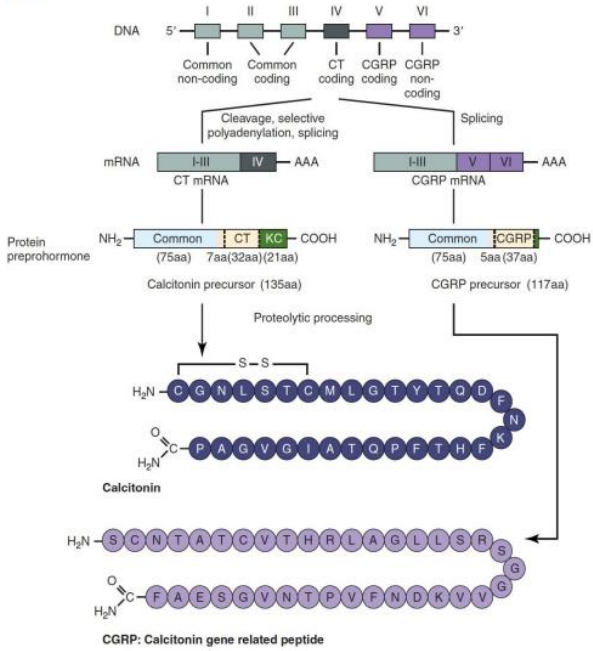




- **Calcitonin is produced by the thyroid.**
- **Vitamin d is a steroid and a derivative of cholesterol.**
- **Fibroblast growth factor 23 is the biggest protein hormone.**

Calcium Regulating Hormones

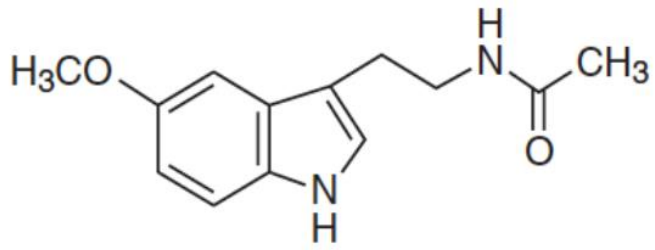




7. PINEAL GLAND

Pineal Gland Hormones

Hormone	Composition (amino acids)
Melatonin	Indolamine (N-acetyl-5- methoxytryptamine)



Melatonin

- **Melatonin is an amino acid derived hormone made from tryptophan.**
- **It's responsible for the control of circadian rhythm (your daily cycle like sleeping waking etc.).**

8. ADRENAL AND SEXUAL GLANDS HORMONES

Adrenal and Sexual Glands' Hormones

Hormone	Composition (amino acids)
Group of hormones	steroids
Norepinephrine	Amino acid derivative

- **Most of these hormones are steroids.**
- **Norepinephrine is an amino acid derivative (tyrosine)**

***these hormones will have a separate lecture later.**

SYNTHESIS AND DEGRADATION OF HORMONES

In general, the synthesis and degradation of the hormone are according to the receptor location (intracellular vs extracellular).

- ➢ according to the receptor location, we can classify the hormones into :
  - Those which have intracellular receptors

1) steroids
2) small molecules like nitric oxide NO
3) amino acid derivates like thyroid hormone

  - Those which have extracellular receptors

1) Catecholamines
2) proteins and peptides
3) FA derivates, eicosanoids (large molecules)

There will be a separate lecture to the steroids concept so for know just focus on the doctor's tips

Steroid hormone synthesis In general they are made from cholesterol

They are divided to these categories according to the number of carbon atoms:

• C21:

- Progesterone: directly from pregnenolone

- Cortisol & Aldosterone: from progesterone

• C19

– Testosterone

– from progesterone or pregnenolone

– 2c shortage

• C18 (estrogen):

– Aromatase

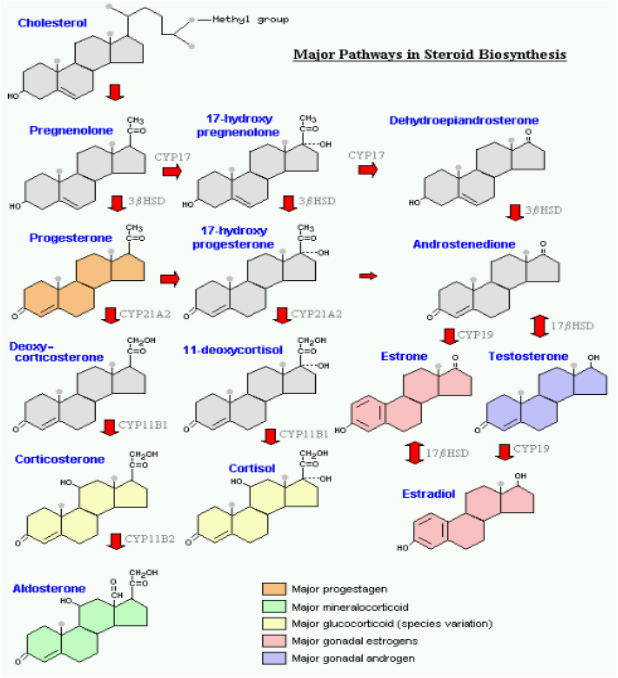
– Cleaves C18

Minimal differences found between the steroid hormones (in the number of carbons and some simple modifications like hydroxylation) but still are able to induce huge functions

– Reduction

Cholesterol isn't a steroidal hormone

First reaction converts cholesterol (27 carbons) to pregnenolone(21 carbons) which is the parent molecule for all steroid hormones



What is the structure of cholesterol?

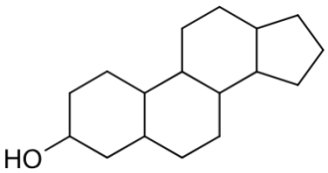
It has 27 carbons ---→17 carbons atoms of them, bounded in four fused rings (three six membrane cyclohexane ring (a, b, c) , one five membrane cyclopentane ring (d) .

question: can we synthesis a cholesterol in our body?

yes, we can. The basic unit is the acetyl coA , synthesized in the liver

Steroid hormone breakdown:

cholesterol can be broken down until reaching the sterol ring which can't be cleaved or further degraded.



Sterol ring

Once the sterol ring (steran core) being synthesized inside the body (steroid genesis) , The body probably cannot break down it again. (Steran core cannot be cleaved)

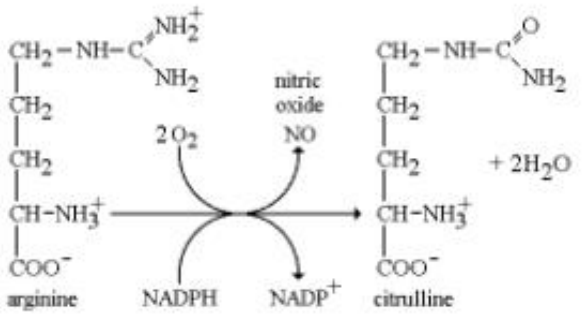
So how can the body get rid of it? By the liver through conjugation with glucuronides or sulphates, glycosylation or maybe hydroxylation, so it will be

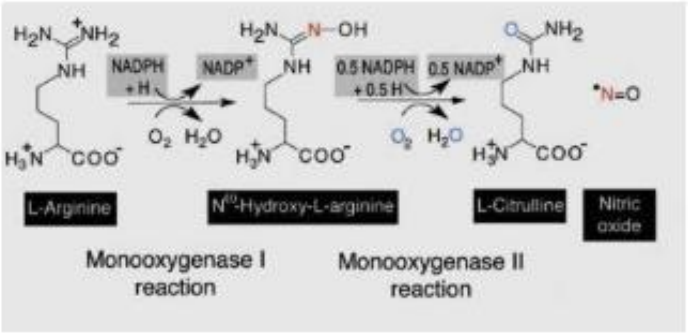
secreted with bile, also if found in low concentration, steroids can be secreted with urine

Nitric oxide (NO)

A small molecules, it's a byproduct of the reaction that converts the arginine (a basic amino acid) to the citrulline (intermediat of urine cycle , also it is a basic amino acid) by the enzyme NO-synthase..

- This reaction is dependent on NADPH , so is considered a reduction reaction.
- NO: synthetized by NO-synthase.





The nitic oxide has many function in the body , and there are 3 isoform of nitic oxide synthase , we called them nitric oxide synthase isozymes that will be in :

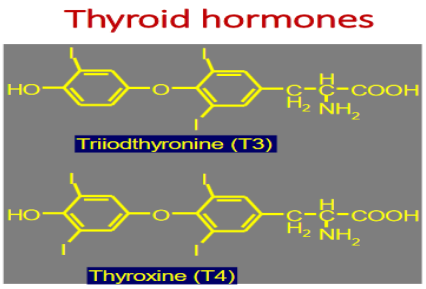
- In neurons (NOS-I): as neurotransmission
- In macrophages (NOS-II): because it has free radicals so it can kill the bacteria.
- Endothelial (NOS-III): by cascade through cGMP can cause vasodilation. (smooth muscle → cGMP → vasodilation)

nitric oxide can save life in case of angina(ذبحة) by immediately secreting the NO by the endothelial cell, this is why the drugs like trinitroglycerin which is composed of glycerin and 3 nitrous groups can help in this situation (vasodialtor).

Clinical correlation to nitric oxide:

- Nitrates in the treatment of angina
- Refractory hypotension during septic shock

Thyroid hormones synthesis:



Its adapted from tyrosine , the starting point is phenylalanine that is hydroxylated through phenylalanine hydroxylase to form tyrosine .

Then the modification can happen to tyrosine, iodination of tyrosine inside the thyroid gland by the thyroid peroxidase .

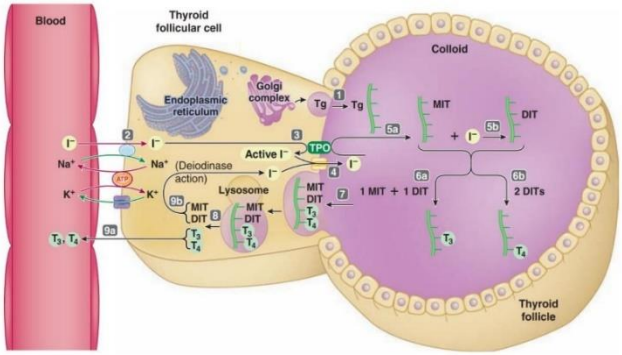
This thyroid peroxidase will oxidize the iodide (I-) to iodine (I2) and then it will do iodination to tyrosine forming Monoiodotyrosine (MIT) by adding one Iodine molecule or diiodotyrosine (DIT) by adding two iodine molecules, all of this with the helping of thyroglobulin protein.

the thyroid peroxidase also couples the two molecules of tyrosine , (if MIT was coupled with DIT --→ form T3) & (DIT with DIT-→ form T4) inside the thyroid gland .

Note that MIT can't be coupled with another MIT.

For further understanding please refer to the physiology lecture about thyroid hormones , this pic is from the physiology lecture

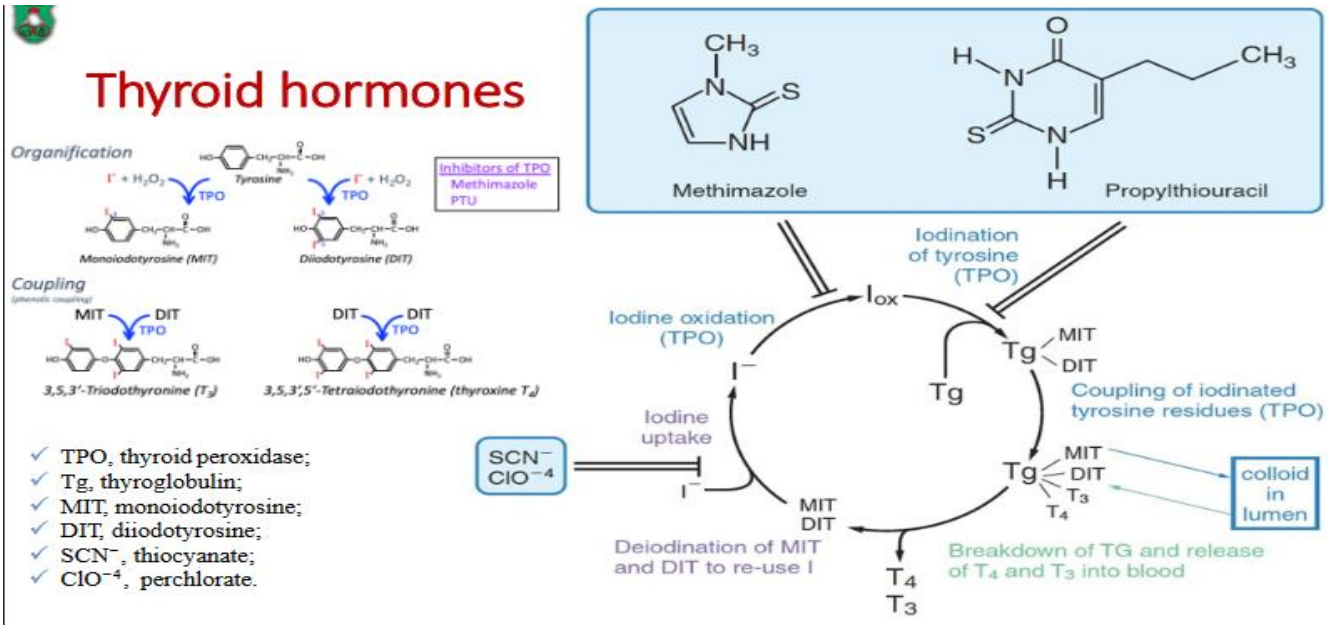
https://youtu.be/dRaSZvD-Ku8(فيديو قصير وممتع).



Cyanide & perchlorate are toxic substances that limits iodine uptake from bloodstream.

the thiocyanate generated during detoxification of cyanide in the body is believed to interfere with iodine uptake because of its structural similarity.

هذه الصور موجودة في السلايدات :



Thyroid hormone degradation:

Deiodinase is an enzyme that removes iodine , converts T4 to T3 which is the active form , found normally in lower concentration than T4 and have a lower half life .

How can the body get rid of T4 ?

1) deiodination by the deiodinase enzyme converting it to T3 then another deiodination reaction inactivates it.

2) conjugation directly into the bile

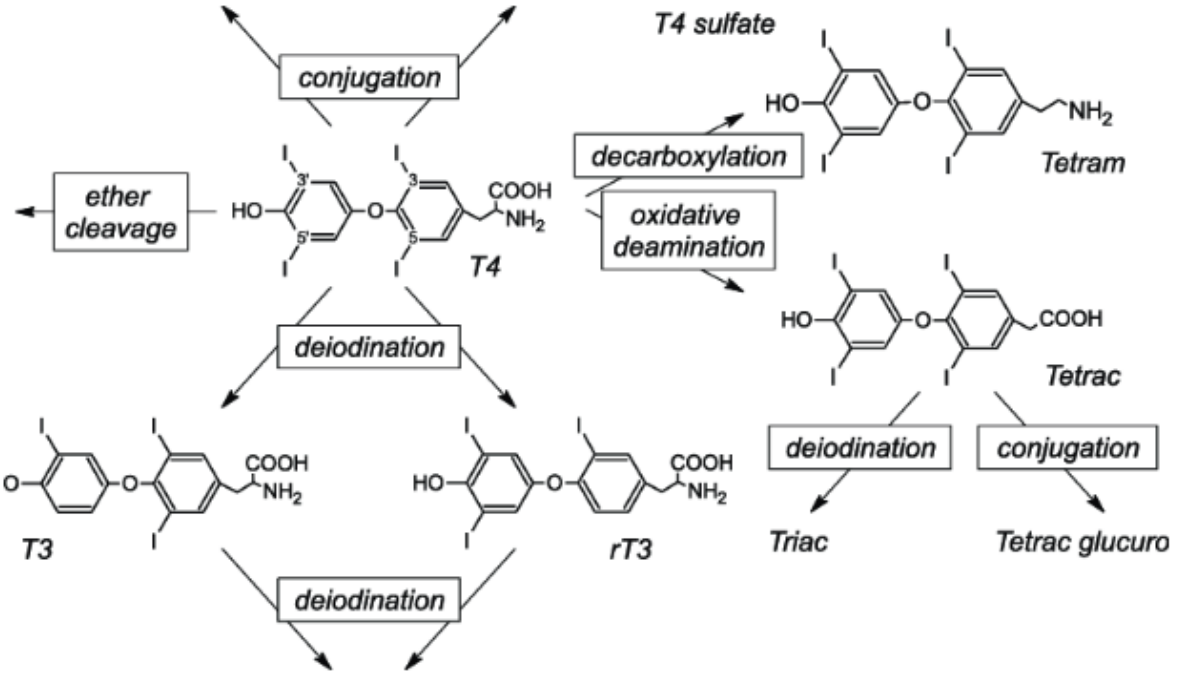
3) any modification to its structure will inactivate it :

(removing carboxyl group from the backbone of tyrosine or by oxidative deamination (removing the amino group)will end the effect of hormone.

How can the body get rid of T3?

By deiodination making it inactive then through bile or other mechanisms

Thyroid hormones degradation



CATECHOLAMINE:

Possess a catechol ring (phenylic group) like tyrosine and phenylalanine.

We called them Amine because it have an amino group, and all of them are tyrosine derived .

Synthesis is in: adrenal medulla, nerve tissue (norepinephrine).

PRODUCTS:

– DOPAMINE, ADRENALINE (HORMONES)

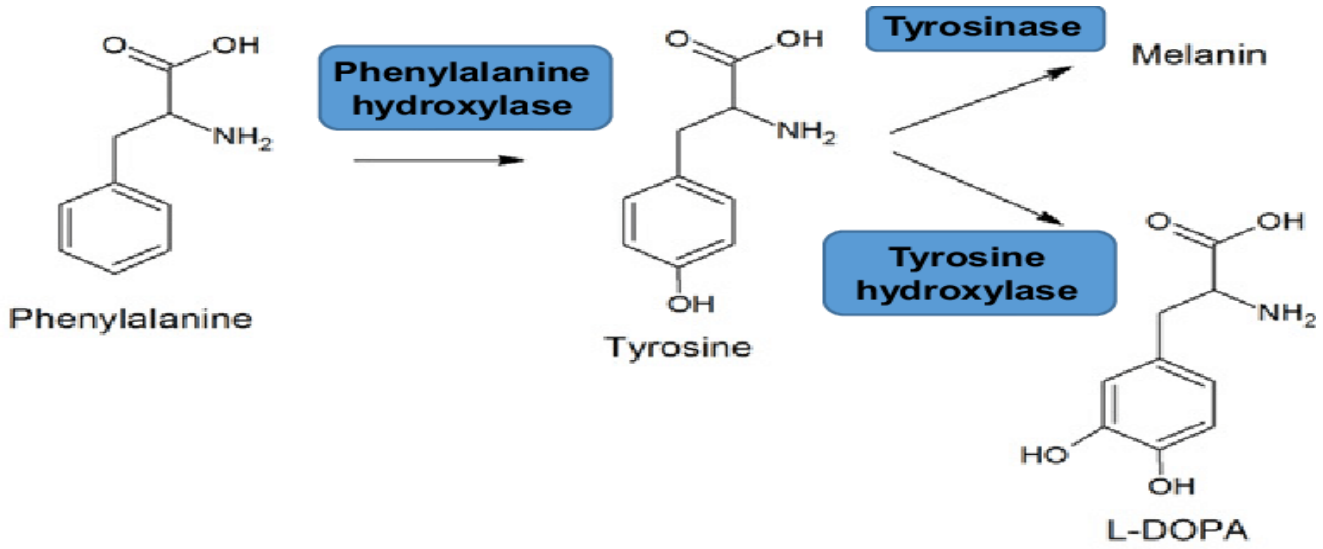
– NORADRENALINE (NEUROTRANSMITTER)

The reaction start with phenylalanine , which is hydroxylated (addition of OH) by phenylalanine hydroxylase (if this enzyme is deficient the patient will suffer from phenylketonuria) to produce tyrosine (hydroxy phenylalanine)

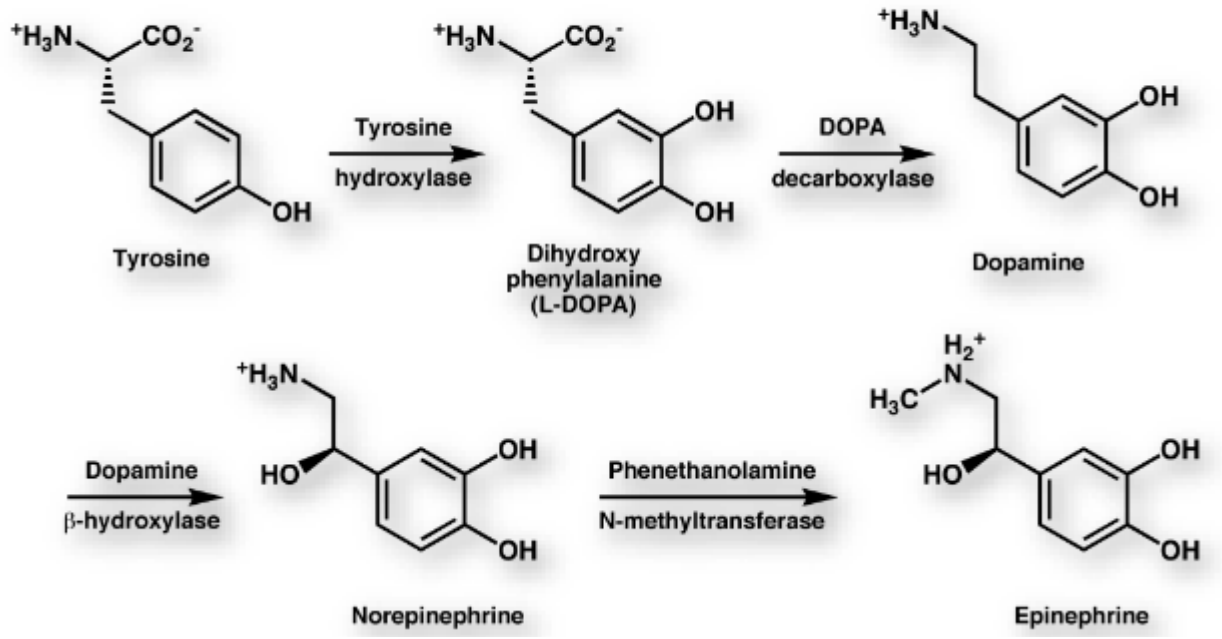
Again the tyrosine is hydroxylated by tyrosine hydroxylase producing dihydroxy phenylalanine (L-DOPA).

Now a decarboxylation reaction (by decarboxylase enzyme) removes the carboxyl group producing dopamine.

The dopamine may produce norepinephrine by hydroxylation and then methylation reaction will produce epinephrine by methyltransferase enzyme.



Catecholamine synthesis



To sum up the reactions:

1) hydroxylation
2) hydroxylation
3) decarboxylation
4) hydroxylation
5) methylation

In the last two steps there are epinephrine and norepinephrine .

Why is the norepinephrine called by this name?

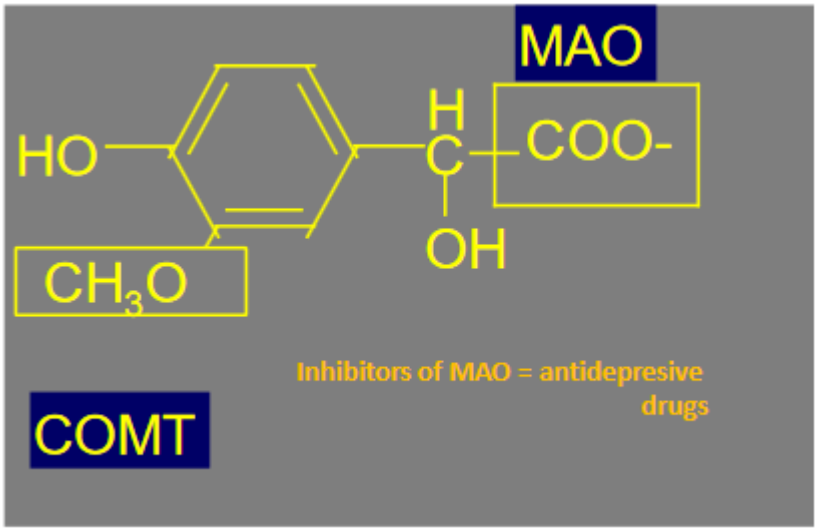
Nor -----→ no r (methyl) group in the structure.

Catecholamine breakdown

to degrade the catecholamine molecules, we start with:

1) acting on the catechol ring by COMT enzyme

2) removing the (amino group) by monoamine oxidase



So, there is two enzymes: 1) monoamine oxidase (MOA) -→ this enzyme removes the amino group by an oxidation reaction.

(recall the biochemistry ---→ **oxidative deamination**)

And this process will end the effect of the dopamine, norepinephrine, epinephrine.

- There is a clinical condition related with MOA --→ depression or psychological disorder ---→ there is a high concentration of the MOA (decrease the concentration of dopamine and nor, epinephrine).

- So, this patient will take MOA inhibiters (antidepressive drugs) to increase the concentration of the dopamine, nor ,epinephrine.

2) catechol o methyl transferase (COMT)
the structure of the dopamine and nor, epinephrine have two hydroxyl groups bound to the catechol ring, COMT transmits a methyl group to the oxygen in place of the hydrogen.

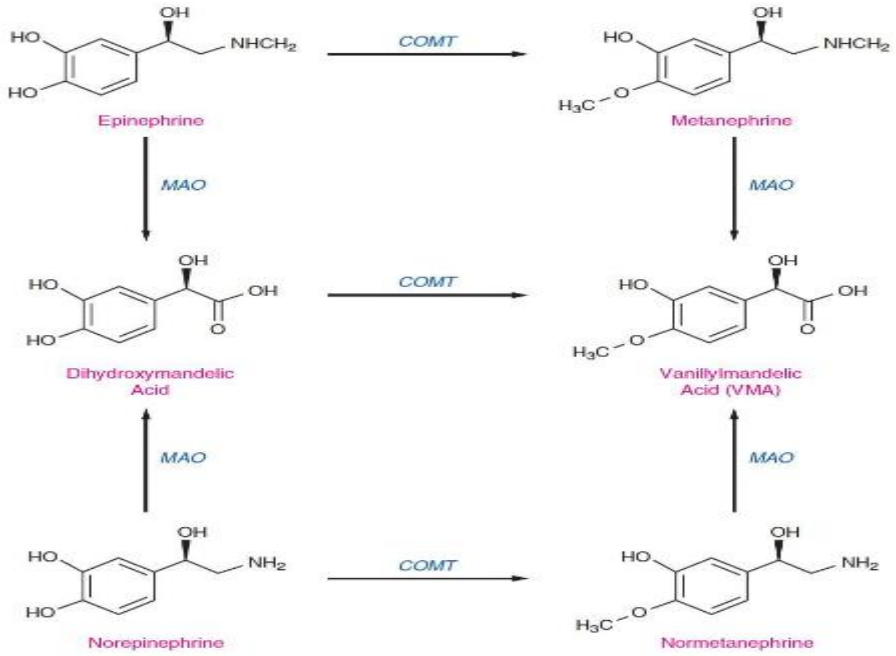
These two enzymes will end the effect of the dopamine and nor, epinephrine.

This diagram explains the integration between the two enzymes.

التفاعل ممكن يبدأ بأي نوع من الأنزيمات (COMT, MOA)

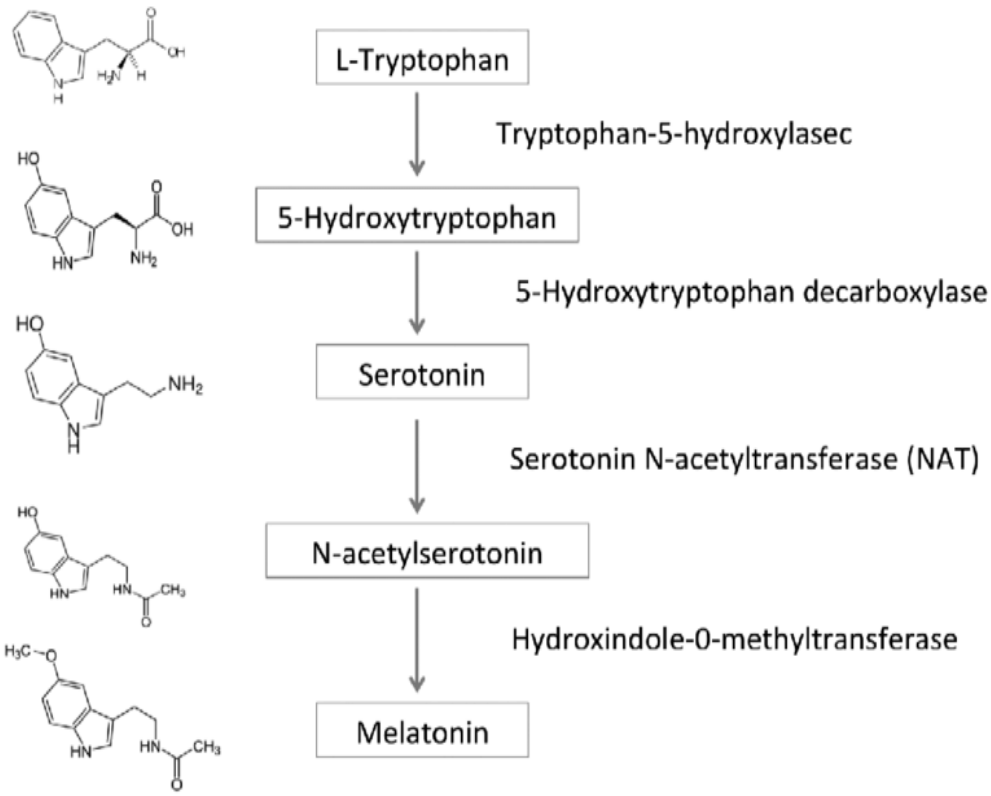
Both of them are involved in degradation and follow each other

MOA then COMT or COMT then MOA

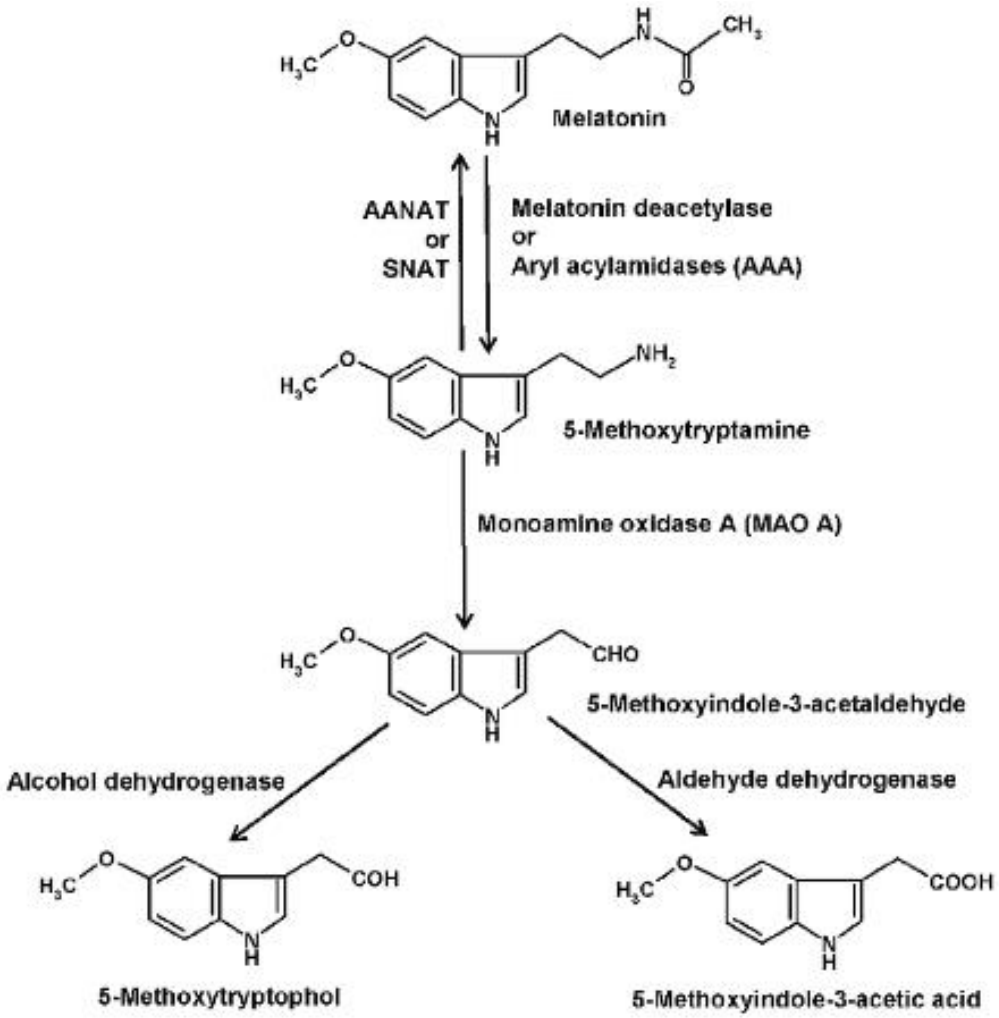


Melatonin

- The synthesis of the melatonin starts with tryptophan amino acid by hydroxylation reaction to produce (5-hydroxytryptophan) , then decarboxylation to the back bone of the amino acid to produce serotonin (5-hydroxytryptamine), then by acetylation to the back bone of serotonin that will produce the (N-acetyl serotonin) , followed by methyl group transfer to indole ring of serotonin that eventually produces melatonin.



- To degrade melatonin we delete what was added ,for instance : (acetyl group) or amino group by the MOA enzyme(MOA acts on any aminoacid's derivative) .



Protein and peptide hormones

Example:

CNS mediators: neuropeptides, opioids

- Hypothalamic releasing hormones and pituitary peptides
- Insulin and glucagon
- Growth factors: IGF, CSF, EPO …and many others

They share the same synthesis pathway.

Gene –transcription→mature m-RNA –translation→ signaling peptide →to ER→cleavage of signal peptide → modifications in Golgi (forming disulfide bridges)→secreted out

Most of them are produced as proprotein or preproproteins.

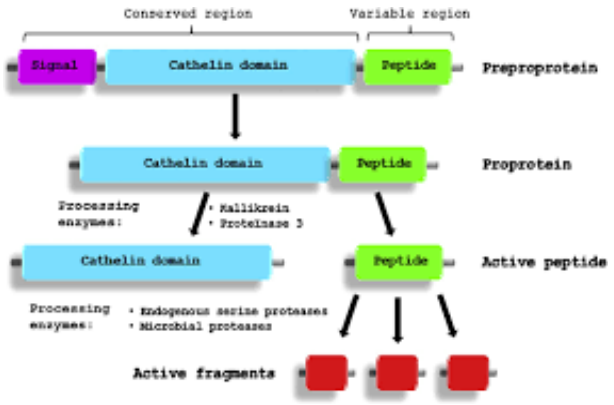
- Proproteins inactive (non-functioning) form (have extra inhibitory part removed by proteolysis).
- Preproproteins require two steps of cleaving to be activated.

Proprotein = precursor

Preprotein isn't a precursor

Remember when we studied about plasma proteins

Albumin had a precursor called proalbumin while there was another protein called prealbumin which is not related to albumin it is another distinctive protein



Due to the presence of signaling sequence they are triggered to the rough endoplasmic reticulum then they get modified in golgi apparatus to be secreted as hormones

General steps of peptide synthesis

"Precursor Polypeptides"

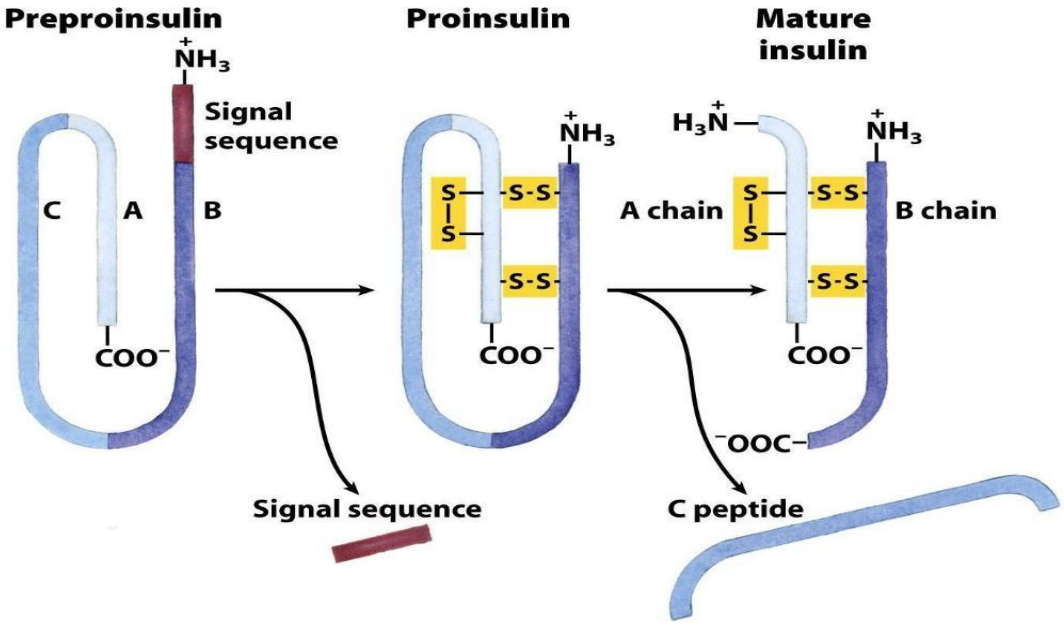
- **Expression of "pre-pro" protein**
- **Transport to ER** (due to a signaling sequence)
- **Splitting the signaling sequence**
- **Cleavage to definite peptide(s) and final modification in Golgi**

Examples include :

– Proinsulin to insulin

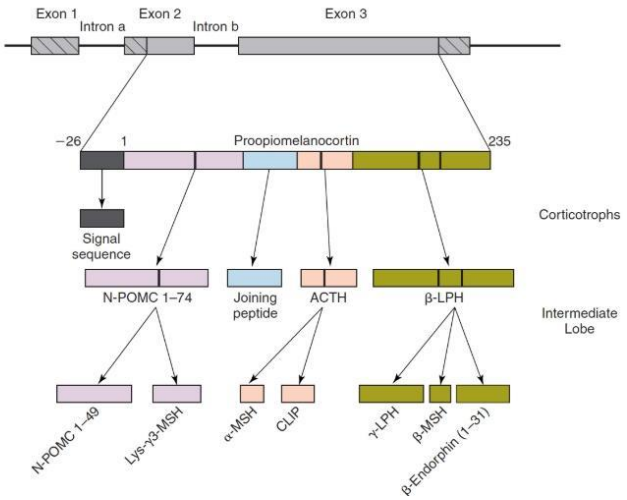
 A larger precursor preproinsulin -> 23 amino acids signal sequence is removed -> 3 disulfide bonds form between chain A&B

 Proinsulin -> after forming 3 disulfide bridges ,Removal of the C peptide (every insulin hormone had 1 c peptide , so I can know the insulin concentration by measuring c peptide concentration) -> Mature insulin which is composed only of A and B chains (not considered a quaternary structure because A &B are parts from a single peptide)



– Proopiomelanocortin (POMC) to MSH and ACTH

I synthesize a large protein (POMC) then I splice it into smaller functioning proteins (MSH & ACTH)

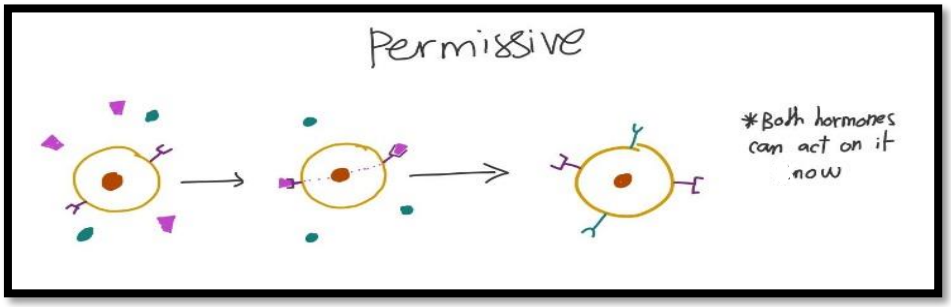


Degradation of peptide hormones

- endocytosis of complex hormone-receptor then joining with a lysosome which contains proteases
- Chemical modification (liver): rearrangement of S-S bridges, cleavage
- Renal excretion of small peptides

Target cell interactive effects (if two hormones reached the cell how they affect each other's function)

- Permissive effects – one hormone enhances the effect of a later hormone (the first hormone binds to its target receptor and induces upregulation of receptors targeted by the second hormone giving the second the permission to affect the cell)



Examples:

- Estrogen up-regulates progesterone receptors in uterus
- Thyroid hormone increases the effect of epinephrine on breakdown of triglycerides in adipocytes

- Integrative effects – hormones produce complementary effects on different tissues (both of hormones have the same effect on the same cell where the net effect is expressed as 1+1=2)

- PTH and calcitriol increase ECF calcium

- Synergistic effects: (if the first hormone is present alone it will produce minimal effect on the cell ,same for the secondI but when combining them together they will produce a huge response, 1+1=10)

- Both FSH and estrogen necessary for normal oocyte development
- FSH and testosterone together increase spermatogenesis

- Antagonistic effects:

- Insulin and glucagon (not found at high concentration at same time or they neutralize each other's effect)