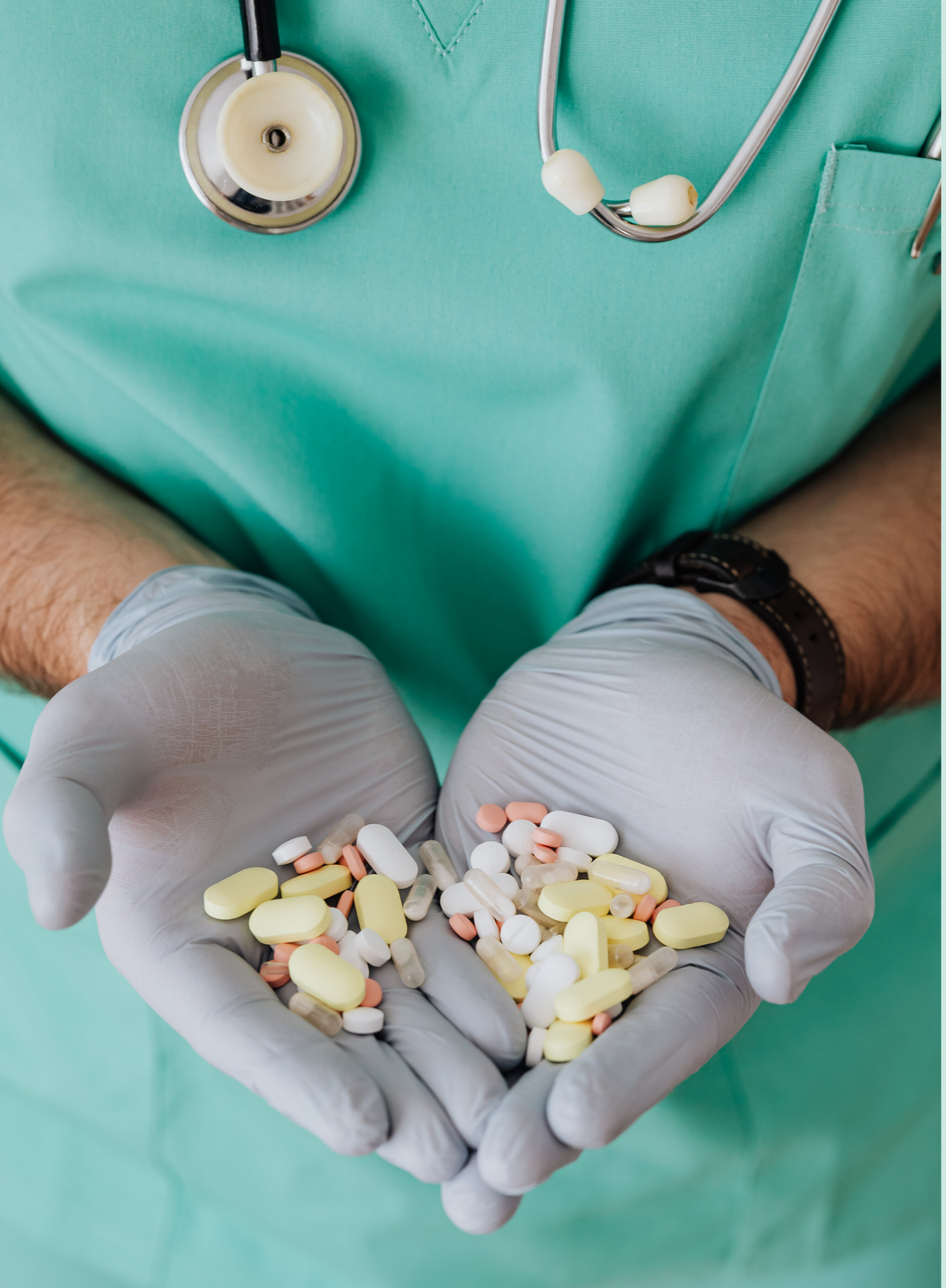


Sheet# 2

PASSION ACADEMIC TEAM YU - MEDICINE

Endocrine system

Lec. Title : Introduction to Endocrinology (Part 2)

Written By : Sawsan Radi

IF YOU COME BY ANY MISTAKE , PLEASE KINDLY REPORT IT TO SHAGHAFBATCH@GMAIL.COM

(الملف الأول - 22 سلايد)

Subject: Biochem of Endocrine | Lec (2) | Date | No. (1)

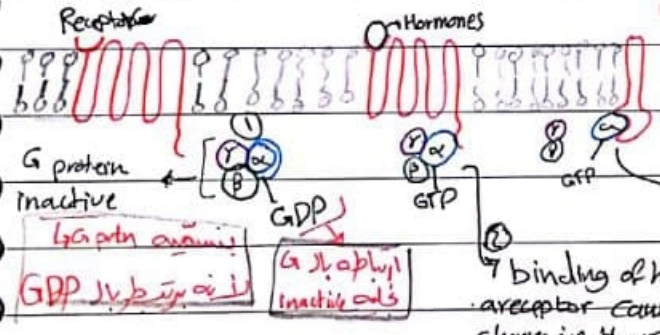
* Signal Transduction System :

slide 22

the pathway through which kinds of proteins that the signal will tranduce to the cell after binding of ligands/hormones.

Pathways	second messenger (used as a Kinase)
1) Gproteins coupled to Adenylyl cyclase: (activation of Gprtns then cyclase)	→ cAMP
2) G proteins coupled to phospholipasec	→ IP_3 (Inositol trisphosphate), DAG (diacyl glycerde molecule)
3) // // // to Phospholipase A_2	→ Archidonic acid metabolies
4) receptor tyrosine Kinases phosphoproteins	→ No second messenger (this receptor is a kinase itself)
5) tyrosine kinase-associated Receptors	→ phosphoproteins
6) Guanylyl cyclase (this are which produces cGMP from GTP)	→ cGMP

slide 23



* why would (G protein) dissociate?

↳ the receptor (adenylyl cyclase) has more affinity to (α+GTP) than β subunit.

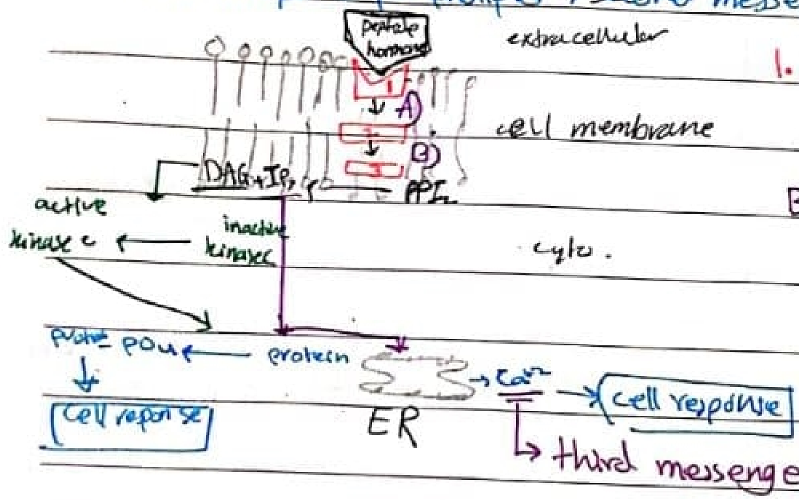
slide 24

* cyclic adenosine monophosphate (cAMP) second messenger mechanism.

α subunit with GTP will activate adenylyl cyclase → ④ the receptor will for cAMP from ATP to be the second messenger → converts inactive form of prtns to active form by phosphorelation/or cause deactivation by dephosphorelation depending on the pathway

* Cell membrane phospholipid, second messengers

slide 25



1. receptor 2. G protein 3. Phospholipase C

A) → the same story in slide 22 & 23

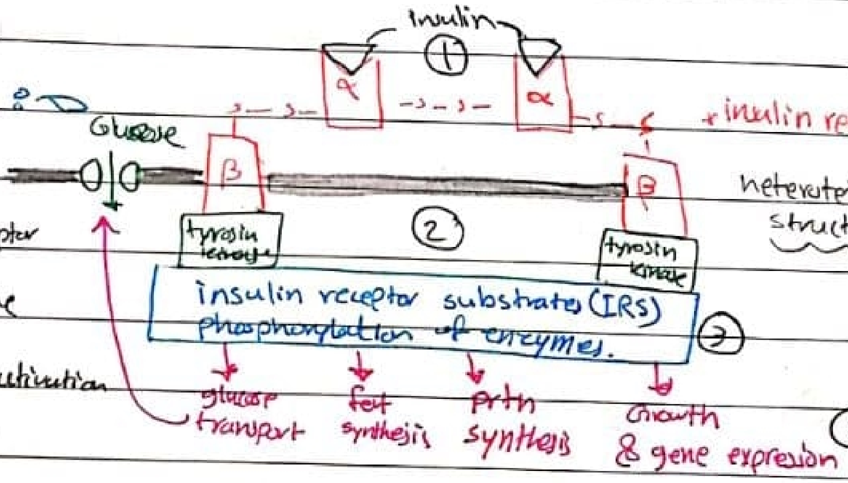
B) → α + GTP → active phospholipase C → lipase activity

↓ (DAG + IP_3) ← degrade PIP_2

both are second messengers.

* The insulin receptor :

slide 26



+ insulin receptor → heterotetrameric structure

(1) insulin bind with its receptor

(2) a conformation change in the receptor cause tyrosin kinase activation

(3) IRS will activate

(4) these are the cell responses.

فبالبداية حكى ما تحفظوهم صرفنا بعدين حكى لا تقرأ طريقة تميزهم وهم فرحها :(

slide 27

← طريقة مش لا تمتة الالم بصفة.

Guanylate cyclase (بسارعة) → ANP

Tyrosine... → insulin + (growth أزغلطة) IGF-1 + GH + prolactin ← واحد برّاني

Phospholipid.. → غلا ترجيت آنجي وبنتها الأدرك

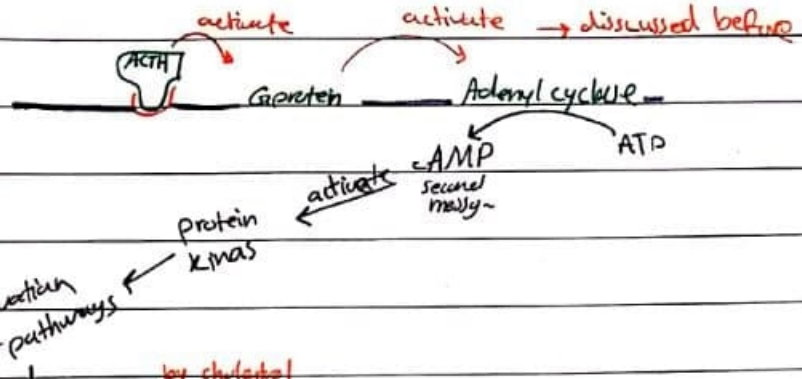
angiotensin II, GnRH, TRH, ola = Oxytocin, PTH

بنتها يعني مرضت كويلة ما رأى بيني ، V_1 ← ADH (V_1 receptor)

Adenylyl → سي سي سي طرها نجلة أنفت قيصه

Glucagon, PTH, CRH, MSH, HCG, somatostatin, TSH, FSH, LH, ACTH, HCG, GHRH, Glucagon

* Steroid Hormone synthesis & secretion: slide 28



ex: cholestrate ester → (by cholesterol esterase) Cholestrol → start steroids production (we have a lot of steroids)

in mitochondria

→ scc (site chain cleavage)

pregenolone → Cortisol

* the action of steroids going through the binding of intercellular receptor slide 29

they will translocated to nucleus

OR the hormon go throw nucleus where it binel to its receptor

* the receptor binel to responce elements (sequence in DNA responed to hormone) by indirect way. → activation or inactivation of genes.

* synthesis of Amine Hormones: slide 30

Hormones derived from amino acids

Tyrosin → Thyroid Hormones

Tyrosin hydroxibute → L-Dopa → (hydroxylase) Dopamine → (hydroxylase) Norepinephrine → (methaleration) Epinphrine

* Why this diversity? due to the source of hormones →

- in thyroid glanels the hormones will be Thyrad hormone
- in adrenal they will be the others

} due to different enzy in each type of glanel

N O T E B O O K

Lec 2

Subject: Biochem of Endocrine — Date — No. 4

ما شرحها أولاً، حكى منتعرف عليها قدام — Slide 32

" " " " " " " — Slide 33

* Processing of prepropiomelanocortin: — Slide 34

long prepropiomelanocortin (with signal peptide) → cleavage → fragments → (different hormones)

prostructure

* we use this way to save energy in the cells, so we will have different hormones that will integrate eventually in order to homeostasis, rather than having one hormone which may have many problems.

* prepro-oxyphysin & prepropressophysin: — Slide 35

prepro structure —Cleavage→ one hormones + transporter for this hormone

* you must know that the numbers show the activity of the hormone. — Slide 36

ex: oxytocin will be more oxytocic & milk ejection.

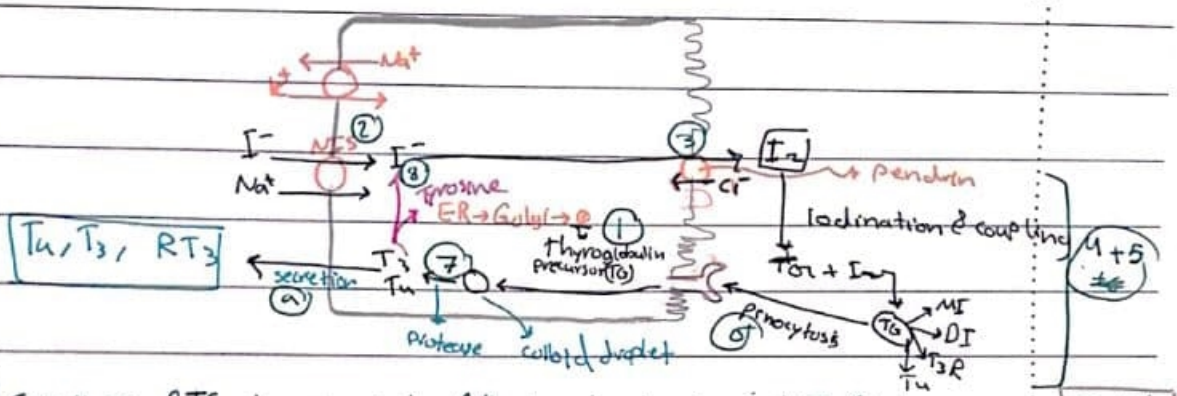
AVP " " " Vasopressor & Antidiuretic

dDAVP " " antidiuretic

→ these hormones have some similarity & all of them have (S-S) bridge, the difference in the site of the bridge or in amino acids included, will make the difference in their activity

* Thyroid hormone synthesis & secretion:

37 ن ل



1) Synthesis of TG, ejrusion into follicular lumin in rough ER, Golgi

2) I^- pump by basal membrane cells → inhibitors are perchlorate, thiocyanate

3) oxidation of $I^- \longrightarrow I_2$ in apical side (luminal) by peroxidase → inhibitor is PTU

4) Organification of I_2 into MIT & DIT

5) coupling reaction of MIT & DIT into T_3 & T_4 } apical membrane by peroxidase

6) endocytosis of TG by apical membrane — inhibitor is propylthiouracil (PTU)

7) Hydrolysis of Tu, T_3, RT_3, MIT, DIT by proteases in lysosomes

8) Deiodination of residual MIT & DIT, (recycling of I^-), intracellularly by: deiodinase

* Thyroglubulin exist as a ~~poly~~peptide with side chains → modification

Slide 39

give us: Tyrosine, MIT, DIT, I_2, RT_3, Tu

Slide 40

in peripheral tissues

Tu → active T_3

Tu → inactive RT_3

Slide 41

Slide 42

* Basic structure of adrenocortical & gonadal steroids: Slide 43

+steroid hormone depends on the site of synthesis.

Cholestrol → progestron, corticoids (differentiate)

↳ the precursor as trogens, androgens (depending on gonadal system) of all steroids

* we have 3 layers in adrenal gland: Zona fasiculata & Reticularis & glumerulosa, all of them are responsable for steroids synthesis Slide 44

* In Zona fasiculata & Reticularis ⇐

→ cortisol, curticosteron, adrostenedione, Dehydroepandrosteron. due to action of ACTH

* in glomerulosa ⇐ Slide 45

Aldosteron, due to action of ACTH

↳ the key molecule is pregnenolone, used in different zone & as a result many different hormones

* Hepatic metabolism of Cortisol: Slide 46

↳ to generate tetrahydro (+4 OH) cortisole, tetrahydro cortisole glucuronide with carbohydrate molecule

cortisone (used as a drug), Ketosteroids

* in gonadal system → testesterone production Slide 47

Slide 48

* Insulin in the liver → activation → activate glycolysis prosses — slide 49
  - formation of cholestrol
  - inhibit gluconeogenesis
  - inhibit break down of fats → we have enough glucose to make energy
  - formation of glycogen → Glycogenesis
  - or inactivation.

* processing of preproglucagon * — slide 50

preproglucagon (179) → GRPP & glucagon (29) (in pancreatic islets) (A-cells)

→ GLP-1, GLP-2 & glicentin (intestine) (L-cells)

we use there agonists for treatments in Diabetis.

* formation of Vitami D_3 — slide 51

cholestrol → provitamin —UV light (from sun)→ Cholecalciferol → activation prosses

1,25-(OH_2) cholecalciferol "active form" (by PTH → parathyroid hormone)

or

24,25-(OH_2) cholecalciferol in kidney