

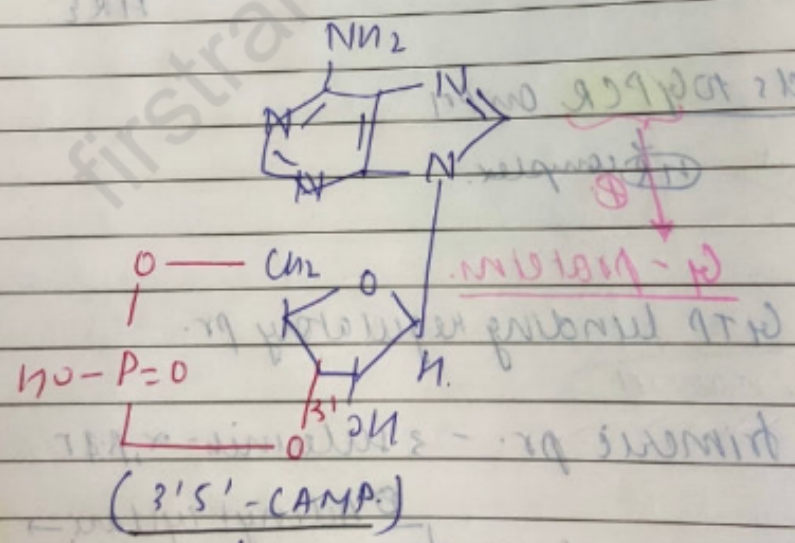
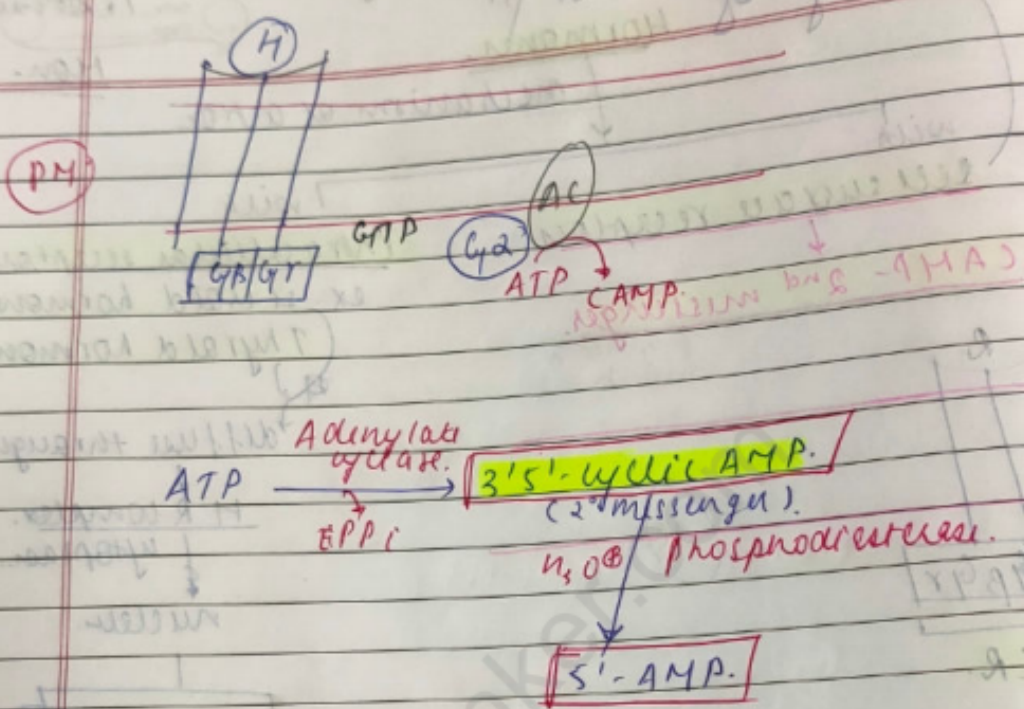
Mon.

Mechanism of action

Adenylate cyclase.
(inv in PM)

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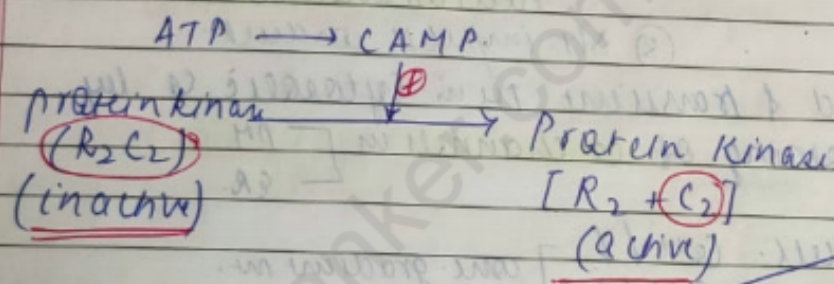
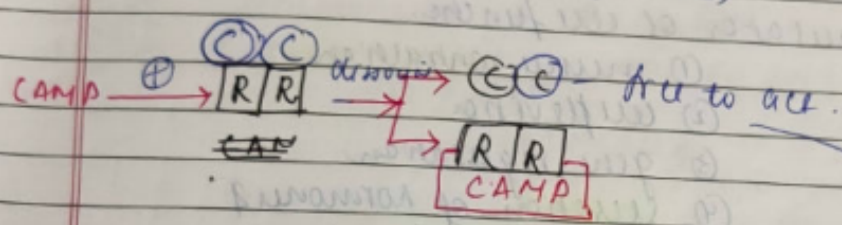


(3',5'-cAMP) → PKA
cyclic AMP dependent protein kinase

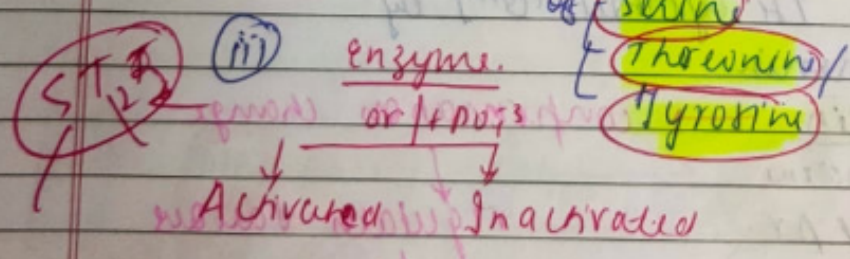
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② Protein Kinase (PKA)

↳ tetrameric molecule
↳ 2 Regulatory + 2 catalytic subunits ($R_2 C_2$)



- ① transfers PO_4^{3-} group from ATP $\rightarrow$ diff enzyme pr.
- ② phosphorylation usually takes place at the OH group of serine/threonine/tyrosine



④ Ex - Covalent Modification.

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Hormones with cell surface receptors

(2) Ca²⁺ messengers - neuroamine

- (i) imp. regulators of cell function.
 - ① muscle contraction
 - ② cell division
 - ③ gene regulation
 - ④ secretion of hormones & neurotransmitters.
 - ⑤ N.Y. impulse conduct.

(ii) Rapid & transient rise in cytosolic Ca by opening of Ca channels in PM & ER.

(iii) intracell. $Ca^{++} \downarrow$
extracell. $Ca^{++} \uparrow$] conc. gradient m.

(iv) Ca⁺⁺ transporting ATPase transporters
accumulate Ca^{++} within the lumen of ER (Sarcoplasmic Reticulum) in muscle.

(v) Hormones rise cytosolic Ca^{++} by

④ mechanism.

① Calmodulin → conformation change
Ca⁺⁺ dependent
regulatory pr.
4 Ca⁺⁺ binding
sites.

↑ binds
Ca⁺⁺

Ex. AD-adenylate cyclase
② Ca⁺⁺ dependent pr. kinase

HORMONES WITH CELL SURFACE RECEPTORS

PIP2 cascade:

phosphatidylinositol diP₂

Hormones + Receptor
(ex- serotonin) (m on pm)

HR complex

Gpr or Gq

PL-C major player

PLD

phosphatidylcholine
H₂O PLD Acid

PIP2

1,4,5-IP₃ + DAG

(membrane lipid)

opens Ca channels

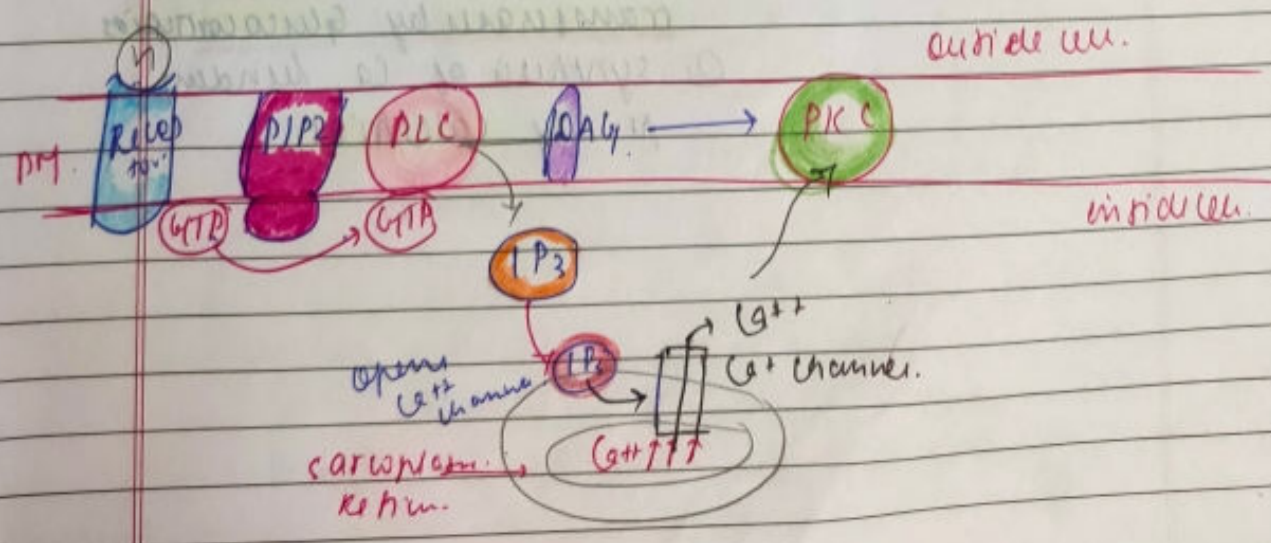
PKC

Ca⁺⁺ ↑ from intracellular stores [ER sarcoplasmic reticulum]

① smooth muscle contracts

② glycogen breakdown

③ exocytosis



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MECHANISM OF ACTION OF STEROID HORMONES HORMONES WITH INTRACELLULAR RECEPTORS

Ex - Steroid hormones +
Thyroid hormones.

nuclear
receptor

↓
diffuse through PM.
(lipid soluble)

H-R complex

(cytoplasm)

↓ translated
nucleus

H-R binds to

sp. sequences bind
sp. hormones.

HRE

Hormone Response
Element

SRE

Steroid Response
Element on DNA

↓
enhances

↑ transcription

↓ mRNA

↓ translation

protein

enzymes or
hormones

Ex: Synthesis of amino

transferases by Glucocorticoids

② synthesis of Ca binding
pr. by calcitriol

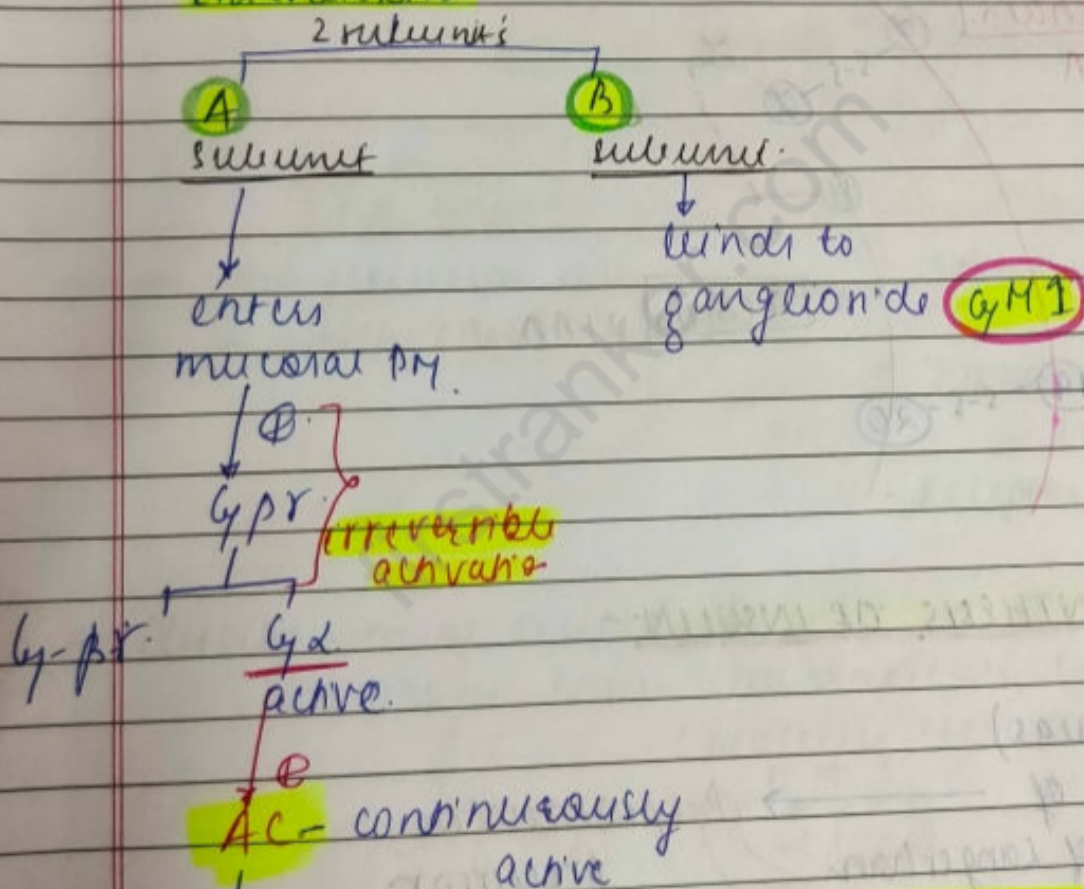
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Abnormal G-pr. signalling

CHOLERA.

~> Cholera toxin - int inside bacterium Vibrio cholerae.
enterotoxin.

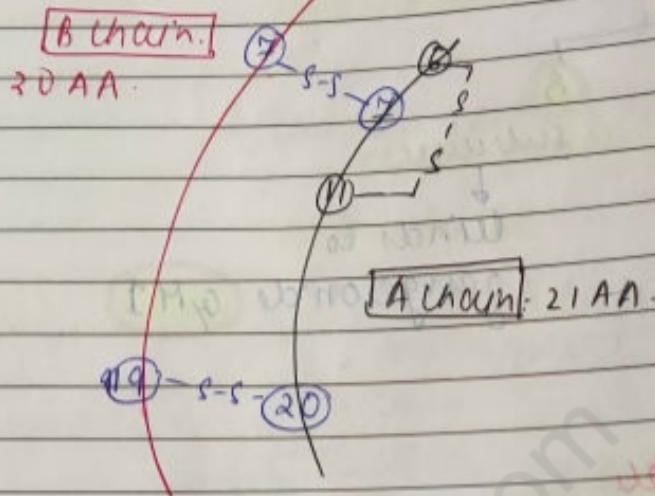


~> 3'5 CAMP ↑↑ ① prevents absorption of salts from intestine leading to watery diarrhoea.
② H₂O loss from body.
③ loss of NaCl → fatal results.

INSULIN

pr. hormone - 2 pp. chain

Structure of I



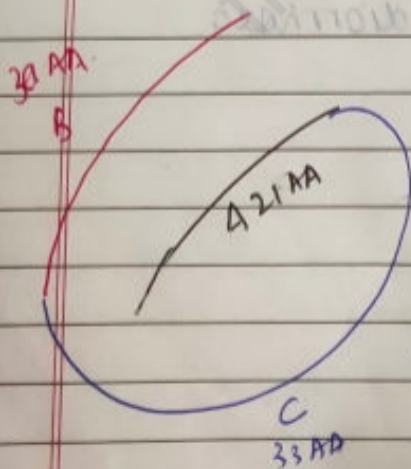
BIOSYNTHESIS OF INSULIN

(Pancreas)
β cells of Islet of Langerhans → Preproinsulin precursor

109 AA

Leads to 23 AA ER

Proinsulin
86 AA



Carboxyl app.

Cleaved by proteases

↳ connecting peptide removed

→ No. of AA in C peptide vary w/c species.

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Mechanism of Action of Insulin:

①

Insulin + Receptor on target cells (intracellular)

Insulin Receptor: Glycoprotein

4 subunits

2 α units

2 β units

on extracellular side to which Insulin binds.

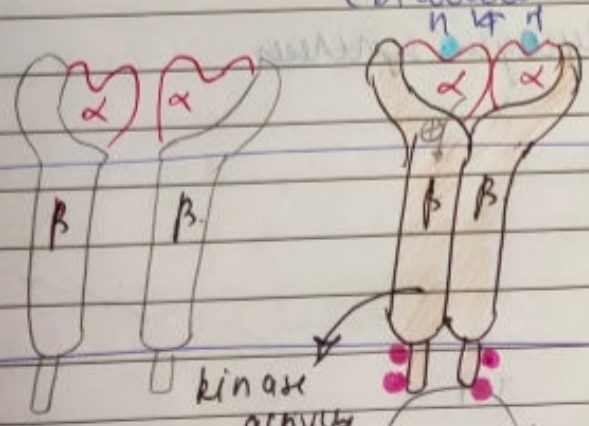
- exposed on cytoplasmic side

- Tyrosine Kinase activity.

- Receptor Tyrosine Kinase

②

Decrease in no. of receptors & target tissue less sensitive to Insulin (diabetes Mellitus Type II)



kinase activity
↓
Tyrosine residues phosphorylated

→ cellular response.

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Insulin + α subunit



α units oligomerise



β receptor

[Tyrosine kinase activity

[Transmits signal to cytoplasm

- phosphorylated sites act as locking Htg ^{receptor} ^{hand/lock}
for Insulin Response Substrate ^{receptor}
IRS 1 & IRS 2. ^{receptor}



recruits GLUT 4

to cell surface



Glycogen synthesis