Types of Hormones (According to what they are made of)

- **Protein, Peptide Hormones**
  - made of Amino Acids
- **Amine Hormones**
  - Derived from Amino acids like tyrosine
  - Catecholamines
    - Dopamine
    - Epinephrine
    - Norepinephrine
  - Thyroid Hormones
    - T_3
    - T_4
- **Steroid Hormones**
  - Derived from Cholesterol

Hormones (According to solubility)

lipid solube

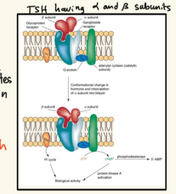
1. Steroid Hormones
2. Eicosanoid
3. Thyroid Hormones
   - it is an amine hormone but lipid soluble

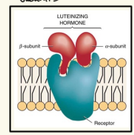
water Soluble

1. Amine Hormones (Catecolamines)
2. Protein and Peptide Hormones
3. Glycoproteins
   - FSH
   - LH
   - hCG
   - TSH

one important feature of those is that they have 2 subunits

- α subunit → common in all glycoproteins
- β subunit → different for each glycoprotein; the one that activates G-protein

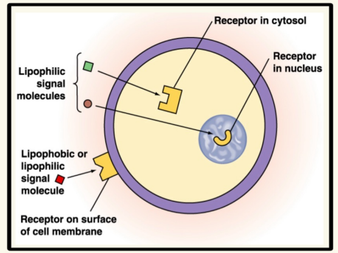


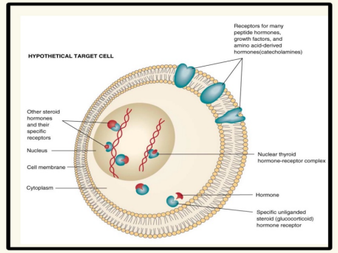


Receptors (According to their location)

- **Receptors on the plasma membrane**
  - ☑ water soluble Hormones
  - ☑ Lipid soluble Hormones
  - → the hormone - receptor complex travels to the nucleus to form its job
- **Receptors in the cytoplasm**
  - ☒ water soluble Hormones
  - ☑ Lipid soluble Hormones
- **Receptors in the nucleus**
  - ☒ water soluble Hormones
  - ☑ Lipid soluble Hormones

Hormones binding to these receptors Have Genomic effect ⇒ they cause Protein Synthesis





Notes :-

- Protein kinase → Increases phosphorylation
  - ↳ Addition of a phosphate group
  - this causes ↑
  - Activation OR Inhibition
  - ⇐ According to the Protein phosphorylated and its job
- Protein phosphatase → Decreases phosphorylation
  - ↳ Addition of a Phosphate group
  - this causes ↓
  - Activation OR Inhibition
  - ⇐ According to the Protein phosphorylated and its job

Plasma membrane Receptors

1 Ion channel-Linked Receptors

[they open/close ion channels ⟹ causing change in membrane Potential]

2 G Protein-coupled Receptors

[Activate G Proteins which activate second messengers]

- **Gs** ⟹ Has a β-adrenergic receptor
- **Gi** ⟹ Has an α_2-adrenergic receptor
- **Gq** ⟹ Has an α_1-adrenergic receptor

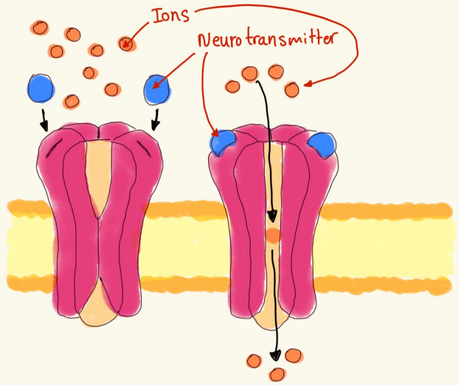
3 Enzyme-Linked Receptors

- insulin receptor → **Receptor Tyrosine kinase** → Growth factor receptors
- **Receptor Serine/Threonine kinase**
- leptin Receptor (JAK-STAT Pathway)

4 Guanylate Cyclase-linked Receptors

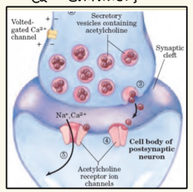
- **Membrane bound Guanylyl Cyclase** → Activated by Peptides like ANP
- **Soluble Guanylyl cyclase** → Activated by (NO)

1 Ion channel- Linked Receptors



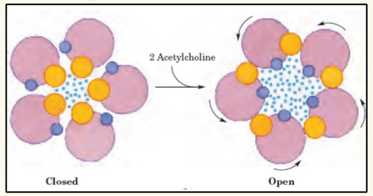
* the binding of neurotransmitters to an ion channel linked receptor causes it to either open or close the channel which causes changes in membrane potential (ionotropic receptors)

ligand gated Na^+ and Ca^{+2} channels

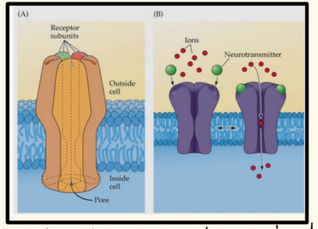


Ionotropic receptors

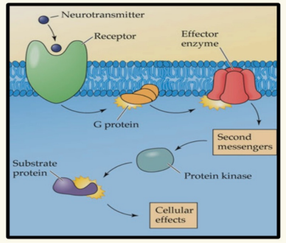
A closed channel VS An open Channel

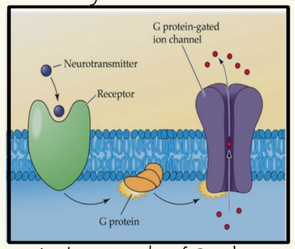


metapotropic receptor opening or closing an ion channel

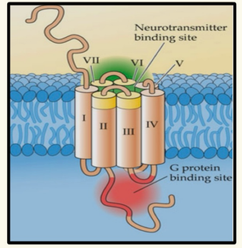


metapotropic receptor activating second messenger system

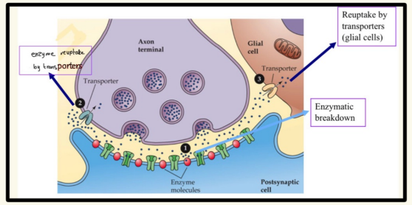




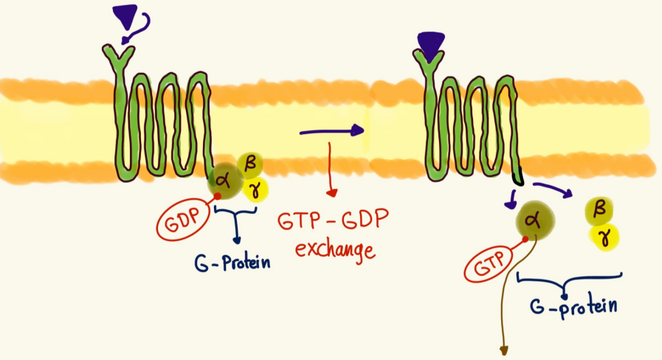
metapotropic receptor (G protein receptor)



enzyme recycling and enzyme reuptake



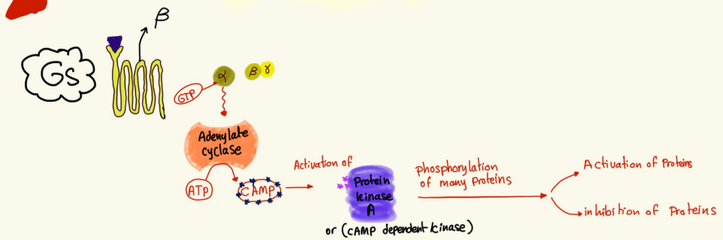
2 G Protein - coupled Receptors

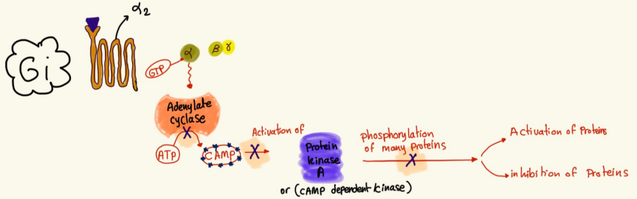


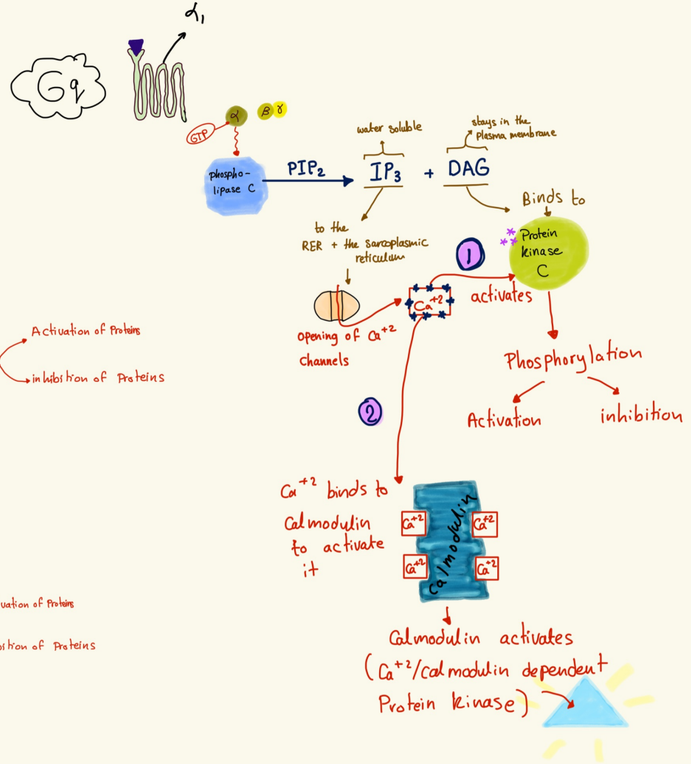
what a released α can do (metabotropic receptors)

1. open / close ion channels
2. Activation of intracellular enzymes
3. Activation of gene transcription
4. Activating second messenger systems

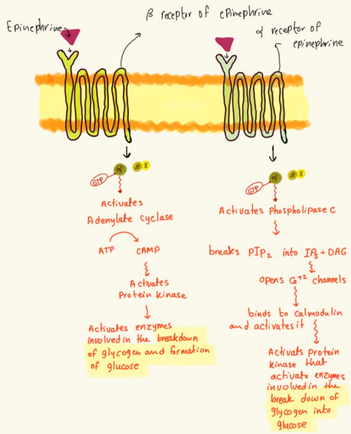
An important note :-
the complex βγ released from the G protein has an inhibitory effect specially visible in Gi

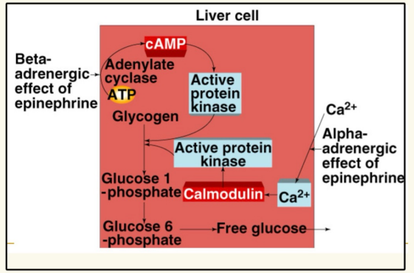




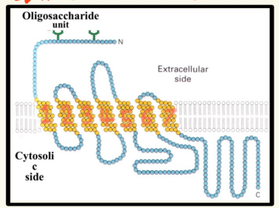


Epinephrine action through 2 second messenger systems

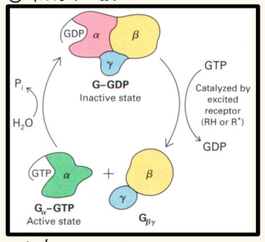




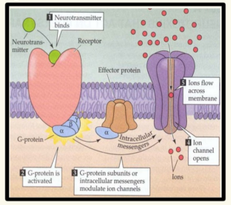
The G protein receptor
↳ it is a 7-helices transmembrane receptor



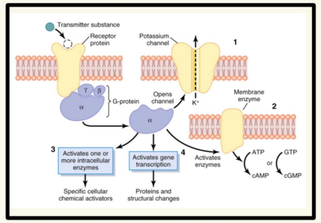
The General mechanism of G Protein work



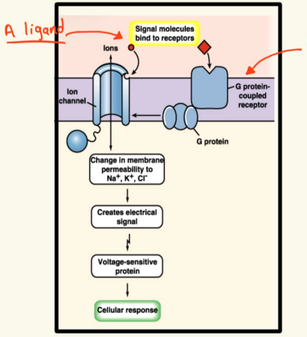
what a G Proteins Can do



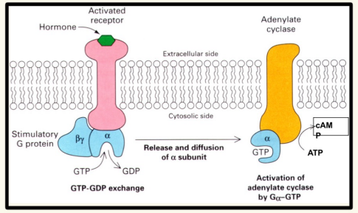
Some things G Proteins Can do



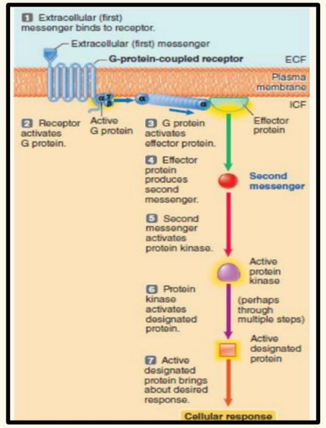
How an ion channel opens → by a ligand binding to it
↳ by a G Protein coupled receptor



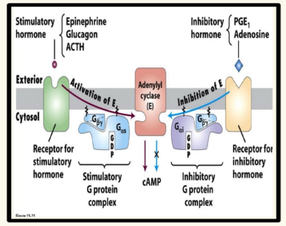
How G Proteins and their receptors work



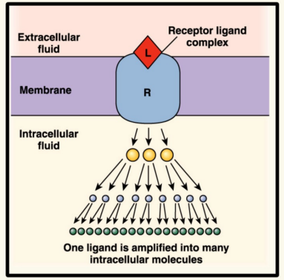
G Protein and its Job



the effect of stimulatory and inhibitory G complexes and stimulatory and inhibitory hormones

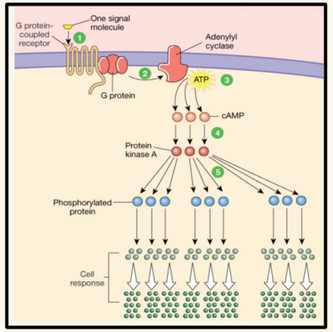


the cascade effect of G Protein coupled receptors

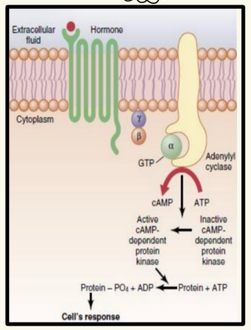


how a small amount of the ligand can cause hundreds of intracellular changes

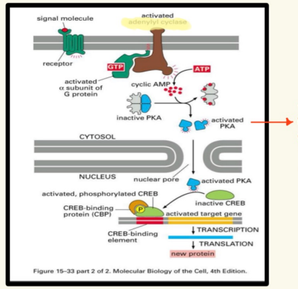
the cascade effect of G Protein coupled receptors



Adenylate cyclase 2nd messenger system (Gs)

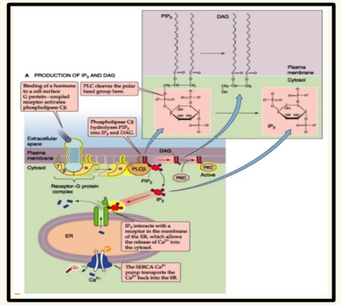


the role of cAMP in Activating transcription

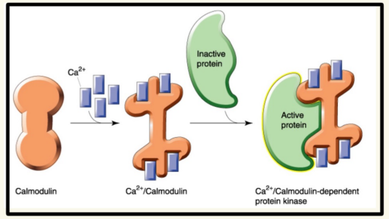


the activated protein kinase enters the nucleus to activate the inactive CREB (cAMP response Element-binding protein) which binds to A specific DNA sequence called CRE (cAMP response element) to increase or decrease expression of downstream genes

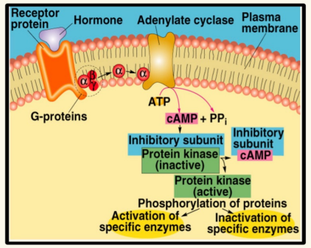
Phospholipase C and its effect directed by (Gq)



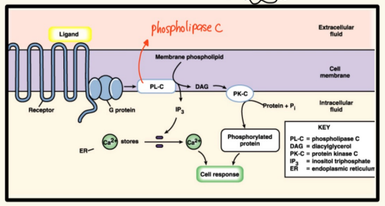
Ca^{+2} activating Calmodulin and the Ca^{+2}/Calmodulin-dependent Protein kinase



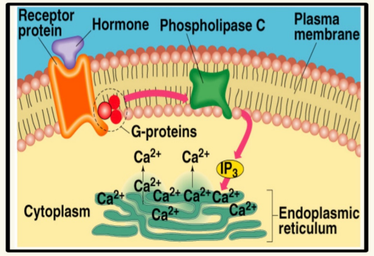
the intracellular role of adenylate Cyclase activated by (Gs)



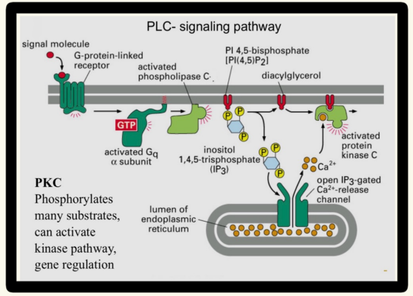
the effect of phospholipase C and Ca^{+2} activated by (Gq)



The effect of phospholipase C of Opening Ca^{+2} channels

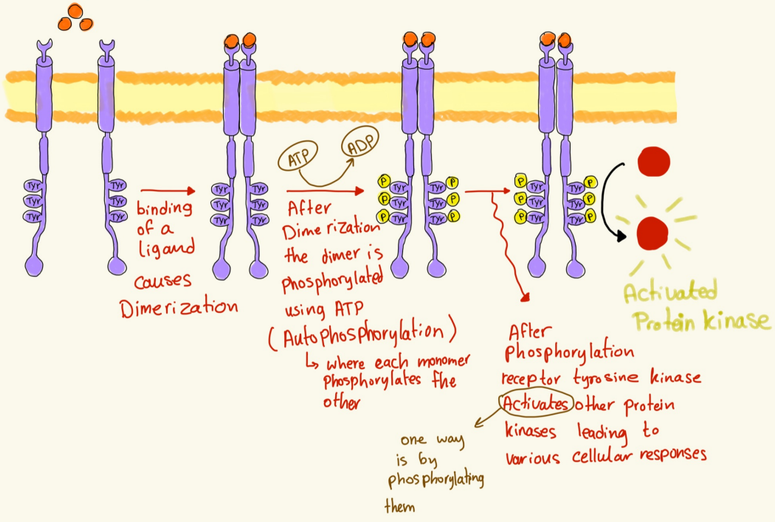


Phospholipase C's Pathway

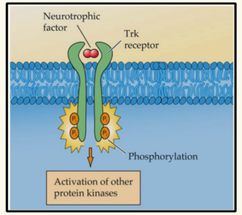


3 Enzyme - Linked Receptors

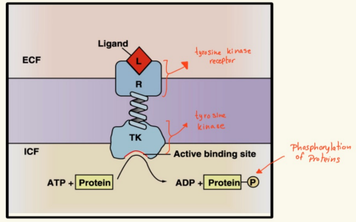
Receptor tyrosine kinase — phosphorylates tyrosine on the target Protein that is going to be activated



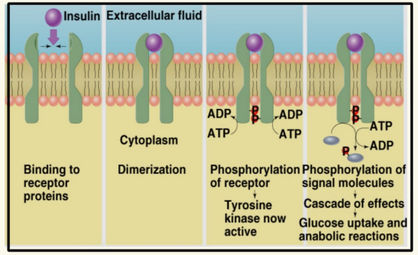
Tyrosine kinase receptor



Tyrosine kinase and its receptor

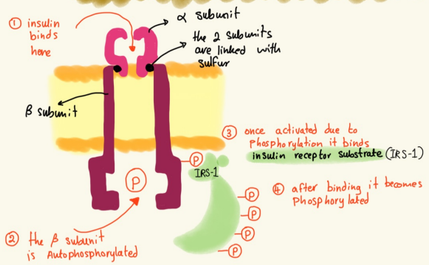


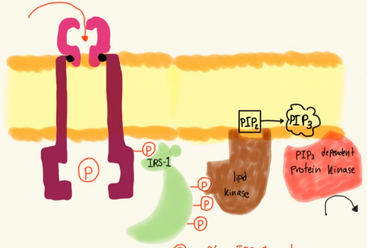
Tyrosine kinase + Tyrosine kinase receptor



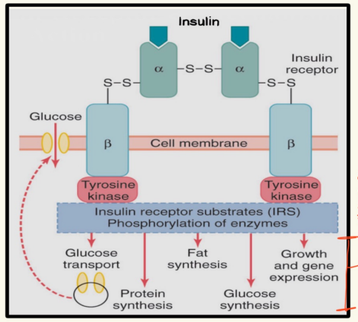
which is an example of a receptor tyrosine kinase

Insulin signal transduction Pathway

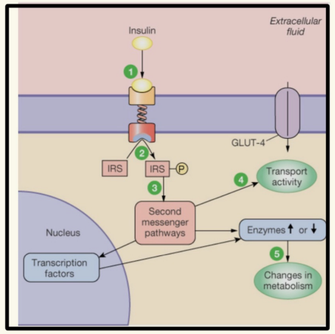




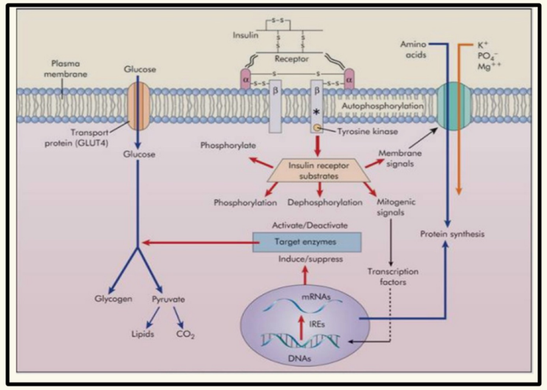
insulin receptor is a tyrosine kinase receptor



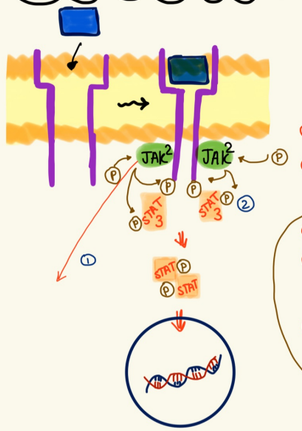
Insulin effect in cells



insulin effect in cells



JAK-STAT Pathway



Like leptin ↑ (ligand)

① when the ligand binds it attracts JAK

② JAK activates enzymes leading to different effects on the cells ----① JAK's first Job

③ JAK guides the phosphorylation of STAT ----② JAK's second Job

④ phosphorylated STAT units bind together

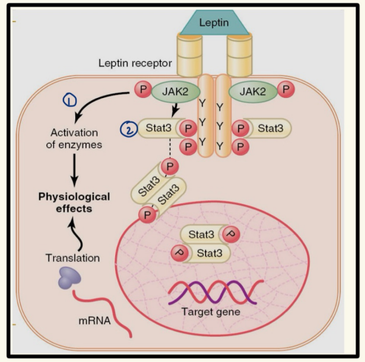
⑤ STAT complex then enters the nucleus And causes transcription

① it causes Autophosphorylation of the 2 monomers of the ligand receptor

② when STAT binds to the phosphorylated receptor it gets phosphorylated

*** there are multiple JAKs and STATs but the ones mentioned are JAK 2 and STAT 3

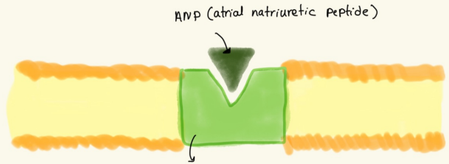
JAK - STAT Pathway (leptin receptor)



4 Guanylate cyclase - linked Receptors

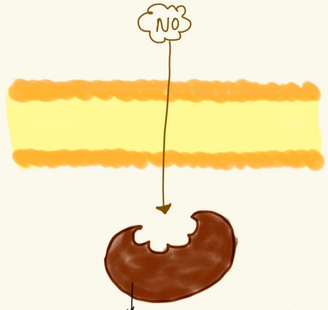
⇒ the key difference in here is that the receptor is the enzyme that does intracellular effect

membrane bound Pathway



Can cause many effects like ① vasodilation ② ↑ Na^+ excretion (kidney)

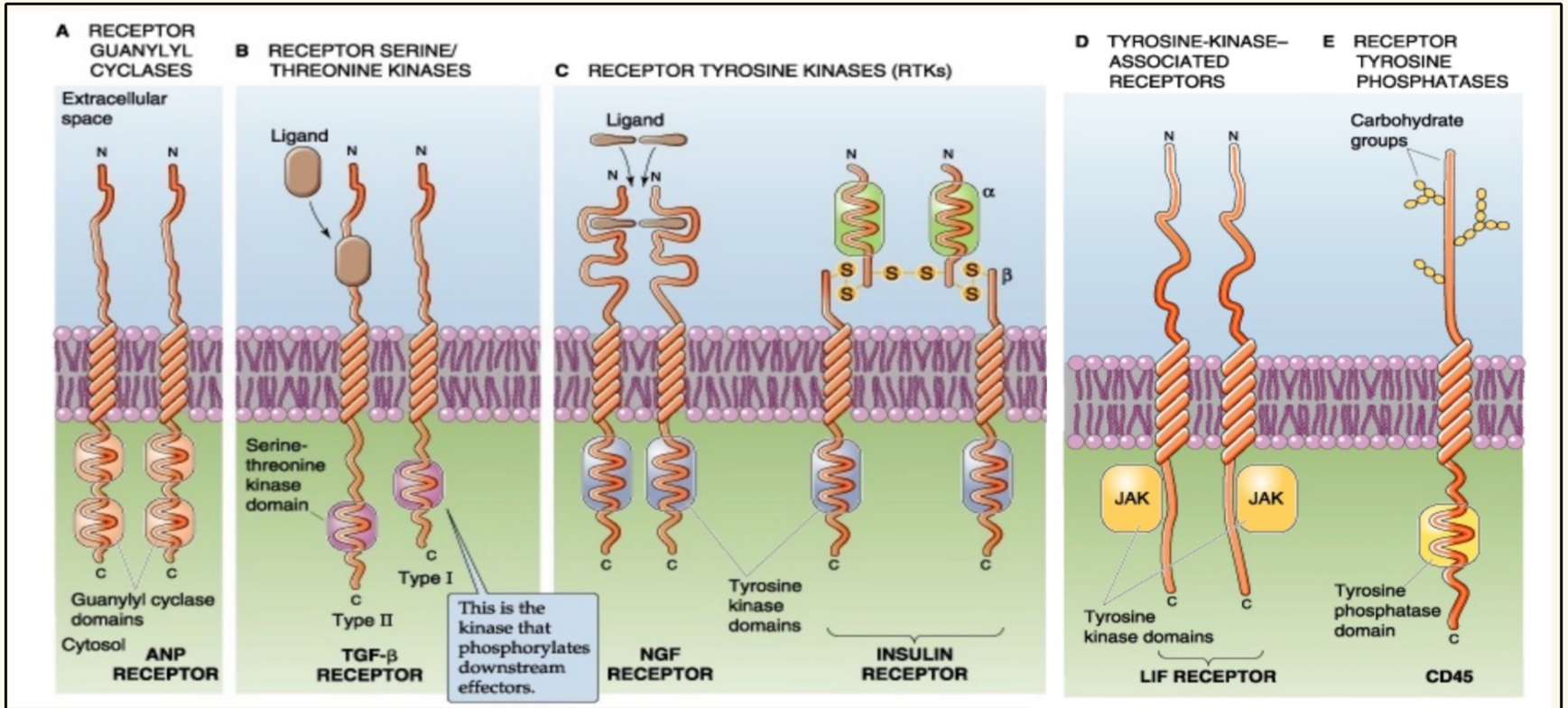
Nitric oxide pathway



Activates Protein kinase G

↓ Decreases Ca^{+2} causing muscle relaxation

Guanylyl cyclase = Guanylate cyclase



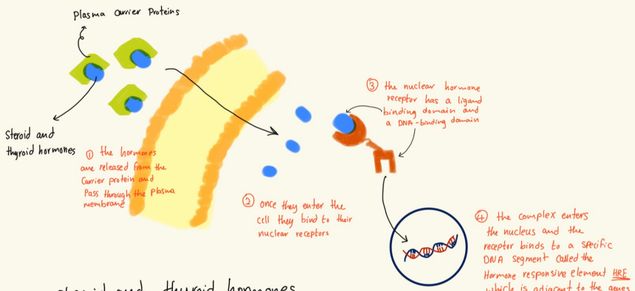
Note :-

→ tyrosine kinases phosphorylate tyrosine residues on target proteins

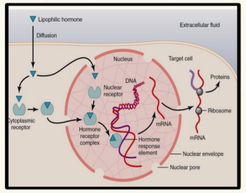
→ serine / Threonine kinases phosphorylate serine / Thrionine residues on target proteins

Nuclear Receptors

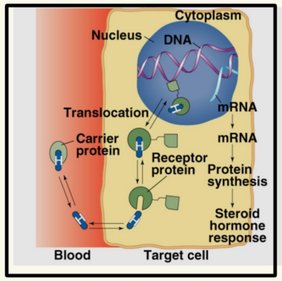
↳ Receptors that cause gene transcribtion (genomic effect)



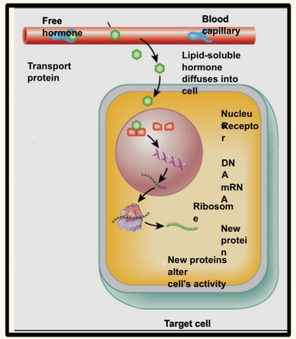
Steroid and thyroid hormones receptors general mechanism



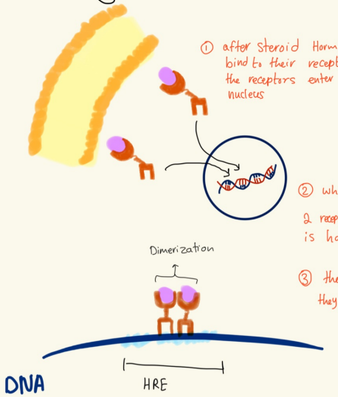
Nuclear receptor – the receptor is in the cytoplasm



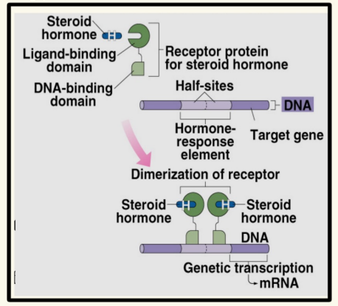
Nuclear receptor – the receptor is in the nucleus



① Steroid Hormones action

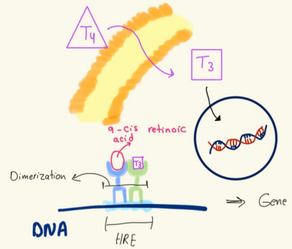


Steroid hormone receptor

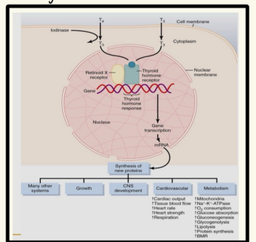


② thyroid hormone action

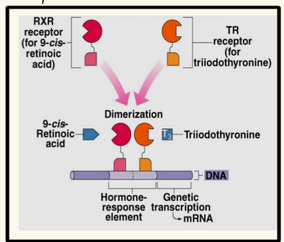
① T_4 (Prohormone) is converted into T_3 (Hormone) in the cytoplasm
② T_3 binds to the ligand binding domain of its receptor that is in the nucleus
* * * Vitamin A derivative (9 cis-retinoic acid) is the half side of the hormone-receptor complex
③ the 2 half sides Dimerize and bind to the HRE
④ gene transcribtion is then stimulated



thyroid hormone's effect

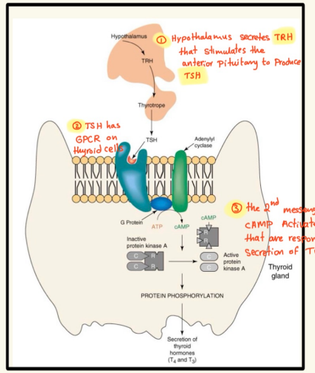


thyroid hormone receptor

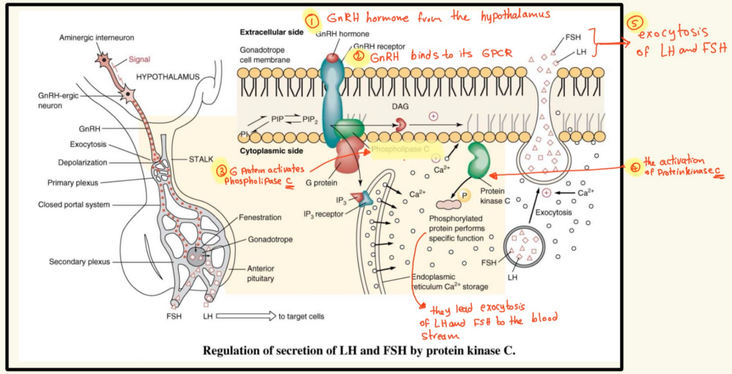


Regulation of some enzymes

TSH stimulates the Production and release of thyroid hormones



Regulating LH and FSH Secretion by Protein Kinase C



Regulation of secretion of LH and FSH by protein kinase C.

First messenger

First messenger from outside to inside

Second messengers work inside the cell

Second messenger

intracellular effects

Third messengers go from inside to outside the nucleus and vice versa

Third messenger

Third messenger