



Pharmacodynamics2

By

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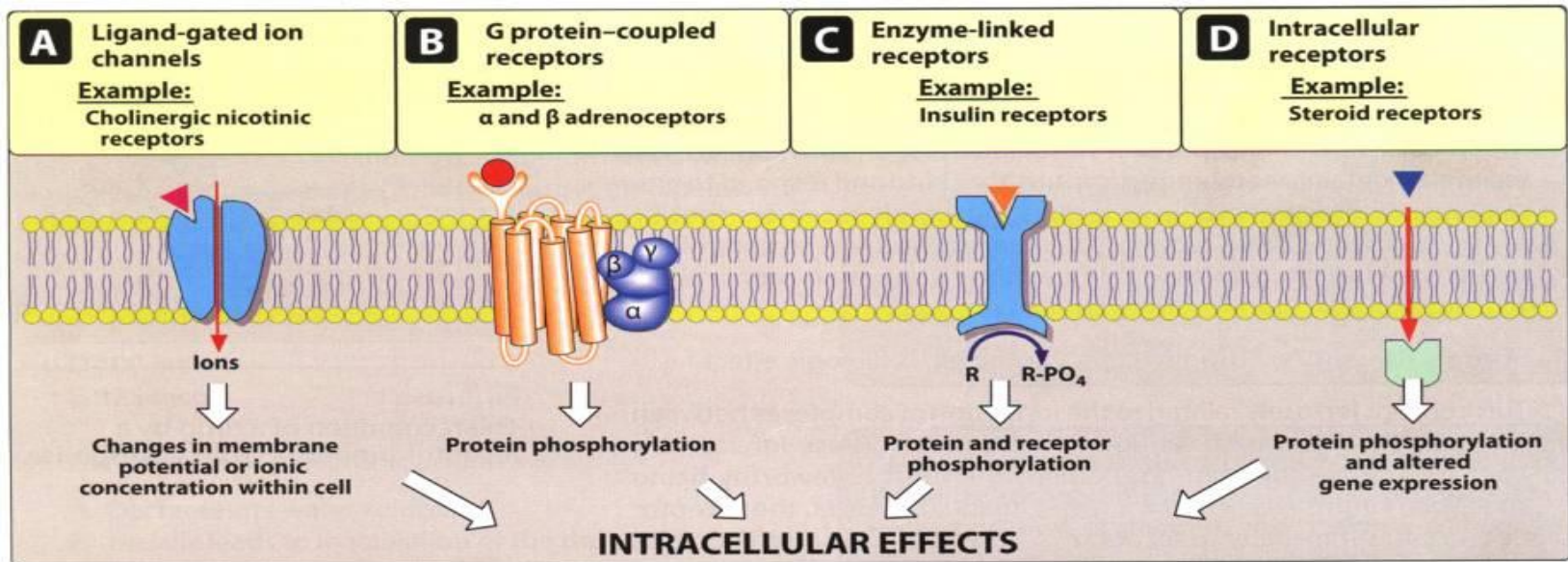


ILOS



- Define receptors
- Outline different types of receptors and mention examples

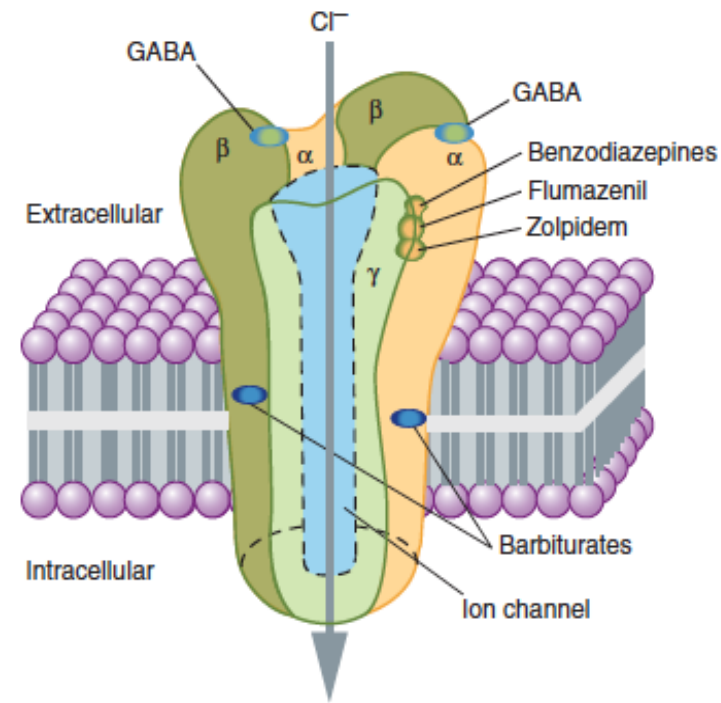
Types of receptors and signal transduction mechanism



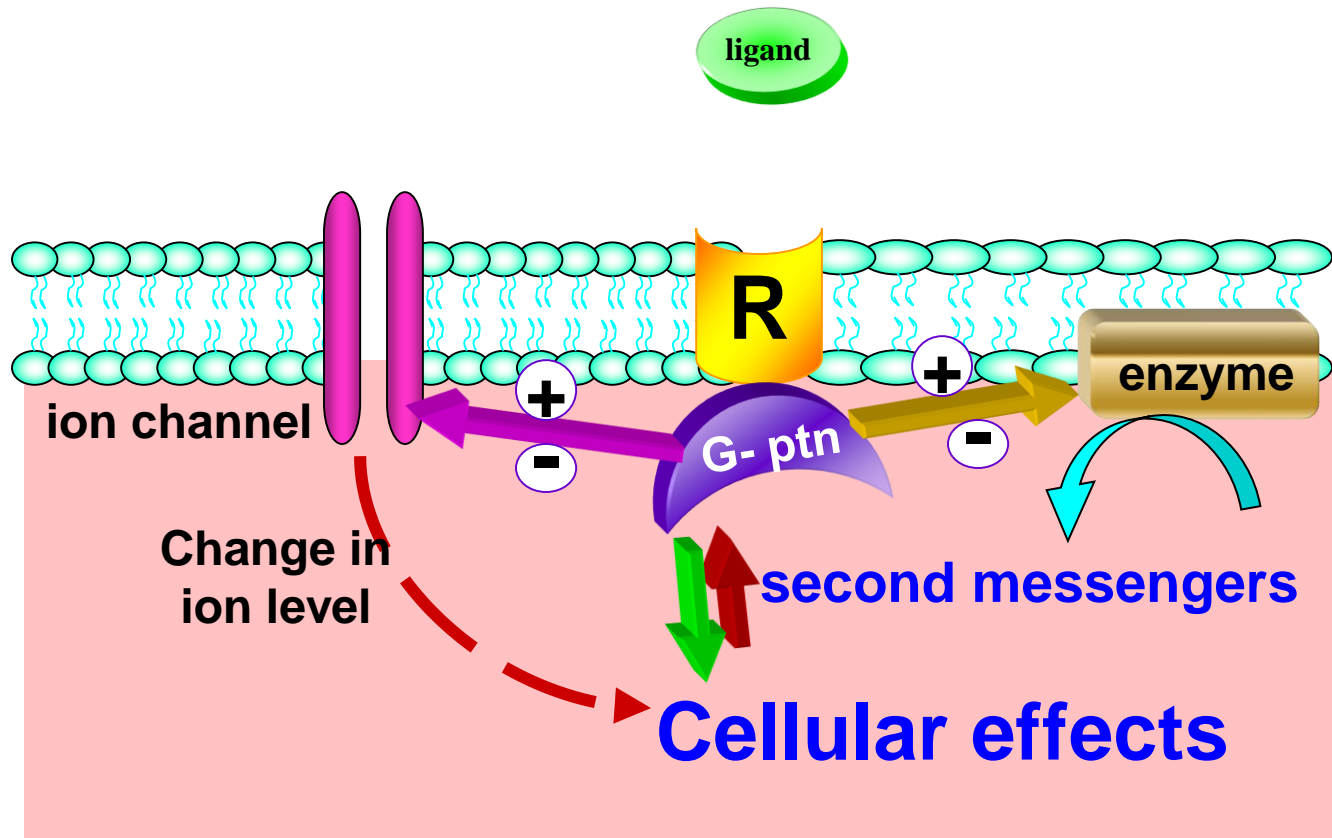
- A) Ligand binds to the **extracellular domain of a ligand-gated ion channel**.
- B) Ligand binds to a domain of a **transmembrane receptor, which is coupled to a G protein**.
- C) Ligand binds to the **extracellular domain of a receptor that activates a kinase enzyme**.
- D) Lipid-soluble ligand diffuses across the membrane to **interact with its intracellular receptor**.

A) Ligand gated ionic channel receptors:

- They are **membrane receptors** located on the gate of ionic channels.
- **Binding of the ligand** to the receptor will lead to a **conformational change in the receptor** and **change in cell membrane permeability to ions**.
- **Milliseconds** between binding of the ligand and cellular response
- **Examples:**
 - Acetylcholine (A.Ch) + Nicotinic receptors $\Rightarrow \uparrow \text{Na}^+$ influx \Rightarrow depolarization.
 - GABA + GABA_A receptors $\Rightarrow \uparrow \text{Cl}^-$ influx \Rightarrow hyperpolarization

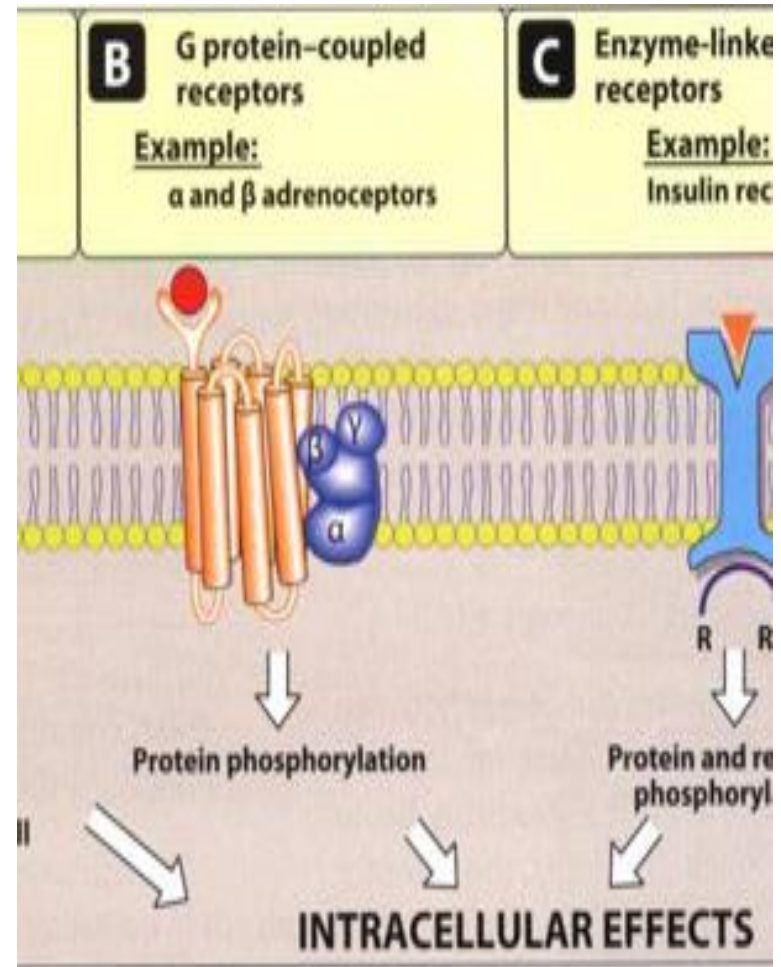


B)G. protein-coupled receptors and second messengers:



B) G. protein-coupled receptors and second messengers:

- The G-protein is a membrane protein comprising three subunits (α , β , γ)
- G-proteins either:
 - Regulate intracellular 2nd messengers (α -subunits with GTPase activity) or
 - Control opening of ion channels (β , γ - subunits)
- There are different G α subunits (G α_s - G α_i - G α_q)
- Few seconds - minutes between binding of the ligand and the cellular response.



Examples of G-protein coupled receptors

- **Adrenaline + β receptors** → **G α s-protein** → **stimulation** of AC → increase of cAMP concentration
- **Adrenaline + α 2 receptors** → **G α i-protein** → **inhibition** of AC → decrease of cAMP concentration
- **A.Ch + M1&3- receptors** → **G α q-protein** → stimulation of Phospholipase C enzyme → Inositol triphosphate (IP3) & Di-acyl glycerol (DAG) → Ca²⁺ + Calmodulin → Response.
- **Acetylcholine + M2-receptors** → **G $\beta\gamma$** → **K⁺ Efflux** → Hyperpolarization



C) Enzyme (Tyrosine kinase)-linked receptors:

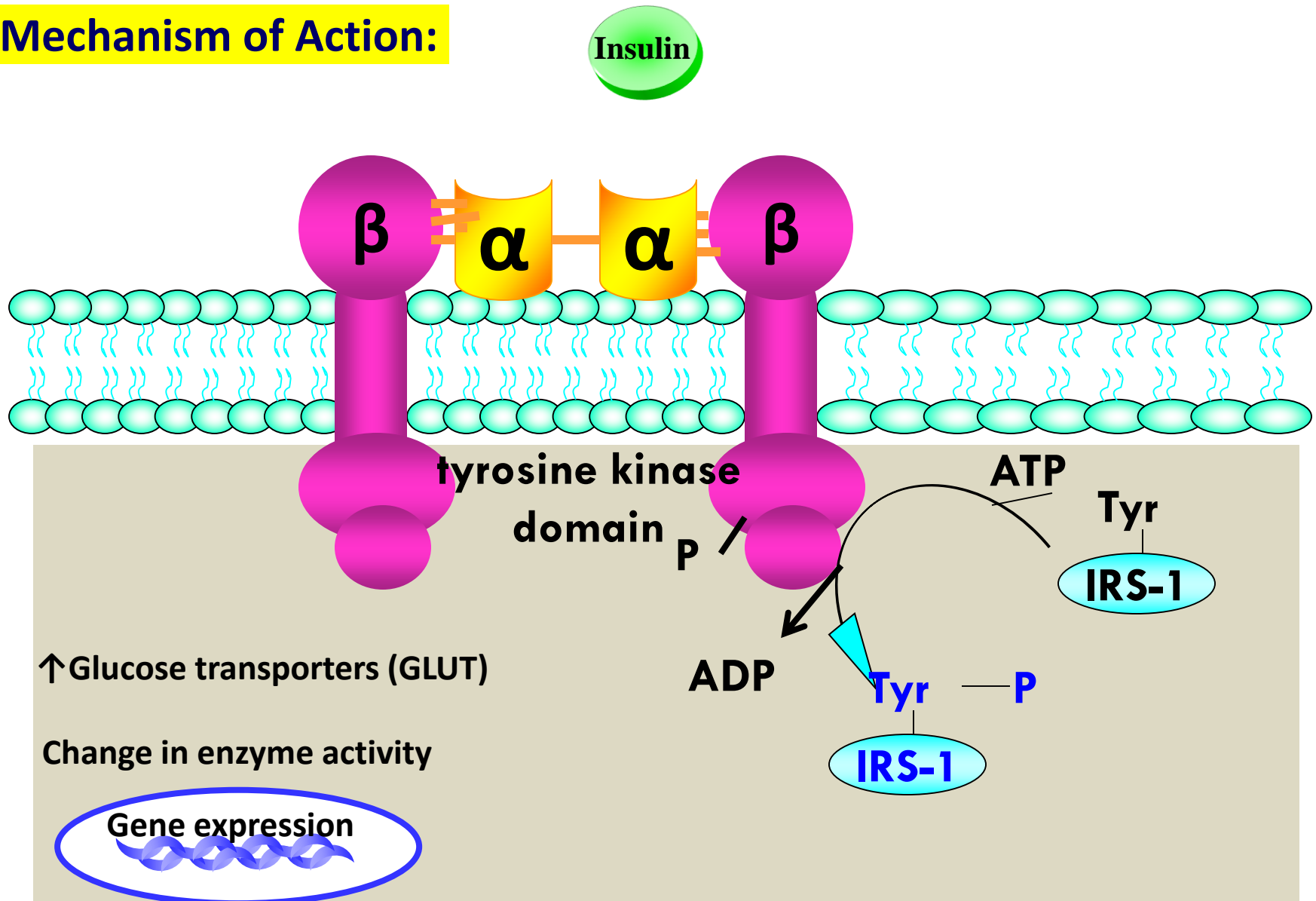
- They are **polypeptide receptors** consisting of an **extracellular ligand-binding domain** (to which insulin or growth hormone binds). It is connected to **cytoplasmic enzymatic domain** containing tyrosine kinase enzyme, which when activated will phosphorylate and activate:

i. Signal transducer → **Non-genomic actions** →
Seconds – Minutes e.g. hypoglycemia of insulin.

ii. Activator of transcription that will separate from the receptor to cross the nuclear membrane and modulate gene transcription → **Genomic actions** → **Hours e.g. anabolic effect of insulin and growth hormone.**

Tyrosine- kinase linked receptors

Mechanism of Action:



D) Gene-active intracellular receptors (DNA linked receptors):

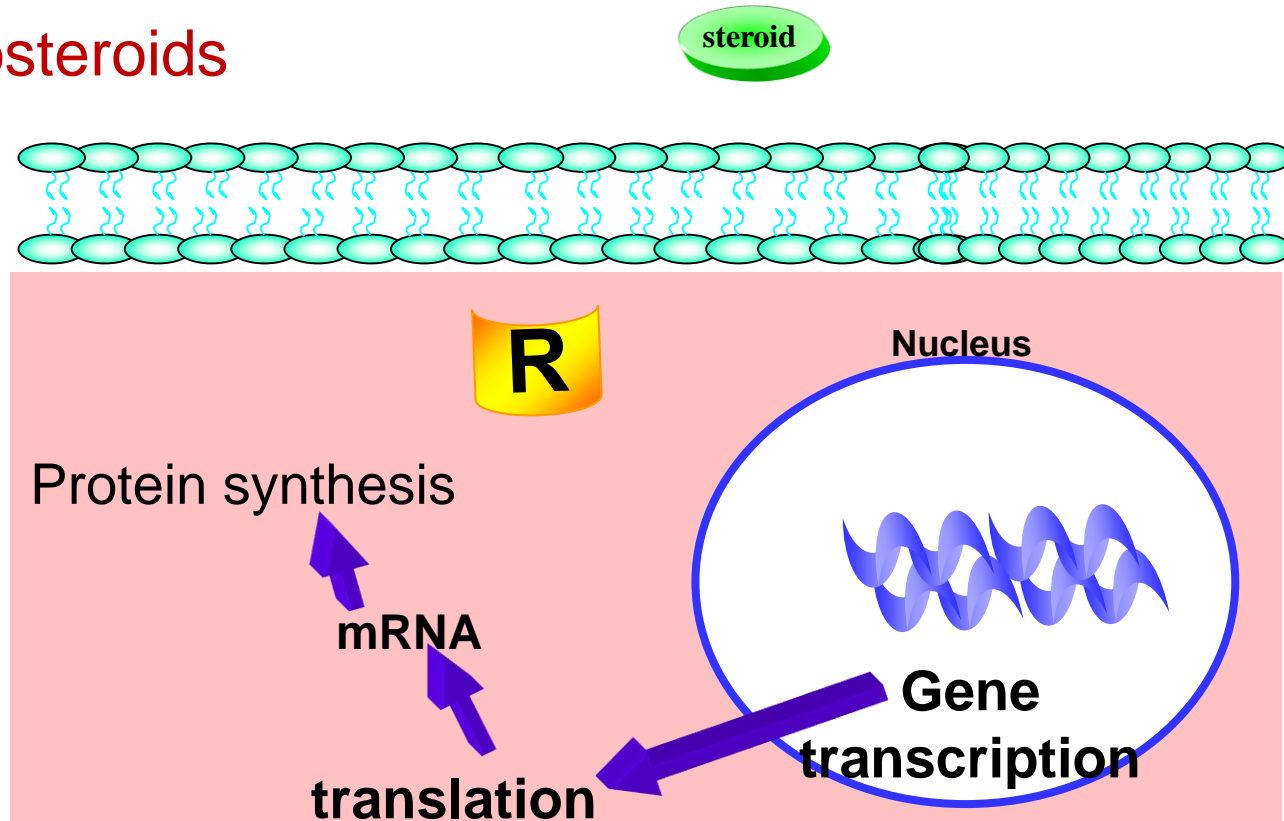
- They are cytosolic or nuclear receptors that modulate the transcription of genes in the nucleus leading to change in protein synthesis.

e.g. **Lipid soluble ligands (steroid hormones, thyroxine, vit. D) + Intracellular receptors → DNA transcription → mRNA → change in protein synthesis.**

- **Delayed lasting effect (hours between binding of the ligand and cellular response).**

D) Gene-active intracellular receptors (DNA linked receptors):

- corticosteroids





Questions



1-Mention different types or receptors.

2-Explain :

Rapid onset of action of neurotransmitters.

3- Discuss mechanism of action of steroid.



THANK YOU

