G-Protein–Coupled Receptors (

Receptor:

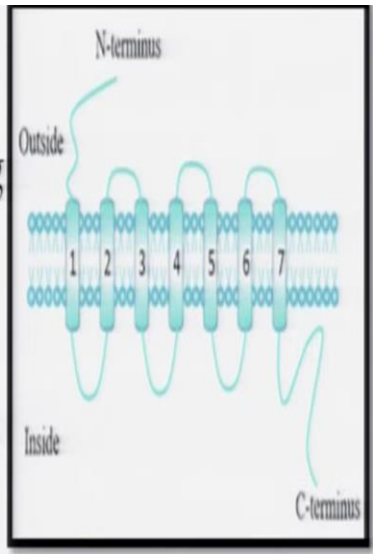
- ✓ Receptors are proteins found on the cell surface, cytoplasm or nuclear membrane to which specific molecules such as neurotransmitters, hormones or other ligands will bind and initiate the cellular response

G-Protein–Coupled Receptor:

- ✓ It is also called GPCR.
- ✓ GPCR is also called as Serpentine receptor
- ✓ It is 7 trans membrane /metabotropic
- ✓ It is a cell surface receptor.

G-Protein–Coupled Receptor (Contd..):

- ✓ The molecule has 7 α-helical membrane spanning hydrophobic amino acid (AA) segments
- ✓ GPCR has 6 loops- 3 intracellular ,3 extracellular.

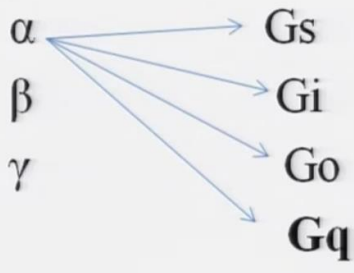


- ✓ The agonist binding site is located somewhere between the helices on the extracellular face, while another recognition site formed by cytosolic segments (in side the cell membrane)

Some of the examples of GPCR are

- ✓ Muscarinic acetylcholine receptors
- ✓ Adrenergic receptors
- ✓ Opioid receptors
- ✓ Adenosine receptors
- ✓ Histamine receptors
- ✓ Serotonin receptors(Expect 5 HT3)
- ✓ γ-amino butyric acid (GABA-B)
- ✓ Dopamine receptors,
- ✓ Glucagon receptors
- ✓ Metabotropic glutamate receptors
- ✓ Olfactory receptors.

- ✓ 30 -40% of marketing drug target site is GPCR
- ✓ These are large family of cell membrane receptors.
- ✓ G protein is trimeric composition consists of



G-protein coupled receptors (GPCRs) (Pharmacodynamics Part 9)

GPCRs are the receptors that are linked to effector (enzyme/channel/carrier protein) through G-proteins (GTP activated proteins).

GPCR is a seven transmembrane receptor

G-Protein is heterotrimeric & is made of three different subunits α, β and γ.

→ Ligand binds to GPCR.

→ GDP dissociates while GTP binds to α-subunit.

→ α-subunit detach from $\beta\gamma$ subunits & regulate target proteins

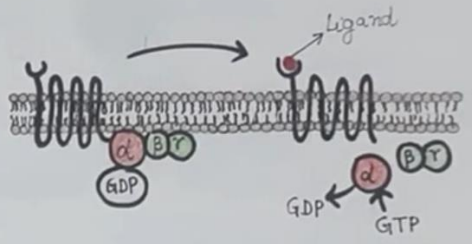
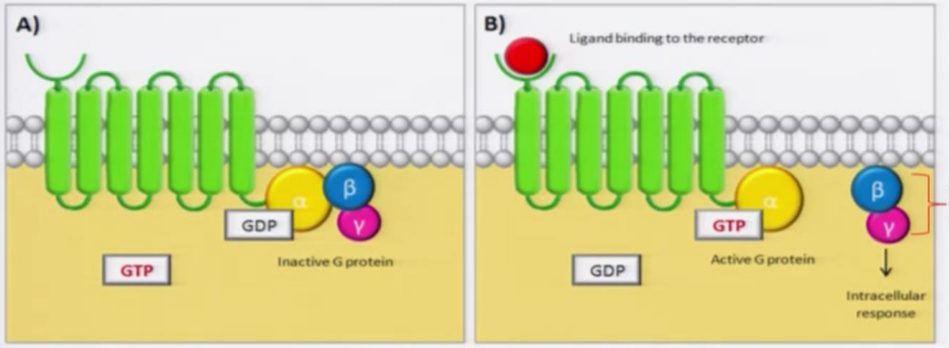


Fig: Structure of GPCR

G-proteins are classified into four families based on α-subunit

G_s	G_i	G_o	G_q
Stimulation of Adenylyl Cyclase ↓ Open Ca^{2+} channels	Inhibition of Adenylyl Cyclase ↓ Open K^+ channels	Inhibition of Calcium Channel	Activation of Phospholipase C.

Conformational changes seen when drug bind to the receptors



Also activates other proteins

G-Protein–Cou

✓Activation of receptor leads to replacement of GDP by GTP by guanine nucleotide exchange factor

G-Protein–Coupled Receptors (GPCR)

- ✓ They are two important pathway through which G.protein receptor function

A. Adenylyl Cyclase pathway(C AMP pathway)

B. Phospholipase pathway(IP3- DAG pathway)