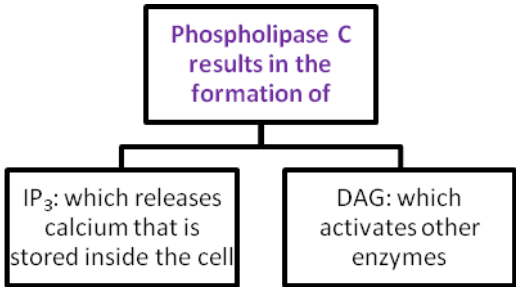
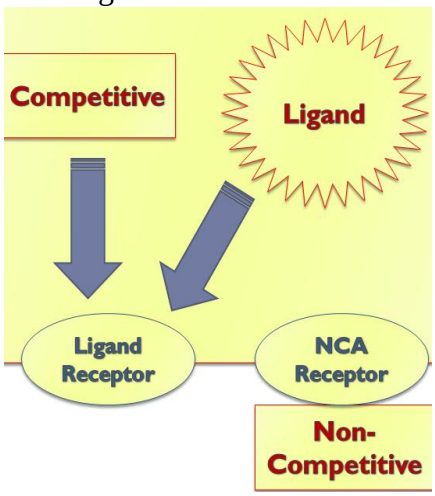
- **Pharmacodynamics**: it studies the effects of drugs on the body (what they do to the body) and this differs from pharmacokinetics which is represented by: Absorption, distribution, biotransformation (metabolism) and elimination.
- **There are four receptors which drugs can act on:**
  - **Ligand-gated ion channels**: their action is very fast (milliseconds). They are found in nicotinic receptors. For example, when two acetylcholine molecules bind to a nicotinic receptor they open sodium channels on the cell membrane of target tissues leading to influx of sodium from extracellular fluid (ECF) to intracellular fluid (ICF).
  - **G-protein-coupled receptors**: the action of these receptors is also rapid (seconds). These receptors are coupled with other proteins such as G_s-protein (which will stimulates the target enzyme when activated) and G_i-protein (which will inhibit the target enzyme when activated). The main mechanism by which these receptors operate is the (second messenger system):

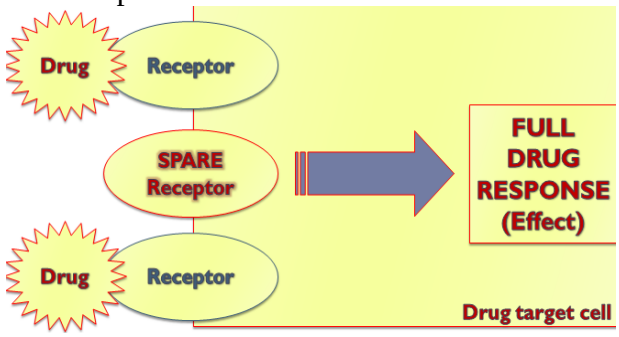


  - **Kinase-linked receptors**: the action of these receptors is slow (hours). A good example is insulin-receptor which if activated will lead to the phosphorelation of other molecules inside the cell deriving a biological effect.
  - **Nuclear receptors**: the action of these receptors is also slow (hours). Steroids are considered as a good example. They penetrate cells directly because they are lipid-soluble. Then, they bind to their receptors which are found in the nucleus and this complex will attach to the DNA leading to transcription and translation of new enzymes.
- **Compare between affinity and efficacy.**
  - Affinity is the strength of attraction between a drug and its receptor while efficacy is the maximum effect which a drug can reach. Affinity of a drug to its receptor is affected by the following factors:
    - ✓ Molecular size.
    - ✓ Molecular shape.
    - ✓ Electrical charge.
- **What is an agonist?**
  - It is a substance or molecule that will activate a receptor leading to a full response. If the response is not full, then it is called a partial agonist.
- **What is an inverse agonist?**
  - It is a substance or molecule that will bind to a receptor leading to an opposite response.
- **What are antagonists?**
  - They are substances or molecules which will bind to the receptor and prevent agonists from binding to it. Therefore, this will inhibit the action of agonists on the receptor.
    Antagonists are of two types:
    - ✓ Competitive: they will bind to the same site in the receptor which an agonist binds to (thus affinity of the receptor to the agonist will decrease). Notice that increasing the amount of agonists can result in displacement of competitive antagonists.

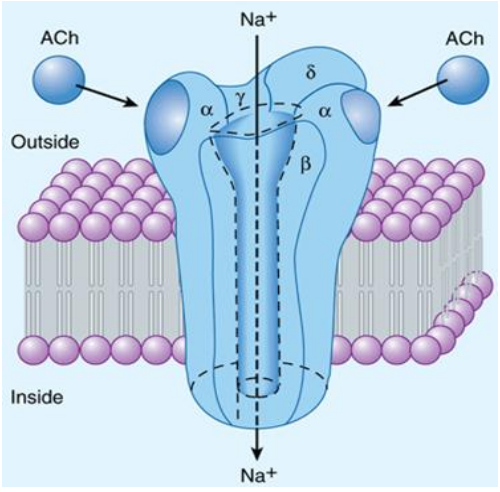
✓ Non-competitive: they will bind to the receptor on another site than the active site (which an agonist binds to) leading to conformational changes (thus efficacy will be decreased). Increasing the amount of agonists will not displace non-competitive antagonists.



- **What are spare receptors?**
  - These receptors are found when a drug acts on tissues to produce the maximum effect without using all of the receptors which are available.



- **Upregulation vs. downregulation:**
  - **Upregulation**: when the body is exposed to a lot of antagonists, the body will respond by increasing the number of receptors and their sensitivity to prevent harmful effects of blocking the receptors by antagonists.
  - **Downregulation**: when the body is exposed to a lot of agonists, the body will respond by decreasing the number of receptors and their sensitivity to prevent harmful effects of over-activation by agonists.
- **Ion channels are divided into:**
  - **Voltage-gated channels**: they are opened when there is a change in membrane potential.



  - **Ligand-gated channels**: an agonist such as acetylcholine must bind to the channel to open it.

- **What is the mechanism of action of local anesthetics?**
  - They block sodium (Na^+) –channels present on the membrane of neurons, so even if there is a stimulus, sodium channels will remain closed and the patient will feel nothing.
- **Some drugs and enzymes which they act on:**
  - **Aspirin**: cyclooxygenase.
  - **Orlistat**: lipase.
  - **Fomepizole**: alcohol dehydrogenase.
  - **Organophophates**: acetycholine esterase.

- **DOSE-RESPONSE RELATIONSHIPS:**
  - **Graded-dose**: it means that different doses will be administered to the same patient or tissue over time and response will be visualized.
  - **EC_{50}**: it is the dose which will give 50% of the maximum effect.
  - **Potency**: It is related to different EC_{50} of different drugs (low EC_{50}: the drug is more potent).
  - **Efficacy**: different drugs have different maximum effects.
  - **Quantal dose**: it means that the same dose will be given to a certain population instead of an individual. Response is measured among this population.
  - **Theraputic index:**
    - ✓ **In animals = $\frac{LD_{50}}{ED_{50}}$ (if more than 1: the drug is effective)**
      - ❖ *LD_{50}:* it is lethal dose by which 50% of the animals will die.
      - ❖ *ED_{50}:* It is the effective dose by which 50% of the animals will show the desired effect.
    - ✓ **In humans = $\frac{TD_{50}}{ED_{50}}$**
      - ❖ *TD_{50}:* it is the toxic dose by which toxicity will occur in 50% of the population.