

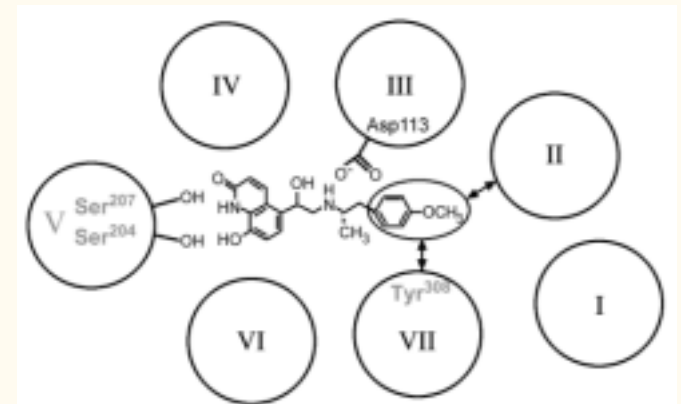
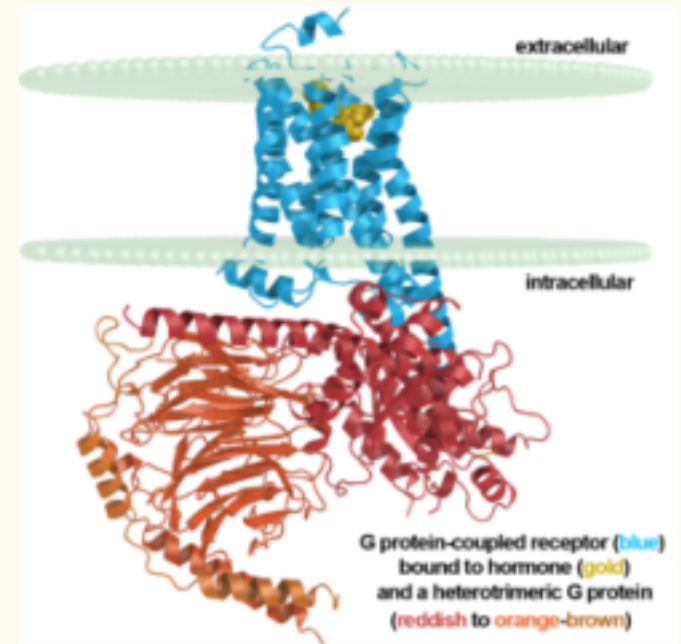
β -2 Adrenergic Receptor

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By Meghan Williams and Jack Nguyen

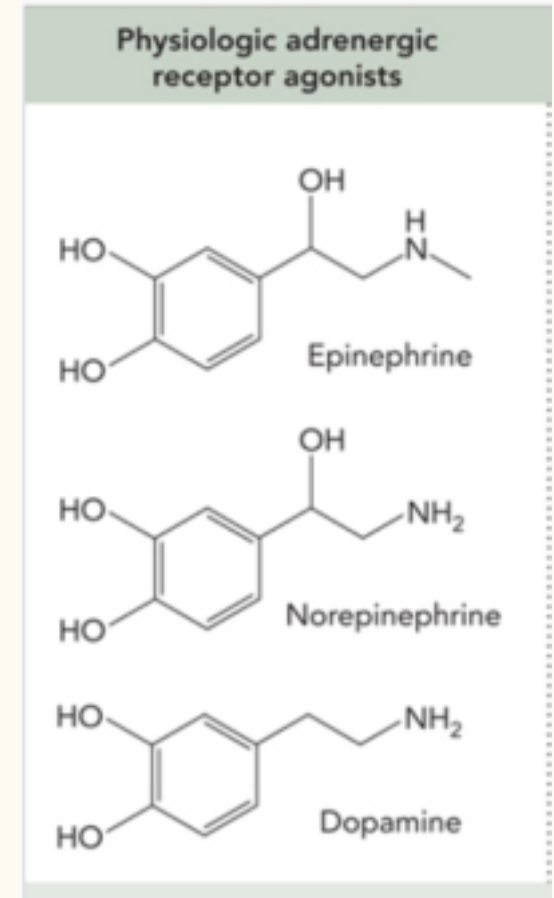
Class and Structure

- GPCR
- 7 transmembrane domains: α helices and loops
 - 3 extracellular loops
 - 3 intracellular loops
 - PKA phosphorylates the 3rd loop and cytoplasmic tail (Ser 207 and Ser 204)
 - Domain 7 involved in high specificity binding (Tyr 308)



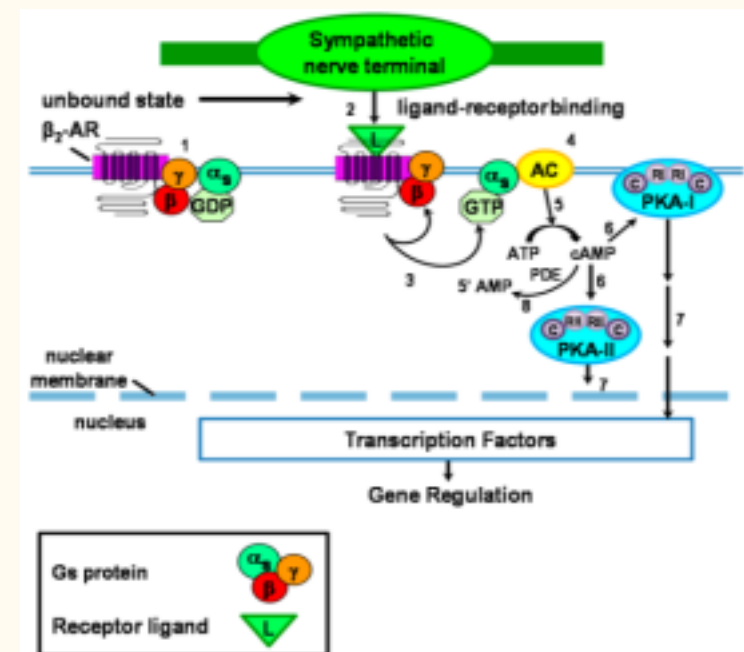
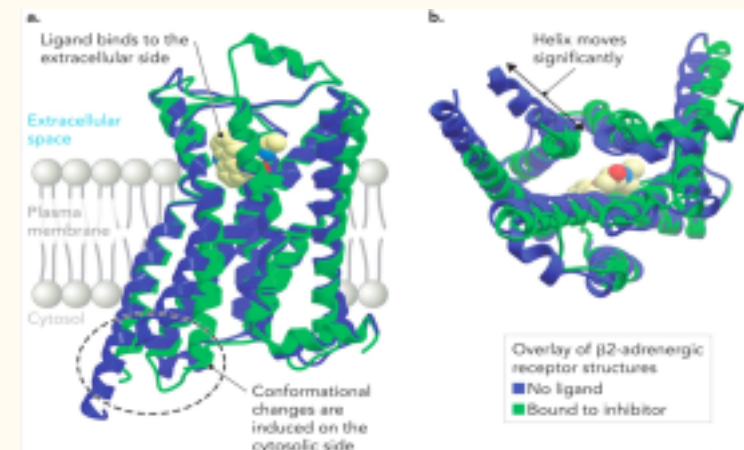
The ligands

- Epinephrine (adrenaline) and Norepinephrine (noradrenaline): fight or flight
 - Catecholamine 1st messengers
 - released from adrenal medulla during times of acute stress
 - Cause: relaxation of smooth muscle (bronchodilation) and release of glucose to bloodstream
- Dopamine
 - Catecholamine 1st messenger
 - Activates pathway similarly
- Epinephrine>Norepinephrine>Dopamine



Activation

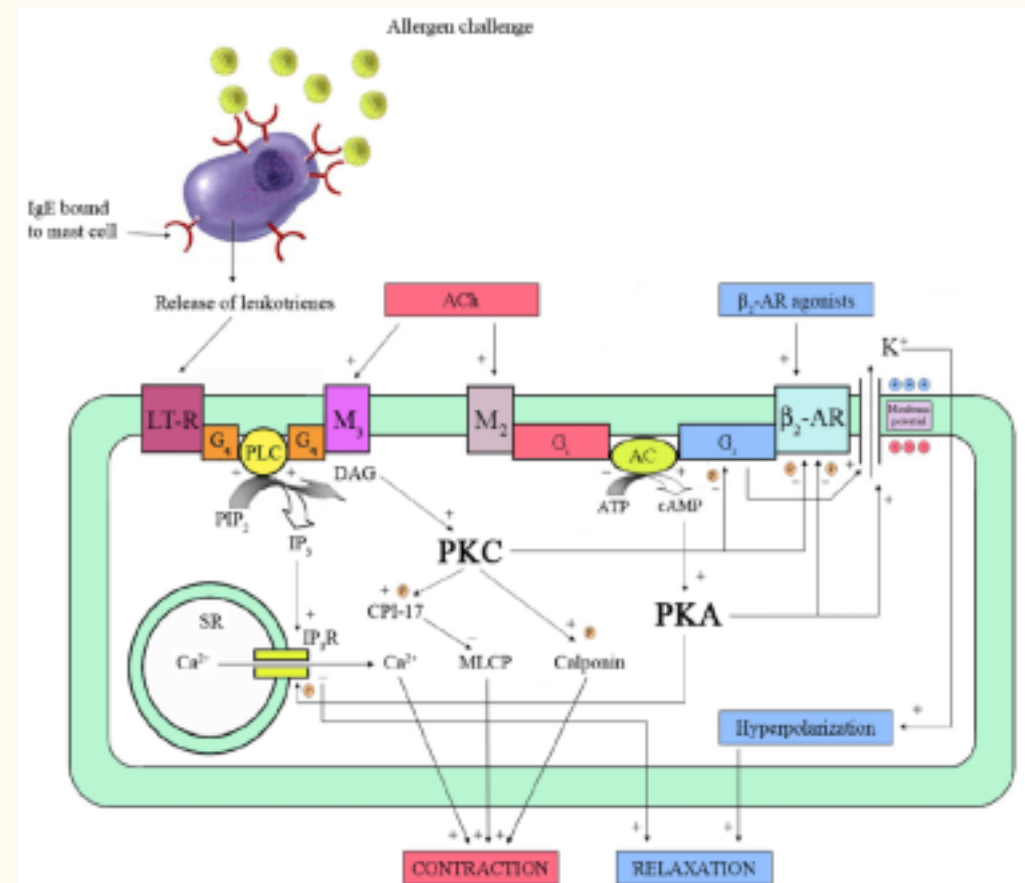
1. Ligand binds & exchanges GDP→GTP causing a conformational change in switch II helix of Gsa
2. Gsa separates and stimulates AC.
3. AC stimulates the production of cAMP.
4. cAMP activates PKA.
5. PKA phosphorylates target proteins which trigger specific responses depending on body location.



Bronchioles Downstream Mechanism

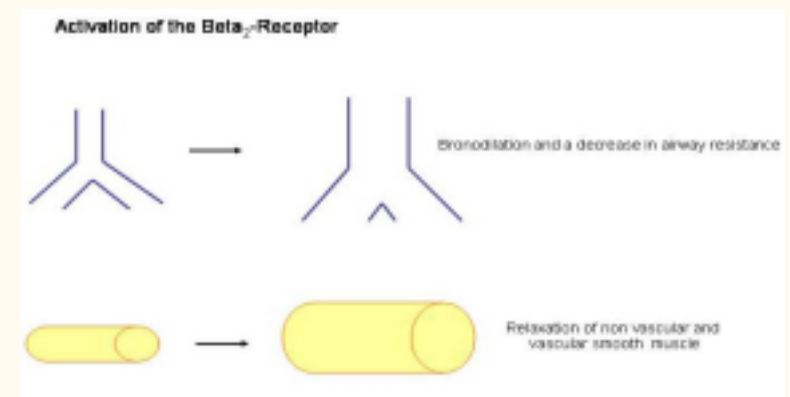
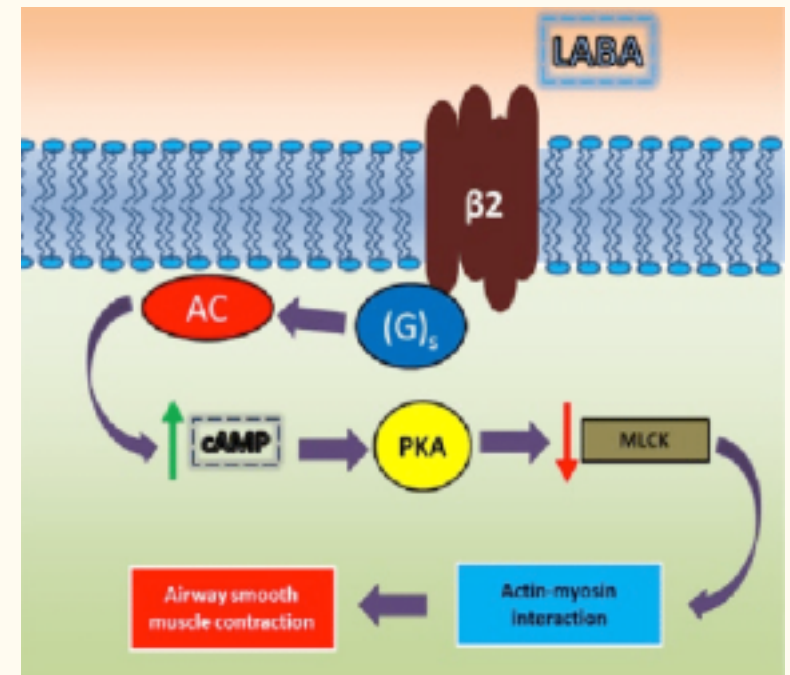
6. PKA then:

- inhibits myosin-light-chain kinase (MLCK) and phosphoinositide hydrolysis
- Promotes $\text{Ca}^{2+}/\text{Na}^{+}$ exchange thus decreasing Ca^{2+} in smooth muscle cells allowing muscles to relax
- Stimulates $\text{Na}^{+}/\text{K}^{+}$ ATPase



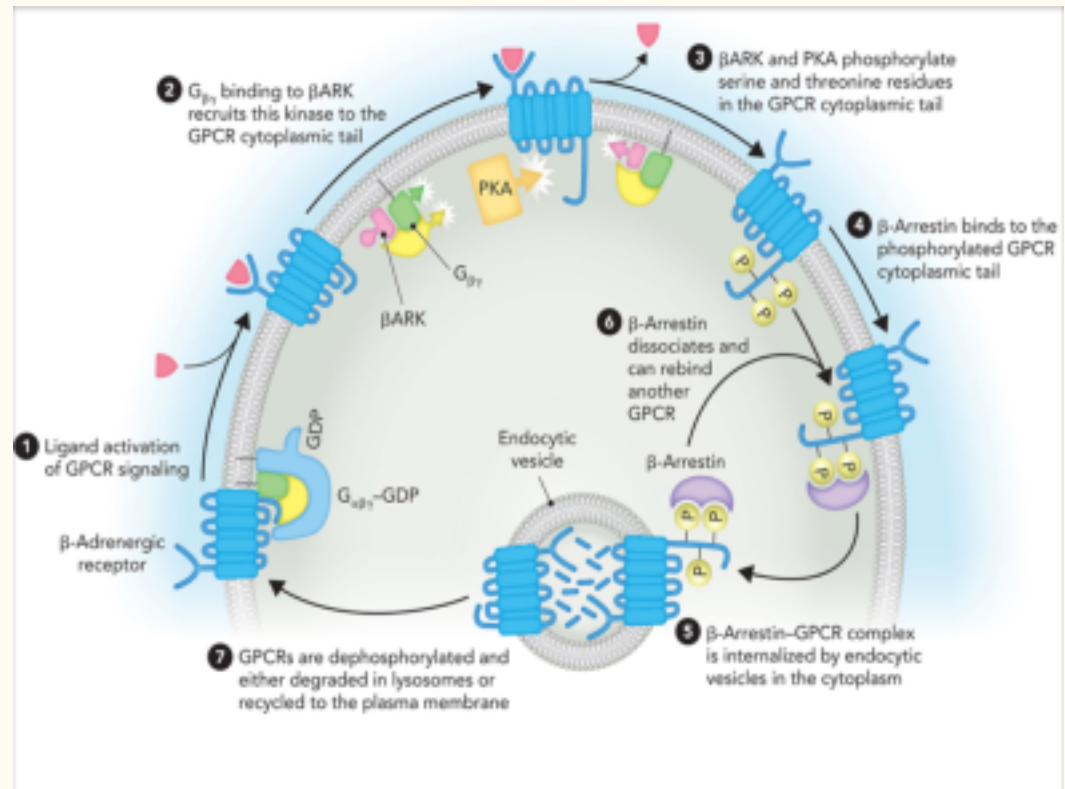
Function

- In smooth muscle → relaxation
 - Lungs = bronchodilation
 - Gut = pause digestion by stopping peristalsis
 - Note: LABA is a long-acting beta-agonist drug (such as formoterol and salmeterol) used to treat asthma
- In the liver
 - Stop glycogen synthesis
 - Start glycogen breakdown to glucose
 - Start glucose synthesis



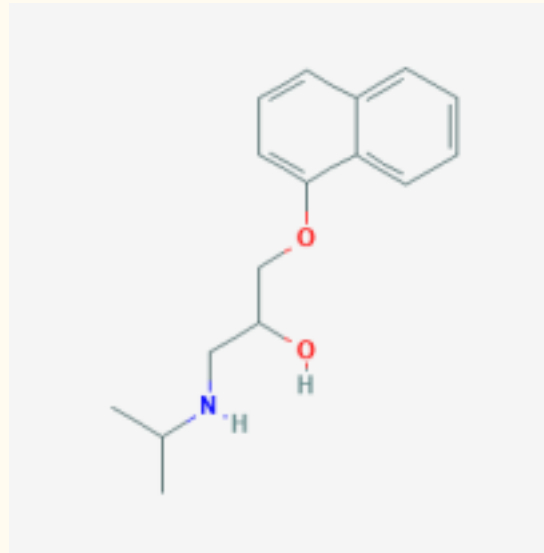
Inhibition: β -arrestin

1. β ARK recruited to membrane by $G\beta\gamma$
2. β ARK & PKA phosphorylate cytoplasmic tail
3. β -arrestin binds
4. Receptor internalized
5. β -arrestin dissociates
6. Phosphates removed
 - a. Recycled to plasma membrane
 - b. Degraded by lysosomes



Inhibition Cont.

- The B-2 Adrenergic Receptor can be inhibited by a class of drugs called beta blockers.
- Beta blockers competitively competes with agonists like Epinephrine for the binding site.
 - Ex. Propranolol



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Questions?