ß2-ADRENERGIC RECEPTOR

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WHAT IS A β2-ADRENERGIC RECEPTOR (β2-AR)?

• β2-AR is a type of G protein-coupled Receptor.

• G-PCRs contain 7 transmembrane alpha helices.
2β-AR CYCLE SUMMARY

1. Ligand Specificity
2. Ligand Binding
3. Message Amplification
4. Message is Turned Off
5. Receptor is Recycled
1. LIGAND SPECIFICITY

- Epinephrine (adrenaline)
- Norepinephrine (noradrenaline)
- Dopamine
- Albuterol (β2-AR agonist)
2. LIGAND BINDING

A. Epinephrine binds to β2-AR.
B. This causes a conformational change in the receptor that induces Ga to release GDP and then bind to GTP.
   A. Gsa is specific to β2-AR
C. This causes the dissociation of Ga from Gβγ and the activation of both Ga and Gβγ.
D. Ga binds to Adenylate Cyclase and stimulates the production of cAMP.
2. LIGAND BINDING
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3. MESSAGE AMPLIFICATION

- Adenylate Cyclase cAMP production from ATP is increased.
- Four cAMP molecules bind to the R2C2 tetramer.
- PKA is activated. This leads to:
  1. Inhibition of glycogen synthesis
  2. Activation of glycogen degradation
  3. Activation of glucose synthesis

- **Net Result = Glucose export**
3. MESSAGE AMPLIFICATION
4. MESSAGE IS TURNED OFF

• β-adrenergic receptor kinase (βARK) is attracted to the membrane by GβY and binds to it.
• βARK phosphorylates β2-AR at the C-terminus (Ser and Thr).
  • PKA can also phosphorylate the β2 receptor.
• β-Arrestin binds to the phosphorylated C-terminal domain of the protein.
• An endocytic vesicle forms around the receptor via membrane invagination.
4. MESSAGE IS TURNED OFF
WHAT ABOUT GA SIGNAL TERMINATION?

- A GAP binds to Ga-GTP complex.
- This stimulates Ga to hydrolyze GTP to GDP.
  - The GAP leaves

- Gaβγ reassociates with a GPCR
5. RECEPTOR IS RECYCLED (OR NOT)

The receptor is dephosphorylated and sent back to the plasma membrane (or sent to the lysosome).
RECALL: THE B2-AR SHARES THE SAME EXACT PATHWAY AS THE GLUCAGON RECEPTOR
WHY DOES THE B2-ADRENERGIC RECEPTOR HAVE A DIFFERENT EFFECT THAN THE GLUCAGON RECEPTOR EVEN THOUGH THEY SHARE THE SAME PATHWAY?
• Different tissues respond to different hormones based on receptor type, receptor location, and what is targeted.
  • Skeletal muscles have on epinephrine receptors, but they don't have glucagon receptors.
    • The liver, however, has both epinephrine and glucagon receptors.
  • Different enzymes are available for the same kinase
    • Glycogen breaks down into lactate in muscles and lactate is released into the blood.
    • Glycogen breaks down into glucose in the liver and glucose is released into the blood.
REFERENCES


ANY QUESTIONS?