Beta-2 adrenergic receptor

The **beta-2 adrenergic receptor** (β_2 adrenoreceptor), also known as **ADRB2**, is a cell membrane-spanning beta-adrenergic receptor that interacts with (binds) epinephrine, a hormone and neurotransmitter (ligand synonym, adrenaline) whose signaling, via a downstream L-type calcium channel interaction, mediates physiologic responses such as smooth muscle relaxation and bronchodilation. Unlike other adrenergic receptors, norepinephrine does not produce β_2 receptor stimulation.

The official symbol for the human gene encoding the β_2 adrenoreceptor is ADRB2.[3]

1 Gene

The *ADRB2* gene is intronless. Different polymorphic forms, point mutations, and/or downregulation of this gene are associated with nocturnal asthma, obesity and type 2 diabetes.[4]

2 Structure

The 3D crystallographic structure (see figure and links to the right) of the β_2-adrenergic receptor has been determined[5][1][2] by making a fusion protein with lysozyme to increase the hydrophilic surface area of the protein for crystal contacts.

3 Mechanism

This receptor is directly associated with one of its ultimate effectors, the class C L-type calcium channel CaV1.2. This receptor-channel complex is coupled to the G_s G protein, which activates adenylyl cyclase, catalysing the formation of cyclic adenosine monophosphate (cAMP) which then activates protein kinase A, and the counterbalancing phosphatase PP2A. The assembly of the signaling complex provides a mechanism that ensures specific and rapid signaling. A two-state biophysical and molecular model has been proposed to account for the pH and REDOX sensitivity of this and other GPCRs.[6]

Beta-2 Adrenergic Receptors have also been found to couple with G_i, possibly providing a mechanism by which response to ligand is highly localized within cells. In contrast, Beta-1 Adrenergic Receptors are coupled only to G_s, and stimulation of these results in a more diffuse cellular response.[7] This appears to be mediated by cAMP induced PKA phosphorylation of the receptor.[8]

4 Function

Actions of the β_2 receptor include:

4.1 Muscular system

4.2 Circulatory system

- Heart muscle contraction
- Increase cardiac output (minor degree compared to β_1).
  - Increase heart rate [11] in sinoatrial node (SA node) (chronotropic effect).
  - Increase atrial cardiac muscle contractility. (inotropic effect).
  - Increases contractility and automaticity[11] of ventricular cardiac muscle.
- Dilate hepatic artery.
- Dilate arterioles to skeletal muscle.

4.3 Eye

In the normal eye, beta-2 stimulation by salbutamol increases intraocular pressure via net:

- Increase in production of aqueous humour by the ciliary process,
- Subsequent increased pressure-dependent uveoscleral outflow of humour, *despite* reduced drainage of humour via the Canal of Schlemm.

In glaucoma, drainage is reduced (open-angle glaucoma) or blocked completely (closed-angle glaucoma). In such cases, beta-2 stimulation with its consequent increase in humour production is highly contra-indicated, and conversely, a topical beta-2 antagonist such as timolol may be employed.

4.4 Digestive system

- Glycogenolysis and gluconeogenesis in liver.[11]
- Glycogenolysis and lactate release in skeletal muscle.[11]
- Contract sphincters of GI tract.
- Thickened secretions from salivary glands.[11]
- Insulin secretion from pancreas

4.5 Other

- Inhibit histamine-release from mast cells.
- Increase protein content of secretions from lacrimal glands.
- Increase renin secretion from kidney.
- Receptor also present in cerebellum.
- Bronchiole dilation (targeted while treating asthma attacks)
- Involved in brain - immune - communication [13]

5 Agonists

Main article: $Beta_2$-adrenergic agonist

- spasmolytics in asthma and COPD
- Short acting beta agonist (SABA)
  - Salbutamol (albuterol in USA)
  - Terbutaline
  - Bitolterol mesylate
  - Isoproterenol
  - Levosalbutamol (levalbuteral in USA)
  - Ritodrine (tocolytic)
  - Orciprenaline Sulfate / Metaproterenol
- Long lasting beta agonist (LABA)
  - Formoterol
  - Salmeterol
  - Clenbuterol
- Ultra long lasting beta agonist (LABA)
  - Arformeterol
  - Carmoterol
  - Indacaterol
  - GSK-159797, −597901, −159802, −642444 and −678007

6 Antagonists

(Beta blockers)

- butoxamine*[10]
- First generation (non-selective) β-blockers
- ICI-118,551

* denotes selective agonists to the receptor.

7 Interactions

Beta-2 adrenergic receptor has been shown to interact with:

- AKAP12,[14][15]
- OPRD1,[16]
- Grb2,[17]
- SNX27[18] and
- SLC9A3R1.[19][20][21]

8 See also

- Other adrenergic receptors
  - Alpha-1 adrenergic receptor
  - Alpha-2 adrenergic receptor
  - Beta-1 adrenergic receptor
  - Beta-3 adrenergic receptor
- Discovery and development of beta2 agonists

9 References

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11 External links

- "β_2-adrenoceptor". *IUPHAR Database of Receptors and Ion Channels*. International Union of Basic and Clinical Pharmacology.

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