Adrenoceptors, α_2

Overview: α_2-Adrenoceptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Adrenoceptors; Bylund *et al*., 1994) are 7TM receptors, activated by endogenous agonists with a relative potency of adrenaline > noradrenaline. UK14304 (brimonidine) and BHT920 are agonists selective for α_2-adrenoceptors relative to α_1-adrenoceptors. Rauwolscine (9.0) and yohimbine (9.0) are antagonists selective for α_2-adrenoceptors relative to α_1-adrenoceptors. [^{3}H]-Rauwolscine (1 nM), [^{3}H]-UK14304 (5 nM) and [^{3}H]-RX821002 (0.5 nM and 0.1 nM at α_{2C}) are relatively selective radioligands. There is species variation in the pharmacology of the α_{2A}-adrenoceptor; for example, yohimbine, rauwolscine and oxymetazoline have an ~20-fold lower affinity for rat, mouse and bovine α_{2A}-adrenoceptors compared with the human receptor. These α_{2A} orthologues are sometimes referred to as α_{2D}-adrenoceptors. Multiple mutations of α_2-adrenoceptors have been described, some of which are associated with alterations in function.

Nomenclature	α_{2A}	α_{2B}	α_{2C}
Other names	α_{2D}	–	–
Ensembl ID	ENSG00000150594	ENSG00000181210	ENSG00000184160
Principal transduction	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$
Selective agonists	Oxymetazoline	–	–
Selective antagonists	BRL44408 (8.0)	ARC239 (8.0), prazosin (7.5), imiloxan (7.3)	ARC239 (8.0), prazosin (7.5)

The effects of classical (not subtype selective) α_2-adrenoceptor agonists such as clonidine, guanabenz and brimonidine (UK14304) on central baroreflex control (hyoptension; bradycardia), hypnotic, analgesic, seizure modulation and platelet aggregation are mediated by α_{2A}-adrenoceptors. The roles of α_{2B}- and α_{2C}-adrenoceptors are less clear but the α_{2B} subtype appears to be involved in neurotransmission in the spinal cord and α_{2C} in regulating catecholamine release from adrenal chromaffin cells. Oxymetazoline is a reduced efficacy agonist. Binding sites for imidazolines, distinct from α_2-adrenoceptors, have been identified and classified as I_1, I_2 and I_3 sites, but with a function other than coupling to G proteins; catecholamines have a low affinity for these sites.

Abbreviations: **ARC239**, 2-(2,4-[*O*-methoxyphenyl]-piperazin)-1-yl; **BHT920**, 6-allyl-2-amino-5,6,7,8-tetrahydro-4*H*-thiazolo-[4,5-d]-azepine; **BRL44408**, 2-(2*H*-[1-methyl-1,3-dihydroisoindole]methyl)-4,5-dihydroimidazole; **MK912**, (2*S*,12*bS*)1′,3′-dimethylspiro(1,3,4,5′,6,6′,7,12*b*-octahydro-2*H*-benzo[*b*]furo[2,3-a]quinolizine)-2,4′-pyrimidin-2′-one; **RX821002**, 2-(2-methoxy-1,4-benzodioxan-2-yl)-2-imidazoline; **UK14304**, 5-bromo-6-[2-imidazolin-2-ylamino]quinoxaline, also known as brimonidine

Further Reading

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