

Adrenoceptors, α_1

Overview: α_1 -Adrenoceptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Adrenoceptors, Bylund *et al.*, 1994) are 7TM receptors activated by the endogenous agonists adrenaline and noradrenaline with equal potency. Phenylephrine, methoxamine and cirazoline are agonists selective for α_1 -adrenoceptors relative to α_2 -adrenoceptors, while prazosin (8.5–10.5) and corynanthine (6.5–7.5) are considered selective for α_1 -adrenoceptors relative to α_2 -adrenoceptors. [³H]-Prazosin (0.25 nM) and [¹²⁵I]-HEAT (0.1 nM; also known as BE2254) are relatively selective radioligands. Numerous splice variants of the α_1 -adrenoceptors exist, some of which may display a different spectrum of signalling properties. One polymorphism of the α_{1A} -adrenoceptor has been described but is not associated with disease.

Nomenclature	α_{1A}	α_{1B}	α_{1D}
Other names	α_{1a} , α_{1c}	α_{1b}	$\alpha_{1A/D}$, $\alpha_{1a/d}$
Ensembl ID	ENSG00000120907	ENSG00000170214	ENSG00000171873
Principal transduction	G _{q/11}	G _{q/11}	G _{q/11}
Selective agonists	A61603, dabuzalgron (Blue <i>et al.</i> , 2004)	—	—
Selective antagonists	Tamsulosin (10.5), KMD3213 (10.4), (+)niguldipine (10.0), SNAP5089 (9.7)	—	BMY7378 (8.4)

The clone originally called the α_{1C} -adrenoceptor corresponds to the pharmacologically defined α_{1A} -adrenoceptor (see Ford *et al.*, 1994; Hieble *et al.*, 1995). Some tissues possess α_1 -adrenoceptors that display relatively low affinity in functional and binding assays for prazosin ($pK_i < 9$) that might represent different receptor states (termed α_{11} -adrenoceptors, Ford *et al.*, 1997; Morishima *et al.*, 2007). α_{1A} -Adrenoceptor C-terminal splice variants form homo and heterodimers, but fail to generate a functional α_{11} adrenoceptor (Ramsay *et al.*, 2004). α_{1D} -Adrenoceptors form heterodimers with α_{1B} - or β_2 -adrenoceptors that show increased cell-surface expression (Uberti *et al.*, 2005). Heterodimers formed between α_{1D} - and α_{1B} -adrenoceptors have distinct functional properties (Hague *et al.*, 2004). (+)Niguldipine also has high affinity for L-type Ca²⁺ channels.

Abbreviations: **A61603**, N-(5-[4,5-dihydro-1H-imidazol-2-yl]-2-hydroxy-5,6,7,8-tetrahydronaphthalen-1-yl)methanesulfonamide hydrobromide; **BMY7378**, 8-(2-[4-[2-methoxyphenyl]-1-piperazinyl]ethyl)-8-azaspiro[4,5]decane-7,9-dione dihydrochloride; **HEAT**, 2- β -4-hydroxy-3-iodophenylethylaminomethyltetralone; **ICI118551**, (-)-1-(2,3-[dihydro-7-methyl-1H-inden-4-yl]oxy)-3-([1-methylethyl]-amino)-2-butanol; **KMD3213**, (-)-(R)-1-(3-hydroxypropyl)-5-(2-[2-(2,2,2-trifluoroethoxy)phenoxy]ethylamino]propyl)indoline-7-carboxamide, also known as silodosin; **RS17053**, N-[2-(2-cyclopropylmethoxyphenoxy)ethyl]-5-chloro- α,α -dimethyl-1H-indole-3-ethanamide; **SNAP5089**, 2,6-dimethyl-4-(4-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate-N-[3-(4,4-diphenylpiperidin-1-yl)propyl]amide methyl ester; **SNAP5272**, carbamate-2,6-diethyl-1,4-dihydro-3-[N-(3-[4-hydroxy-4-phenylpiperidinyl]propyl)]carboxamido-4-(4-nitrophenyl)

Further Reading

- Bylund DB, Eikenberg DC, Hieble JP, Langer SZ, Lefkowitz RJ, Minneman KP *et al.* (1994). International Union of Pharmacology IV. Nomenclature of adrenoceptors. *Pharmacol Rev* **46**: 121–136.
- Cotecchia S (2007). Constitutive activity and inverse agonism at the α_1 adrenoceptors. *Biochem Pharmacol* **73**: 1076–1083.
- Ford APDW, Williams TJ, Blue DR, Clarke DE (1994). α_1 -Adrenoceptor classification: sharpening Occam's razor. *Trends Pharmacol Sci* **15**: 167–170.
- Hein L (2006). Adrenoceptors and signal transduction in neurons. *Cell Tissue Res* **326**: 541–551.
- Hieble JP, Bylund DB, Clarke DE, Eikenburg DC, Langer SZ, Lefkowitz RJ *et al.* (1995). International Union of Pharmacology. X. Recommendation for nomenclature of α_1 -adrenoceptors: consensus update. *Pharmacol Rev* **47**: 267–270.
- Koshimizu TA, Tanoue A, Tsujimoto G (2007). Clinical implications from studies of α_1 adrenergic receptor knockout mice. *Biochem Pharmacol* **73**: 1107–1112.
- Tanoue A, Koshimizu TA, Shibata K, Nasa Y, Takeo S, Tsujimoto G (2003). Insights into α_1 adrenoceptor function in health and disease from transgenic animal studies. *Trends Endocrinol Metab* **14**: 107–113.

References

- Blue DR *et al.* (2004). *BJU Int* **93**: 162–170.
- Ford APDW *et al.* (1997). *Br J Pharmacol* **121**: 1127–1135.
- Hague C *et al.* (2004). *J Pharmacol Exp Ther* **309**: 388–397.
- Morishima S *et al.* (2007). *J Urol* **177**: 377–381.
- Ramsay D *et al.* (2004). *Mol Pharmacol* **66**: 228–239.
- Uberti MA *et al.* (2005). *J Pharmacol Exp Ther* **313**: 16–23.

Citation Information

We recommend that any citations to information in the Guide are presented in the following format:

Alexander SPH, Mathie A, Peters JA (2008). Guide to Receptors and Channels (GRAC), 3rd edn. *Br J Pharmacol* **153** (Suppl. 2): S1–S209.