

Adenosine

Overview: Adenosine receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Adenosine Receptors; Fredholm *et al.*, 2001) are activated by the endogenous ligand adenosine (potentially inosine also at A₃ receptors). NECA is a non-selective agonist, while XAC and CGS15943 display submicromolar affinity at all four adenosine receptors (Klotz *et al.*, 1998; Ongini *et al.*, 1999). A crystal structure for the A_{2A} receptor has recently been described (Jaakola *et al.*, 2008).

Nomenclature	A ₁	A _{2A}	A _{2B}	A ₃
Ensembl ID	ENSG00000163485	ENSG00000128271	ENSG00000170425	ENSG00000121933
Principal transduction	G _{i/o}	G _s	G _s	G _{i/o}
Selective agonists	CPA, CCPA, S-ENBA, GR79236	CGS21680, HENECA, ATL-146e (Peirce <i>et al.</i> , 2001)	Bay60-6583 (Eckle <i>et al.</i> , 2007)	2-Cl-IB-MECA, IB-MECA
Selective antagonists	PSB36 (9.8, Abo-Salem <i>et al.</i> , 2004), DPCPX (8.5), SLV320 (9.0, Kalk <i>et al.</i> , 2007)	SCH442416 (10.3, Todde <i>et al.</i> , 2000), ZM241385 (9.0), SCH58261 (7.9–9.5)	PSB603 (9.3, Borrmann <i>et al.</i> , 2009), MRS1754 (8.7), MRS1706 (8.4), PSB1115 (7.7)	MRS1220 (8.8), VUF5574 (8.4, van Muijlwijk-Koezen <i>et al.</i> , 2000), MRS1523 (7.7), MRS1191 (7.0)
Probes	[³ H]-CCPA, [³ H]-DPCPX (0.6–1.2 nM)	[³ H]-CGS21680, [³ H]-ZM241385 (0.8 nM)	[³ H]-MRS1754 (1.1 nM)	[¹²⁵ I]-AB-MECA (0.6 nM)

Adenosine inhibits many intracellular ATP-utilizing enzymes, including adenylyl cyclase (P-site). A pseudogene exists for the A_{2B} adenosine receptor (ENSG00000182537) with 79% identity to the A_{2B} adenosine receptor cDNA coding sequence, but which is unable to encode a functional receptor (Jacobson *et al.*, 1995). DPCPX also exhibits antagonism at A_{2B} receptors (pK_i ca 7, Alexander *et al.*, 1996; Klotz *et al.*, 1998). HENECA also shows activity at A₃ receptors (Varani *et al.*, 1998). Antagonists at A₃ receptors exhibit marked species differences, such that only MRS1523 and MRS1191 are selective at the rat A₃ receptor. In the absence of other adenosine receptors, [³H]-DPCPX and [³H]-ZM241385 can also be used to label A_{2B} receptors (K_D ca 30 and 60 nM respectively). [¹²⁵I]-AB-MECA also binds to A₁ receptors (Klotz *et al.*, 1998). [³H]-CGS21680 is relatively selective for A_{2A} receptors, but may also bind to other sites in cerebral cortex (Johansson and Fredholm, 1995; Cunha *et al.*, 1996). [³H]-NECA binds to other non-receptor elements, which also recognize adenosine (e.g. Lorenzen *et al.*, 1996). XAC-BY630 has been described as a fluorescent antagonist for labelling A₁ adenosine receptors in living cells, although activity at other adenosine receptors was not examined (Bridson *et al.*, 2004).

Adenosine has also been reported to act as a partial agonist at the ghrelin receptor (Smith *et al.*, 2000), but this has been questioned (Johansson *et al.*, 2005).

Abbreviations: 2Cl-IB-MECA, 2-chloro-N⁶-(3-iodobenzyl)adenosine-5'-N-methyluronamide; AB-MECA, N⁶-(4-aminobenzyl)-adenosine-5'-N-methyluronamide; ATL-146e, 4-[3-[6-amino-9-(5-ethylcarbamoyl-3,4-dihydroxy-tetrahydro-furan-2-yl)-9H-purin-2-yl]-prop-2-ynyl]-cyclohexanecarboxylic acid methyl ester; Bay60-6583, 2-(6-amino-3,5-dicyano-4-(4-(cyclopropylmethoxy)phenyl) pyridin-2-ylthio)acetamide; CCPA, 2-chloro-N⁶-cyclopentyladenosine; CGS15943, 5-amino-9-chloro-2-(2-furyl)1,2,4-triazolo[1,5-c]quinazoline; CGS21680, 2-(4-[2-carboxyethyl]-phenethylamino)adenosine-5'-N-ethyluronamide; CPA, N⁶-cyclopentyladenosine; DPCPX, 8-cyclopentyl-1,3-dipropylxanthine; GR79236, N-[(1s,2s)-2-hydroxycyclopentyl adenosine; HENECA, 2-(1-(E)-hexenyl)adenosine-5'-N-ethyluronamide; MRS1191, 1,4-dihydro-2-methyl-6-phenyl-4-(phenylethynyl)-3,5-pyridinedicarboxylic acid, 3-ethyl 5-(phenylmethyl) ester; MRS1220, 9-chloro-2-(2-furyl)-5-phenylacetamino[1,2,4]triazolo[1,5-c]quinazoline; MRS1523, 2,3-ethyl-4,5-dipropyl-6-phenylpyridine-3-thiocarboxylate-5-carboxylate; MRS1706, N-(4-acetylphenyl)-2-(4-[2,3,6,7-tetrahydro-2,6-dioxo-1,3-dipropyl-1H-purin-8-yl]phenoxy)acetamide; MRS1754, 8-(4-[[4-(cyanophenyl)carbamoylmethyl]oxy]phenyl)-1,3-di(n-propyl)xanthine; NECA, adenosine-5'-N-ethyluronamide; PSB1115, 4-[2,3,6,7-tetrahydro-2,6-dioxo-1-propyl-1H-purin-8-yl]benzenesulphonic acid; PSB36, 1-butyl-8-(3-noradamantanyl)-3-(3-hydroxypropyl)xanthine; PSB603, 8-[4-[4-(4-chlorophenyl)piperazine-1-sulfonyl]phenyl]-1-propylxanthine; S-ENBA, (2S)-N⁶-(2-endonorbanyl)adenosine; SCH442416, 2-(2-furanyl)-7-[3-(4-methoxyphenyl)propyl]-7H-pyrazolo [4,3-e][1,2,4]triazolo[1,5-c]pyrimidin-5-amine; SCH58261, 5-amino-2-(2-furyl)-7-phenylethyl-pyrazolo[4,3-e]-1,2,4-triazolo[1,5-c]pyrimidine; SLV320, trans-4-[(2-phenyl-7H-pyrrolo[2,3-d]pyrimidin-4-yl)amino]cyclohexanol; VUF5574, N-(2-methoxyphenyl)-N-(2-[3-pyridyl]quinazolin-4-yl)urea; XAC, 8-(4-[[[(2-aminoethyl)amino]carbonyl]methyl]oxy]phenyl)-1,3-dipropylxanthine; also known as xanthine amine congener; XAC-BY630, N-(2-aminoethyl)-2-[4-(2,6-dioxo-1,3-dipropyl-7H-purin-8-yl)phenoxy]acetamide; ZM241385, 4-(2-[7-amino-2-(2-furyl)[1,2,4]triazolo[2,3-a][1,3,5]triazin-5-yl amino]ethyl)phenol

Further Reading

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