Melatonin

Overview: Melatonin receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on melatonin receptors, see Dubocovich *et al.*, 1998; 2000) are activated by the endogenous ligands melatonin and *N*-acetylserotonin.

Nomenclature	MT_1	MT_2
Other names	MEL_{1A}, ML_{1A}, Mel_{1a}	MEL_{1B}, ML_{1B}, Mel_{1b}
Ensembl ID	ENSG00000168412	ENSG00000134640
Principal transduction	$G_{i/o}$	$G_{i/o}$
Selective agonists	–	IIK7 (Sugden *et al.*, 1999), 5-methoxyluzindole (Dubocovich *et al.*, 1998)
Selective antagonists	–	K185 (9.3, Sugden *et al.*, 1999), 4P-PDOT (8.8, Dubocovich *et al.*, 1997; Dubocovich *et al.*, 1998), DH97 (8.0, Teh and Sugden, 1998)
Probes	[^{3}H]-melatonin (Browning *et al.*, 2000)	[^{3}H]-melatonin (Browning *et al.*, 2000)

Melatonin, 2-iodo-melatonin, S20098, GR196429, LY156735 and TAK375 (Kato *et al.*, 2005) are non-selective agonists for MT_1 and MT_2 receptors. 2-Iodo-[^{125}I]-melatonin can be used to label all three melatonin receptor subtypes. (-)-AMMTC displays an ~400-fold greater agonist potency than (+)-AMMTC at rat MT_1 receptors (Ting *et al.*, 1999). Luzindole is a non-selective melatonin receptor antagonist with some selectivity for the MT_2 receptor (Dubocovich *et al.*, 1998). MT_1/MT_2 heterodimers present different pharmacological profiles from MT_1 and MT_2 receptors (Ayoub *et al.*, 2004).

The *MT$_3$* binding site of hamster kidney, also termed the Mel_2 receptor, which binds 2-iodo-[^{125}I]-5MCA-NAT (Molinari *et al.*, 1996), was identified as the hamster homologue of human quinone reductase 2 (ENSG00000124588, Nosjean *et al.*, 2000; Nosjean *et al.*, 2001). Pharmacological investigations of *MT$_3$* binding sites have primarily been conducted in hamster and guinea-pig tissues. At this site, *N*-acetylserotonin (Eison and Mullins, 1993; Popova and Dubocovich, 1995; Molinari *et al.*, 1996; Lucchelli *et al.*, 1997) and 5MCA-NAT (Popova and Dubocovich, 1995) appear to function as agonists, while prazosin (Lucchelli *et al.*, 1997) functions as an antagonist. A suggested physiological function of the *MT$_3$* receptor is in the control of intraocular pressure in rabbits (Pintor *et al.*, 2003). *Xenopus* melanophores and chick brain express a distinct receptor (x420, P49219; c346, P49288, initially termed Mel_{1C}) coupled to the $G_{i/o}$ family of G proteins, for which GPR50 has recently been suggested to be a mammalian counterpart (see Dufourny *et al.*, 2008).

Abbreviations: 4P-PDOT, 4-phenyl-2-propionamidotetraline; **5MCA-NAT**, 5-methoxy-carbonylamino-*N*-acetyltryptamine; **AMMTC**, *N*-acetyl-4-aminomethyl-6-methoxy-9-methyl-1,2,3,4-tetrahydrocarbazole; **DH97**, 2-benzyl-*N*-pentanoyltryptamine; **GR196429**, *N*-(2-[2,3,7,8-tetrahydro-1*H*-furo(2,3-*g*)indol-1-yl]ethyl)acetamide; **IIK7**, *N*-butanoyl-2-(2-methoxy-6*H*-isoindolo [2,1-*a*]indol-11-yl)ethanamine; **K185**, *N*-butanoyl-2-(5,6,7-trihydro-11-methoxybenzo[3,4]cyclohept[2,1-*a*]indol-13-yl)ethanamine; **LY156735**, β-methyl-6-chloromelatonin; **S20098**, *N*-(2-[7-methoxy-1-naphthalenyl]ethyl)acetamide; **TAK375**, (S)-N-[2(1,6,7,8-tetrahydro-2H-indeno[5,4-b]furan-8-yl)ethyl]propionamide

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