Orexin

Overview: Orexin receptors (provisional nomenclature) are activated by the endogenous polypeptides orexin-A and orexin-B (also known as hypocretin-1 and 2; 33 and 28 aa) derived from a common precursor, preproorexin or orexin precusror (ENSG00000161610), by proteolytic cleavage (Sakurai *et al.*, 1998). Binding to both receptors may be accomplished with [^{125}I]-orexin A (Holmqvist *et al.*, 2001).

Nomenclature	OX_1	OX_2
Other names	Hypocretin receptor type 1	Hypocretin receptor type 2
Ensembl ID	ENSG00000121764	ENSG00000137252
Principal transduction	$G_{q/11}$	$G_{q/11}$
Rank order of potency	Orexin-A > orexin-B	Orexin-A = orexin-B
Selective agonists	–	[Ala^{11},D-Leu^{15}]orexin-B (Asahi *et al.*, 2003)
Selective antagonists	SB408124 (7.5, Langmead *et al.*, 2004), SB334867A (7.2–7.3, Porter *et al.*, 2001)	JNJ10397049 (7.9–8.3, McAtee *et al.*, 2004)

Coupling of both receptors to $G_{i/o}$ and G_s has also been reported (Kukkonen and Åkerman, 2005; Ramanjaneya *et al.*, 2009).

Loss-of-function mutations in the gene encoding the OX_2 receptor underlies canine hereditary narcolepsy (Lin *et al.*, 1999).

Abbreviations: **JNJ10397049**, 1-(2,4-dibromo-phenyl)-3-((4S,5S)-2,2-dimethyl-4-phenyl-[1,3]dioxan-5-yl)-urea; **SB334867A**, 1-(2-methyylbenzoxanzol-6-yl)-3-[1,5]naphthyridin-4-yl-urea hydrochloride; **SB408124**, 1-(6,8-difluoro-2-methyl-quinolin-4-yl)-3-(4-dimethylamino-phenyl)-urea

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