Galanin

Overview: Galanin receptors (provisional nomenclature, see Foord *et al.*, 2005) are activated by the endogenous peptides galanin (ENSG00000069482) and galanin-like peptide (GALP, ENSG00000105099). Human galanin is a 30 amino-acid non-amidated peptide (Evans and Shine, 1991); in other species, it is 29 amino-acids long and C-terminally amidated. Amino-acids 1–14 of galanin are highly conserved in mammals, birds, reptiles, amphibia and fish. Shorter peptide species (e.g. human galanin-1–19, (Bersani *et al.*, 1991a) and porcine galanin-5–29 (Sillard *et al.*, 1992) and *N*-terminally extended forms [e.g. N-terminally seven and nine residue elongated forms of porcine galanin (Bersani *et al.*, 1991b; Sillard *et al.*, 1992)] have been reported.

Nomenclature	GAL_1	GAL_2	GAL_3
Other names	Galanin-1 receptor, GALR1	Galanin-2 receptor, GALR2	Galanin-3 receptor, GALR3
Ensembl ID	ENSG00000166573	ENSG00000182687	ENSG00000128310
Principal transduction	$G_{i/o}$	$G_{i/o}$, $G_{q/11}$	$G_{i/o}$
Rank order of potency	Galanin > GALP (Ohtaki *et al.*, 1999)	GALP ≥ galanin (Ohtaki *et al.*, 1999)	GALP > galanin (Lang *et al.*, 2005)
Selective agonists	–	Galanin-(2–29) (Fathi *et al.*, 1997; Wang *et al.*, 1997), D-Trp^2-galanin-(1–29) (Smith *et al.*, 1997)	–
Selective antagonists	2,3-Dihydro-dithiin and -dithiepine-1,1,4,4-tetroxides (Scott *et al.*, 2000)	M871 (7.9, Sollenberg *et al.*, 2006)	–

Galanin-(1–11) is a high-affinity agonist at GAL_1/GAL_2 (pK_i 9), and galanin-(2–11) is selective for GAL_2 and GAL_3 compared with GAL_1 (Lu *et al.*, 2005). [^{125}I]-[Tyr^{26}]galanin binds to all three subtypes with K_d values ranging from 0.05 to 1 nM (Skofitsch *et al.*, 1986; Smith *et al.*, 1997; 1998; Wang *et al.*, 1997; Fitzgerald *et al.*, 1998). Porcine galanin-(3–29) does not bind to cloned GAL_1, GAL_2 or GAL_3 receptors, but a receptor that is functionally activated by porcine galanin-(3–29) has been reported in pituitary and gastric smooth muscle cells (Wynick *et al.*, 1993; Gu *et al.*, 1995). Additional galanin receptor subtypes are also suggested from studies with chimeric peptides (e.g. M15, M35 and M40), which act as antagonists in functional assays in the cardiovascular system (Ulman *et al.*, 1993), spinal cord (Wiesenfeld-Hallin *et al.*, 1992), locus coeruleus, hippocampus (Bartfai *et al.*, 1991) and hypothalamus (Leibowitz and Kim, 1992; Bartfai *et al.*, 1993), but exhibit agonist activity at some peripheral sites (Bartfai *et al.*, 1993; Gu *et al.*, 1995). The chimeric peptides M15, M32, M35, M40 and C7 are agonists at GAL_1 receptors expressed endogenously in Bowes human melanoma cells (Ohtaki *et al.*, 1999), and at heterologously expressed recombinant GAL_1, GAL_2 and GAL_3 receptors (Smith *et al.*, 1997; Fitzgerald *et al.*, 1998; Smith *et al.*, 1998).

Abbreviations: C7, galanin-(1–13)-spantide; **M15**, galanin-(1–13)-substance P-5–11 amide, also known as galantide; **M32**, galanin-(1–13)-neuropeptide Y amide-(25–36) amide; **M35**, galanin-(1–13)-bradykinin-(2–9) amide; **M40**, galanin-(1–13)-Pro-Pro-Ala-Leu-Ala-Leu-Ala-Leu-Ala amide; **M871**, galanin-(2–13)-Glu-His-(Pro)$_3$-(Ala-Leu)$_2$-Ala-amide

Further Reading

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