Vasopressin and oxytocin

Overview: Vasopressin (AVP) and oxytocin (OT) receptors (nomenclature as agreed by NC-IUPHAR Subcommittee on Vasopressin and Oxytoxcin Receptors) are activated by the endogenous cyclic nonapeptides AVP and OT. These peptides are derived from precursors (ENSG00000101200 and ENSG00000101405 respectively), which also produce neurophysins.

Nomenclature	V_{1a}	V_{1b}	V_2	OT
Ensembl ID	ENSG00000166148	P47901	ENSG00000126895	ENSG00000180914
Principal transduction	$G_{q/11}$	$G_{q/11}$	G_s	$G_{q/11}$, $G_{i/o}$
Rank order of potency	AVP > OT	AVP > OT	AVP > OT	OT ≥ AVP
Selective agonists	F180, [Phe^2,Orn^8]VT	d[D-3-Pal^2]VP, d(Cha^4]AVP (Derick *et al.*, 2002), d[Leu^4,Lys^8]VP (Pena *et al.*, 2007)	d[Val^4,DArg^8]VP, OPC51803, VNA932	[Thr^4,Gly^7]OT (Elands *et al.*, 1988)
Selective antagonists	d(CH$_2$)$_5$[Tyr(Me)^2,Arg^8]VP (9.0), SR49059 (8.9), YM087 (8.2)	SSR149415 (8.4; Griebel *et al.*, 2002; Serradeil-Le Gal *et al.*, 2002)	VPA985 (8.9; Albright *et al.*, 1998), d(CH$_2$)$_5$[D-Ile^2, Ile^4]AVP (8.4), SR121463A (8.4; Serradeil-Le Gal *et al.*, 1996), OPC31260 (7.6; Yamamura *et al.*, 1992), YM087 (8.96)	SSR126768A (9.3; Serradeil-Le Gal *et al.*, 2004), desGlyNH$_2$-d(CH$_2$)$_5$ [Tyr(Me)^2,Thr^4,Orn^8]OT (8.5), L372662 (8.4),
Probes	[^{3}H]-AVP, [^{3}H]-SR49059 (1.5 nM), [^{3}H]-d(CH$_2$)$_5$[Tyr(Me)^2,Arg^8]AVP (1.1 nM), [^{125}I]-HO-Phaa,D-Tyr(Me)-Phe-Gln-Asn-Arg-Pro-Arg-NH$_2$ (50 pM)	[^{3}H]-AVP, [^{3}H]-SSR149415 (1 nM; Serradeil-Le Gal *et al.*, 2007)	[^{3}H]-AVP, [^{3}H]-desGly-NH$_2$[D-Ile^2,Ile^4]AVP (2.8 nM), [^{3}H]-d[D-Arg^8]AVP (0.8 nM), [^{3}H]-SR121463A (4.1 nM)	[^{3}H]-OT, [^{35}S]-non-peptide OT antagonist (42 pM; Lemaire *et al.*, 2002), [^{125}I]-d(CH$_2$)$_5$[Tyr(Me)^2, Thr^4,Orn^8,Tyr-NH$_2^9$]OVT (90 pM), [^{111}In]-DOTA-dLVT (4.5 nM; Chini *et al.*, 2003)

The V_2 receptor exhibits marked species differences, such that many ligands (d(CH$_2$)$_5$[D-Ile^2,Ile^4]VP and [^{3}H]-desGly-NH$_2$[D-Ile^2,Ile^4]VP) exhibit low affinity at human V_2 receptors (Ala *et al.*, 1997). Similarly, [^{3}H]-d[D-Arg^8]VP is V_2-selective in the rat, not in the human (Saito *et al.*, 1997). The gene encoding the V_2 receptor is polymorphic in man, underlying nephrogenic diabetes insipidus (Bichet, 1998). YM087 display high affinity for both human V_{1a} and V_2 receptors (Tahara *et al.*, 1998). d[Cha^4]AVP is selective only for the human and bovine V_{1b} receptors (Derick *et al.*, 2002), while d[Leu^4,Lys^8]VP has high affinity for the rat V_{1b} receptor (Pena *et al.*, 2007).

Abbreviations: **[^{111}In]-DOTA-dLVT**, [^{111}In]-DOTA-Lys^8-deamino-vasotocin; **[^{35}S]-non-peptide OT antagonist**, [^{35}S]-(1-(1-(2-(2,2,2-trifluoroethoxy)-4-(1-methylsulfonyl-4-piperidinyloxy)phenylacetyl)-4-piperidinyl)-3,4-dihydro-2(1*H*)-quinolinone); **F180**, Hmp-Phe-Ile-Hgn-Asn-Cys-Pro-Dab(Abu)-Gly-NH$_2$; **L372662**, 1-(1-{4-[1-(2-methyl-1-oxidopyridin-3-ylmethyl)piperidin-4-yloxyl]-2-methoxybenzoyl} piperidin-4-yl)-1,4-dihydrobenz[*d*][1,3]oxazin-2one; **OPC31260**, 5-dimethylamino-1-(4-[2-methylbenzoylamino]benzoyl)-2,3,4,5-tetrahydro-1*H*-benzazepine; **OPC51803**, (5*r*)-2-(1-[2-chloro-4-{1-pyrrolidinyl}benzoyl]-2,3,4,5-tetrahydro-1*H*-1-benzazepin-5-yl)-*N*-isopropylacetamide; **SR121463A**, 1-(4-Boc-2-methoxybenzenesulfonyl)-5-ethoxy-3-spiro-(4-[2-morpholinoethoxy]cyclohexane)indol-2-one fumarate; equatorial isomer; **SR49059**, (2*s*)-1-([2*r*,3*s*]-[5-chloro-3-{chlorophenyl}-1-{3,4-dimethoxysulfonyl}-3-hydroxy]-2,3-dihydro-1*H*-indole-2-carbonyl)-pyrrolidine-2-carboxamide; **SSR149415**, (2*S*,4*R*)-1-[5-chloro-1-[(2,4-dimethoxyphenyl)sulfonyl]-3-(2-methoxy-phenyl)-2-oxo-2,3-dihydro-1*H*-indol-3-yl]-4-hydroxy-*N*,*N*-dimethyl-2-pyrrolidine carboxamide; **SSR126768A**, 4-chloro-3-[(3R)-(+)-5-chloro-1-(2,4-dimethoxybenzyl)-3-methyl -2-oxo-2,3-dihydro-1*H*-indol-3-yl]-*N*-ethyl-*N*-(3-pyridylmethyl)-benzamide, hydrochloride; **VNA932**, (2-chloro-4-[3-methyl-pyrazol-1-yl]-phenyl)-(5*H*,11*H*)-pyrrolo(2,1-*c*)(1,4)benzodiazepin-10-yl-methanone; **VPA985**, 5-fluoro-2-methyl-*N*-(4-[5*H*-pyrrolo[2,1-*c*][1,4]benzodiazepin-10 (11*H*)-ylcarbonyl]-3-chlorophenyl)benzamide; **YM087**, (4′-[(2-methyl-1,4,5,6-tetrahydroimidazo[4,5-d][1]benzazepin-6-yl) carbonyl]-2-phenylbenzanilide monohydrochloride)

Further Reading

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