Neuropeptide Y

Overview: Neuropeptide Y (NPY) receptors (nomenclature agreed by NC-IUPHAR on Neuropeptide Y Receptors, see Michel *et al*., 1998) are activated by the endogenous peptides NPY, NPY-(3-36), peptide YY (PYY), PYY-(3-36) and pancreatic polypeptide (PP). The receptor originally identified as the Y3 receptor has been identified as the CXCR4 chemokine recepter (originally named LESTR, Loetscher *et al*., 1994). The y6 receptor is a functional gene product in mouse, absent in rat, but contains a frame-shift mutation in primates producing a truncated non-functional gene (Gregor *et al*., 1996). Many of the agonists exhibit differing degrees of selectivity dependent on the species examined. For example, the relative potency of PP is greater at the rat Y_4 receptor than at the human receptor (Eriksson *et al*., 1998). In addition, many agonists lack selectivity for individual subtypes, but can exhibit comparable potency against pairs of NPY receptor subtypes, or have not been examined for activity at all subtypes. [^{125}I]-PYY or [^{125}I]-NPY can be used to label Y_1, Y_2, Y_5 and Y_6 subtypes non-selectively, while [^{125}I]-[cPP(1-7),NPY(19-23),Ala^{31},Aib^{32},Gln^{34}]hPP may be used to label Y_5 receptors preferentially.

Nomenclature	Y_1	Y_2	Y_4	Y_5	y_6
Other names	–	–	PP_1	–	Y_5, PP_2, Y_{2B}
Ensembl ID	ENSG00000164128	ENSG00000185149	ENSG00000169556	ENSG00000164129	ENSG00000159279
Principal transduction	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$	$G_{i/o}$
Rank order of potency	NPY ≥ PYY >> PP	NPY ≥ PYY >> PP	PP > NPY = PYY	NPY ≥ PYY ≥ PP	NPY = PYY > PP
Selective agonists	[Leu^{31},Pro^{34}]NPY, [Pro^{34}]NPY, [Leu^{31},Pro^{34}]PYY, [Pro^{34}]PYY	NPY-(3-36), PYY-(3-36)	PP	[Ala^{31},Aib^{32}]NPY (Cabrele *et al*., 2000)	–
Selective antagonists	BIBO3304 (9.5, Wieland *et al*., 1998), BIBP3226 (8.2, Gerald *et al*., 1996)	BIIE0246 (8.5, Doods *et al*., 1999), JNJ5207787 (Bonaventure *et al*., 2004)	–	L152804 (7.6, Kanatani *et al*., 2000)	–
Probes	[^{125}I]-[Leu^{31},Pro^{34}] NPY, [^{3}H]-BIBP3226 (2.1 nM)	[^{125}I]-PYY-(3-36)	[^{125}I]-PP	[^{125}I]-[cPP(1-7),NPY(19-23), Ala^{31},Aib^{32},Gln^{34}]hPP (Dumont *et al*., 2004)	–

The Y_1 agonists indicated are selective relative to Y_2 receptors. BIBP3226 is selective relative to Y_2, Y_4 and Y_5 receptors (Gerald *et al*., 1996). NPY-(13-36) is Y_2-selective relative to Y_1 and Y_5 receptors. PYY-(3-36) is Y_2 selective relative to Y_1-receptors.

Abbreviations: **BIBO3304:** (R)-*N*-([4-{aminocarbonylaminomethyl}-phenyl]methyl)-*N*^{2}-(diphenylacetyl)-argininamide trifluoroacetate; **BIBP3226:** R-*N*^{2}-(diphenylacetyl)-*N*-(4-hydroxyphenyl)methyl-argininamide; **BIIE0246:** (S)-*N*^{2}-([1-{2-(4-[(R,S)-5,11-dihydro-6(6*H*)-oxodibenz[*b*,*e*]azepin-11-yl]-1-piperazinyl)-2-oxoethyl}cyclopentyl]acetyl)-*N*-(2-[1,2-dihydro-3,5(4*H*)-dioxo-1,2-diphenyl-3*H*-1,2,4-triazol-4-yl]ethyl)-argininamide; **JNJ5207787**, *N*-(1-acetyl-2,3-dihydro-1*H*-indol-6-yl)-3-(3-cyano-phenyl)-*N*-[1-(2-cyclopentylethyl)piperidin-4-yl]acrylamide; **L152804**: 2-(3,3-dimethyl-1-oxo-4H-1*H*-xanthen-9-yl)-5,5-dimethyl-cyclohexane-1,3-dione

Further Reading

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