Urotensin-II

Overview: The urotensin-II (U-II) receptor (UT, nomenclature as agreed by NC-IUPHAR, see Douglas and Ohlstein, 2000; Foord *et al*., 2005) is activated by the endogenous dodecapeptide U-II, originally isolated from the urophysis, the endocrine organ of the caudal neurosecretory system of teleost fish (Bern *et al*., 1985). Several structural forms of U-II exist in fish and amphibians. The Goby orthologue was used to identify U-II as the cognate ligand for the predicted receptor encoded by the rat gene *gpr14* (Coulouarn *et al*., 1998; Liu *et al*., 1999; Mori *et al*., 1999; Nothacker *et al*., 1999). Human U-II (derived from ENSG00000049247), an 11-amino-acid peptide (Coulouarn *et al*., 1998), retains the cyclohexapeptide sequence of goby U-II that is thought to be important in ligand binding (Kinney *et al*., 2002; Brkovic *et al*., 2003). This sequence is also conserved in the deduced amino-acid sequence of rat (14 amino-acids) and mouse (14 amino-acids) U-II, although the *N*-terminal is more divergent from the human sequence (Coulouarn *et al*., 1999). A second endogenous ligand for UT has been discovered in rat (Sugo and Mori, 2008). The urotensin II-related peptide (URP), an octapeptide, is derived from a different gene, but shares the C-terminal sequence (CFWKYCV) common to U-II from other species. Identical sequences to rat URP are predicted for the mature mouse and human peptides.

Nomenclature	UT
Other names	GPR14, SENR, UR-IIR
Ensembl ID	ENSG00000181408
Principal transduction	$G_{q/11}$
Selective agonists	[Pen^5]U-II-(4–11), U-II-(4–11), U-II (Grieco *et al*., 2002), AC7954 (Lehmann *et al*., 2005), FL104 and analogues (Lehmann *et al*., 2006; 2007)
Selective antagonists	Urantide (8.3, Patacchini *et al*., 2003), SB706375 (7.5–8.0, Douglas *et al*., 2005), palosuran (pIC_{50} 7.1, Clozel *et al*., 2004), SB611812 (6.6, Rakowski *et al*., 2005)
Probes	[^{125}I]-hU-II (0.24 nM, Maguire *et al*., 2000)

In human vasculature, human U-II elicits both vasoconstrictor (pD_2 9.3–10.1, Maguire *et al*., 2000) and vasodilator (pIC_{50} 10.3–10.4, Stirrat *et al*., 2001) responses.

Abbreviations: **[Pen^5]U-II-(4-11)**, [pencillamine, *β,β*-dimethylcysteine]^{5}U-II-(4-11); **AC7954**, 3-(4-chlorophenyl)-3-(2-dimethylaminoethyl)-isochroman-1-one HCl; **FL104**, (+)*N*-(1-[4-chlorophenyl]-3-dimethylaminopropyl)-4-phenylbenzamide oxalate; **palosuran**, 1-[2-(4-benzyl-4-hydroxy-piperidin-1-yl)-ethyl]-3-(2-methyl-quinolin-4-yl)-urea sulphate, also known as ACT058362; **SB611812**, 2,6-dichloro-*N*-(4-chloro-3-{[2-(dimethylamino)ethyl]oxy}phenyl)-4-(trifluoromethyl)benzenesulfonamide; **SB706375**, 2-bromo-4,5-dimethoxy-*N*-[3-(R)-1-methyl-pyrrolidin-3-yloxy)-4-trifluromethyl-phenyl]-benzenesulphonamide HCl; **urantide**, [Pen^5,DTrp^7,Orn^8]hU-II(4-11)

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