Anaphylatoxin and formyl peptide

Overview: Anaphylatoxin and formyl peptide receptors (ENSFM00510000502765, the latter nomenclature as agreed by NC-IUPHAR Subcommittee on the formyl peptide receptor family, see Ye *et al.*, 2009) are activated by the endogenous ~75 amino-acid anaphylatoxin polypeptides C3a (ENSG00000125730) and C5a (ENSG00000106804), generated upon stimulation of the complement cascade. The fMLP receptor responds to exogenous ligands such as the bacterial product formyl-Met-Leu-Phe (fMLP) and endogenous ligands such as annexin I (ENSG00000135046), cathepsin G (ENSG00000100448) and spinorphin, derived from β-haemoglobin (ENSG00000188170). FPR2/ALX receptors (ENSG00000171049) respond to the endogenous fatty acid metabolite lipoxin A_4 (see page S64), as well as annexin I, while the pharmacology of FPR3 (ENSG00000187474) is still developing.

Nomenclature	C3a	C5a	FPR1
Other names	AZ3B, HNFAG09	CD88	Formyl peptide, fMLP, FPR
Ensembl ID	ENSG00000171860	ENSG00000134830	ENSG00000171051
Principal transduction	Gi/o, Gz	Gi/o, Gz, G16 (Buhl *et al.*, 1993)	Gi/o, Gz
Rank order of potency	C3a > C5a (Ames *et al.*, 1996)	C5a, C5a des Arg > C3a (Ames *et al.*, 1996)	fMLP > Cathepsin G > Annexin I (Le *et al.*, 2002; Sun *et al.*, 2004)
Selective agonists	Trp-Trp-Gly-Lys-Lys-Tyr-Arg-Ala-Ser-Lys-Leu-Gly-Leu-Ala-Arg (Ames *et al.*, 1997)	Phe-Lys-Pro-Cha-Cha-Phe-Lys-D-Cha-Cha-D-Arg (Konteatis *et al.*, 1994), S19 (Yamamoto, 2000)	fMLP (Le *et al.*, 1999)
Selective antagonists	SB290157 (pIC_{50} 7.5, Ames *et al.*, 2001)	NMe-Phe-Lys-Pro-D-Cha-Trp-D-Arg (Konteatis *et al.*, 1994), AcPhe-Orn-Pro-D-Cha-Trp-Arg (Wong *et al.*, 1998), W54011 (8.7, Sumichika *et al.*, 2002), CHIPS (Postma *et al.*, 2004)	Cyclosporin H (6.3–7.0, Wenzel-Seifert and Seifert, 1993), BOC-PLPLP (6.0–6.5, Wenzel-Seifert and Seifert, 1993), spinorphin (4, Liang *et al.*, 2001)
Probes	[^{125}I]-C3a	[^{125}I]-C5a	[^{3}H]-fMLP

SB290157 has also been reported to have agonist properties (Mathieu *et al.*, 2005). A putative chemoattractant receptor termed C5L2 (also known as GPR77, ENSG00000134830) binds [^{125}I]-C5a, with no clear signalling function, but a putative role opposing inflammatory responses (Cain and Monk, 2002; Gao *et al.*, 2005; Gavrilyuk *et al.*, 2005). Binding to this site may be displaced with the rank order C5a des Arg > C5a (Cain and Monk, 2002; Okinaga *et al.*, 2003), while there is controversy over the ability of C3a and C3a des Arg to compete (Kalant *et al.*, 2003; Okinaga *et al.*, 2003; Honczarenko *et al.*, 2005; Kalant *et al.*, 2005).

Abbreviations: BOC-PLPLP, Boc-Phe-Leu-Phe-Leu-Phe; **CHIPS**, chemotaxis inhibitory protein of *Staphylococcus aureus*; **SB290157**, N^2-([2,2-diphenylethoxy]acetyl)-L-arg; **W54011**, *N*-([4-dimethylaminophenyl]methyl)-*N*-(4-isopropylphenyl)-7-methoxy-1,2,3,4-tetrahydronaphthalen-1-carboxamide hydrochloride

Further Reading

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