Free fatty acid

Overview: Free fatty acid receptors (FFA, nomenclature as agreed by NC-IUPHAR Subcommittee on free fatty acid receptors, Stoddart *et al*., 2008) are activated by free fatty acids, such that long-chain saturated and unsaturated fatty acids (C16:0, C18:0, C18:1, C18:2, C18:3,n-6, C20:4, C20:5,n-3, C22:6,n-3, Briscoe *et al*., 2003; Itoh *et al*., 2003; Kotarsky *et al*., 2003) activate FFA_1 receptors, while short-chain fatty acids (C2, C3, C4 and C5) activate FFA_2 (Brown *et al*., 2003; Le Poul *et al*., 2003; Nilsson *et al*., 2003) and FFA_3 (Brown *et al*., 2003; Le Poul *et al*., 2003) receptors. In addition, thiazolidinedione PPARγ agonists such as rosiglitazone activate FFA_1 (pEC_{50} 5.2; Kotarsky *et al*., 2003; Stoddart *et al*., 2007; Smith *et al*., 2009).

Nomenclature	FFA_1	FFA_2	FFA_3
Other names	GPR40 (Sawzdargo *et al*., 1997)	GPR43 (Sawzdargo *et al*., 1997)	GPR41 (Sawzdargo *et al*., 1997) LSSIG (Senga *et al*., 2003)
Ensembl ID	ENSG00000126266	ENSG00000126262	ENSG00000185897
Principal transduction	$G_{q/11}$ (Briscoe *et al*., 2003; Itoh *et al*., 2003; Stoddart *et al*., 2007)	$G_{q/11}$, $G_{i/o}$ (Brown *et al*., 2003; Le Poul *et al*., 2003; Nilsson *et al*., 2003)	$G_{i/o}$ (Brown *et al*., 2003; Le Poul *et al*., 2003; Stoddart *et al*., 2007)
Selective agonists	Linoleic acid (Briscoe *et al*., 2003); Itoh *et al*., 2003), GW9508 (pEC_{50} 7.3; Briscoe *et al*., 2006; Sum *et al*., 2007), Cpd B (pEC_{50} 6.1; Tan *et al*., 2008)	(*S*)-2-(4-chlorophenyl)-*N*-(5-fluorothiazol-2-yl)-3-methylbutanamide (pEC_{50} 6.4; Lee *et al*., 2008)	–
Selective antagonists	GW1100 (Briscoe *et al*., 2006; Stoddart *et al*., 2007)	–	–

GW1100 is also an oxytocin receptor antagonist (Briscoe *et al*., 2006).

GPR42 (ENSG00000126251) was originally described as a pseudogene within the family, but the recent discovery of several polymorphisms suggests that some versions of GPR42 may be functional (Liaw and Connolly, 2009) (ENSFM00250000002583). GPR120 (ENSG00000186188) and GPR84 (ENSG00000139572) are structurally unrelated 7TM receptors. GPR120 is activated by unsaturated long-chain free fatty acids (Hirasawa *et al*., 2005; Katsuma *et al*., 2005; Gotoh *et al*., 2007) and GW9508 (pEC_{50} 5.7; Briscoe *et al*., 2006), while GPR84 was found to respond to medium chain fatty acids (Wang *et al*., 2006).

Abbreviations: C16:0, palmitic acid; **C18:0**, stearic acid; **C18:1**, oleic acid; **C18:2**, linoleic acid; **C18:3,n-6**, γ-linolenic acid; **C2**, acetic acid; **C20:4**, arachidonic acid; **C20:5,n-3**, 5z,8z,11z,14z,17z-eicosapentaenoic acid, EPA; **C22:6,n-3**, 4z,7z,10z,13z,16z,19z-docosahexaenoic acid, DHA; **C3**, propionic acid; **C4**, butyric acid; **C5**, valeric acid; **Cpd B**, 3-chloro-5-trifluoromethyl-pyridin-2-yl-methoxy(4-(3-methylphenyl)methyl-1, 3-thiazolidinedione-2, 4-dione; **GW1100**, ethyl 4-(5-[{2-(ethyloxy)-5-pyrimidinyl}methyl]-2-[{(4-fluorophenyl)methyl]thio}-4-oxo-1[4*H*]-pyrimidinyl)benzoate; **GW9508**, 3-(4-[{(3-[phenyloxy]phenyl)methyl}amino]phenyl)propanoic acid

Further Reading

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