Peroxisome proliferator-activated

Overview: Peroxisome proliferator-activated receptors (PPARs, nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Michalik *et al*., 2006) are nuclear hormone receptors of the NR1C family, with diverse roles regulating lipid homeostasis, cellular differentiation, proliferation and the immune response. PPARs have many potential endogenous agonists (see Michalik *et al*., 2006), including 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2, prostacyclin, many fatty acids and their oxidation products, lysophosphatidic acid (McIntyre *et al*., 2003), 13-HODE, 15-HETE, Paz-PC, azelaoyl-PAF and leukotriene B4. These receptors also bind hypolipidaemic drugs (PPARα) and anti-diabetic thiazolidinediones (PPARγ), as well as many non-steroidal anti-inflammatory drugs, such as sulindac and indomethacin. Once activated by a ligand, the receptor forms a heterodimer with members of the retinoid X receptor family and can act as a transcription factor. Although radioligand binding assays have been described for all three receptors, the radioligands are not commercially available.

Nomenclature	PPARα	PPARβ	PPARγ
Systematic nomenclature	NR1C1	NR1C2	NR1C3
Other names	–	PPARδ, NUC1, FAAR	–
Ensembl ID	ENSG00000100406	ENSG00000112033	ENSG00000132170
Selective agonists	GW7647, WY14643, clofibrate, fenofibrate, ciprofibrate, gemfibrozil	L165041, GW501516, GW0742	Rosiglitazone, ciglitazone, troglitazone, pioglitazone, CDDO, GW1929
Selective antagonists	GW6471 (Xu *et al*., 2002)	GSK0660 (Shearer *et al*., 2008)	GW9662 (Huang *et al*., 1999), CDDO-Me (Wang *et al*., 2000), diclofenac (6.2, Adamson *et al*., 2002), BADGE (4.0, Wright *et al*., 2000), T0070907 (Lee *et al*., 2002)

As with the oestrogen receptor antagonists, many agents show tissue-selective efficacy (e.g. Bishop-Bailey, 2000; Rocchi *et al*., 2001; Nakamuta *et al*., 2002). Agonists with mixed activity at PPARα and PPARγ have recently been described (e.g. Doebber *et al*., 2004; Guo *et al*., 2004; Xu *et al*., 2004).

Abbreviations: 13-HODE, 13-hydroxyoctadecadienoic acid; **15-HETE**, 15-hydroxyeicosatetraenoic acid; **azelaoyl-PAF**, 1-O-hexadecyl-2-O-(9-carboxyoctanoyl)-sn-glyceryl-3-phosphocholine; **BADGE**, bisphenol A diglycidyl ether; **CDDO**, 2-cyano-3,12-dioxooleana-1,9-dien-28-oic acid; **CDDO-Me**, 2-cyano-3,12-dioxooleana-1,9-dien-28-oic acid methyl ester; **GSK0660**, 3-([{2-methoxy-4-(phenylamino)phenyl}amino]sulfonyl)-2-thiophenecarboxylic acid methyl ester; **GW1929**, (2*S*)-([2-benzoylphenyl]amino)-3-(4-[2-{methylpyridin-2-ylamino}ethoxy]phenyl) propionic acid; **GW501516**, 2-methyl-4([{(4-methyl-2-[4-trifluoromethylphenyl]-1,3-thiazol-5-yl)methyl}sulfanyl]phenoxy)acetic acid, **GW7647**, 2-([4-{2-([{cyclohexylamino}carbonyl][4-cyclohexylbutyl]amino)ethyl}phenyl]thio)-2-methylpropanoic acid; **GW9662**, 2-chloro-5-nitro-*N*-phenylbenzamide; **L165041**, (4-[3-{4-acetyl-3-hydroxy-2-propylphenoxy}propoxyl]phenoxy)acetic acid; **Paz-PC**, 1-palmitoyl-2-azelaoyl-*sn*-glycero-3-phosphocholine; **T0070907**, 2-chloro-5-nitro-*N*-(4-pyridyl)benzamide; **WY14643**, *N*-(3-[2-quinolinylmethoxy]phenyl)-trifluoromethanesulphonamide

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