Retinoic acid, retinoid X and retinoic acid-related orphan

Overview: Retinoic acid receptors (nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Germain *et al*., 2006a) are nuclear hormone receptors of the NR1B family activated by the vitamin A-derived agonists all-*trans* retinoic acid (ATRA) and 9-*cis*-retinoic acid, and the RAR-selective synthetic agonist TTNPB. Retinoid X receptors (nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Germain *et al*., 2006b) are NR2B family members activated by 9-*cis*-retinoic acid and the RXR-selective agonists LGD1069 and LG100268. These receptors form RXR–RAR heterodimers and RXR–RXR homodimers (Mangelsdorf and Evans, 1995; Chambon, 1996). Retinoic acid-related orphan receptors (ROR, nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Benoit *et al*., 2006) have yet to be assigned a definitive endogenous ligand, although RORα may be synthesized with a 'captured' agonist such as cholesterol (Kallen *et al*., 2002; 2004).

Cytoplasmic cellular retinoid binding proteins I (ENSG00000114115), II (ENSG00000114113), III (ENSG00000139194) and IV (ENSG00000162444) are thought to control the levels of intracellular retinoids available for interaction with their receptors (Li, 1999). [^{3}H]-ATRA and [^{3}H]-9-*cis*-retinoic acid have been used to label RARs and RXRs respectively.

Nomenclature	RARα	RARβ	RARγ
Systematic nomenclature	NR1B1	NR1B2	NR1B3
Other names	–	HBV-activated protein	–
Ensembl ID	ENSG00000131759	ENSG00000077092	ENSG00000172819
Selective agonists	Ro406055 (Delescluse *et al*., 1991)	–	AHPN (Martin *et al*., 1992)
Selective antagonists	Ro415253 (Apfel *et al*., 1992)	–	–

Ro415253 has been suggested to be a PPARγ agonist (Schupp *et al*., 2007). LE135 is an antagonist with selectivity for RARα and RARβ compared with RARγ (Li *et al*., 1999).

Nomenclature	RXRα	RXRβ	RXRγ
Systematic nomenclature	NR2B1	NR2B2	NR2B3
Ensembl ID	ENSG00000078380	ENSG00000112472	ENSG00000143171

Nomenclature	RORα	RORβ	RORγ
Systematic nomenclature	NR1F1	NR1F2	NR1F3
Other names	RZRα	RZRβ	RZRγ
Ensembl ID	ENSG00000069667	ENSG00000198963	ENSG00000143365
Selective agonists	Cholesterol sulfate, cholesterol, 7-OHC (Bitsch *et al*., 2003)	ATRA (Stehlin-Gaon *et al*., 2003)	–

ATRA shows selectivity for RORβ within the ROR family. RORα has been suggested to be a nuclear receptor responding to melatonin (Wiesenberg *et al*., 1995).

Abbreviations: **AHPN**, 6-[3-(1-adamantyl)-4-hydroxyphenyl]-2-naphthalene carboxylic acid, also known as CD437; **ATRA**, all-*trans*-retinoic acid; 4-(6-hydroxy-7-tricyclo[3.3.1.13,7]dec-1-yl-2-naphthalenyl)benzoic acid; **LE135**, 4-(7,8,9,10-tetrahydro-5,7,7,10,10-pentamethyl-5*H*-benzo[*e*]naphtho[2,3-*b*][1,4]diazepin-13-yl)benzoic acid; **LG100268**, 6-(1-[3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydronaphthalen-2-yl]cyclopropyl) nicotinic acid; **LGD1069**, 4-(1-[3,5,5,8,8-pentamethyl-5,6,7,8-tetrahydro-2-naphthyl]ethenyl) benzoic acid; **OHC**, hydroxycholesterol; **Ro406055**, 4-([5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl]carboxamido)benzoic acid (also known as AM580); **Ro415253**, 4-[2-(7-heptoxy-4,4-dimethyl-1,1-dioxo-2,3-dihydrothiochromen-6-yl)prop-1-enyl]benzoic acid, also known as LG629; **TTNPB**, (*E*)-4-(2-[5,6,7,8-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl]-1-propenyl)benzoic acid

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