



Kent Academic Repository

Alexander, Stephen P. H., Cidlowski, John A., Gibb, Alasdair J., Kelly, Eamonn, Mathie, Alistair A., Peach, Chloe J., Veale, Emma L., Armstrong, Jane F., Faccenda, Elena, Harding, Simon D. and others (2025) *The Concise Guide to PHARMACOLOGY 2025/26: Nuclear hormone receptors*. *British Journal of Pharmacology*, 182 (S1). S242-S258. ISSN 0007-1188.

Downloaded from

<https://kar.kent.ac.uk/114868/> The University of Kent's Academic Repository KAR

The version of record is available from

<https://doi.org/10.1111/bph.70232>

This document version

Publisher pdf

DOI for this version

Licence for this version

CC BY (Attribution)

Additional information

Versions of research works

Versions of Record

If this version is the version of record, it is the same as the published version available on the publisher's web site. Cite as the published version.















Author Accepted Manuscripts

If this document is identified as the Author Accepted Manuscript it is the version after peer review but before type setting, copy editing or publisher branding. Cite as Surname, Initial. (Year) 'Title of article'. To be published in **Title of Journal**, Volume and issue numbers [peer-reviewed accepted version]. Available at: DOI or URL (Accessed: date).

Enquiries

If you have questions about this document contact ResearchSupport@kent.ac.uk. Please include the URL of the record in KAR. If you believe that your, or a third party's rights have been compromised through this document please see our [Take Down policy](https://www.kent.ac.uk/guides/kar-the-kent-academic-repository#policies) (available from <https://www.kent.ac.uk/guides/kar-the-kent-academic-repository#policies>).

The Concise Guide to PHARMACOLOGY 2025/26: Nuclear hormone receptors

Stephen P. H. Alexander¹ , John A. Cidlowski² , Alasdair J. Gibb³ , Eamonn Kelly⁴ , Alistair A. Mathie⁵ ,
 Chloe J. Peach⁶ , Emma L. Veale⁷ , Jane F. Armstrong⁸ , Elena Faccenda⁸ , Simon D. Harding⁸ ,
 Christopher Southan⁸ , Jamie A. Davies⁸ , Laurel Coons⁹, Peter J. Fuller¹⁰, Kenneth S. Korach¹¹,
 Donald P. McDonnell¹², Robert Oakley¹¹, Sarah Radi¹³ , Rachid Safi¹², Frances Sladek¹³  and Morag J. Young¹⁴

¹Division of Physiology, Pharmacology & Neuroscience, School of Life Sciences, University of Nottingham Medical School, Nottingham, NG7 2UH, UK, ²National Institute of Environmental Health Sciences, National Institutes of Health, Department of Health and Human Services, Research Triangle Park, NC 27709, USA, ³Research Department of Neuroscience, Physiology and Pharmacology, Division of Biosciences, University College London, Gower Street, London, WC1E 6BT, UK, ⁴School of Psychology and Neuroscience, University of Bristol, Bristol, BS8 1TD, UK, ⁵School of Life Sciences, University of Westminster, London, W1W 6UW, UK, ⁶Division of Physiology, Pharmacology & Neuroscience, School of Life Sciences, Centre of Membrane Proteins and Receptors (COMPARE), University of Nottingham Medical School, Nottingham, NG7 2UH, UK, ⁷Medway School of Pharmacy, Universities of Kent and Greenwich, Chatham Maritime, Kent, ME4 4TB, UK, ⁸Institute for Neuroscience and Cardiovascular Research, University of Edinburgh, Edinburgh, EH8 9XD, UK, ⁹Duke University Medical Center, Durham, USA, ¹⁰Hudson Institute of Medical Research, Clayton, Australia, ¹¹National Institutes of Health, Research Triangle Park, USA, ¹²Duke University School of Medicine, Durham, USA, ¹³University of California, Riverside, Riverside, USA, ¹⁴Monash University, Melbourne, Australia



Abstract

The Concise Guide to Pharmacology 2025/26 marks the seventh edition in this series of biennial publications in the *British Journal of Pharmacology*. Presented in landscape format, the guide provides a comparative overview of the pharmacology of drug target families. The concise nature of the Concise Guide refers to the style of presentation, being clear, accessible, and well-structured, rather than the scope of the content, which spans approximately 500 pages. The Concise Guide summarises the key pharmacological properties of around 1900 human drug targets, and nearly 7000 interactions, involving around 4400 ligands. While the content is a substantially condensed version of the more detailed information and links available at the www.guidetopharmacology.org website, the printed guide serves as a permanent, citable, point-in-time record, that remains stable despite ongoing updates to the online database. The full contents of this publication can be found at <https://bpspubs.onlinelibrary.wiley.com/doi/10.1111/bph.70232>.

The Concise Guides provide expert-curated recommendations of ‘Gold Standard’ selective pharmacological tools, available either commercially or as donations, which enable the identification of individual drug targets or families of drug targets. While the Concise Guide offers a more streamlined overview, more comprehensive information, including detailed pharmacological profiles and links to multiple online databases, is available through the Guide to Pharmacology website. The 2025/26 edition of the Concise Guide is based on material current as of mid-2025, and supersedes all previous editions, including the 2023/24 Guide, and earlier Guides to Receptors and Channels. It is produced in close conjunction with the Nomenclature and Standards Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR), and as such provides official IUPHAR classification and nomenclature for human drug targets, where applicable.

Nuclear hormone receptors are one of the six major pharmacological targets into which the Guide is divided, with the others being: G protein-coupled receptors, ion channels, catalytic receptors, enzymes and transporters. Each section includes nomenclature guidance, concise summaries information of the best available pharmacological tools, key references, and suggestions for further reading.

Conflict of interest

The authors state that there are no conflicts of interest to disclose.

© 2025 The Author(s). *British Journal of Pharmacology* published by John Wiley & Sons Ltd on behalf of British Pharmacological Society.

This is an open access article under the terms of the Creative Commons Attribution License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

Searchable database: <https://www.guidetopharmacology.org/>

Full Contents of ConciseGuide: <http://onlinelibrary.wiley.com/doi/10.1111/bph.70232/full>

Nuclear hormone receptors S242

Introduction: Nuclear receptors are specialised transcription factors with commonalities of sequence and structure, which bind as homo- or heterodimers to specific consensus sequences of DNA (response elements) in the promoter region of particular target genes. They regulate (either promoting or repressing) transcription of these target genes in response to a variety of endogenous ligands. Endogenous agonists are hydrophobic entities which, when bound to the receptor promote conformational changes in the receptor to allow recruitment (or dissociation) of protein partners, generating a large multiprotein complex [23].

Two major subclasses of nuclear receptors with identified endogenous agonists can be identified: steroid and non-steroid hormone receptors. Steroid hormone receptors function typically as dimeric entities and are thought to be resident outside the nucleus in the unliganded state in a complex with chaperone proteins, which are liberated upon agonist binding. Migration to the nucleus and interaction with other regulators of gene transcription, including RNA polymerase, acetyltransferases and deacetylases, allows gene transcription to be regulated. Non-steroid hormone receptors typically exhibit a greater distribution in the nucleus in the unliganded state and interact with other nuclear receptors to form heterodimers, as well as with other regulators of gene transcription, leading to changes in gene transcription upon agonist binding.

Selectivity of gene regulation is brought about through interaction of nuclear receptors with particular consensus sequences of DNA, which are arranged typically as repeats or inverted palindromes to allow accumulation of multiple transcription factors in the promoter regions of genes.

Family structure

S243	1A. Thyroid hormone receptors	S249	2A. Hepatocyte nuclear factor-4 receptors	S253	5A. Fushi tarazu F1-like receptors
S244	1B. Retinoic acid receptors	S249	2B. Retinoid X receptors	S253	6A. Germ cell nuclear factor receptors
S245	1C. Peroxisome proliferator-activated receptors	S250	2C. Testicular receptors	S254	0B. DAX-like receptors
S246	1D. Rev-Erb receptors	S251	2E. Tailless-like receptors	S254	Steroid hormone receptors
S246	1F. Retinoic acid-related orphans	S251	2F. COUP-TF-like receptors	S255	3A. Estrogen receptors
S247	1H. Liver X receptor-like receptors	S252	3B. Estrogen-related receptors	S255	3C. 3-Ketosteroid receptors
S248	1I. Vitamin D receptor-like receptors	S252	4A. Nerve growth factor IB-like receptors		

1A. Thyroid hormone receptors

Nuclear hormone receptors → 1A. Thyroid hormone receptors

Overview: Thyroid hormone receptors (TRs, nomenclature as agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [1, 46]) are nuclear hormone receptors of the NR1A family, with diverse roles regulating macronutrient metabolism, cognition and cardiovascular homeostasis. TRs are activated by thyroxine (T_4) and thyroid hormone (**triiodothyronine**). Once activated by a ligand, the receptor acts as a transcription factor either as a monomer, homodimer or heterodimer with members of the retinoid X receptor family. **NH-3** has been described as an antagonist at TRs with modest selectivity for TR β [121].

Nomenclature	Thyroid hormone receptor- α	Thyroid hormone receptor- β
Systematic nomenclature	NR1A1	NR1A2
HGNC, UniProt	THRA , P10827	THRB , P10828
Rank order of potency	triiodothyronine > T_4	triiodothyronine > T_4
Agonists	dextrothyroxine [22]	dextrothyroxine [22]
Selective agonists	–	sobetirome [29, 147]

Comments: An interaction with integrin $\alpha V\beta 3$ has been suggested to underlie plasma membrane localization of TRs and non-genomic signalling [11]. One splice variant, TR α_2 , lacks a functional DNA-binding domain and appears to act as a transcription suppressor. Although radioligand binding assays have been described for these receptors, the radioligands are not commercially available.

Further reading on 1A. Thyroid hormone receptors

- Elbers LP *et al.* (2016) Thyroid Hormone Mimetics: the Past, Current Status and Future Challenges. *Curr Atheroscler Rep* **18**: 14 [PMID:26886134]
- Mendoza A *et al.* (2017) New insights into thyroid hormone action. *Pharmacol Ther* **173**: 135-145 [PMID:28174093]
- Flamant F *et al.* (2006) International Union of Pharmacology. LIX. The pharmacology and classification of the nuclear receptor superfamily: thyroid hormone receptors. *Pharmacol Rev* **58**: 705-11 [PMID:17132849]

1B. Retinoic acid receptors

Nuclear hormone receptors → 1B. Retinoic acid receptors

Overview: Retinoic acid receptors (nomenclature as agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 53]) are nuclear hormone receptors of the NR1B family activated by the vitamin A-derived agonists **tretinoin** (ATRA) and **alitretinoin**, and the RAR-selective synthetic agonists **TTNPB** and **adapalene**. **BMS493** is a family-selective antagonist [55].

Nomenclature	Retinoic acid receptor- α	Retinoic acid receptor- β	Retinoic acid receptor- γ
Systematic nomenclature	NR1B1	NR1B2	NR1B3
HGNC, UniProt	RARA , P10276	RARB , P10826	RARG , P13631
Agonists	tretinoin [28]	tretinoin [28]	tretinoin [28]
Sub/family-selective agonists	tazarotene [28]	tazarotene [28], adapalene [27]	tazarotene [28], adapalene [27]
Selective agonists	BMS753 [52], tamibarotene [168], Ro 40-6055 [37]	AC261066 [100], AC55649 [99, 100]	AHPN [27]
Selective antagonists	Ro 41-5253 (pIC ₅₀ 6.3–7.2) [3, 78]	–	MM 11253 [87]

Comments: [Ro 41-5253](#) has been suggested to be a PPAR γ agonist [146]. [LE135](#) is an antagonist with selectivity for RAR α and RAR β compared with RAR γ [96].

Further reading on 1B. Retinoic acid receptors

- Duong V *et al.* (2011) The molecular physiology of nuclear retinoic acid receptors. From health to disease. *Biochim Biophys Acta* **1812**: 1023-31 [PMID:20970498]
- Larange A *et al.* (2016) Retinoic Acid and Retinoic Acid Receptors as Pleiotropic Modulators of the Immune System. *Annu Rev Immunol* **34**: 369-94 [PMID:27168242]
- Germain P *et al.* (2006) International Union of Pharmacology. LX. Retinoic acid receptors. *Pharmacol Rev* **58**: 712-25 [PMID:17132850]
- Saeed A *et al.* (2017) The interrelationship between bile acid and vitamin A homeostasis. *Biochim Biophys Acta* **1862**: 496-512 [PMID:28111285]

1C. Peroxisome proliferator-activated receptors

Nuclear hormone receptors → 1C. Peroxisome proliferator-activated receptors

Overview: Peroxisome proliferator-activated receptors (**PPARs**, nomenclature as agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 112]) 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 [16, 112], including 15-deoxy- $\Delta^{12,14}$ -PGJ₂, prostacyclin

(PGL₂), many fatty acids and their oxidation products, lysophosphatidic acid (LPA) [109], 13-HODE, 15S-HETE, Paz-PC, azelaoyl-PAF and leukotriene B₄ (LTB₄). Bezafibrate acts as a non-selective agonist for the PPAR family [177]. These receptors also bind hypolipidaemic drugs (PPAR α) and anti-diabetic thiazolidinediones (PPAR γ), 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. Commonly, receptor occupancy studies are conducted using fluorescent ligands and truncated forms of the receptor limited to the ligand binding domain.

Nomenclature	Peroxisome proliferator-activated receptor- α	Peroxisome proliferator-activated receptor- β/δ	Peroxisome proliferator-activated receptor- γ
Systematic nomenclature	NR1C1	NR1C2	NR1C3
HGNC, UniProt	<i>PPARA</i> , Q07869	<i>PPARD</i> , Q03181	<i>PPARG</i> , P37231
Selective agonists	GW7647 [20, 21], CP-775146 [75], pirinixic acid [177], gemfibrozil [34]	GW0742X [58, 159], GW501516 [125]	GW1929 [20], bardoxolone (Partial agonist) [171], rosiglitazone [66, 92, 184], troglitazone [66, 184], pioglitazone [66, 144, 184], ciglitazone [66]
Selective antagonists	GW6471 (pIC ₅₀ 6.6) [181]	GSK0660 (pIC ₅₀ 6.5) [148]	T0070907 (pK _i 9) [88], GW9662 (Irreversible inhibition) (pIC ₅₀ 8.1) [90], CDDO-Me (pK _i 6.9) [171]

Comments: As with the estrogen receptor antagonists, many agents show tissue-selective efficacy (*e.g.* [15, 120, 141]). Agonists with mixed activity at PPAR α and PPAR γ have also been described (*e.g.* [38, 62, 182]).

Further reading on 1C. Peroxisome proliferator-activated receptors

Cheang WS *et al.* (2015) The peroxisome proliferator-activated receptors in cardiovascular diseases: experimental benefits and clinical challenges. *Br J Pharmacol* **172**: 5512-22 [PMID:25438608]
 Gross B *et al.* (2017) PPARs in obesity-induced T2DM, dyslipidaemia and NAFLD. *Nat Rev Endocrinol* **13**: 36-49 [PMID:27636730]
 Hallenborg P *et al.* (2016) The elusive endogenous adipogenic PPAR γ agonists: Lining up the suspects. *Prog Lipid Res* **61**: 149-62 [PMID:26703188]

Michalik L *et al.* (2006) International Union of Pharmacology. LXI. Peroxisome proliferator-activated receptors. *Pharmacol Rev* **58**: 726-41 [PMID:17132851]
 Sauer S. (2015) Ligands for the Nuclear Peroxisome Proliferator-Activated Receptor Gamma. *Trends Pharmacol Sci* **36**: 688-704 [PMID:26435213]

1D. Rev-Erb receptors

Nuclear hormone receptors → 1D. Rev-Erb receptors

Overview: Rev-erb receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 10]) have yet to be officially paired with an endogenous ligand, but are thought to be activated by heme.

Nomenclature	Rev-Erb- α	Rev-Erb- β
Systematic nomenclature	NR1D1	NR1D2
HGNC, UniProt	NR1D1 , P20393	NR1D2 , Q14995
Endogenous agonists	heme [138, 183]	heme [108, 138, 183]
Selective agonists	GSK4112 [60], GSK4112 [83]	–
Selective antagonists	SR8278 (pIC ₅₀ 6.5) [83]	–

Further reading on 1D. Rev-Erb receptors

Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]

Gonzalez-Sanchez E *et al.* (2015) Nuclear receptors in acute and chronic cholestasis. *Dig Dis* **33**: 357-66 [PMID:26045270]

Gustafson CL *et al.* (2015) Emerging models for the molecular basis of mammalian circadian timing. *Biochemistry* **54**: 134-49 [PMID:25303119]

Sousa EH *et al.* (2017) Drug discovery targeting heme-based sensors and their coupled activities. *J Inorg Biochem* **167**: 12-20 [PMID:27893989]

1F. Retinoic acid-related orphans

Nuclear hormone receptors → 1F. Retinoic acid-related orphans

Overview: Retinoic acid receptor-related orphan receptors (ROR, **nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 10]) have yet to be assigned a definitive endogenous ligand, although ROR α may be synthesized with a 'captured' agonist such as [cholesterol](#) [73, 74].

Nomenclature	RAR-related orphan receptor- α	RAR-related orphan receptor- β	RAR-related orphan receptor- γ
Systematic nomenclature	NR1F1	NR1F2	NR1F3
HGNC, UniProt	RORA , P35398	RORB , Q92753	RORC , P51449
Endogenous agonists	cholesterol [74, 127]	–	–
Selective agonists	7-hydroxycholesterol [17], cholesterol sulphate [17, 74]	–	–
Comments	–	–	The immune system function of RORC proteins most likely resides with expression of the ROR γ t isoform by immature CD4 ⁺ /CD8 ⁺ cells in the thymus [40, 158] and in lymphoid tissue inducer (LTi) cells [41].

Comments: [Tretinoin](#) shows selectivity for ROR β within the ROR family [154]. ROR α has been suggested to be a nuclear receptor responding to [melatonin](#) [176].

Further reading on 1F. Retinoic acid-related orphans

Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
 Cyr P *et al.* (2016) Recent progress on nuclear receptor ROR γ modulators. *Bioorg Med Chem Lett* **26**: 4387-4393 [PMID:27542308]
 Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]

Guillemot-Legris O *et al.* (2016) Oxysterols in Metabolic Syndrome: From Bystander Molecules to Bioactive Lipids. *Trends Mol Med* **22**: 594-614 [PMID:27286741]
 Mutemberezi V *et al.* (2016) Oxysterols: From cholesterol metabolites to key mediators. *Prog Lipid Res* **64**: 152-169 [PMID:27687912]

1H. Liver X receptor-like receptors

Nuclear hormone receptors → 1H. Liver X receptor-like receptors

Overview: Liver X and farnesoid X receptors (LXR and FXR, **nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 116]) are members of a steroid analogue-activated nuclear receptor subfamily, which form heterodimers with members of the retinoid X receptor family. Endogenous ligands for LXRs include hydroxycholesterols (OHC), while FXRs appear to be activated by bile acids. In humans and primates, *NR1H5P* is a pseudogene. However, in other mammals, it encodes a functional nuclear hormone receptor that appears to be involved in cholesterol biosynthesis [126].

Nomenclature	Farnesoid X receptor	Farnesoid X receptor- β	Liver X receptor- α	Liver X receptor- β
Systematic nomenclature	NR1H4	NR1H5	NR1H3	NR1H2
HGNC, UniProt	NR1H4 , Q96R11	NR1H5P , –	NR1H3 , Q13133	NR1H2 , P55055
Potency order	chenodeoxycholic acid > lithocholic acid, deoxycholic acid [103, 128]	–	20S-hydroxycholesterol, 22R-hydroxycholesterol, 24(S)-hydroxycholesterol > 25-hydroxycholesterol, 27-hydroxycholesterol [70, 91]	20S-hydroxycholesterol, 22R-hydroxycholesterol, 24(S)-hydroxycholesterol > 25-hydroxycholesterol, 27-hydroxycholesterol [70, 91]
Endogenous agonists	–	lanosterol [126] – Mouse	–	–
Selective agonists	tropifexor [163], GW4064 [105], obeticholic acid [129], fexaramine [39]	–	–	BMS-852927 [80], GSK9772 [26], CE9A215 [7, 122]
Selective antagonists	DY268 (pIC ₅₀ 8.1) [186], guggulsterone (pIC ₅₀ 5.7–6) [165, 179]	–	–	–

Comments: [T0901317](#) [139] and [GW3965](#) [30] are synthetic agonists that activate both LXR α and LXR β with less than 10-fold selectivity between the two isoforms. In contrast, [SR9243](#) [47] and [BE1218](#) [180] are synthetic inverse agonists of both LXR α and LXR β .

Further reading on 1H. Liver X receptor-like receptors

- Courtney R *et al.* (2016) LXR Regulation of Brain Cholesterol: From Development to Disease. *Trends Endocrinol Metab* **27**: 404-414 [PMID:27113081]
- El-Gendy BEM *et al.* (2018) Recent Advances in the Medicinal Chemistry of Liver X Receptors. *J Med Chem* **61**: 10935-10956 [PMID:30004226]
- Gadaleta RM *et al.* (2010) Bile acids and their nuclear receptor FXR: Relevance for hepatobiliary and gastrointestinal disease. *Biochim Biophys Acta* **1801**: 683-92 [PMID:20399894]
- Merlen G *et al.* (2017) Bile acids and their receptors during liver regeneration: "Dangerous protectors". *Mol Aspects Med* **56**: 25-33 [PMID:28302491]
- Moore DD *et al.* (2006) International Union of Pharmacology. LXII. The NR1H and NR1I receptors: constitutive androstane receptor, pregnane X receptor, farnesoid X receptor alpha, farnesoid X receptor beta, liver X receptor alpha, liver X receptor beta, and vitamin D receptor. *Pharmacol Rev* **58**: 742-59 [PMID:17132852]
- Mouzat K *et al.* (2016) Liver X receptors: from cholesterol regulation to neuroprotection-a new barrier against neurodegeneration in amyotrophic lateral sclerosis? *Cell Mol Life Sci* **73**: 3801-8 [PMID:27510420]
- Schulman IG. (2017) Liver X receptors link lipid metabolism and inflammation. *FEBS Lett* **591**: 2978-2991 [PMID:28555747]

1I. Vitamin D receptor-like receptors

Nuclear hormone receptors → 1I. Vitamin D receptor-like receptors

Overview: Vitamin D (VDR), Pregnane X (PXR) and Constitutive Androstane (CAR) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 116]) are members of the NR1I family of nuclear receptors, which form heterodimers with members of the retinoid X receptor family. PXR and CAR are activated by a range of exogenous compounds, with no established endogenous physiological agonists, although high concentrations of bile acids and bile pigments activate PXR and CAR [116].

Nomenclature	Vitamin D receptor	Pregnane X receptor	Constitutive androstane receptor
Systematic nomenclature	NR1I1	NR1I2	NR1I3
HGNC, UniProt	VDR, P11473	NR1I2, O75469	NR1I3, Q14994
Endogenous agonists	1,25-dihydroxyvitamin D3 [14, 44]	17 β -estradiol [72]	–
Selective agonists	seocalcitol [31, 175], doxercalciferol	hyperforin [117, 174], 5 β -pregnane-3,20-dione [72], lovastatin [93], rifampicin [18, 93]	TCPOBOP [164] – Mouse, CITCO [102]
Selective antagonists	TEI-9647 (pIC ₅₀ 8.2) [143] – Chicken, ZK159222 (pIC ₅₀ 7.5) [48, 67]	–	–
Comments	–	–	Clotrimazole [118] and T0901317 [76] although acting at other sites, function as antagonists of the constitutive androstane receptor.

Further reading on 1I. Vitamin D receptor-like receptors

- Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
- Long MD *et al.* (2015) Vitamin D receptor and RXR in the post-genomic era. *J Cell Physiol* **230**: 758-66 [PMID:25335912]
- Moore DD *et al.* (2006) International Union of Pharmacology. LXII. The NR1H and NR1I receptors: constitutive androstane receptor, pregnane X receptor, farnesoid X receptor alpha, farnesoid X receptor beta, liver X receptor alpha, liver X receptor beta, and vitamin D receptor. *Pharmacol Rev* **58**: 742-59 [PMID:17132852]

2A. Hepatocyte nuclear factor-4 receptors

Nuclear hormone receptors → 2A. Hepatocyte nuclear factor-4 receptors

Overview: The nomenclature of hepatocyte nuclear factor-4 receptors is agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 10]. While linoleic acid has been identified as the endogenous ligand for HNF4 α its function remains ambiguous [187]. HNF4 γ has yet to be paired with an endogenous ligand.

Nomenclature	Hepatocyte nuclear factor-4 α	Hepatocyte nuclear factor-4 γ
Systematic nomenclature	NR2A1	NR2A2
HGNC, UniProt	HNF4A , P41235	HNF4G , Q14541
Endogenous agonists	linoleic acid [187]	–
Agonists	alverine [89], benfluorex [89]	–
Selective agonists	HNF4α inhibitor	–
Selective antagonists	BI6015 [81]	–
Comments	HNF4 α was purified originally from liver but is also found in other tissues including the kidney, intestines, pancreas and stomach [137, 151]. Its expression is driven by two promoters, leading to several isoform variants, the abundance of which vary between the tissues where HNF4 is expressed [82]. HNF4 α has constitutive transactivation activity [187] and binds DNA as a homodimer [71].	HNF4 γ is structurally very similar to HNF4 α although its expression is restricted to the intestinal tract. HNF4 γ has two known isoforms, though it is unknown if this is due to alternative promoter usage or alternative splicing. The two HNF4 receptors can bind DNA as heterodimers as well as homodimers [167].

Further reading on 2A. Hepatocyte nuclear factor-4 receptors

- Garattini E *et al.* (2016) Lipid-sensors, enigmatic-orphan and orphan nuclear receptors as therapeutic targets in breast-cancer. *Oncotarget* **7**: 42661-42682 [PMID:26894976]
- Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
- Herrera-Pulido JA *et al.* (2023) Hepatocyte nuclear factor 4 α multiple isoforms, their functions, and their interactomes. *Proteomics* **23**: e2200372 [PMID:37232233]
- Van Dender C *et al.* (2025) Balancing metabolism and regeneration in liver diseases through HNF4 α targeting. *Trends Endocrinol Metab* [PMID:40328612]
- Vemuri K *et al.* (2023) Multiple roles and regulatory mechanisms of the transcription factor HNF4 in the intestine. *Front Endocrinol (Lausanne)* **14**: 1232569 [PMID:37635981]
- Walesky C *et al.* (2015) Role of hepatocyte nuclear factor 4 α (HNF4 α) in cell proliferation and cancer. *Gene Expr* **16**: 101-8 [PMID:25700366]

2B. Retinoid X receptors

Nuclear hormone receptors → 2B. Retinoid X receptors

Overview: Retinoid X receptors (nomenclature as agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 54]) are NR2B family members activated by [alitretinoin](#) and the RXR-selective agonists [bexarotene](#) and [LG100268](#), sometimes referred to as rexinoids. [UVI3003](#) [119] and [HX 531](#) [42] have been described as a pan-RXR antagonists. These receptors form RXR-RAR heterodimers and RXR-RXR homodimers [25, 107].

Nomenclature	Retinoid X receptor-α	Retinoid X receptor-β	Retinoid X receptor-γ
Systematic nomenclature	NR2B1	NR2B2	NR2B3
HGNC, UniProt	RXRA , P19793	RXRB , P28702	RXRG , P48443
Sub/family-selective agonists	bexarotene [19, 24, 160]	bexarotene [19, 24, 160]	bexarotene [19, 24, 160]
Selective agonists	CD3254 [56]	–	–

Further reading on 2B. Retinoid X receptors

- Germain P *et al.* (2006) International Union of Pharmacology. LXIII. Retinoid X receptors. *Pharmacol Rev* **58**: 760-72 [PMID:17132853]
- Long MD *et al.* (2015) Vitamin D receptor and RXR in the post-genomic era. *J Cell Physiol* **230**: 758-66 [PMID:25335912]
- Menéndez-Gutiérrez MP *et al.* (2017) The multi-faceted role of retinoid X receptor in bone remodeling. *Cell Mol Life Sci* **74**: 2135-2149 [PMID:28105491]

2C. Testicular receptors

Nuclear hormone receptors → 2C. Testicular receptors

Overview: Testicular receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand, although testicular receptor 4 has been reported to respond to retinoids.

Nomenclature	Testicular receptor 2	Testicular receptor 4
Systematic nomenclature	NR2C1	NR2C2
HGNC, UniProt	NR2C1 , P13056	NR2C2 , P49116
Endogenous agonists	–	retinol [193], tretinoin [193]
Comments	Forms a heterodimer with TR4; gene disruption appears without effect on testicular development or function [149].	Forms a heterodimer with TR2.

Further reading on 2C. Testicular receptors

- Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
- Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
- Safe S *et al.* (2014) Minireview: role of orphan nuclear receptors in cancer and potential as drug targets. *Mol Endocrinol* **28**: 157-72 [PMID:24295738]
- Wu D *et al.* (2016) The emerging roles of orphan nuclear receptors in prostate cancer. *Biochim Biophys Acta* **1866**: 23-36 [PMID:27264242]

2E. Tailless-like receptors

Nuclear hormone receptors → 2E. Tailless-like receptors

Overview: Tailless-like receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	TLX	PNR
Systematic nomenclature	NR2E1	NR2E3
HGNC, UniProt	NR2E1 , Q9Y466	NR2E3 , Q9Y5X4
Agonists	BMS493 [61], tretinoin [61]	–
Comments	Gene disruption is associated with abnormal brain development [86, 115].	–

Further reading on 2E. Tailless-like receptors

- Benod C *et al.* (2016) TLX: An elusive receptor. *J Steroid Biochem Mol Biol* **157**: 41-7 [PMID:26554934]
 Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
 Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
 O'Leary JD *et al.* (2018) Regulation of behaviour by the nuclear receptor TLX. *Genes Brain Behav* **17**: e12357 [PMID:27790850]

2F. COUP-TF-like receptors

Nuclear hormone receptors → 2F. COUP-TF-like receptors

Overview: COUP-TF-like receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	COUP-TF1	COUP-TF2	V-erbA-related gene
Systematic nomenclature	NR2F1	NR2F2	NR2F6
HGNC, UniProt	NR2F1 , P10589	NR2F2 , P24468	NR2F6 , P10588
Comments	Gene disruption is perinatally lethal [136].	Gene disruption is embryonically lethal [130].	Gene disruption impairs CNS development [173].

Further reading on 2F. COUP-TF-like receptors

- Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
 Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
 Wu D *et al.* (2016) The emerging roles of orphan nuclear receptors in prostate cancer. *Biochim Biophys Acta* **1866**: 23-36 [PMID:27264242]
 Wu SP *et al.* (2016) Choose your destiny: Make a cell fate decision with COUP-TFII. *J Steroid Biochem Mol Biol* **157**: 7-12 [PMID:26658017]

3B. Estrogen-related receptors

Nuclear hormone receptors → 3B. Estrogen-related receptors

Overview: Estrogen-related receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	Estrogen-related receptor- α	Estrogen-related receptor- β	Estrogen-related receptor- γ
Systematic nomenclature	NR3B1	NR3B2	NR3B3
HGNC, UniProt	ESRRA , P11474	ESRRB , O95718	ESRRG , P62508
Comments	Activated by some dietary flavonoids [155]; activated by the synthetic agonist GSK4716 [196] and blocked by XCT790 [178].	May be activated by DY131 [185].	May be activated by DY131 [185].

Further reading on 3B. Estrogen-related receptors

Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]

Divekar SD *et al.* (2016) Estrogen-related receptor β (ERR β) - renaissance receptor or receptor renaissance? *Nucl Recept Signal* **14**: e002 [PMID:27507929]

Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]

Tam IS *et al.* (2016) There and back again: The journey of the estrogen-related receptors in the cancer realm. *J Steroid Biochem Mol Biol* **157**: 13-9 [PMID:26151739]

Wu D *et al.* (2016) The emerging roles of orphan nuclear receptors in prostate cancer. *Biochim Biophys Acta* **1866**: 23-36 [PMID:27264242]

4A. Nerve growth factor IB-like receptors

Nuclear hormone receptors → 4A. Nerve growth factor IB-like receptors

Overview: Nerve growth factor IB-like receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand, although preliminary evidence suggests that they bind fatty acid metabolites and fatty acid mimetic drugs [6, 35, 133].

Nomenclature	Nerve Growth factor IB	Nuclear receptor related 1	Neuron-derived orphan receptor 1
Systematic nomenclature	NR4A1	NR4A2	NR4A3
HGNC, UniProt	NR4A1 , P22736	NR4A2 , P43354	NR4A3 , Q92570
Comments	An endogenous agonist, cytosporone B , has been described [188], although structural analysis and molecular modelling has not identified a ligand binding site [5, 45, 172].	–	–

Further reading on 4A. Nerve growth factor IB-like receptors

- Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
- Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
- Ranhotra HS. (2015) The NR4A orphan nuclear receptors: mediators in metabolism and diseases. *J Recept Signal Transduct Res* **35**: 184-8 [PMID:25089663]
- Rodríguez-Calvo R *et al.* (2017) The NR4A subfamily of nuclear receptors: potential new therapeutic targets for the treatment of inflammatory diseases. *Expert Opin Ther Targets* **21**: 291-304 [PMID:28055275]
- Safe S *et al.* (2016) Nuclear receptor 4A (NR4A) family - orphans no more. *J Steroid Biochem Mol Biol* **157**: 48-60 [PMID:25917081]

5A. Fushi tarazu F1-like receptors

Nuclear hormone receptors → 5A. Fushi tarazu F1-like receptors

Overview: Fushi tarazu F1-like receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	Steroidogenic factor 1	Liver receptor homolog-1
Systematic nomenclature	NR5A1	NR5A2
HGNC, UniProt	NR5A1 , Q13285	NR5A2 , O00482
Comments	Reported to be inhibited by AC45594 [36] and SID7969543 [101].	–

Further reading on 5A. Fushi tarazu F1-like receptors

- Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
- Garattini E *et al.* (2016) Lipid-sensors, enigmatic-orphan and orphan nuclear receptors as therapeutic targets in breast-cancer. *Oncotarget* **7**: 42661-42682 [PMID:26894976]
- Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]
- Zhi X *et al.* (2016) Structures and regulation of non-X orphan nuclear receptors: A retinoid hypothesis. *J Steroid Biochem Mol Biol* **157**: 27-40 [PMID:26159912]
- Zimmer V *et al.* (2015) Nuclear receptor variants in liver disease. *Dig Dis* **33**: 415-9 [PMID:26045277]

6A. Germ cell nuclear factor receptors

Nuclear hormone receptors → 6A. Germ cell nuclear factor receptors

Overview: Germ cell nuclear factor receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	Germ cell nuclear factor
Systematic nomenclature	NR6A1
HGNC, UniProt	NR6A1 , Q15406

Further reading on 6A. Germ cell nuclear factor receptors

Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
 Garattini E *et al.* (2016) Lipid-sensors, enigmatic-orphan and orphan nuclear receptors as therapeutic targets in breast-cancer. *Oncotarget* **7**: 42661-42682 [PMID:26894976]
 Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]

Safe S *et al.* (2014) Minireview: role of orphan nuclear receptors in cancer and potential as drug targets. *Mol Endocrinol* **28**: 157-72 [PMID:24295738]
 Zhi X *et al.* (2016) Structures and regulation of non-X orphan nuclear receptors: A retinoid hypothesis. *J Steroid Biochem Mol Biol* **157**: 27-40 [PMID:26159912]

0B. DAX-like receptors

Nuclear hormone receptors → 0B. DAX-like receptors

Overview: Dax-like receptors (nomenclature as agreed by the [NC-IUPHAR Subcommittee on Nuclear Hormone Receptors](#) [10]) have yet to be officially paired with an endogenous ligand.

Nomenclature	DAX1	SHP
Systematic nomenclature	NROB1	NROB2
HGNC, UniProt	NROB1 , P51843	NROB2 , Q15466

Further reading on 0B. DAX-like receptors

Benoit G *et al.* (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
 Garattini E *et al.* (2016) Lipid-sensors, enigmatic-orphan and orphan nuclear receptors as therapeutic targets in breast-cancer. *Oncotarget* **7**: 42661-42682 [PMID:26894976]
 Germain P *et al.* (2006) Overview of nomenclature of nuclear receptors. *Pharmacol Rev* **58**: 685-704 [PMID:17132848]

Safe S *et al.* (2014) Minireview: role of orphan nuclear receptors in cancer and potential as drug targets. *Mol Endocrinol* **28**: 157-72 [PMID:24295738]
 Wu D *et al.* (2016) The emerging roles of orphan nuclear receptors in prostate cancer. *Biochim Biophys Acta* **1866**: 23-36 [PMID:27264242]

Steroid hormone receptors

Nuclear hormone receptors → Steroid hormone receptors

Overview: Steroid hormone receptors (nomenclature as agreed by the [NC-IUPHAR Subcommittee on Nuclear Hormone Receptors](#) [2, 33, 98]) are nuclear hormone receptors of the NR3 class, with endogenous agonists that may be divided into 3-hydroxysteroids (estrone and 17 β -estradiol) and 3-ketosteroids (dihydrotestosterone [DHT], aldosterone, cortisol, corticosterone, progesterone and testosterone). These receptors exist as dimers coupled with chaperone molecules (such as hsp90 β [HSP90AB1, P08238] and immunophilin FKBP52:FKBP4, Q02790), which are shed on binding the steroid hormone. Al-

though rapid signalling phenomena are observed [95, 135], the principal signalling cascade appears to involve binding of the activated receptors to nuclear hormone response elements of the genome, with a 15-nucleotide consensus sequence AGAACAnnTGTTCT (*i.e.* an inverted palindrome) as homo- or heterodimers. They also affect transcription by protein-protein interactions with other transcription factors, such as activator protein 1 (AP-1) and nuclear factor κ B (NF- κ B). Splice variants of each of these receptors can form functional or non-functional monomers that can dimerize to form functional or non-functional receptors.

For example, alternative splicing of PR mRNA produces A and B monomers that combine to produce functional AA, AB and BB receptors with distinct characteristics [166].

A 7TM receptor responsive to estrogen (*GPER1*, Q99527, also known as GPR30, see [134]) has been described. Human orthologues of 7TM 'membrane progesterin receptors' (*PAQR7*, *PAQR8* and *PAQR5*), initially discovered in fish [194, 195], appear to localize to intracellular membranes and respond to 'non-genomic' progesterone analogues independently of G proteins [152].

3A. Estrogen receptors

Nuclear hormone receptors → Steroid hormone receptors → 3A. Estrogen receptors

Overview: Estrogen receptor (ER) activity regulates diverse physiological processes *via* transcriptional modulation of target genes [2]. The selection of target genes and the magnitude of the response, be it induction or repression, are determined by many factors, including the effect of the hormone ligand and DNA binding on ER structural conformation, and the local cellular regulatory environment. The cellular environment defines the specific complement of DNA enhancer and promoter elements present and the availability of coregulators to form functional transcription complexes. Together, these determinants control the resulting biological response.

Nomenclature	Estrogen receptor- α	Estrogen receptor- β
Systematic nomenclature	NR3A1	NR3A2
HGNC, UniProt	ESR1 , P03372	ESR2 , Q92731
Endogenous agonists	estriol [85], estrone [85]	–
Selective agonists	propylpyrazoletriol [84, 153], ethinylestradiol [69]	WAY200070 [104], diarylpropionitrile [111, 153], prinaberel [32, 104]
Sub/family-selective antagonists	bazedoxifene (pIC ₅₀ 7.6) [114]	bazedoxifene (pIC ₅₀ 7.1) [114]
Selective antagonists	clomiphene (pK _i 8.9) [4], methyl-piperidino-pyrazole (pK _i 8.6) [156]	R,R-THC (pK _i 8.4) [110, 157], PHTPP (pK _i 6.9) [192]

Comments: R,R-THC exhibits partial agonist activity at ER α [110, 157]. Estrogen receptors may be blocked non-selectively by [tamoxifen](#) and [raloxifene](#) and labelled by [³H]17 β -estradiol and [³H]tamoxifen. Many agents thought initially to be antagonists at estrogen receptors appear to have tissue-specific efficacy (*e.g.* [Tamoxifen](#) is an antagonist at estrogen receptors in the breast, but is an agonist at estrogen receptors in the uterus), hence the descriptor SERM (selective estrogen receptor modulator) or SnuRM (selective nuclear receptor modulator). [Y134](#) has been suggested to be an ER α -selective estrogen receptor modulator [123].

Further reading on 3A. Estrogen receptors

- Coons LA *et al.* (2017) DNA Sequence Constraints Define Functionally Active Steroid Nuclear Receptor Binding Sites in Chromatin. *Endocrinology* **158**: 3212-3234 [PMID:28977594]
- Dahlman-Wright K *et al.* (2006) International Union of Pharmacology. LXIV. Estrogen receptors. *Pharmacol Rev* **58**: 773-81 [PMID:17132854]
- Gonzalez-Sanchez E *et al.* (2015) Nuclear receptors in acute and chronic cholestasis. *Dig Dis* **33**: 357-66 [PMID:26045270]
- Hewitt SC *et al.* (2016) What's new in estrogen receptor action in the female reproductive tract. *J Mol Endocrinol* **56**: R55-71 [PMID:26826253]
- Jameera Begam A *et al.* (2017) Estrogen receptor agonists/antagonists in breast cancer therapy: A critical review. *Bioorg Chem* **71**: 257-274 [PMID:28274582]
- Warner M *et al.* (2017) Estrogen Receptor β as a Pharmaceutical Target. *Trends Pharmacol Sci* **38**: 92-99 [PMID:27979317]

3C. 3-Ketosteroid receptors

Nuclear hormone receptors → Steroid hormone receptors → 3C. 3-Ketosteroid receptors

Overview: Steroid hormone receptors (nomenclature as agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors** [2, 33, 98]) are nuclear hormone receptors of the NR3 class, with endogenous agonists that may be divided into 3-hydroxysteroids ([estrone](#) and [17 \$\beta\$ -estradiol](#)) and 3-ketosteroids ([dihydrotestosterone](#) [DHT], [aldosterone](#), [cortisol](#), [corticosterone](#), [progesterone](#) and [testosterone](#)). For rodent GR and MR, the physiological ligand is corticosterone rather than cortisol. Clinically-used drugs interacting with the 3-ketosteroid receptors include testosterone (AR), methylprednisolone (GR), eplerenone (MR), and medroxyprogesterone (PR).

Nomenclature	Androgen receptor	Glucocorticoid receptor
Systematic nomenclature	NR3C4	NR3C1
HGNC, UniProt	AR , P10275	NR3C1 , P04150
Rank order of potency	dihydrotestosterone > testosterone	cortisol , corticosterone >> aldosterone , deoxycortisone [142]
Endogenous agonists	dihydrotestosterone [161]	–
Selective agonists	testosterone propionate [106], mibolerone [57], flouxymesterone [68], methyltrienolone [170], dromostanolone propionate	fluticasone propionate [13], flunisolide [4], beclomethasone [4], methylprednisolone [4], beta-methasone [4], budesonide [113]
Selective antagonists	bicalutamide (pK _i 7.7) [79], PF0998425 (pIC ₅₀ 7.1–7.5) [97], enzalutamide (pIC ₅₀ 7.4) [162], nilutamide (pIC ₅₀ 7.1–7.1) [150], hydroxyflutamide (pEC ₅₀ 6.6) [170], galeterone (pIC ₅₀ 6.4) [64], flutamide (Displacement of ³ [H] testosterone from wild-type androgen receptors) (pK _i 5.4) [169]	onapristone (pIC ₅₀ 7.6) [189], ZK112993
Labelled ligands	[³H]dihydrotestosterone (Selective Agonist), [³H]methyltrienolone (Selective Agonist), [³H]mibolerone (Agonist)	[³H]dexamethasone (Agonist)

Nomenclature	Mineralocorticoid receptor	Progesterone receptor
Systematic nomenclature	NR3C2	NR3C3
HGNC, UniProt	NR3C2 , P08235	PGR , P06401
Rank order of potency	corticosterone , cortisol , aldosterone , progesterone [142]	progesterone
Endogenous agonists	deoxycorticosterone [142], aldosterone [65, 142], cortisol [65, 142], corticosterone	progesterone [43]
Selective agonists	fludrocortisone [142]	medroxyprogesterone (Affinity at human PR-A) [190], ORG2058 , levonorgestrel [12, 145]
Endogenous antagonists	progesterone (pIC ₅₀ 11) [142]	–
Antagonists	spironolactone (pK _i 8.6) [9], eplerenone (pIC ₅₀ 6.4), canrenone , drospirenone [132]	–
Selective antagonists	esaxerenone (pIC ₅₀ 8.6) [77, 131], finerenone (pIC ₅₀ 7.7) [8], balcirenone (pIC ₅₀ 6.4) [59], onapristone (pIC ₅₀ 6.3) [189]	ulipristal acetate (pIC ₅₀ 9.7) [140], mifepristone (Mixed) (pK _i 9) [191], onapristone (pK _i 7.7) [63], ZK112993
Labelled ligands	[³H] corticosterone (Agonist) [124], [³H] cortisol (Agonist) [124], [³H]aldosterone (Agonist) [49]	[³H]ORG2058 (Selective Agonist)
Comments	Pre-receptor ligand specificity is provided for the MR in tissues associated with maintenance of sodium homeostasis by the co-expression of 11β-hydroxysteroid dehydrogenase type II which converts cortisol (corticosterone in rodents) to their inactive forms. Given the increasing use of <i>Danio rerio</i> (zebrafish) as an experimental model, it is important to note that progesterone (and spironolactone) is a MR agonist in fish [50]. For GR and MR in rodents, the physiological ligand is corticosterone rather than cortisol.	–

Comments: [³H]dexamethasone also binds to MR *in vitro*. PR antagonists have been suggested to subdivide into Type I (e.g. **onapristone**) and Type II (e.g. **ZK112993**) groups. These groups appear to promote binding of PR to DNA with different efficacies and evoke distinct conformational changes in the receptor, leading to a transcription-neutral complex [51, 94]. Mutations in AR underlie testicular feminization and androgen insensitivity syndromes, spinal and bulbar muscular atrophy (Kennedy's disease).

Further reading on 3C. 3-Ketosteroid receptors

- Baker ME *et al.* (2017) 30 YEARS OF THE MINERALOCORTICOID RECEPTOR: Evolution of the mineralocorticoid receptor: sequence, structure and function. *J Endocrinol* **234**: T1-T16 [PMID:28468932]
- Carroll JS *et al.* (2017) Deciphering the divergent roles of progestogens in breast cancer. *Nat Rev Cancer* **17**: 54-64 [PMID:27885264]
- Cohen DM *et al.* (2017) Nuclear Receptor Function through Genomics: Lessons from the Glucocorticoid Receptor. *Trends Endocrinol Metab* **28**: 531-540 [PMID:28495406]
- Lu NZ *et al.* (2006) International Union of Pharmacology. LXV. The pharmacology and classification of the nuclear receptor superfamily: glucocorticoid, mineralocorticoid, progesterone, and androgen receptors. *Pharmacol Rev* **58**: 782-97 [PMID:17132855]
- Lucas-Herald AK *et al.* (2017) Genomic and non-genomic effects of androgens in the cardiovascular system: clinical implications. *Clin Sci* **131**: 1405-1418 [PMID:28645930]
- Weikum ER *et al.* (2017) Glucocorticoid receptor control of transcription: precision and plasticity via allosterity. *Nat Rev Mol Cell Biol* **18**: 159-174 [PMID:28053348]

Further reading on Nuclear hormone receptors

- Burris TP *et al.* (2023) International Union of Basic and Clinical Pharmacology CXIII: Nuclear Receptor Superfamily-Update 2023. *Pharmacol Rev* **75**: 1233-1318 [PMID:37586884]

References

1. Alexander SP *et al.* (2021) [34529827]
2. Alexander SPH *et al.* (2019) [31710718]
3. Apfel C *et al.* (1992) [1323127]
4. Auerbach SS *et al.* DrugMatrix. Accessed on 02/05/2014.
5. Baker KD *et al.* (2003) [12809604]
6. Ballarotto M *et al.* (2023) [37256819]
7. Ban SY *et al.* (2025) [39919463]
8. Bärfacker L *et al.* (2012) [22791416]
9. Bell MG *et al.* (2007) [18038968]
10. Benoit G *et al.* (2006) [17132856]
11. Bergh JJ *et al.* (2005) [15802494]
12. Bergink EW *et al.* (1983) [6645495]
13. Biggadike K *et al.* (2000) [10633034]
14. Bishop JE *et al.* (1994) [7976510]
15. Bishop-Bailey D *et al.* (2000) [11030710]
16. Bishop-Bailey D *et al.* (2003) [12749590]
17. Bitsch F *et al.* (2003) [14622968]
18. Blumberg B *et al.* (1998) [9784494]
19. Boehm MF *et al.* (1994) [8071941]
20. Brown KK *et al.* (1999) [10389847]
21. Brown PJ *et al.* (2001) [11354382]
22. Brun LD *et al.* (1980) [6777394]
23. Burreis TP *et al.* (2023) [37586884]
24. Canan Koch SS *et al.* (1999) [10052980]
25. Chambon P. (1996) [8801176]
26. Chao EY *et al.* (2008) [18800767]
27. Charpentier B *et al.* (1995) [8544175]
28. Charton J *et al.* (2009) [19058965]
29. Chiellini G *et al.* (1998) [9653548]
30. Collins JL *et al.* (2002) [11985463]
31. Colston KW *et al.* (1992) [1472092]
32. Cvorro A *et al.* (2008) [18097065]
33. Dahlman-Wright K *et al.* (2006) [17132854]
34. De Filippis B *et al.* (2011) [21889235]
35. de Vera IM *et al.* (2016) [27128111]
36. Del Tredici AL *et al.* (2008) [18055761]
37. Delescluse C *et al.* (1991) [1656191]
38. Doebber TW *et al.* (2004) [15120604]
39. Downes M *et al.* (2003) [12718892]
40. Eberl G *et al.* (2004) [15247480]
41. Eberl G *et al.* (2004) [14691482]
42. Ebisawa M *et al.* (1999) [10748721]
43. Edwards JP *et al.* (1998) [9667968]
44. Erben RG *et al.* (2002) [12089348]
45. Flaig R *et al.* (2005) [15716272]
46. Flamant F *et al.* (2006) [17132849]
47. Flaveny CA *et al.* (2015) [26120082]
48. Fujishima T *et al.* (2003) [12901907]
49. Fuller PJ *et al.* (1976) [966452]
50. Fuller PJ *et al.* (2019) [31439819]
51. Gass EK *et al.* (1998) [9528977]
52. Géhin M *et al.* (1999) [10421757]
53. Germain P *et al.* (2006) [17132850]
54. Germain P *et al.* (2006) [17132853]
55. Germain P *et al.* (2009) [19477412]
56. Germain P *et al.* (2002) [11805839]
57. Giwerzman A *et al.* (2000) [10852459]
58. Graham TL *et al.* (2005) [15939051]
59. Granberg KL *et al.* (2019) [30596500]
60. Grant D *et al.* (2010) [20677822]
61. Griffett K *et al.* (2020) [32763139]
62. Guo Q *et al.* (2004) [14701675]
63. Hamann LG *et al.* (1996) [8627601]
64. Handratta VD *et al.* (2005) [15828836]
65. Hellal-Levy C *et al.* (1999) [10611474]
66. Henke BR *et al.* (1998) [9836620]
67. Herdick M *et al.* (2000) [11094341]
68. Higuchi RI *et al.* (2007) [17439112]
69. Jain N *et al.* (2006) [16722623]
70. Janowski BA *et al.* (1996) [8878485]
71. Jiang G *et al.* (1995) [7651430]
72. Jones SA *et al.* (2000) [10628745]
73. Kallen J *et al.* (2004) [14722075]
74. Kallen JA *et al.* (2002) [12467577]
75. Kane CD *et al.* (2009) [18971326]
76. Kanno Y *et al.* (2013) [23665929]
77. Kato M *et al.* (2018) [29688582]
78. Keidel S *et al.* (1994) [8264595]
79. Kinoyama I *et al.* (2006) [16420057]
80. Kirchgessner TG *et al.* (2016) [27508871]
81. Kiselyuk A *et al.* (2012) [23675769]
82. Ko HL *et al.* (2019) [30840880]
83. Kojetin D *et al.* (2011) [21043485]
84. Kraichely DM *et al.* (2000) [11014206]
85. Kuiper GG *et al.* (1997) [9048584]
86. Land PW *et al.* (2003) [12902391]
87. Le Q *et al.* (2000) [10723137]
88. Lee G *et al.* (2002) [11877444]
89. Lee SH *et al.* (2013) [23675775]
90. Leesnitzer LM *et al.* (2002) [12022867]
91. Lehmann JM *et al.* (1997) [9013544]
92. Lehmann JM *et al.* (1997) [9013583]
93. Lehmann JM *et al.* (1998) [9727070]
94. Leonhardt SA *et al.* (1998) [9849965]
95. Levin ER. (2008) [18784332]
96. Li E. (1999) [10331664]
97. Li JJ *et al.* (2008) [18921992]
98. Lu NZ *et al.* (2006) [17132855]
99. Lund BW *et al.* (2009) [19239230]
100. Lund BW *et al.* (2005) [16302793]
101. Madoux F *et al.* (2008) [18334597]
102. Maglich JM *et al.* (2003) [12611900]
103. Makishima M *et al.* (1999) [10334992]
104. Malamas MS *et al.* (2004) [15456246]
105. Maloney PR *et al.* (2000) [10956205]
106. Manfredi MC *et al.* (2007) [17574413]
107. Mangelsdorf DJ *et al.* (1995) [8521508]
108. Matta-Camacho E *et al.* (2014) [24872411]
109. McIntyre TM *et al.* (2003) [12502787]
110. Meyers MJ *et al.* (1999) [10395487]
111. Meyers MJ *et al.* (2001) [11708925]
112. Michalik L *et al.* (2006) [17132851]
113. Millan DS *et al.* (2011) [21880489]
114. Miller CP *et al.* (2001) [11356100]
115. Monaghan AP *et al.* (1997) [9394001]
116. Moore DD *et al.* (2006) [17132852]
117. Moore LB *et al.* (2000) [10852961]
118. Moore LB *et al.* (2000) [10748001]
119. Nahoum V *et al.* (2007) [17947383]
120. Nakamuta M *et al.* (2002) [11991651]
121. Nguyen NH *et al.* (2002) [12109914]
122. Nguyet Nguyen TM *et al.* (2024) [39032762]
123. Ning M *et al.* (2007) [17115070]
124. Nixon M *et al.* (2016) [27535620]
125. Oliver WR *et al.* (2001) [11309497]
126. Otte K *et al.* (2003) [12529392]
127. Paravicini G *et al.* (1996) [8858107]
128. Parks DJ *et al.* (1999) [10334993]
129. Pellicciari R *et al.* (2002) [12166927]
130. Pereira FA *et al.* (1999) [10215630]
131. Piotrowski DW. (2012) [22866979]
132. Pollow K *et al.* (1992) [1493716]
133. Prossnitz ER *et al.* (2017) [28252961]
134. Prossnitz ER *et al.* (2008) [18271749]
135. Prossnitz ER *et al.* (2009) [19389460]
136. Qiu Y *et al.* (1997) [9271116]
137. Radi SH *et al.* (2023) [37600688]
138. Raghuram S *et al.* (2007) [18037887]
139. Repa JJ *et al.* (2000) [10968783]
140. Rewinkel J *et al.* (2008) [18243712]
141. Rocchi S *et al.* (2001) [11684010]
142. Rupperecht R *et al.* (1993) [8282004]
143. Saito N *et al.* (2006) [17125259]
144. Sakamoto J *et al.* (2000) [11095972]
145. Schindler AE *et al.* (2003) [14670641]
146. Schupp M *et al.* (2007) [17290005]
147. Sharma SK *et al.* (1977) [269396]
148. Shearer BG *et al.* (2008) [17975020]
149. Shyr CR *et al.* (2002) [12052874]
150. Simard J *et al.* (1997) [9111629]
151. Sladek FM *et al.* (1990) [2279702]
152. Smith JL *et al.* (2008) [18603275]
153. Stauffer SR *et al.* (2000) [11150164]
154. Stehlin-Gaon C *et al.* (2003) [12958591]
155. Suetsugi M *et al.* (2003) [14638870]
156. Sun J *et al.* (2002) [11861516]
157. Sun J *et al.* (1999) [9927308]
158. Sun Z *et al.* (2000) [10875923]
159. Sznajdman ML *et al.* (2003) [12699745]
160. Thacher SM *et al.* (2000) [10637371]
161. Tilley WD *et al.* (1989) [2911578]
162. Tran C *et al.* (2009) [19359544]
163. Tully DC *et al.* (2017) [29148806]
164. Tzamelis I *et al.* (2000) [10757780]
165. Urizar NL *et al.* (2002) [11988537]
166. Vegeto E *et al.* (1993) [8264658]
167. Vemuri K *et al.* (2023) [37635981]
168. Vizirianakis IS *et al.* (2010) [20925433]
169. Wakabayashi K *et al.* (2008) [18571420]
170. Wang LG *et al.* (1998) [10076535]
171. Wang Y *et al.* (2000) [11043571]
172. Wang Z *et al.* (2003) [12774125]
173. Warnecke M *et al.* (2005) [15741322]
174. Wentworth JM *et al.* (2000) [10974665]
175. Wiberg K *et al.* (1995) [8573413]
176. Wiesenberg I *et al.* (1995) [7885826]
177. Willson TM *et al.* (2000) [10691680]
178. Willy PJ *et al.* (2004) [15184675]
179. Wu J *et al.* (2002) [12089353]
180. Xu H *et al.* (2021) [34124002]
181. Xu HE *et al.* (2002) [11845213]
182. Xu Y *et al.* (2004) [15115385]
183. Yin L *et al.* (2007) [18006707]
184. Young PW *et al.* (1998) [9454824]
185. Yu DD *et al.* (2005) [15713377]
186. Yu DD *et al.* (2014) [24775917]
187. Yuan X *et al.* (2009) [19440305]
188. Zhan Y *et al.* (2008) [18690216]
189. Zhi L *et al.* (2003) [12781198]
190. Zhi L *et al.* (1998) [9464360]
191. Zhi L *et al.* (2003) [12781197]
192. Zhou HB *et al.* (2007) [17228884]
193. Zhou XE *et al.* (2011) [21068381]
194. Zhu Y *et al.* (2003) [12601167]
195. Zhu Y *et al.* (2003) [12574519]
196. Zuercher WJ *et al.* (2005) [15857113]