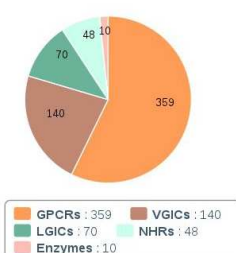


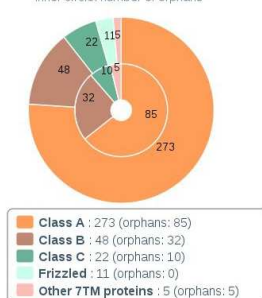
Number of human genes



Highcharts.com

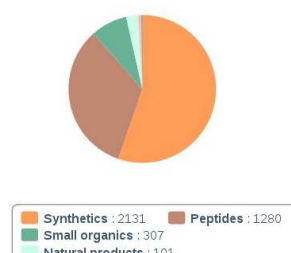
GPCR classes

Inner circle: number of orphans*



Highcharts.com

Ligand classes



Highcharts.com

IUPHAR-DB features include:

- Detailed pharmacological, structural, functional, genomic and physiological information about human and rodent receptors, using IUPHAR-approved nomenclature.
- Content is peer reviewed by members of the IUPHAR Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR); the data are provided through manual curation of the primary literature by a network of over 60 subcommittees.
- Aim is to provide a rigorously curated “gold standard” set of recommended pharmacological tools (licensed drugs, commercially available experimental compounds and radioligands) that have the best profile of “off-target” actions, effectiveness across commonly used experimental species and proven efficacy both in vitro and in vivo.
- Search the database by keyword, reference, gene symbol, id, ligand structure.

Agonists

Key to terms and symbols View all chemical structures Click column headers to sort

Ligand	Sp.	Action	Affinity	Units	Reference
(*)aceclidine	Hs	Full agonist	5.7	pEC ₅₀	76
(*)aceclidine	Hs	Partial agonist	5.1	pEC ₅₀	76
Mch-A-343	Hs	Partial agonist	5.0 – 5.3	pK _i	11
HNHC 11-1314	Hs	Full agonist	7.1 – 7.7	pK _i	39
HNHC 11-1585	Hs	Full agonist	8.3	pK _i	39
HNHC 11-1607	Hs	Full agonist	8.1	pK _i	39
acetylcholine	Rn	Full agonist	5.6	pK _i	79
acetylcholine	Hs	Full agonist	4.5 – 5.4	pK _i	46,79-80
arecaidine propargyl ester	Hs	Full agonist	5.7	pK _i	80
arecoline	Hs	Full agonist	5.4	pK _i	80
bethanecol	Hs	Full agonist	4.2	pK _i	80
carbachol	Hs	Full agonist	4.0 – 4.4	pK _i	79-80,82
carbachol	Rn	Full agonist	4.2	pK _i	79
surmethide	Hs	Full agonist	4.1	pK _i	80

Ligand 16: 298

Ligand name: **carbachol**

2D Structure

Calculated Physical-Chemical Properties

Hydrogen bond acceptors	3
Hydrogen bond donors	1
Rotatable bonds	4
Topological polar surface area	62.32
Molecular weight	147.11
XLogP	-0.98
No. Lipinski's rules broken	0

Molecular properties generated using the CDK.

Summary | Biological activity | References | Structure | Similar ligands

Classification

Compound class	Synthetic organic
Approved drug	Yes (source: DrugBank)

Chair

Michael Spedding, France

Vice Chairs

Anthony Davenport, UK - Evolving
Pharmacology

Anthony Harmar, UK – Database

Rick Neubig, USA - GPCRs

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~600 Contributors

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International Union of Basic and Clinical Pharmacology. LXXXV: Calcium-Activated Chloride Channels

Fen Huang, Xiuming Wong, and Lily Y. Jan

Department of Physiology, Howard Hughes Medical Institute, University of California, San Francisco, California

BJP British Journal of
Pharmacology

Themed Section: Secretin Family (Class B) G Protein-Coupled Receptors –
from Molecular to Clinical Perspectives

International Union of Basic and Clinical Pharmacology Review

Pharmacology and functions of receptors for vasoactive intestinal peptide and pituitary adenylate cyclase-activating polypeptide: IUPHAR Review 1

Anthony J Harmar¹, Jan Fahrenkrug², Ilana Gozes³, Marc Laburthe⁴,
Victor May⁵, Joseph R Pisegna⁶, David Vaudry⁷, Hubert Vaudry⁷,
James A Waschek⁸ and Sami I Said⁹

GPR183 (EBI2) & oxysterols.

Statement by NC-IUPHAR on GPR183 (EBI2)

"Two independent reports (1, 2) propose 7 α , 25-dihydroxycholesterol (7 α ,25-OHC) as an endogenous ligand of this receptor. 7 α ,25-OHC is synthesised from cholesterol by the sequential action of cholesterol 25-hydroxylase (CH25H) and CYP7B1 (25-hydroxycholesterol 7- α -hydroxylase). Consistent with 7 α ,25-OHC as an endogenous ligand, inhibition of CYP7B1 with clotrimazole reduced the content of 7 α ,25-OHC in the mouse spleen and mimicked the phenotype of pre-activated B cells from EBI2-deficient mice (2) and mice deficient in CH25H had a similar phenotype to EBI2 knockout mice."

1. Hannedouche S, Zhang J, Yi T, Shen W, Nguyen D, Pereira JP, Guerini D, Baumgarten BU, Roggo S, Wen B, Knochenmuss R, Noël S, Gessier F, Kelly LM, Vanek M, Laurent S, Preuss I, Miault C, Christen I, Karuna R, Li W, Koo DI, Suply T, Schmedt C, Peters EC, Falchetto R, Katopodis A, Spanka C, Roy MO, Dethoux M, Chen YA, Schultz PG, Cho CY, Seuwen K, Cyster JG, Sailer AW. (2011) Oxysterols direct immune cell migration via EBI2. *Nature*. **475** (7357): 524-7. [PMID: [21796212](#)]
2. Liu C, Yang XV, Wu J, Kuei C, Mani NS, Zhang L, Yu J, Sutton SW, Qin N, Banie H, Karlsson L, Sun S, Lovenberg TW. (2011) Oxysterols direct B-cell migration through EBI2. *Nature*. **475** (7357): 519-23. [PMID: [21796211](#)]

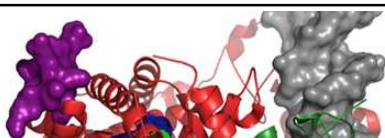
Crystal structures of the μ and κ opioid receptors

Comments by Brian M. Cox:

It is now almost 60 years since Beckett and Casy first proposed that morphine and related drugs must act through a specific receptor in brain to induce analgesia (1), and nearly 40 years since three groups independently showed the presence of high affinity binding sites for such drugs in the central nervous system (2, 3, 4). Another milestone in our understanding of the actions of morphine like drugs comes with the publication this month of the crystal structures of two of the four closely related opioid peptide receptors, the κ opioid receptor (5) and the μ opioid receptor (6). Morphine and other opiates used therapeutically act predominantly through the μ receptor while the κ receptor is activated predominantly by some ketocyclazocines, by the hallucinogenic agent salvinorin A, and by the endogenous opioid dynorphin.

The new reports follow closely on reports earlier this year of other GPCRs. The two groups responsible for these latest developments used similar strategies; the receptors were crystallized as complexes with very tightly binding highly receptor-type-selective antagonist ligands; JD1c in the case of the κ receptor and β -FNA for the μ receptor. Thus in each case the receptor is visualized in an inactive conformation. Nevertheless, some interesting features are immediately apparent. Both receptors crystallized as dimers, with more than one potential interface between adjacent receptor monomers as possible dimerization sites. Higher polymerization states and heterodimerization with other GPCRs are possible. These observations provide a structural basis for earlier proposals that opioid receptors might function as dimers or higher polymers (7). Opiate drugs are also known for their rapid reversibility - the immediacy of the reversal of opiate-induced respiratory depression by naloxone can be dramatic. The new studies show that the ligand binding pockets of both the μ and κ receptors are unusually exposed or open relative to other GPCRs. The accessibility of the binding pocket favors rapid dissociation (except in the case of irreversible antagonists such as β -FNA). Since the affinity of many agonist and antagonists at μ or κ receptors is high despite their rapid reversibility, their association rates must also be very high.

Another feature of opioid receptors is the apparent ability of different ligands acting through the same receptor type to direct signaling through different effector pathways. Ligands for opioid receptors are chemically very heterogeneous. The reported structures for the μ and κ receptors point to accessory sites around the common ligand binding pocket for each receptor that provide additional points of receptor interaction for some ligands. Much work needs to be done to understand the basis of agonism at these receptors, but it is tempting to speculate that these additional interaction sites for some ligands might be exploited in the design of agonists preferentially driving signaling through alternative transduction pathways.



Guide to PHARMACOLOGY

<http://www.guidetopharmacology.org>

A new collaboration between IUPHAR and the British Pharmacological Society (BPS).

The Guide to Pharmacology is intended to become a "one-stop shop" source of quantitative information on drug targets and the prescription medicines and experimental drugs that act on them.

It provides a single entry point to a database of information from the 5th edition of the BPS Guide to Receptors and Channels (GRAC) and the IUPHAR database.



Guide to Pharmacology features include:

- Succinct overview of the key properties of >1600 established or potential human drug targets.
- Background reading, expert summaries, recommended agonists and inhibitors.
- Links to detailed information and ligand lists in IUPHAR-DB.
- Fully searchable by keyword, gene symbol, ligand and reference.

5-Hydroxytryptamine receptors

More information on this family may be found on the [IUPHAR-DB](#) family and introduction pages.

Overview Hide

5-HT receptors [nomenclature as agreed by [ICUPHAR Subcommittee on 5-HT receptors](#) (Hoyer *et al.*, 1994 [88]) and subsequently revised (Hartig *et al.*, 1996 [8]) ionotropic 5-HT₁ class, GPCR receptors where the endogenous agonist is 5-HT. The diversity of metabotropic 5-HT receptors is increased by alternative splicing that produces (non-functional), 5-HT_{1C} (non-functional), 5-HT_{1D}, 5-HT_{1E} (non-functional) and 5-HT_{1F} receptors. Unique amongst the GPCRs, RNA editing produces 5-HT_{2C} receptor isoforms that and specificity of coupling to G_{q/11} and also pharmacology [8,89]. Most 5-HT receptors (except 5-HT_{1A} and 5-HT_{2A/2C}) play specific roles mediating functional responses in the CNS [89]. Ramage and Villalón, 2008 [79].

Receptors Hide


Unless otherwise stated all data refer to the human proteins. Gene information is provided for human (Hs), mouse (Mm) and rat (Rn).

5-HT _{1A} <small>Hide</small>	
Nomenclature	5-HT _{1A}
Other names	-
IUPHAR-DB	5-HT _{1A}
Genes	HTR1A (Hs), H01a (Mm), HR1a (Rn)
Ensembl ID	ENSG00000178394 (Hs), ENSMUSG00000021721 (Mm), ENSRNOG00000010254 (Rn)
Principal transduction	G _{1A}
Selective agonists (pK_i)	U92016A (9.7) [56] 8-OH-DPAT (8.4 – 9.4) [19,32,41,49,61,66-68] F15599 (8.6) [69]
Selective antagonists (pK_i)	WAY-100635 (9.9 – 9.2) [66-67] (S)-UK-381 (7.9 – 8.6)
Radio ligands (K_d)	p-[³ H]mPPF [³ H]WAY-100635 (Antagonist) [³ H]PF-234008 (1.4 x 10 ⁻⁸ M) [80]

Ligand 86-7

Ligand name: 8-OH-DPAT

2D Structure Hide



Calculated Physical-Chemical Properties Hide

Hydrogen bond acceptors	5
Hydrogen bond donors	3
Polarizable bonds	9
Topological polar surface area	23.47
Molecular weight	247.19
KLlogP	0.74
Hb: Lipinski's rules broken	0

Molecular properties generated using the CDK.

Summary | **Biological activity** | **References** | **Structure** | **Similar ligands** | **Radio analogues**

GRAC BIP Guide to Receptors and Channels

Selectivity data from the Guide to Receptors and Channels (GRAC), 9th Edition.

Selectivity at human receptors (unless otherwise stated)

Key to terms and symbols Click column headers to sort

Receptor	Type	Action	Affinity	Units	Concentration range (nM)	Reference
5-HT _{1A}	Agonist	Full agonist	8.4 – 9.4	pK _i	-	1-8

IUPHAR DATABASE International Union of Basic and Clinical Pharmacology

Selectivity data from IUPHAR-DB

Selectivity at human GPCRs Click column headers to sort

Key to terms and symbols

Receptor	Type	Action	Affinity	Units	Concentration range (nM)	Reference
5-HT _{1A}	Agonist	Full agonist	8.4 – 9.4	pK _i	-	1-8
5-HT _{1D}	Agonist	Full agonist	6.9 – 7.3	pK _i	-	9-11
5-HT _{1F}	Agonist	Full agonist	6.3 – 7.6	pK _i	-	22-25