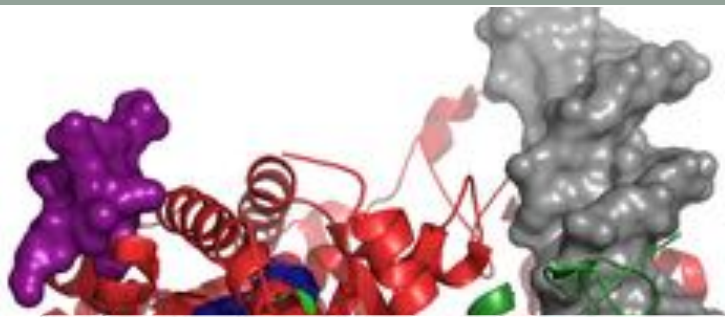


IUPHAR/BPS Guide to PHARMACOLOGY

Generic slides for use in presentations and teaching materials

- These slides are provided for public use to facilitate the production of teaching materials and presentations describing the IUPHAR/BPS Guide to PHARMACOLOGY (www.guidetopharmacology.org).
- The slide set is divided up into sections which can be mixed and matched as required.
- They are provided under the [CC BY license](#) allowing you to adapt and use them for any purpose as long as we are acknowledged as the original authors.
- The data described herein are current as of December 2017.
- These slides are available to download as a Microsoft PowerPoint file at http://www.guidetopharmacology.org/slides/GtoPdb_Generic_Slides.pptx and a PDF at http://www.guidetopharmacology.org/slides/GtoPdb_Generic_Slides.pdf
- They are also available on SlideShare at <https://www.slideshare.net/GuidetoPHARM/gtopdb-generic-slides-201718>



IUPHAR/BPS
Guide to PHARMACOLOGY

The IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb)

<http://www.guidetopharmacology.org>

Name

Date, Venue



BRITISH
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THE UNIVERSITY
of EDINBURGH



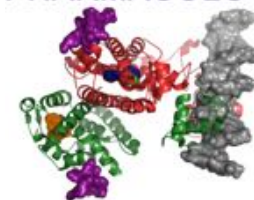
Contents

- Background and history of the database
- About NC-IUPHAR
- Database content
- Navigating the website and search tools
- Recent additions and expansions
- The Concise Guide to PHARMACOLOGY
- The IUPHAR Guide to IMMUNOPHARMACOLOGY
- The IUPHAR/MMV Guide to MALARIA PHARMACOLOGY
- Additional features and resources
- The Pharmacology Education Project
- Acknowledgements

BACKGROUND AND HISTORY OF THE DATABASE

Introducing GtoPdb (1)

IUPHAR/BPS
Guide to
PHARMACOLOGY



- In early 2011 a collaboration was initiated between The International Union of Basic and Clinical Pharmacology (IUPHAR) and the British Pharmacological Society
- Aim: to develop a single entry point to information on pharmacological targets and their ligands



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SOCIETY**

Introducing GtoPdb (2)

- A single entry point to previously **separate but complementary** information originally contained in the IUPHAR database (IUPHAR-DB) and the Guide to Receptors and Channels (GRAC) series of publications



Remit of GtoPdb

GtoPdb aims to:

- Provide access to data on all known biological targets
- Make recommendations on ligands for use in characterising those targets
- Provide an entry point into the pharmacological literature
- Provide an integrated educational resource with high quality training in the principles of basic and clinical pharmacology and techniques
- Foster innovative drug discovery

A brief history of IUPHAR-DB

- Development of the IUPHAR database of receptors and channels began in 2000
- Developed by a team of curators, guided by the IUPHAR Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR) and its international network of expert subcommittees
- In-depth coverage of the properties and pharmacology of G protein-coupled receptors, voltage- and ligand-gated ion channels, and nuclear hormone receptors.



A brief history of GRAC

- The Guide to Receptors and Channels (GRAC)
- Published biennially since 2004 in the *British Journal of Pharmacology*
- Provides a rapid overview of the key properties of a wide range of established or potential pharmacological targets
- Information arranged succinctly, so that a newcomer to a particular target group can identify the main elements '**at a glance**'.



ABOUT NC-IUPHAR

About NC-IUPHAR

The International Union of Basic and Clinical Pharmacology Committee on Receptor Nomenclature and Drug Classification

- Objectives:
 - Issue guidelines for the nomenclature and classification of human biological targets
 - Facilitate the designation of newly discovered sequences as functional biological targets and potential drug targets
 - Designate the polymorphisms and variants which are functionally important
 - Develop an authoritative and freely available, global online resource, the Guide to PHARMACOLOGY (<http://www.guidetopharmacology.org>)
- NC-IUPHAR expert reviews:
 - Nomenclature articles published in *Pharmacological Reviews*
 - Articles and editorials on varied topics published in *British Journal of Pharmacology*
 - Cumulative H-Index for NC-IUPHAR is >70.

<http://www.guidetopharmacology.org/nciuphar.jsp>

NC-IUPHAR membership (1)

Executive Committee

Stephen Alexander, UK (Chair)
Arthur Christopoulos, Australia (Deputy Chair)
Anthony Davenport, UK (Funding Liaison)
Jamie A. Davies (Database Chair/PI)
Doriano Fabbro, Switzerland (Industry Liaison)
Adam Pawson, UK (Executive Secretary)

Core members

Stephen Alexander, UK
Arthur Christopoulos, Australia
John Cidlowski, USA
Anthony Davenport, UK
Doriano Fabbro, Switzerland
Kozo Kaibuchi, Japan
Yoshikatsu Kanai, Japan
Francesca Levi-Schaffer, Israel
Eliot Ohlstein, USA - Editor
John A. Peters, UK
Alex Phipps, UK
Joerg Striessnig, Austria

Ex Officio

Ingolf Cascorbi, Germany (IUPHAR President)
Michael Spedding, France (IUPHAR Secretary-General)
James Barrett, USA (IUPHAR Treasurer)
Amrita Ahluwalia, UK (BJP Editor-in-Chief)
Elspeth Bruford, UK (HGNC Group Coordinator)
Simon Maxwell, UK (Educational Site Project Leader)
Jamie A. Davies, UK (Database Chair/Principal Investigator)
Jane Armstrong, UK (Database Curator)
Elena Faccenda, UK (Database Curator)
Simon D. Harding, UK (Senior Database Developer)
Adam Pawson, UK (Senior Database Curator)

Past Chairs (ex officio)

Paul Vanhoutte, China
Robert Ruffolo, USA

NC-IUPHAR membership (2)

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Tom I. Bonner, USA
Michel Bouvier, Canada
Thomas Burris, USA
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Stephen Charlton, UK
Moses Chao, USA
Mark Coles, UK
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Philippe Delerive, France
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Gillian Gray, UK
Debbie Hay, New Zealand
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Michael F. Jarvis, USA
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Terry Kenakin, USA
Janos Kiss, Hungary
Stefan Knapp, UK
Andrew Knight, UK
Chris Langmead, Australia
Vincent Laudet, France

Margaret (Mandy) MacLean, UK
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Fiona Marshall, UK
Alistair Mathie, UK
Ian McGrath, UK
Graeme Milligan, UK
Richard Neubig, USA
Stefan Offermanns, Germany
Richard Olsen, USA
Jean-Philippe Pin, France
Helgi Schiöth, Sweden
David Searls, USA
Graeme Semple, USA
Patrick M. Sexton, Australia
Joanna L. Sharman, UK
Christopher Southan, Sweden
Roland Staal, USA
Bart Staels, France
Georg Terstappen, Germany
Katerina Tiligada, Greece
Mary Vore, USA

Clinical Translational Pharmacology Group

Ed Bullmore, UK
Robert Dow, UK
Garrett Fitzgerald, USA
Alex Phipps, UK
Patrick du Souich, Canada
David Webb, UK
Don Birkett, Australia

NC-IUPHAR subcommittees

NC-IUPHAR Subcommittee Chairs/Liaisons (96 subcommittees; >500 scientists)

G protein-coupled receptors Subcommittees

5-Hydroxytryptamine: Nick Barnes, John Neumaier
alpha₁-adrenoceptors: Dianne Perez
Apelin: Anthony Davenport
Bombesin: Robert Jensen
Calcium-sensing: Ed Brown, Hans Bräuner-Osborne
Cholecystokinin: Laurence Miller
Dopamine: Raul Gainetdinov
Formylpeptide family: Richard Ye
GABA_B: Bernhard Bettler
Glucagon receptor family: Laurence Miller
Histamine: Paul Chazot
Leukotriene: Magnus Bäck
Melanin-concentrating hormone: Jean-Louis Nahon
Metabotropic glutamate: Jean-Philippe Pin
Neuropeptide FF/neuropeptide AF: Jean-Marie Zajac
Neuropeptide Y: Dan Larhammar
Orexin: Christopher Winrow
Peptide P518: Jerome Leprince
Prolactin-releasing peptide: Helgi Schiöth
Relaxin family peptide: Roger Summers
Tachykinin: Susan Leeman, Steven Douglas
Urotensin: Hubert Vaudry

Ligand-gated ion channels Subcommittees

John Peters (Liaison for all LGIC subcommittees)

5-HT₃: John Peters
GABA_A: Richard Olsen
Glycine: Joseph Lynch
Ionotropic glutamate: Graham Collingridge
Nicotinic acetylcholine: Neil Millar
P2X: Charles Kennedy
ZAC: Timothy Hales

Antibodies Subcommittee

Alex Phipps

Adenylyl cyclases Subcommittee

Carmen Dessauer

Drug Target and Chemistry Curation Subcommittee

Christopher Southan

Epigenetics Subcommittee

Rabinder Prinjha

Acetylcholine (muscarinic): Arthur Christopoulos
alpha₂-adrenoceptors: VACANT
beta-adrenoceptors: Terry Hébert
Bradykinin: VACANT
Cannabinoid: Roger Pertwee, Allyn Howlett
Complement peptide: Peter Monk
Endothelin: Anthony Davenport
Free fatty acid: VACANT
Galanin: Andrew Gundlach
Glycoprotein hormone: Deborah Segaloff
Hydroxycarboxylic acid: Stefan Offermanns
Lysophospholipid (LPA): Jerold Chung
Melanocortin: Tung Fong, Helgi Schiöth
Motilin: Anthony Davenport
Neuropeptide S: Girolamo Calo
Neurotensin: Jean Mazella
P2Y: Maria-Pia Abbracchio
Platelet-activating factor: VACANT
Prostanoid: Xavier Norel
Relaxin-like: Nick Barker
Trace amine: Janet Maguire
Vasopressin and oxytocin: Bernard Mouillac

Voltage-gated ion channels Subcommittees

Joerg Striessnig (Liaison for all VGIC subcommittees)

Calcium-activated potassium: George Gutman
CatSper and Two-Pore: David Chapman
Cyclic nucleotide-regulated: Martin Biel
Inwardly rectifying potassium: Yoshihiro Kubo
Transient Receptor Potential: David Clapham
Two-P potassium: Steven Goldstein
Voltage-gated calcium: William Catterall
Voltage-gated potassium: George Gutman
Voltage-gated sodium: William Catterall

Gasotransmitters Subcommittee

Andreas Papapetropoulos and Csaba Szabo

Guanylyl cyclases Subcommittee

Adrian Hobbs and Scott Waldman

Non-coding RNAs Subcommittee

Andrew Baker

Adenosine: Adriaan Izjerma
Angiotensin: Sadashiva Karnik
Bile acid: Anthony Davenport
Calcitonin: Debbie Hay, David Poyner
Chemokine: Philip Murphy
Corticotropin-releasing factor: Richard Hauger, Frank Dautzenberg
Estrogen (G protein coupled): VACANT
Frizzled: Gunnar Schulte
Ghrelin: Birgitte Holst
Gonadotrophin-releasing hormone: Adriaan Izjerma
Kisspeptin: Anthony Davenport
Lysophospholipid (S1P): Sarah Spiegel
Melatonin: Ralf Jockers
Neuromedin U: Gary Willars
Neuropeptide W/neuropeptide B: Anthony Davenport
Opioid: Larry Toll
Parathyroid hormone: Jean-Pierre Vilardaga
Prokineticin: Philippe Rondard
Protease-activated: Nigel Bunnett
Somatostatin: Stephan Schulz
Thyrotropin-releasing hormone: Marvin Gershengorn
VIP and PACAP: VACANT

Nuclear hormone receptors Subcommittees

John Cidlowski and Thomas Burris (Liaisons for all NHR subcommittees)

NHR subcommittees are currently being reformed

Kinases Subcommittee

Doriano Fabbro

Pattern Recognition Receptors Subcommittee

Clare Bryant

Proteases Subcommittee

Anthony Turner

Transporters Subcommittee

Stephen Alexander

'Concise Guide to PHARMACOLOGY' Editors

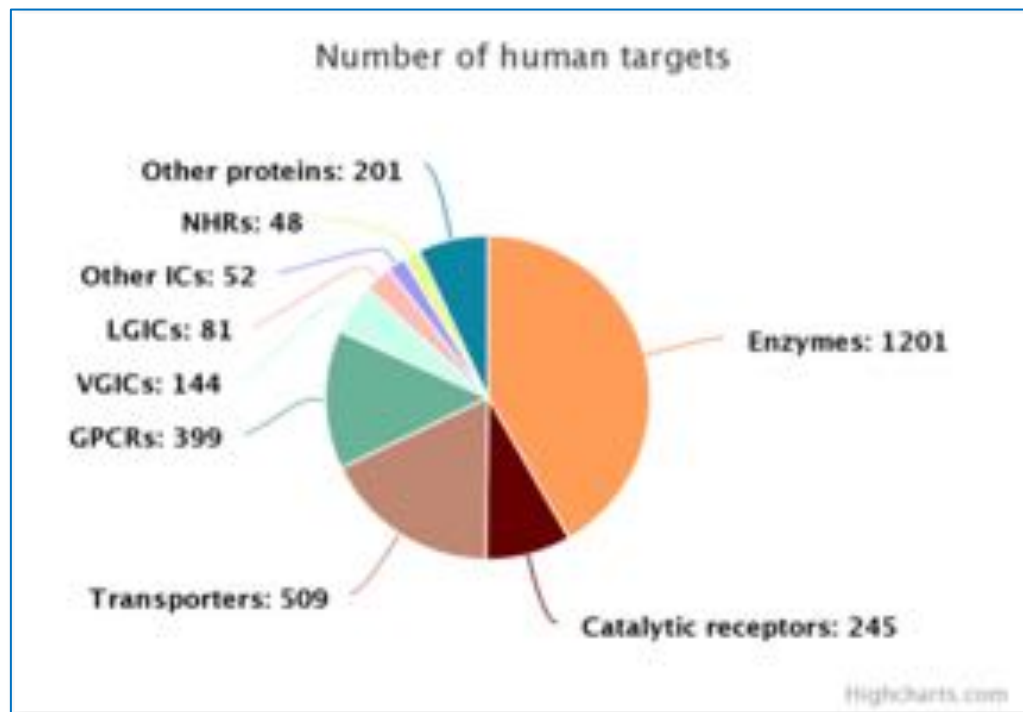
Stephen Alexander, Eamonn Kelly, Neil Marrion, John Peters

DATABASE CONTENT

GtoPdb content - targets

>1,700 established or potential drug targets and ~1,100 related proteins:

- G protein-coupled receptors (Class A, B, C, frizzled, adhesion and orphan GPCRs)
- Ligand-gated ion channels
- Voltage-gated ion channels
- Other ion channels
- Nuclear hormone receptors
- Catalytic receptors
- Kinases
- Proteases
- Other enzymes
- Transporters
- Other protein targets

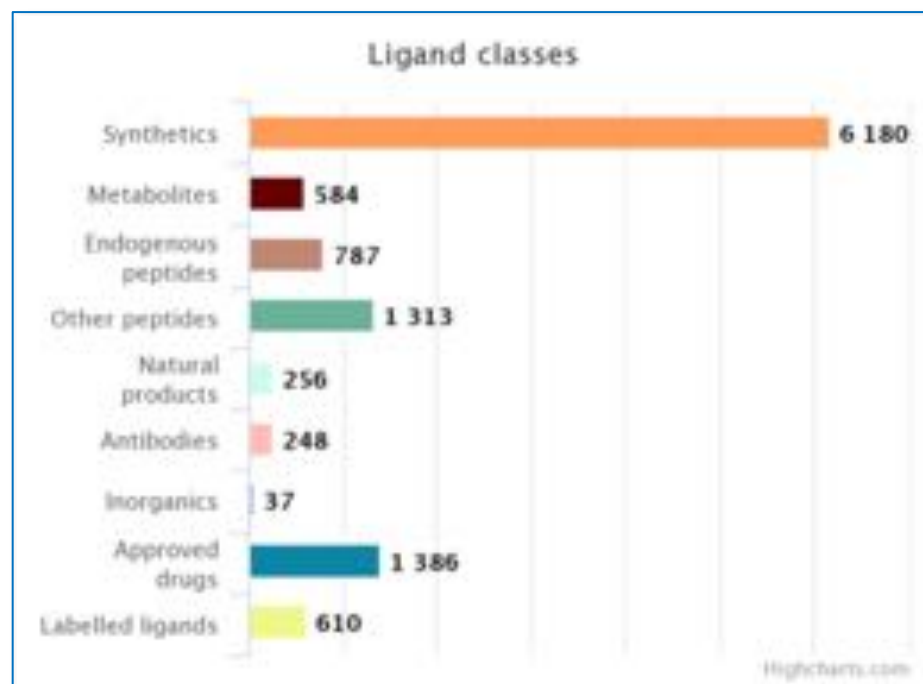


Target numbers as of the 2018.4 release

GtoPdb content - ligands

~9,000 ligands and drugs:

- Approved drugs
- Synthetic organic compounds
- Metabolites, hormones, neurotransmitters
- Natural products
- Endogenous peptides
- Other peptides
- Inorganics
- Antibodies
- Labelled ligands



Ligand numbers as of the 2018.4 release

Concise target family summaries

- Concise target family summaries introducing the main properties
- Expert overviews and comments
- “Gold-standard” selective ligands, clinically-used drugs, endogenous ligands and probes (radioligands and PET ligands where available)
- Further reading lists

Detailed annotation for selected targets

Data are collected and reviewed by NC-IUPHAR subcommittees and individual experts:

- Gene and protein information
- IUPHAR nomenclature and synonyms
- Extensive pharmacology: agonist, antagonist and allosteric regulator affinities, ion channel blockers, enzyme/transporter inhibitors and substrates
- Signal transduction mechanisms; Tissue distribution
- Functional assays; Physiological functions
- Mouse gene knockout phenotypes
- Clinically-relevant mutations and pathophysiology
- Gene expression changes in disease; Biologically significant variants

Other features

- Extensively referenced and linked to primary literature in PubMed
- Focus is on human data but where species differences exist or literature data unavailable other species are given
- Linked to corresponding entries in other resources, e.g. UniProt, Ensembl, Entrez Gene, KEGG, OMIM, ChEMBL
- Ligand information including structure, peptide sequences, clinical data and nomenclature, linked up to chemistry resources including PubChem

NAVIGATING THE WEBSITE AND SEARCH TOOLS

Navigating GtoPdb

- Browse lists of targets and ligands
- Target families are listed under expandable family trees
- Target information is presented in two levels of detail
 1. **Concise** family summary pages
 2. **Detailed** pages for selected targets
- Ligand pages are provided for all compounds in GtoPdb
- Use the search tools to search by name, keyword, identifier or ligand structure



IUPHAR/BPS Guide to PHARMACOLOGY

 Search Database

Home About Targets Ligands Diseases Resources Advanced search Guide to IMMUNOPHARMACOLOGY Portal

An expert-driven guide to pharmacological targets and the substances that act on them.

Quick links

Targets

G protein-coupled receptors
Ion channels
Nuclear hormone receptors
Kinases
Catalytic receptors
Transporters
Enzymes
Other protein targets

Ligands

Approved drugs
Synthetic organics
Metabolites
Natural products
Endogenous peptides
Other peptides
Inorganics
Antibodies
Labeled ligands

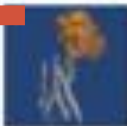
Resources

Help documentation
FAQ
Tutorial
Download data & reports
REST web services

Recent Twitter activity

What's new to Guide to PHARMACOLOGY

Latest database release, version 2018.4 released 19th September 2018



- Read full release details in our blog post
- Updates to targets in >30 families across all target classes
- Added immunology/inflammation targets with novel pharmacological modulators (FCGR2A, RASGRP1, TGM2, SIGLEC8, CD37, STAT3, STAT6)
- Continued curation on both the antimalarial ligand family and antimalarial target family. The database now hold 41 tagged anti-malarial ligands and 9 *P. falciparum* (307) targets
- Curation of SMILES strings for around 40 peptide structures
- First-ever curation of paper from a pre-print archive (ChemRxiv)
- Major extension to coverage of our webservices to include main immunological datatypes and disease data (see our web services page)

Latest News and Hot Topics in Pharmacology

Hot Topic: GPR37/GPR37L1 and the putative pairing with prosapride/PSAP

Comments by Dr. Nicola J. Smith, National Heart Foundation Future Leader Fellow & ...

Dec 12, 2018

Hot Topic: Somatic APP gene recombination in normal and Alzheimer's disease neurons

A new facet of the human brain has been reported [1] involving a first example of ...

Dec 12, 2018

GtoImmuPdb **NEW!**

ELTHAIE Guide to
IMMUNO
PHARMACOLOGY



Visit the IUPHAR Guide to IMMUNOPHARMACOLOGY portal for a unique, immunological access-point to the Guide to PHARMACOLOGY.

The Concise Guide to PHARMACOLOGY 2017/18



A **FREE** publication snapshot created from the database summary pages.

Access the table of contents

Please see the 5 minute introductory video on the Concise Guide:

G protein-coupled receptors

View a list of class A GPCRs, class B GPCRs, class C GPCRs, class Fizzled GPCRs, adhesion class GPCRs or other 7TM proteins

Expand all nodes

Collapse all nodes

[[G protein-coupled receptors OVERVIEW

[- Orphan and other 7TM receptors OVERVIEW

- Class A Orphans
- Class B Orphans
- Class C Orphans
- Taste 1 receptors
- Taste 2 receptors
- Other 7TM proteins
- 5-Hydroxytryptamine receptors
- Acetylcholine receptors (muscarinic)
- Adenosine receptors
- Adhesion Class GPCRs
- Adrenoceptors
- Angiotensin receptors
- Apelin receptor
- Bile acid receptor
- Bombesin receptors
- Bradykinin receptors
- Calcitonin receptors
- Calcium-sensing receptors
- Cannabinoid receptors
- Chemerin receptor
- Chemokine receptors
- Cholecystokinin receptors
- Class Fizzled GPCRs
- Complement peptide receptors
- Corticotropin-releasing factor receptors
- Dopamine receptors
- Endothelin receptors
- Estrogen (G protein-coupled) receptor
- Formylpeptide receptors
- Free fatty acid receptors
- GABA_A receptors
- Galanin receptors
- Ghrelin receptor
- Glucagon receptor family
- Glycoprotein hormone receptors
- Gonadotrophin-releasing hormone receptors
- GPR13, GPR55 and GPR119
- Histamine receptors
- Hydroxycarboxylic acid receptors
- Kisspeptin receptor
- Leukotiene receptors
- Lysophospholipid (LPL) receptors
- Lysophospholipid (S1P) receptors





Histamine receptors

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

Overview

[?](#) [Hide](#) [More detailed introduction](#)

Histamine receptors (nomenclature as agreed by [ICUPHAR Subcommittee on Histamine Receptors](#), [16]) are activated by the endogenous ligand histamine. Marked species differences exist between histamine receptor orthologues (see [16]).

Receptors

?	H₁ receptor Show summary > More detailed page
	H₂ receptor Show summary > More detailed page
	H₃ receptor Show summary > More detailed page
	H₄ receptor Show summary > More detailed page



Comments

[?](#) [Show >](#)

Further reading

[?](#) [Show >](#)

References

[?](#) [Show >](#)

Histamine receptors family summary page



H₁ receptor [Show summary >](#)

[More detailed page](#)

H₂ receptor [Hide summary](#)

[More detailed page](#)

Target id	263
Nomenclature	H₂ receptor
Previous and unofficial names	gastric receptor I H2R HH2R
Genes	HRH2 (Hs), Hrh2 (Mm), Hrh2 (Rn)
Ensembl ID	ENSG00000113749 (Hs), ENSMUSG00000034987 (Mm), ENSRNOG00000018260 (Rn)
UniProtKB AC	P25021 (Hs), P97292 (Mm), P25102 (Rn)
Principal transduction	G _s
Selective agonists	amthamine [19]
Selective antagonists	iodine pK _i 7.5 [3] - Rat ranitidine pK _i 7.1 [21] cimetidine pK _i 6.8 [5]
Labelled ligands	[¹²⁵ I]iodoaminopotentidine (Antagonist) pK _d 8.7 [20] - Rat [³ H]iodine (Antagonist) pK _d 7.7 – 8.7 [30]

H₃ receptor [Show summary >](#)

[More detailed page](#)

H₄ receptor [Show summary >](#)

[More detailed page](#)



IUPHAR/BPS Guide to PHARMACOLOGY

21. Leurs R, Smit MJ, Menge WM, Timmerman H. (1994)

Pharmacological characterization of the human histamine H2 receptor stably expressed in Chinese hamster ovary cells.

Br. J. Pharmacol., 112 (3): 847-54. [PMID:7921611]



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Br. J. Pharmacol. 1994 Jul;112(3):847-54

Pharmacological characterization of the human histamine H2 receptor stably expressed in Chinese hamster ovary cells.

Leurs R¹, Smit MJ, Menge WM, Timmerman H

Author information

Abstract

1. The gene for the human histamine H2 receptor was stably expressed in Chinese hamster ovary (CHO) cells and characterized by [125I]-iodoaminopotentidine binding studies. In addition, the coupling of the expressed receptor protein to a variety of signal transduction pathways was investigated. 2. After cotransfection of CHO cells with pCMVhumH2 and pUT626, a phleomycine-resistant clonal cell line (CHOhumH2) was isolated that expressed 565 +/- 35 fmol kg-1 protein binding sites with high affinity (0.21 +/- 0.02 nM) for the H2 antagonist, [125I]-iodoaminopotentidine. 3. Displacement studies with a variety of H2 antagonists indicated that the encoded protein was indistinguishable from the H2 receptor identified in human brain membranes and guinea-pig right atrium. The Ki-values observed in the various preparations correlated very well (r2 = 0.996-0.920). 4. Displacement studies with histamine showed that a limited fraction (32 +/- 6%) of the binding sites

Full text links

Free PMC Full-text archive

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Related citations in PubMed

Two distinct pathways for histamine H2 [J Biol Chem. 199

Structural and functional analysis of the [Biochem J. 199

Independent coupling of the [Leibergs Arch Pharmacol. 199

Reference information and linkout to PubMed

[H₁ receptor](#) [Show summary](#) >[More detailed page](#) [H₂ receptor](#) < [Hide summary](#)[More detailed page](#)

Target id	263
Nomenclature	H₂ receptor
Previous and unofficial names	gastric receptor I H2R HH2R
Genes	HRH2 (Hs), Hrh2 (Mm), Hrh2 (Rn)
Ensembl ID	ENSG00000113749 (Hs), ENSMUSG00000034987 (Mm), ENSRNOG00000018260 (Rn)
UniProtKB AC	P25021 (Hs), P97292 (Mm), P25102 (Rn)
Principal transduction	G _s
Selective agonists	amthamine [19]
Selective antagonists	tioidine pK _i 7.5 [3] - Rat ranitidine pK _i 7.1 [21] cimetidine pK _i 6.8 [5]
Labelled ligands	[¹²⁵I]iodoaminopotentidine (Antagonist) pK _D 8.7 [20] - Rat [³H]tioidine (Antagonist) pK _D 7.7 – 8.7 [30]

[H₃ receptor](#) [Show summary](#) >[More detailed page](#) [H₄ receptor](#) [Show summary](#) >[More detailed page](#)

H₂ receptor



Target id: 263

Nomenclature: H₂ receptor

Family: Histamine receptors

Annotation status: Annotated and reviewed, awaiting update [» Email us](#)

Contents:

- Gene and Protein Information
- Previous and Unofficial Names
- Database Links
- Natural/Endogenous Ligands
- Agonists
- Antagonists
- Transduction Mechanisms
- Tissue Distribution
- Expression Datasets
- Functional Assays
- Physiological Functions
- Physiological Consequences of Altering Gene Expression
- Phenotypes, Alleles and Disease Models
- Biologically Significant Variants
- Available Assays
- References
- Citation information

Gene and Protein Information

class A G protein-coupled receptor

Species	TM	AA	Chromosomal Location	Gene Symbol	Gene Name	Reference
Human	7	358	5q35.2	HHR2	histamine receptor H2	11
Mouse	7	358	13 B1	Hh2	histamine receptor H2	18
Rat	7	358	17p14	Hh2	histamine receptor H 2	40

Previous and Unofficial Names

gastric receptor I

H2R

HH2R

Database Links

Specialist databases

GPCRDB [hrh2_human \(Hs\)](#), [hrh2_mouse \(Mm\)](#), [hrh2_rat \(Rn\)](#)

Other databases

ChEMBL Target [102 \(Hs\)](#), [11297 \(Mm\)](#), [11298 \(Rn\)](#)

DrugBank Target [P25021 \(Hs\)](#)

Ensembl Gene [ENSG00000113749 \(Hs\)](#), [ENSMUSG00000034987 \(Mm\)](#), [ENSRNOG00000018260 \(Rn\)](#)

Entrez Gene [3274 \(Hs\)](#), [15466 \(Mm\)](#), [25461 \(Rn\)](#)

GenitoUrinary Development Molecular Anatomy Project [Hrh2 \(Mm\)](#)

Human Protein Atlas [ENSG00000113749 \(Hs\)](#)

KEGG Gene [hsa:3274 \(Hs\)](#), [mmu:15466 \(Mm\)](#), [mo:25461 \(Rn\)](#)

OMIM [142703 \(Hs\)](#)

RefSeq Nucleotide [NM_022304 \(Hs\)](#), [NM_008286 \(Mm\)](#), [NM_012965 \(Rn\)](#)

RefSeq Protein [NP_071640 \(Hs\)](#), [NP_032312 \(Mm\)](#), [NP_037097 \(Rn\)](#)

UniProtKB [P25021 \(Hs\)](#), [P97292 \(Mm\)](#), [P25102 \(Rn\)](#)

Wikipedia [HRH2 \(Hs\)](#)

Natural/Endogenous Ligands

[Histamine](#)

Agonists

Key to terms and symbols

[View all chemical structures](#)

[Click column headers to sort](#)

Ligand		Sp.	Action	Affinity	Units	Reference
impromidine			Hs Full agonist	7.2	pK_i	47
arpromidine			Hs Full agonist	6.3 - 8.0	pK_i	47
UR-PC136			Hs Full agonist	7.0	pK_i	47
UR-PC146			Hs Full agonist	6.0	pK_i	47
histamine			Rn Full agonist	3.8	pK_i	3
amthamine			Hs Full agonist	6.4	pEC_{50}	20
burimamide			Hs Full agonist	5.6 - 5.7	pEC_{50}	1

[View species-specific agonist tables](#)

Antagonists

Key to terms and symbols

[View all chemical structures](#)

[Click column headers to sort](#)

Ligand		Sp.	Action	Affinity	Units	Reference
[¹²⁵ I]aminopotentidine			Rn Antagonist	8.7	pK_D	21
[³ H]nizatidine			Hs Antagonist	7.7 - 8.7	pK_D	34
isodaminopotentidine			Rn Antagonist	9.2	pK_i	3
foldine			Rn Antagonist	7.5	pK_i	3
nizatidine			Hs Antagonist	7.1	pK_i	23
omebidine			Hs Antagonist	6.85	pK_i	6
ranitidine			Rn Antagonist	6.2	pK_i	3
omebidine			Rn Antagonist	5.9	pK_i	3
metamide			Rn Antagonist	5.8	pK_i	3
burimamide			Rn Antagonist	5.5	pK_i	44
dobenpropil			Hs Antagonist	5.2	pK_i	9
ABT-239			Hs Inverse agonist	5.2	pK_i	8
famotidine			Hs Antagonist	-	-	

[View species specific antagonist tables](#)

Antagonist Comments

Nizatidine is a H_2 antagonist clinically in use to block histamine-induced gastric acid secretion [35].

Famotidine is also a selective H_2 antagonist. The only affinity data, in free access journals, found to date relates to the canine H_2 receptor, where famotidine has an IC_{50} of 26.3nM [17].

Interaction tables

Click for species-specific selectivity table

Ligand is endogenous in this species

Ligand is labelled

Ligand is radioactive

Approved drug

Primary target of this compound

ranitidine

🔍 Ligand ID: 1234

Name: ranitidine

 View more information in the IUPHAR Pharmacology Education Project [ranitidine](#)

Structure and Physico-chemical Properties

2D Structure 🔍



Calculated Physico-chemical Properties 🔍

Hydrogen bond acceptors	3
Hydrogen bond donors	2
Rotatable bonds	10
Topological polar surface area	109.89
Molecular weight	314.14
XLogP ₃	1.52
No. Lipinski's rules broken	0

Molecule properties generated using the [CDK](#)

Summary [Biological activity](#) [Clinical data](#) [References](#) [Structure](#) [Similar ligands](#)

Classification 🔍

Compound class: [Synthetic organic](#)

Approved drug? [Yes \(FDA \(3377\)\)](#)

IUPAC Name 🔍

N#C1=NC(=C(C=C1)CSCCN2C=NC(=N2)C)N

International Nonproprietary Names 🔍

INN number	INN
4060	ranitidine

Synonyms 🔍

Am-13005 | Gantacil | GR-122111X | Zantac®

Database Links 🔍

CAS Registry No: [46357-35-5 \(source: Solfinder\)](#)

ChEBI: [CHEBI:9776](#)

ChEMBL Ligand: [ChEMBL:152](#)

DrugBank Ligand: [DB00863](#)

Ligand page for the approved drug
ranitidine

Structure and Physico-chemical Properties

2D Structure ?



Calculated Physico-chemical Properties ?

Hydrogen bond acceptors	3
Hydrogen bond donors	2
Rotatable bonds	10
Topological polar surface area	108.88
Molecular weight	314.14
XLogP	2.12
No. Lipinski's rules broken	0

Molecular properties generated using the [CDK](#)


Summary **Biological activity** Clinical data References Structure Similar ligands

 [View interactive charts of activity data from ChEMBL and GtoPdb across species \(new!\)](#)

Selectivity at human GPCRs

Key to terms and symbols

Click column headers to sort

Target	Type	Action	Affinity	Units	Reference	
H ₂ receptor	 Antagonist	Antagonist	7.1	pK _i	2	▼

Selectivity at rat GPCRs

Key to terms and symbols

Click column headers to sort

Target	Type	Action	Affinity	Units	Reference	
H ₂ receptor	Antagonist	Antagonist	6.2	pK _i	1	▼

Ligand mentioned in the following text fields

[Histamine receptors overview](#)

Biological activity data for ranitidine at targets in the database

Structure and Physico-chemical Properties

2D Structure ?



Calculated Physico-chemical Properties ?

Hydrogen bond acceptors	3
Hydrogen bond donors	2
Rotatable bonds	10
Topological polar surface area	108.88
Molecular weight	314.14
XLogP	2.12
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

Summary Biological activity **Clinical data** References Structure Similar ligands

Summary of Clinical Use ?

Ranitidine is used in the treatment of gastric ulcers, where blocking of H₂ receptors reduces gastric acid secretion and ameliorates disease symptoms.

Mechanism Of Action and Pharmacodynamic Effects ?

Competitive inhibition of H₂ receptors on parietal cells leads to suppression of gastric acid secretion.

External links ?

For extended ADME data see the following:

[Electronic Medicines Compendium \(eMC\)](#)

Peptide ligand information

endothelin-1

Ligand ID: 509

Name: endothelin-1

Abbreviated name: ET-1

Species: Human, Mouse, Rat

View more information in the IUPHAR Pharmacology Education Project: [endothelin, et 1](#)

Summary | Biological activity | References | Structure | Similar ligands | (Un)labelled forms

Classification

Compound class	Endogenous peptide in human, mouse or rat
Ligand family/group	Neuropeptides

Gene/precursor

Gene symbol	Gene name	Species	Precursor protein name	Synonyms
EDN1	endothelin 1	Human	propro-endothelin 1	ET1
Edn1	endothelin 1	Mouse	propro-endothelin 1	ET-1
Edn1	endothelin 1	Rat	propro-endothelin 1	endothelin-1, Et1, ET-1, PRET1, proproendothelin-1

Database Links

BindingDB Ligand	50279793
CAS Registry No.	117399-94-7
UniProtKB	P05293 (hdc), P05305 (hdc), P05306 (hdc)

- Curated sequence information
- Post-translational and chemical group modifications
- Precursor proteins and encoding genes
- Similar sequences
- Gene families

Summary | Biological activity | References | **Structure** | Similar ligands | (Un)labelled forms

Peptide Sequence

CSCSSLMDKECVYFCHLDIW

Cys-Ser-Cys-Ser-Ser-Leu-Met-Asp-Lys-Glu-Cys-Val-Tyr-Phe-Cys-His-Leu-Asp-Ile-Ile-Tip

Post-translational Modification

There are two disulfide bonds formed, between cysteine residues at positions 1 and 15 and cysteine residues at positions 3 and 11.

Ligand page for the endogenous peptide endothelin-1

Bespoke tables for different targets

- Heteromeric complexes: subunit composition
- GPCRs: signal transduction mechanism
- Ion channels: ion conductance and voltage-dependence
- Nuclear receptors: DNA co-binding partners, target genes
- Enzymes: substrates, cofactors, reaction mechanisms
- Transporters: substrates
- Antimalarial targets: whole organism assays

Enzyme Reaction 	
EC Number: 5.3.3.2	isopentenyl diphosphate + dimethylallyl diphosphate

Cofactors 			
Cofactor	Species	Comments	Reference
Mg ²⁺	Human	Enzyme activity increases with increasing Mg ²⁺ up to 20mM.	2
Mn ²⁺	Human	Activity increases up to a concentration of 100 micromolar Mn ²⁺ then sharply decreases.	2.5

isopentenyl-diphosphate Δ -isomerase 1

Subunits
KCTD8 (Accessory protein)
KCTD12 (Accessory protein)
KCTD12b (Accessory protein)
KCTD16 (Accessory protein)
GABA _{B1}
GABA _{B2}

GABA_B receptor

Database search functionality

- Quick search box at the top of every page with autocomplete for target, family and ligand names



- Advanced searches are available on the Target Search and Ligand Search pages

Target search tools

- Search by name or keyword, identifier (e.g. UniProtKB accession) or reference (e.g. PubMed id)

The image displays a web-based target search tool interface. On the left, there are three search methods: 'Target text search', 'Search by database identifier', and 'Search for data by literature reference'. The 'Target text search' section includes a text input field, a 'Search the database' button, and dropdown menus for 'Search field to search' (set to 'All') and 'Limit by species' (set to 'All'). Below this, there are additional dropdowns for 'Limit by target type' (set to 'All') and a 'Search the database' button. A red arrow points from this button to the 'Search results' section on the right. The 'Search results' section shows a list of search results for 'Methicillin', including details for 'Family: Methicillin receptor', 'Target: MDR1 receptor (Methicillin receptor)', and 'Target: MDR1 receptor (Methicillin receptor)'. The results are presented in a structured format with various identifiers and descriptions.

Ligand search tools

- Search by name, identifier (e.g. PubChem CID, InChI) or structure (exact match, similarity, substructure, SMARTS)

Ligand network search

Enter name or formula search:

Select fields to search: All Ligands Names/synonyms Comments

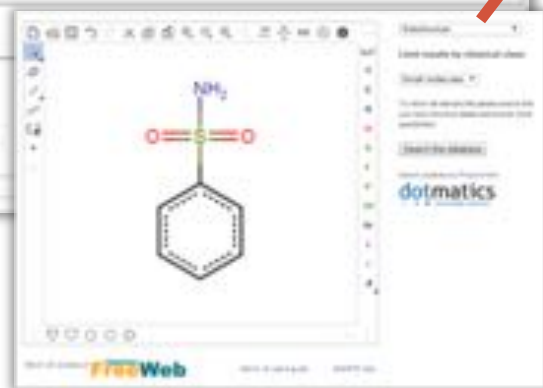
Search by chemical identifier

Enter identifier to search:

Identifier type:

Chemical structure search

1. Load or draw a structure into the editor below



Chemical structure search results

Test structure:

Test SMILES: NS(=O)(=O)c1ccccc1

Five query returned 107 matches

View results by: Sort results by:

SMILES	SMILES	SMILES
 <input type="button" value="View structure"/>	 Tegapic SMILES: <chem>NS(=O)(=O)c1ccc2c(c1)nc3ccccc23</chem> <input type="button" value="View structure"/>	 Tegapic SMILES: <chem>NS(=O)(=O)c1ccc2c(c1)nc3ccccc23</chem> <input type="button" value="View structure"/>

Advanced search by keyword

- Keyword searches, for example by disease name, can facilitate retrieval of associated ligands and targets



A search for “Alzheimer’s disease” returns implicated targets and ligands tested in clinical trials

RECENT ADDITIONS AND EXPANSIONS

Recent additions and expansions

- Antibodies
- Kinases
- Proteases and hydrolases
- Epigenetic targets
- Regulators of G protein Signaling (RGS) proteins
- Targets relevant to immunopharmacology, including:
 - Transcription factors
 - Immune checkpoint proteins
 - Fc epsilon receptors
 - Absent in melanoma (AIM)-like receptors (ALRs) and C-type lectin-like receptors (CLRs) within Pattern Recognition Receptors
- Antimalarial ligands and targets
- Ligand families

Information on antibodies

- Collaboration with IMG-T®, the international ImMunoGeneTics information system®
- Pharmacological data on 224 approved and experimental therapeutic monoclonal antibodies

golimumab

Update on 07/16

Name golimumab

View more information on the Clinical Pharmacology Database Project [golimumab](#)

Summary Biological activity Clinical data References Immunopharmacology

Classification

Compound class [Antibody](#)

Approved drug? [Yes \(FDA \(2006\), EMA \(2006\)\)](#)

International Nomenclature

INN	INN number	INN
golimumab		

Summary

[DVT] (L1), [CNS] (L1), [Stimulant]

Database links

Specialized databases

ACTIVITY (G)	[17]
--------------	------

Other databases

PubChem (G)	[17822881]
Search PubMed clinical trials	golimumab
Search PubMed titles	golimumab
Search PubMed abstracts	golimumab

Summary Biological activity Clinical data References Immunopharmacology

View interactive charts of activity data from ChEMBL and GtoPdb across species [\(new!\)](#)

Selectivity at human ligand targets

Key to terms and symbols Click column headers to sort

Target	Type	Action	Affinity	Units	Reference
tumour necrosis factor shed form	Antibody	Binding	10.7	pIC ₅₀	2

Summary Biological activity Clinical data References Immunopharmacology

Summary of Clinical Use

Used in adults with various inflammatory conditions [1] e.g. moderate to severe active rheumatoid arthritis [2] active psoriatic arthritis, active ankylosing spondylitis and moderate to severe ulcerative colitis.

Mechanism of Action and Pharmacodynamic Effects

Anti-TNF α monoclonal antibody which binds and neutralises soluble and membrane human TNF α , a pro-inflammatory cytokine associated with chronic inflammation.

External links

For extended ACME data see the following:

- [Electronic Medicines Compendium \(EMC\)](#)
- [Drugs.com](#)
- [European Medicines Agency \(EMA\)](#)

Database page for the antibody golimumab

Information on kinases

- Database pages created for *all* the human protein kinases and selected lipid kinases
- Detailed annotation for the ~30 clinically-used kinase inhibitors, including target affinities, clinical use, and ADME (absorption, distribution, metabolism and excretion) data
- Panel data from published screening assays by DiscoverRx, EMD Millipore and Reaction Biology
- Links to the DiscoverRx TREEspot™ compound profile visualisation tool

- ☐ Kinases (EC 2.7.x.x)
 - ☑ AGC: Containing PKA, PKG, PKC families
 - ☑ Atypical
 - ☑ CAMK: Calcium/calmodulin-dependent protein kinases
 - ☑ CK1: Casein kinase 1
 - ☑ CMGC: Containing CDK, MAPK, GSK3, CLK families
 - ☑ Lipid modifying kinases
 - ☑ Other protein kinases
 - ☑ Miscellaneous protein kinases
 - ☑ STE: Homologs of yeast Sterile 7, Sterile 11, Sterile 20 kinases
 - ☑ TK: Tyrosine kinase
 - ☑ TKL: Tyrosine kinase-like



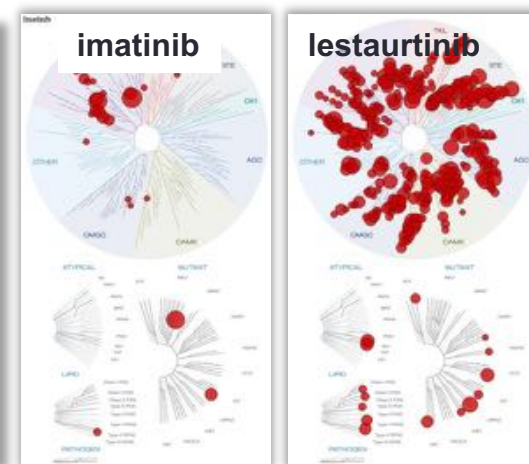
DiscoverRx Kinase Inhibitor Panel

A screen of 170 inhibitors against 100 human kinases. Quantitative data were derived using DiscoverRx KinomeScan™ product. <http://www.discoverrx.com/kinase-inhibitor-panel>

Reference: 1,4

Key to terms and symbols

Target	Name in screen	No.	Type	Action	Affinity	Units
phosphoinositide-3-OH kinase (class II group 1)	PI3K1	10	inhibitor	inhibitor	0.0	(μ M)
collagen-induced protein-tyrosine kinase kinase 2	FAK2	10	inhibitor	inhibitor	0.0	(μ M)
src kinase protein kinase 2	SH2PTK2	10	inhibitor	inhibitor	0.0	(μ M)
src kinase protein kinase 2	SH2PTK2	10	inhibitor	inhibitor	0.0	(μ M)
large tumor suppressor kinase 2	LATS2	10	inhibitor	inhibitor	0.0	(μ M)
tyrosine kinase, SH2-like kinase 2	SH2TK2	10	inhibitor	inhibitor	0.0	(μ M)
src kinase protein kinase 2	SH2PTK2	10	inhibitor	inhibitor	0.0	(μ M)
src kinase protein kinase 2	SH2PTK2	10	inhibitor	inhibitor	0.0	(μ M)



Information on proteases and hydrolases

- MEROPS classification system adopted
- Database pages for 175 proteases and 14 hydrolases/lipases with activity records in ChEMBL
- Ligand activity (K_i or IC_{50}) data curated for approved drugs, prodrugs, clinical candidates (e.g. BACE1 for Alzheimer's), and selected research compounds

Peptidases and proteinases
AA: Aspartic (A) Peptidases
AD: Aspartic (A) Peptidases
CA: Cysteine (C) Peptidases
CD: Cysteine (C) Peptidases
CE: Cysteine (C) Peptidases
M-: Metallo (M) Peptidases
MA: Metallo (M) Peptidases
MC: Metallo (M) Peptidases
ME: Metallo (M) Peptidases
MF: Metallo (M) Peptidases
MG: Metallo (M) Peptidases
MH: Metallo (M) Peptidases
MJ: Metallo (M) Peptidases
MP: Metallo (M) Peptidases
PA: Serine (S) Peptidases
PB: Threonine (T) Peptidases
PC: Cysteine (C) Peptidases
SB: Serine (S) Peptidases
SC: Serine (S) Peptidases

presenilin 1

Inhibitors						
Key to terms and symbols		View all chemical structures			Click column headers to sort	
Ligand		Sp.	Action	Affinity	Units	Reference
begacestat	 	Hs	Inhibition	7.83	IC_{50}	5
CHF-5074	 	Hs	Binding	4.4	IC_{50}	7
evapacestat	 	Hs	Inhibition	9.5	IC_{50}	8
ELND006	 	Hs	Inhibition	9.47	IC_{50}	6
RG4129037	 	Hs	Inhibition	8.4	IC_{50}	3
senapacestat	 	Hs	Inhibition	7.82	IC_{50}	2
AZ400	 	Hs	Inhibition	7.59	IC_{50}	1

Information on epigenetic targets

- GtoPdb includes ~130 epigenetic targets (chromatin modifying enzymes and bromodomain-containing proteins), along with activity data for published inhibitors

- ▣ Chromatin modifying enzymes
 - ▣ Enzymatic bromodomain-containing proteins
 - Bromodomain kinase (BRDK) family
 - TAF1 family
 - TIF1 family
 - 1.14.11.- Histone demethylases
 - 2.1.1.43 Histone methyltransferases (HMTs)
 - 2.3.1.48 Histone acetyltransferases (HATs)
 - 3.6.1.3 ATPases
 - 2.1.1.- Protein arginine N-methyltransferases
 - 3.5.1.- Histone deacetylases (HDACs)

Tough DF *et al.* (2014) Epigenetic pathway targets for the treatment of disease: accelerating progress in the development of pharmacological tools: IUPHAR Review 11. *Br J Pharmacol.*, **171**: 4981–5010.

Information on RGS proteins

- Includes all members of the four RGS protein subfamilies, along with information about interacting proteins, activity data for published pharmacological tools, tissue distribution, physiological functions, and disease relevance for the more extensively studied RGS proteins

RGS4 (regulator of G protein signaling 4) [Hide summary](#)

Target id 2811

Names **regulator of G-protein signaling 4**

Common abbreviation RGS4

Previous and unofficial names ESTM48 | ESTM50

Genes RGS4 (Hs), Rgs4 (Mm), Rgs4 (Rn)

Ensembl ID ENSG00000117152 (Hs), ENSMUSG0000038530 (Mm), ENSRNOG0000002773 (Rn)

UniProtKB AC P49799 (Hs), O08899 (Mm), P49799 (Rn)

Selective inhibitors RGS4 inhibitor 11b pIC₅₀ 7.8 [2]
CCG-50014 pIC₅₀ 7.5 [1-2]
RGS4 inhibitor 13 pIC₅₀ 7.3 [2]

Clinically-Relevant Mutations and Pathophysiology ?

Disease: **Parkinson Disease**
Synonyms: Parkinson's disease [Disease Ontology: [DOID:14330](#)]
Disease Ontology: [DOID:14330](#)
OMIM: [168600](#)

References: [20,24](#)

Disease: **Schizophrenia**
Disease Ontology: [DOID:5419](#)
OMIM: [181500](#)
Orphanet: [ORPHA3140](#)

References: [6-7,26,28](#)

Associated Proteins ?

G Proteins		Interacting Proteins		
Name	References	Name	Effect	References
Gz	16	GPCR-Kir3 channel complex	Accelerated GIRK activation and deactivation	17
Gaq/11	1,16	μ receptor	Reduced agonist potency G-protein-coupling specificity	13,23
Gas		δ receptor	G-protein-coupling specificity	13,23
Goi1		Gβγ and PLCβ1	Signaling complex formation	11
Goi0	1-2,16	calmodulin	Reverses PIP3-mediated GAP inhibition	30
Ge12/13		spinophilin	Scaffolding	25,42

Associated Protein Comments

Affinity for Gαq is lower than that for Gαi.

Information on transcription factors (relevant to immunopharmacology)

- This is a small but dynamic family with new members and pharmacological data being added when reported in the literature

Transcription factors

- BTB (POZ) domain containing TFs
- Forkhead box TFs

Overview

Hide [More detailed introduction](#)

The BTB/POZ transcription factor family has four members, BCL6, Kaiso (ZBTB33), HIC1, and PLZF (ZBTB16). They all also belong to the much larger C2H2-type zinc finger transcription factor family.

Targets

B-cell CLL/lymphoma 6 [Show summary](#) [More detailed page](#)

Inhibitors

Key to terms and symbols [View all chemical structures](#) [Click column headers to sort](#)

Ligand	Sp.	Action	Affinity	Units	Reference
FX1	Hs	Binding	5.2	pK _d	2
compound 8c [PMD: 28780529]	Hs	Binding	6.1 – 7.0	pIC ₅₀	6

Inhibitor Comments

The BCL6 inhibitor 79-6 (PubChem CID 5721353) is commercially available but it is less potent (K_d 138 μM) than the compounds listed in the table above. 79-6 is active in vivo and in vitro, and is reported to be selective for BCL6 over the related transcription factors Kaiso (ZBTB33), HIC1, and PLZF (ZBTB16) [3].

Immunopharmacology Comments

BCL6/corepressor complexes are important for the formation of germinal centers and differentiation and proliferation of lymphocytes. Oncogenic mutations in BCL6 lead to the development of diffuse large B-cell lymphoma cells from germinal center B cells. Disruption of BCL6/corepressor complex formation by pharmacological inhibitors has therefore been identified as a novel drug mechanism with potential for the treatment of autoimmune diseases and cancer [2-3].

Targets

forkhead box N1 [Show summary](#) [More detailed page](#)

Immunopharmacology Comments

FOXN1 deficiency has been identified as the cause of the nude severe combined immunodeficiency (SCID) phenotype in mice and humans [2-3].

Information on immune checkpoint proteins

- This family consolidates existing GtoPdb targets with new family members in a single place for easy user access

The image shows a screenshot of the GtoPdb website's 'Immune checkpoint proteins' page. The page is divided into several sections: 'Contents', 'Overview', and 'Subfamilies'. The 'Subfamilies' section is currently expanded, showing a list of immune checkpoint proteins. A red arrow points from the 'Other immune checkpoint proteins' link in the 'Subfamilies' section to the detailed view of the 'CD40 / TNFRSF5' subfamily. Another red arrow points from the 'Toggle GtoImmuPdb View' button to the 'CD40 / TNFRSF5' subfamily entry.

Immune checkpoint proteins

Contents

- Overview
- Subfamilies
- How to cite this family page

Overview

Immune checkpoint pathway blockade has revolutionized cancer treatment for some patients, with targeted immunopembrolizumab, nivolumab, atezolizumab, durvalumab, and avelumab making it to the clinic.

Subfamilies

Guide to Immunopharmacology view: OFF

- Immune checkpoint catalytic receptors
- Other immune checkpoint proteins

[Toggle GtoImmuPdb View](#) [Expand all](#)

CD40 / TNFRSF5 [Show summary »](#)

HVEM (herpes virus entry mediator / TNFRSF14) [Show summary »](#)

CD86 [Show summary »](#)

CD80 [Show summary »](#)

CD28 [Show summary »](#)

LAG3 (CD223) / CD223 [Show summary »](#)

CTLA-4 (cytotoxic T-lymphocyte-associated protein 4 (CD152)) [Show summary »](#)

PD-1 (programmed cell death 1 (CD279)) [Show summary »](#)

B7-H3 (CD276) [Show summary »](#)

ICOS (CD278) [Show summary »](#)

SIGLEC-2 (CD22) [Show summary »](#)

SIGLEC-3 (CD33) [Show summary »](#)

TIM3 (CD366) [Show summary »](#)

TIGIT [Show summary »](#)

V.set immunoregulatory receptor [Show summary »](#)

Information on Fc epsilon receptors

- This family is included because these receptors are crucial in the development of allergic reactions, although specific pharmacology is sparse

Fc epsilon receptors

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

UniProtKB view: OFF [Toggle UniProtKB View](#) [Toggle CGTP status](#) [Expand all sections](#) [Collapse all sections](#)

Overview

[?](#) [Hide](#) [More detailed introduction](#)

The type I high affinity IgE receptor (FcεR1) is crucial for the production of allergic reactions. It is a tetramer composed of 1 alpha, 1 beta, and 2 gamma chains. The gamma chains are also subunits of other Fc receptors. The FcεR1 has a lower affinity for IgE.

Targets

[?](#)

FcεR1α (Fc fragment of IgE receptor 1α) Show summary	More detailed page
FcεR1β (membrane spanning 4-domains A2) Show summary	More detailed page
FcεR1γ (Fc fragment of IgE receptor 1γ) Show summary	More detailed page
FcεR2 (Fc fragment of IgE receptor 2) Show summary	More detailed page

Information on pattern recognition receptors

- This family consolidates existing GtoPdb targets across different target classes, with new family members, in a single place for easy user access

The screenshot shows a web page titled "Non-catalytic pattern recognition receptors". It features a "Contents" section with links for "Overview", "Subfamilies", and "How to cite this family page". The "Overview" section includes a question mark icon, a "More detailed introduction" link, and text explaining that these receptors are non-catalytic DNA-sensing proteins that induce an innate immune response. It lists catalytic receptor PRRs included in the Guide to PHARMACOLOGY: Toll-like receptors (TLRs), Nucleotide-binding oligomerization domain-like receptors (NLRs, also known as NOD-like receptors), and RIG-I like receptors (RLRs). The "Subfamilies" section has a "Toggle GtoImmuPdb View" button and "Expand all nodes" and "Collapse all nodes" buttons. Below, it shows the "Guide to Immunopharmacology view: OFF" and a list of subfamilies: "Absent in melanoma (AIM)-like receptors (ALRs)", "C-type lectin-like receptors (CLRs)", and "Other pattern recognition receptors".

Bryant *et al.* (2015) International Union of Basic and Clinical Pharmacology. XCVI. Pattern recognition receptors in health and disease. *Pharmacol Rev.* 67(2):462-504.

Information on antimalarial ligands and targets

- New families introduced as part of the IUPHAR/MMV Guide to Malaria Pharmacology project (GtoMPdb)

Antimalarial targets

ChemBL view: OFF [Toggle ChemBL view](#) [Toggle CDF status](#) [Expand all sections](#) [Collapse all sections](#)

Overview

4 hits

This family encompasses antimalarial targets identified and validated in *Plasmodium*, the genus of protozoan parasite known to cause malaria. The genome of *P. falciparum*, the species that is responsible for the majority of malaria-related deaths, has been sequenced and analysed contributing to an increased understanding of potential biological targets in the parasite. More than half of the predicted gene products exhibit little homology outside the *Plasmodium* genus and have not been given functional assignments, while a considerable number are unique to *P. falciparum* [2]. In recent years, genetic methods have facilitated the identification of new molecular targets in the parasite and it is hoped that novel cross-species targets will be elucidated to help inform antimalarial drug discovery [3].

Targets

1

PF3X4 (<i>Plasmodium falciparum</i> ATPase4) Show summary +
PF3X5 (<i>Plasmodium falciparum</i> phenylalanine-tRNA ligase alpha subunit) Show summary +
PF3X7-TS (<i>Plasmodium falciparum</i> bifunctional dihydrofolate reductase/thymidylate synthase) Show summary +
PF3X8 (<i>Plasmodium falciparum</i> dihydroorotate dehydrogenase) Show summary +
PF3X9 (<i>Plasmodium falciparum</i> 1-deoxy-D-xylulose 5-phosphate reductoisomerase) Show summary +
PF3F2 (<i>Plasmodium falciparum</i> elongation factor 2) Show summary +
PF3M1 (<i>Plasmodium falciparum</i> N-Methyltransferase) Show summary +
PF3K4 (<i>Plasmodium falciparum</i> phosphatidylinositol 4-kinase) Show summary +

Antimalarial ligands

ChemBL view: OFF [Toggle ChemBL view](#) [Toggle CDF status](#) [Expand all sections](#) [Collapse all sections](#)

Overview

4 hits

This family contains agents that are used for the prevention and treatment of malaria infection. It includes approved drugs, clinical candidates and investigational compounds.

Ligands

1

ACT-42546 Show summary +	Show detailed page PDF
amodiaquine Show summary +	Show detailed page PDF
AN681 Show summary +	Show detailed page PDF
AR1592 Show summary +	Show detailed page PDF
artemether Show summary +	Show detailed page PDF
artemether Show summary +	Show detailed page PDF
artemisinin Show summary +	Show detailed page PDF
artemisinin Show summary +	Show detailed page PDF
artemisinin Show summary +	Show detailed page PDF
artemisinin Show summary +	Show detailed page PDF

Information on ligand families

- New ligand family and group listing gives easy access to groups of ligands with shared homology, functions or mechanism of action

Ligand families and groups

ImmunePdb view: **OFF**

Ligand families

- Activin and inhibin
- Antimalarial ligands
- Bone morphogenetic proteins
- CD molecules (ligands)
- Chemokines
- Complement components and ligands
- Ephrins
- Fibroblast growth factor (FGF) family ligands
- Galectins
- Glycoprotein hormones
- Immune checkpoint modulators
- **Interferons**
- Interleukins
- Neuropeptides
- Non-steroidal anti-inflammatory ligands
- Tumor necrosis factor superfamily ligands
- Vascular endothelial growth factor (VEGF) family ligands
- Wnt family ligands

Interferons

ImmunePdb view: **OFF** [Toggle ImmunePdb View](#) [Expand all sections](#) [Collapse all sections](#)

Overview

Classification

Type I interferons: Interferon interferons alpha (IFN- α), IFN β , IFN ϵ , IFN ω , IFN κ , which all signal through the IFN- α/β receptor (IFNAR) that is a dimer of IFNAR1 and IFNAR2 subunits.

Type II interferon: IFN γ which acts through the IFNGR, which comprises IFNGR1 and IFNGR2 subunits.

Type III interferons: IFN λ which signal through a receptor complex containing IL28RA and IFNL1.

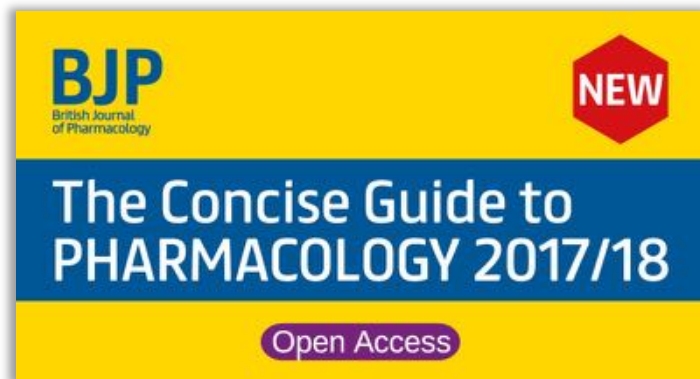
Ligands

IFN- α 1C2 (Sp. Human) View summary	More detailed page
IFN- α 2 (Sp. Human) View summary	More detailed page
IFN- α 4 (Sp. Human) View summary	More detailed page
IFN- α 5 (Sp. Human) View summary	More detailed page

THE CONCISE GUIDE TO PHARMACOLOGY

The Concise Guide to PHARMACOLOGY

- A publication snapshot created from the target family summaries in GtoPdb
- At-a-glance view of target properties - a quick desktop reference guide
- Published biennially in the *British Journal of Pharmacology* (the basic pharmacology journal of the BPS)
- PDFs include embedded hyperlinks to target and ligand entries in GtoPdb, PubMed, HGNC and UniProt

The image is a screenshot of a web page titled 'Somatostatin receptors'. The page contains a table with columns for 'Accession', 'Gene Symbol', 'Gene Name', 'EC Number', 'EC Name', 'EC Class', 'EC Subclass', 'EC Sub-subclass', 'EC Class Name', 'EC Subclass Name', and 'EC Sub-subclass Name'. The table lists various somatostatin receptors and their associated EC numbers and names. The page also includes a 'References' section at the bottom.

Alexander SPH *et al.* (2017) The Concise Guide to PHARMACOLOGY 2017/18. *Br J Pharmacol.* **174** (Suppl 1): S1-S446.

THE IUPHAR GUIDE TO IMMUNOPHARMACOLOGY



IUPHAR Guide to **IMMUNOPHARMACOLOGY**

- A new portal linking GtoPdb targets and ligands to immunological cell types, processes and diseases
- Developed in conjunction with immunologists to include the data types and navigation routes most relevant to immunology
- Immuno-relevant targets and ligands in GtoPdb have been flagged and annotated with supporting data
- Officially launched in October 2018

www.guidetoimmunopharmacology.org

Browsing new GtoImmuPdb data types

- Browse by cell type or immunological process to find targets
- Browse by disease to find targets and drugs

Targets Associated to Immune Processes - Inflammation

Select Immune Process category: Inflammation

Jump to: GPCR (see ChemoKin (GPCR)) | Enzymes | Catalysts | Receptors | Transporters

GPCRs

GPCR receptor name (family)	Process Association Comments	GO Association	Immunopharmacology Comments
ACXK1 (Chemokine receptors)		• inflammatory response (GO:0009814) &A	ACXK1 is one of more than 20 chemokine receptors expressed in human leukocytes. Chemokines promote leukocyte chemotaxis to sites of inflammation.
ACXK2 (Chemokine receptors)		• inflammatory response (GO:0009814) &A	ACXK2 is one of more than 20 chemokine receptors expressed in human leukocytes. Chemokines promote leukocyte chemotaxis to sites of inflammation.
ADGRG2 (Adhesion Class GPCRs)			

Targets Associated to Immune Cell Types - T cells

Select Immune Cell Type category: T cells

Jump to: GPCR (see ChemoKin (GPCR)) | Enzymes | Catalysts | Receptors | Other Protein Targets

The T cells category includes the following Cell Ontology parent terms:

- alpha beta T cell (CL:0000719) - A T cell that expresses an alpha-beta T cell receptor complex.
- effector T cell (CL:0000911) - A differentiated T cell with ability to traffic to peripheral tissues and is capable of mounting a specific immune response.
- regulatory T cell (CL:0000923) - A T cell which regulates several immune responses as well as the responses of other T cell subsets through direct cell-cell contact and cytokine release.

This group encompasses most cytotoxic and helper T cells, as well as regulatory T cells.

GPCRs

GPCR receptor name (family)	Cell Type Association Comments	Cell Ontology Association	Immunopharmacology Comments
A2A receptor (Adenosine receptors)	A2A and A2B receptor antibody shows expression in CD4+ and CD8+ T cell subpopulations. More than 95% of Jurkat T cells were shown to be A2A receptor positive.		A2A receptor is decreased in the immune-enriching stroma [2].
A2B receptor (Adenosine receptors)	CD8+ T cells from patients with rheumatoid arthritis express lower levels of A2B mRNA compared with healthy subjects.	• CD8(positive), TCR(positive), T cell (CL:0000720)	A2B mRNA is expressed on innate and adaptive immune cells of humans and rodents, and are reported to have an immune-modulating effect [2].

The IUPHAR Guide to IMMUNOPHARMACOLOGY Disease list

Targets | Ligands

List of immunological diseases and the ligands contained in GtoImmuPdb

Disease: Activated PMR delta syndrome | Ligand associations: none

Disease X Refs: OMIM 613513
Orphanet ORPHA167094

Disease: Acute lymphocytic leukemia (ALL) | Ligand associations: entosilumab (agonist); blinatumomab

Disease X Refs: OMIM 613065

Ligand	Disease Association Comments	Clinical Use	References
Entosilumab (agonist) [EMA & FDA (2017)] [DrugBank]	Approved therapy for ALL.	The EMA has granted entosilumab orphan designation for the treatment of the rare disease B-cell acute lymphoblastic leukemia.	
Blinatumomab [FDA (2014)] [DrugBank]	Approved specifically for Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukemia (B-cell ALL), an	In December 2014 the FDA approved blinatumomab for use in the treatment of Philadelphia chromosome-negative (Ph-)	

Browsing immunological targets

- GtoPdb families with immuno-relevant targets are highlighted

The image shows a screenshot of the GtoPdb website's 'protein-coupled receptors' page. The main page lists various receptor families, with several highlighted in blue. An overlay window shows a detailed view of a specific target, including its name, comments, and associated biological processes.

Target Page Details:

Immuno-Pharmacology Comments:
 CD3, receptor is involved in controlling natural killer cell degranulation and inhibition [1], and mediates production of MCP-1 by macrophages which results in recruitment of monocyte chemoattractant receptor only with immunosuppressive outcome [2]. High levels of CD3, expression in the CNS suggest a possible role in neuroinflammation and potential as a drug target [3].

Immune Cell Type Associations:

Immune Cell Type	Natural killer cell
Cell Ontology Term	macr cell (E: 0000947)
Comment	Macr cells express both conventional receptors, although the CD3, receptor is most abundantly expressed in the central nervous system.
References	

Immune Process Associations:


Immune Process	Inflammation
Immune Process ID	I
Comment	
GO Annotation	Associated to GO processes, EA only
GO Processes	positive regulation of acute inflammatory response to antigenic stimulus (GO:0002966) EA, positive regulation of leukogenesis (GO:0030532) EA, negative regulation of leukocyte activation (GO:0030534) EA
References	
Immune Process	Immune regulation
Immune Process ID	I
Comment	
GO Annotation	Included in GO processes, EA only
GO Processes	positive regulation of acute inflammatory response to antigenic stimulus (GO:0002966) EA, positive regulation of leukogenesis (GO:0030532) EA, negative regulation of leukocyte activation (GO:0030534) EA
References	

Antagonists

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

Ligand	Sp.	Action	Affinity	Units	Reference
SR144528	Hs	Antagonist	8.3 – 9.2	pKi	30-31
AM-630	Hs	Antagonist	7.5	pKi	31

Detailed target page with immunopharmacology data

 Immuno-ligand icon

Browsing immunological ligands

- Immuno-relevant ligands are highlighted
- Portal includes a list of all immuno-ligands

The IUPHAR Guide to IMMUNOPHARMACOLOGY Ligand List

Approved Synthetic ligands Receptors Natural products Enzymes/peptides Other proteins Targets Antibody Ligands **Immuno**

Toggle ImmunPub View

ABCDEFGHIJKLMNOPQRSTUVWXYZ

Ligand name	ID	Synonyms
A		
8529	8529	
A289982	8582	A 289982, A289982
A439078	4128	A 439078, A-439078
Abatacept	8881	8881 [8881], CTLA-4IgDn, DenaliR, RG-1046, RG-2077
Abatacept	8529	LAS 100877
ABT 727	8529	ABT 727, ABT727, compound 2 [PMID 2125804]
AC 428	8571	AC-428
acalabrutinib	8911	ACP-295, Example 1 [US2014019395 A1]
ACT 388849	8911	
ACTH (hp Human)	8633	ActharIL, adrenocorticotrophic hormone (1-39), corticotropin
acungromast	8058	8CT 187, 8CT 287, 8CT187, compound A [WO201109606]
adalmumab	4886	22E7, PR83CT, Nurxcel

ImmunPub

Ligand 8529

Name: 8529

Structure and Physico-chemical Properties

2D Structure



Estimated Physico-chemical Properties

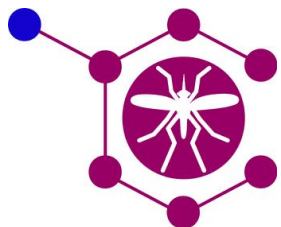
Property	Value
Hydrogen bond acceptors	8
Hydrogen bond donors	2
Rotatable bonds	9
Topological polar surface area	78.06
Molecular weight	440.33
logP	0.78
No. Lipinski's rule broken	0

Secondary Biological activity Chemical data References Structure **Immunopharmacology**

Immunopharmacology Disease

Disease	IC50s	Comment	References
Activated PPAR alpha synthesis	IC50: 12212 IC50: 20742 [20742]	Phase 2 clinical candidate for the condition (see AC75165586)	
Asthma	Disease Therapy: 000 284 IC50: 30007	Complete Phase 1 trial in asthma (see AC75165587)	
Chronic obstructive pulmonary disease	Disease Therapy: 000 284	Phase 2 clinical candidate for COPD (see AC75165588)	1

THE IUPHAR/MMV GUIDE TO MALARIA PHARMACOLOGY



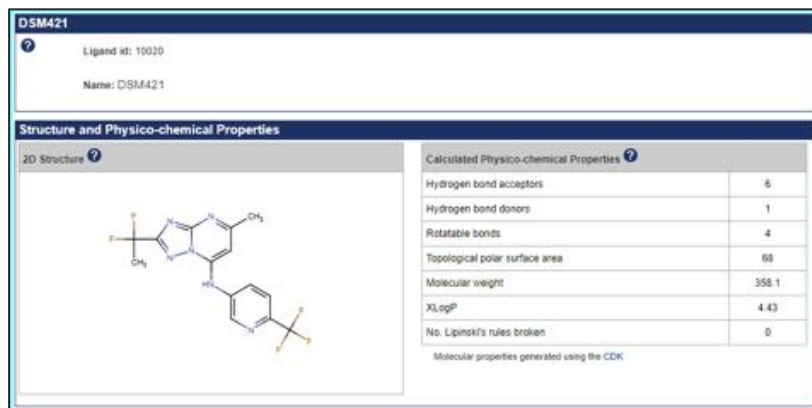
IUPHAR/MMV Guide to **MALARIA PHARMACOLOGY**

- Funded by Medicines for Malaria Venture (MMV) to curate antimalarial compounds and their *Plasmodium* molecular targets
- Provide a new portal to the existing GtoPdb that is optimized for the malaria research community
- Includes lead structures, target sequences and efficacy data integrated across global efforts
- The new resource, the IUPHAR/MMV Guide to Malaria Pharmacology (GtoMPdb), will be freely available, richly annotated and regularly updated

The screenshot displays the homepage of the IUPHAR/MMV Guide to Malaria Pharmacology. The header features the logo and title. Below the header is a navigation menu with tabs for Home, Search, Targets, Ligands, Parasites, and Species. A search bar is located in the top right corner. The main content area is divided into several sections: 'Targets' with a search box, 'Parasite Lifecycle Stages' with a list of stages, 'Target Species' with a list of species, and 'Recent Updates & Help' with a list of updates. A 'Search & Log' button is visible in the top right corner of the main content area.

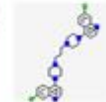
GtoMPdb Data

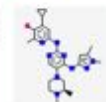
- New target classification – Antimalarial Targets
 - Initial set included 9 *Plasmodium falciparum* targets
- New ligand classification – Antimalarial Ligands
 - An initial set of ~40 were available in the 2018.4 release
- Categories are likely to be further sub-divided
- Includes a tag for submitted structures to PubChem

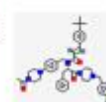



Items: 1 to 20 of 40

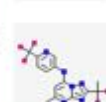
Limits Activated: IUPHAR/BPS Guide to PHARMACOLOGY [Change](#) | [Reset](#)

- 

piperazine: [GTP1-10025](#): [7-chloro-4-\[4-\(3-\[4-\(7-chloroquinolin-4-yl\)piperazin-1-yl\]piperazin-1-yl\)butyl\]piperazine](#)
Source: [IUPHAR/BPS Guide to PHARMACOLOGY](#)
Deposit Date: 2018-09-19 Available Date: 2018-09-19 Modify Date: 2018-09-19
SID: 375973214 [CID: 122262]
[Summary](#) [PubChem](#) [Same Compound](#)
- 

MMV253: [GTP1-10024](#): [AZ13721412](#)
Source: [IUPHAR/BPS Guide to PHARMACOLOGY](#)
Deposit Date: 2018-09-19 Available Date: 2018-09-19 Modify Date: 2018-09-19
SID: 375973213 [CID: 92045019]
[Summary](#) [PubChem](#) [Same Compound](#)
- 

Actelion-451840: [ACT-451840](#): [GTP1-10022](#)
Source: [IUPHAR/BPS Guide to PHARMACOLOGY](#)
Deposit Date: 2018-09-19 Available Date: 2018-09-19 Modify Date: 2018-09-19
SID: 375973212 [CID: 53303762]
[Summary](#) [PubChem](#) [Same Compound](#)
- 

ELQ-300: [ELQ300](#): [GTP1-10021](#)
Source: [IUPHAR/BPS Guide to PHARMACOLOGY](#)
Deposit Date: 2018-09-19 Available Date: 2018-09-19 Modify Date: 2018-09-19
SID: 375973211 [CID: 67016606]
[Summary](#) [PubChem](#) [Same Compound](#)
- 

DSM421: [GTP1-10020](#): [2-\(1-\(1-\(difluoroethyl\)-5-methyl-N-\(6-\(trifluoromethyl\)pyridin-3-yl\)pyrimidin-7-yl\)amino](#)
Source: [IUPHAR/BPS Guide to PHARMACOLOGY](#)
Deposit Date: 2018-09-19 Available Date: 2018-09-19 Modify Date: 2018-09-19
SID: 375973210 [CID: 122552962]
[Summary](#) [PubChem](#) [Same Compound](#)

GtoMPdb Portal

- Customised views of the data have been developed
- Ability to browse not only by target and ligand, but by target species and parasite lifecycle stage (shown here)

Plasmodium asexual blood stage [erythrocytic merozoite, trophozoite, erythrocytic schizont]

Step ID: 3
Name: Plasmodium asexual blood stage (erythrocytic merozoite, trophozoite, erythrocytic schizont)
Associated with T targets: 29 ligands

Description

The collective lifecycle stage that occurs as a result of asexual reproduction in erythrocytes of the host organism and can include:

- **erythrocytic merozoite**, non-invasive but recognises specific proteins on the surface of the erythrocyte and has an apical complex that facilitates entry into the host cell. This form of the parasite is also found in host hepatocytes (see [hepatic merozoites](#)).
- **trophozoite**, the intracellular trophic form that develops from the merozoite. The young trophozoite has a distinctive 'ring' morphology in Giemsa-stained blood smears but this disappears as the parasite grows in size. During the trophic period the parasite ingests the host cell cytoplasm and breaks down the haemoglobin, producing non-toxic hemozoin as a by-product. After feeding and growth is complete the trophozoite undergoes asexual reproduction (schizogony) and develops into a schizont.
- **erythrocytic schizont**, a multicellular form of the parasite that develops in erythrocytes from the trophozoite by schizogony with incomplete cytokinesis. This developmental form is also found in host hepatocytes (see [hepatic schizont](#)).

Completion of cytokinesis produces several thousand merozoites from a single schizont, leading to rupture of the infected erythrocyte and release of merozoites into the bloodstream. These merozoites invade new erythrocytes and initiate either another cycle of schizogony or, under certain conditions, a small percentage of merozoites commit to sexual reproduction (gametogony) (see [Plasmodium asexual blood stage](#)).

It is the repeated cycle of schizogony in erythrocytes that leads to clinical symptoms; the simultaneous rupture of infected erythrocytes and the associated release of antigens and waste products accounts for the intermittent bouts of fever associated with malaria. As a result, almost all available antimalarial therapies target the asexual blood stage.

Interactions

Key to terms and symbols Click column headers to sort

Target	Ligand	Sto.	Action	Affinity	Units	Reference
Plasmodium falciparum (Erythrocyte) (Schizontogenesis)	OSAA41	1:1	-	7.8 - 7.8	µM	18
Plasmodium falciparum (Erythrocyte) (Schizontogenesis)	OSAA26	1:1	-	1.8	µM	18

ADDITIONAL FEATURES AND RESOURCES

Additional features and resources

- FAQ, Tutorial and Help pages (<http://www.guidetopharmacology.org/helpPage.jsp>)
- NC-IUPHAR nomenclature guidelines (<http://www.guidetopharmacology.org/nomenclature.jsp>)
- NC-IUPHAR and GtoPdb publication list (<http://www.guidetopharmacology.org/nciupharPublications.jsp>)
- Hot topics in pharmacology and latest receptor-ligand pairings (<http://www.guidetopharmacology.org/news.jsp>)
- GtoPdb data downloads (<http://www.guidetopharmacology.org/download.jsp>)
- RDF flat files of target-ligand interaction data (<http://www.guidetopharmacology.org/download.jsp#rdf>)
- REST web services for computational access to data in JSON form (<http://www.guidetopharmacology.org/webServices.jsp>)
- Blog posts about database updates, curatorial and technical aspects, and hot topic commentaries (<http://blog.guidetopharmacology.org/>)

THE PHARMACOLOGY EDUCATION PROJECT

An IUPHAR learning resource

IUPHAR Pharmacology Education Project

A free learning resource to support education and training in the pharmacological sciences

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enquiries@guidetopharmacology.org



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- Database team:
 - Jamie Davies (Principal Investigator)
 - Simon Harding, Joanna Sharman (Developers)
 - Adam Pawson, Elena Faccenda, Christopher Southan, Jane Armstrong (Curators)
 - Toni Wigglesworth (Project Administrator)
- All database team alumni
- All current and past NC-IUPHAR and website sponsors
- IUPHAR/BPS Guide to PHARMACOLOGY funders:



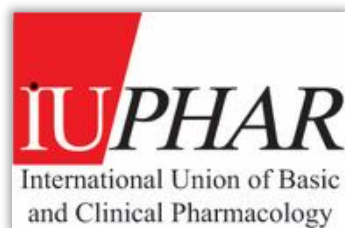
THANK YOU FOR YOUR ATTENTION



APPENDIX

TEMPLATE SLIDES

Live demos at this meeting



- Booth # X

- Booth # X

