# IUPHAR/BPS Guide to PHARMACOLOGY Generic slides for use in presentations and teaching materials

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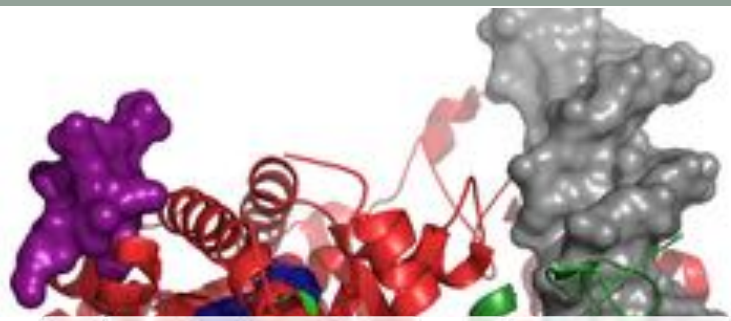
- They are also available on SlideShare at https://www.slideshare.net/GuidetoPHARM/gtopdb-generic-slides-201718



IUPHAR/BPS
Guide to PHARMACOLOGY

# The IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb)

**http://www.guidetopharmacology.org**

**Name**

Date, Venue

IUPHAR
International Union of Basic and Clinical Pharmacology

BRITISH PHARMACOLOGICAL SOCIETY

THE UNIVERSITY of EDINBURGH

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- Background and history of the database
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- 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)


- 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

IUPHAR
International Union of Basic and Clinical Pharmacology

BRITISH PHARMACOLOGICAL 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

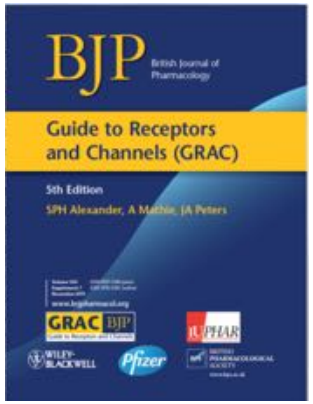
# A brief history of IUPHAR-DB

- 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***'.

GRAC BJP
Guide to Receptors and Channels



# 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 Ediotr-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)

**Corresponding members**

Susan Amara, USA
Tom I. Bonner, USA
Michel Bouvier, Canada
Thomas Burris, USA
William A. Catterall, USA
Stephen Charlton, UK
Moses Chao, USA
Mark Coles, UK
Steven L. Colletti, USA
Graham Collingridge, UK
Philippe Delerive, France
Sir Colin T. Dollery, UK
Richard Eglen, UK
Sam J. Enna, USA
Steven Foord, UK
David Gloriam, Denmark
Gillian Gray, UK
Debbie Hay, New Zealand
Allyn Howlett, USA
Franz Hofmann, Germany
Yu Huang, Hong Kong
Ad P. Ijzerman, The Netherlands
Michael F. Jarvis, USA
Bong-Kiun Kaang, Korea
Terry Kenakin, USA
Janos Kiss, Hungary
Stefan Knapp, UK
Andrew Knight, UK
Chris Langmead, Australia
Vincent Laudet, France
Margaret (Mandy) MacLean, UK
Neil Marrion, UK
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
$alpha_1$-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)**

$5\text{-}HT_3$: 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
$alpha_2$-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 Izjerman
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 Ijzerman
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

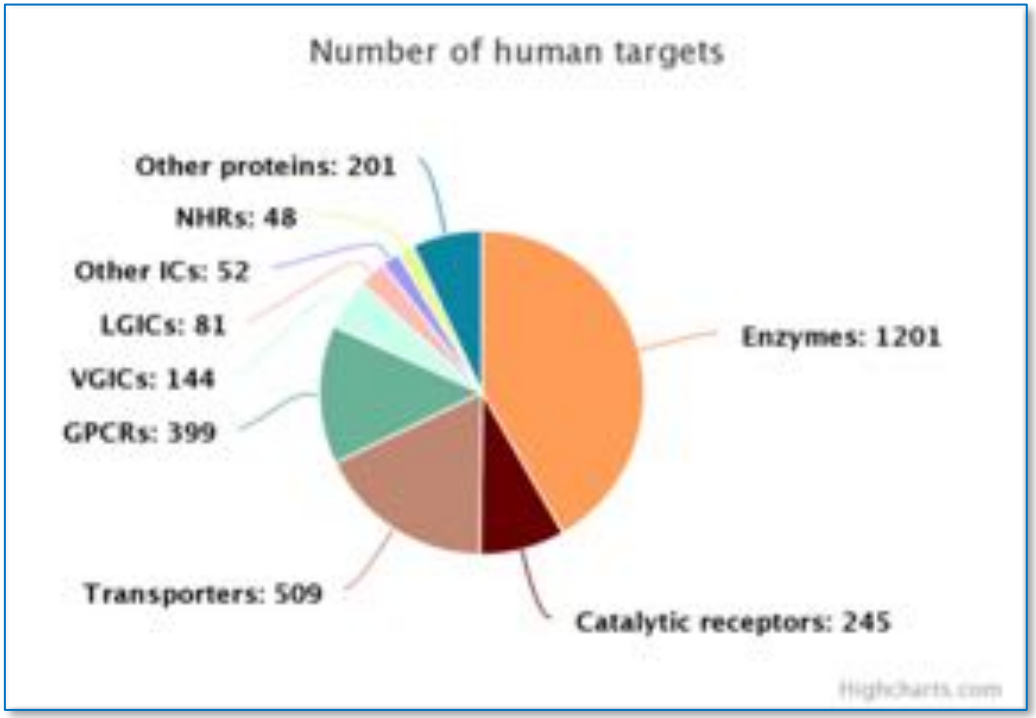
**'Concise Guide to PHARMACOLOGY' Editors**
Stephen Alexander, Eamonn Kelly, Neil Marrion, John Peters

# 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

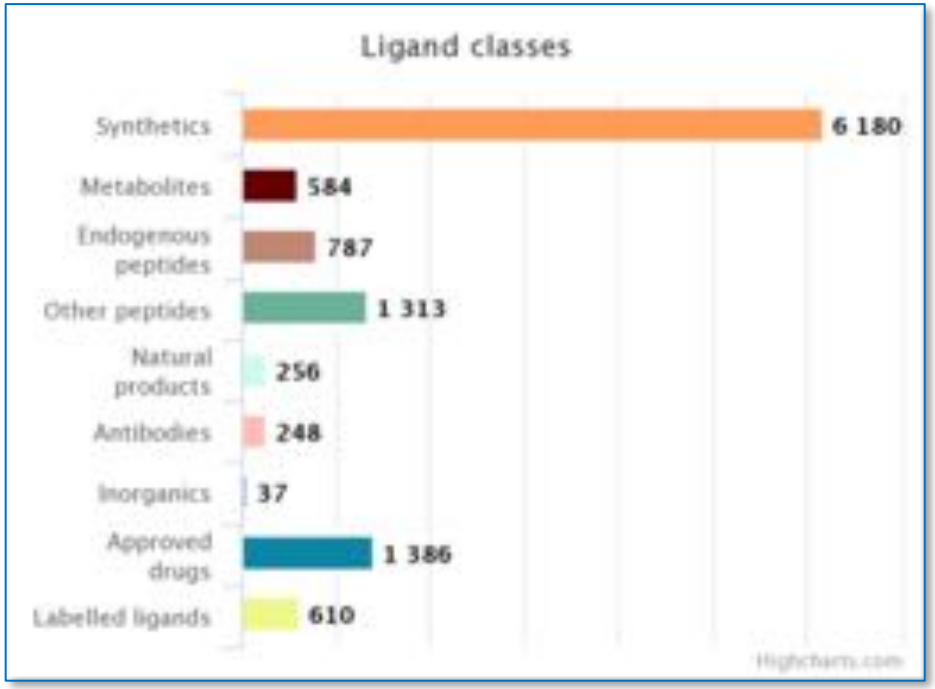



Target numbers as of the 2018.4 release

# 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

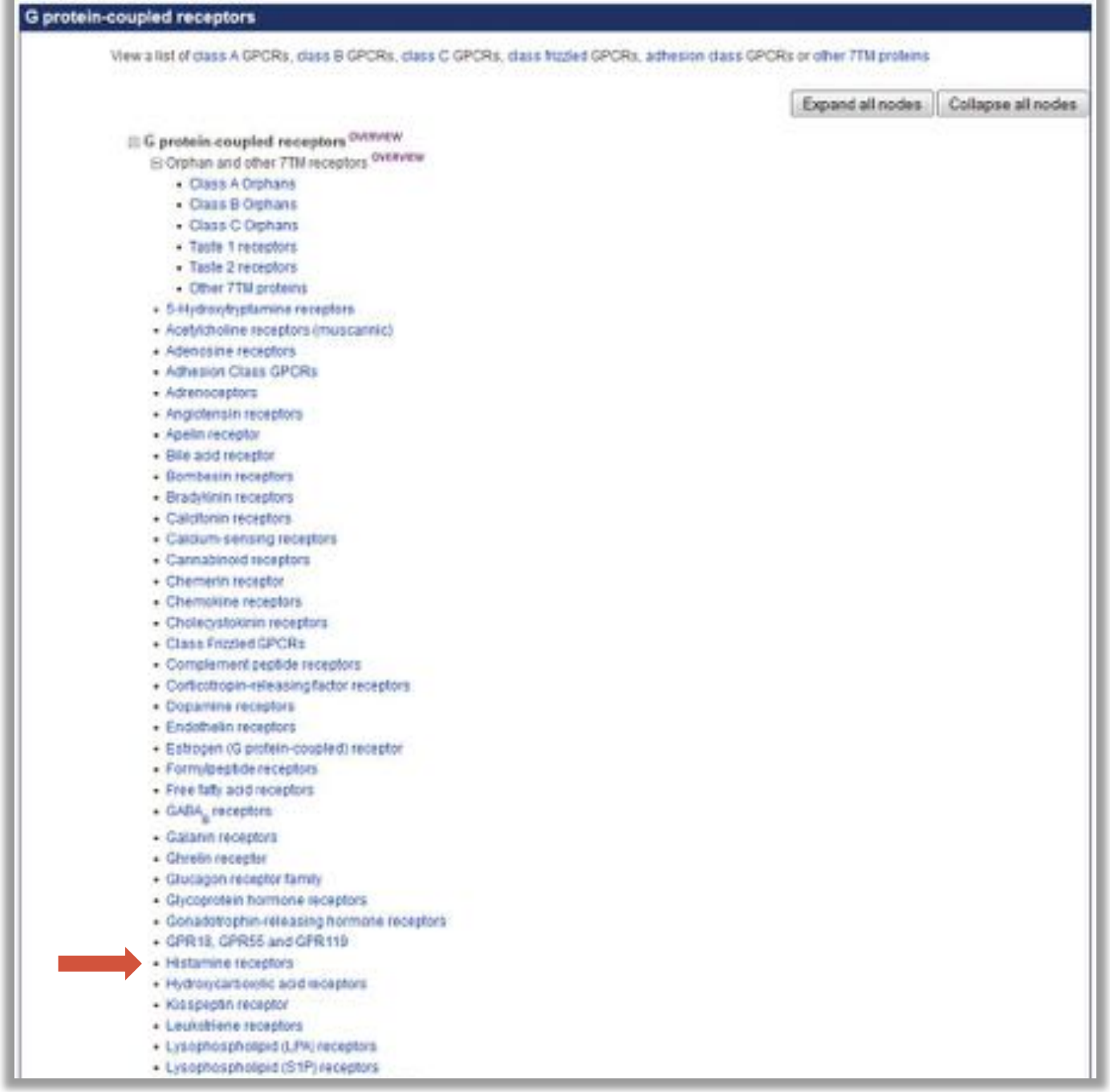
- Extensively referenced and linked to primary literature in PubMed
- Focus is on human data but where species differences exist or literature data unavailable other species are given
- Linked to corresponding entries in other resources, e.g. UniProt, Ensembl, Entrez Gene, KEGG, OMIM, ChEMBL
- Ligand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

# NAVIGATING THE WEBSITE AND SEARCH TOOLS

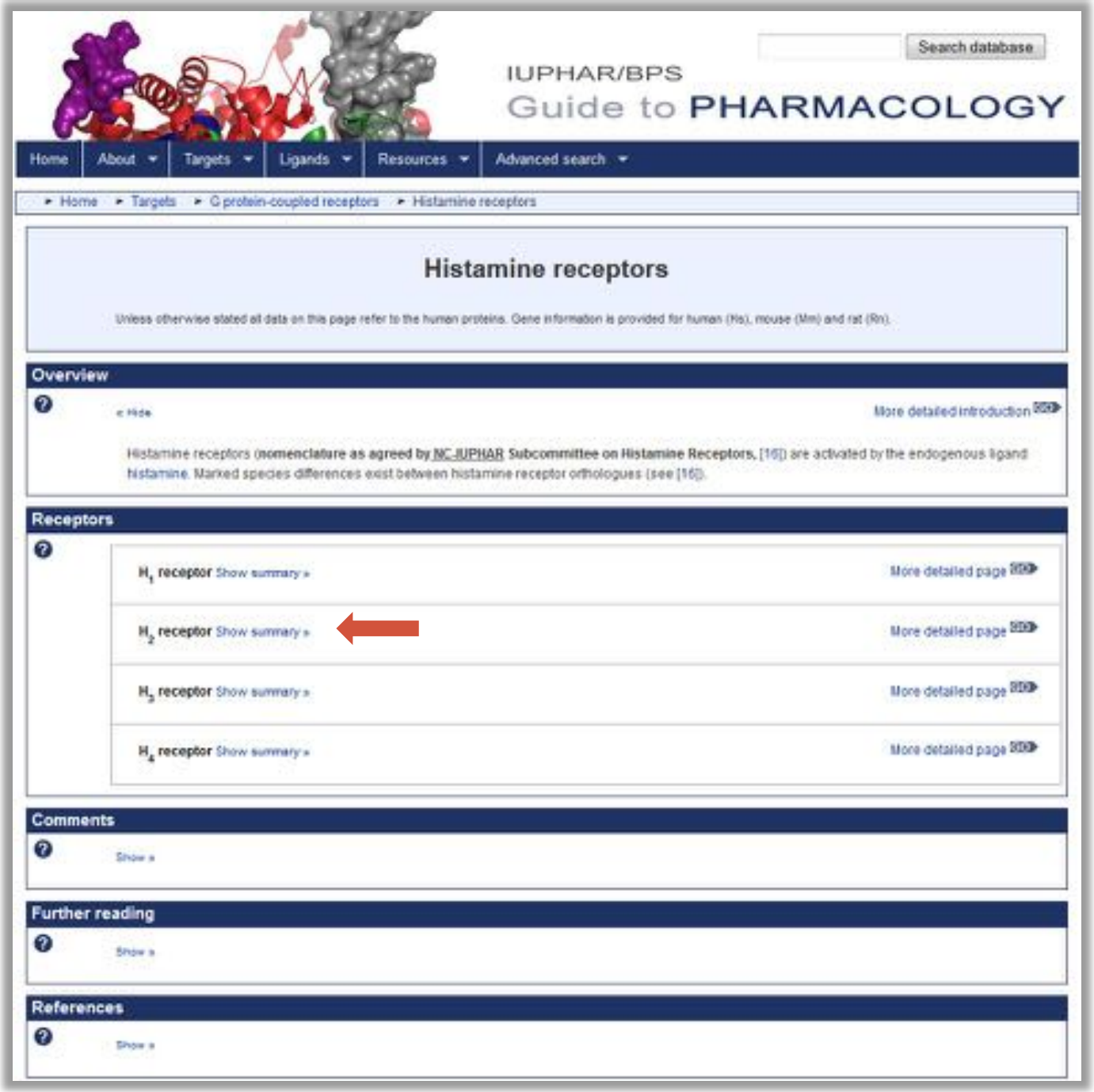
# Navigating GtoPdb

- 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

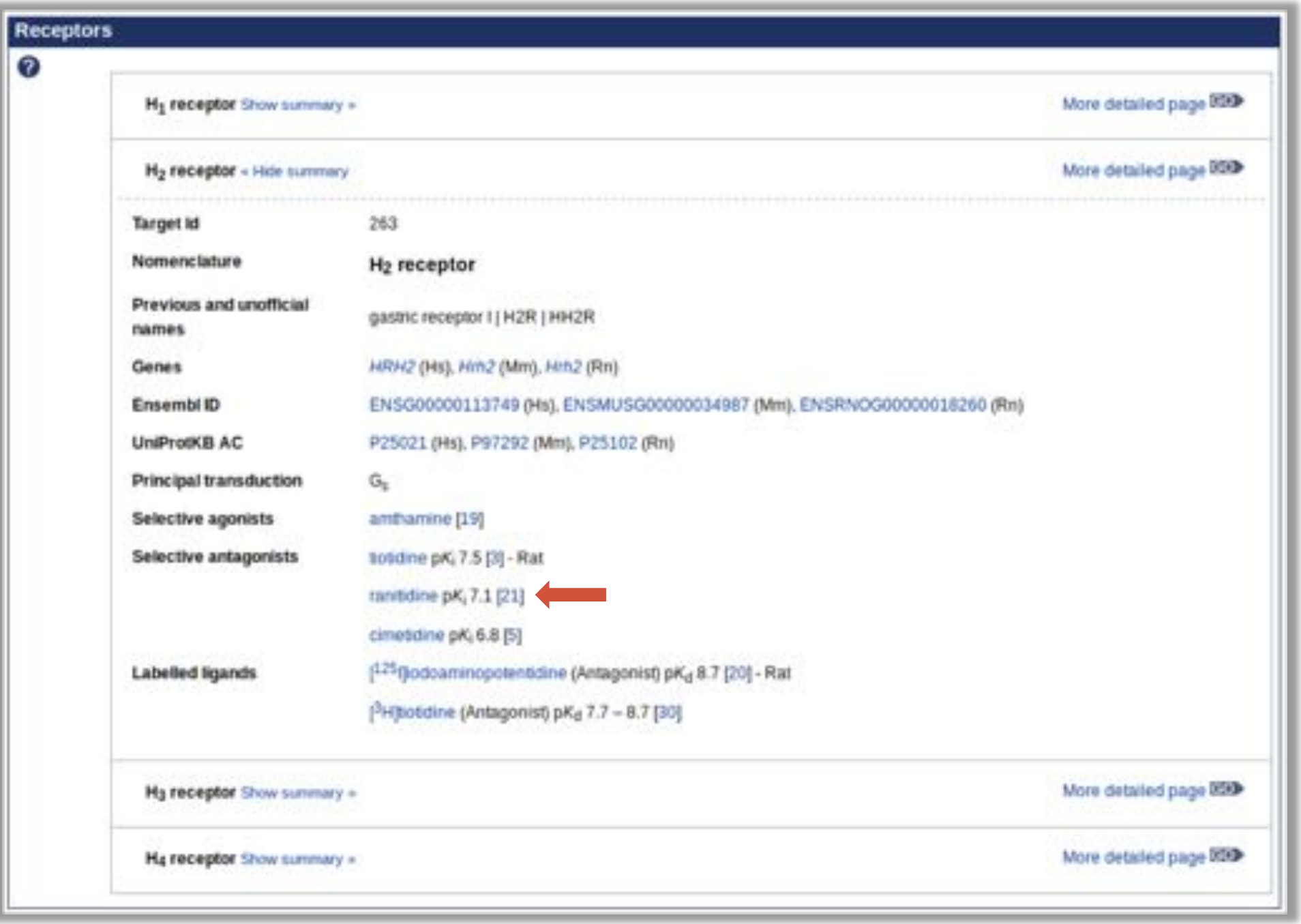

GtoPdb home page



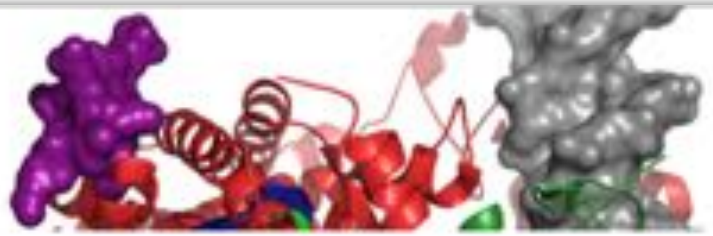

GtoPdb home page




Histamine receptors family summary page




Histamine $H_2$ receptor concise summary view



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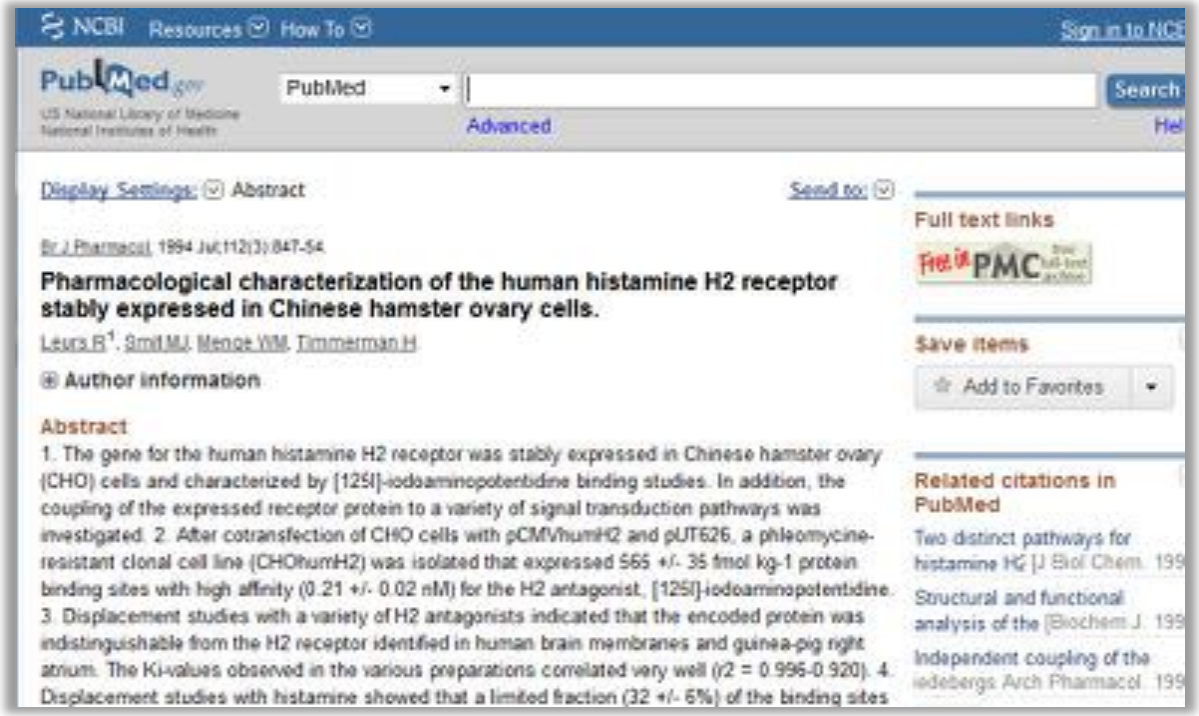
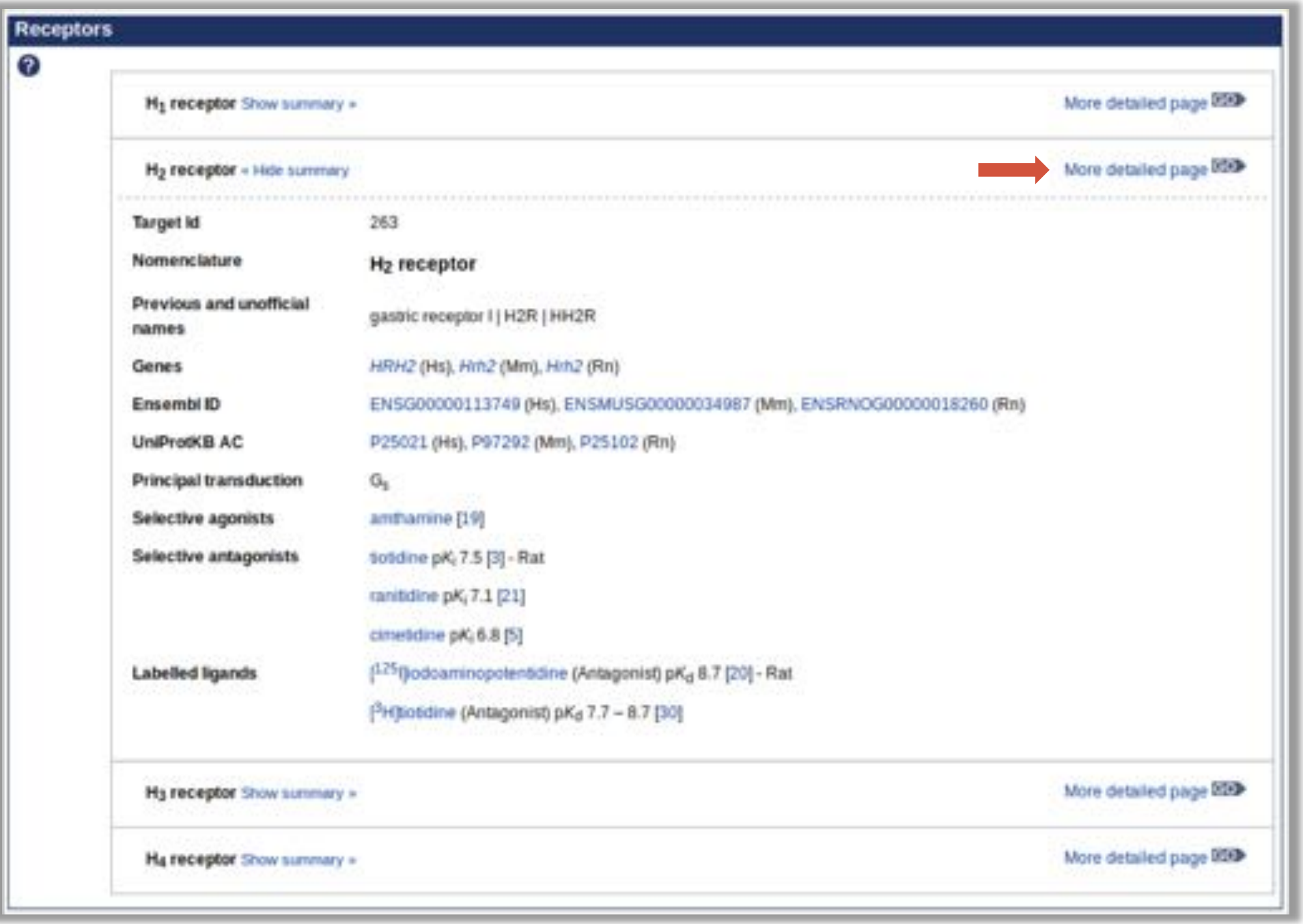
**21. Leurs R, Smit MJ, Menge WM, Timmerman H. (1994)**
Pharmacological characterization of the human histamine H2 receptor stably expressed in Chinese hamster ovary cells.
*Br. J. Pharmacol.*, **112** (3): 847-54. [PMID:7921611]




Reference information and linkout to PubMed




Link to more details for the $H_2$ receptor

## $H_2$ receptor

Target id: 263

Nomenclature: $H_2$ receptor

Family: Histamine receptors

Annotation status: Annotated and reviewed, awaiting update » Email us

**Contents:**



### Gene and Protein Information

class A G protein-coupled receptor

| Species | TM | AA | Chromosomal Location | Gene Symbol | Gene Name | Reference |
|---|---|---|---|---|---|---|
| Human | 7 | 359 | 5q35.2 | *HRH2* | histamine receptor H2 | 11 |
| Mouse | 7 | 358 | 13 B1 | *Hrh2* | histamine receptor H2 | 18 |
| Rat | 7 | 358 | 17p14 | *Hrh2* | histamine receptor H 2 | 40 |

### Previous and Unofficial Names

| |
|---|
| gastric receptor I |
| H2R |
| HH2R |

$H_2$ receptor detailed annotation page

| 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), rno: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 |

Linkouts to other gene and protein resources

## 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-PG136 | Hs | Full agonist | 7.0 | $pK_i$ | 47 |
| UR-PG148 | 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]tiotidine | Hs | Antagonist | 7.7 – 8.7 | $pK_d$ | 34 |
| iodoaminopotentidine | Rn | Antagonist | 9.2 | $pK_i$ | 3 |
| tiotidine | Rn | Antagonist | 7.5 | $pK_i$ | 3 |
| ranitidine | Hs | Antagonist | 7.1 | $pK_i$ | 23 |
| cimetidine | Hs | Antagonist | 6.85 | $pK_i$ | 6 |
| ranitidine | Rn | Antagonist | 6.2 | $pK_i$ | 3 |
| cimetidine | Rn | Antagonist | 5.9 | $pK_i$ | 3 |
| metiamide | Rn | Antagonist | 5.8 | $pK_i$ | 3 |
| burimamide | Rn | Antagonist | 5.5 | $pK_i$ | 44 |
| clobenpropit | 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

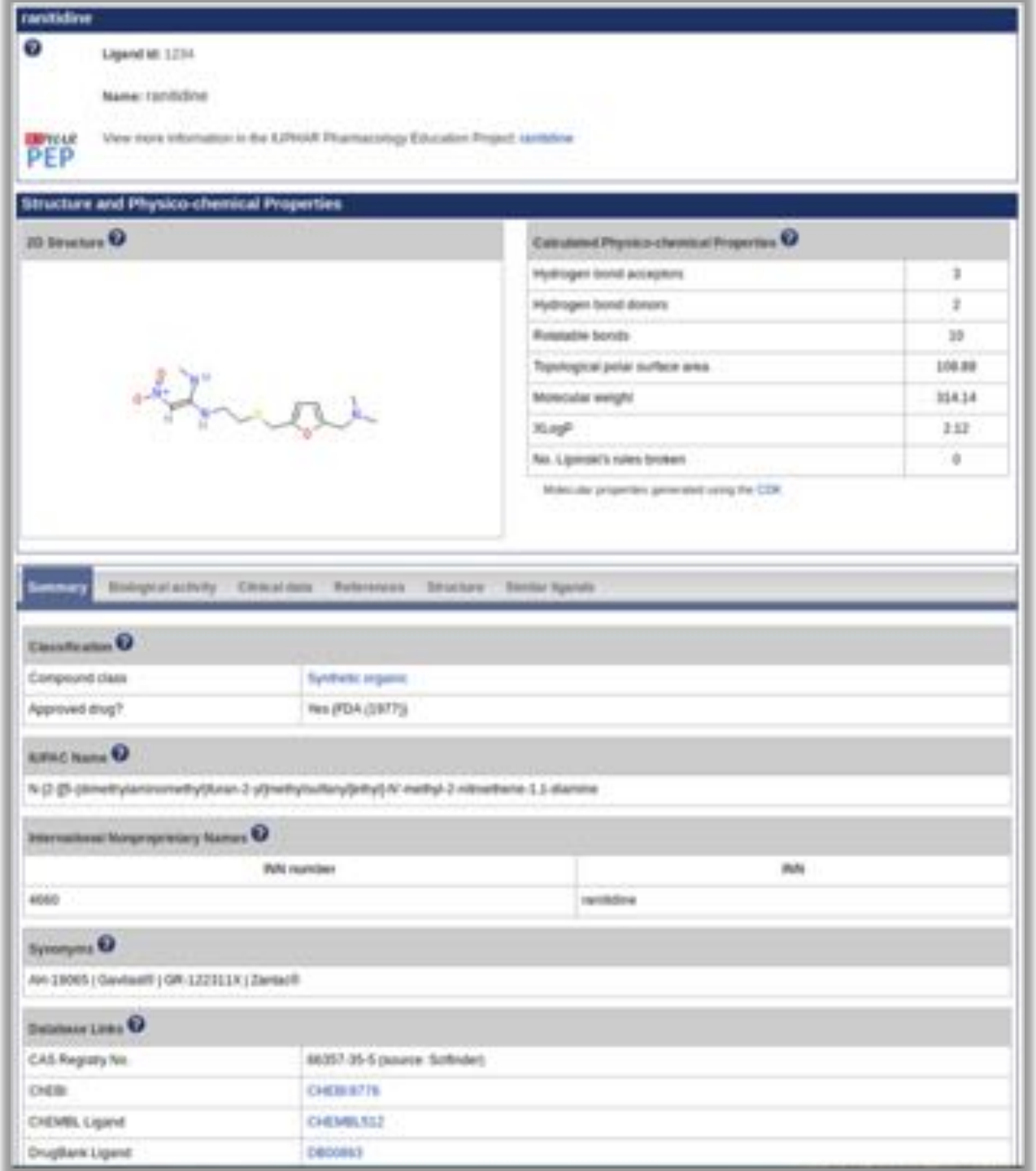
## Antagonist Comments

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




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 |

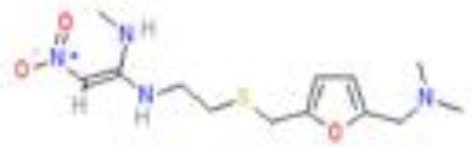
### Ligand mentioned in the following text fields

Histamine receptors overview

Biological activity data for ranitidine at targets in the database

## Structure and Physico-chemical Properties

### 2D Structure



### Calculated Physico-chemical Properties

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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 gastic ulcers, where blocking of $H_2$ receptors reduces gastric acid secretion and ameliorates disease symptoms.

### Mechanism Of Action and Pharmacodynamic Effects

Competitive inhibition of $H_2$ receptors on parietal cells leads to supression of gastric acid secretion.

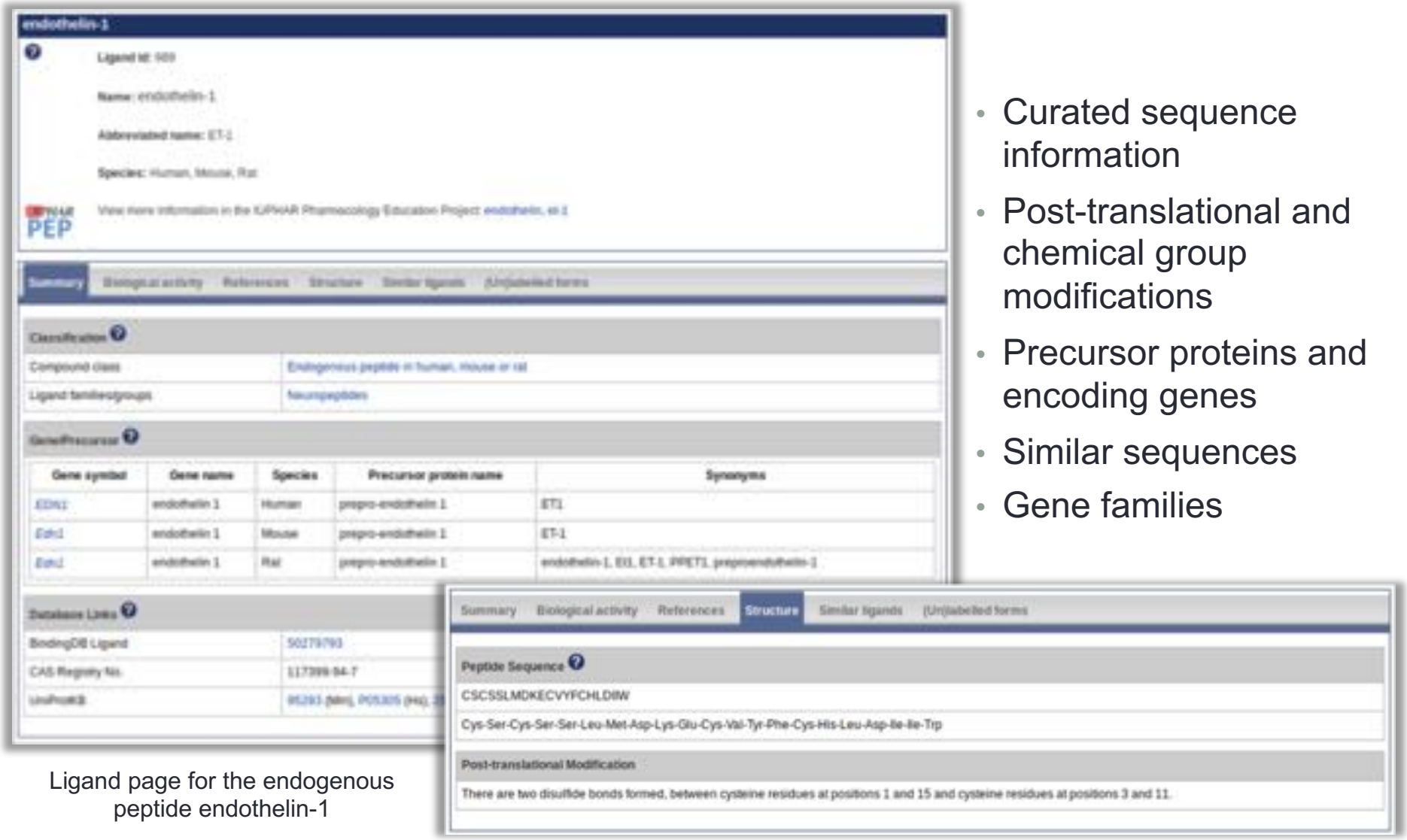
### External links

For extended ADME data see the following:

Electronic Medicines Compendium (eMC)

Clinical use and mechanism of action for ranitidine

# Peptide ligand information

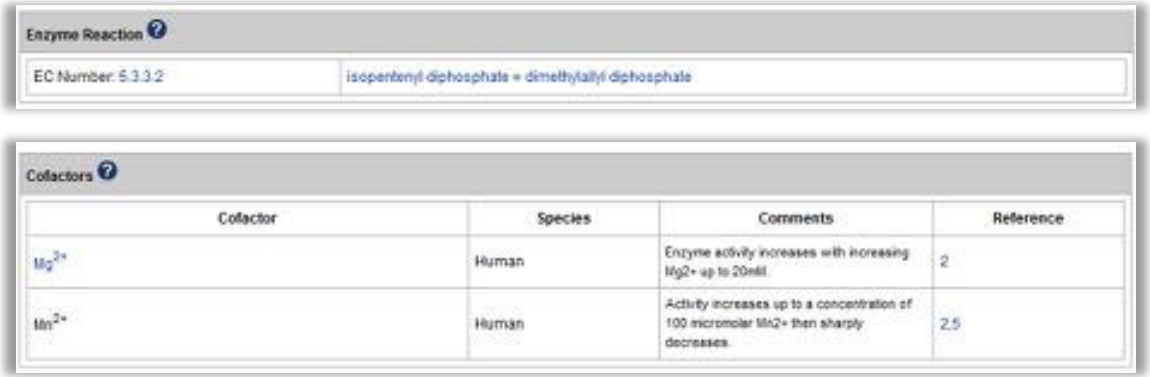



Ligand page for the endogenous peptide endothelin-1

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

# 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



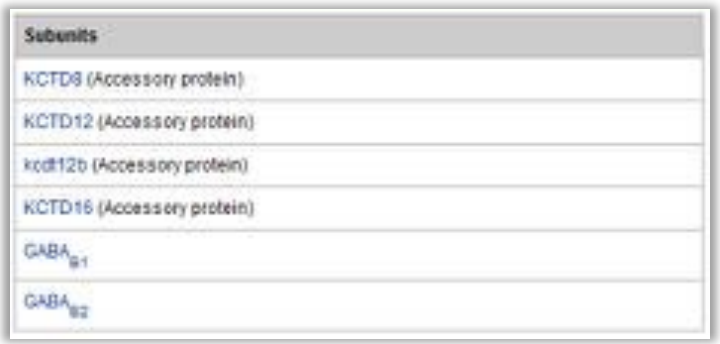
Enzyme Reaction

| EC Number: 5.3.3.2 | isopentenyl diphosphate = dimethylallyl diphosphate |
|---|---|

Cofactors

| Cofactor | Species | Comments | Reference |
|---|---|---|---|
| $Mg^{2+}$ | Human | Enzyme activity increases with increasing Mg2+ up to 20mM. | 2 |
| $Mn^{2+}$ | Human | Activity increases up to a concentration of 100 micromolar Mn2+ then sharply decreases. | 2,5 |

isopentenyl-diphosphate Δ-isomerase 1



| Subunits |
|---|
| KCTD8 (Accessory protein) |
| KCTD12 (Accessory protein) |
| kcdt12b (Accessory protein) |
| KCTD16 (Accessory protein) |
| $GABA_{B1}$ |
| $GABA_{B2}$ |

$GABA_B$ receptor

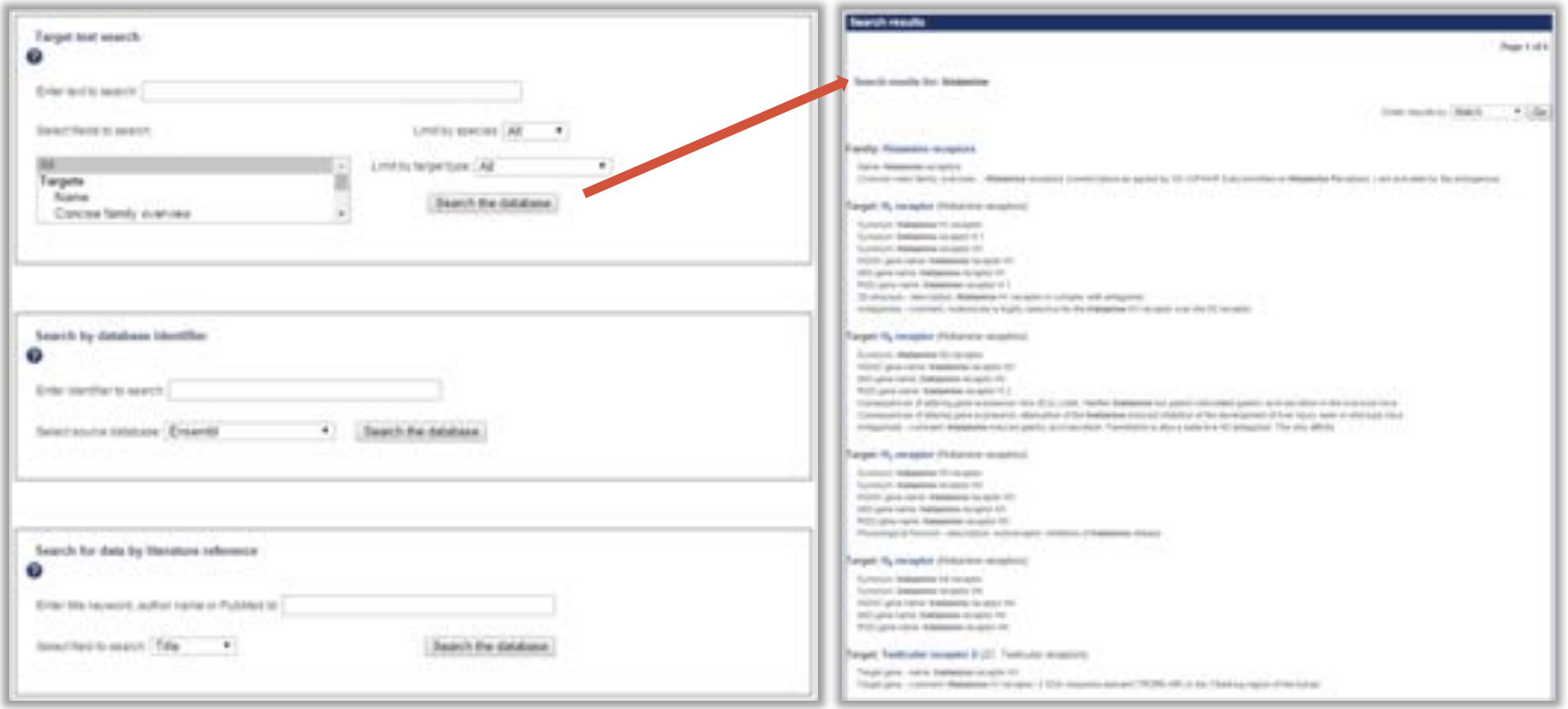
# Database search functionality

- 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

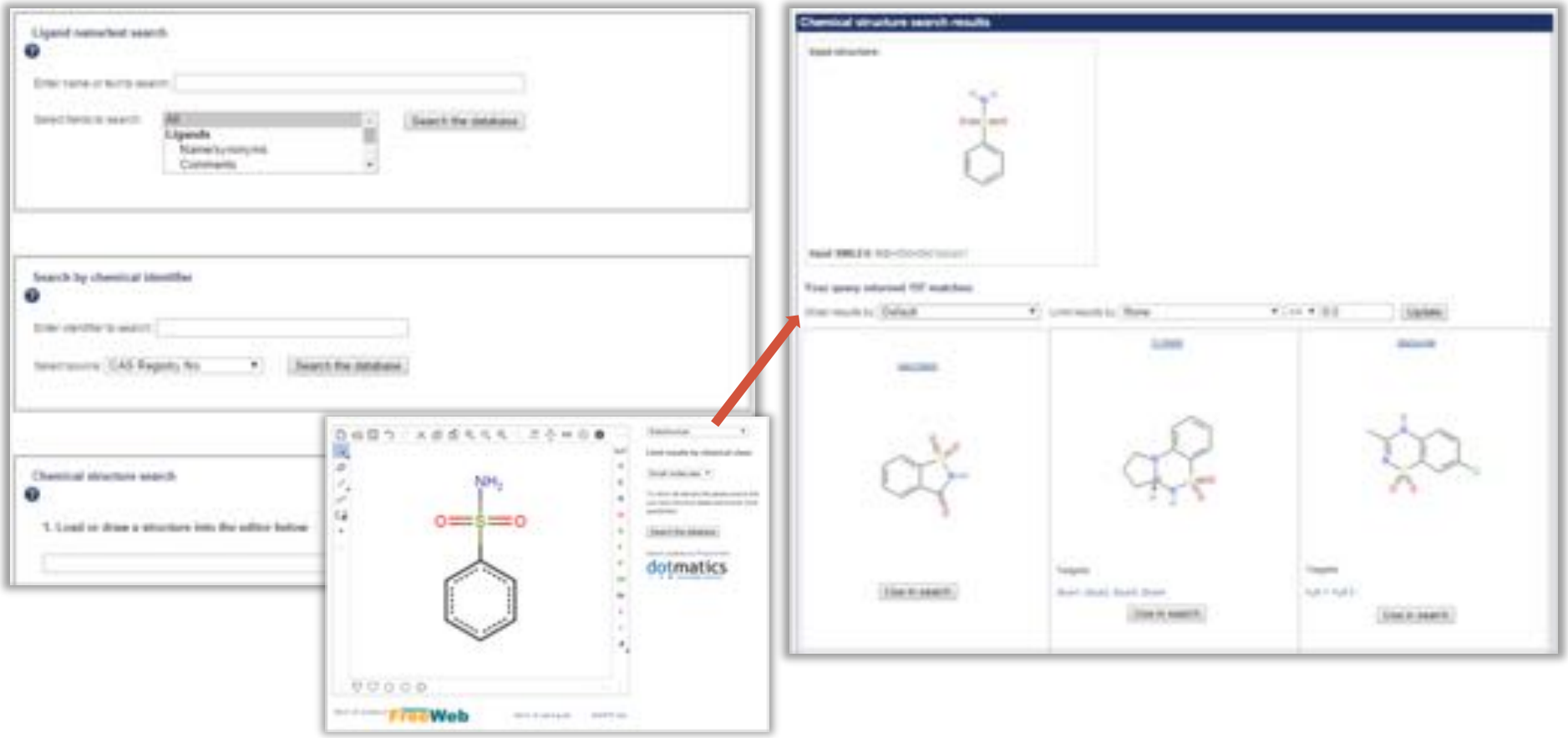
# Target search tools

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



# Ligand search tools

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



# 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

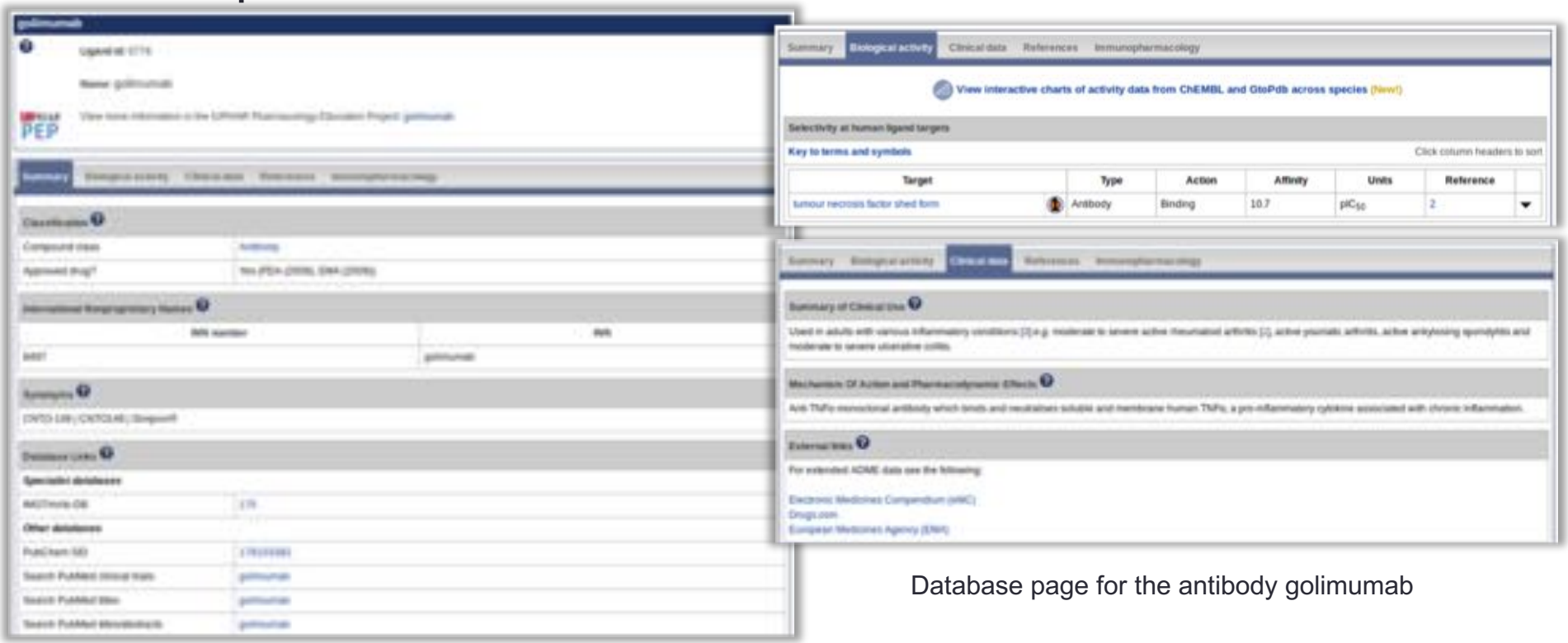
# RECENT ADDITIONS AND EXPANSIONS

# 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

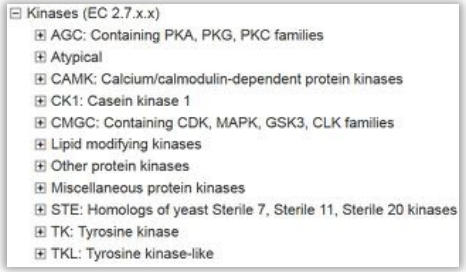
- Collaboration with IMGT®, the international ImMunoGeneTics information system®
- Pharmacological data on 224 approved and experimental therapeutic monoclonal antibodies

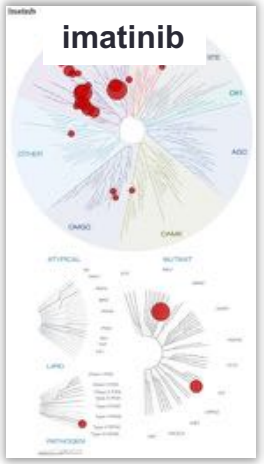


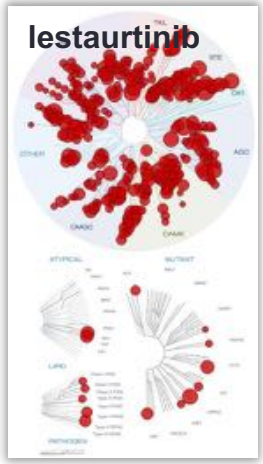

Database page for the antibody golimumab

# 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 DiscoveRx, EMD Millipore and Reaction Biology
- Links to the DiscoveRx TREE*spot*™ compound profile visualisation tool



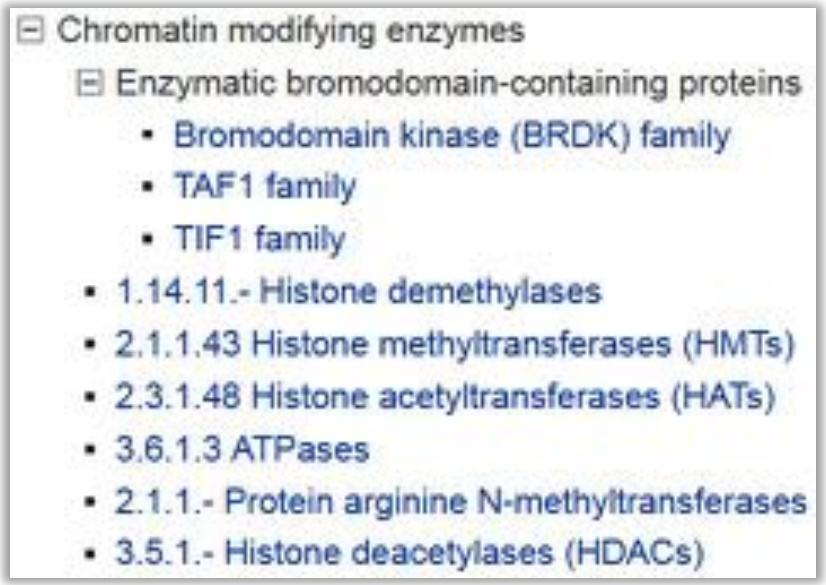
# Information on proteases and hydrolases

- 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


presenilin 1

# Information on epigenetic targets

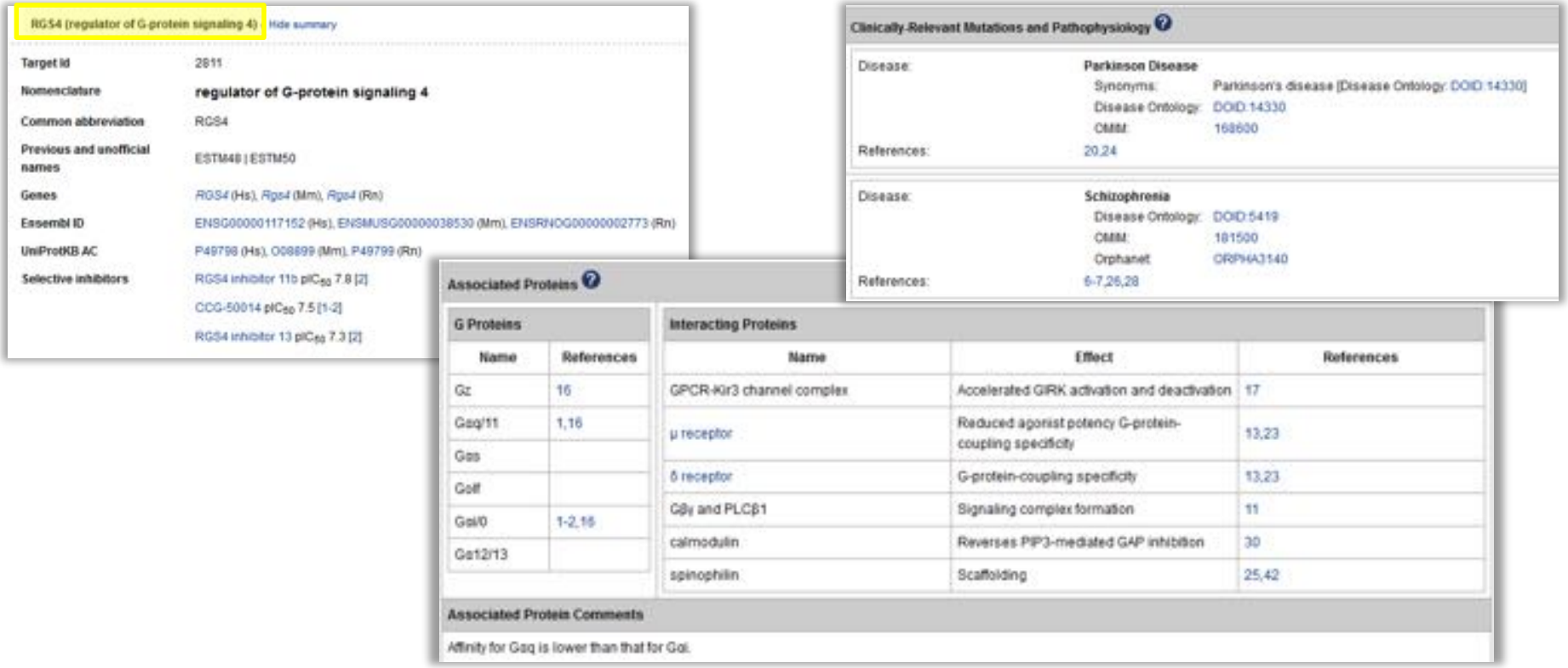
- GtoPdb includes ~130 epigenetic targets (chromatin modifying enzymes and bromodomain-containing proteins), along with activity data for published inhibitors




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 |
| Nomenclature | 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), ENSMUSG00000038530 (Mm), ENSRNOG00000002773 (Rn) |
| UniProtKB AC | P49798 (Hs), O08899 (Mm), P49799 (Rn) |
| Selective inhibitors | RGS4 inhibitor 11b $pIC_{50}$ 7.8 [2] |
| | CCG-50014 $pIC_{50}$ 7.5 [1-2] |
| | RGS4 inhibitor 13 $pIC_{50}$ 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

| Name | References |
|---|---|
| Gz | 16 |
| Gαq/11 | 1,16 |
| Gαs | |
| Golf | |
| Gαi/0 | 1-2,16 |
| Gα12/13 | |

Interacting Proteins

| Name | Effect | References |
|---|---|---|
| GPCR-Kir3 channel complex | Accelerated GIRK activation and deactivation | 17 |
| μ receptor | Reduced agonist potency G-protein-coupling specificity | 13,23 |
| δ receptor | G-protein-coupling specificity | 13,23 |
| Gβγ and PLCβ1 | Signaling complex formation | 11 |
| calmodulin | Reverses PIP3-mediated GAP inhibition | 30 |
| spinophilin | Scaffolding | 25,42 |

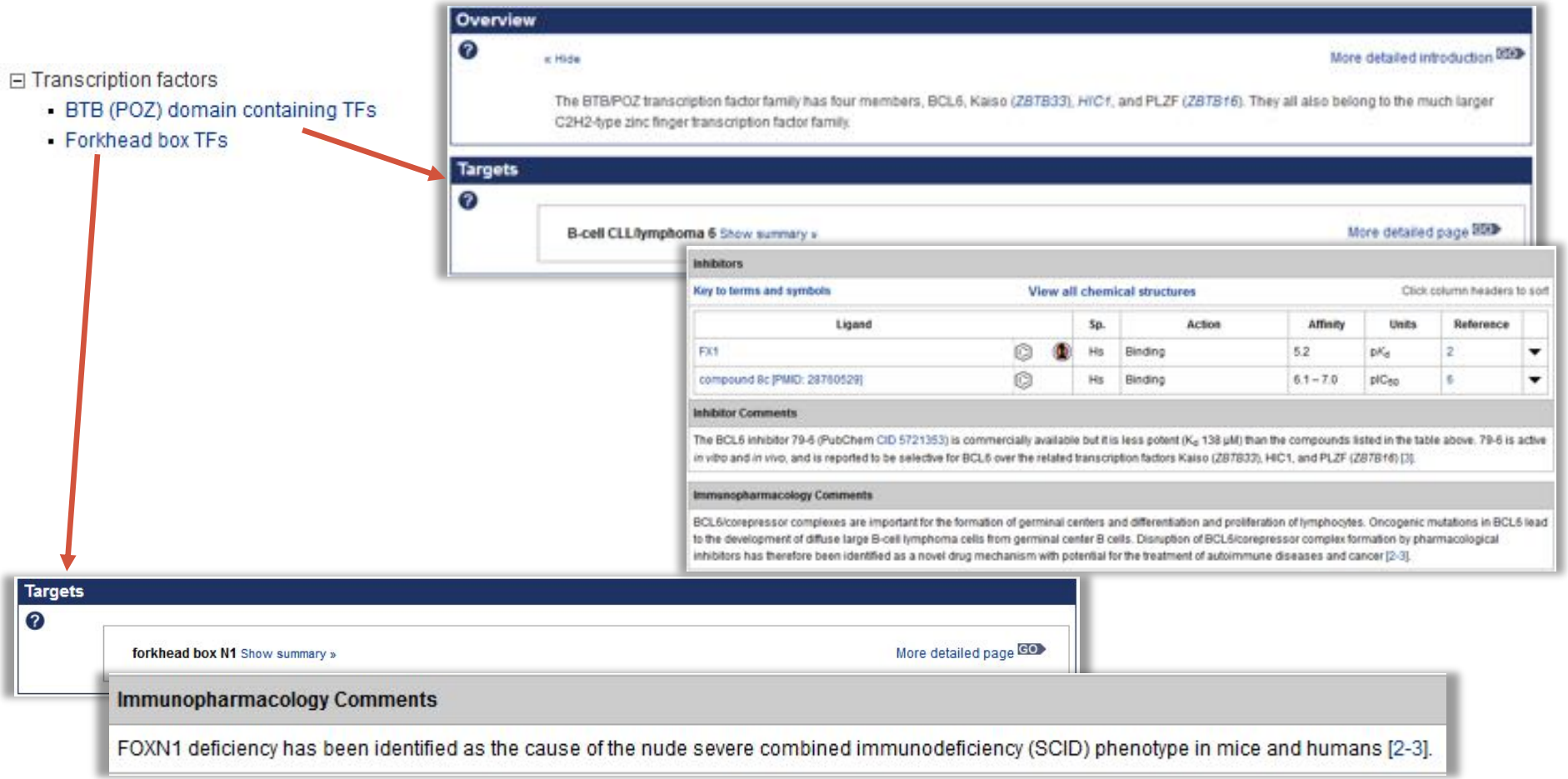
Associated Protein Comments

Affinity for Gαq is lower than that for Gαi.

Sjögren B. (2017) The evolution of regulators of G protein signalling proteins as drug targets - 20 years in the making: IUPHAR Review 21. *Br J Pharmacol*. 174(6):427-437.

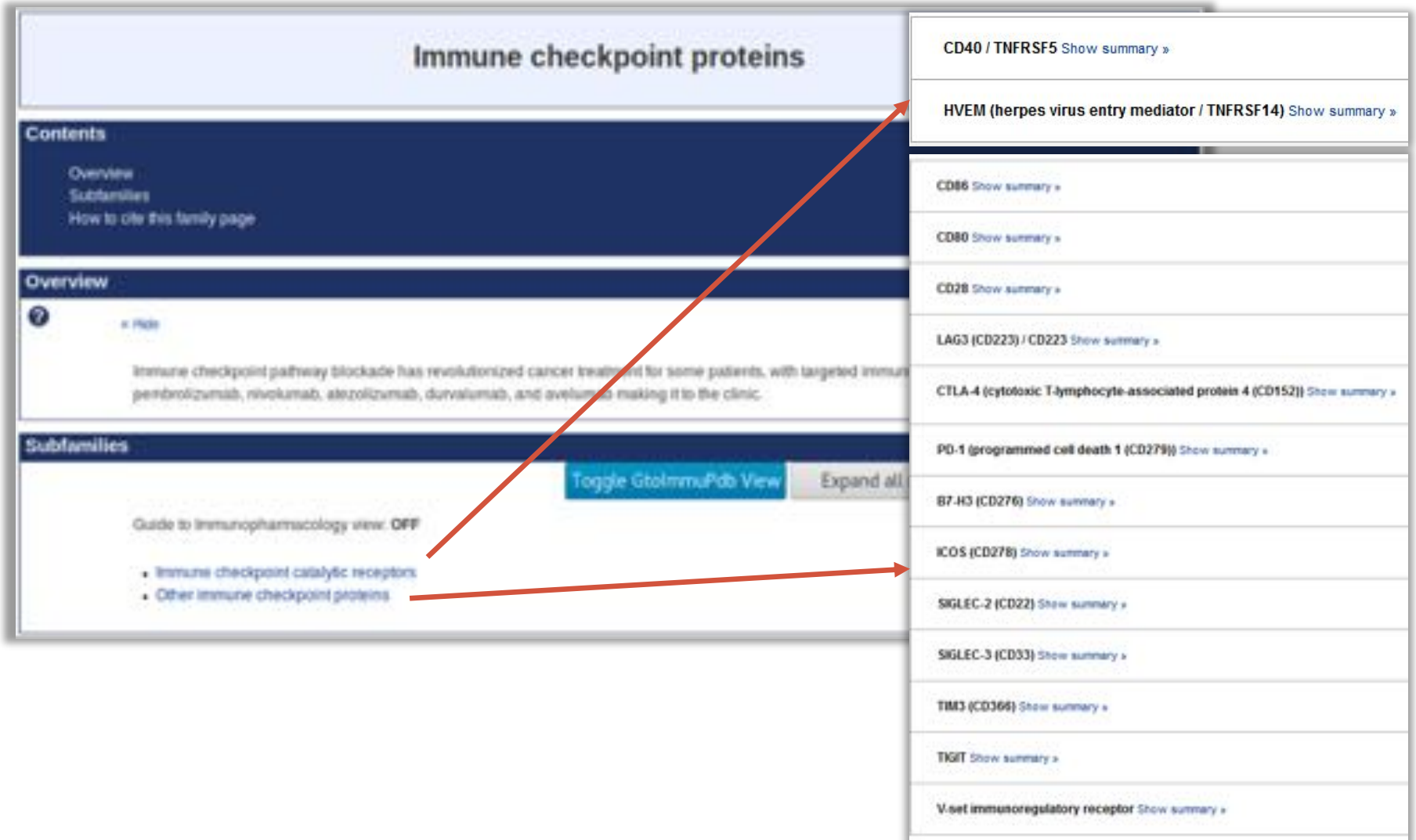
# Information on transcription factors (relevant to immunopharmacology)

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



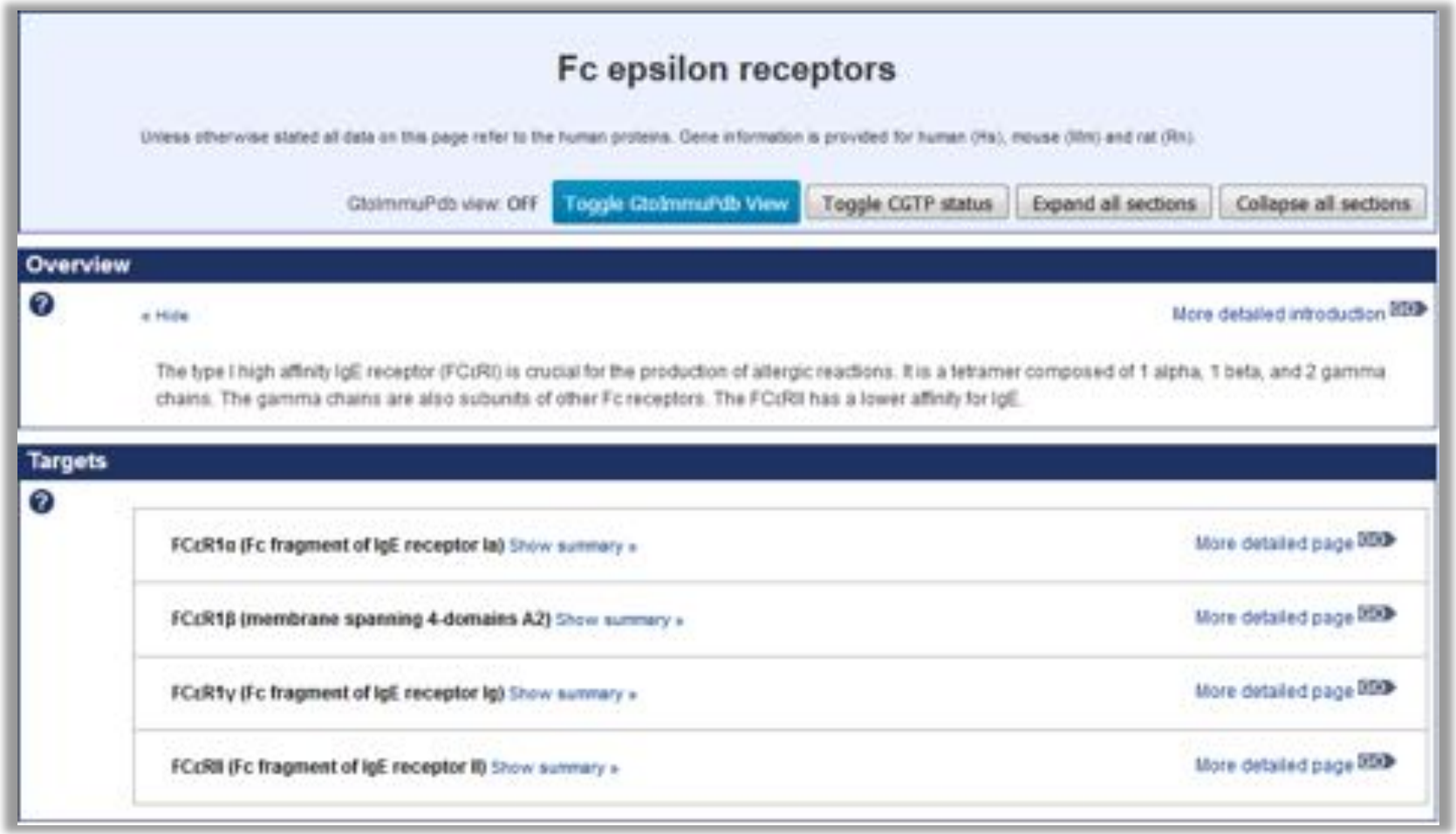
# Information on immune checkpoint proteins

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



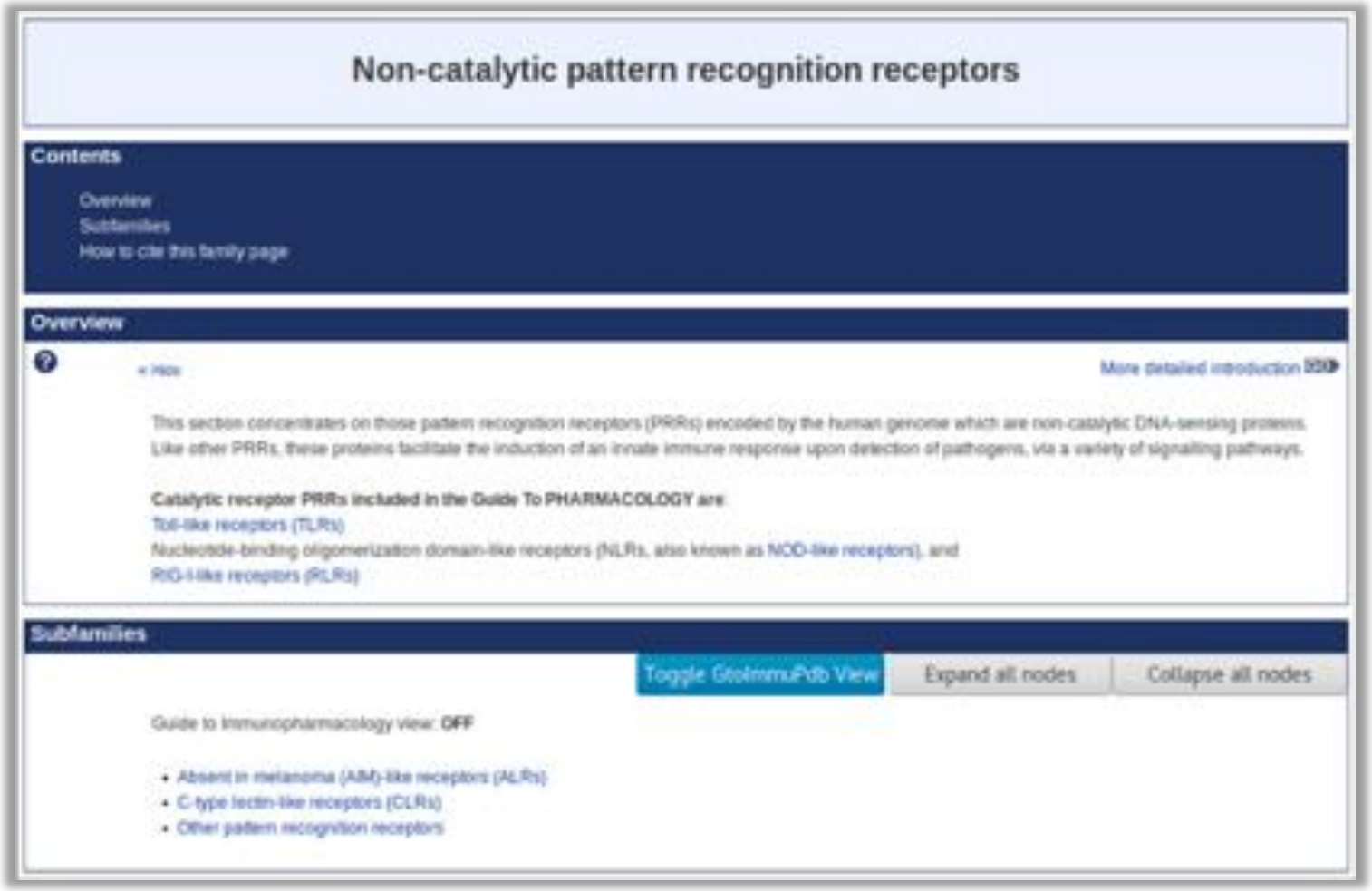
# Information on Fc epsilon receptors

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



# 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



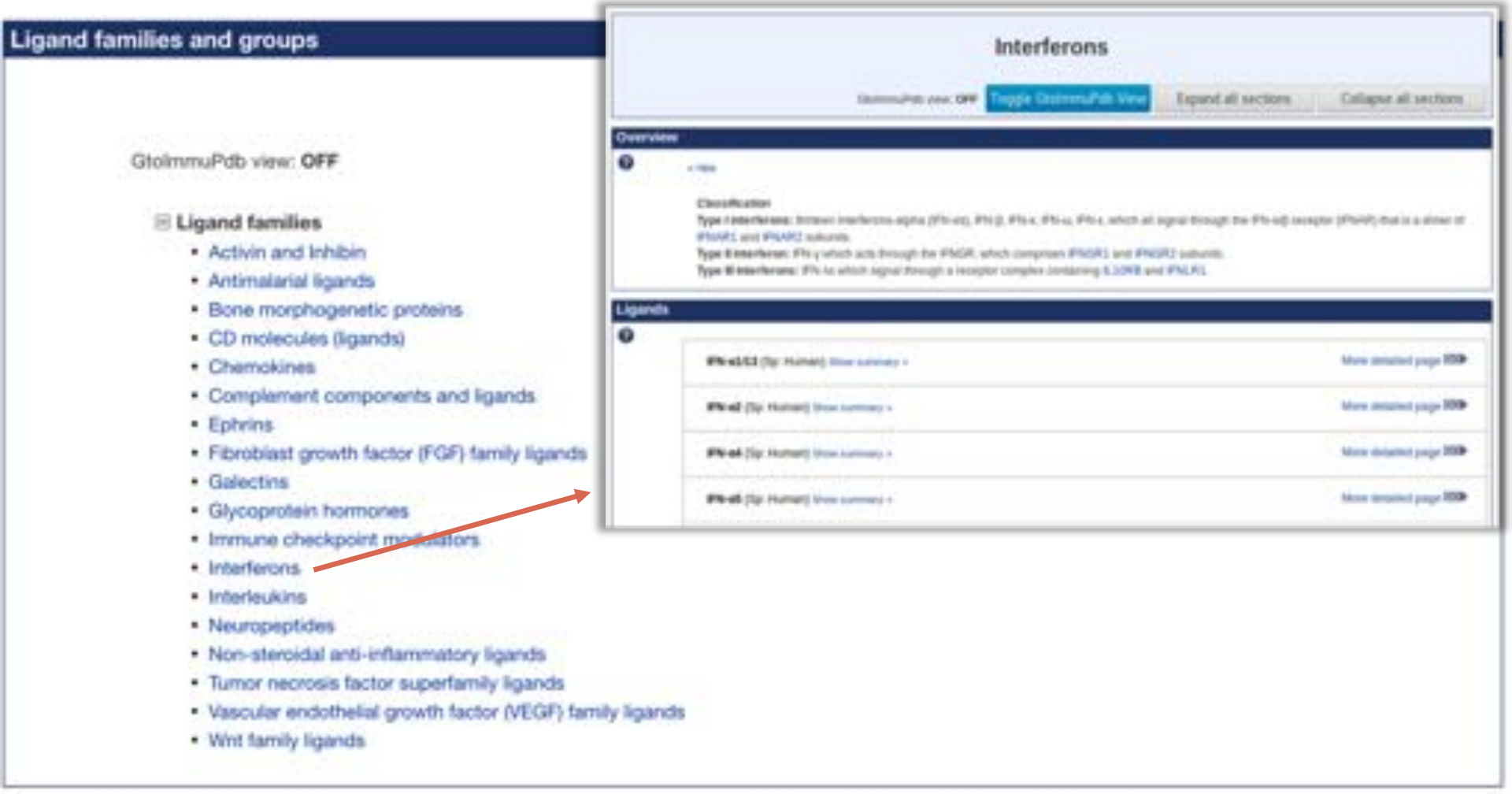

Bryant *et al.* (2015) International Union of Basic and Clinical Pharmacology. XCVI. Pattern recognition receptors in health and disease. *Pharmacol Rev*. 67(2):462-504.

# Information on antimalarial ligands and targets

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


# 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



# 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



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

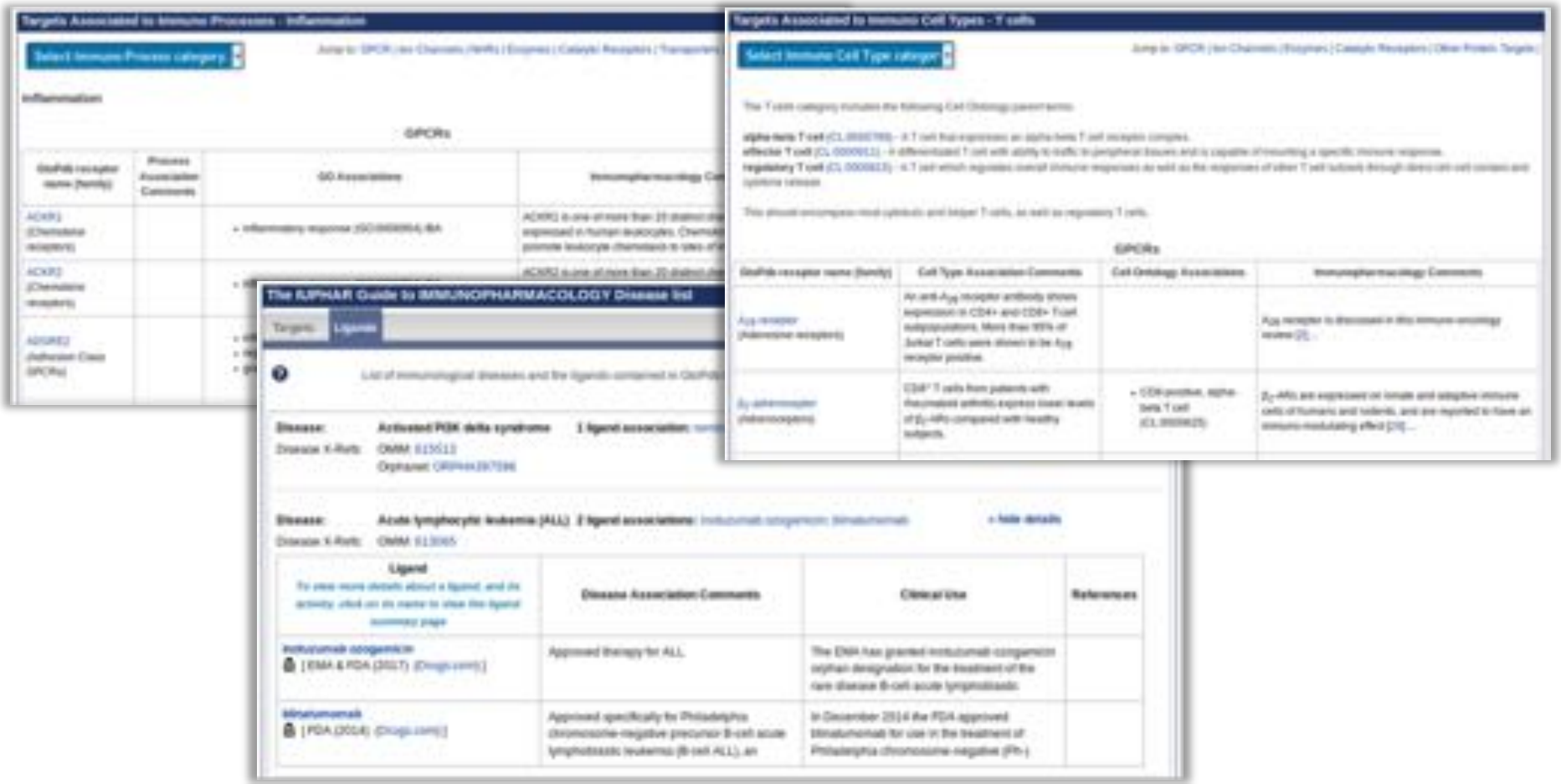
# IUPHAR Guide to IMMUNOPHARMACOLOGY

- 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](http://www.guidetoimmunopharmacology.org)

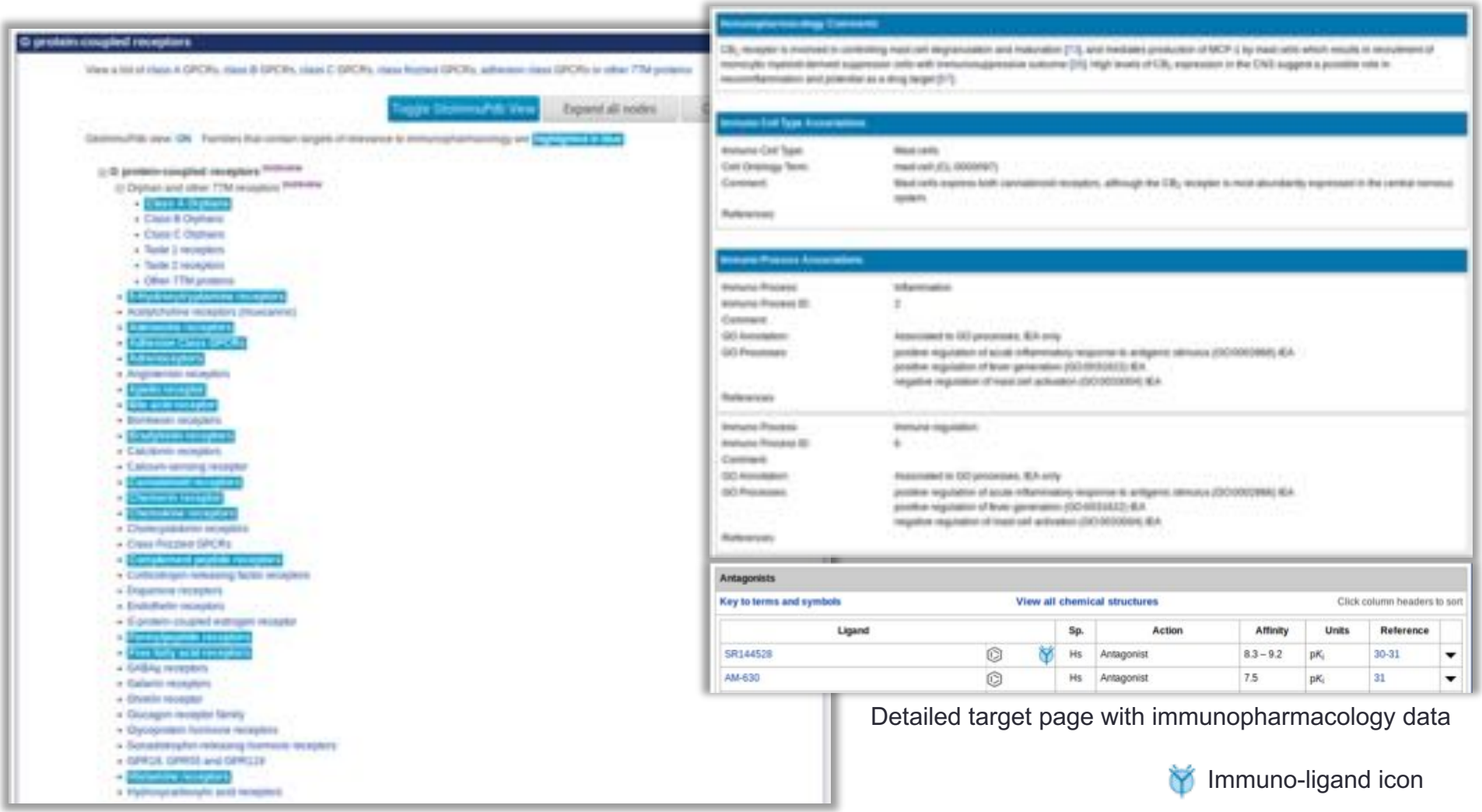
# Browsing new GtoImmuPdb data types

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



# Browsing immunological targets

- GtoPdb families with immuno-relevant targets are highlighted

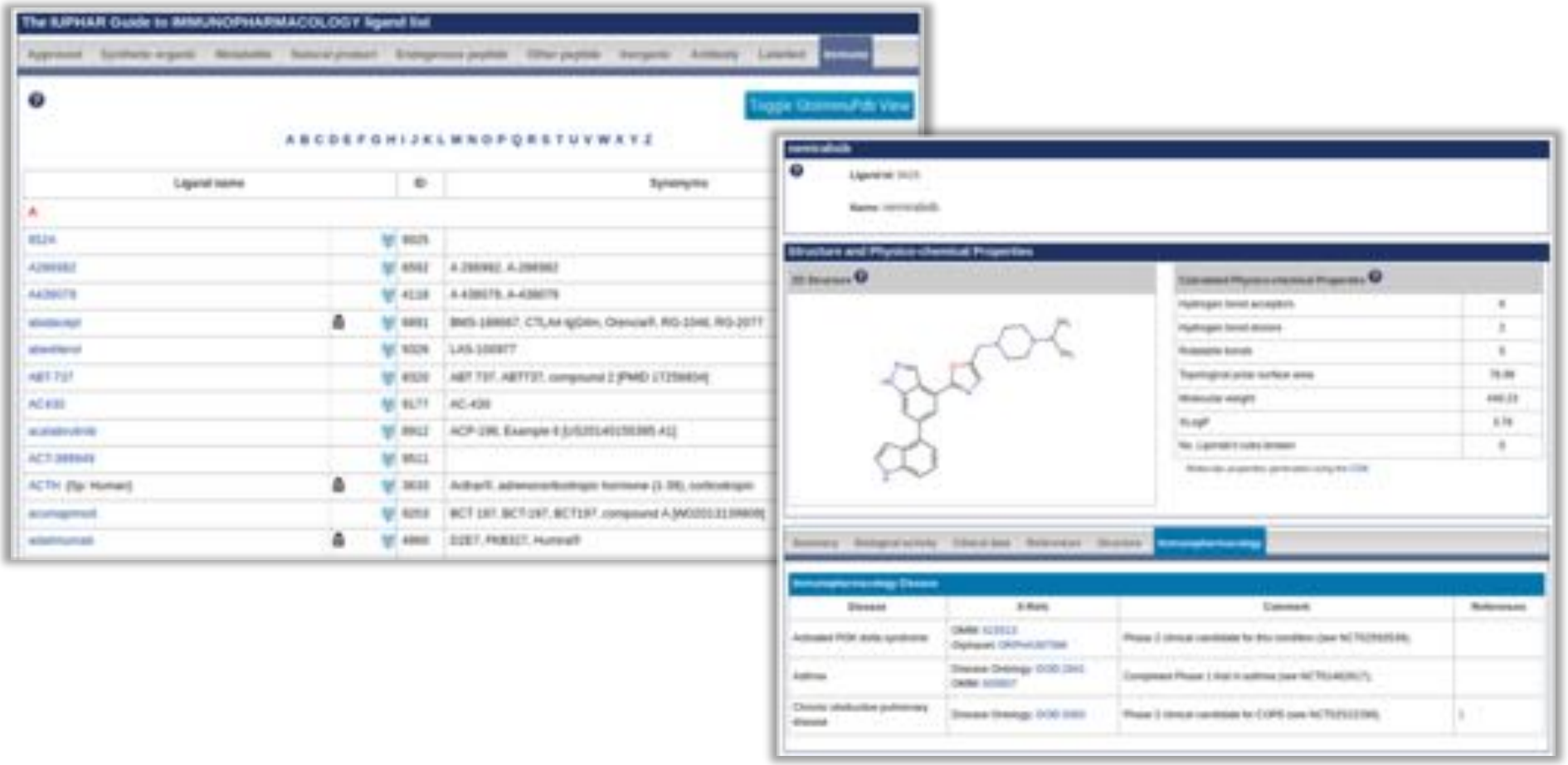



Detailed target page with immunopharmacology data

Immuno-ligand icon

# Browsing immunological ligands

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



# THE IUPHAR/MMV GUIDE TO MALARIA PHARMACOLOGY

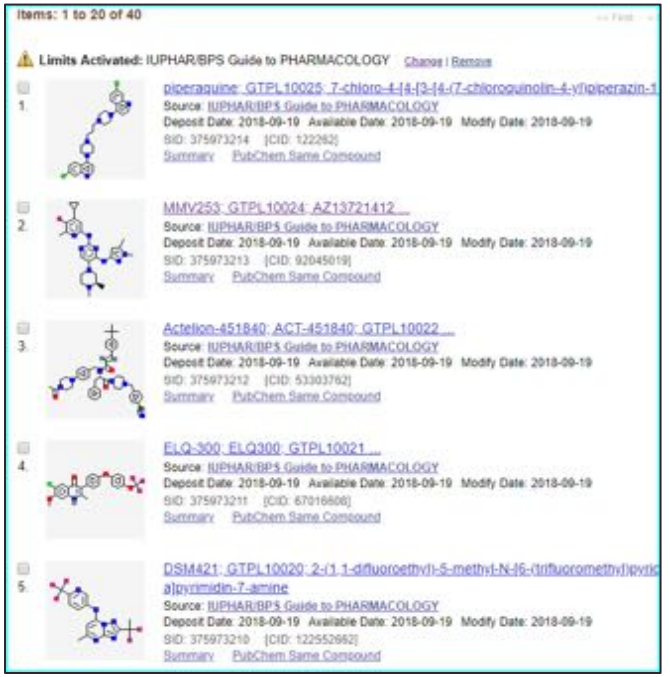
# IUPHAR/MMV Guide to MALARIA PHARMACOLOGY

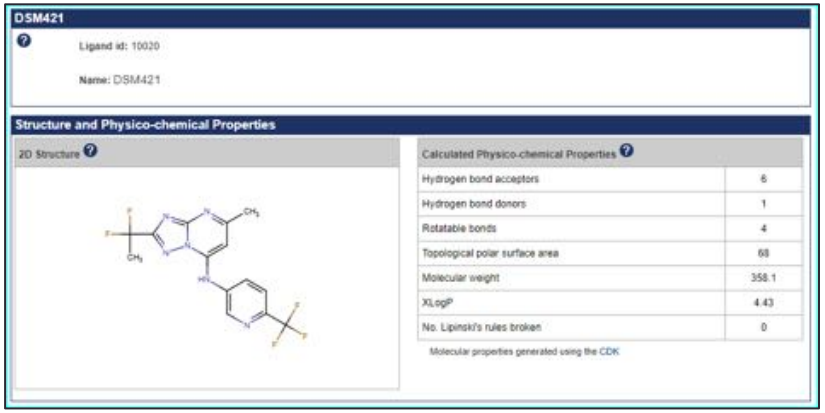
- Funded by Medicines for Malaria Venture (MMV) to curate antimalarial compounds and their *Plasmodium* molecular targets
- Provide a new portal to the existing GtoPdb that is optimized for the malaria research community
- Includes lead structures, target sequences and efficacy data integrated across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


www.guidetomalariapharmacology.org

# GtoMPdb Data

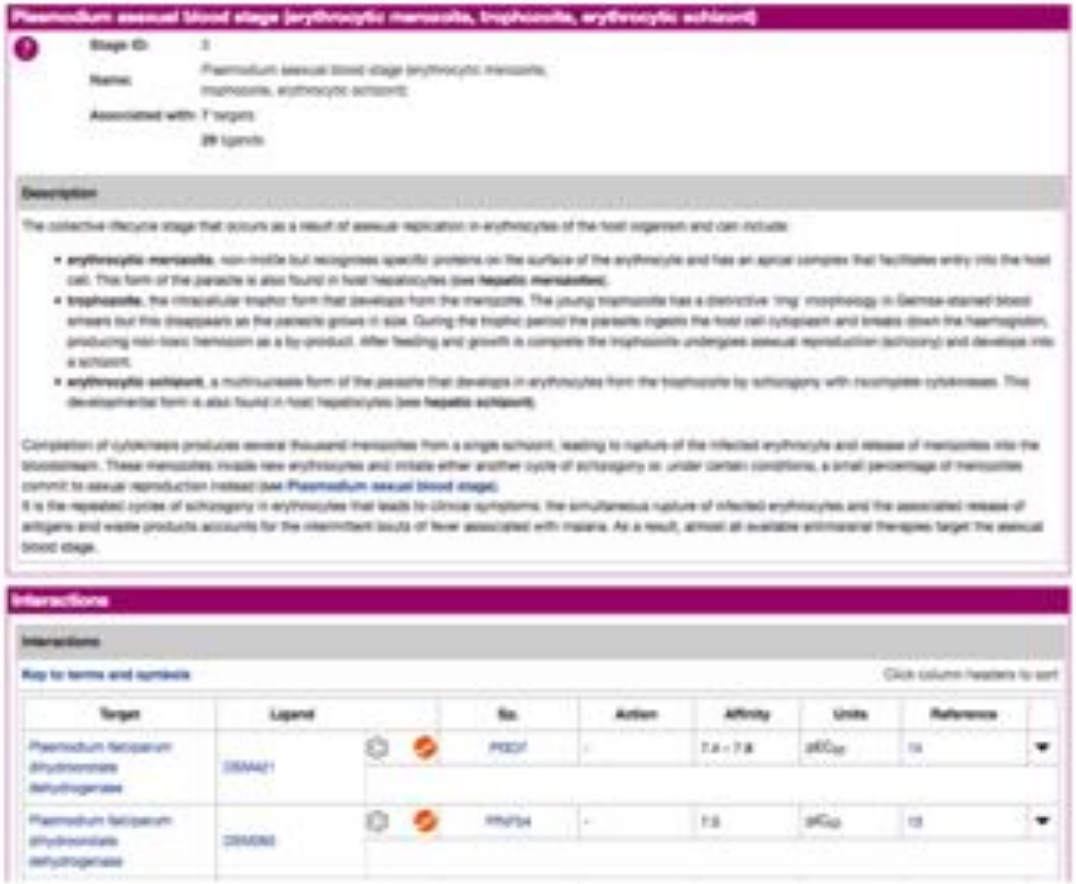
- New target classification – Antimalarial Targets
  - Initial set included 9 *Plasmodium falciparum* targets
- New ligand classification – Antimalarial Ligands
  - An initial set of ~40 were available in the 2018.4 release
- Categories are likely to be further sub-divided
- Includes a tag for submitted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



# 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)



# 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

## www.pharmacologyeducation.org
## @PharmacologyEd


**Pharmacology**
**Clinical pharmacology**
**Drugs**
**Therapeutics**

Please contribute content to this growing resource by visiting the website or email **admin@pharmacologyeducation.org**

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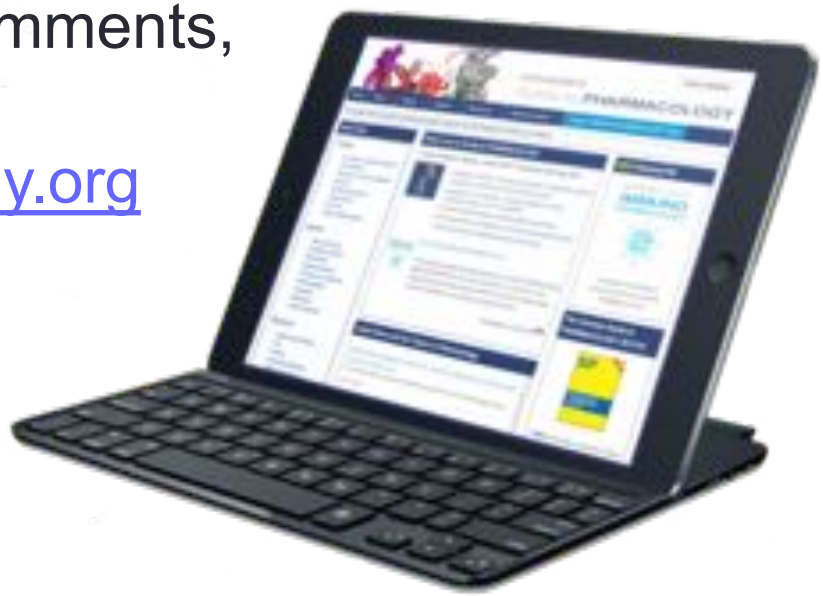
- Download slides and posters SlideShare
- Email us with any questions, comments, suggestions
  enquiries@guidetopharmacology.org



# Acknowledgements


- The late Prof Tony Harmar, founder and original PI
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- NC-IUPHAR subcommittees and *Concise Guide to PHARMACOLOGY* editors and contributors
- 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:

IUPHAR International Union of Basic and Clinical Pharmacology

BRITISH PHARMACOLOGICAL SOCIETY

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# APPENDIX

TEMPLATE SLIDES

# Live demos at this meeting

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International Union of Basic and Clinical Pharmacology

- Booth # X

BRITISH PHARMACOLOGICAL SOCIETY

- Booth # X