IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

November 2024

www.guidetopharmacology.org

enquiries@guidetopharmacology.org

Introduction **4**
Key Updates / Notifications 4
The Guide to Pharmacology Database (GtoPdb) **5**
GtoPdb Website Analytics 5
GtoPdb Website Access Statistics 5
Download Statistics 8
GtoPdb Content 8
GtoPdb Entity Growth 9
GtoPdb Updates 10
Targets 10
Ligands 13
Tracking requests from BJP/BJCP authors for new ligand and target entries 16
Natural products project with SIF 16
Analysis of journals contributing to curated data 17
AntibioticDB and Global Antibiotic Research and Development Partnership 18
GtoPdb Web-Application Developments 19
Web-Application Updates 19
Natural Products 19
Nucleic Acids 19
Connectivity 21
Links to other resources 21
Pubchem Connectivity 22
PubChem Statistics for GtoPdb 23
NCBI LinkOuts 23
Europe PMC 24
Bibliometrics and Scholarly Portals 25
Nucleic Acids Research Database Issue 25
Concise Guide to Pharmacology 25
Bibliometrics 25
SARS-CoV-2 Review 26
Other 26
EBI UniProtKB/Swiss-Prot cross-references 27
HGNC 28
GPCRdb 28
General overview of database team activities **29**
GtoPdb Team Interactions 29
Global Core Biodata Resource 29
ELIXIR 29
Publications 30
Outreach and Social Media 30
X (formerly Twitter) 30

LinkedIn 30
Guide to Pharmacology Blog 30
Hot Topics 31
Slides 31
Engaging with Us 31

Introduction

This database report provides an overview of recent progress and the current status of the IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb) since our last NC-IUPHAR meeting held in April 2024. Previous reports are online for Apr 2024, Nov 2023, Apr 2023, Nov 2022, Apr 2022, Nov 2021 and April 2021. We have reduced redundancy between the reports by purging sections without significant changes. Thus, if you remember any aspect that is not here, it may well be in a previous report (and by all means enquire).

Zenodo repository of reports:

- April 2024 doi: 10.5281/zenodo.11046804
- November 2023 doi: 10.5281/zenodo.1007801
- April 2023 doi: 10.5281/zenodo.7915909
- November 2022 doi: 10.5281/zenodo.7458274
- April 2022 doi: 10.5281/zenodo.7786340
- November 2021 doi: 10.5281/zenodo.7786355

Key Updates / Notifications

- 2 Database release (2024.2, 2024.3)
    - 22 new targets added, 11 with quantitative interactions.
    - 15 human targets with new quantitative interactions
    - 136 new quantitative interaction added across all targets
    - 273 new ligands added (21 approved drugs), 259 with quantitative interactions (3 approved drugs)
    - 245 ligands with new quantitative interactions (total 9356)
    - 310 new ligand-target interactions

- ~44,000 Engaged Sessions per month
- ~32,500 Users per month

The Guide to Pharmacology Database (GtoPdb)

GtoPdb Website Analytics

GtoPdb Website Access Statistics

Monthly statistics	**Oct 2023 - Sep 2024** (*last report figures*)
Engaged Sessions	43,936 (48,364)
Users	32,549 (36,113)
Page views	266,390 (291,706)
Pages / Session	5.12 (5.09)
Avg. Session Duration	00:04:09 (00:04:06)
Views per User	8.19 (8.08)

The above table summarises the access statistics for the Guide to Pharmacology over the last year, comparing against our previous reporting period (Apr 2023 - Mar 2024). Data are generated using Google Analytics GA4.

The website has had just short of 3.2 million page views during the last 12 months. This is a slight decrease on the previous reporting period of April 2023-March 2024. While the pages viewed per session, session duration and page views per user have all marginally increased, overall engaged sessions, users and page views have slightly decreased.

This second table shows the access stats by country (ordered by most engaged sessions). Very similar to our last reporting period, around 54% of all engaged sessions come from the USA, China, UK and India. Engaged sessions are sessions lasting longer than 10 seconds, or containing 2 or more screen/page views.

	Country	Total users	Sessions	↓ Engaged sessions	Engaged sessions per active user	Views	Views per session
	Totals	**390,479**	**624,745**	**527,232**	**1.35**	**3,196,682**	**5.12**
1	United States	117,005	167,454	139,771	1.2	621,548	3.71
2	United Kingdom	32,999	67,965	58,310	1.77	511,642	7.53
3	India	38,487	53,859	48,975	1.27	216,127	4.01
4	China	27,813	53,432	41,833	1.51	308,286	5.77
5	Germany	10,286	18,896	16,089	1.57	109,388	5.79
6	Japan	10,401	18,951	15,974	1.54	98,952	5.22
7	Australia	9,238	17,744	14,686	1.59	97,393	5.49
8	Canada	9,224	15,912	13,900	1.51	97,180	6.11
9	South Korea	8,904	14,313	12,337	1.39	70,417	4.92
10	France	7,121	11,138	9,595	1.35	62,097	5.58
11	Italy	5,933	9,450	8,283	1.4	51,336	5.43
12	Brazil	4,791	9,339	8,220	1.72	53,803	5.76
13	Spain	5,284	9,444	8,048	1.53	67,354	7.13
14	Mexico	4,460	8,482	7,517	1.69	63,396	7.47
15	Netherlands	4,491	7,518	6,531	1.46	43,150	5.74
16	Russia	4,001	7,110	6,235	1.56	38,699	5.44
17	Hong Kong	3,757	8,060	6,181	1.65	44,278	5.49
18	Indonesia	5,141	6,447	5,916	1.15	20,072	3.11
19	Philippines	4,101	5,468	4,958	1.21	19,029	3.48
20	Denmark	2,884	5,855	4,899	1.7	35,523	6.07

The third table, shown below, shows access stats from countries with a Human Development Index (HDI) of less than 0.8. The Human Development Index (HDI) is a summary measure of average achievement in key dimensions of human development: a long and healthy life, being knowledgeable and having a decent standard of living. The HDI is the geometric mean of normalised indices for each of the three dimensions. Countries with a HDI of 0.8 or above are considered ones with ‘very high human development’.

Around 114,000 users for HDI<0.8 countries have accessed GtoPdb, which covers over 155,000 engaged sessions. This is about 29% of all sessions. If India and China are excluded it is around 64,000 sessions (~12% of all sessions). Previously we had reported around 125,000 users and 170,000 engaged sessions from HDI < 0.8 countries.

	Total users	Sessions	Engaged sessions	Engaged sessions per user	Views
India	38,487	53,859	48,975	1.27	216,127
China	27,813	53,432	41,833	1.51	308,286
Brazil	4,791	9,339	8,220	1.72	53,803
Mexico	4,460	8,482	7,517	1.69	63,396
Indonesia	5,141	6,447	5,916	1.15	20,072
Philippines	4,101	5,468	4,958	1.21	19,029
Egypt	3,655	4,754	4,449	1.22	17,742
Pakistan	3,107	4,160	3,751	1.21	11,860
Nigeria	2,467	3,048	2,879	1.17	8,708
Colombia	1,346	2,543	2,205	1.64	19,646
Iran	1,697	2,397	2,191	1.29	9,667
Vietnam	1,685	2,200	2,014	1.20	7,283
Iraq	1,725	2,037	1,914	1.11	6,329
Peru	1,006	2,050	1,792	1.78	14,319
Bangladesh	1,233	1,606	1,483	1.20	4,913
Ukraine	826	1,530	1,366	1.66	13,017
South Africa	1,133	1,490	1,359	1.20	5,481
Jordan	699	1,111	1,025	1.47	4,762
Algeria	561	797	742	1.33	6,272
Bulgaria	505	713	664	1.31	4,741
Ethiopia	548	678	615	1.12	1,934
Kenya	539	640	594	1.10	1,651
Sri Lanka	399	610	553	1.39	2,815
Ghana	475	557	523	1.10	1,486
Morocco	319	552	509	1.60	2,500
Total for all HDI <0.8	**114,721**	**178,164**	**155,039**	**130**	**853,700**

Download Statistics

Data for October 2023 to September 2024 shows total file downloads of 6,890 during this period, which is a significant increase on our previous reporting period (4,247 (Apr 23-Mar 24)).

Year	Jan-Sep 2024	Oct-Dec 2023	Totals
Event name	Event count	Event count	↓ Event count
Totals	**5,452** 79.1% of total	**1,438** 20.9% of total	**6,890** 100.0% of total
1 file_download	5,452	1,438	6,890

GtoPdb Content

These database statistics were compiled on 3rd October 2024 from the 2024.3 release. All database statistics can be found at https://www.guidetopharmacology.org/databaseContent.jsp.

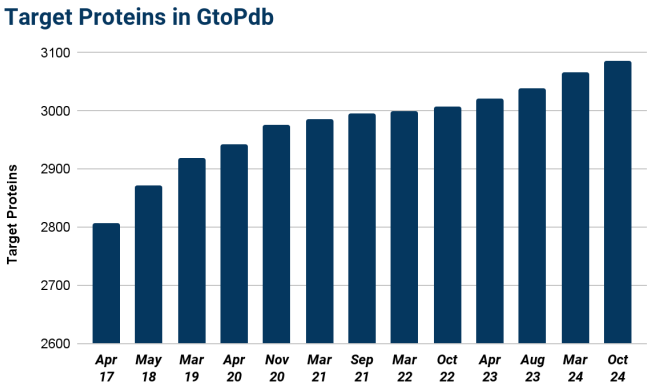
Targets	**Number of (Human) UniProt IDs**
7TM receptors	399
Nuclear hormone receptors	48
Catalytic receptors	253
Ligand-gated ion channels	81
Voltage-gated ion channels	144
Other ion channels	53
Enzymes	1306
Transporters	555
Other protein targets	247
Human targets with ligand interactions	1999
Human targets with quantitative ligand interactions	1747
Human targets with approved drug interactions	751
Human Primary Targets with approved drug interactions	353
Total number of targets	**3086**

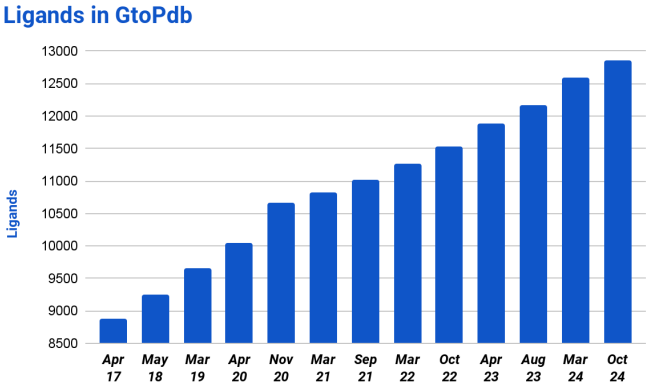
Ligands	**Number of Ligands**
Synthetic organics	9094
Metabolites	512

Endogenous peptides	819
Other peptides including synthetic peptides	1524
Natural products	458
Antibodies	399
Inorganics	39
Approved drugs	2019
Withdrawn drugs	112
Drugs with INNs	3538
Labelled ligands	649
Unique PubChem CIDs	10469
Ligands with target interactions	10581
Ligands with quantitative interactions (approved drugs)	9356 (1138)
Ligands with clinical use summaries (approved drugs)	3826 (2009)
Total number of ligands (PubChem SIDs)	**12862**
Number of binding constants curated from the literature	**21,268**

GtoPdb Entity Growth

Growth rates are documented in earlier reports and our 2016, 2018, 2020, 2022 and 2024 NAR papers. Updates come via subcommittee contributions to the Concise Guide, and the continued tagging of pre-existing targets and ligands with comments and references to GtoImmuPdb and GtoMPdb. Note that, while we highlight newly-liganded targets in release notes, the growth of new targets is slow but ligand expansion continues.





	Mar 19	Apr 20	Nov 20	Mar 21	Sep 21	Mar 22	Oct 22	Apr 23	Aug 23	Mar 24	Oct 24
Target protein IDs	**2920**	**2943**	**2976**	**2985**	**2995**	**3000**	**3007**	**3021**	**3039**	**3067**	**3068**
Ligands total	**9662**	**10053**	**10659**	**10821**	**11025**	**11271**	**11532**	**11893**	**12164**	**12590**	**12862**
Approved drugs	1421	1471	1614	1643	1689	1734	1787	1865	1919	1981	2019
PubChem CIDs	7407	7483	7994	8102	8262	8462	8633	9307	9852	10168	10469

GtoPdb Updates

Targets

New protein targets:

We curated three new protein targets for the October release of version 2024.3, and three others(*) expected to be available in our next release. These were primarily added in response to evidence of pharmacologic modulation and therapeutic potential.

TID	Family	Gene	Name	Comment
3293	5.-.-.- Isomerases	*PDIA3*	protein disulfide isomerase family A member 3	Required for protein folding in ER; aberrant expression has been detected in cancers and downregulation/inhibition has antitumour effects; punicalagin (natural product) curated as an inhibitor
3294	Zinc finger TFs	*WIZ*	WIZ zinc finger	Sickle cell disease target- its inhibition increases fetal hemoglobin (HbF) expression; molecular glue degrader dWIZ-1 curated
3295	CD molecules	*CD226*	CD226 molecule	Stimulatory immune checkpoint in the CD155 (PVR)-TIGIT/CD226 axis; molecular target for cancer immunotherapy development;

				salvianolic acid B (natural product) curated as an inhibitor
3296*	Cholesterol biosynthesis pathway	*SC5D*	sterol-C5-desaturase	SC5D deficiency causes a rare autosomal recessive cholesterol biosynthesis disorder known as lathosterolosis
3297*	Cholesterol biosynthesis pathway	*NSDHL*	NAD(P) dependent steroid dehydrogenase-like	Therapeutic potential for cholesterol-related diseases and carcinomas. Variants in *NSDHL* are associated with the lipid metabolism disorder CHILD syndrome. An inhibitor compound was curated
3298*	Hydrolases & Lipases	*CES2*	carboxylesterase 2	detoxification of xenobiotics and activation of ester and amide prodrugs; natural product (+)-Yanhusanine B is an inhibitor

19 new protein targets were added to the Guide at the 2024.2 release (June 2024). They represent molecular targets for cancer, inflammation, immunity, viral infection and Parkinson's disease. Experimental tool compounds or clinical candidates that modulate protein functions have been curated where available.

TID	Family	Gene	Name	Comment
3274	Methyllysine reader proteins	SPIN1	spindlin 1	Overexpressed in malignancies, making it a target for anti-cancer drug development- two inhibitors tool compounds curated (MS8535, MS31)
3275	Coronavirus (CoV) proteins	n/a	CoV Non-structural protein 10	subunit of the betacoronavirus 2'-O-methyltransferase (mRNA capping enzyme)
3276	Coronavirus (CoV) proteins	n/a	CoV Non-structural protein 16	subunit of the betacoronavirus 2'-O-methyltransferase (mRNA capping enzyme)

3277	Coronavirus (CoV) proteins	n/a	CoV 2'-O-methyltransferase (complex)	Target for coronavirus antivirals-sinefungin curated as an inhibitor
3278	Gasdermins (GSDM)	GSDMD	gasdermin D	Inflammasome component & pyroptosis effector. Target for the development of drugs with anti-inflammatory effects. disulfiram and LDC7559 curated as inhibitor tools.
3279	High Mobility Group (HMG) proteins	HMGB1	high mobility group box 1	Endogenous ligand for Toll-like receptors 2 and 4, and RAGE-inhibitor tools 3-AESA and methotrexate curated
3280	NF-kappa B TF proteins	RELA	RELA proto-oncogene, NF-kB subunit	Key to regulating the interferon response to SARS-CoV-2 infection-2 inhibitor toll compounds curated
3281	NF-kappa B TF proteins	NFKB1	nuclear factor kappa B subunit 1	dimerises with RELA to form most abundant NF-kB TF, promotes expression of genes that drive the immune response and acute phase responses to infection and tissue trauma
3282	NF-kappa B TF proteins	NFKB2	nuclear factor kappa B subunit 2	Transcriptional activator or repressor of genes involved in inflammation and the immune response
3283	NF-kappa B TF proteins	REL	REL proto-oncogene, NF-kB subunit	Involved in apoptosis, inflammation and the immune response- can be oncogenic
3284	NF-kappa B TF proteins	RELB	RELB proto-oncogene, NF-kB subunit	RelB-NFκB/p50 and RelB-NFκB/p52 heterodimers are transcriptional activators

3285	Synuclein proteins	SNCA	synuclein alpha	Two anti-SNCA mAbs that block toxic synuclein alpha oligomer/fibril formation have been curated
3286	Synuclein proteins	SNCB	synuclein beta	non-amyloid component in Alzheimer's disease plaques
3287	Synuclein proteins	SNCG	synuclein gamma	Third member of this small protein family
3288	N6-methyladenosine readers	YTHDC1	YTH N6-methyladenosine RNA binding protein C1	target for the development of cancer therapeutics- selective inhibitor curated
3289	M28: Aminopeptidase Y	QPCTL	glutaminyl-peptide cyclotransferase like	Small molecule gQC inhibitors offer an approach to promote tumour-specific immunity- 4 inhibitors curated
3290	Hydrolases & Lipases	LYPLA1	lysophospholipase 1	Synthetic and natural product tool inhibitors curated
3291	Hydrolases & Lipases	LYPLA2	lysophospholipase 2	Synthetic and natural product tool inhibitors curated
3292	RAB subfamily	RAB32	RAB32, member RAS oncogene family	RAB32 S71R identified as a risk factor in familial Parkinson's disease, in same pathway as LRRK2 activation

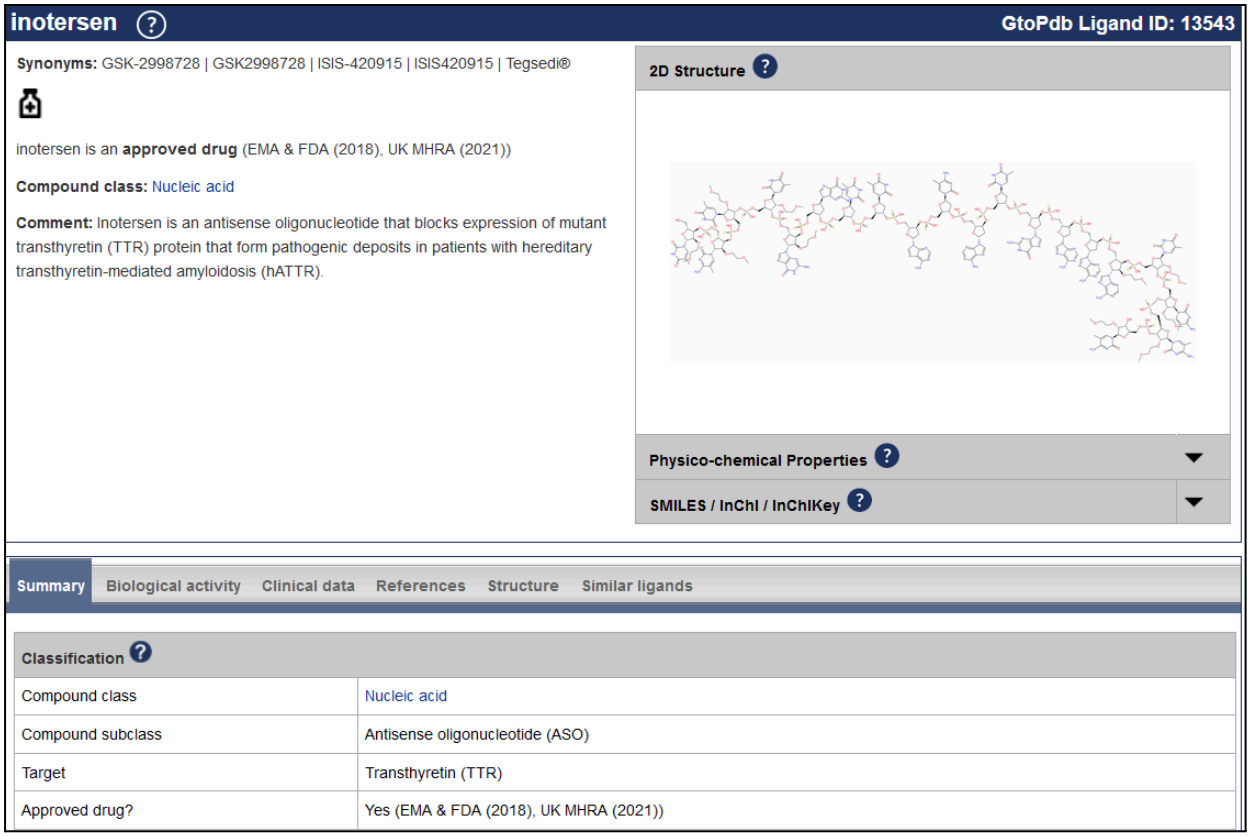
Ligands

Curation of new ligands is generally guided by the target family subcommittees as part of routine update processes. Where targets don't have a formal GtoPdb subcommittee, curators are able to independently add ligands when pharmacological relevance is demonstrated. Caveat: new ligands will only be added to GtoPdb when the curators can confirm name-to-structure associations, find citable evidence that confirms MMOA and a source of quantitative interaction data.

Additional ligand sources include the medicinal chemistry literature, INN lists from the WHO, DrugHunter (https://drughunter.com/), first disclosures from scientific meetings (such as AACR and ACS) and patents. New ligands (and less frequently, targets) are also added on request by BJP/BJCP/PR&P authors as part of the journal submission process, so that hyperlinks to the GtoPdb can be included in the published articles. The requests are vetted by the senior curator to ensure relevance before the decision is made to include in the GtoPdb (or not).

A few ligand highlights for this report:

- We continue efforts to curate potential antiviral compounds that target SARS-CoV-2 proteins such as Mpro, PLpro, RdRp, nsp10/16 2'-O-methyltransferase complex, nsp13 helicase, and Mac1 domain of nsp3. We have 110 Mpro inhibitors with quantitative interaction data.
- Only 8/45 of newly FDA-approved drugs for 2024 are not curated in the GtoPdb. The omissions have been reviewed and do not meet our inclusion criteria.
- The August 2024 release of WHO proposed INNs (PL131; with 213 INNs) offered the opportunity for curatorial sleuthing to try to match INNs either with lead compounds in declared company development pipelines, or to structures claimed in patents. We currently have 29 of this set of INNs in the GtoPdb, 18 of which are kinase inhibitors. We will continue to analyse PL131 to identify either new drug targets, or new pharmacological modalities for existing targets, to expand our coverage of emerging therapeutic targets.
- There are now 120 molecules in the GtoPdb 'PROTACs, molecular glues and other degraders' ligand family https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=1030, with >10 of these degraders in early stage clinical trials. The majority of the PROTACs in CT are intended for use in cancer indications, and targets include the estrogen (ER) and androgen (AR) receptors, BRD9, BCL-XL, BTK and mutant BRAF. One clinical stage PROTAC with anti-inflammatory potential is designed to degrade IRAK4. Four of the chemical structures for clinical candidate PROTACs have been matched to INNs; zelebrudomide (NX2127) is a BTK PROTAC, zomiradomide (KT-413) degrades IRAK4, Ikaros and Aiolos, bavdegalutamide (ARV110) degrades the AR and vepdegrestrant (ARV471) targets the ER.
- In collaboration with Peter Ferdinandy and his team in Hungary, we have begun curation of nucleic acid class drugs/ligands. The new ligand class tab https://www.guidetopharmacology.org/GRAC/LigandListForward?type=Nucleic-acid was published as part of our Database Release 2024.3 at the beginning of October. This has required the inclusion of a new ligand type (Nucleic acid) and subtypes (e.g. aptamer, antisense oligonucleotide, siRNA, miRNA) in our schema. This set already has 17 ligands, a few of which had already been curated but were classified as synthetic organics. We also include approval information for any in clinical use, structural information where it is available (either as nucleic acid structures/HELM notation or full chemical structures with SMILES) and indicate the target for each ligand. The page for inotersen (below) shows the new summary page structure. Clinical data and biological data are curated in line with our other ligand classes. See the Web-Application Update section to see how these are now displayed on the website



More information about new ligands and targets is included in our Database Updates blog posts https://blog.guidetopharmacology.org/category/database-updates/, which we generate for each Database release.

Summary of ligands added to GtoPdb in 2024.3 release (compared to 2024.1)

	New Ligands	Updated Ligands	Total Ligands (2024.3)	Total Ligands (2024.1)
Approved Drugs	21	17	2019	1981
Antibacterials	51	6	594	537
Ligands with Quantitative Interaction Data	152	0	9376	9224
All Ligands	273	-	12862	12590

We also track the comment fields in GtoPdb to see which comments have been applied to new ligands, but also any updates to comments for existing ligands. Nearly all new ligands will have a general comment added.

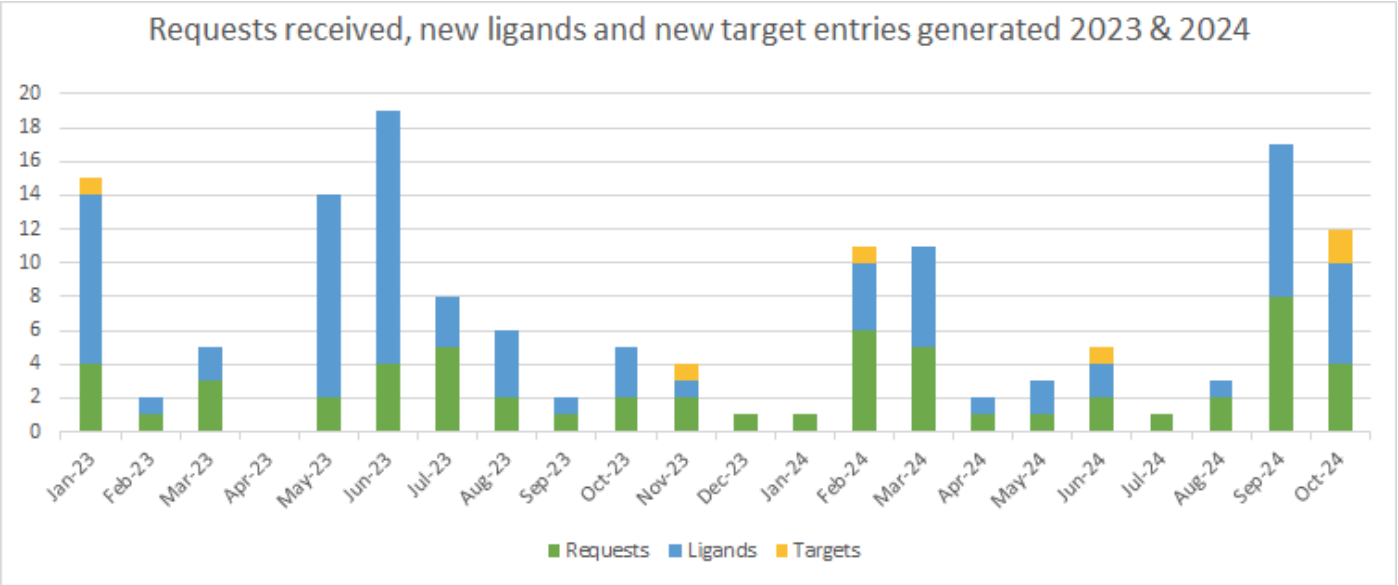
Comment Type	New Ligands	Updated Ligands
General	273	108
Clinical Use	110	98
Bioactivity	133	20
MOA	18	5

Tracking requests from BJP/BJCP authors for new ligand and target entries

Over the 2 years (to end Oct 24) we have received 58 requests from authors for additions to the GtoPdb; 27 from 2023, and 31 so far in 2024.

This process has resulted in the addition of 83 new ligands and 6 new targets, distributed as shown in the chart below.

The green bars show the count of individual requests made. Every inquiry that is received is carefully evaluated by the curators, before any decision is made to add new entries. Requests may result in multiple targets and/or ligands being added to the GtoP. However, it is also the case that for some requests, the targets and ligands don't meet our criteria for inclusion (exemplified by the green-only bars in the graph).



Natural products project with SIF

This project began at the end of 2023, with SIF providing funding via IUPHAR that supports 0.4 FTE for a curator for 3 years. Our main liaison contact is Francesco Visoli, who earlier this year published a short editorial position piece to the BJP which outlines best-practice in NP research.

Visioli F. Natural products: Call for hard evidence. Br J Pharmacol. 2024 181(16):3010-3011. doi:10.1111/bph.16437. PMID: 38783822

The first curation task was to review all of the ligands that were selected as 'natural product' in the GtoPdb dataset, and to rationalise which were truly NPs. A few were either semi-synthetic analogues or derivatives, so these were removed from the NP ligands set. The heading descriptor on the NPs page of the website https://www.guidetopharmacology.org/GRAC/LigandListForward?type=Natural-product will be amended so that 'synthetic derivatives' is no longer included.

Many of the existing NP pages have been updated either with general comments, or information and references to targets, and interaction data where available.

Going forwards new ligands that meet the GtoPdb inclusion criteria will be added, with regular updates provided to SIF via Francesco.

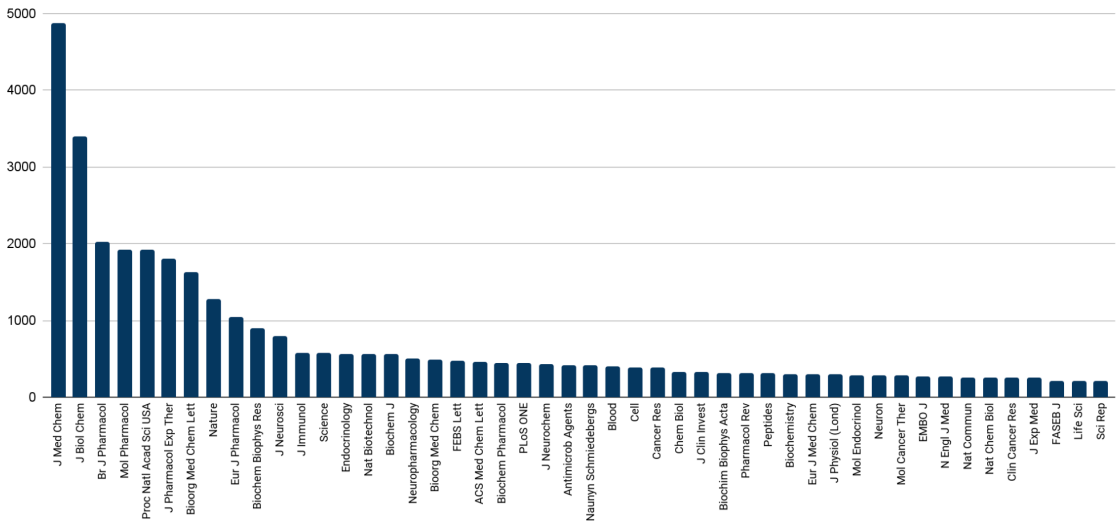
Since our last report >40 new NPs have been added. These have been screened from primary med chem literature, natural product-specific journals and a few from BJP/BJCP author requests.

See the Web-Application Update section for information about a new natural products landing page

Analysis of journals contributing to curated data

The following table and graph show the count of unique articles from journals curated in the GtoPdb. The table is restricted to those journals with over 500 unique curated articles. The graph expands this to all journals with over 200 unique curated articles.

Title	Count
J Med Chem	4865
J Biol Chem	3393
Br J Pharmacol	2019
Mol Pharmacol	1929
Proc Natl Acad Sci USA	1925
J Pharmacol Exp Ther	1805
Bioorg Med Chem Lett	1629
Nature	1283
Eur J Pharmacol	1045
Biochem Biophys Res Commun	904
J Neurosci	797
J Immunol	574
Science	573
Endocrinology	564
Nat Biotechnol	558
Biochem J	558
Neuropharmacology	500



AntibioticDB and Global Antibiotic Research and Development Partnership

We have collaborated with AntibioticDB (ADB; www.antibioticdb.com) since 2019, with the aim of extending the coverage of antibacterial compounds in GtoPdb and providing comprehensive chemistry and pharmacology for select antibacterials curated within ADB. This collaboration is supported by the Global Antibiotic Research and Development Partnership (GARDP; https://gardp.org/), with funding in place until March 2025. This includes continued financial support for a curator (with an increase from 0.2FTE to 0.3FTE) and additional funding for a software developer (0.5FTE), who is working on developing a 'Guide to ANTIMICROBIAL PHARMACOLOGY' portal to GtoPdb and the new ADB database and website (please see the section on GtoPdb Web-Application Developments for further details of this work).

Currently we have **594 ligands** tagged in GtoPdb as 'antibacterial' and **566** of these have links to compounds at ADB. The antibacterials in the GtoPdb include approved drugs, WHO essential Medicines-listed medicines, drugs in clinical development, and a number of investigational and experimental compounds. The focus of recent work has been the curation of antibacterial agents included in the WHO's report "2023 Antibacterial agents in clinical and preclinical development: an overview and analysis" (https://www.who.int/publications/i/item/9789240094000).

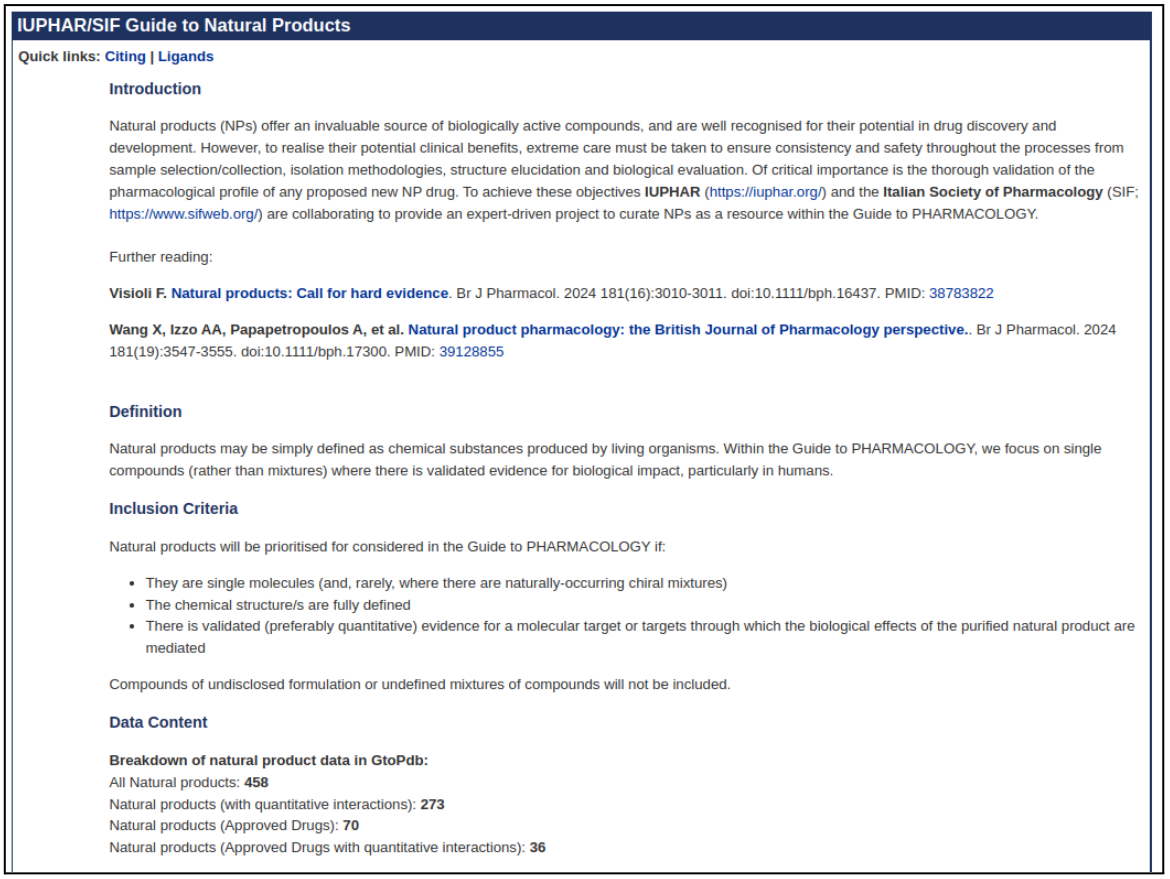
For further information about our work with ADB please refer to previous Database Reports. This collaboration has also been described in more detail in our 2022 NAR update:

> Harding SD, Armstrong JF, Faccenda E, Southan C, Alexander SPH, Davenport AP, Pawson AJ, Spedding M, Davies JA; NC-IUPHAR. The IUPHAR/BPS Guide to PHARMACOLOGY in 2022: curating pharmacology for COVID-19, malaria and antibacterials. *Nucleic Acids Research*, Volume 50, Issue D1, 7 January 2022, Pages D1282–D1294, https://doi.org/10.1093/nar/gkab1010. PMID: 34718737.

Web-Application Updates

Natural Products

NEW: We have developed a new natural products landing page (https://www.guidetopharmacology.org/GRAC/NaturalProductsForward) on the Guide to Pharmacology website. This provides information about the collaborations with SIF as well as defining natural products and explaining our curation inclusion criteria. The page also shows content statistics for natural products and provides tables of the natural products curated in GtoPdb.



IUPHAR/SIF Guide to Natural Products

Quick links: Citing | Ligands

Introduction

Natural products (NPs) offer an invaluable source of biologically active compounds, and are well recognised for their potential in drug discovery and development. However, to realise their potential clinical benefits, extreme care must be taken to ensure consistency and safety throughout the processes from sample selection/collection, isolation methodologies, structure elucidation and biological evaluation. Of critical importance is the thorough validation of the pharmacological profile of any proposed new NP drug. To achieve these objectives **IUPHAR** (https://iuphar.org/) and the **Italian Society of Pharmacology** (SIF; https://www.sifweb.org/) are collaborating to provide an expert-driven project to curate NPs as a resource within the Guide to PHARMACOLOGY.

Further reading:

Visioli F. Natural products: Call for hard evidence. Br J Pharmacol. 2024 181(16):3010-3011. doi:10.1111/bph.16437. PMID: 38783822

Wang X, Izzo AA, Papapetropoulos A, et al. Natural product pharmacology: the British Journal of Pharmacology perspective.. Br J Pharmacol. 2024 181(19):3547-3555. doi:10.1111/bph.17300. PMID: 39128855

Definition

Natural products may be simply defined as chemical substances produced by living organisms. Within the Guide to PHARMACOLOGY, we focus on single compounds (rather than mixtures) where there is validated evidence for biological impact, particularly in humans.

Inclusion Criteria

Natural products will be prioritised for considered in the Guide to PHARMACOLOGY if:

- They are single molecules (and, rarely, where there are naturally-occurring chiral mixtures)
- The chemical structure/s are fully defined
- There is validated (preferably quantitative) evidence for a molecular target or targets through which the biological effects of the purified natural product are mediated

Compounds of undisclosed formulation or undefined mixtures of compounds will not be included.

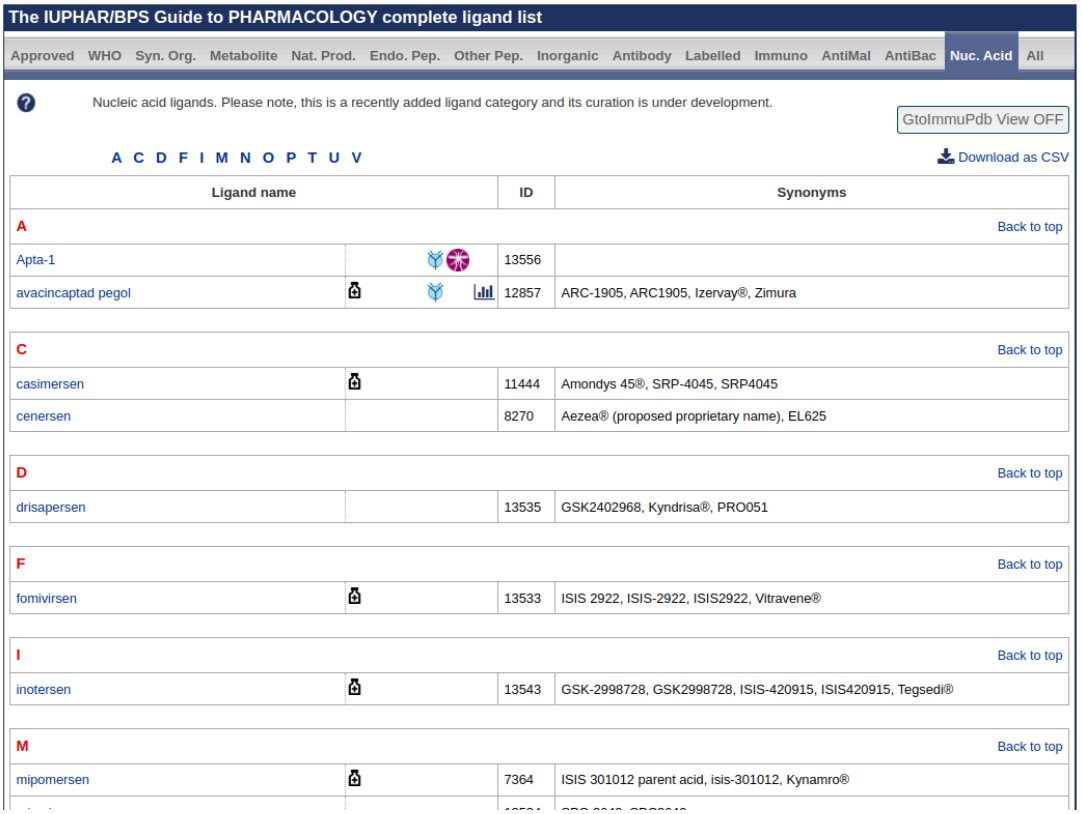
Data Content

Breakdown of natural product data in GtoPdb:
All Natural products: **458**
Natural products (with quantitative interactions): **273**
Natural products (Approved Drugs): **70**
Natural products (Approved Drugs with quantitative interactions): **36**

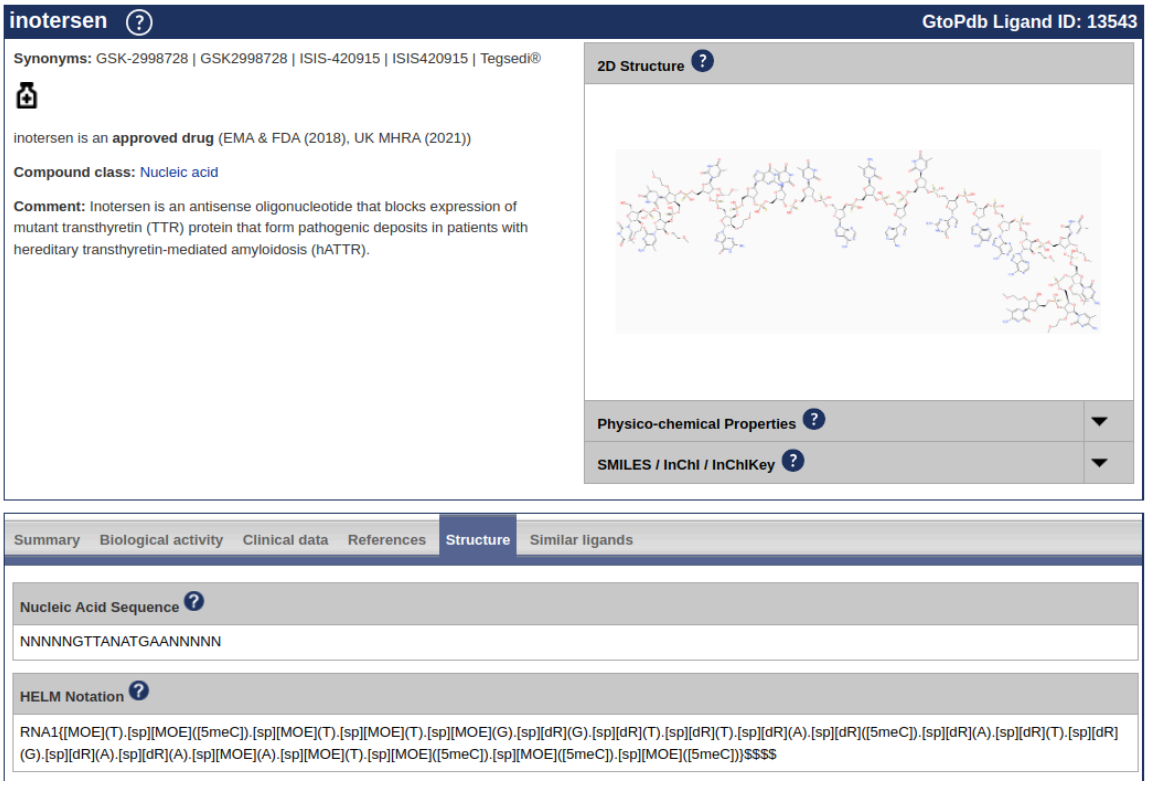
Nucleic Acids

As mentioned, we have been collaborating with Prof Peter Ferdinandy's group at the Semmelweis University, Budapest, Hungary on curating nucleic acid ligands in GtoPdb.

This has led to a couple of developments on the website so that nucleic acid ligands can be viewed and their data displayed. The new ligand category is now available on our ligand list page, https://www.guidetopharmacology.org/GRAC/LigandListForward?type=Nucleic-acid, note the new tab at the top of the page.



On a ligand summary page for a nucleic acid ligand there are now fields displaying nucleic acid subclass and target, along with the nucleic acid sequence and HELM notation (where curated) under the Structure tab



Links to other resources

GtoPdb has built many collaborative connections with other resources, many of which are reciprocal. The table below shows the number of ligands and targets with out-links to each of the named resources. The table is not exhaustive, but shows those specialist resources we link with and resources that have reciprocal links back into GtoPdb.

Given we submit our ligand data to PubChem, all ligands with structural data linked to PubChem have out-links. Our recent and ongoing work with AntibioticDB has built links between antibacterials in GtoPdb (455) and AntibioticDB (https://antibioticdb.com/). Links from antibodies in GtoPdb are made to the IMGT/mAb-DB (https://www.imgt.org/mAb-DB/) database. We also link out to Wikipedia pages that describe ligands - often there are reciprocal links from these Wikipedia pages back to GtoPdb via the main 'chemical infoboxes'.

For our targets, we use UniProtKB identifiers as our primary protein identifier. We use HGNC IDs to provide the primary human gene identifier for our targets. We also provide links to NCBI and Ensembl Gene resources. Specialist resources include GPCRdb (https://gpcrdb.org/), who we have a longstanding collaboration with, linking with GPCR targets. For transporter targets, we have links with Resolute and SLC tables at Bioparadigms.

We ensure that the cross-links are regularly refreshed through formal and informal contacts with database providers.

Site	Ligand Links	Site	Target Links
PubChem	10396	GPCRdb	372
ChEMBL	6688	ChEMBL	2256
Reactome	322	Resolute (SLC)	421
AntibioticDB	512	BioParadigms (SLC)	387
IMGT/mAb-DB	352	HGNC	3084
DrugCentral	1709	NCBI (Entrez) Gene	3063
Wikipedia	3031	Ensembl Gene	3087
GPCRdb	4246	UniProt	3149

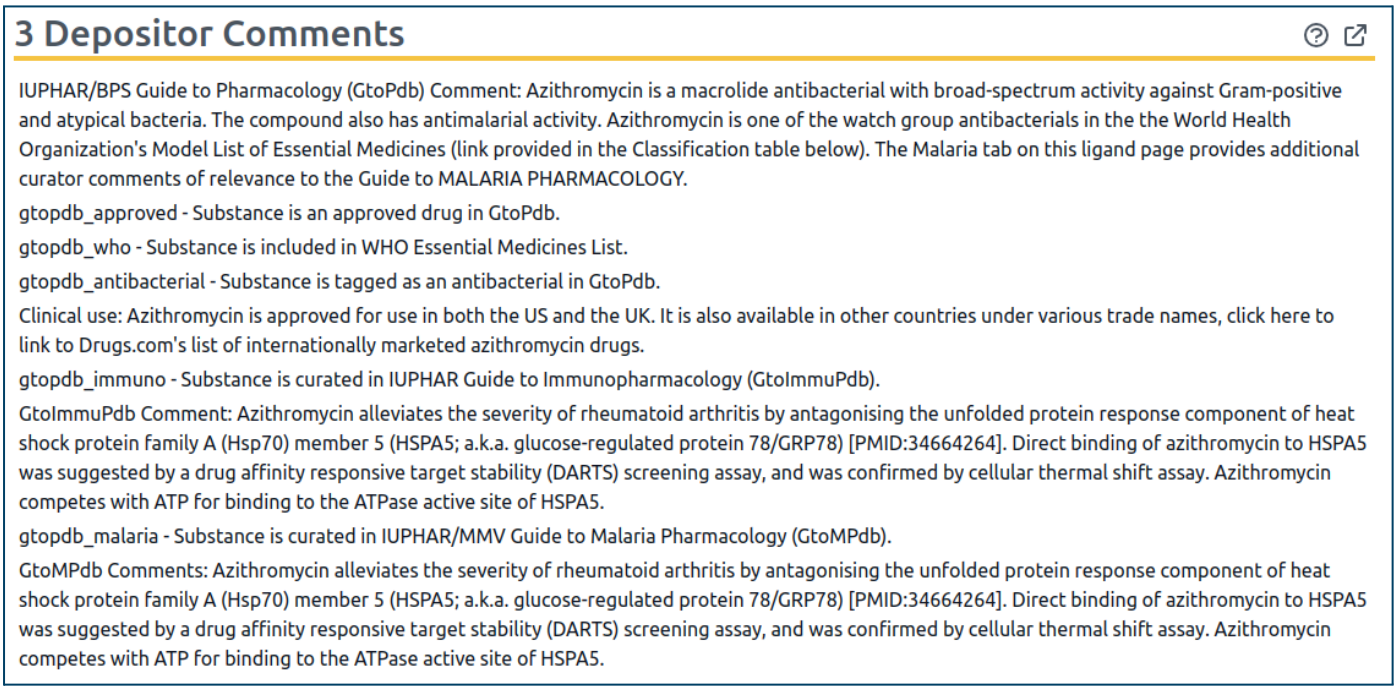
Pubchem Connectivity

All GtoPdb ligands are submitted to PubChem after each database release, this gives them a PubChem Substance ID (SID).

PubChem Substances are community-provided compounds, and many entries may exist for the same molecule. Each may contain different information about the molecule, depending on the information provided by the submitter. PubChem extracts the unique chemical structures from Substance records (standardisation) and stores them as PubChem Compounds. This means that substance records from different data sources about the same molecule are aggregated in a common Compound record in PubChem.

Following our last database release, 2024.3, all 12,874 ligands in GtoPdb have been submitted to PubChem and therefore have PubChem SIDs.

Our PubChem connectivity is enhanced by the addition of curatorial (depositor) comments that we provide when submitting compounds. These depositor comments can be viewed on a substance page at PubChem (see example for azithromycin below). We include ligand general comments, clinical use comments and flagged whether the compound is an approved drug and whether it is tagged as relevant to immunopharmacology, antimalarial pharmacology or antibacterial.



3 Depositor Comments

IUPHAR/BPS Guide to Pharmacology (GtoPdb) Comment: Azithromycin is a macrolide antibacterial with broad-spectrum activity against Gram-positive and atypical bacteria. The compound also has antimalarial activity. Azithromycin is one of the watch group antibacterials in the the World Health Organization's Model List of Essential Medicines (link provided in the Classification table below). The Malaria tab on this ligand page provides additional curator comments of relevance to the Guide to MALARIA PHARMACOLOGY.

gtopdb_approved - Substance is an approved drug in GtoPdb.

gtopdb_who - Substance is included in WHO Essential Medicines List.

gtopdb_antibacterial - Substance is tagged as an antibacterial in GtoPdb.

Clinical use: Azithromycin is approved for use in both the US and the UK. It is also available in other countries under various trade names, click here to link to Drugs.com's list of internationally marketed azithromycin drugs.

gtopdb_immuno - Substance is curated in IUPHAR Guide to Immunopharmacology (GtoImmuPdb).

GtoImmuPdb Comment: Azithromycin alleviates the severity of rheumatoid arthritis by antagonising the unfolded protein response component of heat shock protein family A (Hsp70) member 5 (HSPA5; a.k.a. glucose-regulated protein 78/GRP78) [PMID:34664264]. Direct binding of azithromycin to HSPA5 was suggested by a drug affinity responsive target stability (DARTS) screening assay, and was confirmed by cellular thermal shift assay. Azithromycin competes with ATP for binding to the ATPase active site of HSPA5.

gtopdb_malaria - Substance is curated in IUPHAR/MMV Guide to Malaria Pharmacology (GtoMPdb).

GtoMPdb Comments: Azithromycin alleviates the severity of rheumatoid arthritis by antagonising the unfolded protein response component of heat shock protein family A (Hsp70) member 5 (HSPA5; a.k.a. glucose-regulated protein 78/GRP78) [PMID:34664264]. Direct binding of azithromycin to HSPA5 was suggested by a drug affinity responsive target stability (DARTS) screening assay, and was confirmed by cellular thermal shift assay. Azithromycin competes with ATP for binding to the ATPase active site of HSPA5.

Depositor comments section of PubChem SID 178103124.

Our blog post from December 2022 illustrates how users can exploit these tags when using PubChem. This was reproduced with kind permission from Dr. Chris Southan's blog post: Exploiting the Guide to Pharmacology substance (SID) tags in PubChem

PubChem Statistics for GtoPdb

The stats for the 2024.3 release (with 2024.1 in brackets) are as follows (N.B. the links below can be slow but if they do time out try purging your browser cache).

1. Substances (SID) that we submit to PubChem (refreshing previous submissions) are up to 12874 (12601).
2. Those that have defined chemical structures are merged into 10678 (10436) Compound Identifiers, CIDs (i.e. small molecules and peptides below ~ 70 residues)
3. From our 10211 CIDs 8821 have vendor matches
4. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND gtopdb_approved [Comment] now retrieves 2019 SIDs (1981) which link to 1763 approved drug CIDs
5. Of our SIDs, 1468 (1468) are tagged in GtoImmuPdb and 382 (376) of these are approved drugs
6. Of our CIDs 1031 are tagged in GtoImmuPdb
7. Of our SIDs, 139 are tagged in GtoMPdb and 25 of these are approved drugs
8. Of our CIDs 134 are tagged in GtoMPdb
9. Of our SIDs, 592 are tagged as antibacterial and 255 of these are approved drugs
10. Of our CIDs 551 are tagged as antibacterial
11. We have 2472 (2493) structures that ChEMBL does not have, 7810 (7586) not in DrugBank.
12. 114 (116) structures where GtoPdb is unique as the source. In most cases this is because we were first to extract the paper or patent and push the ligand structures into PubChem where they get linked to the PubMed entries (see Link out section below). There may be some cases where our stereo configuration is unique (InChIKey) but related to other entries (InChKey inner layer). Inspection of " Related Compounds" and "Same Connectivity" will indicate this.
13. We continue to curate clinical monoclonal antibodies with the PubChem Substance select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] gtopdb_antibody" returning 399 SIDs. Adding "gtopdb_approved" gives 161.

The ability to combine selects and filters of our own PubChem entries, find related linked sets (e.g. pivoting from Substances to Compounds) and compare these to other sources in PubChem becomes very informative and powerful. Users are also reminded that, via the InChIKeys or SMILES strings, any of our ligand downloads (including combinations or parts of) can be cast against PubChem using their Identifier Exchange Service to allow detailed exploration of the extensive PubChem links. Users needing guidance for PubChem interrogations are welcome to contact us.

NCBI LinkOuts

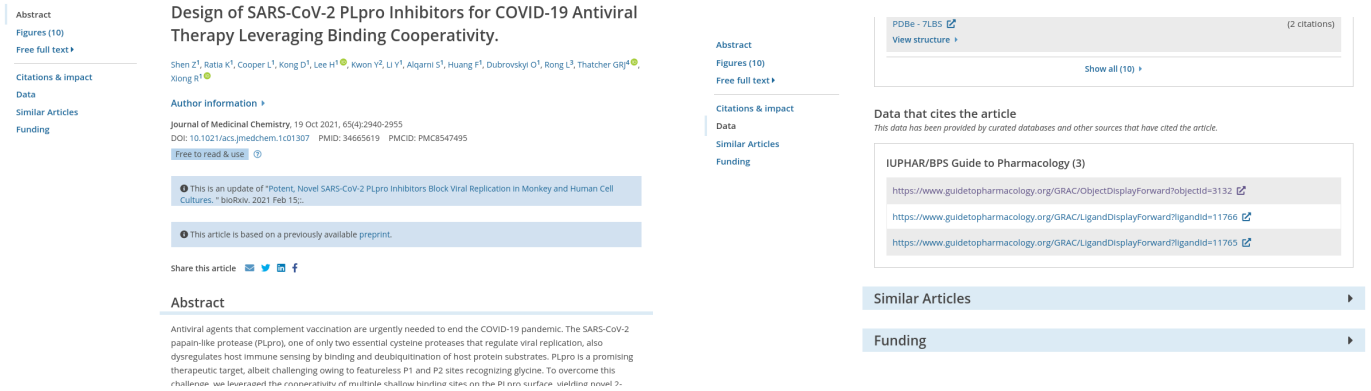
GtoPdb maintains sets of links in the NCBI LinkOut service, to the Protein, Nucleotide, Gene and PubMed databases. Our links are updated frequently. Below is the count of all NCBI database records that contain 'LinkOuts' to GtoPdb. The PubMed count covers all references in the databases including reviews and additional reading for target families. Note that the LinkOut pointers link users back to the database. For various technical reasons associated with NCBI mapping stringencies the three sets of entity links have an

element of over-counting with redundancy. However the PubMed links are clean because they are assigned via our own curation.

Protein	5869
Nucleotide	5130
Gene	8644
PubMed	33,039 (https://pubmed.ncbi.nlm.nih.gov/?term=loprovguidpharm[SB])

Europe PMC

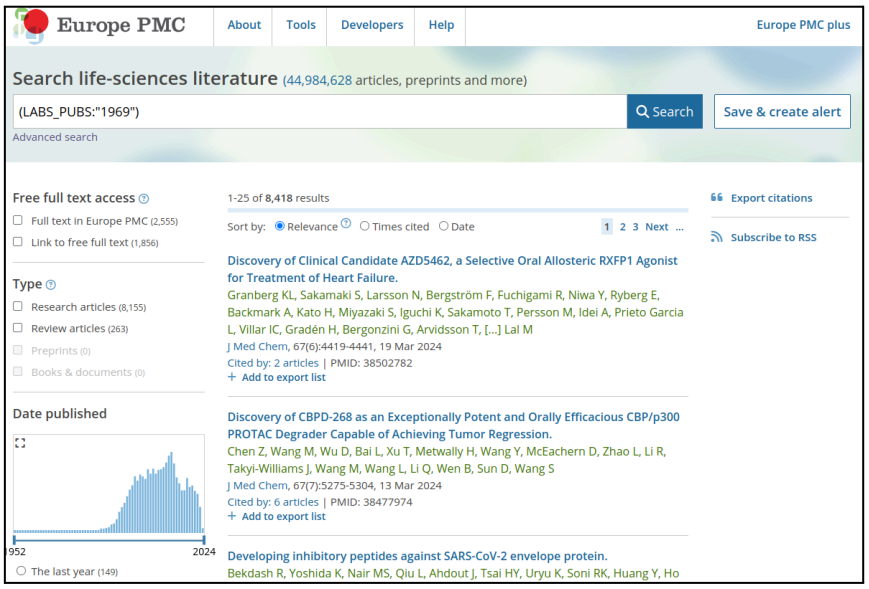
GtoPdb maintains records in the Europe PMC External Links Service. Unlike the larger set of NCBI Outlinks, these publication links are restricted to papers from which GtoPdb interaction data have been curated. These link targets and/or ligands mentioned in the article back to GtoPdb detailed pages.



The above screengrabs show an example of the links from (Shen et al. 2021). Under the 'Data' tab on the left-hand side the data cited in the article can be found. This shows 3 links back to GtoPdb ligands and targets.

As of 28th October 2024 there were 8,418 articles in Europe PMC with links to GtoPdb targets and/or ligands. The EPMC interface query is (LABS_PUBS:"1969")

Full URL: https://europepmc.org/search?query=%28LABS_PUBS%3A%221969%22%29 (screenshot below)



Bibliometrics and Scholarly Portals

Nucleic Acids Research Database Issue

Our latest submission to the Nucleic Acids Research Database Issue was accepted and published online in October 2023 and published in the Database Issue in January 2024.

Harding SD, Armstrong JF, Faccenda E, Southan C, Alexander SPH, Davenport AP, Spedding M, Davies JA. The IUPHAR/BPS Guide to PHARMACOLOGY in 2024. Nucleic Acids Res. 2024 Jan 5;52(D1):D1438-D1449. doi: 10.1093/nar/gkad944. PMID: 37897341; PMCID: PMC10767925

This publication has so far picked up 19 citations (European PMC) or 25 (in PubChem).

We note that the previous NAR update in 2022 (PMID: 34718737), has received 67 citations (69 PubChem), and that our 2020 NAR Database Issue article has picked up 110 citations and (110 PubChem).

Concise Guide to Pharmacology

The 6th Edition (2023/24) of the Concise Guide to Pharmacology was accepted in October 2023 and first published online in December 2023.

The Concise Guide provides concise overviews, mostly in tabular format, of the key properties of approximately 1800 drug targets, and about 6000 interactions with about 3900 ligands. There is an emphasis on selective pharmacology (where available), plus links to the Guide to Pharmacology database, which provides more detailed views of target and ligand properties. It is produced in close conjunction with the Nomenclature and Standards Committee of the International Union of Basic and Clinical Pharmacology (NC-IUPHAR), therefore, providing official IUPHAR classification and nomenclature for human drug targets, where appropriate

Bibliometrics

We continue to get high citation rates in our previous NAR Database Issues and Concise Guide articles because BJP and BJCP select these as reference citations for the GtoPdb outlinks. Top of the list is our NAR 2018 entry (PMC5753190) with 1,341 citations (according to EPMC) or 1,001 (according to PubMed) and 1,710 by Google Scholar. See the table below for links and details of other highly cited NAR and CGTP papers.

	EPMC	PubMed	Google Scholar
NAR 2018	1,341	1,001	1,710
NAR 2016	931	934	1,134
NAR 2014	729	740	890
NAR 2020	110	110	222
NAR 2022	67	69	135
CGTP 17/18 Enzymes	564	564	635
CGTP 15/16 Enzymes	515	514	549

CGTP 13/14 GPCRs	479	465	650
CGTP 17/18 GPCRs	471	465	671

From the most recent edition of the Concise Guide, 2023/24, the G protein-coupled receptors has 16 citations and the Ion Channel chapter and Enzyme chapter both have 7 citations each (all via EPMC).

SARS-CoV-2 Review

Our BJP SARS-Cov-2 review has acquired 38 citations (EPMC).

Alexander SPH et al. A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development: IUPHAR Review 29. Br J Pharmacol. 2020 Nov;177(21):4942-4966.

The Altmetric rankings for all our OA papers are indexed in ScienceOpen. Top of the list by some margin at 275 is our BJP SARS-Cov-2 review.

Other

- As outlined in previous reports we track various metrics for the GtoPdb team and NC-IUPHAR affiliated papers in PubMed, PubMed Central , European PubMed Central (EPMC) Kudos entries and Altmetrics.
- Research output by members of the GtoPdb Curation team can be seen via ORCID IDs for which we have JLS 0000-0002-5275-6446 , EF 0000-0001-9855-7103 , AJP 0000-0003-2280-845X, CS 0000-0001-9580-0446, SDH 0000-0002-9262-8318 and JFA 0000-0002-0524-0260.
- The overall citation performance has resulted in team members JFA, SDH, JLS, EF, AJP, CS and JAD, along with IUPHAR co-authors, SPHA, MS, and APD being listed in the Clarivate 2023 rankings of Highly Cited Researchers.
- GtoPdb team members have 204 cumulative co-authored publications

Below are the (live) April 2024 bibliometric updates compared to the November 2020 metrics. These are given with EPMC links which have the advantage over PubMed of directly generating a citation ranking for any set (but with lower citation rates than PubMed, Google Scholar or WOS).

- The team is on their 9th NAR Database Issue from 2009 to 2024
- IUPHAR reviews in BJP: 45.
- IUPHAR Pharmacological Reviews: 115
- The cumulative BJP “Concise Guide” set now takes us to 47 papers

EBI UniProtKB/Swiss-Prot cross-references

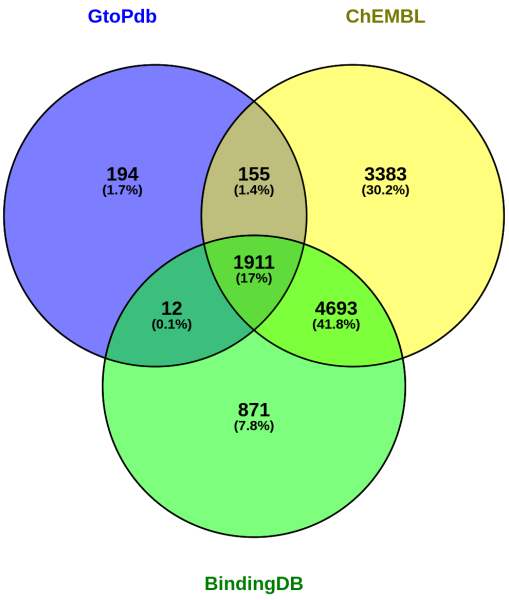
Below are the metrics for [UniProt 2024_04 chemistry sources](). The context for these has been given in previous reports. They provide valuable protein < > chemistry mappings including our own targets where we have curated quantitative ligand interactions of generally < 1uM. Note that SwissLipids curated chemical interactions are for metabolites rather than activity modulators.

Cross-referenced databases 6 results

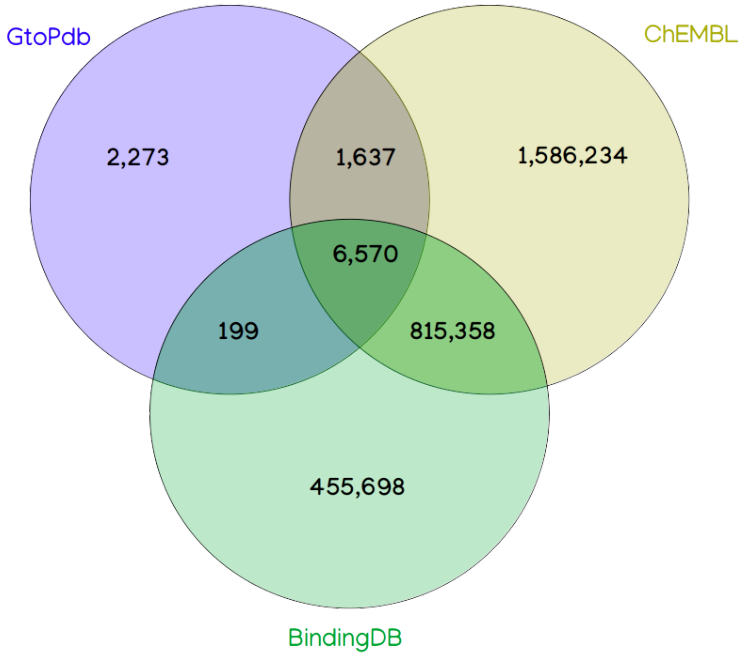
Tools ▾ Download (6) View: Cards ○ Table ◉ Customize columns Share ▾

ID	Name	Abbreviation	Statistics	Category
DB-0019	Drug and drug target database	DrugBank	5,211 UniProtKB entries 4,787 reviewed UniProtKB entries 424 unreviewed UniProtKB entries	Chemistry databases
DB-0127	BindingDB database of measured binding affinities	BindingDB	7,487 UniProtKB entries 6,662 reviewed UniProtKB entries 825 unreviewed UniProtKB entries	Chemistry databases
DB-0174	ChEMBL database of bioactive drug-like small molecules	ChEMBL	10,142 UniProtKB entries 8,951 reviewed UniProtKB entries 1,191 unreviewed UniProtKB entries	Chemistry databases
DB-0182	IUPHAR/BPS Guide to PHARMACOLOGY	GuidetoPHARMACOLOGY	2,272 UniProtKB entries 2,252 reviewed UniProtKB entries 20 unreviewed UniProtKB entries	Chemistry databases
DB-0197	SwissLipids knowledge resource for lipid biology	SwissLipids	1,398 UniProtKB entries 1,394 reviewed UniProtKB entries 4 unreviewed UniProtKB entries	Chemistry databases
DB-0239	DrugCentral	DrugCentral	3,290 UniProtKB entries 2,982 reviewed UniProtKB entries 308 unreviewed UniProtKB entries	Chemistry databases

Even though these sources have different ways of curating, it is informative to compare and contrast. Below is a Venn diagram showing the comparison of UniProtKB identifiers between GtoPdb, ChEMBL and BindingDB. GtoPdb target overlap with both ChEMBL and BindingDB is extensive, GtoPdb has 202 not in ChEMBL and 349 not in BindingDB



This above Venn shows UniProtKB counts are taken from the UniProtKB Chemistry Databases (https://www.uniprot.org/database?query=*&facets=category_exact%3AChemistry+databases). Diagram drawn using Venny 2.1.0 (https://csbg.cnb.csic.es/BioinfoGP/venny.html). The update frequency of these cross-references may be variable depending on the sources.



CID counts are taken using the advanced PubChem Compound search (https://www.ncbi.nlm.nih.gov/pccompound), specifying source name in the query (i.e. 'IUPHAR/BPS Guide to PHARMACOLOGY'[SourceName]).

Around 25% of GtoPdb compounds do not overlap with ChEMBL. ChEMBL extracts all assay data, including ADMET determinations, from a paper whereas GtoPdb usually extracts just the lead compound but will also curate reported secondary target activity. In the comparison with BindingDB, 40% of GtoPdb compounds do not overlap. BindingDB's uniqueness is mainly their patent curation; it also has an arrangement with ChEMBL from which it subsumes just the individual protein target-mapped data..

HGNC

We continued to use HGNC gene identifiers and names for targets in GtoPdb. In total this covers 3,000 human targets. We also use HGNC nomenclature for updating protein names and gene names as part of our regular database update process.

GPCRdb

There are 938 links from 372 GPCR protein targets in GtoPdb to GPCRdb (https://gpcrdb.org/). This gives users specific pointers to GPCRdb's detailed features, curation of mutations, sequence display toolbox and residue numbering system. There are also now 4,263 links from GtoPdb ligand pages to GPCRdb, following work done by GPCRdb to pick up endogenous ligand data from GtoPdb.

General overview of database team activities

GtoPdb Team Interactions

For more details of previous and continuing interactions please see previous reports.

Global Core Biodata Resource

The IUPHAR/BPS Guide to Pharmacology was announced as one of 15 new Global Core Biodata Resources (GCBRs) in December 2023. The announce news article can be viewed here: https://globalbiodata.org/global-biodata-coalition-announces-outcome-of-2023-global-core-biodata-resource-selection-process/

This means that GtoPdb is now one of 52 GCBR designated by the Global Biodata Coalition (GBC). Through the GCBR designation, the Global Biodata Coalition (GBC) seeks to draw attention to the most critical set of global biodata resources and to better understand the challenges and needs for biodata long-term stability. GCBRs are resources of fundamental importance to global life sciences and biomedical research communities, providing open access and long-term preservation of key biological data.

The GCBR selection process was open to biodata resources globally that were able to meet several stringent eligibility criteria and more than 90 resources submitted expressions of interest across the two rounds of GCBR selection. The assessment process for GCBRs was undertaken by a panel of more than 50 independent expert reviewers against a series of criteria that included scientific focus, the size and reach of the user communities, quality of service, governance, and impact on global research.

ELIXIR

Engagement continues with this important Europe-wide bioinformatics infrastructure initiative. Our involvement with ELIXIR-UK brings closer ties with other key UK bioinformatics resources and facilitates collaboration on the use of standard ontologies and identifiers. This is valuable as we continue seeking to ensure GtoPdb is a FAIR-compliant (Findable, Accessible, Interoperable, Reusable) resource.

We are part of ELIXIR-UK though as one facet of the University of Edinburgh's membership. As reported before, we have an entry in the ELIXIR bio-tools directory as one of the official UK ELIXIR Node Services.

We have been engaging locally with other groups in Edinburgh to help strengthen our involvement, this included engaging with the BioFAIR project and their roadshow in Edinburgh on May 22nd 2024.

Publications

Listed here are our most recent publications.

The 6th edition of the Concise Guide to Pharmacology (2023/24) was published in December 2023.

In October 2023 our latest database update paper was accepted and published online in the annual Nucleic Acids Research Database Issue.

Harding SD, Armstrong JF, Faccenda E, Southan C, Alexander SPH, Davenport AP, Spedding M, Davies JA. **The IUPHAR/BPS Guide to PHARMACOLOGY in 2024**. Nucleic Acids Res. 2024 Jan 5;52(D1):D1438-D1449. doi: 10.1093/nar/gkad944. PMID: 37897341; PMCID: PMC10767925

Outreach and Social Media

We use mainstream social media outlets for five primary purposes 1) outreach to potential new users and/or followers 2) informing on new features or releases 3) enhancing awareness of our publications and presentations 4) fostering contacts with our direct collaborators and other followers (including many other databases) 5) establishing reciprocity with key followers and collaborators.

X (formerly Twitter)

@GuidetoPHARM has, as of 25th October 2024, 5,509 followers (increased from 5,465). This platform remains useful as an alerting system for our blog posts, key papers, including from BJP, other pharmacology journals, immunology, biochemistry and medicinal chemistry, new PDB structures, etc.

We also engage in a discrete re-tweeting for reciprocal outreach. These include @BritPharmSoc (who are active in promoting the Concise Guide) @BrJPharmacol, @PharmRevJournal, @PRandP_Journal @IUPHAR, @PharmacologyEd @immunopaedia @cdsouthan and @mqzspa (NC-IUPHAR chair).

(NB readers of this document are most welcome to follow @GuidetoPHARM and Steve Alexander (@mqzspa) and re-tweet posts of interest).

LinkedIn

The Curation Team continues to encourage Subcommittee Chairs and collaborators to increase their reciprocal connectivity as individual LinkedIN users. This expands our collective inter-network reach for posting updates, new papers etc. (N.B. interested readers of this report are encouraged to make connection requests from GtoPdb and IUPHAR scientists they know). Our own LinkedIN group page now has **532 followers**, up from 496 in April 2024.

Guide to Pharmacology Blog

Our Edinburgh blog (http://blog.guidetopharmacology.org/) has received 1,892 visitors between Nov 23 and Oct 24 - an average of 158 visitors per month. Over the same period there have been 3,441 views of our blog (287 per month), which gives an average views per visitor of 1.81.

The blog is our primary news feed and includes database release updates, new features, technical items or articles. Our regular posts with expert commentaries on hot topics relevant to pharmacology are particularly popular, always ranking in the top 5 posts for any given month.

Team member Chris Southan maintains his own (http://cdsouthan.blogspot.com/) where relevant posts include cross-pointers to GtoPdb.

Hot Topics

An established feature, our Hot Topics in Pharmacology track and highlight new significant papers in pharmacology and drug discovery. These are communicated to us from Subcommittee members or picked up from Social Media. For a selection we commission concise commentaries from our expert contacts.

Since the end of April 2024, we have added 41 new hot topic articles.

Slides

We continue to provide a set of generic slides which can be used by anyone presenting or teaching on GtoPdb and a generic poster which can be printed out in various sizes and taken to meetings or handed out as flyers.

Engaging with Us

As is implicit from the Social Media section above, it is crucial to extend our external presence and impact. Thus, the more readers of this document who “connect” with us, (via whichever of the channels above they use for their own professional profile) the more our outreach extends. This also has mutual advantages. In particular re-tweets and LinkedIN likes are useful for extending the alerting network for new releases, publications, meeting slide sets and blog posts. Note also that each time you either save one of our publications to your own Mendeley account or mention it in a tweet, blog or PubMed commons comment (but make sure you specify a DOI or PubMed link for the auto-indexing) the Altmetrics score.