IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

April 2023

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Contents

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 November 2022. Previous reports are online for 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 2023 doi:
- November 2022 doi: 10.5281/zenodo.7458274
- April 2022 doi: 10.5281/zenodo.7786340
- November 2021 doi: 10.5281/zenodo.7786355

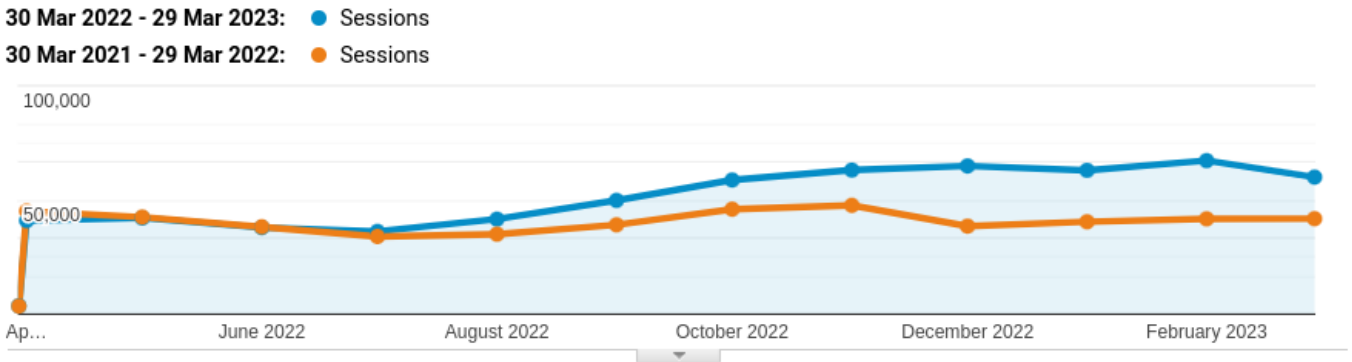
Key Updates / Notifications

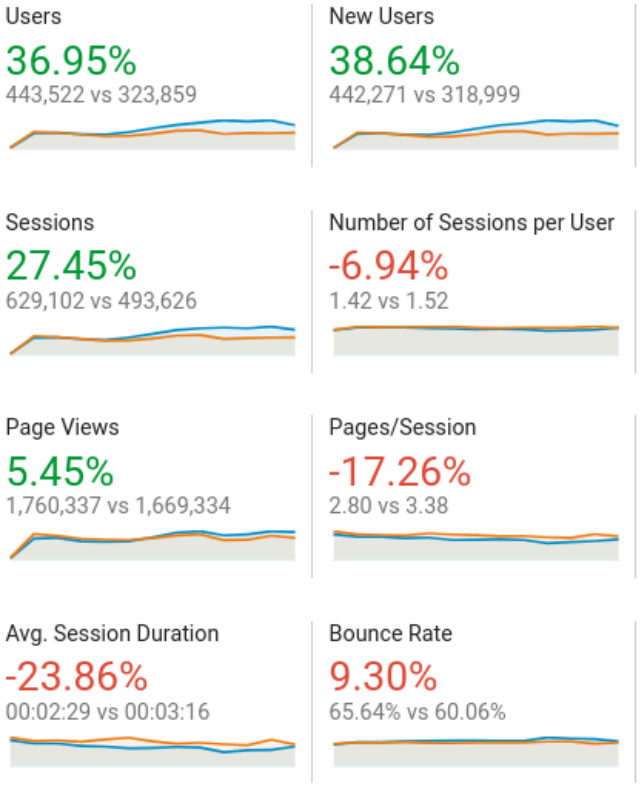
- 2 Database release (2022.4 & 2023.1)
    - 415 new ligands added (78 approved drugs)
    - 16 new targets added
    - 35 human targets with new quantitative interactions (total 1662)
    - 297 ligands with new quantitative interactions (total 8814)
    - 659 new ligand-target interactions

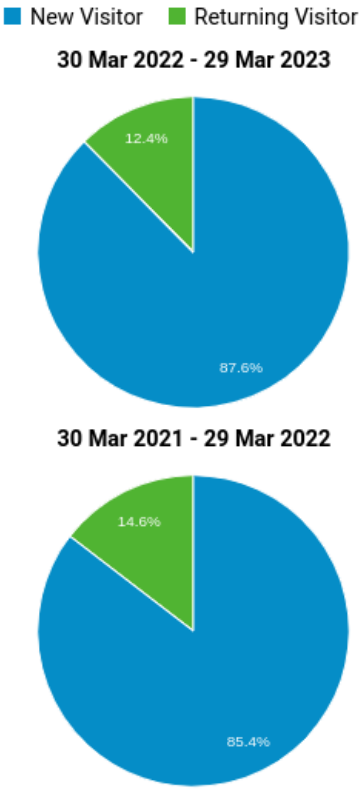
- ~37,000 Users per month (~52,000 sessions)

GtoPdb Website Analytics

GtoPdb Website Access Statistics







Graphs comparing visitors to guidetopharmacology.org for the 12 months from April 2022 to March 2023, with the previous 12 months.

Monthly statistics	**April 2022-March 2023 (previous 12 months)**
Sessions	52,425 (41,135)
Users	36,960 (26,988)
Page views	146,694 (139,111)

Pages / Session	2.80 (3.38)
Avg. Session Duration	00:02:29 (00:03:16)

	Country	Sessions	Sessions
		629,102 % of Total: 100.00% (629,102)	629,102 % of Total: 100.00% (629,102)
1.	United States	165,536	26.31%
2.	China	80,952	12.87%
3.	United Kingdom	59,881	9.52%
4.	India	45,794	7.28%
5.	Germany	18,221	2.90%
6.	Japan	17,446	2.77%
7.	Australia	15,599	2.48%
8.	Canada	15,106	2.40%
9.	South Korea	13,915	2.21%
10.	Russia	11,317	1.80%
11.	France	9,675	1.54%
12.	Italy	9,288	1.48%
13.	Mexico	8,770	1.39%
14.	Spain	8,407	1.34%
15.	Netherlands	6,889	1.10%
16.	Brazil	6,726	1.07%

Total website sessions connecting to the Guide to PHARMACOLOGY website split by country.
Data taken from April 2022 - March 2023.

The figure above shows the breakdown of access to GtoPdb by country. Around 56% of all sessions come from the USA, China, UK and India. A rise under the Google Universal Analytics (UA) for sessions is noted from mid-2022. In the last 12 months, a total of 69 countries have recorded 500 sessions or more and 55 countries have recorded 1000 or more sessions.

	Country	Sessions	Sessions
	HDI<0.8	188,541 % of Total: 29.93% (629,868)	188,541 % of Total: 29.93% (629,868)
1.	China	82,582	43.80%
2.	India	45,210	23.98%
3.	Mexico	8,535	4.53%
4.	Brazil	6,751	3.58%
5.	Philippines	5,755	3.05%
6.	Taiwan	4,751	2.52%
7.	Egypt	4,581	2.43%
8.	Pakistan	4,545	2.41%
9.	Thailand	3,478	1.84%
10.	Indonesia	3,187	1.69%
11.	Iran	3,105	1.65%
12.	Colombia	2,761	1.46%
13.	Iraq	2,346	1.24%
14.	Nigeria	2,201	1.17%
15.	Vietnam	1,864	0.99%
16.	Ukraine	1,784	0.95%
17.	Bangladesh	1,512	0.80%
18.	South Africa	1,420	0.75%
19.	Jordan	1,299	0.69%
20.	Algeria	874	0.46%

Total website sessions connecting to the Guide to PHARMACOLOGY website split by countries with a Human Development Index (HDI) of <0.8.

Data taken from April 2022 - March 2023.

The second table, shown above, shows sessions 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'.

Google Analytics now uses a new GA4 property to manage analytics, which works quite differently to Universal Analytics (being retired mid-2023). Below are the users and session analytics measured by GA4 for GtoPdb. These appear to be similar to what was recorded by UA. UA recorded 376,803 sessions since 1 Oct 2022 (last 6 months) compared to 417,515 by GA4 - however, 331,284 of these are engaged sessions. Engaged sessions are sessions lasting longer than 10 seconds, or containing 2 or more screen/page views.

UA recorded 273,264 users over the last 6 months compared to 277,273 by GA4. Note that GA4 recorded 'Active Users' - this is a user who has an engaged session. This suggests our average users per month is around 45,000 in the last six months.

	Country	Active users	Engaged sessions per user	Sessions	↓Engaged sessions	Views
	Totals	**277,273** 100.0% of total	**1.19** Avg 0%	**417,515** 100.0% of total	**331,284** 100.0% of total	**1,822,069** 100.0% of total
1	United States	79,417	1.1	109,178	87,169	373,439
2	China	45,134	0.95	60,173	43,061	219,629
3	United Kingdom	22,341	1.61	45,462	35,976	320,357
4	India	21,099	1.13	29,731	23,795	101,351
5	Germany	6,947	1.36	11,852	9,447	62,021
6	Canada	6,703	1.26	10,652	8,435	42,341
7	Japan	6,030	1.36	10,323	8,214	52,331
8	South Korea	5,879	1.23	9,185	7,212	39,771
9	Russia	5,973	1.09	7,709	6,521	31,720
10	Australia	4,830	1.29	8,077	6,243	35,682
11	France	3,738	1.33	6,345	4,983	31,204
12	Italy	3,490	1.41	6,017	4,925	31,924
13	Spain	3,409	1.43	6,159	4,884	38,339
14	Mexico	2,703	1.57	5,347	4,244	37,272
15	Netherlands	2,860	1.4	4,919	4,002	25,870

Download Statistics

Yearly period 01 Apr 2022-31 Mar 2023 (comparing with 01 Apr 2021 - 31 Mar 2022)

Google Analytics: Comparison of Downloads

Event Category: Downloads

	Count
2021-2022	3,982
2022-2023	**4,324**
Change	+8.59%

This corresponds to files downloaded from our main downloads page:
http://www.guidetopharmacology.org/download.jsp

A more specific breakdown is shown here:

	2022-2023	2021-2022	Change
Targets CSV/TSV files	***1,534***	*1,377*	**11.47%**
Interactions CSV/TSV file	***375***	*377*	**-0.53%**
Ligands CSV/TSV file	***1,264***	*1,277*	**20.36%**
UniProt Mapping file	***112***	*127*	**-11.81%**
HGNC mapping file	***100***	*126*	**-20.63%**
Ligand ID Mapping	***174***	*170*	**2.35%**
PostgreSQL	***177***	*186*	**-4.84%**

GtoPdb Content

These database statistics were compiled from our development database on 14th April 2023, ahead of our first full database release of 2023 (2023.1). All database statistics can be found at http://www.guidetopharmacology.org/about.jsp#content.

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	1267
Transporters	555
Other protein targets	223
Human targets with ligand interactions	1914
Human targets with quantitative ligand interactions	1662
Human targets with approved drug interactions	723
Human Primary Targets with approved drug interactions	345
Total number of targets	**3023**

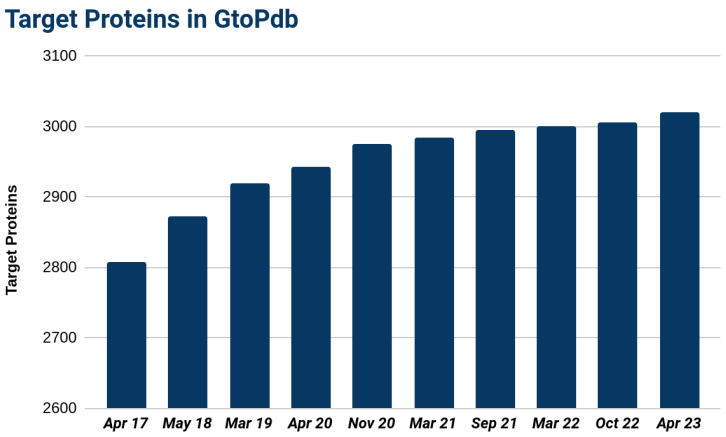
Ligands	**Number of Ligands**
Synthetic organics	8325
Metabolites	526
Endogenous peptides	811
Other peptides including synthetic peptides	1490

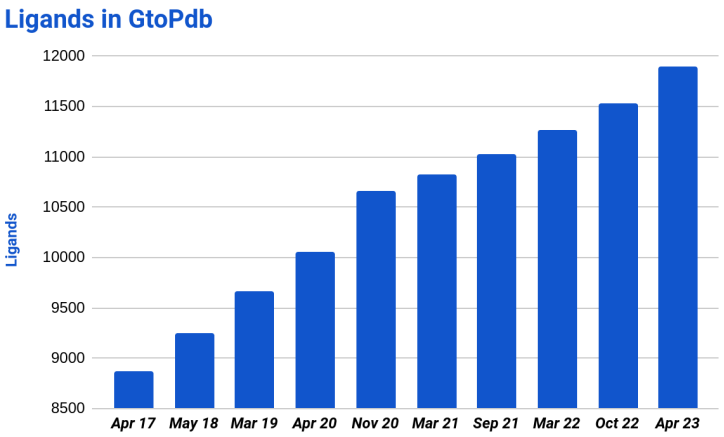
Natural products	409
Antibodies	347
Inorganics	39
Approved drugs	1875
Withdrawn drugs	102
Drugs with INNs	3240
Labelled ligands	642
Unique PubChem CIDs (total CID links)	9349 (9552)
Ligands with target interactions	9981
Ligands with quantitative interactions (approved drugs)	8814 (1098)
Ligands with clinical use summaries (approved drugs)	3387 (1868)
Total number of ligands (PubChem SIDs)	**11,947**
Number of binding constants curated from the literature	**19,890**

GtoPdb Entity Growth

Growth rates over the span of the previous Wellcome Trust grant are documented in earlier reports and our 2016, 2018, 2020 and 2022 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.

	May 18	Mar 19	Apr 20	Nov 20	Mar 21	Sep 21	Mar 22	Oct 22	Apr 23
Target protein IDs	**2872**	**2920**	**2943**	**2976**	**2985**	**2995**	**3000**	**3007**	**3023**
Ligands total	**9251**	**9662**	**10053**	**10659**	**10821**	**11025**	**11271**	**11532**	**11947**
Approved drugs	1364	1421	1471	1614	1643	1689	1734	1787	1875
Antibodies	240	255	270	295	303	317	333	329	347
Peptides	2092	2122	2150	2180	2206	2226	2251	2275	2301
Synthetic small molecules	6048	6401	6816	7303	7428	7593	7797	8026	8325
PubChem SIDs	9251	9662	10053	10659	10821	11025	11271	11532	11947
PubChem CIDs	7109	7407	7483	7994	8102	8262	8462	8633	9349
References	33245	35723	37261	39133	40022	-	-	-	





GtoPdb Updates

Targets

Updates for the Orexin family are complete (Jyrki Kukkonen and Daniel Hoyer).

SIP & LPA Rs were updated as part of the Concise Guide process

Updates for Relaxin Rs, Complement peptide Rs and Succinate R have been requested.

Ligands

New ligand sources (in addition to content from published literature, or via target subcommittees) include the INN lists from the WHO, DrugHunter (https://drughunter.com/) and first disclosures from AACR and ACS meetings. A ligand will only be added to GtoPdb when the curators can confirm name-to-structure associations, and find primary citations for MMOA and quantitative interaction data.

The following table summarises new ligands added and updated in GtoPdb since the 2022.1 release.

The *New Ligands* column shows count of new ligands for each category; *Updated Ligands* shows count of existing ligands, already curated in GtoPdb, now included in the categories. Columns 4 and 5 show the total ligands count for each category from our 2023.1 (Apr 2023) and 2022.1 (Mar 2022) database releases.

NB Additional information about our newly curated ligands will be available in our release notes blog post, following the upcoming 2023.1 release.

Ligands:

- 31 new kinase inhibitors were added, with structures arising from the Jan 2023 proposed INN list
- 12 new ligands with potential anti-CoV activity were added

- 11/14 of the drugs that have been approved by the FDA in 2023 are curated in the GtoPdb. We have not included velmanase alfa-tycv (enzyme), efanesoctocog alfa (factor VIII Fc fusion protein), and rezafungin (anti-fungal) as they don't meet our inclusion criteria.
- 100 new antibacterial compounds were added over the past year. These are from the list of antibacterials provided by the Global Antibiotic Research and Development Partnership (GARDP) and available as part of the encyclopaedia on their REVIVE website (https://revive.gardp.org/resources/encyclopaedia/).

Summary of ligands added to GtoPdb in 2023.1 release (compared to 2022.1)

	New Ligands	Updated Ligands	Total Ligands (2023.1)	Total Ligands (2022.1)
Approved Drugs	97	44	1875	1734
WHO Essential Medicines	4	0	297	293
Ligands with Quantitative Interaction Data	201	261	8814	8352
Anibacterials	45	75	425	305
All Ligands	676	0	11947	11271

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	624	431
Clinical Use	248	154
Bioactivity	274	60
MOA	18	5

Concise Guide to PHARMACOLOGY curation

76 target families have been updated in this process, for the 2023-24 edition of the CG.

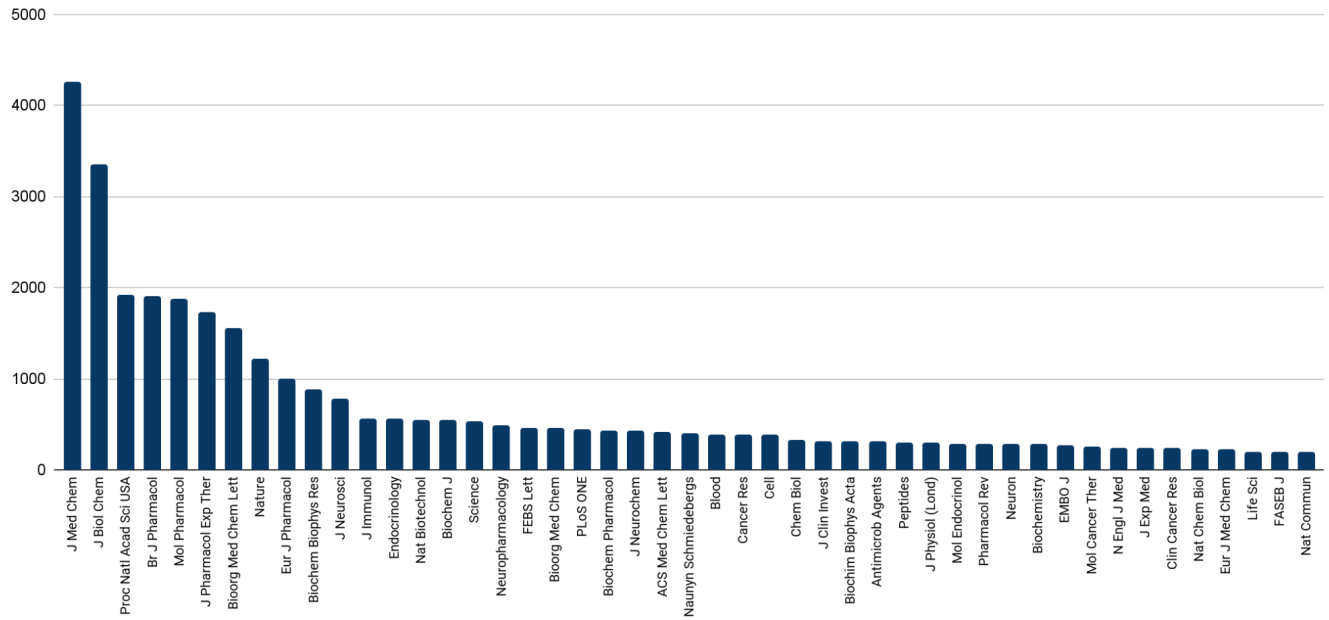
Of note:

- **Orexin R** ligand/interactions sets were substantially re-worked (Jyrki Kukkonen & Dan Hoyer).
- More than 90 ligands (>half of which were new to GtoP) with interactions to the **Taste 2 Rs,** including quantitative interaction data were added- only TAS2R19, TAS2R42, TAS2R45 and TAS2R60 remain 'orphans' (Maik Behrens).
- **$GABA_A$ Rs** ligand/interactions sets were substantially re-worked (Werner Sieghart)

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	4252
J Biol Chem	3356
Proc Natl Acad Sci USA	1920
Br J Pharmacol	1909
Mol Pharmacol	1878
J Pharmacol Exp Ther	1736
Bioorg Med Chem Lett	1561
Nature	1221
Eur J Pharmacol	1001
Biochem Biophys Res Commun	885
J Neurosci	782
J Immunol	569
Endocrinology	560
Nat Biotechnol	555
Biochem J	554
Science	532



GtoPdb Coronavirus (COVID-19) Information Page

As a response to the SARS-CoV-2 pandemic, we have been maintaining a coronavirus information page. This page, available since March 2020, is updated regularly to allow rapid dissemination of reviewed and curated coronavirus therapeutic developments.

Many of these emerging strategies rely on repurposing existing drugs, and others are completely new, but all rely on existing scientific evidence of mechanistic approaches that are effective against either similar viral infections or the serious symptoms that are caused by COVID-19. Compounds that have verified activity, and both established and emerging host and coronavirus targets, are regularly reviewed and updated with detailed curator comments and links to pharmacological data within the GtoPdb.

The page has sections on the key targets and ligands of interest - linked into the more detailed GtoPdb pages. As of April 2023 we have **118 unique entries** in our table of COVID-19 relevant ligands, of these, **107 have ligand summary pages** in GtoPdb.

There are 13 targets on the page, 12 of which have detailed pages in GtoPdb.

In addition to the targets and ligands on the coronavirus page, many more entities in the GtoPdb have curator comments regarding evidence of a relationship to SARS-CoV-2 and/or COVID-19 (a search using SARS-CoV-2 retrieves 294 hits: 237 of which are ligands.

We have expanded coverage of ligands with CoV antiviral potential- adding more Mpro, PLpro and RdRp inhibitors from the literature and from patents (thanks to Chris Southan, for a patent review).

There are also sections providing useful links to other resources and key publications.

The GtoPdb Coronavirus page has been included in the following data hubs:

- European Data COVID-19 Data Portal, related resource (database) https://www.covid19dataportal.org/related-resources
- ELIXIR-UK https://elixiruknode.org/elixir-uk-our-support-to-covid-19-research/
- ELIXIR https://elixir-europe.org/services/covid-19#access
- BPS COVID-19 trusted resources https://www.bps.ac.uk/covid-19/resources-and-trusted-information/journals-and-publications

Antibiotic DB and Global Antibiotic Research and Development Partnership

We are pleased to report that the Global Antibiotic Research and Development Partnership (GARDP; https://gardp.org/) has extended their funding of our collaboration with Antibiotic DB (ADB; www.antibioticdb.com) for a further 2 years. Through this interaction, GtoPdb provides chemistry and pharmacology for a curated set of antibacterial compounds with links to ADB. Currently we have **425 ligands** tagged in GtoPdb as 'antibacterial' and **413** of these have links to compounds at ADB. The antibacterials in the GtoPdb include approved drugs, WHO essential Medicines-listed medicines and a number of investigational and experimental compounds.

For further information about our work with ADB please refer to previous Database Reports (November 2020, April 2021, November 2021, April 2022, November 2022). This collaboration has also been described in more detail in our latest 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.

The next phase of the project will include the current curator position (with an increase from 0.2 FTE to 0.3 FTE) and a software developer (0.5 FTE) who will work on developing a 'Guide to ANTIMICROBIAL PHARMACOLOGY' portal to GtoPdb and the new ADB database and web app (ADB2).

GtoPdb Web-Application Developments

Server Update

We have now made the transition to new servers to host the Guide to PHARMACOLOGY database and web-application and migrated data over. This was essential infrastructure work for us, and means an update in the version of PostGresQL we will be using to version 12.

This upgrade was important to support tools such as ligand activity graphs and pharmacology search.

Chemistry Development Kit

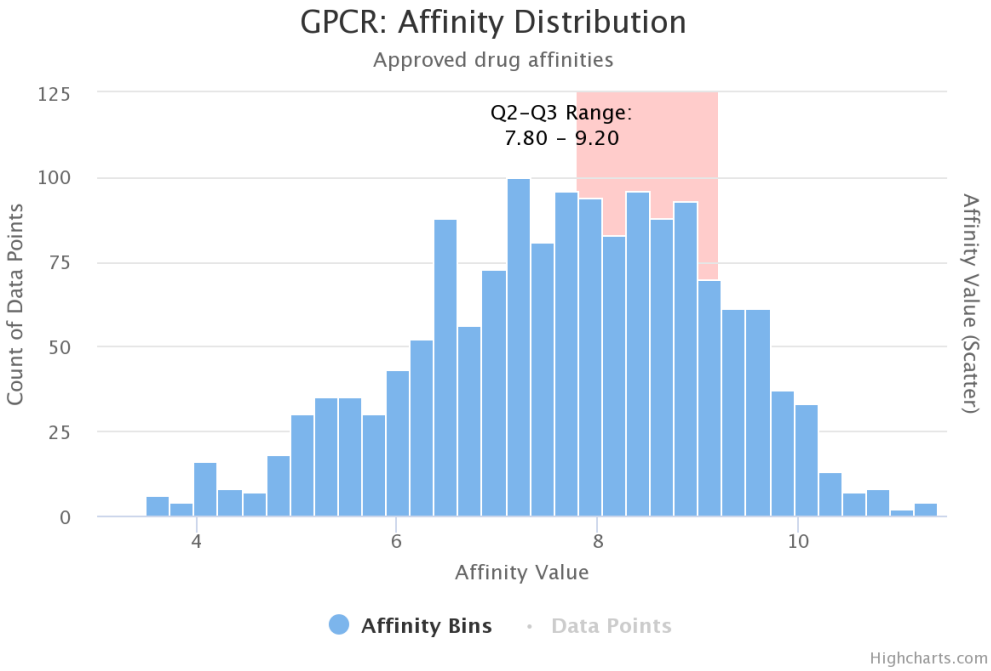
The Chemistry Development Kit (CDK) is a collection of modular Java libraries for processing chemical information (Cheminformatics). The modules are free and open-source and are easy to integrate with other open-source or in-house projects.

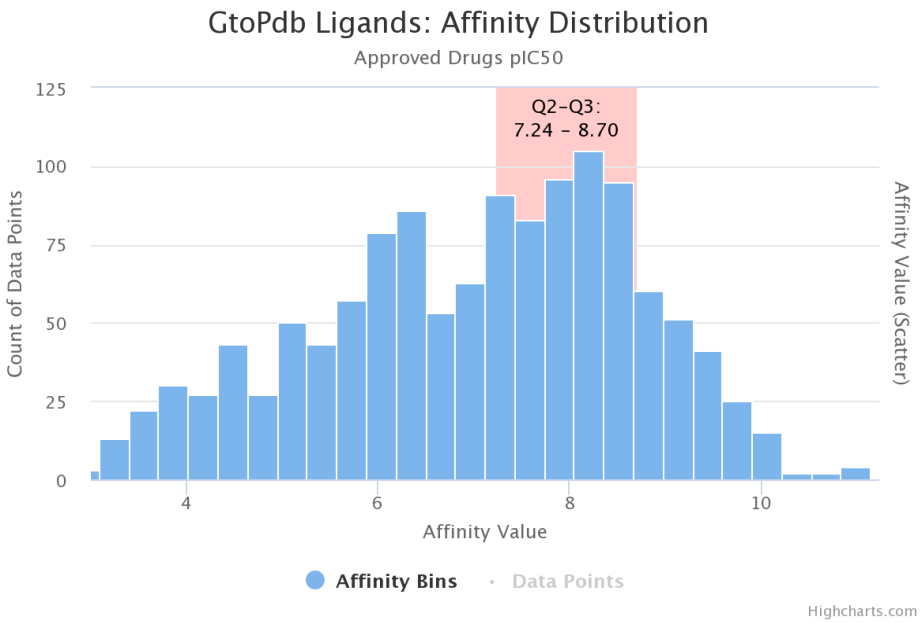
We now use CDK to power our chemical structure search (www.guidetopharmacology.org/GRAC/chemSearch.jsp#structureSearch). We also use features of CDK to calculate physico-chemcial properties of ligands in GtoPdb.

Ligand Affinity Distributions

Using HIghchart JS we have been looking into developing affinity distribution charts on the website. These may provide useful analytical insights into GtoPdb data. They may also be useful ways to summarise and visualise affinity data.

The first example below shows the distribution of all affinity data points for GPCR targets in GtoPdb.





The second chart shows the distribution of pIC50 values for approved drugs in GtoPbd. We expect to be able to develop these further and have something functional on the website by the next release.

Connectivity

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.

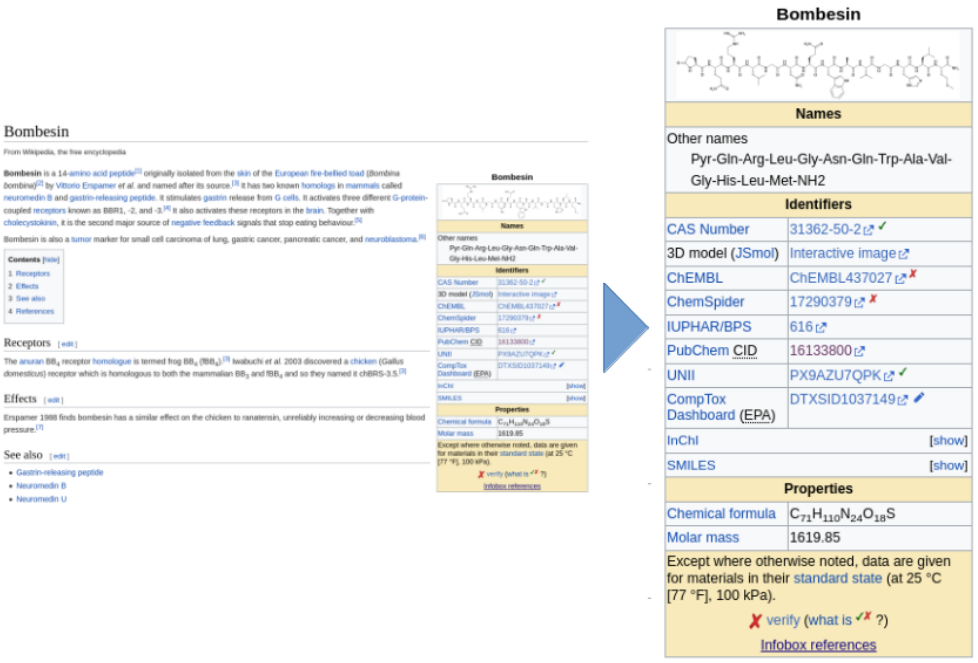
Given we submit our ligand data to PubChem, all ligands with structural data linked to PubChem have out-links (9516). Our recent and ongoing work with AntibioticDB has built links between antibacterials in GtoPdb (442) and AntibioticDB (https://antibioticdb.com/). Links from antibodies in GtoPdb are 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, so the 7602 is the count of UniProtID from all targets across all species. 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	**9516**	**GPCRdb**	**938**
ChEMBL	**6359**	**ChEMBL**	**3794**
Reactome	**344**	**Resolute (SLC)**	**421**
AntibioticDB	**442**	**BioParadigms (SLC)**	**393**
IMGT/mAb-DB	**337**	**HGNC**	**3039**
DrugCentral	**1687**	**NCBI (Entrez) Gene**	**8615**
Wikipedia	**3023**	**Ensembl Gene**	**8756**
GPCRdb	**4073**	**UniProt**	**7602**



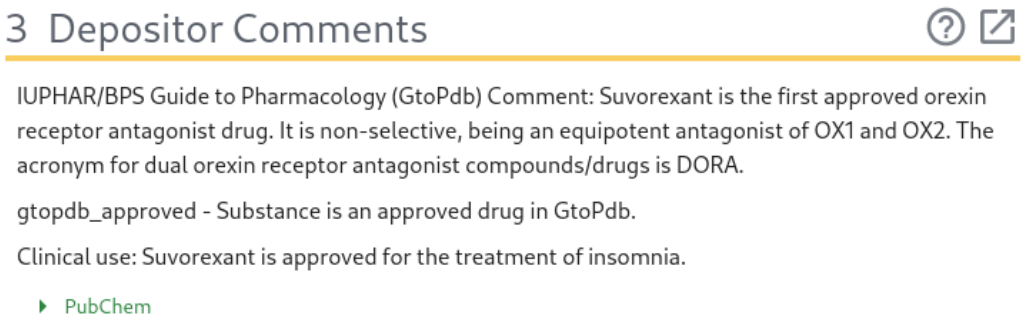
Pubchem Connectivity

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

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 (standardization) 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.

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 suvorexant 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.



Depositor comments section of PubChem SID 135650615.

We recently posted a blog on 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, GtoImmuPdb and GtoMPdb

The stats for the 2023.1 release (with 2022.3 in brackets) are as follows (N.B. the links below can be slow but if they do time out try purging your browser cache). **Please note these are draft numbers and will be update following the full 2023.1 release*

1. Substances (SID) that we submit to PubChem (refreshing previous submissions) are up to 11957 (11539).
2. Those that have defined chemical structures are merged into 9838 (9441) Compound Identifiers, CIDs (i.e. small molecules and peptides below ~ 70 residues)
3. From our 9498 CIDs 7915 have vendor matches
4. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND gtopdb_approved [Comment] now retrieves 1813 SIDs (1787) which link to 1662 approved drug CIDs
5. Of our SIDs, 1384 (1382) are tagged in GtoImmuPdb and 356 (340) of these are approved drugs
6. Of our CIDs 979 are tagged in GtoImmuPdb
7. Of our SIDs, 136 are tagged in GtoMPdb and 25 of these are approved drugs
8. Of our CIDs 134 are tagged in GtoMPdb
9. We have now included an **antibacterial tag in our PubChem upload.** Of our SIDs, 433 are tagged as antibacterial and 197 of these are approved drugs
10. Of our CIDs 432 are tagged in GtoMPdb
11. We have 2331 (2249) structures that ChEMBL does not have, 7076 (6755) not in DrugBank.
12. 359 (337) 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 347 SIDs. Adding "gtopdb_approved" gives 134.

A useful guide/summary of GtoPbd's PubChem substance tagging is given in Dr. Chris Southan's blog post on Exploiting the Guide to Pharmacology substance (SID) tags in PubChem.

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.

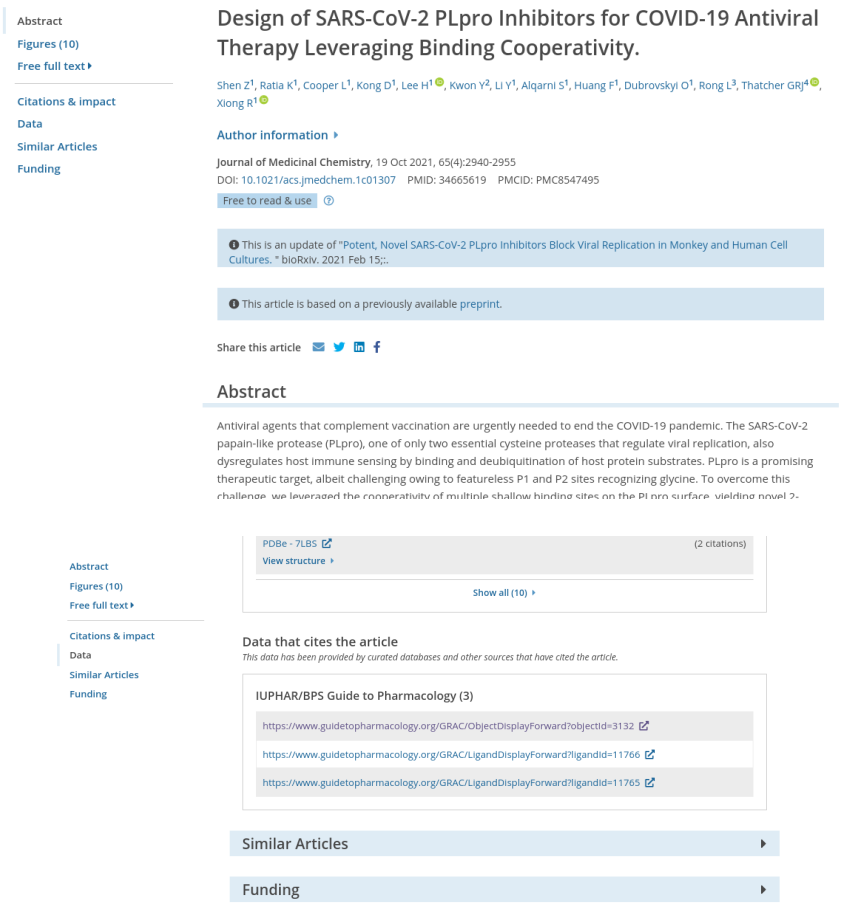
NCBI LinkOuts

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	5955
Nucleotide	5903
Gene	8556
PubMed	31,686 (https://pubmed.ncbi.nlm.nih.gov/?term=loprovguidpharm[SB])

Europe PMC

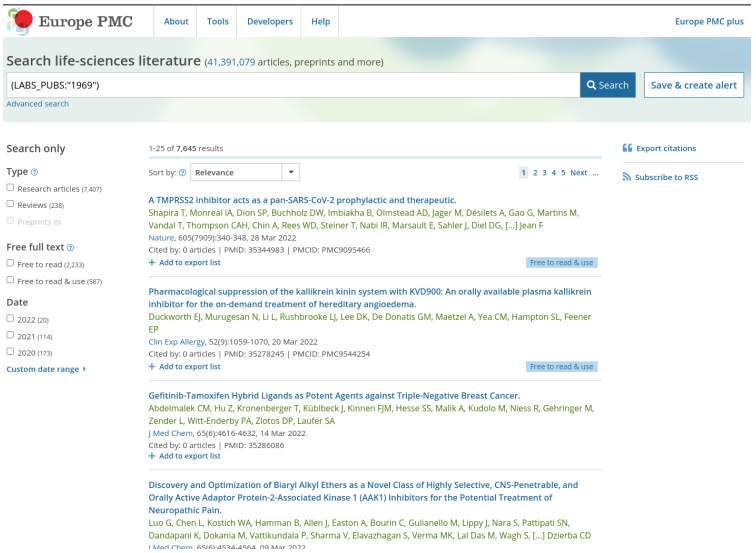
GtoPdb maintains records in the Europe PMC External Links Service. Unlike the larger set of NCBI Outlinks, these publication links are restricted to papers from which GtoPdb interaction data have been curated. These link targets and/or ligands mentioned in the article back to GtoPdb detailed pages.



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 4th May 2023 there were 7,785 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

NAR and CGTP

We are pleased to note that our **2020 NAR Database Issue** article has picked up 90 PubMed citations.

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 1,251 citations (according to EPMC) or 1,295 (according to PubMed) and 1,586 by Google Scholar. This thus overtakes our 2016 paper (PMC4702778) with 924 (EMPC) or 928 (PubMed) citations or 1,082 by Google Scholar, and the 2014 paper (PMC3965070) that reached 712 (EPMC) / 736 (PubMed).

The "Concise Guide" citations are currently led by 2017/18 Enzymes (PMC5650666) at 561 followed by 2015/16: Enzymes (PMC4718211) at 513 and 2013/14: G protein-coupled receptors (PMC3892287) at 473.

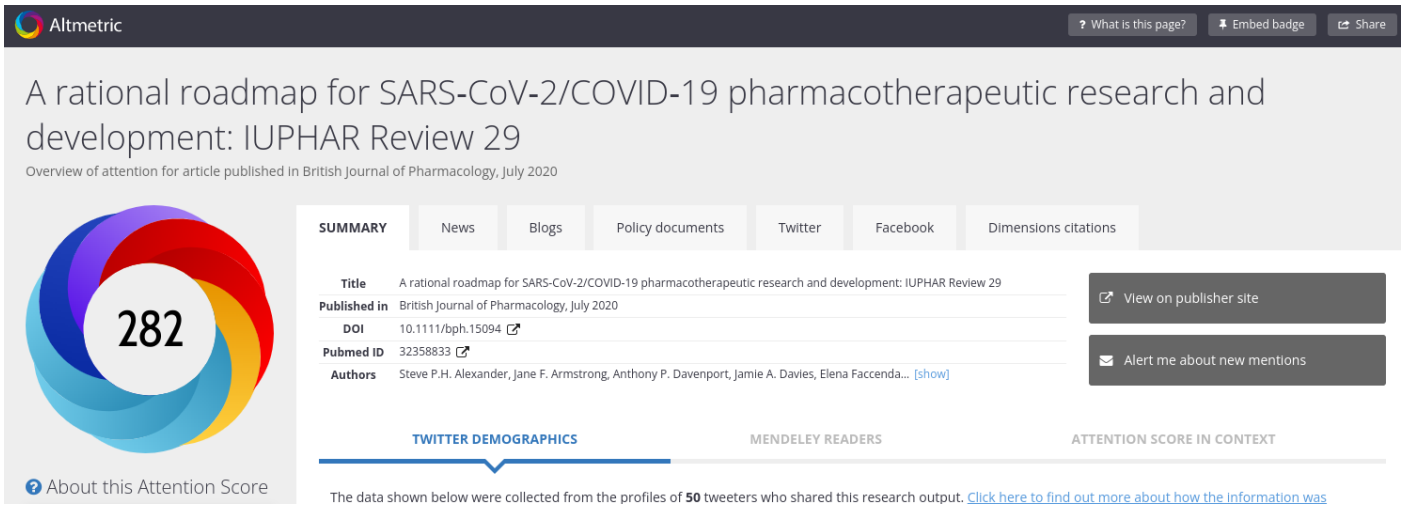
From the most recent edition of the Concise Guide, 2021/22 the G protein-coupled receptors has 71 citations and the Ion Channels has 37 citations.

SARS-CoV-2 Review

Our BJP SARS-Cov-2 review has acquired 50 citations (according to CrossRef).

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 281 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 2022 rankings of Highly Cited Researchers.

- GtoPdb team members have 194 cumulative co-authored publications

Below are the (live) April 2022 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 8th NAR Database Issue from 2009 to 2022

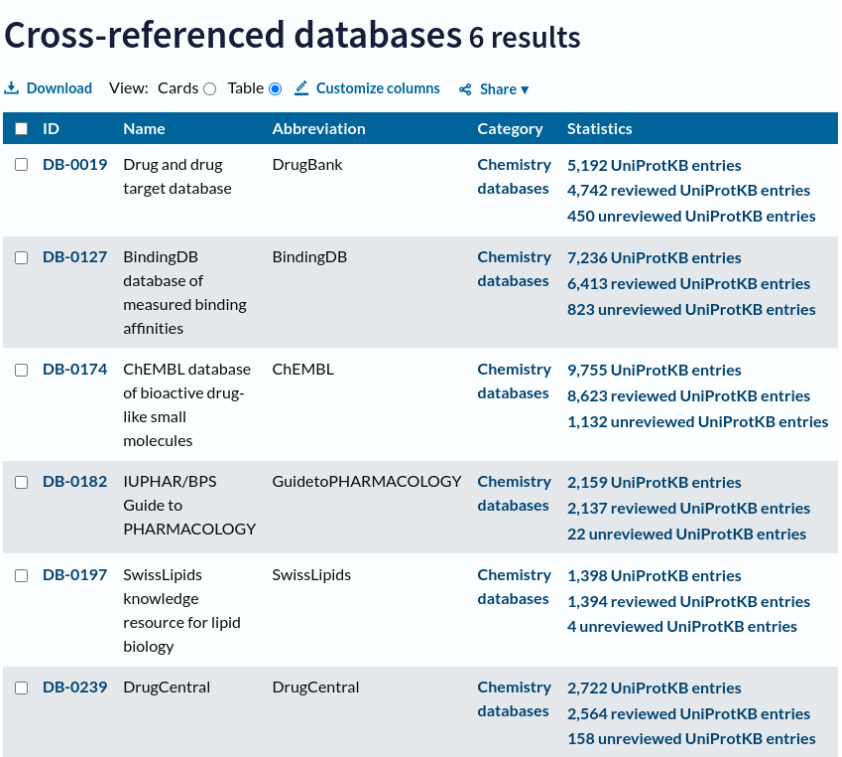
- IUPHAR reviews in BJP: 37.

- IUPHAR Pharmacological Reviews: 109

- The cumulative BJP "Concise Guide" set now takes us to 40 papers

EBI UniProtKB/Swiss-Prot cross-references

Below are the metrics for UniProt 2023_02 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 is the odd-man-out where the curated chemical interactions are for metabolites rather than activity modulators but nonetheless useful.

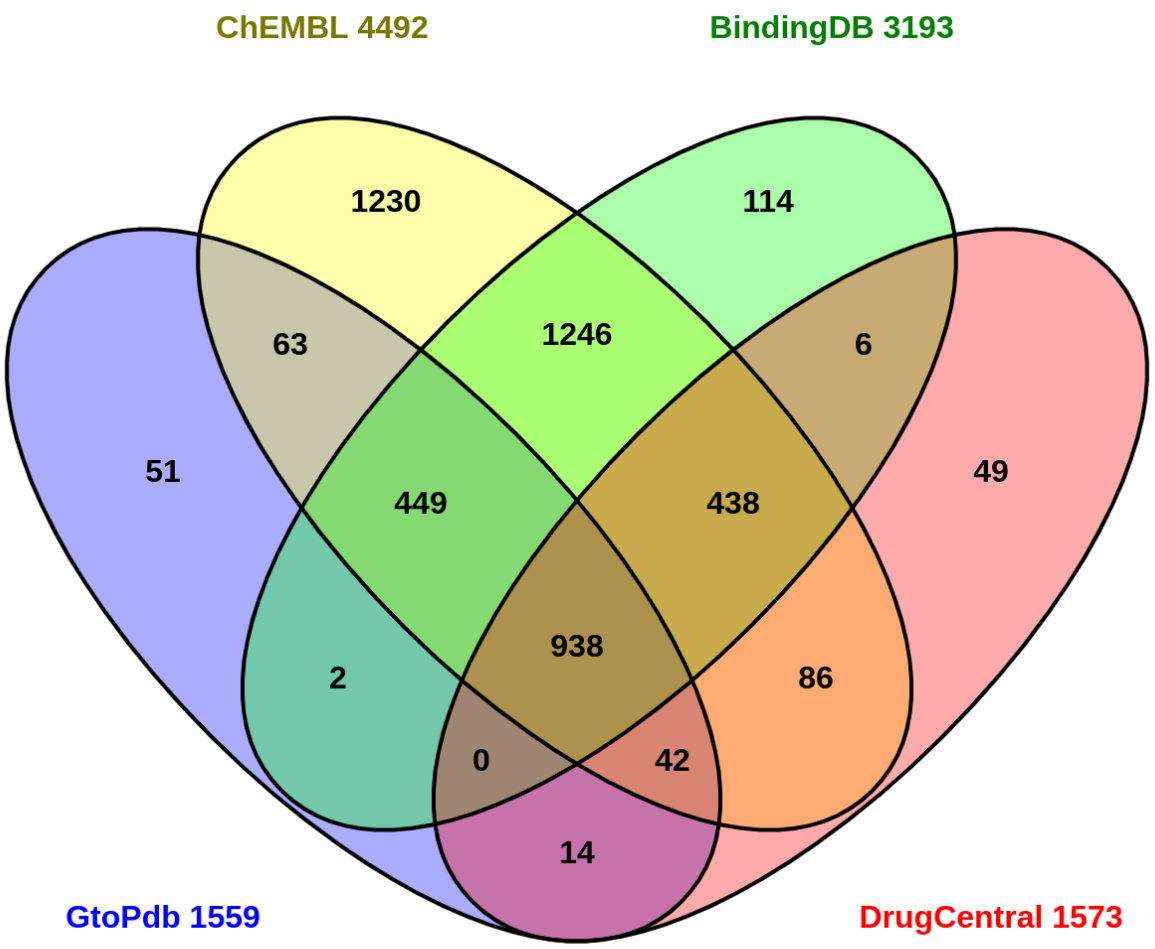


Cross-referenced databases 6 results

Download View: Cards ○ Table ◉ Customize columns Share ▾

ID	Name	Abbreviation	Category	Statistics
DB-0019	Drug and drug target database	DrugBank	Chemistry databases	5,192 UniProtKB entries 4,742 reviewed UniProtKB entries 450 unreviewed UniProtKB entries
DB-0127	BindingDB database of measured binding affinities	BindingDB	Chemistry databases	7,236 UniProtKB entries 6,413 reviewed UniProtKB entries 823 unreviewed UniProtKB entries
DB-0174	ChEMBL database of bioactive drug-like small molecules	ChEMBL	Chemistry databases	9,755 UniProtKB entries 8,623 reviewed UniProtKB entries 1,132 unreviewed UniProtKB entries
DB-0182	IUPHAR/BPS Guide to PHARMACOLOGY	GuidetoPHARMACOLOGY	Chemistry databases	2,159 UniProtKB entries 2,137 reviewed UniProtKB entries 22 unreviewed UniProtKB entries
DB-0197	SwissLipids knowledge resource for lipid biology	SwissLipids	Chemistry databases	1,398 UniProtKB entries 1,394 reviewed UniProtKB entries 4 unreviewed UniProtKB entries
DB-0239	DrugCentral	DrugCentral	Chemistry databases	2,722 UniProtKB entries 2,564 reviewed UniProtKB entries 158 unreviewed UniProtKB entries

Even though these sources have different ways of curating, it is informative to compare and contrast. Taking the four below (omitting DrugBank) gives both a druggable proteome snapshot and our unique contribution to the aggregate coverage. The Venn diagram for the 2023_02 Swiss-Prot entries (Human) are shown below.



There are interesting aspects of relative coverage that cannot be expanded on here (n.b. individual entries can be followed through to their sources via UniProt). However salient observations include that, cumulatively, ~20% of the human proteome is druggable. A second observation is that each source has complementary unique content, including the 51 GtoPdb-only targets. The divergences are of interest but need deeper analysis to discern what curatorial selectivity (e.g. journal choice) explains these differences.

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 943 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 links from GPCRdb and GtoPdb ligand pages following work done by GPCRdb to pick up endogenous ligand data from GtoPdb.

IUPHAR Pharmacology Education project (PEP)

The IUPHAR Pharmacology Education Project continues to be developed “as a learning resource to support education and training in pharmacological sciences” and celebrated its 7th birthday on 1st April 2023.

Financial support is in place for one 0.5 FTE for the next year.

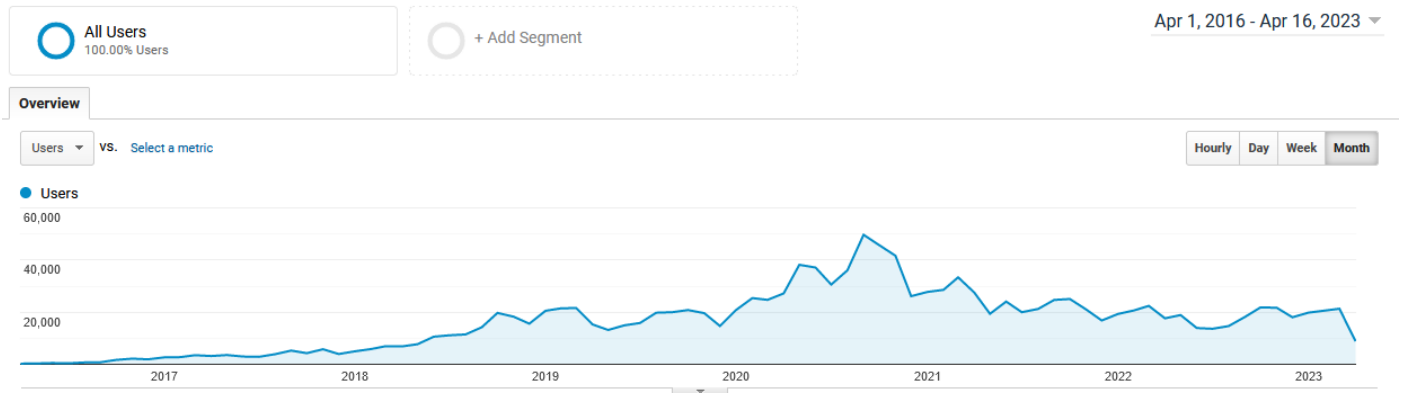
Succession Planning

Under the stewardship of Clare Guilding (PEP Deputy Director; Newcastle University, Vice-Chair of IUPHAR’s Education Section & contributor to BPS Education and Training Committee), John Szarek and Simon Maxwell (PEP co-Directors) PEP has been integrated into the IUPHAR-ed section’s jurisdiction. We hold quarterly combined PEP/IUPHAR-ed meetings. These meetings rotate around reports from PEP, IUPHAR-ed and the Core Concepts working group.

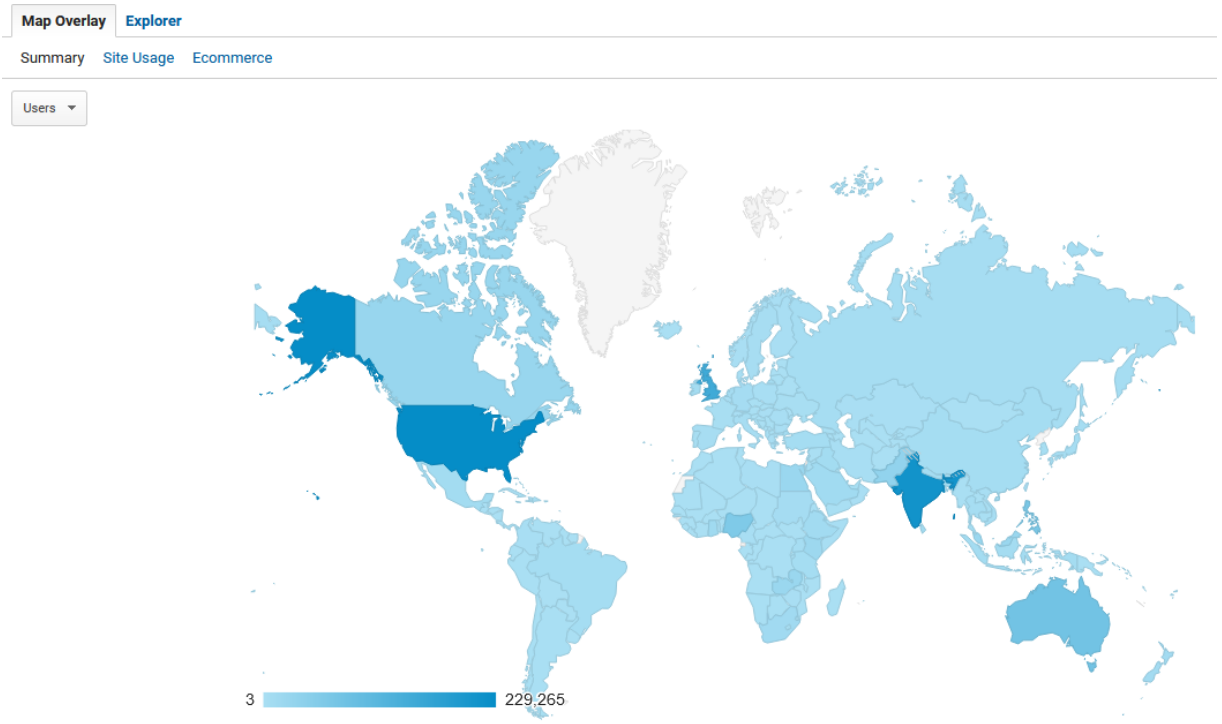
Google Analytics data charts for PEP site usage since 1st April 2016

Google Analytics shows that user sessions continue to average >20K/month. Accumulated page views total >1.7 million.

Monthly user sessions



Global Access



The website has been revised to handle the new Google Analytics 4 (GA4). This required technical input from the University of Edinburgh Drupal team who developed and now maintain the site. To date, data collection is comparable between the current Universal Analytics (UA) and the new GA4 system.

PEP content expansion

- 14 new topics have been published, plus the inclusion of some 'for teachers' resources within the 'Clinical Pharmacokinetics' module (zero & first order PK class exercises, PK visualiser tool).
- 17 new topics are in production, either awaiting editorial review, or being constructed.
- We have received 9 submissions for oncology drugs from Michael Bradaric (Director of Pharmacology, Rush Medical College), and these are in the curation pipeline.
- All modules in the 'Drugs' and 'Therapeutics' sections now have introductory text replacing the 'Under construction' notice that was on the pages.
- The glossary has been expanded, in a collaboration with the CSPT.
- Users from 37 nations have completed our user survey, 21 of which can be considered as 'developing' countries

Social Media

PEP has ~1700 followers of our twitter handle, @PharmacologyEd. IUPHAR-Ed & PEP have established a combined social media team, to try to increase exposure of both resources on social media.

Meetings

- Details for the IUPAR-Ed pharmacology teaching prizes are now hosted on the website https://www.pharmacologyeducation.org/about/iuphar-education-section-teaching-awards, and a banner has been added to the highlights section on the home page that provides a link to the above page for ease of access.
- A banner for the pre-WCP2023 IUPHAR Education Satellite, with a direct link to the meeting's information page is also included on the homepage highlights section
- IUPHAR-Ed have wide representation at WCP2023, with several workshops and a debate on Global Educational Inequalities
- An Education Satellite meeting is arranged for the 2 days in advance of WCP2023. This is being hosted by the University of Strathclyde in Glasgow

The Guide to Immunopharmacology Database (GtoImmuPdb)

GtoImmuPdb is an extension of GtoPdb and its development involved modifications and extensions to the underlying GtoPdb schema to incorporate new immune system specific data types (such as processes, cell types and disease). It also involved further development of the existing GtoPdb website to surface this new data and incorporate it into the existing search and browse mechanisms. The GtoImmuPdb portal is available at (www.guidetoimmunopharmacology.org).

The first public release of the IUPHAR Guide to IMMUNOPHARMACOLOGY was made in June 2018. Technical details on its development and blog posts related to the resource can be found here.

Published information on the project and resource can be found here:

Harding, S.D., Faccenda, E., Southan, C., Pawson, A.J., Maffia, P., Alexander, S.P.H., Davenport, A.P., Fabbro, D., Levi-Schaffer, F., Spedding, M. and Davies, J.A. (2020), **The IUPHAR Guide to Immunopharmacology: connecting immunology and pharmacology**. Immunology, 160: 10-23. doi:10.1111/imm.13175 [PMID:32020584]

Harding SD, Sharman JL, Faccenda E, Southan C, Pawson AJ, Ireland S, Gray AJG, Bruce L, Alexander SPH, Anderton S, Bryant C, Davenport AP, Doerig C, Fabbro D, Levi-Schaffer F, Spedding M, Davies JA; NC-IUPHAR. (2018) **The IUPHAR/BPS Guide to PHARMACOLOGY in 2018: updates and expansion to encompass the new guide to IMMUNOPHARMACOLOGY**. *Nucl. Acids Res.* **46** (Issue D1): D1091-D1106. doi: 10.1093/nar/gkx1121. [PMID:29149325]

GtoImmuPdb target and ligand curation

645 targets tagged as immuno-relevant, 457 have quantitative interaction data

1,403 ligands tagged as immuno-relevant, 318 of which are approved drugs. 1,040 of the immuno ligands have quantitative interaction data, 236 of which are approved drugs

Detailed lists on:

www.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp

This data set remains largely unchanged, as dedicated curation ceased at the end of the grant period. When time allows, coverage is updated/expanded as curators identify new target/ligand pairings that are relevant and pass the curation threshold.

The Guide to Malaria Pharmacology Database (GtoMPdb)

IUPHAR/MMV
Guide to MALARIA PHARMACOLOGY

The GtoMPdb has been developed as an extension to the main GtoPdb database, with the aim of providing optimised access for the malaria research community to the data in GtoPdb. The project was initiated in October 2017, with funding from Medicines for Malaria Venture (MMV; https://www.mmv.org/). The first official release of the GtoMPdb was in September 2019 and the conclusion of MMV funding was at the end of December 2021.

The GtoMPdb portal is available at www.guidetomalariapharmacology.org.

Blog posts related to the resource and technical reports on its development can be found here.

Published information on the project and resource can be found here:

Armstrong JF, Faccenda E, Harding SD, Pawson AJ, Southan C, Sharman JL, Campo B, Cavanagh DR, Alexander SPH, Davenport AP, Spedding M, Davies JA; NC-IUPHAR. (2019) **The IUPHAR/BPS Guide to PHARMACOLOGY in 2020: extending immunopharmacology content and introducing the IUPHAR/MMV Guide to MALARIA PHARMACOLOGY**. *Nucl. Acids Res.* Volume 48, Issue D1, D1006-D1021. https://doi.org/10.1093/nar/gkz951. PMID: 31691834.

GtoMPdb Target and Ligand Curation

The most recent database release (2023.1) contains:

- 136 ligands tagged as in GtoMPdb (selectable in PubChem, see section):

https://www.guidetomalariapharmacology.org/GRAC/LigandListForward?type=AntiMal&database=all

- 40 targets tagged as in GtoMPdb:

https://www.guidetomalariapharmacology.org/GRAC/FamilyDisplayForward?familyId=970

Target and Ligand Review

During the final 6 months of this project we worked with members of the Malaria Drug Accelerator (MalDA; https://www.malariada.org/), an international consortium whose goal is to identify novel druggable targets in *Plasmodium*, to update the 'Antimalarial targets' and 'Antimalarial ligands' families. MalDA provided target descriptions for 25 of our *Plasmodium* targets, allowing us to review the information we display for these targets and to curate any additional data. These target descriptions are also the basis of an IUPHAR review on recent advances in malaria pharmacology and the GtoMPdb resource (manuscript has been submitted and is under revision).

GtoMPdb Page View Analytics

Here is an analysis of page views for malaria content in GtoMPdb. The figures in the table below are taken from our Google Analytics for the period April 2022-March 2023. We analysed the number page views the portal home page received in addition to the malaria focussed lifecycle and species pages.

	Page Views	Page Views per month	Unique Page Views	Unique Page Views per month
Index	5414	451	3943	329
Malaria Species	438	37	282	24
Parasite Lifecycle	5342	445	3478	290

GtoMPdb at WCP2023

A presentation will be given at the 19th World Congress of Basic & Clinical Pharmacology 2023 as part of the Drug discovery and development for Malaria symposium.

General overview of database team activities

GtoPdb Team Interactions

For more details of previous and continuing interactions please see previous reports. Only significant changes since April 21 are reported below.

ELIXIR

Engagements 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.

As reported before, we have an entry in the ELIXIR bio-tools directory as one of the official UK ELIXIR Node Services and part of the Excelerate initiative.

Dr. Simon Harding attended the virtual ELIXIR-UK All-Hands Meeting held in September 2021.

Global Biodata Coalition

We have submitted an expression of interest to the Global Biodata Coalition's (GBC) Global Core Biodata Resource (GCBR) selection process (https://globalbiodata.org/global-core-biodata-resource-selection-process-2023-now-open/).

Public Engagement and Promotion

BPS/BHF Drug Targets in Cardiovascular Disease Webinar

A free-webinar was held on 18th April 2023, hosted by the British Society of Pharmacology and the British Heart Foundation on 'Drug Targets for Cardiovascular Disease: Developing a portal into the Guide to Pharmacology for Cardiovascular clinical and basic researchers.

The aim was to build on the work of the GtoPdb and bring together established leaders in the cardiovascular field to discuss the latest updates in drug development within their area, and the impact that nomenclature and access to tool compounds can have on this.

Presentations were made by Prof. Steve Alexander, Prof. Jamie Davies & Prof. Anthony Davenport

Pharmacology 2022

Pharmacology 2022 was held in Liverpool on 13-14 September 2022.

Dr. Simon Harding attend and gave a flash poster presentation on the The Award-Winning IUPHAR/BPS Guide to PHARMACOLOGY: curating pharmacology for COVID-19, malaria and antibacterials

https://meetings.bps.ac.uk/bpsevents/frontend/reg/absViewDocumentFE.csp?documentID=1560&eventID=68

Prof. Steve Alexander presented a poster on Trends in new drug approvals in 2021 and the GuidetoPharmacology.org database

https://meetings.bps.ac.uk/bpsevents/frontend/reg/absViewDocumentFE.csp?documentID=1564&eventID=68

BioIT World Europe 2022

BioIT World Europe Conference and Expo was held in Berlin on 18-19th October 2022.

Dr. Chris Southan presented on FAIR Obstacles for Curating SARS-CoV-2M-Protease Inhibitors. https://www.bio-itworldeurope.com/data-management#2

Publications

Listed here are our most recent/upcoming publications.

The next edition (6th) of the Concise Guide to Pharmacology (2022/23) is due for submission in May 2023 with online publication expected In late September 2023 the 5th edition of the Concise Guide to Pharmacology (2021/22) was published:

We anticipate submitting an updated database paper to the annual Nucleic Acids Research Database Issue, also in September 2023.

An IUPHAR review 'Advances in Malaria Pharmacology and the online Guide to MALARIA PHARMACOLOGY: IUPHAR Review X' is under revision following submission to BJP.

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.

Twitter

@GuidetoPHARM has, as of 5th April 2023, output 2,442 tweets; followers have increased to 5,080 from 4,938 in November 2022. The value of this platform continues to increase 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.

Most of our Hot Topics are now first picked up from Twitter. 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 404 followers, up from 386 in November 2022.

Guide to Pharmacology Blog

Our Edinburgh blog (http://blog.guidetopharmacology.org/) has received over 1,100 visitors between Nov 2022 and Mar 2023 - an average of 222 visitors per month. Over the same period there have been 1,540 views of our blog, which gives an average views per visitor of 1.38.

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 November 2022 we have added 34 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.