IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

November 2022

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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 2022. Previous reports are online for Apr 2022, Nov 2020, April 2021 and Nov 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).

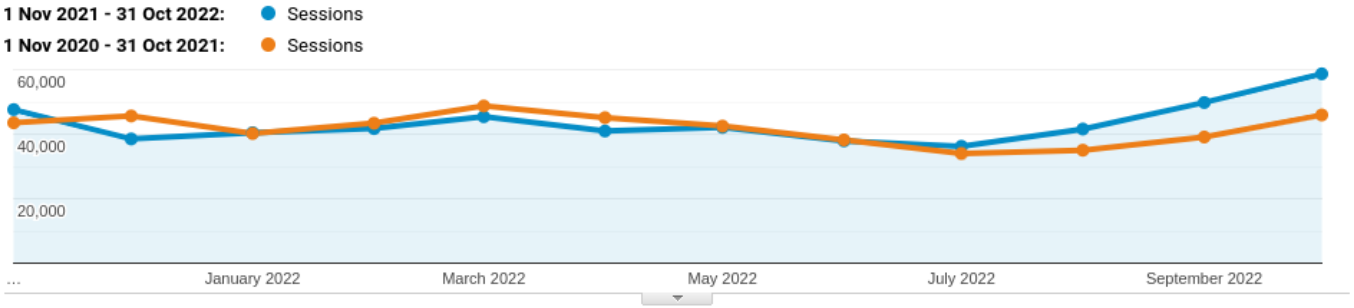
Key Updates / Notifications

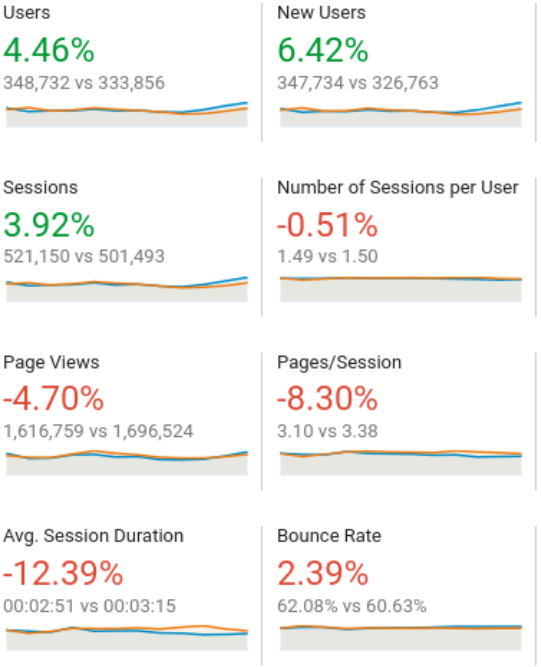
- 2 Database release (2022.2 & 2022.3)
    - 262 new ligands added (40 approved drugs)
    - 10 new targets added
    - 308 new ligand-target interactions
        - 188 ligands, of which 174 are new ligands
        - 192 targets, of which 10 are new targets

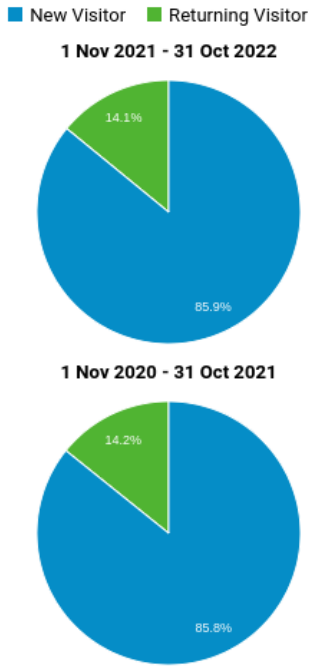
- ~29,000 Users per month (~43,000 sessions)

GtoPdb Website Analytics

GtoPdb Website Access Statistics







Graphs comparing visitors to guidetopharmacology.org for the 12 months from November 2021 to October 2022, with the previous 12 months.

Monthly statistics	**Nov 2021 - Oct 2022 (previous 12 months)**
Sessions	43,429 (41,791)
Users	29,061 (27,821)
Page views	134,729 (141,377)
Pages / Session	3.10 (3.38)
Avg. Session Duration	00:02:51 (00:03:15)

	Country	Sessions	Sessions
		521,150 % of Total: 100.00% (521,150)	521,150 % of Total: 100.00% (521,150)
1.	United States	131,342	25.20%
2.	United Kingdom	54,530	10.46%
3.	China	48,599	9.33%
4.	India	37,668	7.23%
5.	Japan	16,355	3.14%
6.	Germany	16,002	3.07%
7.	Australia	14,456	2.77%
8.	Canada	13,519	2.59%
9.	South Korea	11,478	2.20%
10.	France	9,122	1.75%
11.	Italy	8,369	1.61%
12.	Mexico	8,233	1.58%
13.	Spain	8,105	1.56%
14.	Netherlands	7,308	1.40%
15.	Russia	7,042	1.35%
16.	Brazil	6,607	1.27%

Total website sessions connecting to the Guide to PHARMACOLOGY website split by country.
Data taken from 01 November 2021 to 31 October 2022.

Access to GtoPdb is dominated by the UK and USA (~35% of sessions), which is a slight increase from our previous report, with the vast majority of that increase coming from the USA. Sessions from China have also increased slightly and are nearly on a par with the UK. In the last 12 months, a total of 215 different countries recorded at least one session and 54 countries recorded 1000 or more sessions.

Download Statistics

Yearly period 01 Nov 2021-31 Oct 2022 (comparing with 01 Nov 2020 - 31 Oct 2021)

Google Analytics: Comparison of Downloads

Event Category: Downloads

	Count
2020-2021	4,033
2021-2022	**4,218**
Change	+4.59%

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

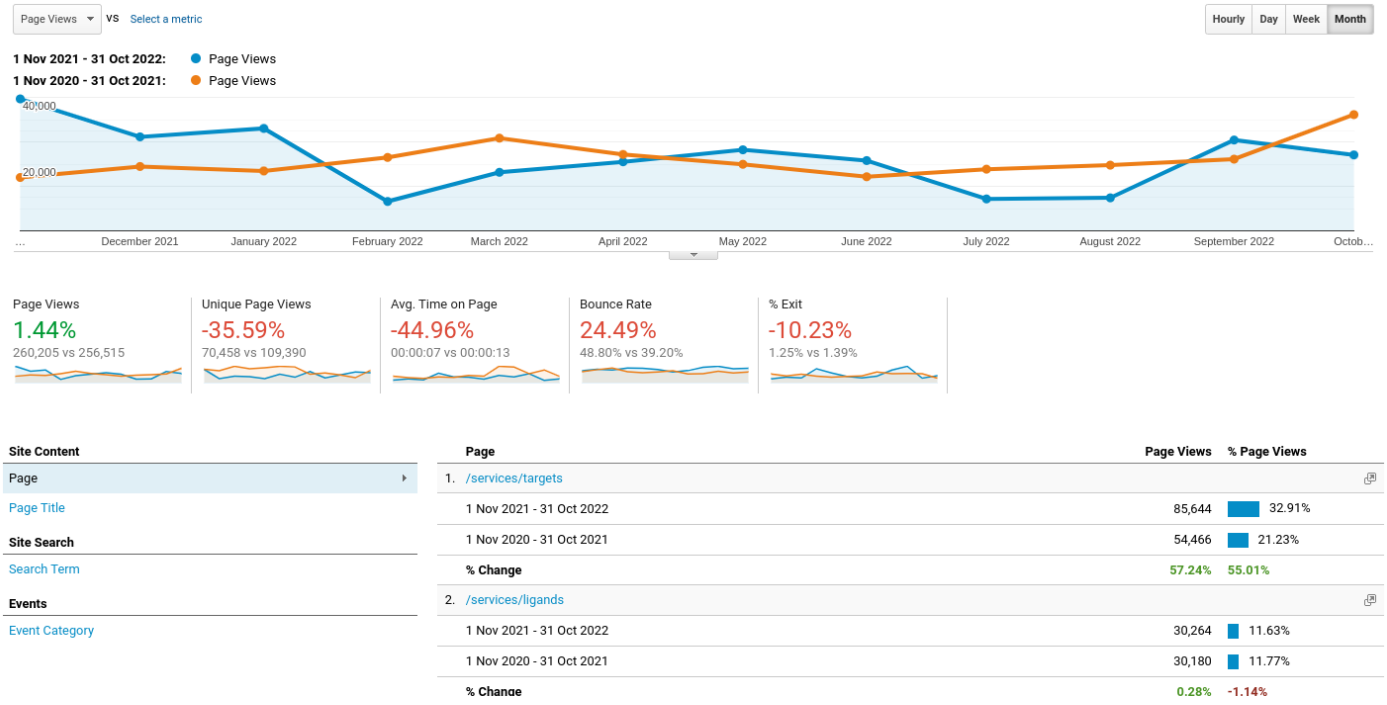
A more specific breakdown is shown here:

	2021-2022	*2020-2021*	**Change**
Targets CSV/TSV files	**1,395**	*1,224*	**13.97%**
Interactions CSV/TSV file	**382**	*384*	**-0.52%**
Ligands CSV/TSV file	**1,264**	*1,141*	**10.78%**
*Covid ligand/target files **	**26**	*89*	**-70.79%**
UniProt Mapping file	**115**	*148*	**-22.30%**
HGNC mapping file	**119**	*135*	**-11.85%**
PostgreSQL	**179**	*189*	**-5.29%**

* This download was available from April 2020, and downloads significantly peaked between April-May 2020.

Web Services

We have tracked our web-services since March 2017. Calls to the web-service are generally from client computers to our server and are not recorded in the same way as visits to our website. Therefore, we can not resolve these to specific users, locations or number of visits but we can record hits for each distinct URL.



The image above shows that there were approximately **260,205 total page views** over the year, which is very similar to the previous year (256,515).

GtoPdb Content

These database statistics were compiled from our 13th October 2022 release (v2022.3). 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	1254
Transporters	555
Other protein targets	220
Targets with ligand interactions	1873
Targets with quantitative ligand interactions	1627
Targets with approved drug interactions	698
Primary Targets with approved drug interactions	344
Total number of targets	**3007**

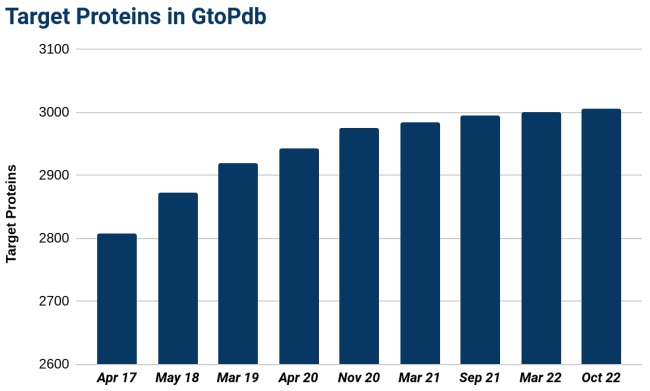
Ligands	Number of Ligands
Synthetic organics	8026
Metabolites	518
Endogenous peptides	811
Other peptides including synthetic peptides	1464
Natural products	345
Antibodies	329
Inorganics	39
Approved drugs	1797
Withdrawn drugs	91
Drugs with INNs	3089
Labelled ligands	634
Unique PubChem CIDs (total CID links)	8462 (8626)
Ligands with target interactions	9641
Ligands with quantitative interactions (approved drugs)	8517 (1057)
Ligands with clinical use summaries (approved drugs)	3234 (1782)
Total number of ligands (PubChem SIDs)	**11,532**
Number of binding constants curated from the literature	**19,267**

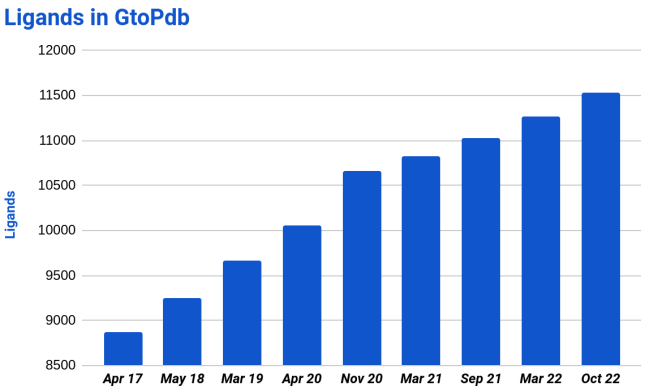
GtoPdb Entity Growth

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.

	Apr 17	May 18	Mar 19	Apr 20	Nov 20	Mar 21	Sep 21	Mar 22	Oct 22
Target protein IDs	**2808**	**2872**	**2920**	**2943**	**2976**	**2985**	**2995**	**3000**	**3007**
Ligands total	**8872**	**9251**	**9662**	**10053**	**10659**	**10821**	**11025**	**11271**	**11532**
Approved drugs	1322	1364	1421	1471	1614	1643	1689	1734	1787
Antibodies	212	240	255	270	295	303	317	333	329
Peptides	2063	2092	2122	2150	2180	2206	2226	2251	2275

Synthetic small molecules	5729	6048	6401	6816	7303	7428	7593	7797	8026
PubChem SIDs	8831	9251	9662	10053	10659	10821	11025	11271	11532
PubChem CIDs	6813	7109	7407	7483	7994	8102	8262	8462	8633
References	-	15851	16864	17695	-	18351	18624	18972	19267





GtoPdb Updates

Targets

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

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 2022.3 (Oct 2022) and 2022.1 (Mar 2022) database releases.

	New Ligands	Updated Ligands	Total Ligands (2022.3)	Total Ligands (2022.1)
Approved Drugs	40	13	1787	1734

WHO Essential Medicines	3	0	296	293
Ligands with Quantitative Interaction Data	164	1	8517	8352
Antimalarials	0	1	135	134
Antibacterials	45	1	351	305
COVID-Relevant Ligands	9	4	97	84

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.

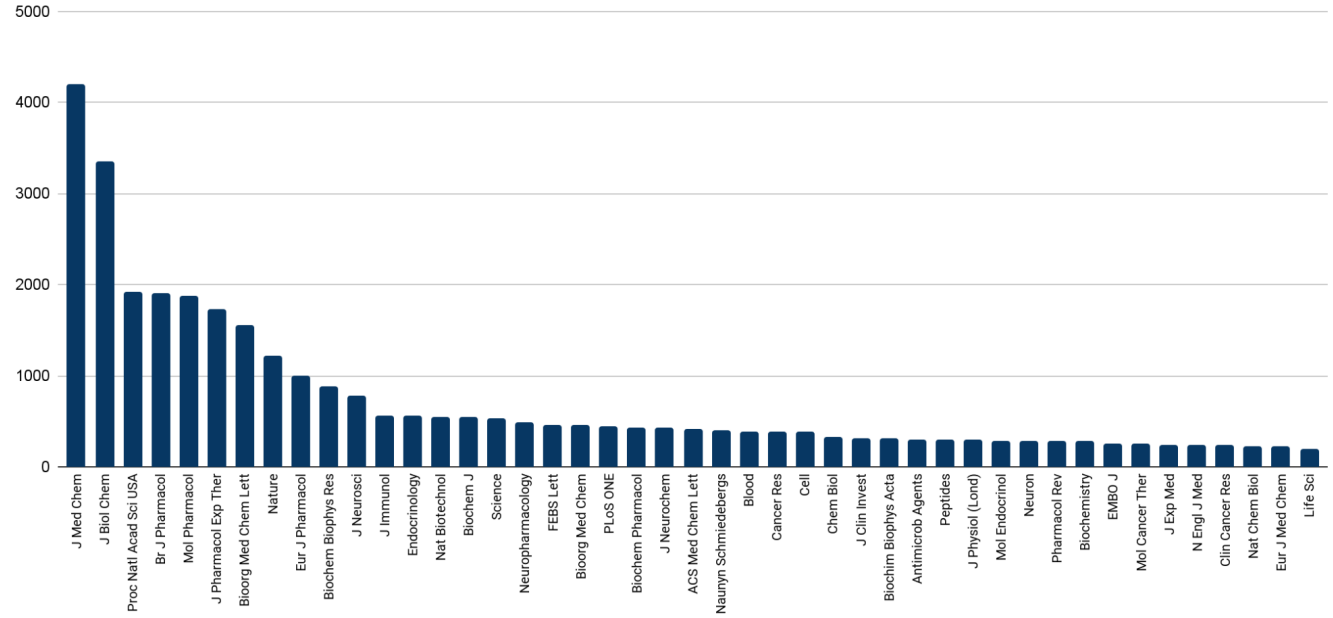
Comment Type	New Ligands	Updated Ligands
General	261	103
Clinical Use	130	75
Bioactivity	142	21
MOA	13	2

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	4206
J Biol Chem	3353
Proc Natl Acad Sci USA	1920
Br J Pharmacol	1902
Mol Pharmacol	1875
J Pharmacol Exp Ther	1735
Bioorg Med Chem Lett	1555
Nature	1220
Eur J Pharmacol	1001
Biochem Biophys Res Commun	885
J Neurosci	782
J Immunol	569
Endocrinology	560

Nat Biotechnol	555
Biochem J	554
Science	531



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 Nov 2022 we have **115 unique entries** in our table of COVID-19 relevant ligands, of these, **104 have ligand summary pages** in GtoPdb, **59 of which are approved drugs**.

There are 11 targets on the page, 9 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 278 hits: 221 ligands and 51 targets, plus 4 hits within target family comments/introductions).

We have expanded coverage of CoV proteins to include more recent evidence of potential druggable targets

- Nsp15 (a uridine specific endoribonuclease) that disrupts activation of host cell dsRNA sensors by degrading viral poly(U) RNA that can generate dsRNA complexes with host poly(A) RNA tails. The uracil derivative tipiracil is an inhibitor.

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 our collaboration with Antibiotic DB (ADB; www.antibioticdb.com) will continue with funding from the Global Antibiotic Research and Development Partnership (GARDP; https://gardp.org/). Through our interaction with ADB, GtoPdb provides chemistry and pharmacology for the antibacterial compounds curated within ADB. Currently we have **351 ligands** tagged in GtoPdb as 'antibacterial' and **326** of these have links to compounds at ADB.

For further information about our work with ADB please refer to previous Database Reports (November 2020, April 2021, November 2021, April 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.

GtoPdb Web-Application Developments

Server Update

We are in the process of setting up new servers to host the Guide to PHARMACOLOGY database and web-application and migrating data over. This is essential infrastructure work for us, and means an update in the version of PostGresQL we will be using to version 12 (from 9.2).

We are setting up two new servers, one for our development/test database and web-server and one to run the live database and web-server.

This upgrade is essential so that we can continue to support tools such as ligand activity graphs and pharmacology search.

As part of this update we are now using the Chemistry Development Kit (CDK) to power our chemical structure search across the PostGresQL database. Previously, we had maintained an Oracle database that contained our chemical structures and had a chemical search plugin. The move to CDK means we can power the search directly on the PostGresQL database.

Currently the new test server is up and running - hosting our development database and web-application.

Work on-going to get the new live server running - expect by the next database release or early 2023.

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.

As mentioned above, we now use CDK to power our chemical structure search (). We also use features of CDK to calculate dphysico-chemcial properties of ligands in GtoPdb

Ligand Download Files

We have added a new download file which lists the physico-chemical properties of the ligands in GtoPdb. This file contains 9,125 ligands for which we have calculated the physio-chemical properties. Properties cannot be calculated for ligands without SMILES structures, such as some of the larger peptides. The data is calculated using the Chemistry Development Kit (CDK)

We have also continued to develop the endogenous/natural ligand pairing file. This file contains all ligands and ligand subunits considered endogenous and the protein target they interact with. The file includes

ligand and target UniProt and Ensembl IDs, and also includes indications of the rank potency of the ligand and any more detailed curatorial comments. A separate (detailed) file also includes quantitative interaction data for the ligand-target pairings. We thank Prof. David Gloriam's research group at the University of Copenhagen and Dr. Joanna Sharma (Novo Nordisk) for their collaboration and advice in preparing these files.

All download files on the GtoPdb website are available in our downloads page.

Connectivity

Sites Linking Into GtoPdb

Google Search Console allows us to pinpoint where external links into the Guide to Pharmacology are coming from. It counts around 530,000 unique external links into GtoPdb.

The following table shows 12 external sites that have significant links into GtoPdb. This covers Wiley, European PMC, nih.gov (PubChem/PubMed/PMC/Pharos), Wikipedia, EBI (ChEMBL), genenames.org (HGNC), UniProt and GPCRdb. Linking pages are the number of pages at the site that have a link to GtoPdb. Target pages are the unique count of GtoPdb pages the site links to.

Site	Linking Pages	Target Pages
nih.gov	65818	5656
wiley.com	65444	4396
orpha.net	17602	757
wikipedia.org	14490	2338
europepmc.org	10645	2546
ebi.ac.uk	6742	2331
gpcrdb.org	4316	945
reactome.org	3840	1334
genecards.org	2456	1568
drugcentral.org	1835	1302
uniprot.org	1665	820
genenames.org	728	647

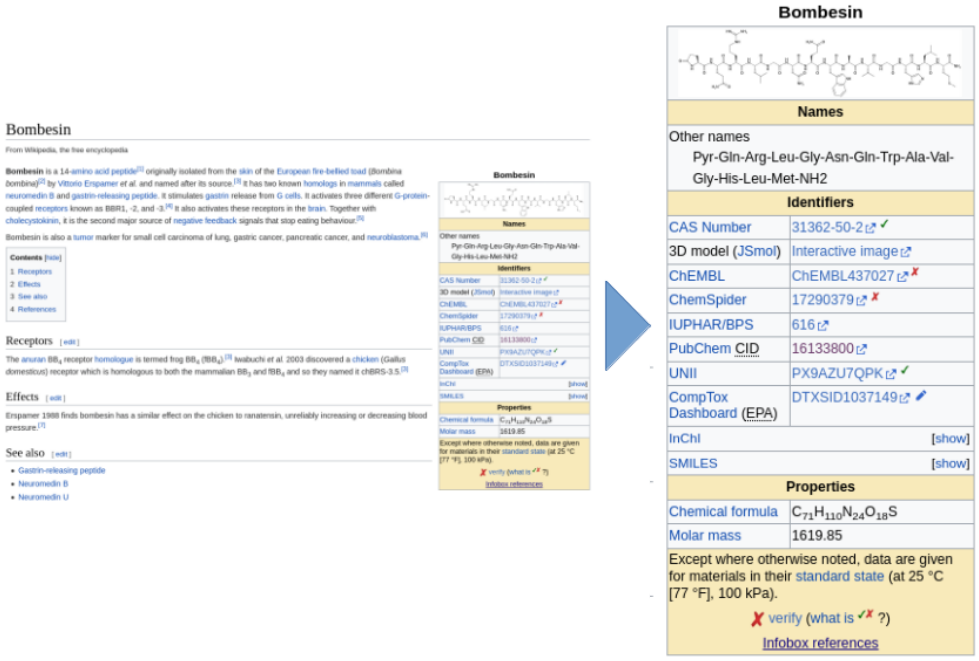
Links to other resources - Ligands

GtoPdb has built many collaborative connections with other resources, many of which are reciprocal. For our ligands, the table below shows the number of ligands 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 (8833). Our recent and ongoing work with AntibioticDB has built links between antibacterials in GtoPdb (356) and AntibioticDB (https://antibioticdb.com/). We have also recently worked with Reactome, linking GtoPdb ligands with relevant Reactome Drug and Reaction entities. 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' (see screenshot below).

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

GtoPdb ligands with links external sites	
Site	**Ligands**
PubChem CID	**8833**
ChEMBL	**6167**
Reactome	**344**
AntibioticDB	**356**
IMGT/mAb-DB *	**318**
DrugCentral	**1640**
Wikipedia	**3017**
*** not reciprocal**	



Links to other resources - Targets

For our targets, the table below shows the number of target links to each of the named resources. We use UniProtKB identifiers as our primary protein identifier, so the 7567 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.

GtoPdb target links to external sites (reciprocal)	
Site	**Target Links**
GPCRdb	943
ChEMBL	3623
Resolute (SLC)	421
BioParadigms (SLC)	393
HGNC	3025
NCBI (Entrez) Gene	8576
Ensembl Gene	8681
UniProt	7567

PubChem Statistics for GtoPdb, GtoImmuPdb and GtoMPdb

The stats for the 2022.3 release (with 2022.1 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 11539 (11277).
2. Those that have defined chemical structures are merged into 9441 (9188) Compound Identifiers, CIDs (i.e. small molecules and peptides below ~ 70 residues)
3. From our 9441 CIDs 7573 have vendor matches
4. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND gtopdb_approved [Comment] now retrieves 1787 SIDs (1734) which link to 1586 approved drug CIDs
5. Of our SIDs, 1382 (1359) are tagged in GtoImmuPdb and 340 (333) of these are approved drugs
6. Of our CIDs 957 are tagged in GtoImmuPdb
7. Of our SIDs, 135 are tagged in GtoMPdb and 25 of these are approved drugs
8. Of our CIDs 133 are tagged in GtoMPdb
9. We have 2249 (2147) structures that ChEMBL does not have, 6755 (6554) not in DrugBank.
10. 337 (348) 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.
11. We continue to curate clinical monoclonal antibodies with the PubChem Substance select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] gtopdb_antibody" returning 329 SIDs. Adding "gtopdb_approved" gives 121.
12. We have now included an **antibacterial tag in our PubChem upload**, the select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND gtopdb_antibacterial[All Fields] " returns 350 SIDs, 139 of which are tagged as approved drugs.

A useful guide/summary of GtoPbd's PubChem substance tagging is given in Dr. Chris OSuthans 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

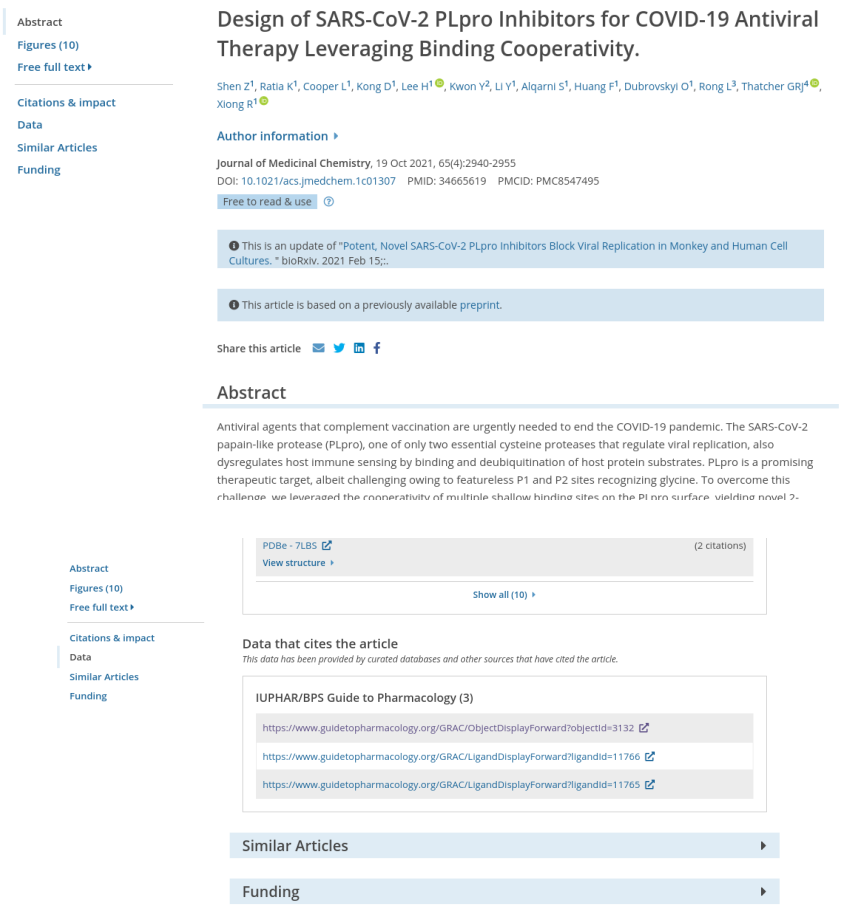
GtoPdb maintains sets of links in the NCBI LinkOut service, to the Protein, Nucleotide, Gene and PubMed databases. Our links are updated frequently. Below is the count of all NCBI database records that contain

'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	5957
Nucleotide	5903
Gene	8508
PubMed	30,626 (https://pubmed.ncbi.nlm.nih.gov/?term=loprovguidpharm[SB])

Europe PMC

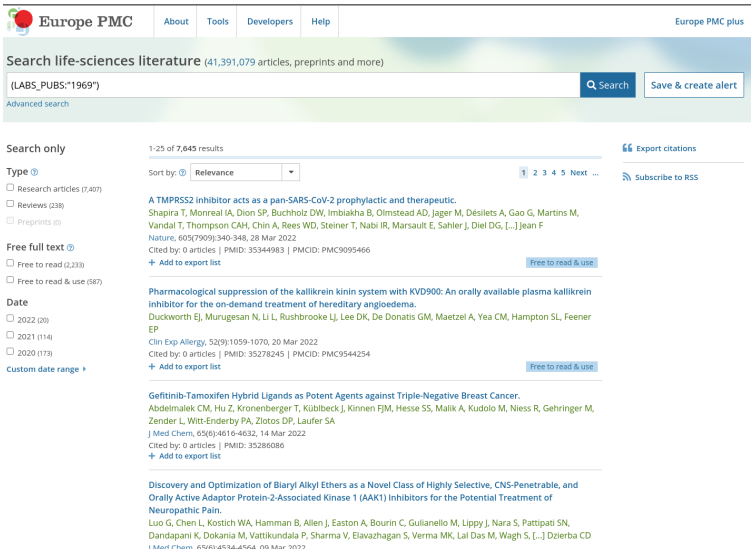
GtoPdb maintains records in the Europe PMC External Links Service. Unlike the larger set of NCBI Outlinks, these publication links are restricted to papers from which GtoPdb interaction data have been curated. These link targets and/or ligands mentioned in the article back to GtoPdb detailed pages.



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 November 2022 there were 7,645 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 86 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 1,202 citations (according to EPMC) or 1,280 (according to PubMed). This thus overtakes our 2016 paper (PMC4702778) with 917 (EMPC) or 927 (PubMed) citations, and the 2014 paper (PMC3965070) that reached 707 / 733.

The "Concise Guide" citations are currently led by 2017/18 Enzymes (PMC5650666) at 560 followed by 2015/16: Enzymes (PMC4718211) at 512 and 2013/14: G protein-coupled receptors (PMC3892287) at 471.

SARS-CoV-2 Review

Our BJP SARS-Cov-2 review has acquired 48 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 JAF, 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 2022_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 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

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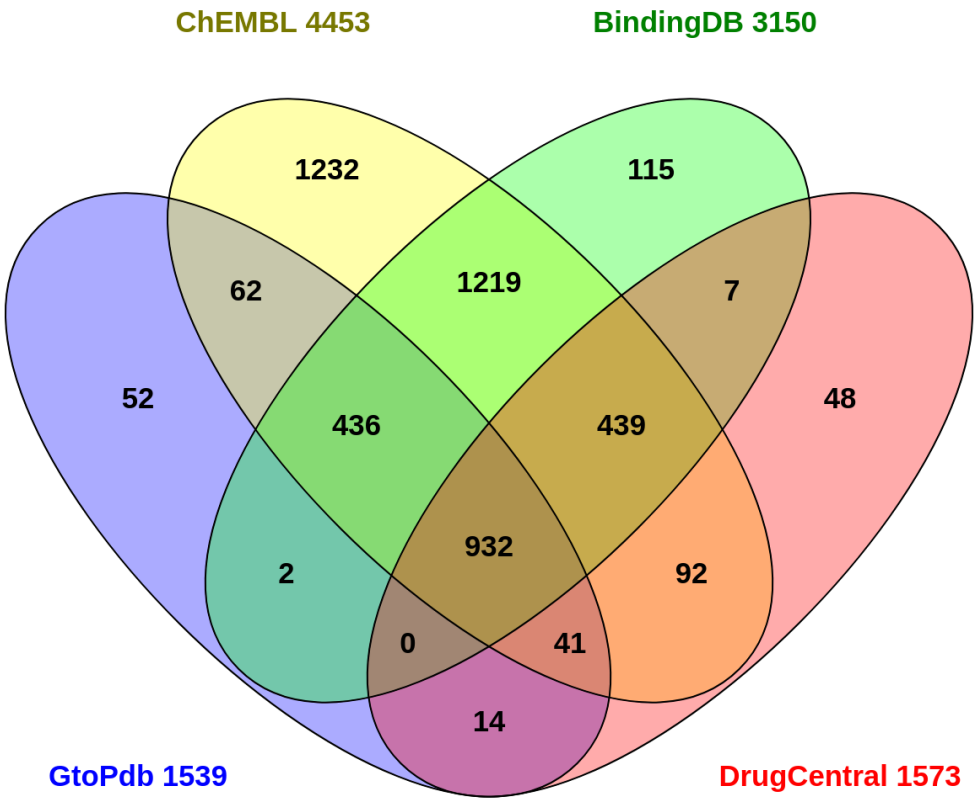
ID	Name	Abbreviation	Category	Statistics
DB-0019	Drug and drug target database	DrugBank	Chemistry databases	5,192 UniProtKB entries 4,741 reviewed UniProtKB entries 451 unreviewed UniProtKB entries
DB-0127	BindingDB database of measured binding affinities	BindingDB	Chemistry databases	8,349 UniProtKB entries 6,291 reviewed UniProtKB entries 2,058 unreviewed UniProtKB entries
DB-0174	ChEMBL database of bioactive drug-like small molecules	ChEMBL	Chemistry databases	9,622 UniProtKB entries 8,488 reviewed UniProtKB entries 1,134 unreviewed UniProtKB entries
DB-0182	IUPHAR/BPS Guide to PHARMACOLOGY	GuidetoPHARMACOLOGY	Chemistry databases	2,141 UniProtKB entries 2,120 reviewed UniProtKB entries 21 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	2,723 UniProtKB entries 2,564 reviewed UniProtKB entries 159 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 2022_04 Swiss-Prot entries 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 52 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 6th birthday on 1st April 2022.

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

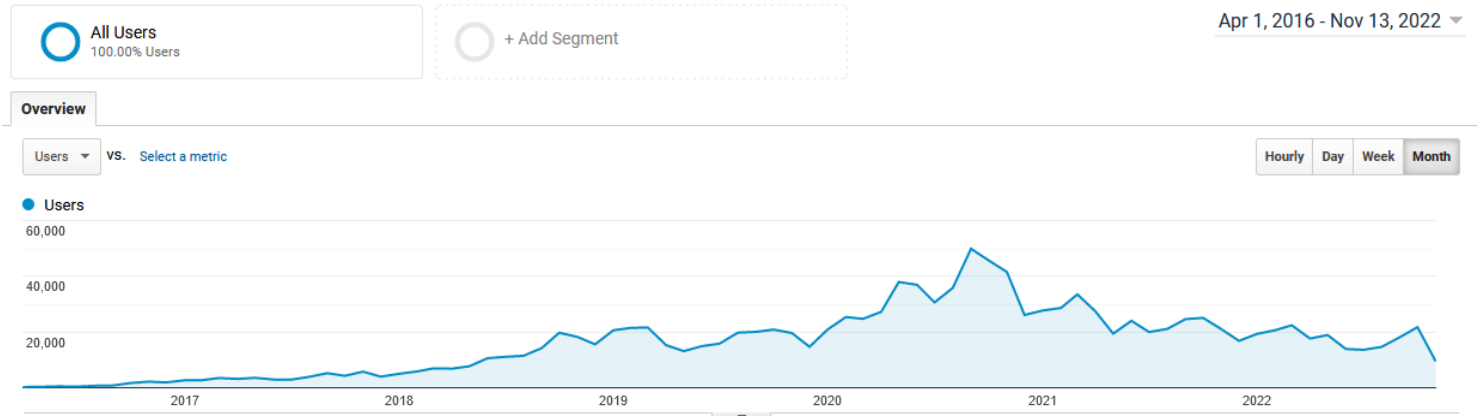
Succession Planning

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 held our first combined PEP/IUPHAR-ed meeting in March, with PEP being the focus. These meetings will rotate around reports from PEP, IUPHAR-ed and the Core Concepts working group. The next meeting is on 7th December 2022.

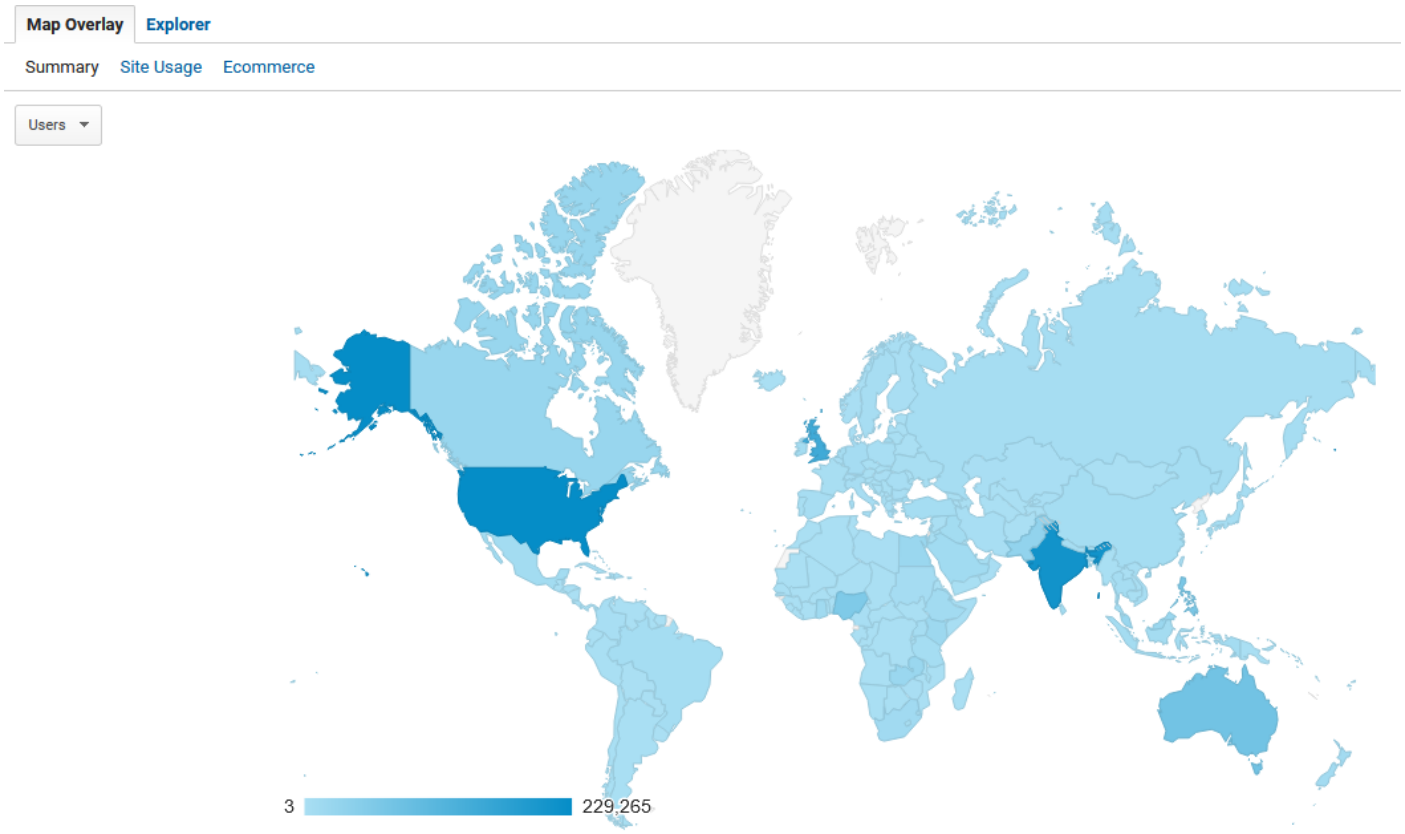
Google Analytics data charts for PEP site usage since 1st April 2016

Google Analytics shows that user sessions continue to average >20K/month. Accumulated page views total >1.5 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.

Potential additions for the PEP website

- Considering a new top level section on the home page to host 'Teaching Resources', which would house a curated selection of resources that would be of benefit to those teaching pharmacology. Links to a couple of examples (created by Kelly Karpa) are included in the Clinical Pharmacology/Clinical pharmacokinetics module as 'Pharmacokinetics exercises (for teaching)' https://www.pharmacologyeducation.org/clinical-pharmacology/clinical-pharmacokinetics
- Also evaluating the possibility of hosting quizzes for pharmacology students, as learning resources, if a suitably effective Drupal module can be implemented.

These types of revisions require the time of the development team, and their delivery will come at some expense for the PEP finances. We are waiting for proposals and costings.

Social Media

PEP has ~1700 followers of our twitter handle, @PharmacologyEd.

Meetings

An Education Satellite meeting is being planned for the 2 days in advance of WCP2023 (Sat/Sun 1st/2nd July 2023). Through collaboration this will be 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

644 targets tagged as immuno-relevant, 496 have quantitative interaction data

1382 ligands tagged as immuno-relevant, 305 of which are approved drugs. 1018 of the immuno ligands have quantitative interaction data, 225 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.

Immuno Process Data

The table below summarises the unique targets (UniProtKB) annotated to each category and the total target-GO annotations (data here is from the 2022.3 release).

Process Category	**GtoPdb Human UniProtKB**	**Target-GO annotations**
Barrier integrity	61	80
Inflammation	575	1436
Antigen presentation	148	222
T cell (activation)	236	530

B cell (activation)	190	335
Immune regulation	536	1399
Tissue repair	47	49
Immune system development	219	383
Cytokine production & signalling	474	1386
Chemotaxis & migration	249	524
Cellular signalling	420	1100

Immuno Cell Type Data

The table below shows the top-level cell type categories used in GtoImmuPdb along with the Cell Ontology (CO) terms mapped to each category. The Cell Ontology provides the formalised vocabulary against which we annotate targets to cell type associations.

Cell Type Category	**Cell Ontology Terms**	**Targets annotated**
B cells	CL:0000945 lymphocyte of B lineage	58
T cells	CL:0000789 alpha-beta T cell CL:0000815 regulatory T cell CL:0000911 effector T cell	85
Dendritic cells	CL:0000451 dendritic cell	44
Other T cells	CL:0000798 gamma-delta T cell CL:0000814 mature NK T cell CL:0000898 naive T cell CL:0000940 mucosal invariant T cell	4
Macrophages & monocytes	CL:0000235 macrophage CL:0000576 monocyte	60
Granulocytes	CL:0000094 granulocyte	48
Natural killer cells	CL:0000623 natural killer cell	31
Mast cells	CL:0000097 mast cell	40
Innate lymphoid cells	CL:0001065 innate lymphoid cell	6
Stromal cells	CL:0000499 stromal cell	1

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 (2022.3) contains:

- 135 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 review).

GtoMPdb Page View Analytics

Here is a detailed analysis of page views for malaria content in GtoMPdb. The figures in the table below are taken from our Google Analytics for the period November 2021 - October 2022. We analysed the number page views malaria tagged targets, ligands and families received in addition to the malaria focussed lifecycle and species pages.

Total shows over 23,733 unique views (1,887 per month).

	Page Views	Page Views per month	Unique Page Views	Unique Page Views per month
Index	4044	225	3266	181.4
Targets	3765	314	2448	204
Ligands	14012	1168	10708	892
Families	3643	304	1932	161
Malaria Species	514	43	328	27
Parasite Lifecycle	5982	499	5051	421
	31960	**2551**	**23733**	**1887**

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 continue 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.

Public Engagement and Promotion

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

hiddenREF Award

We are pleased that in September 2021 the IUPHAR/BPS Guide to PHARMACOLOGY was given a hidden REF award in the category ‘applications of research’.

The hidden Ref (https://hidden-ref.org) is a national 'competition', supported by publishers, learned societies etc. (https://hidden-ref.org/supporters/) , designed to celebrate and recognise the range of important research achievements that may not fit neatly into a REF submission.

"The ways in which the research impact is judged overlooks many of the people who are vital to the success of research. It's only by recognising everyone who is vital to the conduct of research that we will create an environment in which to advance it."

We are of course very grateful to receive this award, and our thanks go to the hidden REF committees.

Being recognised in this way is a testament to the hard work of the entire Guide to PHARMACOLOGY team, both past and present, who's vision and dedication has provided the research community with such an invaluable resource.

Publications

Listed here are our most recent publications.

In late September 2021 the 5th edition of the Concise Guide to Pharmacology (2021/22) was published:

Alexander SP, Kelly E, Mathie A, et al. . THE CONCISE GUIDE TO PHARMACOLOGY 2021/22: Introduction and Other Protein Targets. Br J Pharmacol. 2021;178 Suppl 1:S1-S26. doi:10.1111/bph.15537. PMID: 34529830

Please view the table of contents for all chapters of CGTP 2021/22.

In October 2021 we published 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.

All nine authors on the NAR publication above have made the Clarivate "Highly Cited" list for 2022, consolidating from previous years listings for many of them.

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 18th November 2022, output 2,409 tweets; followers have increased to 4,938 from 4,658 in April 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.

Our tweet announcing the latest database release (made on 31st March) reached 948 impressions with an engagement rate of 3%.

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 386 followers, up from 344 in April 2022.

Guide to Pharmacology Blog

Our Edinburgh blog (http://blog.guidetopharmacology.org/) has received over 1,600 visitors in 2022, which is similar to the number of visitors over the same period in 2021 (Jan-mid-Nov 1,665). Our average views per visitor remains stable at 1.62, slightly down from 1.65.

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 April 2022 we have added 36 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.