IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

April 2022

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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 2021. Previous reports are online for 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).

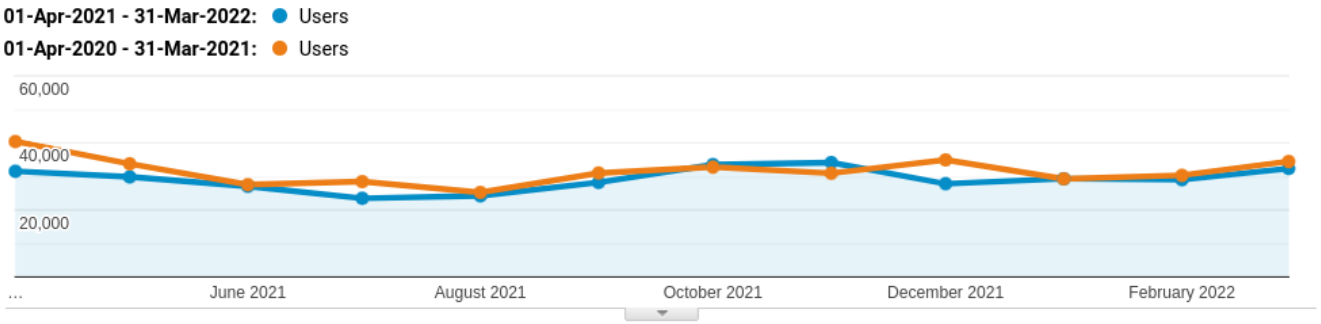
Key Updates / Notifications

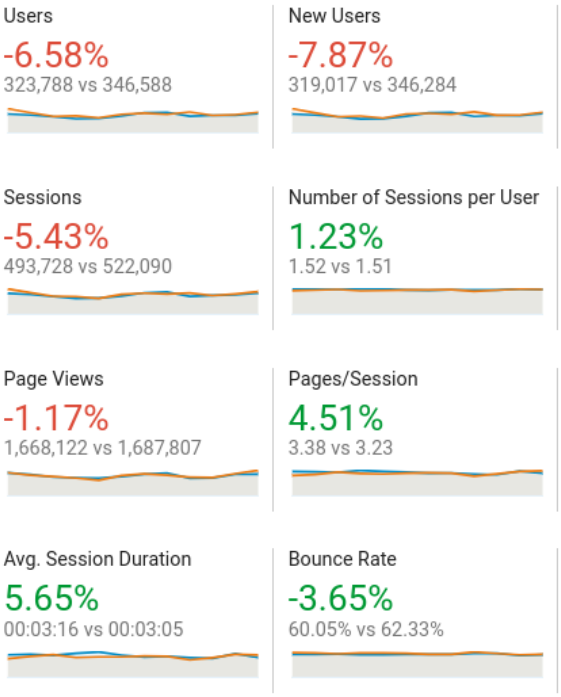
- 2 Database release (2021.4 & 2022.1)
    - 247 new ligands added
    - 6 new targets added
    - 362 new ligand-target interactions
        - 218 ligands
        - 181 targets (5 of which are ligand targets)
        - 2 whole organism assays

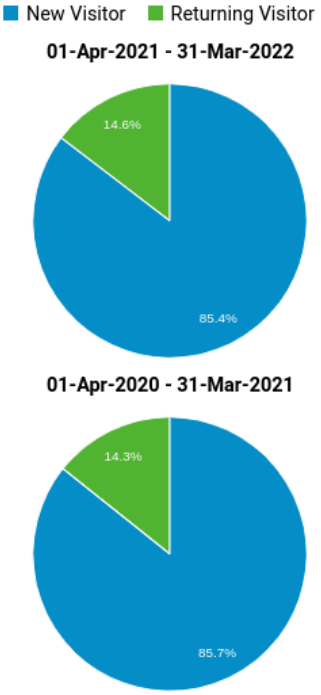
- Received Hidden REF Award
- ~27,000 Users per month (~41,000 sessions)

GtoPdb Website Analytics

GtoPdb Website Access Statistics







Graphs comparing visitors to guidetopharmacology.org for the 12 months from April 2020 to March 2021, with the previous 12 months.

Monthly statistics	**April 2020 - March 2021 (previous 12 months)**
Sessions	41,144 (43,508)
Users	26,982 (28,882)
Page views	139,010 (140650)
Pages / Session	3.38 (3.23)
Avg. Session Duration	00:03:16 (00:03:05)

	Country	Sessions	Sessions
		493,728 % of Total: 100.00% (493,728)	493,728 % of Total: 100.00% (493,728)
1.	United States	109,904	22.26%
2.	United Kingdom	54,586	11.06%
3.	China	44,031	8.92%
4.	India	40,764	8.26%
5.	Germany	16,062	3.25%
6.	Japan	15,937	3.23%
7.	Australia	14,052	2.85%
8.	Canada	12,652	2.56%
9.	South Korea	10,850	2.20%
10.	France	9,060	1.84%

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

Access to GtoPdb continues to be dominated by the UK and USA (~33% of sessions), but has fallen slightly in both these regions. Conversely, access for both China and India has increased, both seeing ~20% in sessions. In the last 12 months, a total of 215 different countries recorded at least one session and 55 countries recorded 1000 or more sessions.

Download Statistics

Yearly period 01 Apr 2021-31 Mar 2022 (comparing with 01 Apr 2020 - 31 Mar 2021)

Google Analytics: Comparison of Downloads

Event Category: Downloads

	Count
2020-2021	4,339
2021-2022	**3,982**
Change	-8.23%

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	**1,377**	*1,510*	**-8.8%**
Interactions CSV/TSV file	**365**	*432*	**-15.5%**

Ligands CSV/TSV file	**1,094**	*1,197*	**-8.6%**
*Covid ligand/target files **	**47**	*202*	**-76.7%**
UniProt Mapping file	**127**	*190*	**-33%**
HGNC mapping file	**126**	*152*	**-17%**
*PostgreSQL***	**186**	*190*	**-2.1%**

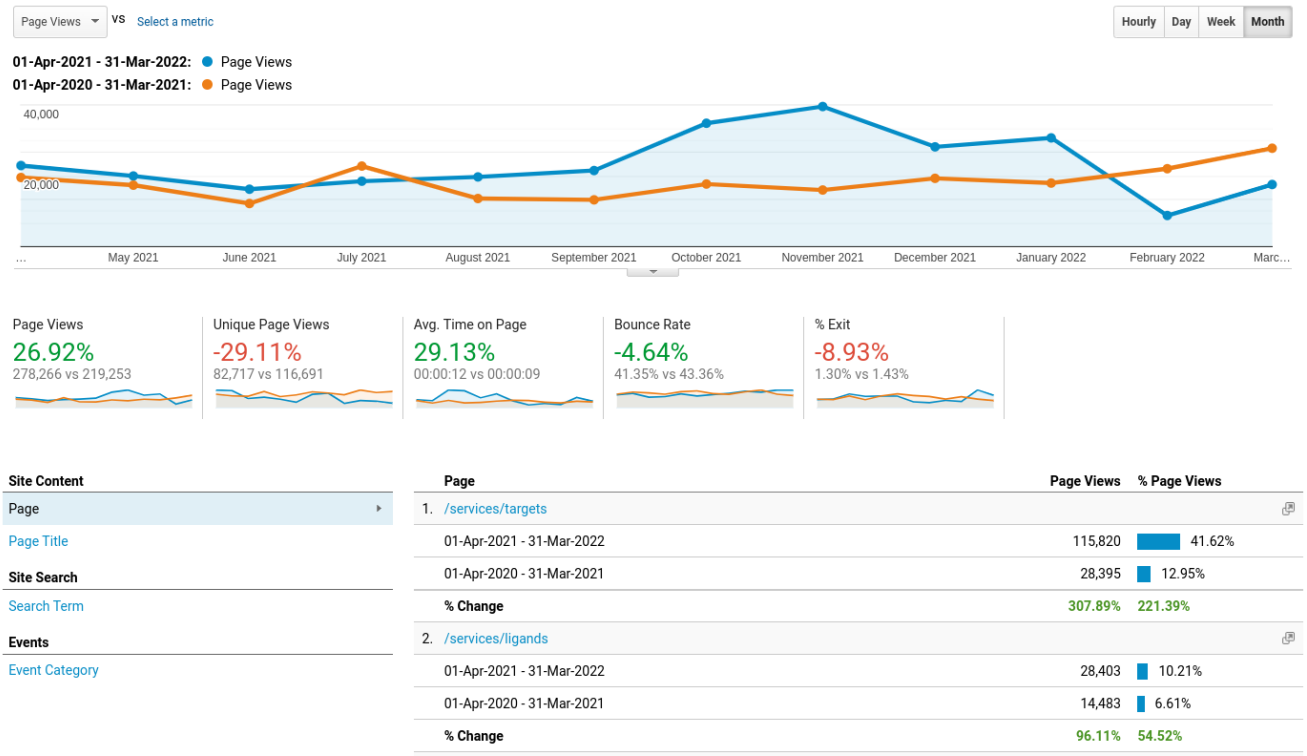
* This download was available from April 2020, and downloads significantly peaked between April-May 2020.

** Total downloads of PostgreSQL database dump files (versions 2020.1 onwards).

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 below shows that there were approximately **278,266 total page views** over the year, which is an increase of ~26% on the previous year (219,253).



Traffic to GtoPdb web services over the past year

GtoPdb Content

These database statistics were compiled from our 31st March 2022 release (v2022.1). 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	1248
Transporters	555
Other protein targets	219
Targets with ligand interactions	1860
Targets with quantitative ligand interactions	1607
Targets with approved drug interactions	693
Primary Targets with approved drug interactions	342
Total number of targets	**3000**

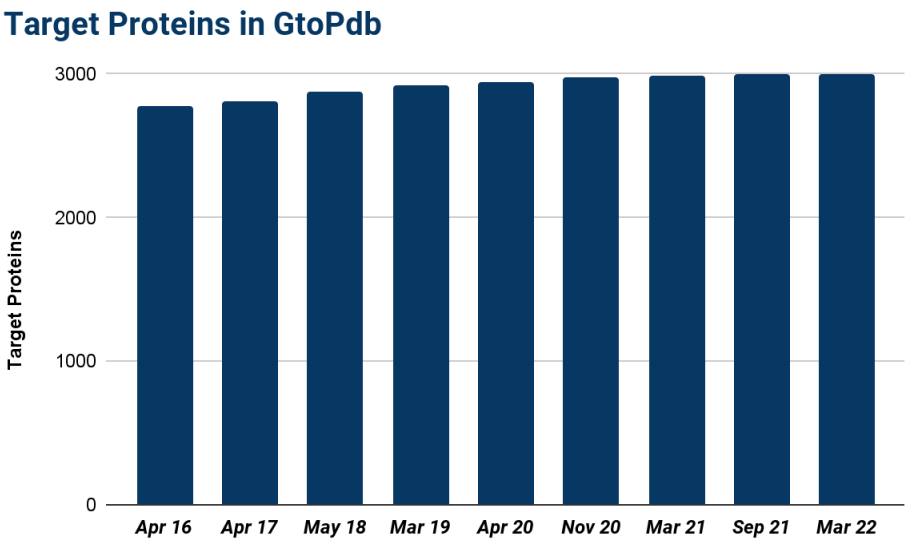
Ligands	**Number of Ligands**
Synthetic organics	7797
Metabolites	517
Endogenous peptides	808
Other peptides including synthetic peptides	1443
Natural products	334
Antibodies	333
Inorganics	39
Approved drugs	1734
Withdrawn drugs	89
Ligands with INNs	2959
Labelled ligands	634
Unique PubChem CIDs (total CID links)	8462 (8626)
Ligands with target interactions	9465
Ligands with quantitative interactions (approved drugs)	8352 (1044)
Ligands with clinical use summaries (approved drugs)	3093 (1730)

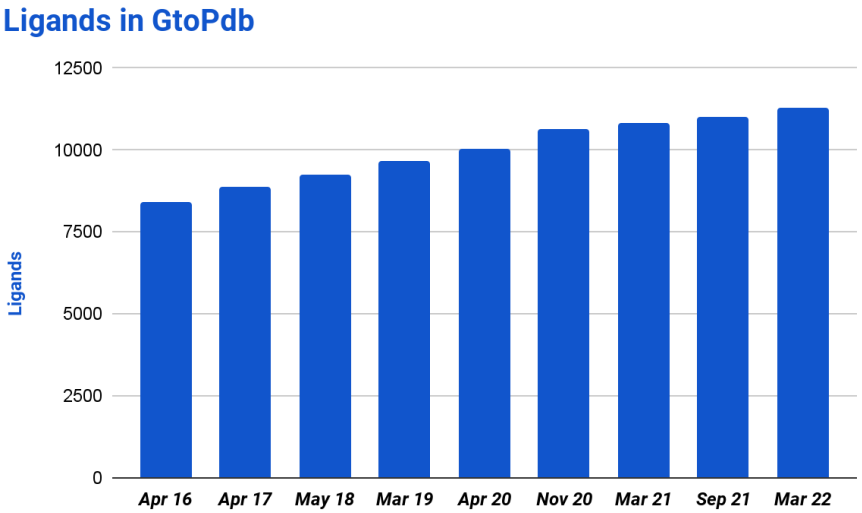
Total number of ligands (PubChem SIDs)	**11271**
Number of binding constants curated from the literature	**18,972**

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 16	Apr 17	May 18	Mar 19	Apr 20	Nov 20	Mar 21	Sep 21	Mar 22
Target protein IDs	**2775**	**2808**	**2872**	**2920**	**2943**	**2976**	**2985**	**2995**	**3000**
Ligands total	**8400**	**8872**	**9251**	**9662**	**10053**	**10659**	**10821**	**11025**	**11271**
Approved drugs	1273	1322	1364	1421	1471	1614	1643	1689	1734
Antibodies	172	212	240	255	270	295	303	317	333
Peptides	2007	2063	2092	2122	2150	2180	2206	2226	2251
Synthetic small molecules	5363	5729	6048	6401	6816	7303	7428	7593	7797
PubChem SIDs	8328	8831	9251	9662	10053	10659	10821	11025	11271
PubChem CIDs	6163	6813	7109	7407	7483	7994	8102	8262	8462
References	-	-	15851	16864	17695	-	18351	18624	18972





GtoPdb Updates

Targets

Since the last report the Relaxin receptors family has been updated (Roger Summers). Updates for the Orexin family are 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 2021.3 release.

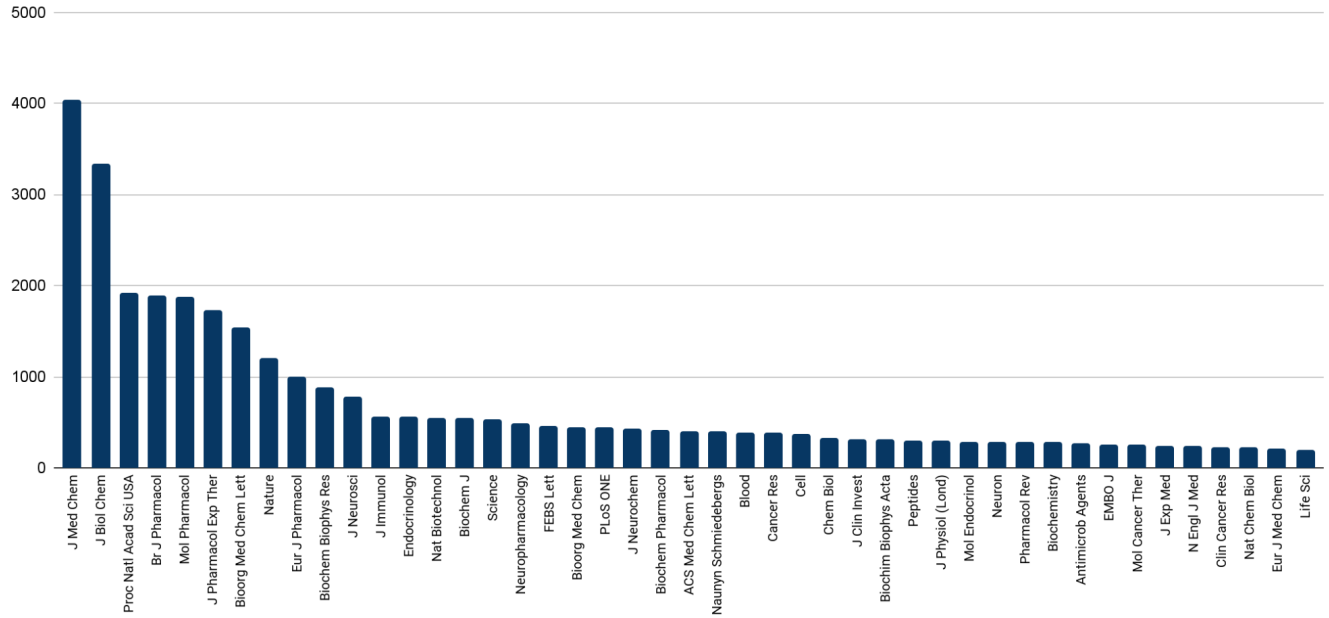
The *New Ligands* column shows count of new ligands for each category; *Updated Ligands* shows count of existing ligands, already curated in GtoPdb, now included in the categories. Columns 4 and 5 show the total ligands count for each category from our 2022.1 (Mar 2022) and 2021.3 (Sep 2021) database releases.

	New Ligands	Updated Ligands	Total Ligands (2022.1)	Total Ligands (2021.3)
Approved Drugs	16	30	1734	1688
WHO Essential Medicines	0	18	293	282
Ligands with Quantitative Interaction Data	189	2	8352	8161
Antimalarials	16	4	134	114
COVID-Relevant Ligands	2	0	84	82
All Ligands	247	0	11271	11025

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	4045
J Biol Chem	3345
Proc Natl Acad Sci USA	1916
Br J Pharmacol	1893
Mol Pharmacol	1875
J Pharmacol Exp Ther	1728
Bioorg Med Chem Lett	1536
Nature	1212
Eur J Pharmacol	998
Biochem Biophys Res Commun	882
J Neurosci	780
J Immunol	567
Endocrinology	560
Nat Biotechnol	555
Biochem J	554
Science	528


5000
4000
3000
2000
1000
0
J Med Chem
J Biol Chem
Proc Natl Acad Sci USA
Br J Pharmacol
Mol Pharmacol
J Pharmacol Exp Ther
Bioorg Med Chem Lett
Nature
Eur J Pharmacol
Biochem Biophys Res
J Neurosci
J Immunol
Endocrinology
Nat Biotechnol
Biochem J
Science
Neuropharmacology
FEBS Lett
Bioorg Med Chem
PLoS ONE
J Neurochem
Biochem Pharmacol
ACS Med Chem Lett
Naunyn Schmiedebergs
Blood
Cancer Res
Cell
Chem Biol
J Clin Invest
Biochim Biophys Acta
Peptides
J Physiol (Lond)
Mol Endocrinol
Neuron
Pharmacol Rev
Biochemistry
Antimicrob Agents
EMBO J
Mol Cancer Ther
J Exp Med
N Engl J Med
Clin Cancer Res
Nat Chem Biol
Eur J Med Chem
Life Sci

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 weekly (compared to quarterly for the main website) 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 Apr 2022 we have 105 unique entries in our table of COVID-19 relevant ligands, of these, 86 have ligand summary pages in GtoPdb, 50 of which are approved drugs.

The list of 9 targets on the page remains at 9 (detailed pages in GtoPdb; Seven of these are curated protein targets: ACE2, CD147, furin, Neurophilin 1, SAR-CoV-2 main protease, SARS-CoV-2 nsp3/PL-pro and TMPRSS2, and one, GM-CSF, is a ligand target. The ninth, OAS1, is a protein target listed but not curated in the database). These are proteins that are current clinical targets.

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 246 hits: 195 ligands and 46 targets, plus 4 hits within target family comments/introductions).

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

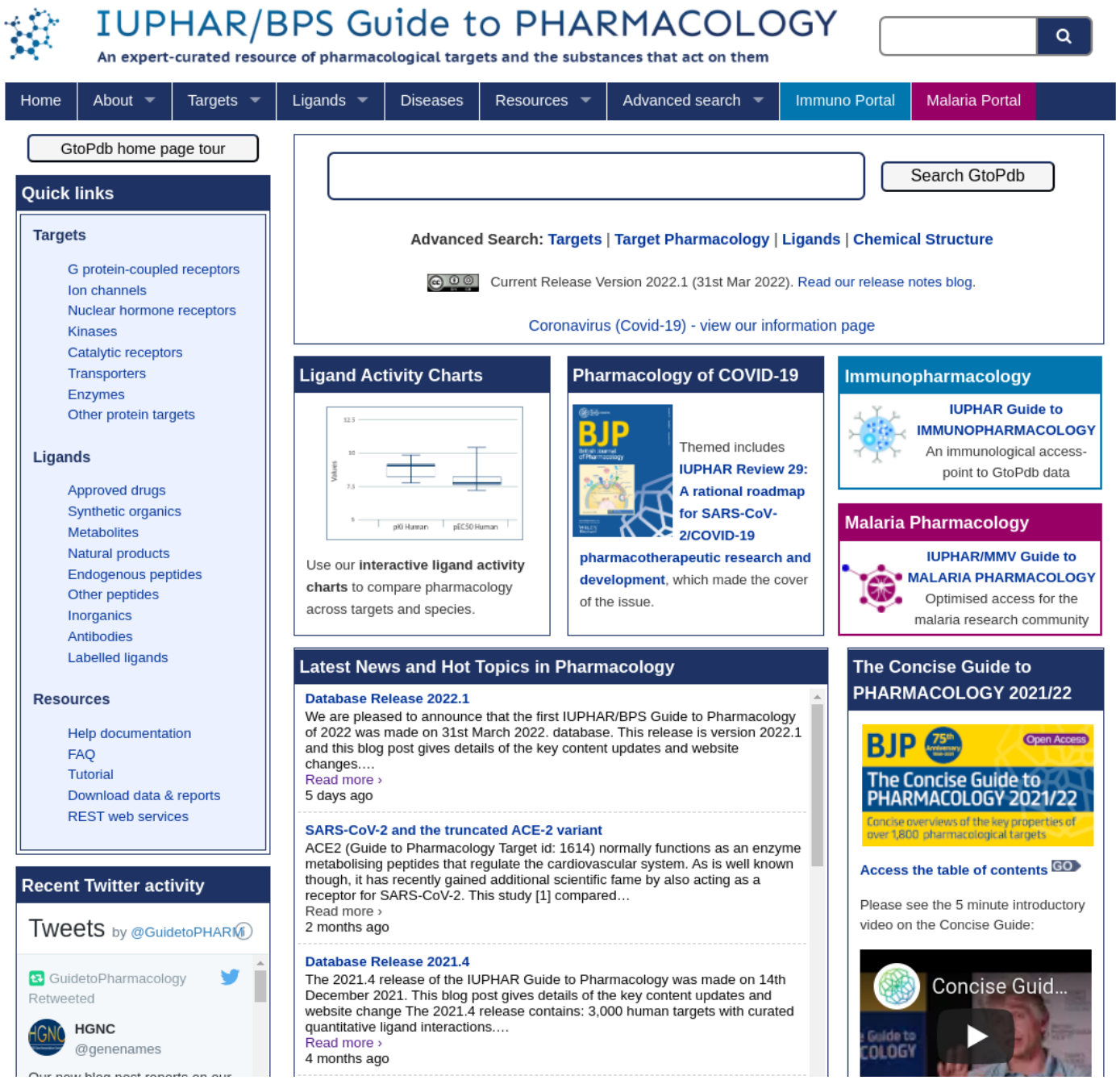
The GtoPdb Coronavirus page has been included in the following data hubs:

- 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

New Home Page

The Guide to PHARMACOLOGY home-page has been revised and was made public at our 2021.4 release. The layout prioritises ways users can access the data. The site search and links to advanced search tools are more prominent, there are panels linking to ligand activity graphs, GtoImmuPdb, GtoMPdb, and current key resources (such as the coronavirus information page and publication).

Page elements are more condensed to the top of the page and the site banner has been updated.



Ligand Download Files

A new, detailed endogenous ligands file is now provided on our downloads page. 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. The 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 now have a line at the top (preceded by a double hash '##') which indicates the database version and release data from which the data was generated. This is important so users can more easily track data provenance.

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 **305 ligands** tagged in GtoPdb as 'antibacterial' and **247** 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). 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.

Connectivity

PubChem Statistics for GtoPdb, GtoImmuPdb and GtoMPdb

The stats for the 2022.1 release (with 2021.3 in brackets) are as follows (N.B. the links below can be slow but if they do time out try purging your browser cache).

1. Substances (SID) that we submit to PubChem (refreshing previous submissions) are up to 11277 (11031).
2. Those that have defined chemical structures are merged into 9188 (8976) Compound Identifiers, CIDs (i.e. small molecules and peptides below ~ 70 residues)
3. From our 9188 CIDs 7165 have vendor matches
4. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND gtopdb_approved [Comment] now retrieves 1734 SIDs (1688) which link to 1538 approved drug CIDs
5. Of our SIDs, 1359 (1345) are tagged in GtoImmuPdb and 333 (324) of these are approved drugs
6. Of our CIDs 941 are tagged in GtoImmuPdb
7. Of our SIDs, 134 are tagged in GtoMPdb and 25 of these are approved drugs
8. Of our CIDs 132 are tagged in GtoMPdb
9. We have 2147 (2093) structures that ChEMBL does not have, 6554 (6367) not in DrugBank.
10. 348 (323) 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 333 SIDs. Adding "gtopdb_approved" gives 126.

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 304 SIDs, 103 of which are tagged as approved drugs.

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.

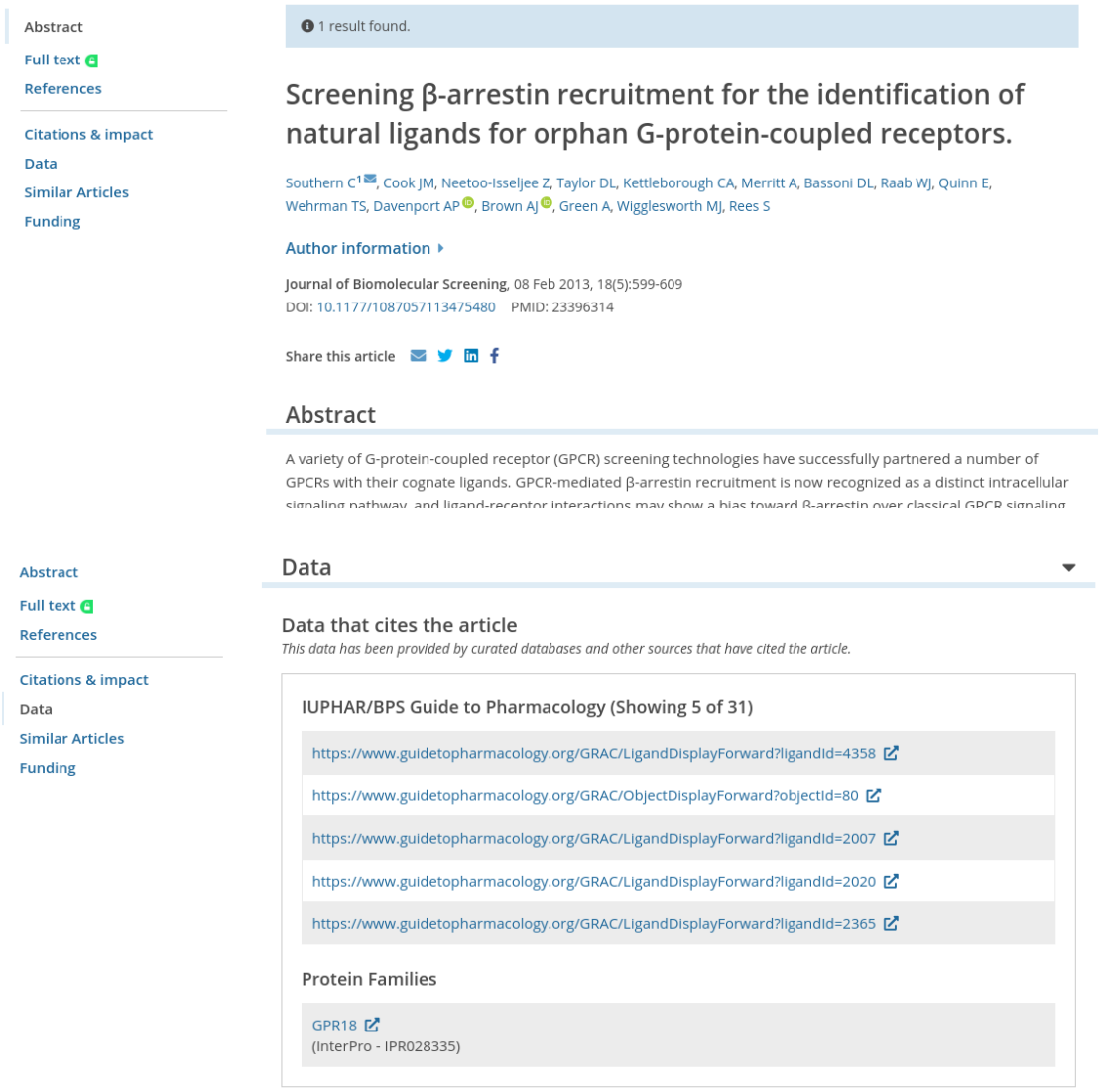
NCBI LinkOuts

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	5963
Nucleotide	5904
Gene	8466
PubMed	30,619 (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 (Southern et al. 2013). Under the 'Data' tab on the left-hand side the data cited in the article can be found. This shows 31 links beach to GtoPdb ligands and targets.

As of April 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

Bibliometrics and Scholarly Portals

NAR and CGTP

We are pleased to note that our **2020 NAR Database Issue** article has already picked up 71 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 1,192 citations (according to EPMC) or 1,235 (according to PubMed). This thus overtakes our 2016 paper (PMC4702778) with 915 (EMPC) or 920 (PubMed) citations, and the 2014 paper (PMC3965070) that reached 702 / 728.

The “Concise Guide” citations are currently led by 2017/18 Enzymes (PMC5650666) at 557 followed by 2015/16: Enzymes (PMC4718211) at 511 and 2013/14: G protein-coupled receptors (PMC3892287) at 468.

SARS-CoV-2 Review

Our BJP SARS-Cov-2 review has acquired 39 PubMed citations.

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 282 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 AJF, SDH, JLS, EF, AJP, CS and JAD, along with IUPHAR co-authors, SPHA, MS, and APD being listed in the Clarivate 2021 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).

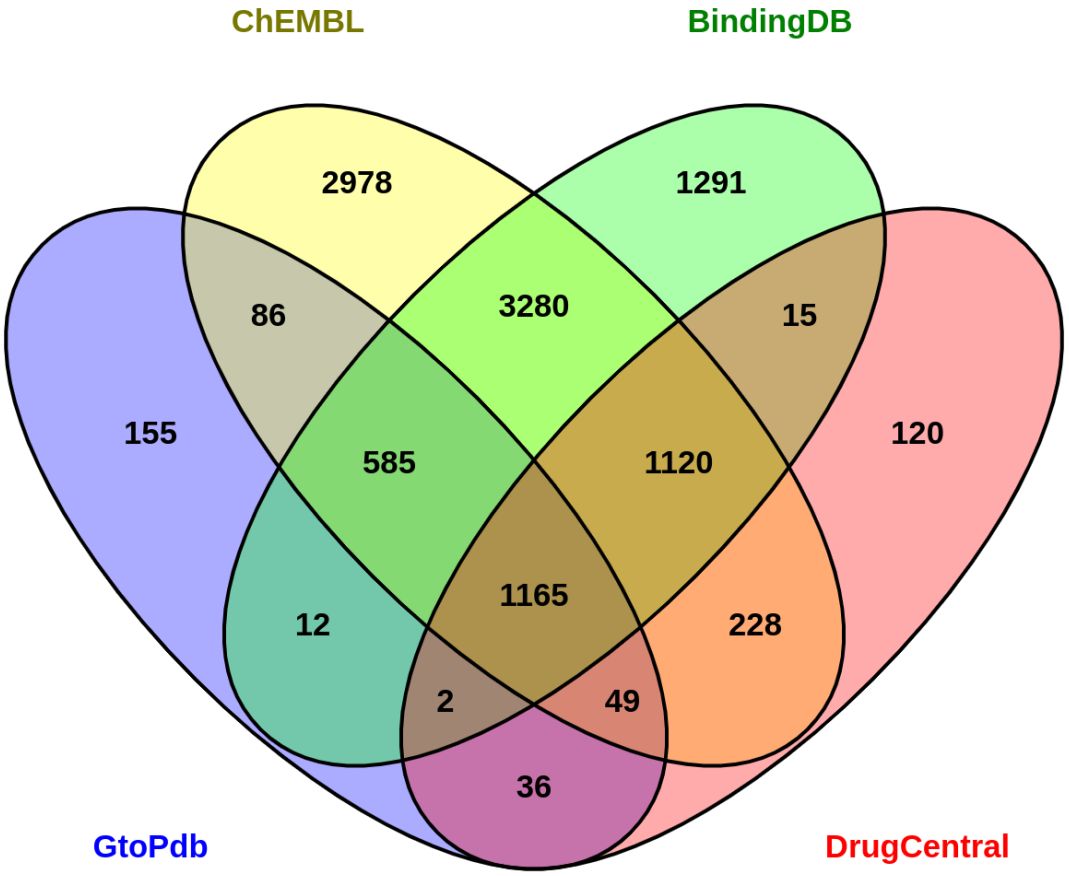
- The team is on their 8th NAR Database Issue from 2009 to 2022
- IUPHAR reviews in BJP: 34.
- IUPHAR Pharmacological Reviews: 109
- The cumulative BJP “Concise Guide” set now takes us to 40 papers

EBI UniProtKB/Swiss-Prot cross-references

Below are the metrics for UniProt 2022_01 chemistry sources. 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-reference
BindingDB BindingDB database of measured binding affinities · UniProtKB (7,470) Category: Chemistry databases
ChEMBL ChEMBL database of bioactive drug-like small molecules · UniProtKB (9,491) Category: Chemistry databases
DrugBank Drug and drug target database · UniProtKB (5,159) Category: Chemistry databases
DrugCentral DrugCentral · UniProtKB (2,735) Category: Chemistry databases
GuidetoPHARMACOLOGY IUPHAR/BPS Guide to PHARMACOLOGY · UniProtKB (2,090) Category: Chemistry databases
SwissLipids SwissLipids knowledge resource for lipid biology · UniProtKB (1,398) Category: Chemistry databases

Even though these sources have slightly different ways of going about their curatorial business it is informative to compare and contrast the four below (omitting DrugBank which has a tendency to over-map and has not recently updated these cross-refs) to give both a druggable proteome snapshot and our unique contribution to the aggregate coverage. The Venn diagram for the November human 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 57 GtoPdb-only targets. The divergences are of interest but need deeper analysis to discern what curatorial selectivity (e.g. journal choice) explains these differences.

There are links from 1,563 GtoPdb ligands to BindingDB.

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.

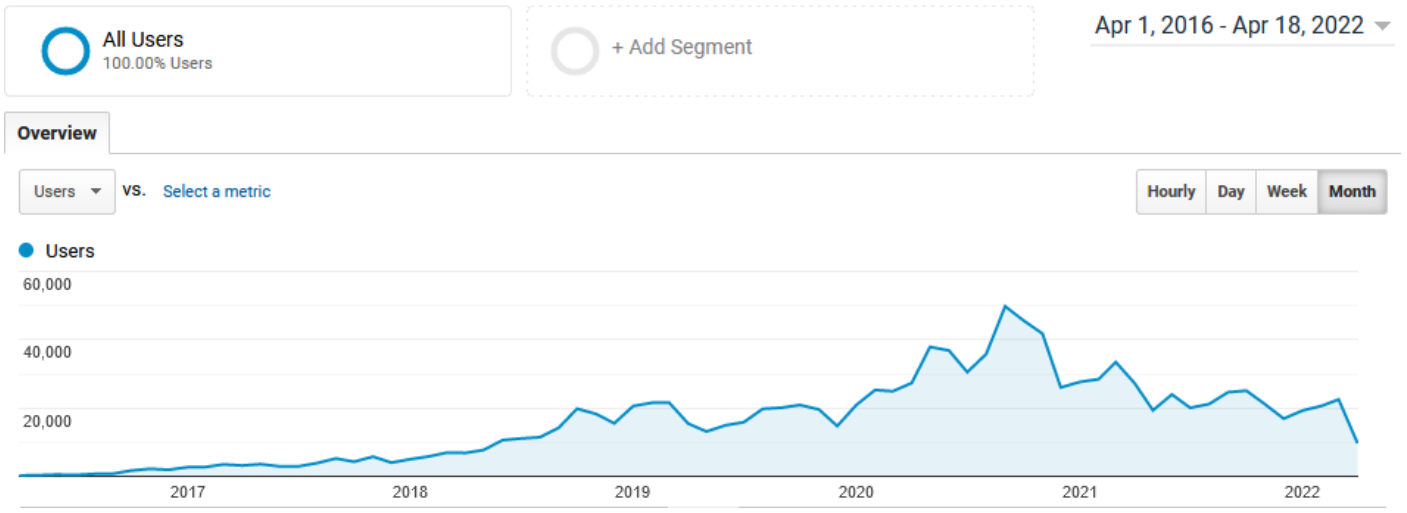
As a result of this amalgamation we have recruited 4 new members to the PEP editorial board

- Gavin Dawe, National University of Singapore (Singapore)
- John Kelly, National University of Ireland Galway (Ireland)
- Zoltan Varga, Semmelweis University (Hungary)
- Paul White Monash University (Australia)

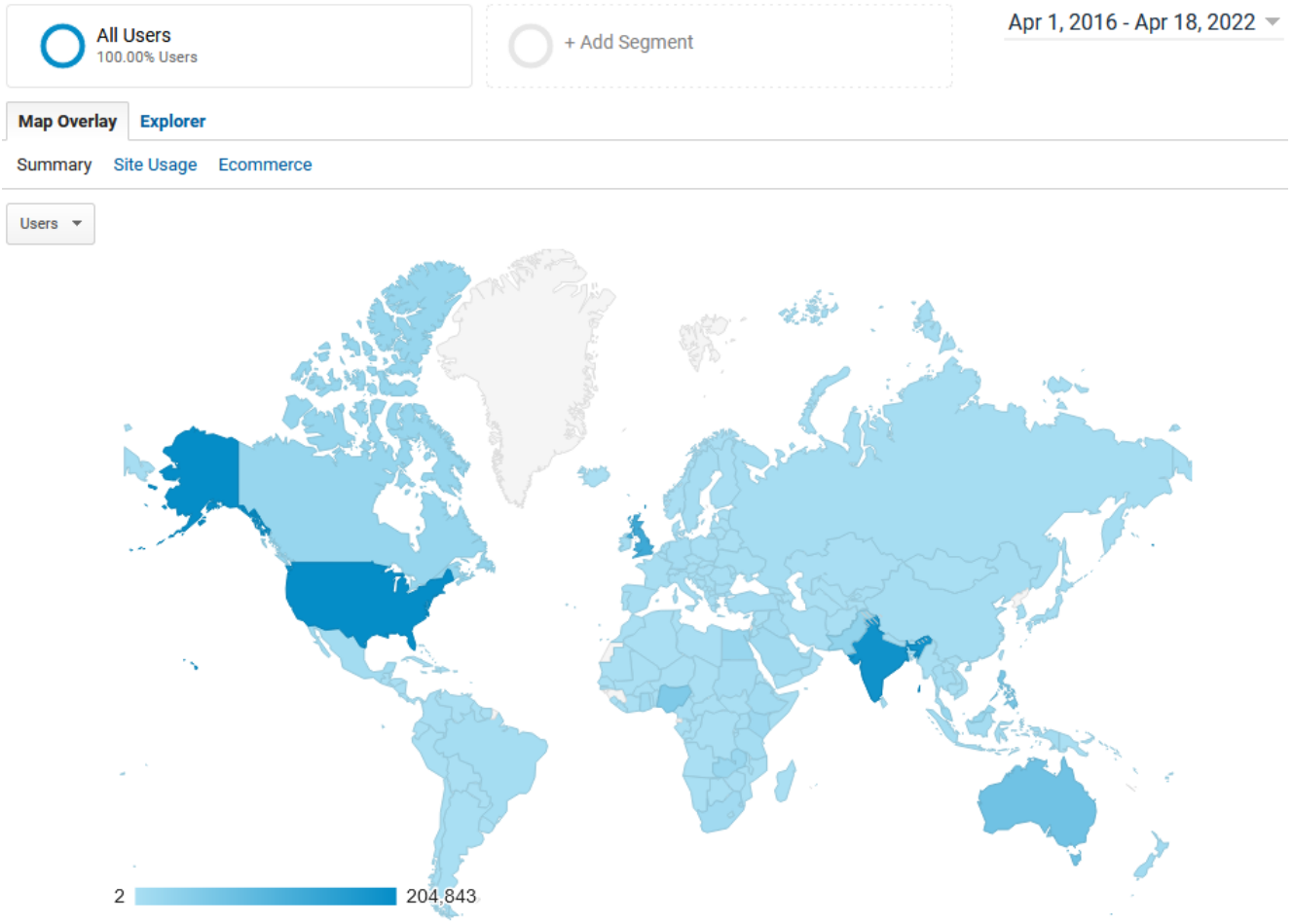
Google Analytics data charts for PEP site usage since 1st April 2016

Google Analytics shows that user sessions continue to average >25K/month.

Monthly user sessions



Global Access



Social Media

PEP has ~1600 followers of our twitter handle, @PharmacologyEd.

Meetings

We are in the process of submitting an abstract for Pharmacology 2022 in Liverpool.

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

641 targets tagged as immuno-relevant, 449 have quantitative interaction data

1359 ligand tagged as immuno-relevant. 999 of the immuno ligands have quantitative interaction data, 220 of which are approved drugs

Detailed lists on:

www.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp

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 2021.5 release).

Process Category	GtoPdb Human UniProtKB	Target-GO annotations
Barrier integrity	60	86
Inflammation	763	1724
Antigen presentation	174	279
T cell (activation)	255	568
B cell (activation)	207	354
Immune regulation	647	1771
Tissue repair	55	60
Immune system development	303	585
Cytokine production & signalling	577	1725
Chemotaxis & migration	290	633

Cellular signalling	555	1435

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)

Introduction

IUPHAR/MMV
Guide to MALARIA PHARMACOLOGY

The Guide to MALARIA PHARMACOLOGY (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.

GtoMPdb Target and Ligand Curation

Curation Summary

The number of ligands in the public database with antimalarial activity has continued to increase. The most recent database release (2022.1) contains:

- 134 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 last 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. This process has helped inform target subfamily classification (see our April 2021 report for more details), identify interaction data for new antimalarial ligands and update a number of existing ligands.

These target descriptions are also the basis of an IUPHAR review on recent advances in malaria pharmacology and the GtoMPdb resource (manuscript ready for submission, pending MMV approval).

GtoMPdb Web Interface and Database Development

The GtoMPdb uses the same underlying database as GtoPdb and in previous reports we have described changes to the database structure and the web interface that were necessary for the capture and presentation of antimalarial data. A summary of the development work undertaken for this project can be found in our November 2020 report.

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 April 21 - March 22. 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 22,807 unique views (1,866 per month).

	Page Views	Page Views per month	Unique Page Views	Unique Page Views per month
Index	1622	90	1256	69.8
Targets	4159	347	2754	230
Ligands	16173	1348	11887	991
Families	5643	470	2784	232
Malaria Species	550	46	420	35
Parasite Lifecycle	4436	370	3706	309
	32583	**2670**	**22807**	**1866**

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

hiddenREF Award

We are pleased that 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.

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 7th April 2022, output 2,351 tweets; followers have increased to 4,658 from 4,489 in November 2021. 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 344 followers, up from 325 in November 2021.

Guide to Pharmacology Blog

Our Edinburgh blog (http://blog.guidetopharmacology.org/) has received over 2,000 visitors in 2021, which is a drop from ~3,600 visitors in 2020. However, 2020 saw us publish almost twice as many blog posts and the average views per visitor has actually risen from 1.59 to 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 November 2021 we've added 40 new hot topic articles, including a commentary by Chris Southan on "SARS-CoV-2 and the truncated ACE-2 variant". The commentary discusses the publication by Williams et al. om differential expression of ACE2 and was published in February 2022 and has received over 50 views.

Williams TL, Strachan G, Macrae RGC, Kuc RE, Nyimanu D, Paterson AL, Sinha S, Maguire JJ, ana Davenport AP. Differential expression in humans of the viral entry receptor ACE2 compared with the short deltaACE2 isoform lacking SARS-CoV-2 binding sites. Sci Rep. 11:24336. (2021). [PMID: 34934117]

And most recently a commentary on endothelin-1 (ET-1) pathway as a new therapeutic target for COVID-19. The study compared ET-1 in the plasma of patients infected with COVID-19 who were hospitalised during the first wave of the pandemic, including those placed on ventilators. Significantly higher levels of ET-1 were measured in these patients, compared with infected individuals with mild or no symptoms. The release of multiple copies of the virus following infection is known to damage endothelial cells and the results show stored ET-1 is also released into the bloodstream.

Abraham GR, Kuc RE, Althage M, Greasley PJ, Ambery P, Maguire JJ, Wilkinson IB, Hoole SP, Cheriyan J, Davenport AP. Endothelin-1 is increased in the plasma of patients hospitalised with Covid-19. J Mol Cell Cardiol. 2022 Mar 23:S0022-2828(22)00051-7. doi: 10.1016/j.yjmcc.2022.03.007. [PMID: 35339512].

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.