IUPHAR

INTERNATIONAL UNION OF BASIC AND CLINICAL PHARMACOLOGY

IUPHAR/BPS
Guide to **PHARMACOLOGY**

IUPHAR
Guide to **IMMUNOPHARMACOLOGY**

IUPHAR/MMV
Guide to **MALARIA PHARMACOLOGY**

BRITISH PHARMACOLOGICAL SOCIETY

BJP

The Concise Guide to PHARMACOLOGY 2019/20

Concise overviews of the key properties of over 1,700 pharmacological targets

Open Access

DATABASE Report

April 2020

enquiries@guidetopharmacology.org

TABLE OF CONTENTS

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 Paris in April 2019. Previous reports are online for May 2018, Oct 2018, and Apr 2019.

Further details are provided on updates to the Wellcome Trust funded project to develop the "The Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb): Integration of targets, diseases and therapies into an expert-driven database". More details can be found in our blog, which includes technical blog posts highlighting aspects of the development of the resource.

We again include details on the Guide to MALARIA PHARMACOLOGY (GtoMPdb), a project funded by Medicines for Malaria Venture (MMV) to add information about antimalarials to GtoPdb and to develop a purpose-built parasitologist-friendly portal for the website interface. This resource was officially launched in September 2019 (see our blog post).

Of particular relevance and importance at this time, are details of our new Coronavirus (COVID-19) information page which was launched in early March 2020.

This report will detail our progress on the GtoPdb, GtoImmuPdb and GtoMPdb projects. It is based on the April 2019 report, as reference. A few general sections have been left in for context, but most have been updated.

GENERAL OVERVIEW OF DATABASE TEAM ACTIVITIES

PUBLIC ENGAGEMENT – PROMOTING OUR RESOURCES

CONFERENCES/MEETINGS (SINCE APRIL 2019 AND UPCOMING)

- BPS Pharmacology 2019, Edinburgh, UK. Dec 2019. Jamie Davies, Simon Harding, Pasquale Maffia and Clare Bryant: "Workshop: Guide to Immunopharmacology - How to Navigate and Use the Database". Chris Southan (posters and flash presentation)
- ELIXIR UK All Hands, Dundee, UK. Dec 2019. Simon Harding and Chris Southan - Updates on Guide to Pharmacology
- 39 Congresso Nazionale della Società Italiana di Farmacologia, Firenze, Italy. Nov 2019. Elena Faccenda presented on IUPHAR/BPS Guide to IMMUNOPHARMACOLOGY.
- ELIXIR All Hands 2019, Lisbon, June 2019, Chris Southan
- BioMalPar XV: Biology and Pathology of the Malaria Parasite, EMBL, Heidelberg, May 2019. Jane Armstrong presented a poster on the Guide to MALARIA PHARMACOLOGY

Our slideshare account includes slide sets and posters presented by team members. Some are also posted on Christopher Southan's own slideshare.

PUBLICATIONS

PUBLISHED OR PRE-PRINTED (SINCE EARLY 2019)

- Steve Alexander, Jane Armstrong, Anthony Davenport, et al. A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development. *Authorea.* April 13, 2020. DOI: https://doi.org/10.22541/au.158679935.58510327
- Cross-tier web programming for curated databases: A case study. Simon Fowler, Simon D. Harding, Joanna Sharman, James Cheney. https://arxiv.org/abs/2003.03845
- Opening up connectivity between documents, structures and bioactivity. Southan C. Beilstein J Org Chem. 2020 Apr 2;16:596-606. doi: 10.3762/bjoc.16.54. eCollection 2020. Review. PMID: 32280387

- [Guide to Immunopharmacology: a database to boost immunology education, research and therapy.](#) Milling S, Spedding M, Maffia P. Immunology. 2020 May;160(1):1-2. doi: 10.1111/imm.13201. PMID: 32297319

- [The IUPHAR Guide to Immunopharmacology: connecting immunology and pharmacology](#). 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). Immunology, 160: 10-23. [doi:10.1111/imm.13175](#) [PMID:32020584]

- [The IUPHAR/BPS Guide to PHARMACOLOGY in 2020: extending immunopharmacology content and introducing the IUPHAR/MMV Guide to MALARIA PHARMACOLOGY.](#) 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. Nucleic Acids Res. 2020 Jan 8;48(D1):D1006-D1021. doi: 10.1093/nar/gkz951. PMID: 31691834

- [THE CONCISE GUIDE TO PHARMACOLOGY 2019/20](#) Alexander SPH, Kelly E, Mathie A, Peters JA, Veale EL, Armstrong JF, Faccenda E, Harding SD, Pawson AJ, Sharman JL, Southan C, Buneman OP, Cidlowski JA, Christopoulos A, Davenport AP, Fabbro D, Spedding M, Striessnig J, Davies JA; CGTP Collaborators. Br J Pharmacol. 2019 Dec;176 Suppl 1:S1-S20. doi: 10.1111/bph.14747. PMIDs: 31710719, 31710718, 31710717, 31710716, 31710715, 31710714, 31710713

- [The IUPHAR Pharmacology Education Project.](#) Faccenda E, Maxwell S, Szarek JL. Clin Pharmacol Ther. 2019 Jan;105(1):45-48. doi: 10.1002/cpt.1278. Epub 2018 Dec 26. Review. PMID: 30588614

- [Inverse pharmacology: Approaches and tools for introducing druggability into engineered proteins.](#) Davies JA, Ireland S, Harding S, Sharman JL, Southan C, Dominguez-Monedero A. Biotechnol Adv. 2019 Dec;37(8):107439. doi: 10.1016/j.biotechadv.2019.107439. Epub 2019 Sep 5. Review. PMID: 31494210

- [A new guide to immunopharmacology](#). Harding SD, Faccenda E, Southan C, Maffia P, Davies JA. Nat Rev Immunol. 2018 Dec;18(12):729. doi: 10.1038/s41577-018-0079-2. No abstract available. PMID: 30327546

CORONAVIRUS (COVID-19) - OUR NEW INFORMATION PAGE

PUBLISHED EARLY MARCH 2020, UPDATED REGULARLY

Given the novelty of SARS-CoV-2 infection (COVID-19), and the lack of proven therapies, a wide variety of strategies are being employed to combat this worldwide epidemic. 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.

- The effects of existing antiviral medications are being evaluated
- The inflammatory aspects of the disease are being targeted using existing medications including glucocorticoids, COX inhibitors, immunosuppressants and immunomodulators
- Strategies to block interaction between the virus and ACE2 on host cells, or inhibition of spike protein activation are being explored
- Novel inhibitors of the main CoV protease are being developed
- Mucolytic drugs and drugs to counter pulmonary edema are in clinical trials

All of these tactics are intended to mitigate against COVID-19 and provide a window during which vaccine development can progress (with the caveat that the search for vaccines to prevent infection by existing circulating coronaviruses has been notoriously unsuccessful).

We quickly set-up a new page as a quick response to the COVID-19 pandemic where we have aimed to collect many of the pharmacological strategies being considered. There are sections on the key targets and ligands of interest - linked into the more detailed GtoPdb pages, where we already have curated information in the database. In cases where we don't currently have a ligand curated in GtoPdb (but plan to add it) we have added the ligand to a new pre-release blog so that this data can be available as soon as possible.

The ligands (therapeutics) table excludes traditional natural product-based medicines, blood-derived products (*e.g.* serum from recovered patients and stem cells), investigational vaccines, anti-bacterials for secondary infections and supportive treatments (oxygen therapy).

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

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) keeping collaborators and other followers (including many other databases) aware of our activities. 5) establishing reciprocity with key followers and collaborators.

FACEBOOK

The number of 'likes' increased to 4,585 (April 2020), from 4,107 (March 2019). We have 4,649 followers.

TWITTER

@GuidetoPHARM has just pipped 2,062 tweets, followers have increased to 3531, from 2670 in March 2019, and our retweet rate also continues to increase year-on-year. 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 have been very active in promoting the Concise Guide) @BrJPharmacol, @PharmRevJournal, @PRandP_Journal @IUPHAR, @PharmacologyEd @immunopaedia @cdsouthan and @mqzspa (NC-IUPHAR chair). From our recent publications listed above we saw useful tweet boosts via @ChemRxiv as well as Wiley @currentprotocol and @ChemMedChem.

LINKEDIN

The Curation Team have been encouraging Subcommittee Chairs and collaborators to increase their reciprocal connectivity as individual LinkedIN users. This expands our collective inter-network outreach 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 250 followers, up from 191 in March 2019.

BLOGGING

Our Edinburgh blog (http://blog.guidetopharmacology.org/) continues to receive over 650 views on average per month. This 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

As an established and popular feature our Hot Topics are seeded in the form of new significant pharmacology, drug discovery and key human genomics papers. These are communicated to us from Subcommittee members or picked up from Twitter. For a selection, as before, we commission concise commentaries from our expert contacts. We've had recent guest commentaries from Jörg Striessnig, Ralf Jockers, Steve Alexander, Michael Spedding, Francesca Levi-Schaffer, Magnus Bäck, Fiona H. Marshall, Dr. Charles Kennedy, Simon R. Foster, David E. Gloriam, Shane D Hellyer and Karen J Gregory (all commentaries are posted under the Hot topic category on our blog).

We have recently made changes to the way we capture Hot Topics publication by formally storing them in the database. This enables us to more easily track hot topic publications and to dynamically generate the Hot Topics page.

SLIDESHARE

Our account (http://www.slideshare.net/GuidetoPHARM) allows the database team to share slide sets and posters with the community thereby extending the reach way beyond conference session direct attendees. Our slide sets received 4296 (+852) views over the past year. 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.

ENQUIRIES RECEIVED FROM USERS

We get a steady stream of user communications coming in to enquiries@guidetopharmacology.org. This is about one a week and they continue to cover a useful spectrum of (mostly minor) fixes that we promptly address. It is useful to catalogue these engagements as they provide valuable information (not readily captured by analytics) in how and why GtoPdb is used. They also provide useful ideas for future development.

Shoumo Bhattacharya (University of Oxford)

Interested in downloading target tissue distribution in chemokine receptors.

Daniela Digles (University of Vienna)

Was again into touch about accessing solute carrier substrates. This helped inform changes to the data we include in the web service API.

Nicholas Allen (National University of Ireland Galway)

Access to Ion channel diagrams.

Mohib Uddin (AstraZeneca)

Mohib reached out with antagonist data for the CXCR2 chemokine receptor and data on the Prostanoid receptor, DP2/CRTh2 and is now included as a contributor to both these families.

Jesper Sorensen (Open Eye Software)

Jesper has been making use of the target tree structure in GtoPdb as part of a modelling service they are planning to provide. He states that the website is extremely useful and the web service API is fantastic.

Mathew O'Meara (University of Michigan)

Matthew used our web services to identify FDA approved drugs and inquired about how this is displayed in our output. He took the time to let us know he was thrilled with the COVID-19 pages we put together.
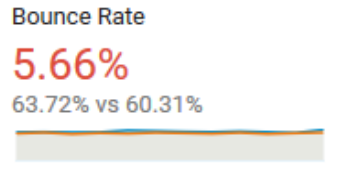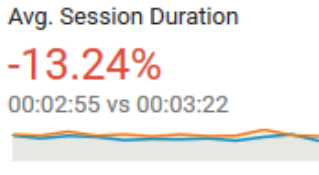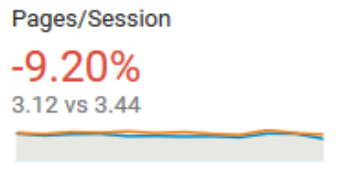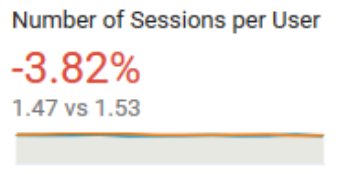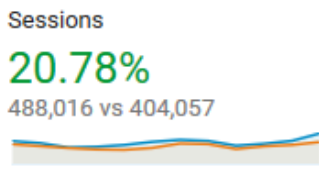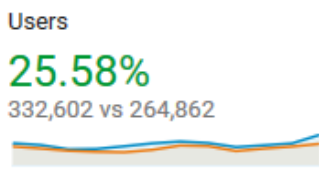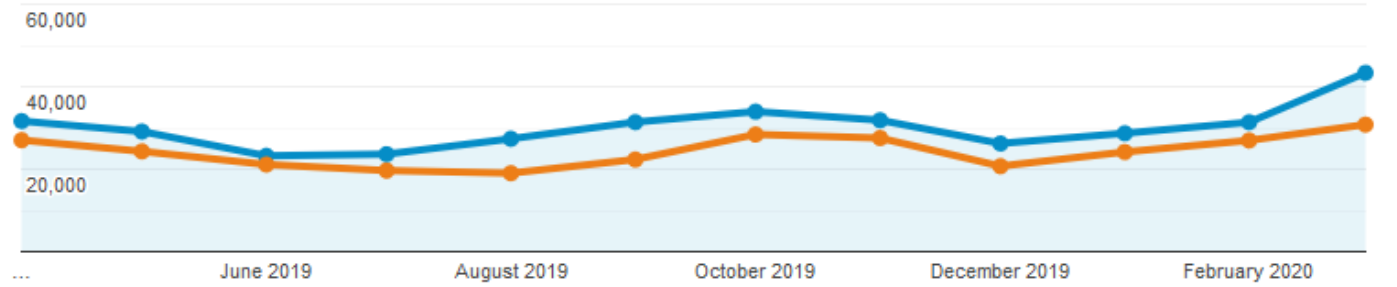
ENGAGING WITH US

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.
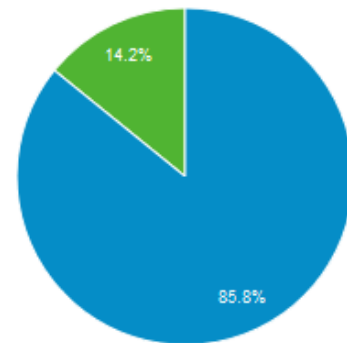
GTOPDB WEBSITE ACCESS STATISTICS

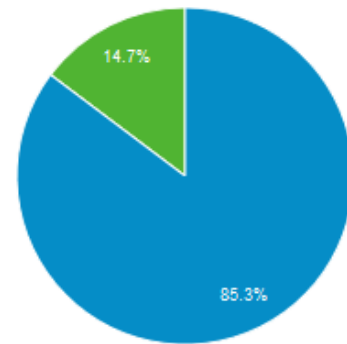01-Apr-2019 - 31-Mar-2020: ● Users
01-Apr-2018 - 31-Mar-2019: ● Users

New Visitor **Returning Visitor**

Users
25.58%
332,602 vs 264,862

New Users
25.60%
329,041 vs 261,967

Sessions
20.78%
488,016 vs 404,057

Number of Sessions per User
-3.82%
1.47 vs 1.53

Page Views
9.67%
1,523,470 vs 1,389,189

Pages/Session
-9.20%
3.12 vs 3.44

Avg. Session Duration
-13.24%
00:02:55 vs 00:03:22

Bounce Rate
5.66%
63.72% vs 60.31%

01-Apr-2019 - 31-Mar-2020

14.2% / 85.8%

01-Apr-2018 - 31-Mar-2019

14.7% / 85.3%

Graphs comparing visitors to guidetopharmacology.org for the 12 months from April 2019 to March 2020, with the previous 12 months.

Monthly statistics	Apr 2019 - Mar 2020 (previous 12 months)
Sessions	40,668 (33,671)
Users	27,716 (22,071)
Page views	126,955 (115,765)
Pages / Session	3.12 (3.44)
Avg. Session Duration	00:02:55 (00:03:22)

ACQUISITION, BROWSERS AND DEVICES

It is useful to be aware of where users are accessing GtoPdb and what devices/browsers they are using. This can help us to better optimise the site and to ensure we test across the most popular platforms.

	Default Channel Grouping	Source	Users	Users
			337,650 % of Total: 100.00% (337,650)	337,650 % of Total: 100.00% (337,650)
1.	Organic Search	google	218,639	63.11%
2.	Direct	(direct)	82,252	23.74%
3.	Organic Search	bing	8,543	2.47%
4.	Referral	baidu.com	3,945	1.14%
5.	Referral	en.wikipedia.org	3,901	1.13%
6.	Referral	ncbi.nlm.nih.gov	3,596	1.04%
7.	Referral	en.m.wikipedia.org	3,092	0.89%
8.	Referral	bpspubs.onlinelibrary.wiley.com	2,129	0.61%
9.	Referral	iuphar-db.org	1,941	0.56%
10.	Organic Search	baidu	1,846	0.53%

This shows acquisition data from Apr 2019 to Apr 2020

	Browser	Device Category	Sessions	Sessions
			493,539 % of Total: 100.00% (493,540)	493,539 % of Total: 100.00% (493,540)
1.	Chrome	desktop	247,477	50.14%
2.	Safari	desktop	43,215	8.76%
3.	Firefox	desktop	43,051	8.72%
4.	Chrome	mobile	42,759	8.66%
5.	Internet Explorer	desktop	33,308	6.75%
6.	Safari	mobile	29,534	5.98%
7.	Edge	desktop	22,212	4.50%
8.	Safari	tablet	6,959	1.41%
9.	Samsung Internet	mobile	4,418	0.90%
10.	UC Browser	mobile	3,957	0.80%

Browser and Device Category of Session on GtoPdb (Apr 19 - Apr 20)

The majority of sessions on GtoPdb come *via* organic search (Google - 63%) and are performed predominantly from desktop devices. Chrome is also the browse of choice. Only about 8-10% of traffic come from referrals, with the following table showing how these break down.

	Source	Sessions ▼ ↓	Sessions ▼
		45,242 % of Total: 9.17% (493,540)	**45,242** % of Total: 9.17% (493,540)
1.	en.wikipedia.org	5,066	11.20%
2.	ncbi.nlm.nih.gov	4,584	10.13%
3.	baidu.com	4,028	8.90%
4.	iuphar-db.org	3,686	8.15%
5.	en.m.wikipedia.org	3,480	7.69%
6.	bpspubs.onlinelibrary.wiley.com	2,853	6.31%
7.	cn.bing.com	2,298	5.08%
8.	pubchem.ncbi.nlm.nih.gov	1,437	3.18%
9.	m.facebook.com	1,121	2.48%
10.	ebl.soms.bris.ac.uk	995	2.20%

We get about 10% of our referrals from NCBI and 6% from Wiley.

These database statistics were compiled from our April 20th release (v2020.2). 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	249
Ligand-gated ion channels	81
Voltage-gated ion channels	144
Other ion channels	53
Enzymes	1219
Transporters	539
Other protein targets	211
Targets with ligand interactions	1799
Targets with quantitative ligand interactions	154
Targets with approved drug interactions	654
Primary Targets with approved drug interactions	332
Total number of targets	**2943**
Ligands	**Number of ligands**
Synthetic organics	6816
Metabolites	509
Endogenous peptides	798
Other peptides including synthetic peptides	1352
Natural products	269
Antibodies	270
Inorganics	39
Approved drugs	1471
Withdrawn drugs	72
Ligands with INNs	2402
Labelled ligands	609
Unique PubChem CIDs (total CID links)	7483 (7684)
Ligands with target interactions	8696
Ligands with quantitative interactions (approved drugs)	7650 (952)
Ligands with clinical use summaries (approved drugs)	2517 (1468)
Total number of ligands (PubChem SIDs)	**10053**
Number of binding constants	48902
Number of binding constants curated from the literature	17695

DOWNLOAD STATISTICS

Yearly period 17th April Year 1 to 16th April Year 2.

GOOGLE ANALYTICS COMPARISON OF DOWNLOADS

Event Category: Downloads

Event Label: Downloaded

	Count
2018-2019	2,840
2019-2020	3,228
Change	13.66%

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

and the slides page: http://www.guidetopharmacology.org/slides.jsp

A more specific breakdown is shown here:

	2018-2019	**2019-2020**	**Change**
Targets CSV/TSV file	1097	1085	-1%
Interactions CSV/TSV file	361	383	6%
Ligands CSV/TSV file	278	255	-8%
UniProt Mapping file	89	96	8%
HGNC mapping file	96	114	18%
PostgreSQL*	184	154	-16%
Generic slides (PPT & PDF)	177	170	-16%
Generic poster	67	73	8.96%
Supplier Links	412	557	35%

* Total downloads of PostgreSQL database dump files (versions 2018.1 onwards).

WEB SERVICES

Tracking of our web-services has been in place 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't report details on specific users, such as location or number of visits. We can only record the number of hits for each distinct URL.

The image below shows that there were approximately **104,500** total hits over the year, which is very similar to the previous year (~105,000). Calls to targets and ligands both saw large increases, with decreases coming in calls to interaction and similarity data.
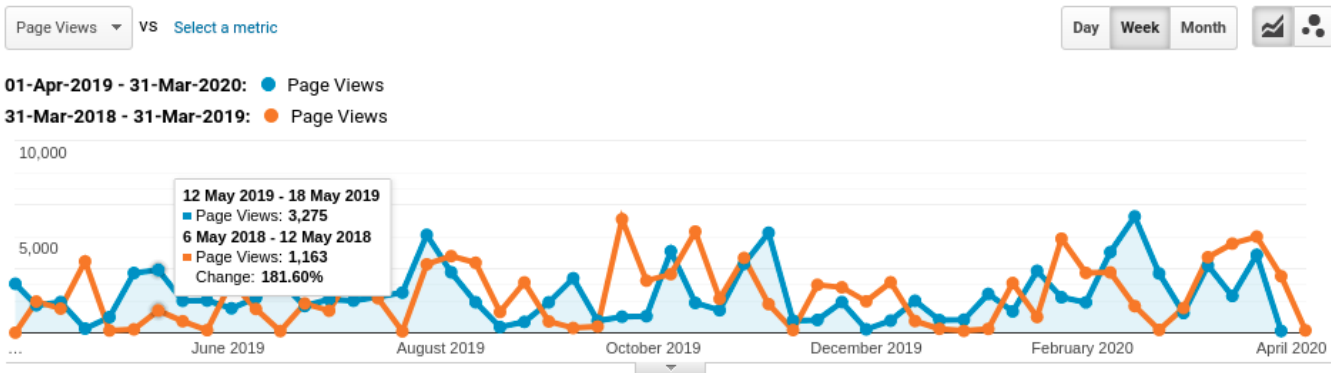
Page	Page Views	Unique Page Views	Avg. Time on Page	Entrances	Bounce Rate	% Exit	Page Value
	0.57% ▼ 104,579 vs 105,178	8.55% ▲ 64,805 vs 59,700	99.91% ▲ 00:00:13 vs 00:00:07	11.67% ▲ 2,076 vs 1,859	7.05% ▲ 50.96% vs 47.61%	12.31% ▲ 1.99% vs 1.77%	0.00% US$0.00 vs US$0.00
1. /services/targets							
01-Apr-2019 - 31-Mar-2020	13,553 (12.96%)	762 (1.18%)	00:00:12	563 (27.12%)	43.69%	2.83%	US$0.00 (0.00%)
31-Mar-2018 - 31-Mar-2019	7,865 (7.48%)	753 (1.26%)	00:00:13	525 (28.24%)	35.43%	4.01%	US$0.00 (0.00%)
% Change	72.32%	1.20%	-7.92%	7.24%	23.33%	-29.44%	0.00%
2. /services/ligands							
01-Apr-2019 - 31-Mar-2020	3,992 (3.82%)	553 (0.85%)	00:00:30	343 (16.52%)	68.22%	8.79%	US$0.00 (0.00%)
31-Mar-2018 - 31-Mar-2019	994 (0.95%)	533 (0.89%)	00:01:57	202 (10.87%)	68.32%	27.36%	US$0.00 (0.00%)
% Change	301.61%	3.75%	-74.32%	69.80%	-0.14%	-67.87%	0.00%

Traffic to GtoPdb web services URLs over the past year

SUPPLIER LINKS

In May 2018 we accepted sponsorship from Tocris (https://www.tocris.com) in return for providing product supplier links on our ligand summary pages.

Tocris supplies a list of their compounds which we mapped to GtoPdb ligand *via* PubChem CIDs and InChi Keys. This sponsorship was continued in 2019 and recently we have made a further update (April 2020) which brings the total mapped compounds to 1420. We have recently been discussing their possible expansion of COVID-19 relevant compounds from our recent curation push, but this will need a lead-in time from their side.

GTOPDB TEAM INTERACTIONS

For more details of previous and continuing interactions please see the October 2018 and April 2019 reports. Only significant changes since April 2019 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 and Dr. Chris Southan attended the ELIXIR-UK All-Hands Meeting held in December 2019 in Dundee, where we presented an update on the IUPHAR/BPS Guide to Pharmacology (slideshare link).

BIOSCHEMAS

An important area of engagement with ELIXIR has been the inclusion of BioSchemas (http://bioschemas.org/) mark-up on Guide to Pharmacology ligand and target pages. Adding schema.org semantic mark-up to GtoPdb makes it simpler for search engines to index the website and makes it easier to collate and analyse the data. Our current focus is on implementing mark-up on all ligand summary pages and target detail pages. This involves including properties from the Bioschemas MolecularEntity profile (https://bioschemas.org/profiles/MolecularEntity/0.5-RELEASE/) and Protein profile (https://bioschemas.org/profiles/Protein/0.11-RELEASE/), which we have been involved in developing. We thank Dr. Alasdair Gray (Heriot-Watt University) for his advice and guidance in incorporating BioSchemas into GtoPdb.

We have also added mark-up to the new coronavirus page, which is now functioning, as tests using the Google Structured Data Testing Tool show.

Google Structured Data Testing Tool run on the GtoPdb coronavirus.jsp page. Left panel shows the mark-up, ight panel shows the validation, showing it detects the 3 proteins, including the SARS-CoV-2 main protease marked up on the page. *Ignore errors - this indicated that 'Protein' is a type not known to Google.*

PROBES AND DRUGS

Since 2019 we have had useful interactions with The Probes & Drugs portal including a Skype session. In particular they have not only picked up the chemistry from each of our releases, but they also managed to index all the compounds that are linked in the Concise Guide papers (see yellow highlight).

The have become a valuable source of stringently collated compound sets that are complementary to those in PubChem. Many of these (e.g. published kinase and probe sets) are uniquely captured by them and are important to be able to intersect with our own records.

ANTIBIOTIC DB

We are engaging with Prof. Laura Piddock on incorporation of data contained in Antibiotic DB (https://www.antibioticdb.com/) into GtoPdb. The initial work has been split between web-application development concerns and data curation. In terms of development we've discussed with Antibiotic DB (ADB)'s developer (Sam Durdy) about altering the ADB code so that it is possible to link directly into individual compound pages at ADB- this will allow for direct links between GtoPdb and ADB. We are also in discussion about longer-term hosting of the ADB at the University of Edinburgh.

In terms of curation, Dr. Elena Faccenda has been in discussion with Laura Piddock about rationalising the compounds in ADB so they can be mapped to GtoPdb compounds and incorporated. Because the historical focus of GtoPdb has been 'human' drug targets, very few antibiotic compounds are currently contained in the GtoPdb. Prof. Piddock is reviewing ADB content as this curation process has highlighted a good number of duplicate ADB entries, as well as many with either no structures and/or no references which would preclude entry into GtoPdb. The final set of ADB compounds which have validated chemical structures will be added to GtoPdb, although technicalities around data curation (*e.g.* species assignment/selectivity, resistance, whole organism data) and organisation of the antibiotics into families that would be recognisable to antimicrobial scientists have still to be finalised.

PUBCHEM

We have extended our important interactions with PubChem, including by both mail and TC conversations with Evan Bolton, Paul Theissen and other members of the team. Aspects of our PubChem ligand content are outlined in our latest NAR paper PMID 31691834 as well as comparative statistics with ChEMBL and BindingDB in PMID 32280387

We continue the important feed of reciprocal GtoPdb < BJP (and BJCP) > PubChem < > PubMed links. For example, our PubChem SID records now link to 427 BJP and 32 BJCP articles as PubMed records. A recent BJP reciprocal navigation example is shown below.

LUF7244, an allosteric modulator/activator of K_v 11.1 channels, counteracts dofetilide-induced torsades de pointes arrhythmia in the chronic atrioventricular block dog model.

Qile M[1], Beekman HDM[1], Sprenkeler DJ[1], Houtman MJC[1], van Ham WB[1,2], Stary-Weinzinger A[2], Beyl S[2], Hering S[2], van den Berg DJ[3], de Lange ECM[3], Heitman LH[4], IJzerman AP[4], Vos MA[1], van der Heyden MAG[1].
⊕ Author information

Abstract
BACKGROUND AND PURPOSE: K_v 11.1 (hERG) channel blockade is an adverse effect of many drugs and lead compounds, associated with lethal cardiac arrhythmias. LUF7244 is a negative allosteric modulator/activator of K_v 11.1 channels that inhibits early afterdepolarizations in vitro. We tested LUF7244 for antiarrhythmic efficacy and potential proarrhythmia in a dog model.

EXPERIMENTAL APPROACH: LUF7244 was tested in vitro for (a) increasing human $I_{Kv11.1}$ and canine I_{Kr} and (b) decreasing dofetilide-induced action potential lengthening and early afterdepolarizations in cardiomyocytes derived from human induced pluripotent stem cells and canine isolated ventricular cardiomyocytes. In vivo, LUF7244 was given intravenously to anaesthetized dogs in sinus rhythm or with chronic atrioventricular block.

KEY RESULTS: LUF7244 (0.5-10 μM) concentration dependently increased $I_{Kv11.1}$ by inhibiting inactivation. In vitro, LUF7244 (10 μM) had no effects on $I_{KIR2.1}$, $I_{Nav1.5}$, I_{Ca-L}, and I_{Ks}, doubled I_{Kr}, shortened human and canine action potential duration by approximately 50%, and inhibited dofetilide-induced early afterdepolarizations. LUF7244 (2.5 mg·kg^{-1} ·15 min^{-1}) in dogs with sinus rhythm was not proarrhythmic and shortened, non-significantly, repolarization parameters (QTc: -6.8%). In dogs with chronic atrioventricular block, LUF7244 prevented dofetilide-induced torsades de pointes arrhythmias in 5/7 animals without normalization of the QTc. Peak LUF7244 plasma levels were

Links from PubMed

GTPL10447; LUF7244; compound 7i [PMID: 26519929] ...
Source: IUPHAR/BPS Guide to PHARMACOLOGY
Deposit Date: 2019-09-19 Available Date: 2019-09-19 Modify Date: 2019-09-19
SID: 385612207 [CID: 127042386]
Summary PubChem Same Compound

Images from this publication. See all images (7) Free text

Related PubChem Substance

(Right sidebar)

Full text links — BJP > PMC Full text FREE

Save items — ☆ Add to Favorites

Similar articles
Allosteric Modulation of Kv11.1 (hERG) Channels Protects Against [Circ Arrhythm Electrophysiol. ...]
Azimilide and dofetilide produce similar electrophysiological and [Eur J Pharmacol. 2001]
Selective late sodium current inhibitor GS-458967 suppresses Torsa [Br J Pharmacol. 2018]
Review Antiarrhythmic and proarrhythmic properties of ([J Cardiovasc Pharmacol Ther. 2...]
Review Dofetilide: Electrophysiologic Effect, Efficacy, and Safe [Card Electrophysiol Clin. 2016]
See reviews...
See all...

Cited by 1 PubMed Central article
LUF7244, an allosteric modulator/activator of K$_v$ 11.1 char [Br J Pharmacol. 2019]

Related information
Articles frequently viewed together
MedGen
PubChem Compound
PubChem Substance
References for this PMC Article
Free in PMC
Cited in PMC

We continue to develop curatorial tagging within the depositor comment sections in the substance records (SIDs). Users are able to make domain-specific queries, related to both immunopharmacology and malaria pharmacology, to be executed from both the PubChem Substance (SID) and PubChem Compound (CID) interfaces, by using an advanced search of 'comments' fields. The example below shows the explicit retrieval of our 1466 approved drug SID records ranked by our submission date (query highlighted in yellow).

1. Rimegepant; BMS-927711; Nurtec ODT ...
Source: IUPHAR/BPS Guide to PHARMACOLOGY
Deposit Date: 2020-03-14 Available Date: 2020-03-14 Modify Date: 2020-03-14
SID: 404859151 [CID: 51049968]
Summary PubChem Same Compound

2. Structure not available
Eptinezumab; Vyepti; eptinezumab-jjmr ...
Source: IUPHAR/BPS Guide to PHARMACOLOGY
Deposit Date: 2020-03-14 Available Date: 2020-03-14 Modify Date: 2020-03-14
SID: 404859141
Summary

3. ambroxol; GTPL10692; 4-[(2-amino-3,5-dibromophenyl)methylamino]cyclohexan-1-ol
Source: IUPHAR/BPS Guide to PHARMACOLOGY
Deposit Date: 2020-03-14 Available Date: 2020-03-14 Modify Date: 2020-03-14
SID: 404859139 [CID: 2132]
Summary PubChem Same Compound

(Right sidebar)

Refine your results · Subsets of your results
BioActivity Experiments
BioAssays, Active (928)
BioAssays, Tested (928)

Find related data
Database: Select ▼
Find items

Search details
gtopdb_approved[comment] AND "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName]

PubChem have recently piloted a new Classification Browser (https://pubchem.ncbi.nlm.nih.gov/classification/#hid=92) which displays the GtoPdb target hierarchy in a way that allows users to browse our PubChem Substances/Compounds. The GtoPdb target classification is also shown on PubChem Target pages (e.g. HTR1A). Note that PubChem specifically selected us for highlighting in this highly-visible global resource because of our acknowledged quality as a submitter.

In later 2018 we completed the submission of BioAssays to PubChem, following on from a pilot exercise for the 5-HT receptor family in 2015. We can report a good working relationship with Ben Shoemaker at PubChem who has been helpfully overseeing the upload of the assays and is advising us on ways to keep these updated in the future. The Bioassays are also shown on Target and Compound pages in PubChem so this will increase exposure of the GtoPdb data.

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*". The PEP celebrated its 4th birthday on 1st April 2020.

Financial support is in place for one 0.5 FTE for the next 4-6 months. This comes from IUPHAR.

Site Usage

The figures below show month to month data from Google Analytics of the recorded PEP user sessions and the global distribution of users, from April 2016 when the PEP was launched up to the most current data. User sessions are continuing to grow, accruing 15-25K sessions/month during 2020. Almost 60% of traffic originates from desktops, 37% from mobiles and the remainder from tablets.
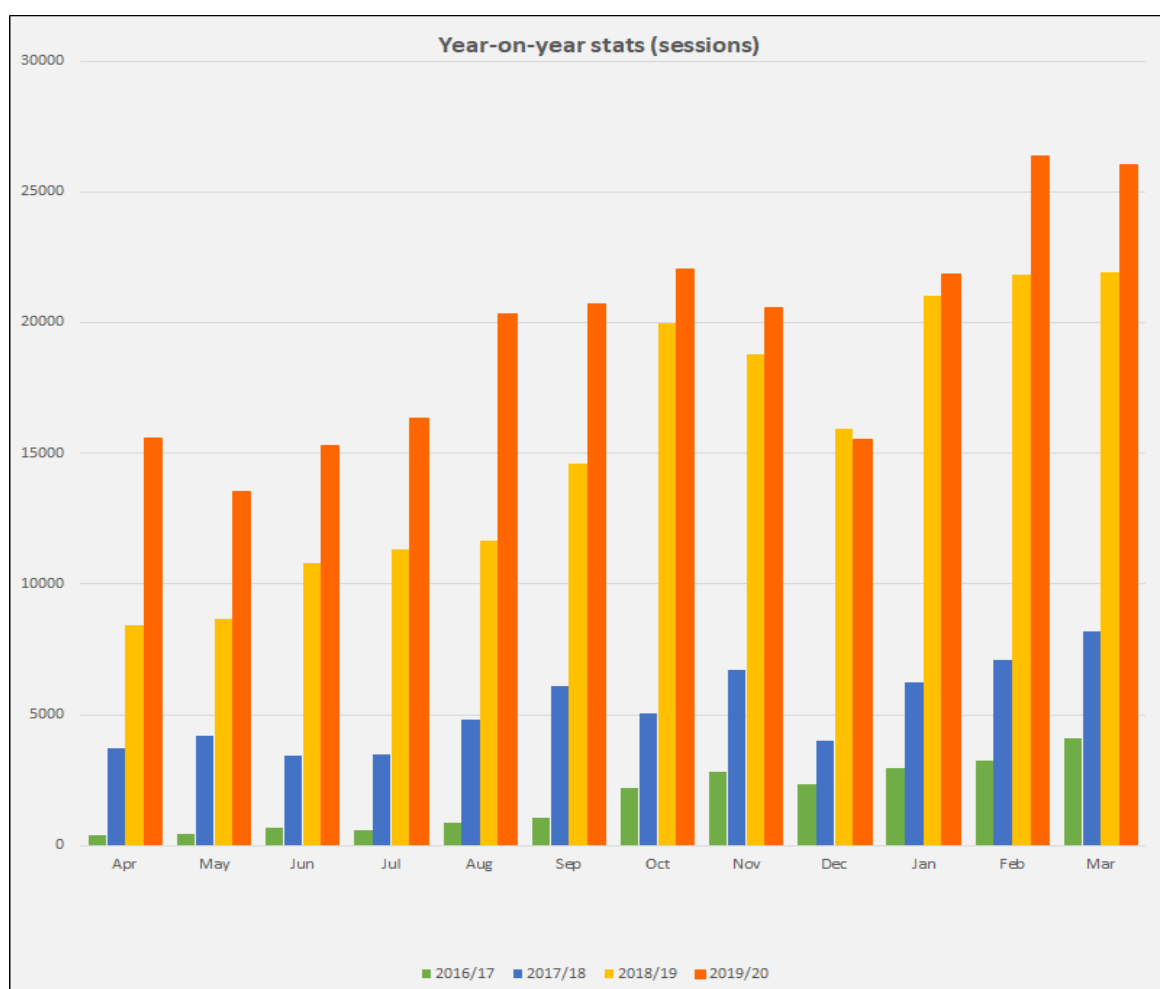
User Sessions

Geographic distribution for entire data set (April 2016-March 2020)
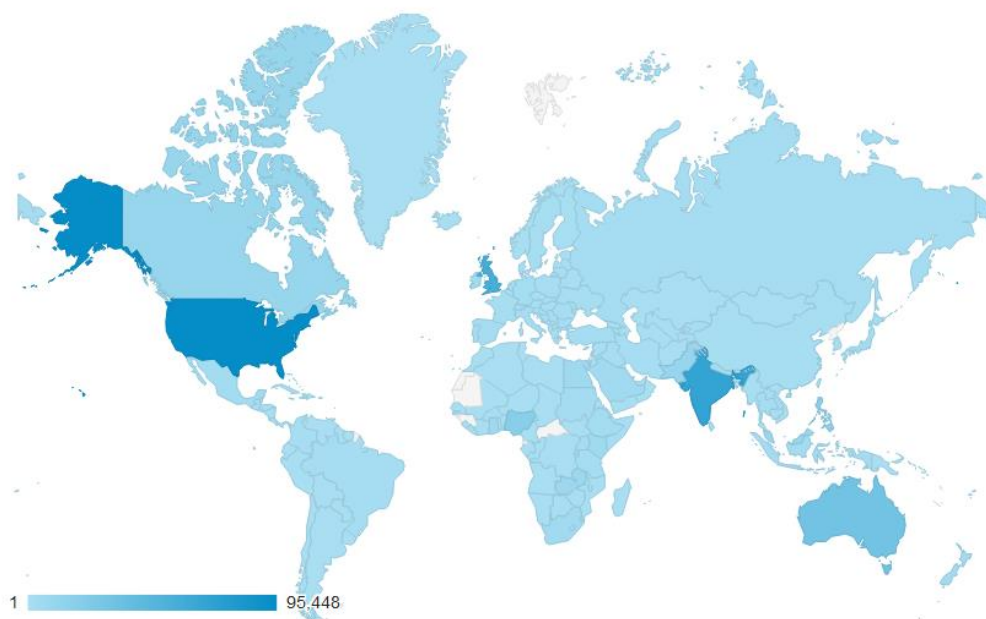
Google Analytics of access to IUPHAR PEP Website

We have noticed relatively high interest in our SlideShare offerings. We currently have 22 slide sets posted, and data analytics has recorded almost 17,000 views, and 600 downloads, in the last year. The top 5 (by number of views) are shown in the panel below.

Top content	
Name	Views
Drugs and blood clotting	2,846
Opioid analgesics- an introduction	2,555
Drugs acting on the kidney lectures 1 and 2	1,867
Physiology and pharmacology of nausea and emesis 2015 jap	1,579
An introduction to general anaesthesia	1,540

We also have embedded Vimeo videos by Simon Maxwell in some sections of PEP, and these have recorded ~3000 views coming from PEP.

PEP has 840 followers of our twitter handle, @PharmacologyEd.

A brief survey designed to collect basic feedback from PEP users was initiated at the end of March 2019. We have had >40 submissions from faculty and students, with most rating both the amount and quality of content as 'Excellent' and reporting that the site is 'Easy to navigate'. So far, IP address data shows completed surveys from users (new in 2020) in Mexico, Nigeria, Colombia, Korea, Mongolia, Myanmar and Papua New Guinea.

The journal-to-GtoPdb linking initiative PMID 25965085) for the BJP since Oct 2014 and BJCP since Nov 2016, can be counted via the reference citations to our Concise Guide and NAR papers. The results indicate out-links for ~ 80% of BJP papers and ~ 50% for BJCP. To ameliorate the retrospective "missing key link" problem we now have a prospective process whereby, on manuscript acceptance followed by their own marking-up of GtoPdb links, authors are advised to alert us directly to key entities that we do not yet have. In appropriate cases we then add these ligands and the new reference. This has the advantages, for both the author and the journal, of not only adding their reference into GtoPdb but also the paper gains PubChem-to-PubMed reciprocal linking derived from our PubChem ligand submissions.

This same principle of increased author and journal exposure actually applies to all the references we curate but is even more so for those for which we submit ligand links into PubChem. A snapshot of the statistics for release 2020.1 is shown below.

Links from PubChem Substance

Items: 1 to 20 of 11696

<< First   < Prev   Page 1   of 585   Next >   Last >>

1. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor.
   Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu NH, Nitsche A, Müller MA, Drosten C, Pöhlmann S.
   Cell. 2020 Apr 16;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052. Epub 2020 Mar 5.
   PMID: 32142651   Free PMC Article
   Similar articles

2. Osilodrostat: First Approval.
   Duggan S.
   Drugs. 2020 Apr;80(5):495-500. doi: 10.1007/s40265-020-01277-0. Review.
   PMID: 32141023
   Similar articles

3. COVID-19: combining antiviral and anti-inflammatory treatments.
   Stebbing J, Phelan A, Griffin I, Tucker C, Oechsle O, Smith D, Richardson P.
   Lancet Infect Dis. 2020 Apr;20(4):400-402. doi: 10.1016/S1473-3099(20)30132-8. Epub 2020 Feb 27. No abstract available.
   PMID: 32113509   Free PMC Article
   Similar articles

4. CSTI-300 (SMP-100); a Novel 5-HT$_3$ Receptor Partial Agonist with Potential to Treat Patients with Irritable Bowel Syndrome or Carcinoid Syndrome.
   Roberts A, Grafton G, Powell AD, Brock K, Chen C, Xie D, Huang J, Liu S, Cooper AJ, Brady CA, Qureshi O, Stamataki Z, Manning DD, Moore NA, Sargent BJ, Guzzo PR, Barnes NM.
   J Pharmacol Exp Ther. 2020 Apr;373(1):122-134. doi: 10.1124/jpet.119.261008. Epub 2020 Feb 26.
   PMID: 32102919
   Similar articles

The distribution of these linkages by Journal is shown below.
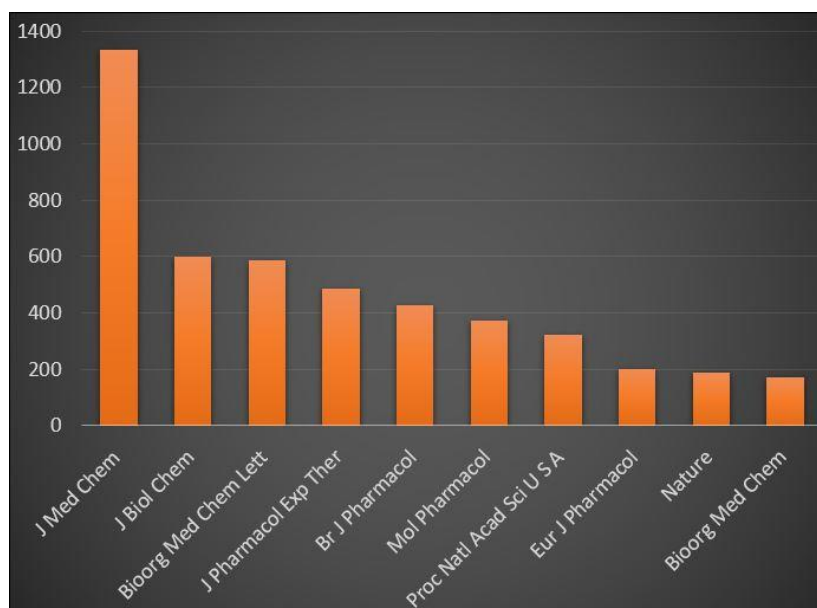
The connection of 10034 SIDs to 11696 PMIDs implies we are curating approximately 0.9 ligands-per-paper. However, this is a slight underestimate because a proportion of ancillary references are included in our PubChem submissions (e.g. reviews and clinical trials). It should also be noted that PMIDs do not cover the entirety of our literature coverage since ligand-associated references include a small number that are patent-only and DOI-only (including pre-prints).

IMMUNOPAEDIA

Engagement continues with Immunopaedia, an open-access online platform freely available for learning and teaching immunology. The resource aims to improve engagement between core immunology and clinical practice, and it is the official International Union of Immunological Societies (IUIS) learning site. Immunopaedia provides clinical case studies to help highlight immunological concepts, an online course to support teaching and learning in immunology, and it provides information on treatment and diagnostics on infectious diseases.

We have extended the immunopharmacology links from ligand summary pages to provide links from relevant ligand to case studies at Immunopaedia.

rituximab				

Ligand id: 6780

Name: rituximab

View more information in the IUPHAR Pharmacology Education Project: rituximab

📊 **View interactive charts of activity data from GtoPdb and ChEMBL (where available) across species**

Summary Biological activity Clinical data References **Immunopharmacology**

Immunopharmacology Comments

Rituximab is the first biological agent to show positive effects on biological and clinical disease parameters in Sjögren's syndrome [1,7].

Immunopharmacology Disease

Disease	X-Refs	Comment	References
Chronic lymphocytic leukemia	Disease Ontology: DOID:1040 OMIM: 151400 Orphanet: ORPHA67038	An anti-CD20 therapy approved for CLL and non-Hodgkins lymphoma.	
Rheumatoid arthritis	Disease Ontology: DOID:7148 OMIM: 180300	An anti-CD20 therapy approved for RA.	
Pemphigus	Disease Ontology: DOID:9182	Rituximab is the first biologic therapy approved for pemphigus vulgaris (PV), and represents the first major PV therapeutic advance in more than 60 years.	

Immunopaedia Case Studies Links

My eyes cross at twilight

A 7 year old with severe muscle weakness and difficulty walking

A case of lymphadenopathy and night sweats

My head hurts and I cannot speak?

Screenshot showing links from rituximab and four Immunopaedia case studies

We are also looking at how we might best include links from targets and families to Immunopaedia. In total we have ~150 links curated in GtoPdb and will continue to engage to add more links in future database releases.

NEW DRUG APPROVALS

For our 2Q 2019 database releases there was a substantially increased coverage of European Medicines Agency (EMA) drug approval data. There are 414 approved drugs with EMA marked as a source, up from 274 in 2018.1. In addition, at about this time of year considerable interest is generated from reviews of the previous year's FDA Drug Approvals (see https://cdsouthan.blogspot.com/2019/01/2018-approved-drugs-in-pubchem.html)
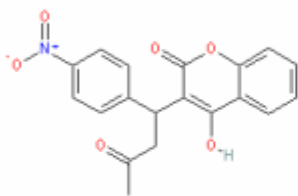
Reaching 59, 2018 was welcomed as a particularly prolific year. However, for our own capture, we have various exclusion criteria such as anti-infectives (with some exceptions including our antimalarials mentioned above), already-approved mixture components, topicals, non-antibody biologicals, undefined extracts (e.g. fish oil) and inorganics. Thus, our scorecard stands at 26 chemical entities that form PubChem Compound Identifiers. We also have database records and PubChem Substance submissions for 11 of the 12 newly-approved antibodies (excepting the anti-HIV one).

- **Ligand Activity Graphs:** This tool provides charts with box plots summarising all the activity data for a ligand taken from ChEMBL and GtoPdb across multiple targets and species. Separate charts are created for each target, and where possible the algorithm tries to merge ChEMBL and GtoPdb targets by matching them on name and UniProt accession, for each available species. However, please note that inconsistency in naming of targets may lead to data for the same target being reported across multiple charts.

  Previously, access to the charts was only found on a ligand's summary page, under the biological activity tab. We've now moved that link so it appears more prominently on these pages.

We have also added a new icon on the ligand list pages which indicated whether there are activity charts available for the ligand. Click the icon takes the users straight to the charts.

- **Clinical trial data:** The ligand summary pages have been updated to improve the display of clinical trials information. Key clinical trials involving the ligand are now displayed in a separate table, under the clinical data tab. The table includes links out to the clinical trial plus trial title, type, source, curator comments and reference

22

- **WHO essential medicines:** We have added a new ligand category for WHO essential medicines. Ligands are marked in the database if they are in the current (21st list, 2019) World Health Organization (WHO) Model List of Essential Medicines. These are displayed under our ligand list view, and also on individual ligand summary pages (shown in the images below).

chloroquine

❓ **Ligand id:** 5535

Name: chloroquine

Structure and Physico-chemical Properties

2D Structure ❓

Calculated Physico-chemical Properties ❓

Hydrogen bond acceptors	3
Hydrogen bond donors	1
Rotatable bonds	8
Topological polar surface area	28.16
Molecular weight	319.18
XLogP	4.27
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

❓ 📊 **View interactive charts of activity data from GtoPdb and ChEMBL (where available) across species**

| Summary | Biological activity | Clinical data | References | Structure | Similar ligands | Immunopharmacology | Malaria |

Classification ❓

Compound class	Synthetic organic
Ligand families/groups	Antimalarial ligands
Approved drug?	Yes (FDA (1949), UK (2000))
WHO Essential Medicine	WHO Model List of Essential Medicines (21st List, 2019). Access PDF version.

● **External links in European PubMed Central:** The GtoPdb has recently been included in the External Links service at Europe PMC (EPMC) (https://europepmc.org/LabsLink). On EPMC pages, links to target and ligand entries have been added to the papers curated by GtoPdb that include a quantitative description of the ligand-target interaction. It is possible to retrieve all these references at EMPC by running an "Advanced Search" and selecting "IUPHAR/BPS Guide to Pharmacology" from the "External Links" drop-down list (LABS_PUBS:"1969″) as the cross-reference query. This currently gives 6,753 results, which can be further combined as Boolean-type queries against all other types of EPMC indexing including Bibliographic Fields, Filters, Data Links, External Links and Annotations.

Showing how GtoPdb links appear in EPMC articles under the 'Data' section. Targets or ligand mentioned in the article (that are curated in GtoPdb) will appear.

- **Update ChEMBL target links:** Our target out-links to ChEMBL have been updated, many thanks to Anna Gaulton for her support in this. Not only have we updated our existing links, but we have added around ~800 new outlinks.

- **New download lists:** We have added a downloadable list of approved drugs and their primary targets. Please see our downloads page for full access.

- **Other minor updates:**
    - Our site-wide search now works using '*' as a wildcard indicator at the end of a search string. This helps make our search behaviour more consistent with other web-resources.
    - Interaction table style modified improve style and better handle wrapped text

Growth rates over the span of the previous Wellcome Trust grant are documented in earlier reports and our 2016, 2018 and 2020 NAR papers. Updates come through subcommittee contributions to the Concise Guide, and the continued tagging of pre-existing targets and ligands with comments and references to GtoImmuPdb and GtoMPdb.

	Oct 2013	Oct 2015	April 2016	Oct 2016	Apr 2017	Oct 2017	May 2018	Sep 2018	Mar 2019	Apr 2020
Target protein IDs	2485	2761	2775	2794	2808	2825	2872	2880	2920	2943
Ligands total	6064	8024	8400	8674	8872	8978	9251	9405	9662	10053
Approved drugs	559	1233	1273	1291	1322	1334	1364	1386	1421	1471
Antibodies	10	138	172	205	212	223	240	248	255	270
Peptides	1776	1981	2007	2039	2063	2079	2092	2100	2122	2150
Synthetic small molecules	3504	5055	5363	5563	5729	5807	6048	6180	6401	6816
PubChem SIDs	3107	8024	8328	8674	8831	8978	9251	9405	9662	10053
PubChem CIDs	2694	6057	6163	6337	6813	6822	7109	7224	7407	7483
Binding constants	41076	44691	45534	45908	46287	46488	47058	47426	48071	48902
References	21774	27880	29247	30251	31239	31733	33245	34382	35723	37261

In preparation for the Concise Guide to PHARMACOLOGY (CGtP 2019/20 edition) our expert subcommittees and collaborators provided updates to the family summary pages across all target classes. Details of additional updates are listed below.

GPCRs:
Acetylcholine receptors (muscarinic)
Apelin receptor
Calcitonin receptor
Calcium-sensing receptor
Cannabinoid receptors
Chemokine receptors
Free fatty acid receptors
Glucagon receptor family
GPR15
GPR68
Leukotriene receptors
Melatonin receptor
Opioid receptors

Channels:
5-HT3 receptors
Nicotinic acetylcholine receptors
Calcium- and sodium-activated potassium channels
Transient Receptor Potential channels

NHRs:

3A. Estrogen receptors
1F. Retinoic acid-related orphans
1H. Liver X receptor-like receptors

Enzymes and Other protein targets:
Carboxylases
epidermal growth factor receptor
2.7.1.40 Pyruvate kinases
Monoacylglycerol lipase
Sphingomyelin phosphodiesterase
Phosphodiesterases, 3′,5′-cyclic nucleotide
CYP2 family
Poly ADP-ribose polymerases
Thrombopoietin receptor

New targets (not including Antimalarial targets):
SARS-CoV-2 proteins
Cereblon protein
Nudix hydrolase 7
carbonic anhydrase 2
carbonic anhydrase 5A
hydroxysteroid 17-beta dehydrogenase 2
PVR cell adhesion molecule

SOS Ras/Rac guanine nucleotide exchange factor 1	dihydropyrimidine dehydrogenase
lysyl oxidase	P-selectin (CD62)
glycine cleavage system protein H	CD36 molecule
5-methyltetrahydrofolate-homocysteine methyltransferase	C1-related protein
perforin 1	tankyrase
O-GlcNAcase	tankyrase 2
	glutathione S-transferase omega 1
	nectin cell adhesion molecule 4

PUBCHEM STATISTICS FOR GTOPDB, GTOIMMUPDB AND GTOMPDB

The stats for the 2019.2 release (with 2018.4 in brackets) are as follows (N.B. because the NCBI Entrez system suffers from overload, the links below may time out but should eventually return the result).
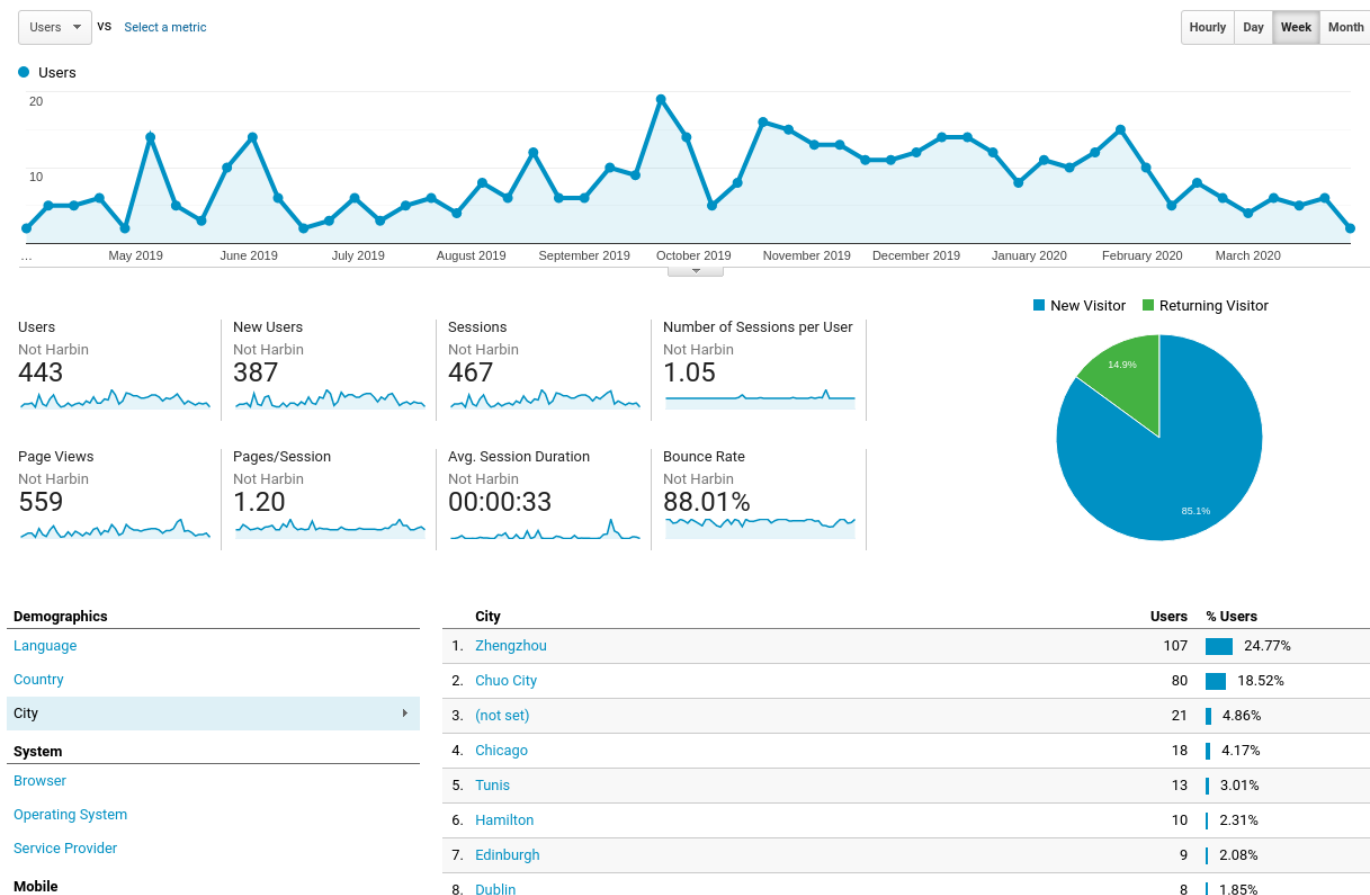
1. Substances (SID) that we submit to PubChem (refreshing previous submissions) are up to 10034 (9670).
2. Those that have defined chemical structures are merged into 7828 (7478) Compound Identifiers, CIDs (i.e. small molecules and moderate peptides)
3. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND approved [Comment] now retrieves 1569 SIDs (1518) .
4. Of these 1368 (1328) have CIDs (use the "Find Related Data" operator and select "same CIDs".
5. Of our SIDs, 1279 (1151) are tagged in GtoImmuPdb and 302 (282) of these are approved drugs
6. Of our CIDs 724 are tagged in GtoImmuPdb
7. Of our SIDs, 81 are tagged in GtoMPdb and 22 of these are approved drugs
8. Of our CIDs 51 are tagged in GtoMPdb
9. We have 1847 (1817) structures that ChEMBL23 does not have, 5461 not in DrugBank and 6491 not in DrugCentral.
10. 166 (182) structures unique to us as a source.

PubChem has released a new interface that expands the indexing and search functionality for our own entries (see example query below) but there are still some minor discrepancies in the exact metrics returned compared to the Entrez interface.

SYNPHARM: A DATABASE OF SMALL MOLECULES AND THEIR DRUG-RESPONSIVE PROTEIN SEQUENCES LINKED TO GTOPDB

For a detailed description of SynPHARM please see the October 2016 report or the website: http://synpharm.guidetopharmacology.org/. It is a database of drug-responsive protein sequences derived from GtoPdb interaction data. A paper describing SynPHARM has been published: Ireland et al. (2018) SynPharm: A Guide to PHARMACOLOGY Database Tool for Designing Drug Control into Engineered Proteins. ACS Omega. Jul 31;3(7):7993-8002. PMID: 30087931. The figure below shows the SynPHARM access statistics for the past year. These stats exclude traffic from Harbin, China as we noted a spike from this location in october 2019 which looked consistent with being a bot.

Users	New Users	Sessions	Number of Sessions per User
Not Harbin	Not Harbin	Not Harbin	Not Harbin
443	387	467	1.05

Page Views	Pages/Session	Avg. Session Duration	Bounce Rate
Not Harbin	Not Harbin	Not Harbin	Not Harbin
559	1.20	00:00:33	88.01%

	City	Users	% Users
1.	Zhengzhou	107	24.77%
2.	Chuo City	80	18.52%
3.	(not set)	21	4.86%
4.	Chicago	18	4.17%
5.	Tunis	13	3.01%
6.	Hamilton	10	2.31%
7.	Edinburgh	9	2.08%
8.	Dublin	8	1.85%

Demographics
Language
Country
City
System
Browser
Operating System
Service Provider
Mobile

SynPharm access statistics for the past year (April 2019 - Mach 2020)

- As outlined in previous reports we track various metrics for the GtoPdb team and NC-IUPHAR affiliated papers in [PubMed](), [PubMed Central](), [European Pub Med Central]() (EPMC) [Kudos entries]() and [Altmetrics]().
- Team members have individual [Google Scholar]() pages as well as [ResearchGate]() entries and [Edinburgh Research Explorer]() profiles.
- However, the profile of choice (as EMPC linked with citation graphs) has now become [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]() and SDH [0000-0002-9262-8318]().

Below are the April 2019 live bibliometric updates compared to the November 2018 metrics. These are given with EPMC links which have the advantage over PubMed of directly generating a citation ranking for any set (but with significantly lower citation rates than PubMed, Google Scholar or WOS).

- Database team members' cumulative co-authored publications have increased from 169 to [170]() (this is a PubMed query that is not so easy to do in EPMC).
- IUPHAR reviews in BJP increased by 1 to [27]().
- IUPHAR Pharmacological Reviews increased by 1 to [104]().
- The BJP "Concise Guide" sets from 2013 and 2015 added up to 17 with the 2017/18 set now taking us to [26]() papers.
- Our publications in the [NAR Database issues]() increased by 1 to [7]()
- We continue to get high citation rates in our NAR and Concise Guide articles because the BJP and BJCP selected these as [reference citations]() for the GtoPdb outlinks. These are topped by our NAR 2016 entry ([PMID 24234439]()) with [689]() citations, overtaking the 2014 paper ([PMID 24234439]()) that reached [631]().
- The "Concise Guide" citations are currently led by 2015/16: Enzymes ([PMID 26650445]()) at [503]() closely followed by 2013/14: G protein-coupled receptors ([PMID 24517644]()) at [450]().
- The overall citation performance of our papers resulted in team members JLS, EF and AJP, along IUPHAR co-authors, SPHA, MS, and APD being listed in the Clarivate 2018 ranking of [Highly Cited Researchers]().
- The [Altmetric]() rankings for all our OA papers are now indexed in [ScienceOpen]().

GTOIMMUPDB WEB INTERFACE AND DATABASE DEVELOPMENT STATUS

GtoImmuPdb is an extension of GtoPdb and its development has 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 involves 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).

In October 2018, we officially launched the IUPHAR Guide to IMMUNOPHARMACOLOGY, having made the first public release back in June 2018. Technical details on its development and blog posts related to the resource can be found here.

As mentioned earlier, we continue to incorporate outlinks to Immunopaedia from immune-tagged targets and ligands.

GUIDE TO IMMUNOPHARMACOLOGY: PUBLICATIONS AND PRESENTATIONS

Following the launch of GtoImmuPdb we have focussed more heavily on disseminating information about the resource.

At the end of 2018, a Nature Web Watch article was published which acted a succinct way to announce the availability of the new resource.

- A new guide to immunopharmacology. Harding SD, Faccenda E, Southan C, Maffia P, Davies JA. Nat Rev Immunol. 2018 Dec;18(12):729. doi: 10.1038/s41577-018-0079-2. No abstract available. PMID: 30327546

In collaboration with Pasquale Maffia (Glasgow University), we have published a review in Immunology on using the Guide to Immunopharmacology, with a particular focus on case studies in targeting vascular inflammation.

- The IUPHAR Guide to Immunopharmacology: connecting immunology and pharmacology. 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). Immunology, 160: 10-23. doi:10.1111/imm.13175 [PMID:32020584]

This has been followed by a more recent Editorial in Immunology.

- Guide to Immunopharmacology: a database to boost immunology education, research and therapy. Milling S, Spedding M, Maffia P. Immunology. 2020 May;160(1):1-2. doi: 10.1111/imm.13201. PMID: 32297319
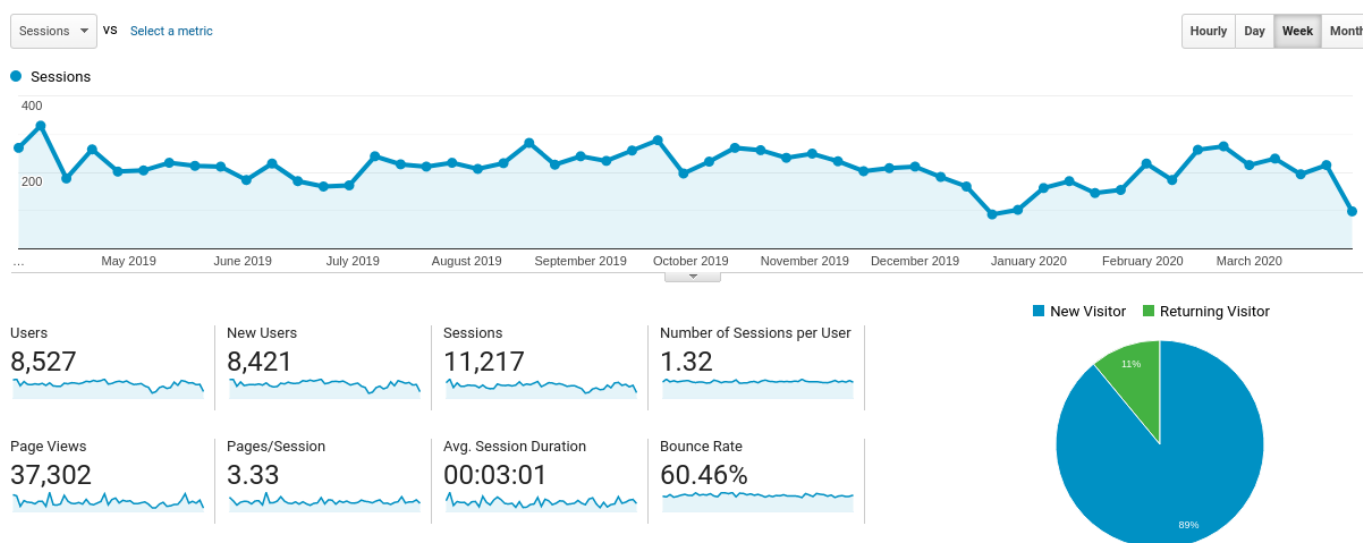
At the end of 2019 we presented the resource at two meetings. These presentations were aimed at being guides to using the resource and built on the case studies presented in the Immunology review article.

- Dr. Elena Faccenda presented at the 39th Congresso Nazionale della Società Italiana di Farmacologia, Firenze, Italy. Nov 2019. Link to slides.
- Prof. Jamie Davies and Dr. Simon Harding then presented in December 2019 at the BPS Pharmacology meeting in Edinburgh, UK. This formed part of the workshop session "Guide to Immunopharmacology - How to Navigate and Use the Database". Dr. Simon Harding's was a tutorial on using the resource (https://www.slideshare.net/GuidetoPHARM/hardingimmunopharmacologyworkshoppharmacology2019).

GTOIMMUPDB ANALYTICS

Our analytics over the last year (Apr 19 - Mar 20) shows an average of ~930 sessions per month.

Users 8,527	New Users 8,421	Sessions 11,217	Number of Sessions per User 1.32
Page Views 37,302	Pages/Session 3.33	Avg. Session Duration 00:03:01	Bounce Rate 60.46%

Access statistics for GtoImmuPdb (March 2019 - April 2020)

DISEASE DATA

Disease	GtoPdb Ligands	GtoPdb Targets
Rheumatoid arthritis	127	11
Asthma	78	6
Psoriasis	58	2
Chronic obstructive pulmonary disease	42	-
Crohn's disease	27	1
Osteoarthritis	25	4
Systemic lupus erythematosus	24	-
Ulcerative colitis	23	1
Psoriatic arthritis	16	-

This table gives a summary of the diseases with the most target and ligand associations in GtoImmuPdb.

IMMUNO PROCESS DATA

The table below summarises the unique target (UniProtKB) annotated to each category and the total target-GO annotations (data here is from 2020.2 release).

Process Category	GtoPdb Human UniProtKB	Target-GO annotations
Barrier integrity	51	68
Inflammation	677	1652
Antigen presentation	162	247
T cell (activation)	230	528
B cell (activation)	183	323
Immune regulation	553	1586
Tissue repair	27	29
Immune system development	290	570
Cytokine production & signalling	558	1702
Chemotaxis & migration	279	607
Cellular signalling	517	1332

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	53
T cells	CL:0000789 alpha-beta T cell CL:0000815 regulatory T cell CL:0000911 effector T cell	80
Dendritic cells	CL:0000451 dendritic cell	41
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	3
Macrophages & monocytes	CL:0000235 macrophage CL:0000576 monocyte	58
Granulocytes	CL:0000094 granulocyte	48
Natural killer cells	CL:0000623 natural killer cell	28
Mast cells	CL:0000097 mast cell	39
Innate lymphoid cells	CL:0001065 innate lymphoid cell	6
Stromal cells	CL:0000499 stromal cell	1

- 618 targets tagged as in GtoImmuPdb:
    - 150 catalytic receptors
    - 204 enzymes
    - 101 gpcrs
    - 40 ion channels
    - 107 other proteins
    - 8 nuclear hormone receptors
    - 10 transporters
- 1277 ligands tagged as in GtoImmuPdb:
    - 820 synthetic organic
    - 159 antibodies
    - 253 peptides
    - 28 metabolites
    - 16 natural products
    - 1 inorganic
    - 272 Approved drugs
- Detailed lists on:
    - www.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp

SEARCHING, COLLATION, ALERTING

The different strategies we had used to retrieve papers was already described in the Oct 2018 report. However, in terms of using open reference managers to collate, tag, add curatorial notes and share papers of interest, we faced a major challenge in 1Q 2019 with the announcement of the closure of CiteUlike (the URL is already dead). We had been usefully using this over the last three years for intra-team and public sharing. Fortunately bulk migrations to Zotero worked fairly well and, crucially preserved the tagging and notes we had added to our CiteUlike entries. Example entries from our "Hot Topic" tagging are shown below from https://www.zotero.org/cdsouthan/items/collectionKey/4ZK4CW8S/tag/htopic

	Title	Creator	Date Modified
☐	Functional characterization of 3D protein structures informe…	Hicks et al.	4/17/2019 10:52 AM
☐	A Brief Note About Alzheimer's	Lowe	4/17/2019 10:51 AM
☐	Prioritization of cancer therapeutic targets using CRISPR-Ca…	Behan et al.	4/14/2019 7:59 PM
☐	A reference map of the human protein interactome	Luck et al.	4/11/2019 10:08 PM
☐	Microdeletion in a pseudogene identified in a patient with h…	Habib et al.	4/1/2019 1:14 PM
☐	The past, present and future of anti-malarial medicines	Tse et al.	4/1/2019 10:27 AM
☐	Biology must develop herd immunity against bad-actor molecul…	Plemper and Cox	4/1/2019 9:57 AM
☐	A Diagnosis for All Rare Genetic Diseases: The Horizon and t…	Boycott et al.	3/30/2019 9:46 PM
☐	Pharma R&D Annual Review 2018	Llyod	2/26/2019 11:34 PM

Team members and collaborators are still adjusting to Zotero sharing features (and collaborators are welcome to connect to us) but we continue to use a variety of tags for our own triage in addition to adding pre-curation (e.g. PubChem IDs and patent numbers) and post curation notes (including to curated ligands). In terms of alerting we follow Twitter feeds from Immune Regulation News , Human Immune News British Society for Immunology, Edinburgh Centre for Inflammation Research as well as journals such as Nature Immunology and Journal of Immunology.

THE GUIDE TO MALARIA PHARMACOLOGY DATABASE (GTOMPDB)

INTRODUCTION

The Guide to MALARIA PHARMACOLOGY (GtoMPdb) has been developed as an extension to the main GtoPdb database, with the aim of providing optimized access for the malaria research community to the data in GtoPdb. The initial phase of the project is now complete and MMV have provided further funding (until December 2020) to allow malaria pharmacology content to be maintained and expanded. In this section of the report we will provide an update on both the curation effort and the status of web interface and database developments, including details of the public release of the GtoMPdb.

OFFICIAL PUBLIC RELEASE

The IUPHAR/MMV Guide to IMALARIA PHARMACOLOGY was officially released in September 2019. The resource is now available at www.guidetomalariapharmacology.org.

PUBLICATIONS AND PRESENTATIONS

To coincide with World Malaria Day 2019 and to raise awareness we issued a blog post and a news release, in conjunction with Edinburgh Infectious Diseases and the School of Biological Sciences. These highlighted the release of the GtoMPdb and also provided an account of the long association malaria research has had with Edinburgh.

During the course of 2019 the resource was presented at a number of meetings.
- BioMalPar XV: Biology and Pathology of the Malaria Parasite, EMBL, Heidelberg, Germany, May 2019. Link to poster.
- 8th Edinburgh Infectious Diseases Symposium, Edinburgh, UK, June 2019. Poster presentation.
- Glasgow-Edinburgh Malaria Mosquito Meeting (GEMM), Edinburgh, UK, December 2019. Link to slides.

An article, published in the annual database issue of the journal *Nucleic Acids Research*, was used to announce the release of the GtoMPdb and provide an introduction to the resource.

- The IUPHAR/BPS Guide to PHARMACOLOGY in 2020: extending immunopharmacology content and introducing the IUPHAR/MMV Guide to MALARIA PHARMACOLOGY. 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. Nucleic Acids Res. 2020 Jan 8;48(D1):D1006-D1021. doi: 10.1093/nar/gkz951. PMID: 31691834

In addition, blog posts related to the resource and technical reports on its development can be found here.

GTOMPDB TARGET AND LIGAND CURATION

COLLECTING AND PRIORITISING CONTENT

The curation team utilizes a similar strategy to the one employed by GtoImmuPdb and described in our previous reports. We have continued to increase our collection of publications, maintained in Zotero, that we have tagged with antimalarial specific tags. In addition, MMV provided an initial list of targets and ligands of high priority and we will continue to build on this list with the advice of both MMV and our expert advisory committee (EAC).

CURATION SUMMARY

The number of ligands in the public database with antimalarial activity has continued to increase and we have also added to the number of *P. falciparum* targets. Our most recent database release (2020.2) contains:

- 80 ligands tagged as in GtoMPdb:
  http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=999
- 33 targets tagged as in GtoMPdb:
  http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=970

GTOMPDB WEB INTERFACE AND DATABASE DEVELOPMENT

The GtoMPdb uses the same underlying database as GtoPdb and in previous reports (May 2018, October 2018 and April 2019) we have described a number of changes to the database structure and the web interface that were necessary for the capture and presentation of antimalarial data. To summarize this development work, we have:

- Introduced a project specific tag allowing us to identify all ligands and targets in the database that are to be included in the GtoMPdb.
- Many antimalarial compounds have a poorly understood mechanism of action and an unknown molecular target and we have extended the interactions table and updated the web interface to accommodate this.
- Introduced a new 'whole organism' assay type to capture data from the whole cell assays used routinely in antimalarial drug discovery.
- Information about the *Plasmodium* lifecycle activity of a ligand is now stored in the database and is provided in the interactions table.
- Details about the *Plasmodium* species/strain can be stored in the database and displayed using a pop-up window that has been added to the interactions table.
- Deployed a new malaria comments field for both ligands and targets.
- Extended the site search to incorporate the malaria comments field and to bring back targets from searches on parasite lifecycle stage or malaria species.

This completed the major part of the required development work, but we have continued to implement improvements and in the last reporting period we have:

- Implemented a table to provide information about a ligand's Target Candidate Profile (TCP), where this is available. TCP details were previously included as a text description in the malaria comments.

P218

Ligand id: 9740

Name: P218

Structure and Physico-chemical Properties

2D Structure ❓
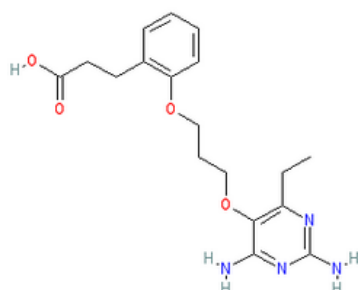
Calculated Physico-chemical Properties ❓

Hydrogen bond acceptors	6
Hydrogen bond donors	3
Rotatable bonds	10
Topological polar surface area	133.58
Molecular weight	360.18
XLogP	1.72
No. Lipinski's rules broken	0

Molecular properties generated using the CDK

❓ 📊 **View interactive charts of activity data from GtoPdb and ChEMBL (where available) across species**

| Summary | Biological activity | Clinical data | References | Structure | **Malaria** |

Guide to Malaria Pharmacology Comments

P218 was selected from a structure-informed drug discovery process to develop inhibitors of the clinically validated target *P. falciparum* dihydrofolate reductase (PfDHFR) [4]. The compound is example 8 from patent WO2009048957 [3].

Potential Target/Mechanism Of Action: P218 potentially inhibits both wild-type and clinically relevant mutated forms of PfDHFR.

Target Candidate Profiles

Profile	Intended Use	Target Stage	Comment	References
TCP-1	reduce parasite burden	asexual blood stages		
TCP-4	chemoprotection	hepatic schizonts		
TCP-5	transmission reduction	gametocytes		

Ligand page for P218, illustrating the Target Candidate Profile (TCP) table

- This has allowed us to add a new category to the GtoMPdb ligand list page: this now has three categories with the addition of a list of ligands with a TCP.

GtoMPdb ligand list page, showing the TCP tab selected.

- Following feedback from a member of our EAC, we have added a direct link to PlasmoDB on our detailed target pages. This update provides a useful search index in addition to ensuring the interface displays the link more prominently (we have also retained the pre-existing link to PlasmoDB, in the Gene Symbol column).
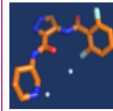

Target page for PfCPSF3, illustrating the new link to PlasmoDB (Database Links table)

GTOMPDB PORTAL DEVELOPMENT

The GtoMPdb portal (www.guidetomalariapharmacology.org) has been designed to provide optimized access to our antimalarial data and has been tailored for those involved in malaria research. Development of this portal was a major focus during the first phase of the project and is now essentially complete (please see previous reports for more details). However, we continue to encourage and welcome feedback and will consider implementing suggested improvements.

The portal provides tailored routes into browsing the antimalarial data. In addition to the existing ligand and target browse/search functionality available on the parent GtoPdb site we have developed customised views of the data that include parasite lifecycle and target species activity. Access to all is from the menu-bar or from the panels on the homepage.
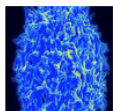
IUPHAR/MMV
Guide to MALARIA PHARMACOLOGY

Search Database

| Home | About ▾ | Targets ▾ | Ligands ▾ | Lifecycle ▾ | Species ▾ | Resources ▾ | Guide to PHARMACOLOGY |

Targets ?

- ► Antimalarial targets

Search for targets GO

Ligands ?

- ► All antimalarial drugs
- ► Approved antimalarial drugs

Search for ligands GO

Latest Updates & Help

Latest updates:

The first full release of GtoMPdb was made on 18th Sep 2019.

GtoMPdb was presented at the EMBL BoMalPar XV meeting in Heidelberg, 28-30 May 2019. See our poster.

Help

View our help page for information about the data in and using the Guide to MALARIA PHARMACOLOGY.

Parasite Lifecycle Stages ?

- ► Plasmodium liver stage
- ► Plasmodium dormant liver stage
- ► Plasmodium asexual blood stage
- ► Plasmodium sexual blood stage
- ► Plasmodium mosquito host

View parasite lifecycle home page GO

Target Species ?

- ► *P. falciparum*
- ► *P. vivax*
- ► *P. berghei*
- ► *P. cynomolgi*
- ► *P. yoelii*

View target species home page GO

GtoPdb Twitter activity

Tweets by @GuidetoPHARM ⓘ

GuidetoPharmacology
@GuidetoPHARM

Guide to Immunopharmacology: a database to boost immunology education, research and therapy onlinelibrary.wiley.com/doi /full/10.11…

Immunology   Guide to Imm…

Embed   View on Twitter

News

- ► GtoMPdb at EMBL BioMalPar XV (May 19) (slideshare)
- ► World Malaria Day 2019: A New Guide to Malaria Pharmacology
- ► GtoMPdb at Pharmacology 2018 (Dec 18) (slideshare)
- ► View GtoPdb news
- ► Medicine for Malaria Venture (MMV) home

GtoMPdb portal