IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

November 2020

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Contents

INTRODUCTION

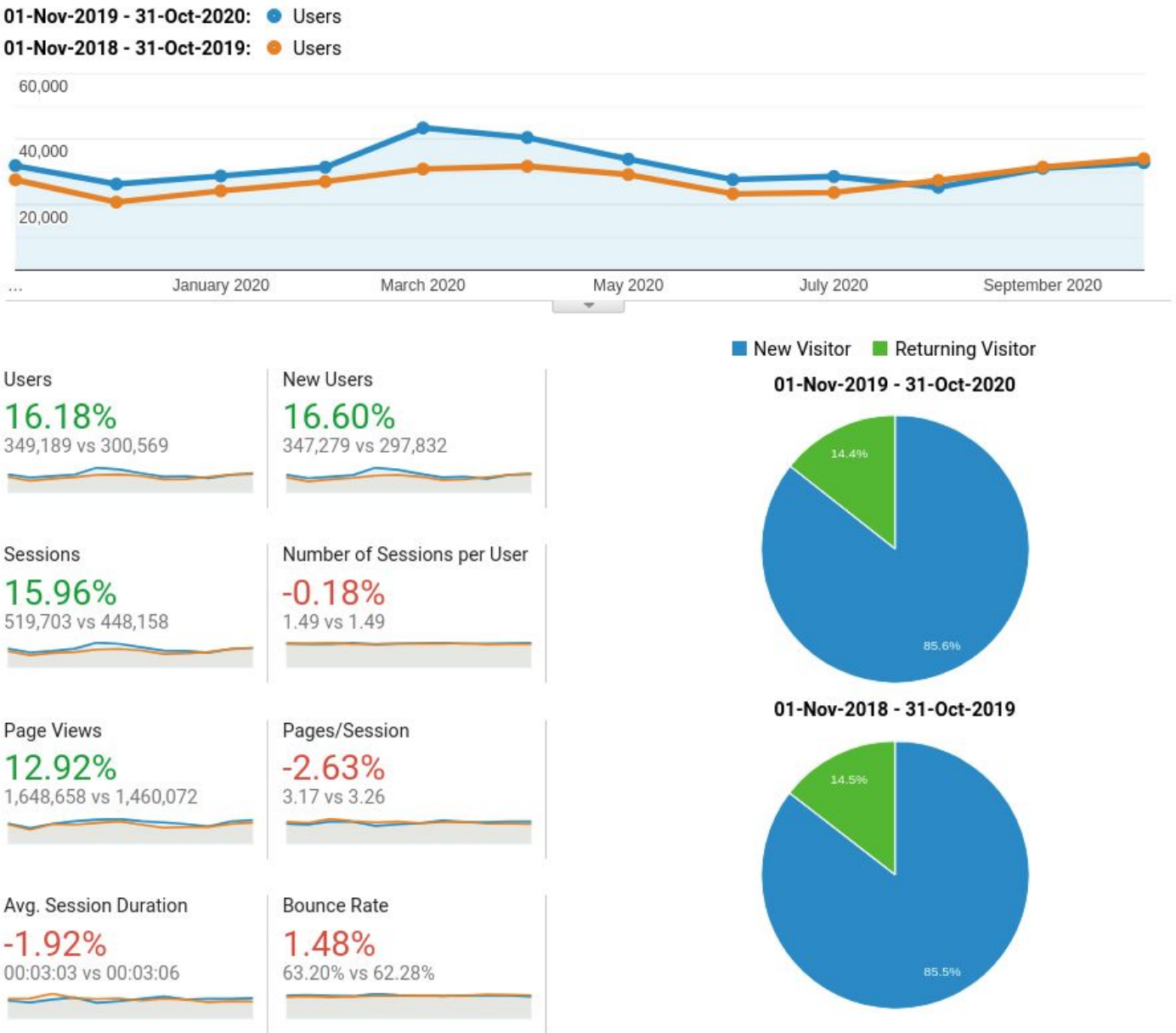
This database report provides an overview of recent progress and the current status of the IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb) since our last NC-IUPHAR meeting held in April 2020. Previous reports are online for Oct 2018, Apr 2019 and Apr 2020.

We update on the curation of data relevant to the pharmacological strategies aimed at mitigating SARS-CoV-2 infection (COVID-19). Since early March 2020 our Coronavirus (COVID-19) information page has been an easily accessible hub where this data has been collated.

This report also includes updates on the Wellcome Trust funded Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb) and the Medicines for Malaria Venture (MMV) funded Guide to MALARIA PHARMACOLOGY (GtoMPdb).

The Guide to Pharmacology Database (GtoPdb)

GtoPdb Website access statistics



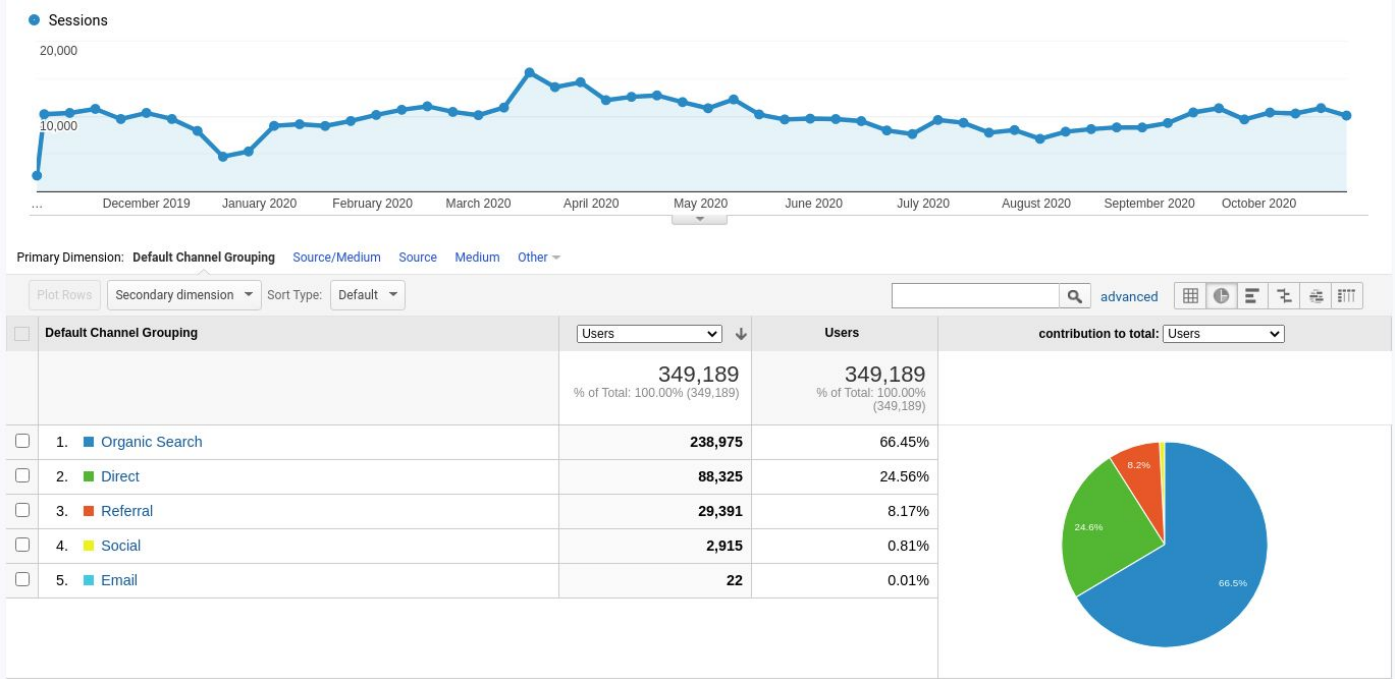
Graphs comparing visitors to guidetopharmacology.org for the 12 months from November 2019 to October 2020, with the previous 12 months.

Monthly statistics	Apr 2019 - Mar 2020 (previous 12 months)
Sessions	43,309 (37,347)
Users	29,099 (25,047)

Page views	137,388 (121,672)
Pages / Session	3.17 (3.26)
Avg. Session Duration	00:03:03 (00:03:06)

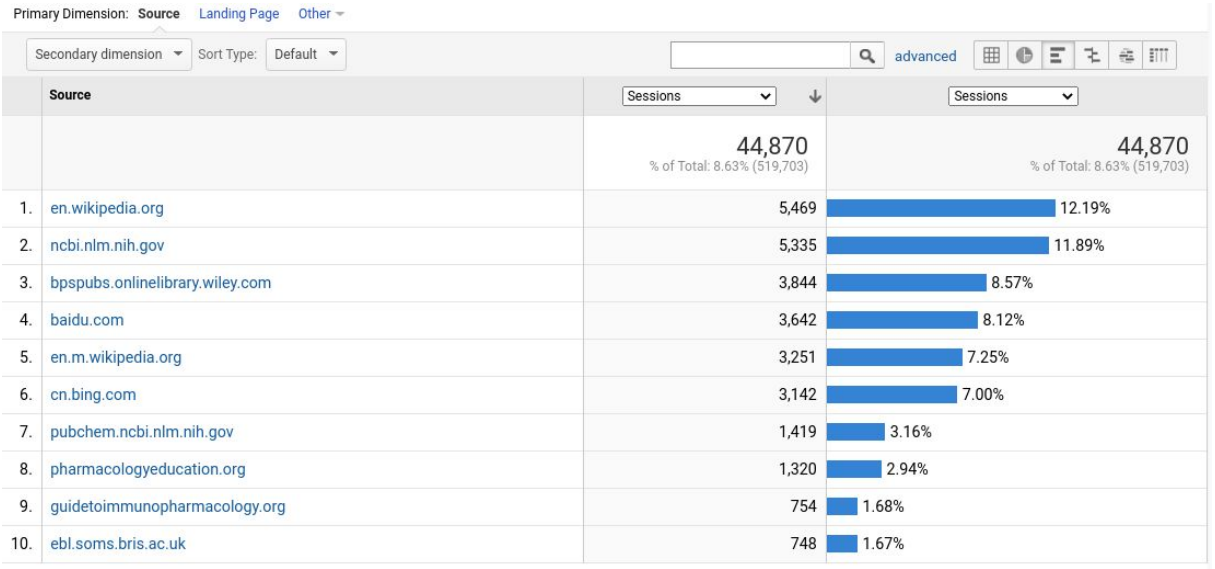
Acquisition, Browsers and Devices

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.



This shows acquisition data from Nov 2019 to Oct 2020

The majority of sessions on GtoPdb come *via* organic search (~66%). Only about ~9% of traffic come from referrals, with the following table showing how these break down.



We get about 12% of our referrals from NCBI and 8-9% from Wiley.

GtoPdb content

These database statistics were compiled from our November 12th release (v2020.5). 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	1231
Transporters	555
Other protein targets	216
Targets with ligand interactions	1819
Targets with quantitative ligand interactions	1567
Targets with approved drug interactions	660
Primary Targets with approved drug interactions	334
Total number of targets	**2976**
Ligands	***Number of ligands***
Synthetic organics	7303
Metabolites	514
Endogenous peptides	802
Other peptides including synthetic peptides	1378
Natural products	328
Antibodies	295
Inorganics	39
Approved drugs	1614
Withdrawn drugs	86
Ligands with INNs	2697
Labelled ligands	618
Unique PubChem CIDs (total CID links)	7994 (8196)
Ligands with target interactions	8959
Ligands with quantitative interactions (approved drugs)	7884 (974)
Ligands with clinical use summaries (approved drugs)	2837 (1610)
Total number of ligands (PubChem SIDs)	**10659**
Number of binding constants	48902
Number of binding constants curated from the literature	17695

Download Statistics

Yearly period 1st November Year 1 to 31st October Year 2.

Google Analytics comparison of Downloads

Event Category: Downloads

Event Label: Downloaded

	Count
2018-2019	2,787
2019-2020	4,134
Change	48.33%

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:

	2019-2020	2018-2019	Change
Targets CSV/TSV file	1311	1064	23.2%
Interactions CSV/TSV file	403	398	1.26%
*Ligands CSV/TSV file **	627	267	12.36%
*Covid ligand/target files ***	286	0	-
UniProt Mapping file	190	154	23.88%
HGNC mapping file	144	122	18.03%
*PostgreSQL****	192	148	29.73%
Generic slides (PPT & PDF)	174	174	0%
Generic poster	68	73	-6.85%

* The large increase in ligand downloads is attributable to the fact that we add a new way to download specific ligand sets from our ligand list pages (https://www.guidetopharmacology.org/GRAC/LigandListForward?database=all). Users can download any of the sets on this page in csv format.

** This download was not available until April 2020.

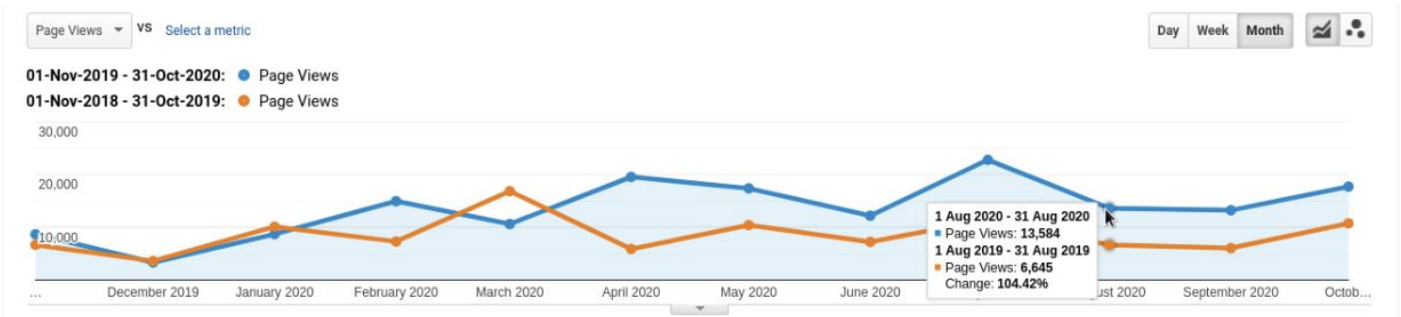
*** Total downloads of PostgreSQL database dump files (versions 2018.4 onwards).

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 **162,463** total hits over the year, which is an increase on the following year (~102,861).



Primary Dimension: Page | Page Title | Other

Plot Rows | Secondary dimension | Sort Type: Default | advanced

	Page	Page Views	Unique Page Views	Avg. Time on Page	Entrances	Bounce Rate	% Exit	Page Value
		57.94% 162,463 vs 102,861	44.57% 92,833 vs 64,215	31.14% 00:00:11 vs 00:00:09	33.38% 2,637 vs 1,977	12.25% 44.79% vs 51.04%	15.55% 1.62% vs 1.92%	0.00% US$0.00 vs US$0.00
	1. /services/targets							
	01-Nov-2019 - 31-Oct-2020	**19,826** (12.20%)	1,043 (1.12%)	00:00:15	699 (26.51%)	38.05%	2.49%	US$0.00 (0.00%)
	01-Nov-2018 - 31-Oct-2019	**13,094** (12.73%)	815 (1.27%)	00:00:09	612 (30.96%)	39.54%	2.93%	US$0.00 (0.00%)
	% Change	**51.41%**	**27.98%**	**63.59%**	**14.22%**	**-3.76%**	**-15.21%**	**0.00%**
	2. /services/ligands							
	01-Nov-2019 - 31-Oct-2020	**6,703** (4.13%)	663 (0.71%)	00:00:29	398 (15.09%)	60.80%	5.58%	US$0.00 (0.00%)
	01-Nov-2018 - 31-Oct-2019	**1,122** (1.09%)	554 (0.86%)	00:01:49	273 (13.81%)	69.96%	31.19%	US$0.00 (0.00%)
	% Change	**497.42%**	**19.68%**	**-73.25%**	**45.79%**	**-13.09%**	**-82.11%**	**0.00%**

Traffic to GtoPdb web services over the past year

Coronavirus (Covid-19) - GtoPdb information page

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 special note regarding publicity around preliminary efficiency of Pfizer and Moderna vaccines, that gives hope that we can vaccinate against this virus.

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. OIn addition to the targets and ligands on the coronavirus page, amny 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 183 hits).

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

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

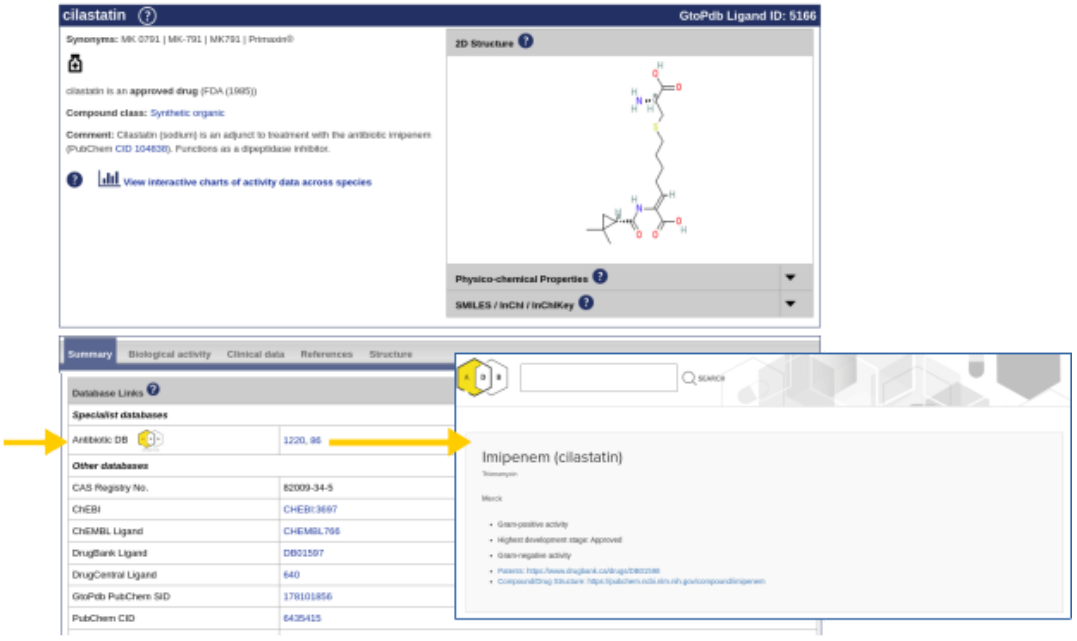
The GtoPdb Coronavirus page has been included in the following data hubs:

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

Antibiotic DB

We have continued our collaboration with Prof. Laura Piddock (University of Birmingham) on incorporation of data contained in Antibiotic DB (https://www.antibioticdb.com/) into GtoPdb.

As part of a collaboration with AntibioticDB (https://www.antibioticdb.com/), we have now begun to identify and tag sets of antibiotic ligands in GtoPdb. Where we have identified mappings between these and compounds in the AntibioticDB repository, we've put in place direct links. The newly curated set includes approved and investigational antibiotics and pre-clinical leads, as well as compounds whose development has been discontinued



Showing the ligand summary page for cilastatin, with ADB links under the Summary tab, and subsequent landing page for compound 1220 (Imipenem (cilastatin)) at Antibiotic DB

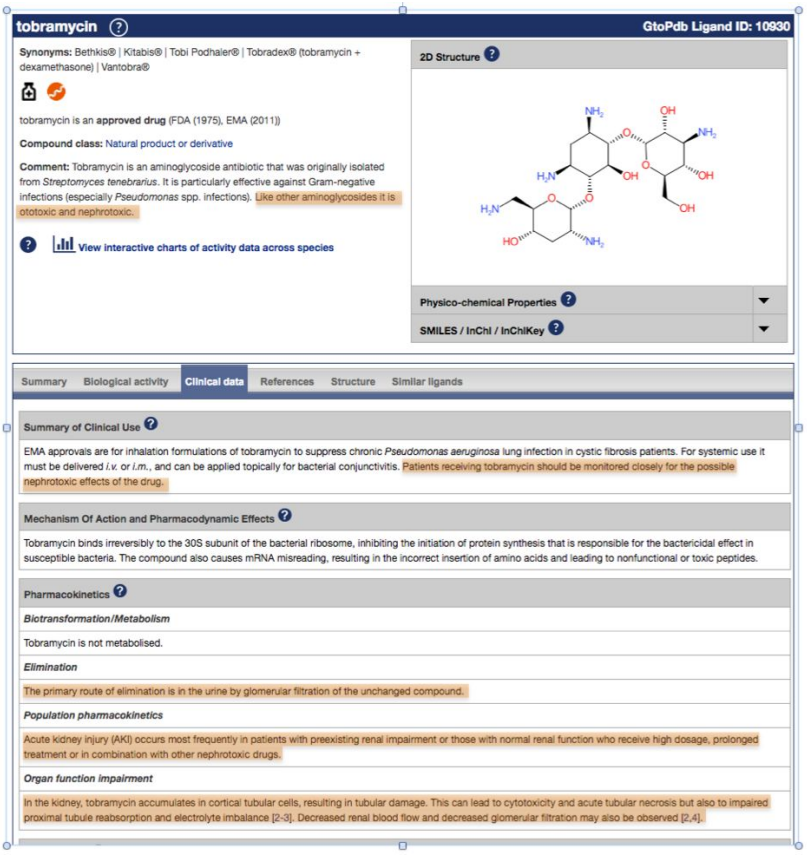
Currently we have 293 ligands tagged in GtoPdb as ‘antibiotic’ and 229 of these have these links to compounds at ADB.

Laura Piddock and her ADB team have spent considerable time updating their database, in response to issues that arose during GtoPdb curatorial review. The GtoPdb now contains a set of antibiotic compounds with validated chemical structures, with hyperlinks to ADB pages. The antibiotics in the GtoPdb include approved drugs, WHO essential Medicines-listed antibiotics and a number of investigational and experimental compounds. The GtoPdb has not added the microbial targets through which the antibiotics function. This would require specific funding for curator time.

Nephrotoxic Drug Information

Drug-induced renal damage is a common adverse event that contributes to morbidity and to significant healthcare costs. Over the summer we were joined by MSc student Isabel Walters, working on a project to identify and collate information about drugs with reported nephrotoxic side-effects. Adding this new data to the GtoPdb will be a valuable addition to the clinical section of the Ligand summary page.

Using our established search strategies and curation methods, Isabel identified 126 ligands of which 86 were already included in the GtoPdb. Additional information about the mechanism of renal injury and cell type involved was also collected. A subset of these ligands (including both new and existing examples) was prioritized for update by the curation team, using the current web interface to display nephrotoxic data (see figure below). During her project, Isabel also designed a number of extensions to the interface that could improve access to the information and the user experience.



Showing the current Ligand summary page for tobramycin, with information about the renal effects of the drug highlighted in orange

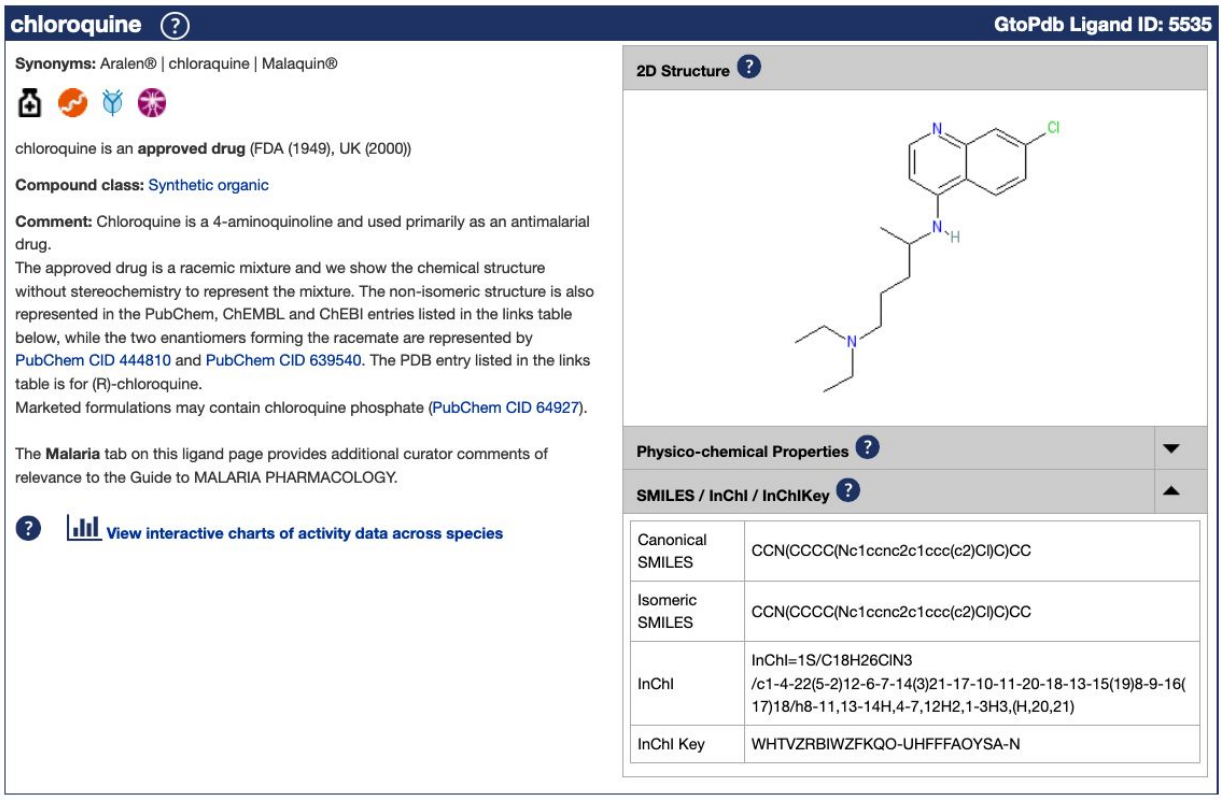
New GtoPdb Website Features (since April 2020)

Ligand Summary Pages

The layout of the ligand summary pages has been changed to provide more of the key information on a ligand at the top of the page. In the example below we show how this looks for chloroquine.

The main information box now contains:

- Synonyms
- Icons to indicate key ligand classifications
- Drug approval indication
- GtoPdb curator comments
- Link to ligand activity graphs



In addition, the 2D ligand structure is displayed beside this information in an expandable/retractable section where users can also view physico-chemical properties and SMILES/InChI/InChI Keys.

Previously the top part of the ligand summary pages contained too much white space, repetitions of the ligand name and emphasised the ligand ID, physico-chemical properties and to some extent buried comments, SMILES/InChI keys and useful links (such as to the ligand activity graphs).

The reorganisation of the page now emphasises key information. GtoPdb curator comments in particular contain a valuable description of the ligand and provide explanations as to why they have been curated in GtoPdb.

WHO essential medicines: - blog post as guide to accessing via PubChem

A blog-post on Accessing WHO Essential Medicines in GtoPdb was published in June that explains how users can access these tagged compounds in PubChem.

Therefore it is now possible, through the query below to easily access the WHO Essential Medicines in GtoPdb through PubChem:

https://www.ncbi.nlm.nih.gov/pcsubstance?term=(%22iuphar%2Fbps%20guide%20to%20pharmacology%22%5BSourceName%5D)%20AND%20%22gtopdb%20who%22%5BComment%5D

Updated ChEMBL target links:

We updated our ChEMBL target outlinks following the ChEMBL 27 release in May 2020.

Accessibility

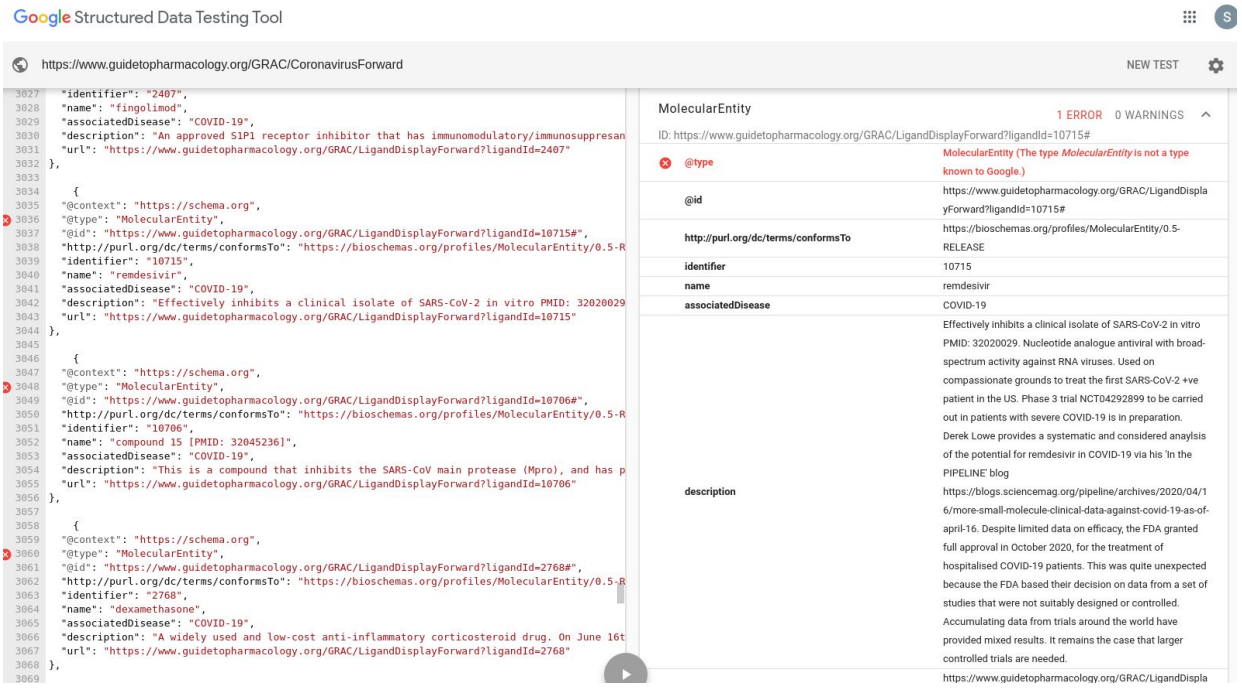
The Public Sector Bodies (Website and Mobile Applications) (No. 2) Accessibility Regulations have prompted us to review and revise our website to make it comply, as far as it can, with Web Content Accessibility Guidelines 2.1 (WCAG 2.1). As such we are working towards publishing a “best effort” accessibility statement and identifying and fixing high-priority accessibility problems.

We have been using the automated testing tools provided by Little Forest to help us identify high priority issues. These include responsiveness, colour contrast, heading structure & labels on forms, fields and buttons.

Bioschemas

As previously mentioned we have been including 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.

In the last 6-months our focus has been on implementing mark-up on the new GtoPdb Coronavirus page. all ligand summary pages and target detail pages. We again thank Alasdair Gray and Petros Papadopoulos from Heriot-Watt University for their guidance on this.



Google Structured Data Testing Tool run on the GtoPdb coronavirus.jsp page. Left panel shows the mark-up, ight panel shows the validation.

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 virtual ELIXIR-UK All-Hands Meeting held in June 2020 in Dundee, where we presented an update on the IUPHAR/BPS Guide to Pharmacology (slideshare link).

Probes and Drugs

We continue to have useful interactions with The Probes & Drugs portal. They remain the quickest of any metasource to pick up the chemistry from each of our releases (even with a lag of one or two versions this is still impressive). .

P&D 03.2020 released with the Probes tab, probe criteria filters and advanced export

On September 22nd, a new version of P&D portal (03.2020) was released with some major data and functionality updates, among these with a new Probes tab, probe criteria filters, and an advanced export.

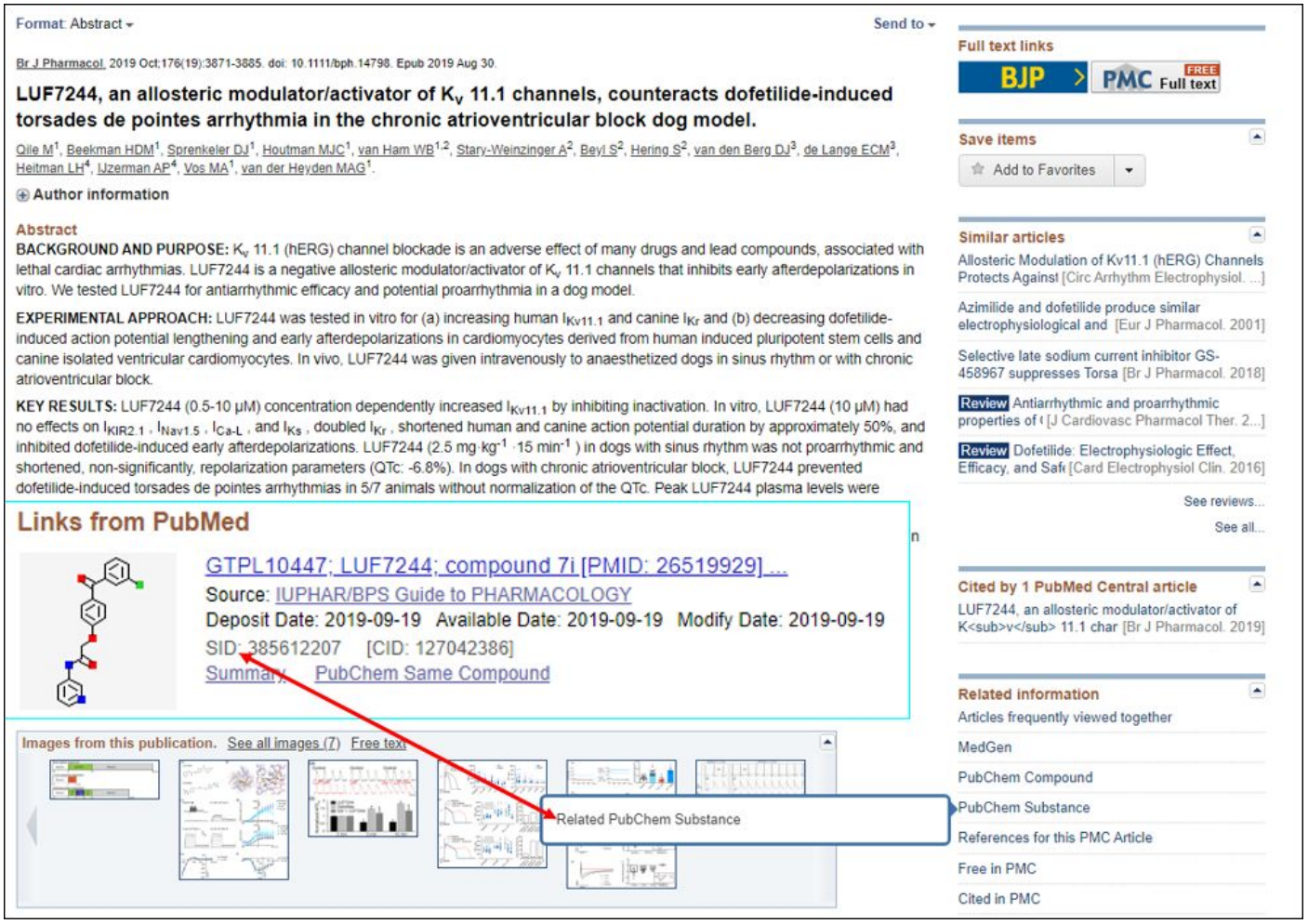
Concerning the data updates, all of the major data sources were updated to their current versions (ChEMBL 27, GtoPDB 2020.03, DrugBank 5.1.7, and others) along with many of the compound sets, including the probe sets such as Chemical probes.org, Open Science Probes, SGC probes, and opnMe portal. We also added one brand new compound set of biased GPCR ligands from BiasDB (BiasDB: A Comprehensive Database for Biased GPCR

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.

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.



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).

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.

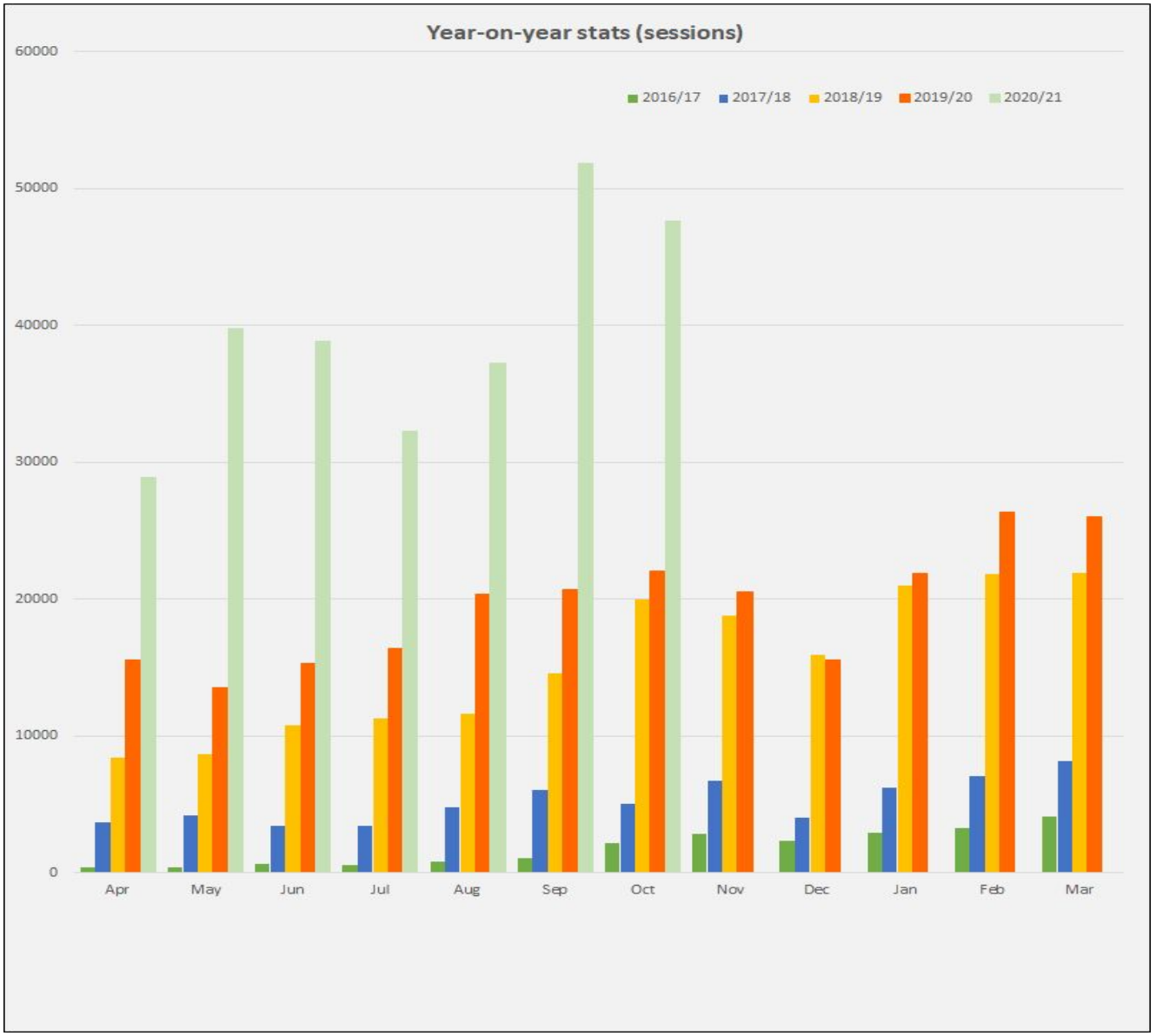
IUPHAR Pharmacology Education project (PEP)

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 6 months. This comes from IUPHAR.

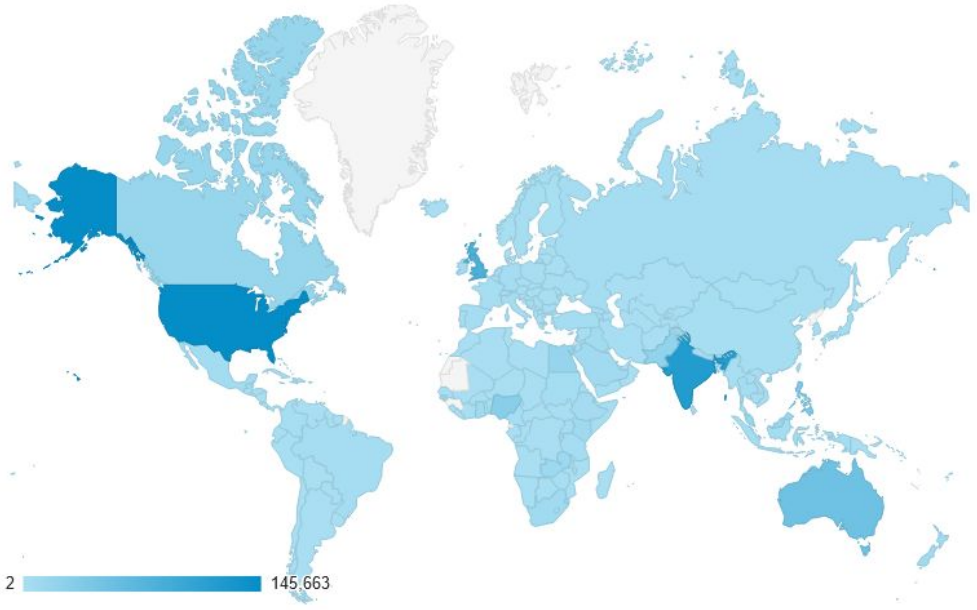
Site Usage

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-Nov 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 22,753 views, and 700 downloads, in the last year. The top 5 (by number of views) are shown in the panel below.

Top content

Name	Views
Opioid analgesics- an introduction	4,805
Drugs and blood clotting	3,272
An introduction to general anaesthesia	2,280
Drugs acting on the kidney lectures 1 and 2	2,213
Introductory receptor pharmacology_2014-15_jap	1,732

Top countries

Name	Views
India	3,424
United States	3,007
Pakistan	840
United Kingdom	634
Egypt	421

We also have embedded Vimeo videos by Simon Maxwell in some sections of PEP, and these have recorded ~4000 views coming from PEP.

PEP has >1200 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.

GtoPdb Entity Growth

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	Nov 2020
Target protein IDs	2485	2761	2775	2794	2808	2825	2872	2880	2920	2943	2976
Ligands total	6064	8024	8400	8674	8872	8978	9251	9405	9662	10053	10659
Approved drugs	559	1233	1273	1291	1322	1334	1364	1386	1421	1471	1614
Antibodies	10	138	172	205	212	223	240	248	255	270	295
Peptides	1776	1981	2007	2039	2063	2079	2092	2100	2122	2150	2180
Synthetic small molecules	3504	5055	5363	5563	5729	5807	6048	6180	6401	6816	7303
PubChem SIDs	3107	8024	8328	8674	8831	8978	9251	9405	9662	10053	10659
PubChem CIDs	2694	6057	6163	6337	6813	6822	7109	7224	7407	7483	7994
Binding constants	41076	44691	45534	45908	46287	46488	47058	47426	48071	48902	49363
References	21774	27880	29247	30251	31239	31733	33245	34382	35723	37261	39133

GtoPdb Target Updates

These are lists of target updated, and new targets added since April 2020.

GPCRs:
Adenosine receptors
Adhesion Class GPCRs
Bombesin receptors
Bradykinin receptor
Calcium-sensing receptor
Complement peptide receptors
Dopamine receptors
Gonadotropin-releasing hormone receptors
G protein-coupled estrogen receptor
Hydroxycarboxylic acid receptors
Leukotriene receptors
Lysophospholipid (LPA) receptors
Lysophospholipid (S1P) receptors
Melanocortin receptors
Melatonin receptors
Motilin receptor
Neuropeptide S receptor
Neurotensin receptors
Orexin receptors
Prolactin-releasing peptide receptor
QRFP receptor

Catalytic Receptors:
Integrins
Nitric oxide (NO)-sensitive (soluble) guanylyl cyclase
Transmembrane guanylyl cyclases
Tumour necrosis factor (TNF) receptor family

NHRs:
3-Ketosteroid receptors

Ion Channels:
Acid-sensing (proton-gated) ion channels (ASICs)
Glycine receptors
P2X receptors
Voltage-gated potassium channels
Voltage-gated proton channel
Voltage-gated sodium channels
VGICs-introduction

Enzymes and Other protein targets:
2-Acylglycerol ester turnover
N-Acyelthanolamine turnover
RGS proteins (R4, 7, 12 families)
Sphingosine 1-phosphate lyase
Sphingosine 1-phosphate phosphatase
Sphingosine 1-phosphate turnover
Sphingosine kinase

Transporters:
Glycine transporter subfamily
Neutral amino acid transporter subfamily
SLC8 family of sodium/calcium exchangers
SLC14 family of facilitative urea transporters
SLC28 family
SLC29 family
SLC51 family of steroid-derived molecule transporters
SLC54 Mitochondrial pyruvate carriers

New targets (not including Antimalarial targets):

Klotho
ABHD2 (α β -Hydrolase 2)
neuroplastin
PDZ domain containing 11
erythrocyte membrane protein band 4.1
FXYD domain containing ion transport regulator 1
FXYD domain containing ion transport regulator 3
P-type ATPases reorganised and new targets added (transmembrane protein 30A
ATPase 13A1, ATPase cation transporting 13A2, ATPase 13A3, ATPase 13A5)
SLC66 Lysosomal amino acid transporters (5)
Cyclic GMP-AMP synthase (cGAS)
Coronavirus proteins (proteins & polyproteins, 15 in total)
Tetraspanin family (incl CD37)

PubChem Statistics for GtoPdb, GtoImmuPdb and GtoMPdb

The stats for the 2020.5 release (with 2019.2 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 10585 (10034).
2. Those that have defined chemical structures are merged into 8371 (7828) Compound Identifiers, CIDs (i.e. small molecules and moderate peptides)
3. The select "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND approved [Comment] now retrieves 1717 SIDs (1569) .
4. Of our SIDs, 1313 (1279) are tagged in GtoImmuPdb and 310 (302) of these are approved drugs
5. Of our CIDs 724 are tagged in GtoImmuPdb
6. Of our SIDs, 91 are tagged in GtoMPdb and 24 of these are approved drugs
7. Of our CIDs 51 are tagged in GtoMPdb
8. We have 2038 (1847) structures that ChEMBL23 does not have, 5844 not in DrugBank and 6930 not in DrugCentral.
9. 189 (166) structures unique to us as a source. \

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. The drop in access after July 2020 might in part be explained by an error with the security certificate to the site which was preventing access.

SynPharm access statistics for the past year (November 2019 - October 2020)

BIBLIOMETRICS AND SCHOLARLY PORTALS

- 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, SDH 0000-0002-9262-8318 and JFA 0000-0002-0524-0260.

Below are the November 2020 live bibliometric updates compared to the April 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 significantly lower citation rates than PubMed, Google Scholar or WOS).

- Database team members' cumulative co-authored publications have increased from 170 to 184 (this is a PubMed query that is not so easy to do in EPMC).
- IUPHAR reviews in BJP increased by 3 to 30.
- IUPHAR Pharmacological Reviews increased by 2 to 106.
- The BJP “Concise Guide” sets from 2013-2017 added up to 26 with the 2019/20 set now taking us to 33 papers.
- 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 2018 entry (PMC5753190) with 734 citations (according to EPMC) or 1034 (according to PubMed) , overtaking the 2016 paper (PMC4702778) with 880 (EMPC) or 903 (PubMed) citations, and the 2014 paper (PMC3965070) that reached 663 / 710 .

- The “Concise Guide” citations are currently led by 2015/16: Enzymes (PMC4718211) at 507 closely followed by 2017/18 Enzymes (PMC5650666) at 471 and 2013/14: G protein-coupled receptors (PMC3892287) at 459.
- The overall citation performance of our papers resulted in team members JLS, EF, AJP and JAD, along IUPHAR co-authors, SPHA, MS, and APD being listed in the Clarivate 2019 ranking of Highly Cited Researchers.
- The Altmetric rankings for all our OA papers are now indexed in ScienceOpen.

The Guide to Immunopharmacology Database (GtoImmuPdb)

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.

Engagement continues with Immunopaedia, an open-access online platform freely available for learning and teaching immunology. 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.

Guide to Immunopharmacology: Publications and Presentations

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

GtoImmuPdb analytics

Our analytics over the last year (Nov 19 - Oct 20) shows an average of ~870 sessions per month.

Access statistics for GtoImmuPdb (November 2019 - October 2020)

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 2020.5 release).

Process Category	**GtoPdb Human UniProtKB**	**Target-GO annotations**
Barrier integrity	51	63
Inflammation	677	1483
Antigen presentation	161	247
T cell (activation)	230	528
B cell (activation)	183	323
Immune regulation	554	1409
Tissue repair	27	29
Immune system development	290	569
Cytokine production & signalling	559	1491
Chemotaxis & migration	281	604
Cellular signalling	517	1164

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	56
T cells	CL:0000789 alpha-beta T cell CL:0000815 regulatory T cell CL:0000911 effector T cell	82
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	47
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

GtoImmuPdb target and ligand curation stats

- 631 targets tagged as in GtoImmuPdb:
  - 150 catalytic receptors
  - 209 enzymes
  - 102 gpcrs
  - 40 ion channels
  - 113 other proteins
  - 9 nuclear hormone receptors
  - 10 transporters
- 1320 ligands tagged as in GtoImmuPdb:
  - 850 synthetic organic
  - 167 antibodies
  - 258 peptides
  - 28 metabolites
  - 16 natural products
  - 1 inorganic
  - 279 Approved drugs
- Detailed lists on:
  - www.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp

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. Although the initial phase of the project has been completed, MMV have provided further funding (until December 2020) to allow malaria pharmacology content to be maintained and expanded.

The IUPHAR/MMV Guide to IMALARIA PHARMACOLOGY was officially released in September 2019. The resource is now available at www.guidetomalariapharmacology.org. Blog posts related to the resource and technical reports on its development can be found here.

In the following section of the report we will provide an update on both the curation effort and the status of web interface and database developments.

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 have been tagged with antimalarial specific tags. In addition, MMV provided an initial list of targets and ligands of high priority and we have continued 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. The most recent database release (2020.5) contains:

- 100 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, April 2019, April 2020) we have described changes to the database structure and the web interface that were necessary for the capture and presentation of antimalarial data. The major part of the required

development work was completed prior to the public release of the GtoMPdb but we have continued to implement improvements. 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.
- Deployed a new malaria comments field for both ligands and targets.
- 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.
- Extended the site search to incorporate the malaria comments field and to bring back targets from searches on parasite lifecycle stage or malaria species.
- Added a table to provide information about a ligand's Target Candidate Profile (TCP), where this is available.

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.

GtoMPdb Portal Homepage

General overview of database team activities

Public Engagement and Promotion

conferences/meetings (since April 2019 and upcoming)

- ELIXIR All Hands 2020 (e-poster - Simon Harding) https://www.slideshare.net/GuidetoPHARM/guide-to-pharmacology-poster-elixir-all-hands-2020
- BPS Live: The Pharmacology of drugs for COVID-19 (21 October 2020). A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development, Dr Steve Alexander, University of Nottingham, UK
- BPS Pharmacology 2020 (iPoster 14 Dec- Simon Harding). IUPHAR/BPS Guide to PHARMACOLOGY: Expansion for antimalarials, antibiotics and COVID-19
- BPS Pharmacology 2020 (Oral Communication 15 Dec - Chris Southan). Curating SARS-CoV-2 viral targets for the IUPHAR/BPS Guide to Pharmacology'
- BPS Pharmacology 2020 (submitted Late Breaking abstract - Chris Southan). SARS-CoV-2/COVID-19 pharmacological roadmap: a strategy for curating and updating drug targets in the Guide to Pharmacology Coronavirus

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 April 2020)

- Steve P.H. Alexander Jane F. Armstrong Anthony P. Davenport Jamie A. Davies Elena Faccenda Simon D. Harding Francesca Levi-Schaffer Janet J. Maguire Adam J. Pawson Christopher Southan Michael Spedding. A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development. *Br J Pharmacol. 2020 Nov;177(21):4942-4966*. April 13, 2020. DOI: https://doi.org/10.1111/bph.15094. PMID: 32358833.
    - front cover of special joint BJP, BJCP & PR&P virtual issue COVID-19 Research
- Simon Fowler, Simon D. Harding, Joanna Sharman, James Cheney. Cross-tier web programming for curated databases: A case study. International Journal of Digital Curation, 2020 Vol 15 No 1. DOI: https://doi.org/10.2218/ijdc.v15i1.717. https://arxiv.org/abs/2003.03845
- Christopher Southan. Opening up connectivity between documents, structures and bioactivity. *Beilstein J Org Chem*. 2020 Apr 2;16:596-606. doi: 10.3762/bjoc.16.54. eCollection 2020. Review. PMID: 32280387
- Simon Milling, Michael Spedding & Pasquale Maffia. 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

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 5,030 (October 2020), from 4,585 (April 2020). We have 5,123 followers.

Twitter

@GuidetoPHARM has, as of 30th October 2020, output 2,179 tweets, followers have increased to 3,977, from 2,531 in April 2020. 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.

At each database release, our Twitter announcement usually gathers impressions ~3,000 impressions and an engagement rate ~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).

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 280 followers, up from 250 in April 2020.

Blogging

Our Edinburgh blog (http://blog.guidetopharmacology.org/) has received ~450 views on average per month since April 2020. This is reduction from an average in the previous 6 months of ~650 views, but the average per post remains steady at ~50.

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 and popular feature, our Hot Topics in Pharmacology track and highlight new significant papers in pharmacology and drug discovery. These are communicated to us from Subcommittee members or picked up from Social Media. For a selection we commission concise commentaries from our expert contacts. Since April 2020 we've had guest commentaries from Chris Southan on GPCR peptides; Charles

Kennedy on TMEM163 regulation of the ATP-gated P2X receptor; and Misty Attwood & Helgi Schiöth on soluble ligands as drug targets. 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.

Slides

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 3,828 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.

WikiData

Guide to Pharmacology has now been added as a source on WikiData.
https://www.wikidata.org/wiki/Property:P5458

FairSharing

FairSharing.org is ‘a curated, informative and educational resource on data and metadata *standards*, inter-related to *databases* and data *policies’.*

The Guide to Pharmacology has an entry as a database on FairSharing.org (https://fairsharing.org/FAIRsharing.f1dv0). Inclusion here will help GtoPdb “be more discoverable, increasing exposure and credit outside of their immediate community and ultimately promote adoption”. It allows us to declare what standards we implement and what collection (or communities) we are part of.

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.

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.

Yi-Chien Chang (Sanofi)

Interested in downloading sets of endogenous ligands.

Li Qingliang (NIH/NCBI)

Helped identify error in synonyms naming.

Cecile Chauvel (Bioaster, France)

Interest in downloading data from Guide to Immunopharmacology, specifically target GO annotations.

Evert Homan (Karolinska Institute)

Understanding definition of agonist versus full agonist

Joanna Sharman (Novo Nordisk)

Jo was interested in getting distributions of the number of drugs vs number of primary targets - for approved drugs, with subsets for primary targets. Our interactions download file can be used to get interaction counts per target, but doesn't distinguish approved drugs. We have since added this as a column to the file.

Anne Bresciani (Novo Nordisk)

Accessing and downloading sets of GPCR primary and secondary transduction mechanisms, including families and references. This was not always 100% clear when comparing downloaded data against the actual database dump. The explanation of how we assign transduction mechanisms could be improved in the help pages.

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.