



IUPHAR/BPS Guide to PHARMACOLOGY

Database Report

November 2020

www.guidetopharmacology.org

enquiries@guidetopharmacology.org

CONTENTS

Contents	1
Introduction	2
The Guide to Pharmacology Database (GtoPdb)	3
GtoPdb Website access statistics	3
Acquisition, Browsers and Devices	4
GtoPdb content	4
Download Statistics	6
Google Analytics comparison of Downloads	6
Web Services	6
Coronavirus (Covid-19) - GtoPdb information page	7
Antibiotic DB	8
Nephrotoxic Drug Information	9
New GtoPdb Website Features (since April 2020)	10
Ligand Summary Pages	10
WHO essential medicines: - blog post as guide to accessing via PubChem	11
Updated ChEMBL target links:	11
Accessibility	12
Bioschemas	12
GtoPdb Team Interactions	12
ELIXIR	12
Probes and Drugs	13
PubChem	13
IUPHAR Pharmacology Education project (PEP)	15
GtoPdb Entity Growth	18
GtoPdb Target Updates	18
PubChem Statistics for GtoPdb, GtoImmuPdb and GtoMPdb	19
synPHARM: a database of small molecules and their drug-responsive protein sequences linked to GtoPdb	19
bibliometrics and scholarly portals	20
The Guide to Immunopharmacology Database (GtoImmuPdb)	22
GtoImmuPdb web interface and DATABASE development status	22
Guide to Immunopharmacology: Publications and Presentations	22

GtoImmuPdb analytics	23
Immuno Process Data	23
Immuno Cell Type Data	23
GtoImmuPdb target and ligand curation stats	24
The Guide to Malaria Pharmacology Database (GtoMPdb)	25
introduction	25
GtoMPdb target and ligand curation	25
collecting and prioritising content	25
curation summary	25
GtoMPdb web interface and database development	25
GtoMPdb portal development	26
General overview of database team activities	28
Public Engagement and Promotion	28
conferences/meetings (since April 2019 and upcoming)	28
Publications	28
published or pre-printed (since early April 2020)	28
Outreach and Social Media	29
Facebook	29
Twitter	29
LinkedIn	29
blogging	29
Hot Topics	29
Slides	30
WikiData	30
FairSharing	30
Enquiries Received From Users	30
ENGAGING WITH US	31

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.

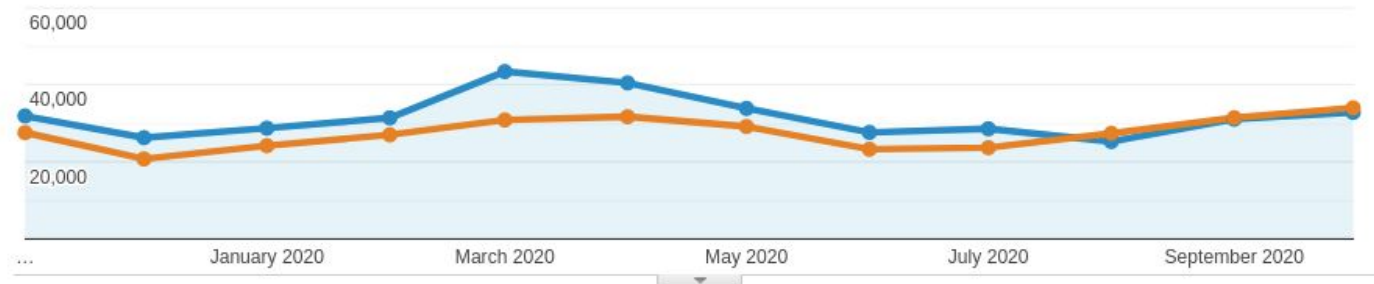
This report also includes updates on the Wellcome Trust funded Guide to IMMUNOPHARMACOLOGY ([GtoImmuPdb](#)) and the Medicines for Malaria Venture (MMV) funded Guide to MALARIA PHARMACOLOGY ([GtoMPdb](#)).

THE GUIDE TO PHARMACOLOGY DATABASE (GTO PDB)

GTO PDB WEBSITE ACCESS STATISTICS

01-Nov-2019 - 31-Oct-2020: ● Users

01-Nov-2018 - 31-Oct-2019: ● Users



Users

16.18%

349,189 vs 300,569



New Users

16.60%

347,279 vs 297,832



Sessions

15.96%

519,703 vs 448,158



Number of Sessions per User

-0.18%

1.49 vs 1.49



Page Views

12.92%

1,648,658 vs 1,460,072



Pages/Session

-2.63%

3.17 vs 3.26



Avg. Session Duration

-1.92%

00:03:03 vs 00:03:06



Bounce Rate

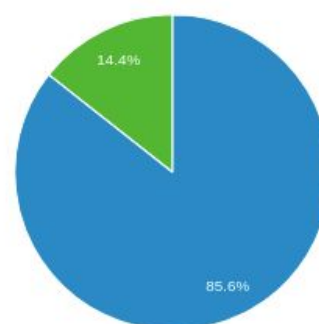
1.48%

63.20% vs 62.28%

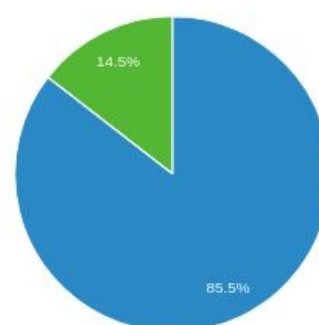


■ New Visitor ■ Returning Visitor

01-Nov-2019 - 31-Oct-2020



01-Nov-2018 - 31-Oct-2019



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)

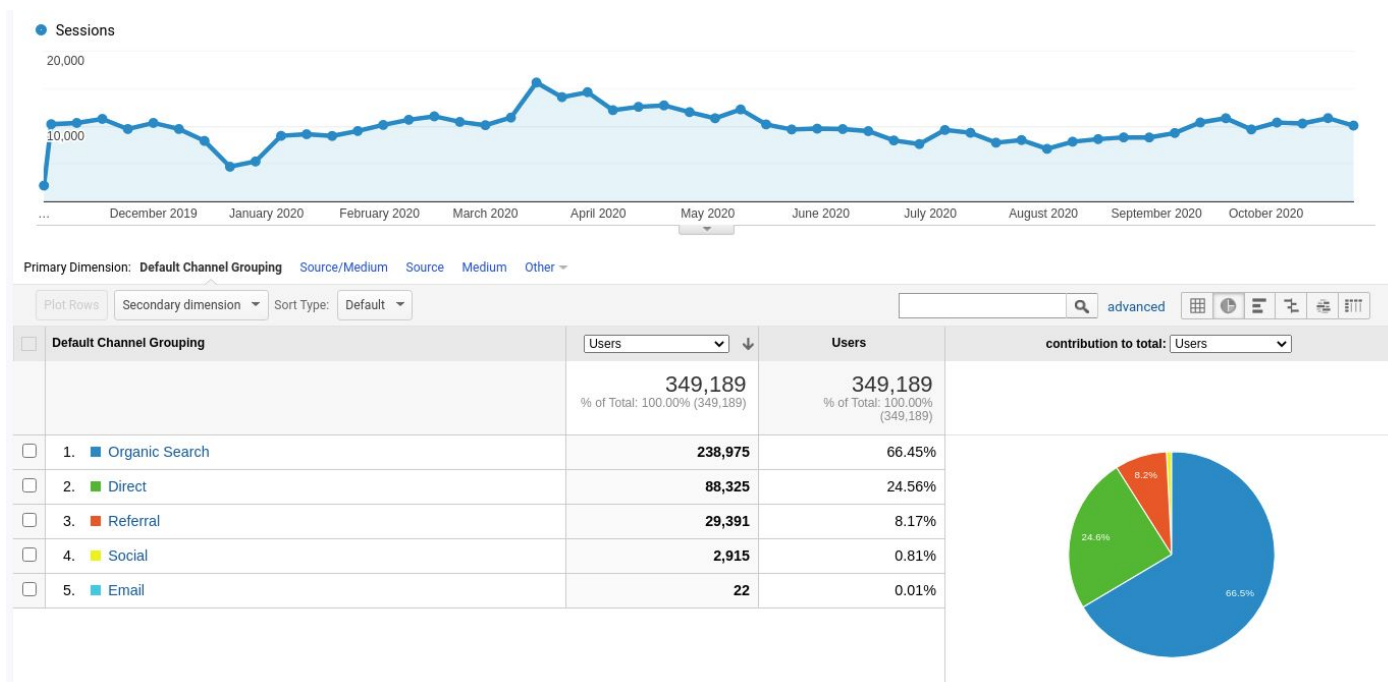
Users

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.

Primary Dimension: Source Landing Page Other

Secondary dimension Sort Type: Default

Source	Sessions	Sessions
	44,870 % of Total: 8.63% (519,703)	44,870 % of Total: 8.63% (519,703)
1. en.wikipedia.org	5,469	12.19%
2. ncbi.nlm.nih.gov	5,335	11.89%
3. bpspubs.onlinelibrary.wiley.com	3,844	8.57%
4. baidu.com	3,642	8.12%
5. en.m.wikipedia.org	3,251	7.25%
6. cn.bing.com	3,142	7.00%
7. pubchem.ncbi.nlm.nih.gov	1,419	3.16%
8. pharmacologyeducation.org	1,320	2.94%
9. guidetoimmunopharmacology.org	754	1.68%
10. ebl.soms.bris.ac.uk	748	1.67%

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
<i>7TM receptors</i>	399
<i>Nuclear hormone receptors</i>	48
<i>Catalytic receptors</i>	249
<i>Ligand-gated ion channels</i>	81
<i>Voltage-gated ion channels</i>	144
<i>Other ion channels</i>	53
<i>Enzymes</i>	1231
<i>Transporters</i>	555
<i>Other protein targets</i>	216
<i>Targets with ligand interactions</i>	1819
<i>Targets with quantitative ligand interactions</i>	1567
<i>Targets with approved drug interactions</i>	660
<i>Primary Targets with approved drug interactions</i>	334
Total number of targets	2976
<u>Ligands</u>	<u>Number of ligands</u>
<i>Synthetic organics</i>	7303
<i>Metabolites</i>	514
<i>Endogenous peptides</i>	802
<i>Other peptides including synthetic peptides</i>	1378
<i>Natural products</i>	328
<i>Antibodies</i>	295
<i>Inorganics</i>	39
<i>Approved drugs</i>	1614
<i>Withdrawn drugs</i>	86
<i>Ligands with INNs</i>	2697
<i>Labelled ligands</i>	618
<i>Unique PubChem CIDs (total CID links)</i>	7994 (8196)
<i>Ligands with target interactions</i>	8959
<i>Ligands with quantitative interactions (approved drugs)</i>	7884 (974)
<i>Ligands with clinical use summaries (approved drugs)</i>	2837 (1610)
Total number of ligands (PubChem SIDs)	10659
<i>Number of binding constants</i>	48902
<i>Number of binding constants curated from the literature</i>	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
<i>Targets CSV/TSV file</i>	1311	1064	23.2%
<i>Interactions CSV/TSV file</i>	403	398	1.26%
<i>Ligands CSV/TSV file *</i>	627	267	12.36%
<i>Covid ligand/target files **</i>	286	0	-
<i>UniProt Mapping file</i>	190	154	23.88%
<i>HGNC mapping file</i>	144	122	18.03%
<i>PostgreSQL ***</i>	192	148	29.73%
<i>Generic slides (PPT & PDF)</i>	174	174	0%
<i>Generic poster</i>	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.

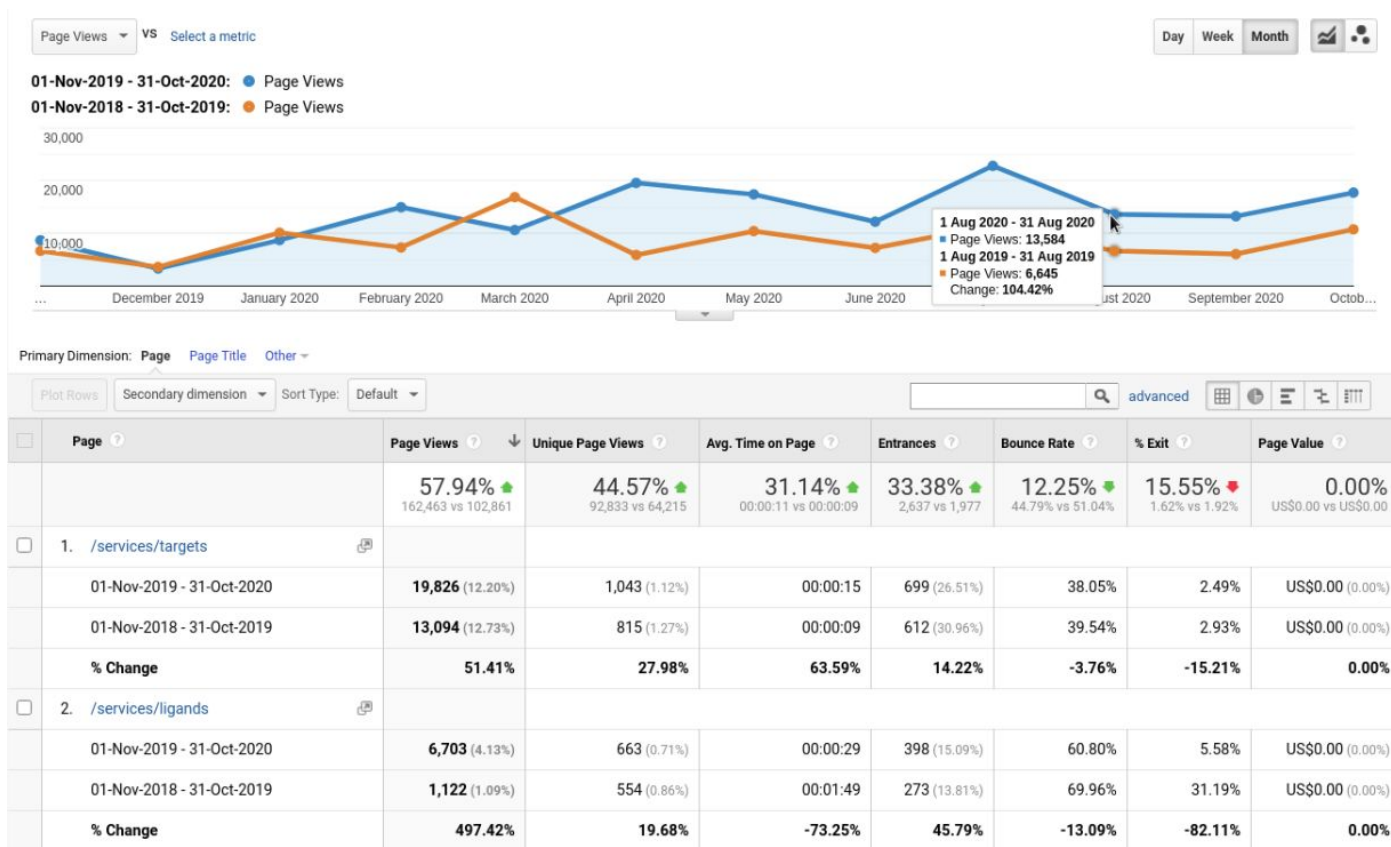
*** Total downloads of PostgreSQL database dump files (versions 2018.4 onwards).

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).



Traffic to GtoPdb web services over the past year

CORONAVIRUS (COVID-19) - GTO PDB 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. On addition to the targets and ligands on the coronavirus page, many more entities in the GtoPdb have curator comments regarding evidence of a relationship to SARS-CoV-2 and/or COVID-19 (a search using SARS-CoV-2 retrieves 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/) (<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

The screenshot displays the GtoPdb interface for the compound cilastatin (GtoPdb Ligand ID: 5166). The top section shows the 2D structure and physico-chemical properties. Below this, a 'Database Links' table lists various databases. A yellow arrow points from the 'Antibiotic DB' entry in this table to a detailed view of Imipenem (cilastatin) in the AntibioticDB repository. The AntibioticDB view shows the compound name, synonyms, and a list of mechanisms of action.

Database Links	Value
Specialist databases	
Antibiotic DB	1220, 96
Other databases	
CAS Registry No.	82009-34-5
CHEBI	CHEBI:3697
ChEMBL Ligand	ChEMBL:795
DrugBank Ligand	DB01597
DrugCentral Ligand	640
GoPdb PubChem: SID	178101856
PubChem CID	6435415

Imipenem (cilastatin)
 Synonyms:
 Mechanism:
 • Gram-positive activity
 • Highest development stage: Approved
 • Gram-negative activity
 • Pubchem: <https://pubchem.ncbi.nlm.nih.gov/compound/Imipenem>
 • CompoundDrug Structure: <https://pubchem.ncbi.nlm.nih.gov/compound/Imipenem>

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.

tobramycin ? GtoPdb Ligand ID: 10930


Synonyms: Bethkis® | Kitabis® | Tobi Podhaler® | Tobradex® (tobramycin + dexamethasone) | Vantobra®



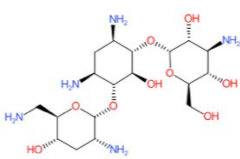
tobramycin is an approved drug (FDA (1975), EMA (2011))

Compound class: Natural product or derivative

Comment: Tobramycin is an aminoglycoside antibiotic that was originally isolated from *Streptomyces tenebrarius*. It is particularly effective against Gram-negative infections (especially *Pseudomonas* spp. infections). Like other aminoglycosides it is ototoxic and nephrotoxic.

 [View interactive charts of activity data across species](#)

2D Structure ?



Physico-chemical Properties ?

SMILES / InChI / InChIKey ?

Summary Biological activity **Clinical data** References Structure Similar ligands

Summary of Clinical Use ?

EMA approvals are for inhalation formulations of tobramycin to suppress chronic *Pseudomonas aeruginosa* lung infection in cystic fibrosis patients. For systemic use it must be delivered *i.v.* or *i.m.*, and can be applied topically for bacterial conjunctivitis. Patients receiving tobramycin should be monitored closely for the possible nephrotoxic effects of the drug.

Mechanism Of Action and Pharmacodynamic Effects ?

Tobramycin binds irreversibly to the 30S subunit of the bacterial ribosome, inhibiting the initiation of protein synthesis that is responsible for the bactericidal effect in susceptible bacteria. The compound also causes mRNA misreading, resulting in the incorrect insertion of amino acids and leading to nonfunctional or toxic peptides.

Pharmacokinetics ?

Biotransformation/Metabolism

Tobramycin is not metabolised.

Elimination

The primary route of elimination is in the urine by glomerular filtration of the unchanged compound.

Population pharmacokinetics

Acute kidney injury (AKI) occurs most frequently in patients with preexisting renal impairment or those with normal renal function who receive high dosage, prolonged treatment or in combination with other nephrotoxic drugs.

Organ function impairment

In the kidney, tobramycin accumulates in cortical tubular cells, resulting in tubular damage. This can lead to cytotoxicity and acute tubular necrosis but also to impaired proximal tubule reabsorption and electrolyte imbalance [2-3]. Decreased renal blood flow and decreased glomerular filtration may also be observed [2,4].

Showing the current Ligand summary page for [tobramycin](#), with information about the renal effects of the drug highlighted in orange

NEW GTOPTDB 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

chloroquine ?
GtoPdb Ligand ID: 5535

Synonyms: Aralen® | chloraquine | Malaquin®




chloroquine is an **approved drug** (FDA (1949), UK (2000))

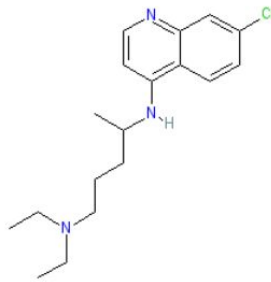
Compound class: Synthetic organic

Comment: Chloroquine is a 4-aminoquinoline and used primarily as an antimalarial drug. The approved drug is a racemic mixture and we show the chemical structure without stereochemistry to represent the mixture. The non-isomeric structure is also represented in the PubChem, ChEMBL and ChEBI entries listed in the links table below, while the two enantiomers forming the racemate are represented by PubChem CID 444810 and PubChem CID 639540. The PDB entry listed in the links table is for (R)-chloroquine. Marketed formulations may contain chloroquine phosphate (PubChem CID 64927).

The **Malaria** tab on this ligand page provides additional curator comments of relevance to the Guide to MALARIA PHARMACOLOGY.

 [View interactive charts of activity data across species](#)

2D Structure ?



Physico-chemical Properties ?

SMILES / InChI / InChIKey ?

Canonical SMILES	<chem>CCN(CCCC(Nc1ccnc2c1ccc(c2)Cl)C)CC</chem>
Isomeric SMILES	<chem>CCN(CCCC(Nc1ccnc2c1ccc(c2)Cl)C)CC</chem>
InChI	InChI=1S/C18H26ClN3/c1-4-22(5-2)12-6-7-14(3)21-17-10-11-20-18-13-15(19)8-9-16(17)18/h8-11,13-14H,4-7,12H2,1-3H3,(H,20,21)
InChI Key	WHTVZRBIWZFKQO-UHFFFAOYSA-N

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

The screenshot displays the Google Structured Data Testing Tool interface. The left panel shows the JSON-LD mark-up for a MolecularEntity, including fields like identifier, name, associatedDisease, and description. The right panel shows the validation results, indicating a 1 ERROR and 0 WARNINGS. The error message states: "MolecularEntity (The type MolecularEntity is not a type known to Google.)". The table below summarizes the validation details:

Property	Value
type	MolecularEntity (The type MolecularEntity is not a type known to Google.)
@id	https://www.guidetopharmacology.org/GRAC/LigandDisplayForward?ligandId=10715#
http://purl.org/dc/terms/conformsTo	https://bioschemas.org/profiles/MolecularEntity/0.5-RELEASE
identifier	10715
name	remdesivir
associatedDisease	COVID-19
description	Effectively inhibits a clinical isolate of SARS-CoV-2 in vitro PMID: 32020029. Nucleotide analogue antiviral with broad-spectrum activity against RNA viruses. Used on compassionate grounds to treat the first SARS-CoV-2 +ve patient in the US. Phase 3 trial NCT04292899 to be carried out in patients with severe COVID-19 is in preparation. Derek Lowe provides a systematic and considered analysis of the potential for remdesivir in COVID-19 via his 'In the PIPELINE' blog https://blogs.sciencemag.org/pipeline/archives/2020/04/16/more-small-molecule-clinical-data-against-covid-19-as-of-april-16. Despite limited data on efficacy, the FDA granted full approval in October 2020, for the treatment of hospitalised COVID-19 patients. This was quite unexpected because the FDA based their decision on data from a set of studies that were not suitably designed or controlled. Accumulating data from trials around the world have provided mixed results. It remains the case that larger controlled trials are needed. https://www.guidetopharmacology.org/GRAC/LigandDispla

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

GTOPTDB 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.

Format: Abstract ▾ Send to ▾

Br J Pharmacol. 2019 Oct;176(19):3871-3885. doi: 10.1111/bph.14798. Epub 2019 Aug 30.

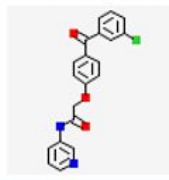
LUF7244, an allosteric modulator/activator of K_v 11.1 channels, counteracts dofetilide-induced torsades de pointes arrhythmia in the chronic atrioventricular block dog model.

Olle M¹, Beekman HDM¹, Sprengeler DJ¹, Houtman MJC¹, van Ham WB^{1,2}, Stary-Weinzinger A², Bevil S², Hering S², van den Berg DJ³, de Lange ECM³, Heltman LH⁴, Ujzerman AP⁴, Vos MA¹, van der Heyden MAG¹.


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_{Kv} 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 μ M) concentration dependently increased $I_{Kv11.1}$ by inhibiting inactivation. In vitro, LUF7244 (10 μ M) had no effects on $I_{KIR2.1}$, $I_{Nav1.5}$, I_{Ca-L} , and I_{Ks} , doubled I_{Kv} , shortened human and canine action potential duration by approximately 50%, and inhibited dofetilide-induced early afterdepolarizations. LUF7244 (2.5 mg kg^{-1} \cdot 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

 [GTP10447; 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

Full text links
  Full text

Save items
Add to Favorites ▾

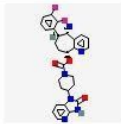
Similar articles
Allosteric Modulation of Kv11.1 (hERG) Channels Protects Against [Circ Arrhythm Electrophysiol. ...]
Azimilide and dofetilide produce similar electrophysiological and [Eur J Pharmacol. 2001]
Selective late sodium current inhibitor GS-458967 suppresses Torsade [Br J Pharmacol. 2018]
Review Antiarrhythmic and proarrhythmic properties of [J Cardiovasc Pharmacol Ther. 2...]
Review Dofetilide: Electrophysiologic Effect, Efficacy, and Saf [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.  [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; GTP10692; 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](#)

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.

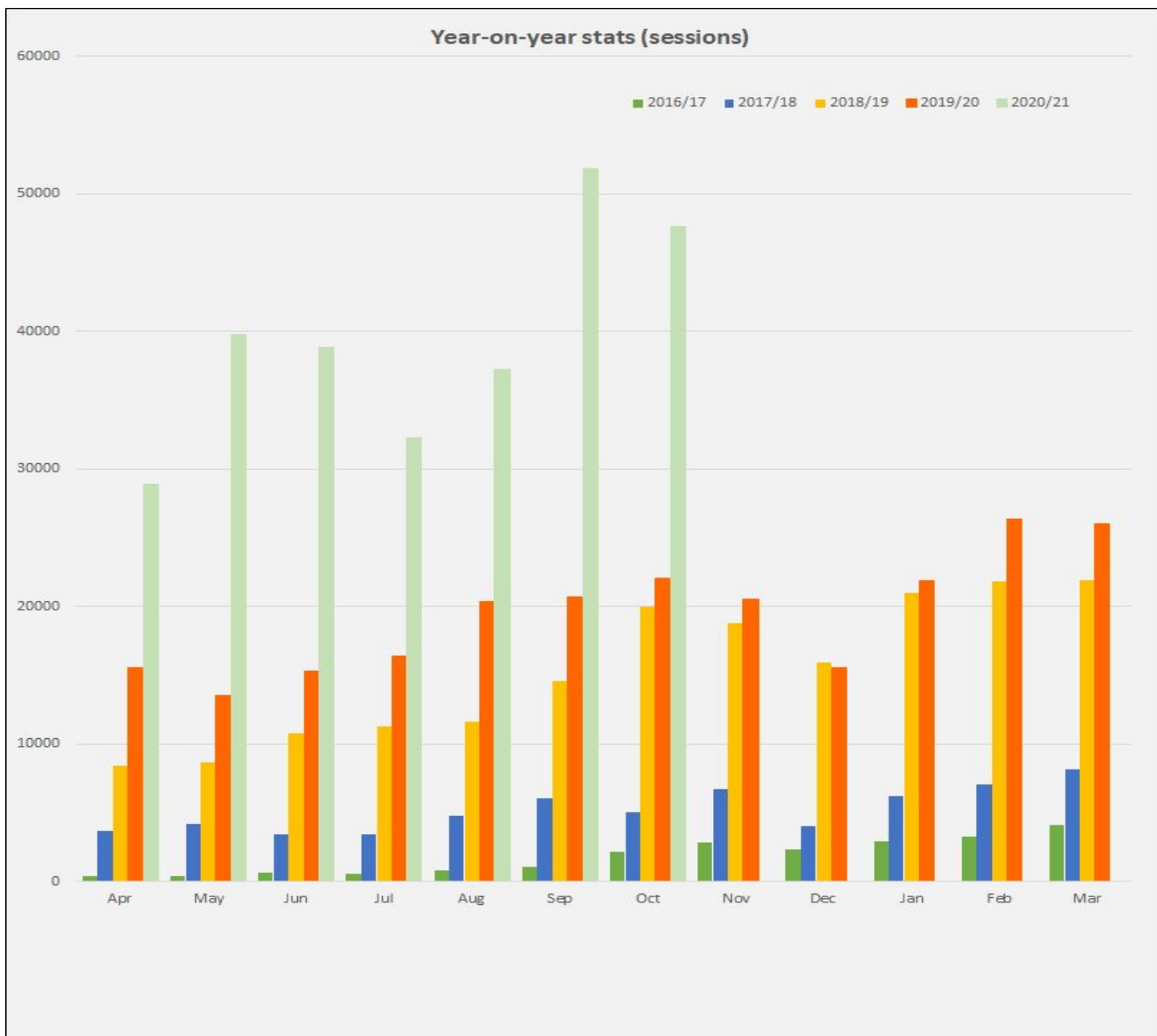
IUPHAR PHARMACOLOGY EDUCATION PROJECT (PEP)

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 6 months. This comes from IUPHAR.

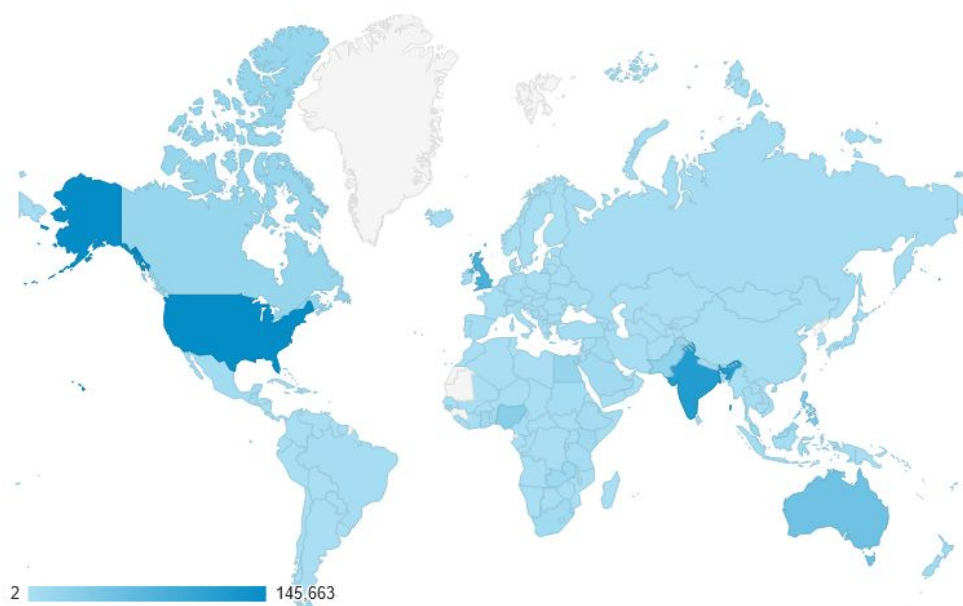
Site Usage

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		Top countries	
Name	Views	Name	Views
Opioid analgesics- an introduction	4,805	India	3,424
Drugs and blood clotting	3,272	United States	3,007
An introduction to general anaesthesia	2,280	Pakistan	840
Drugs acting on the kidney lectures 1 and 2	2,213	United Kingdom	634
Introductory receptor pharmacology_2014-15_jap	1,732	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.

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

GTO_{PDB} 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-Acyl ethanolamine 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)
 neuroligin
 PDZ domain containing 11
 erythrocyte membrane protein band 4.1
 FXFD domain containing ion transport regulator 1
 FXFD 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 GTO_{PDB}, GTO_{IMMUPDB} AND GTO_{MPDB}

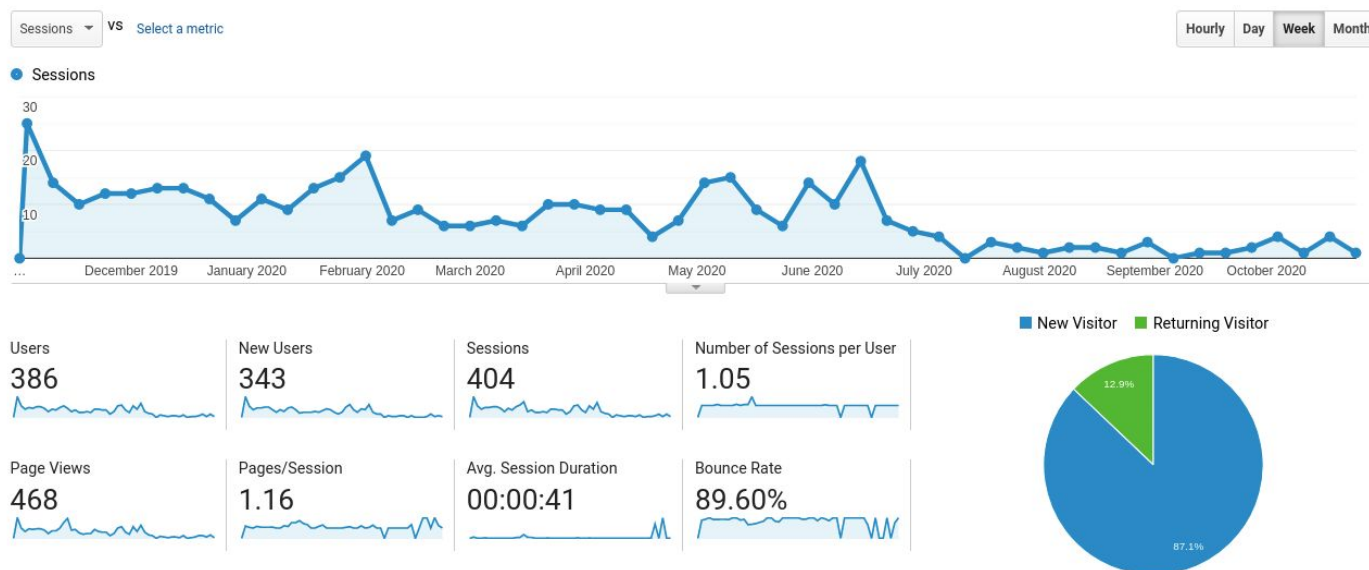
The stats for the 2020.5 release (with 2019.2 in brackets) are as follows (N.B. because the NCBI Entrez system suffers from overload, the links below may time out but should eventually return the result).

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. \

SYNP_{HARM}: A DATABASE OF SMALL MOLECULES AND THEIR DRUG-RESPONSIVE PROTEIN SEQUENCES LINKED TO GTO_{PDB}

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 EPMC 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](https://doi.org/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
<i>Barrier integrity</i>	51	63
<i>Inflammation</i>	677	1483
<i>Antigen presentation</i>	161	247
<i>T cell (activation)</i>	230	528
<i>B cell (activation)</i>	183	323
<i>Immune regulation</i>	554	1409
<i>Tissue repair</i>	27	29
<i>Immune system development</i>	290	569
<i>Cytokine production & signalling</i>	559	1491
<i>Chemotaxis & migration</i>	281	604
<i>Cellular signalling</i>	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
<i>B cells</i>	CL:0000945 lymphocyte of B lineage	56
<i>T cells</i>	CL:0000789 alpha-beta T cell	82
	CL:0000815 regulatory T cell	
	CL:0000911 effector T cell	
<i>Dendritic cells</i>	CL:0000451 dendritic cell	44
<i>Other T cells</i>	CL:0000798 gamma-delta T cell	4
	CL:0000814 mature NK T cell	
	CL:0000898 naive T cell	
	CL:0000940 mucosal invariant T cell	
<i>Macrophages & monocytes</i>	CL:0000235 macrophage	60
	CL:0000576 monocyte	
<i>Granulocytes</i>	CL:0000094 granulocyte	47
<i>Natural killer cells</i>	CL:0000623 natural killer cell	28
<i>Mast cells</i>	CL:0000097 mast cell	39
<i>Innate lymphoid cells</i>	CL:0001065 innate lymphoid cell	6
<i>Stromal cells</i>	CL:0000499 stromal cell	1

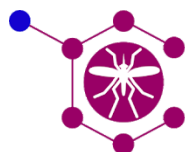
GTOIMMUPDB TARGET AND LIGAND CURATION STATS

- 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.



IUPHAR/MMV Guide to **MALARIA PHARMACOLOGY**

The IUPHAR/MMV Guide to MALARIA 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.

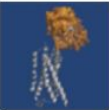
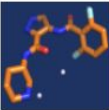



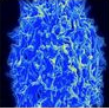
GTOMPDB PORTAL DEVELOPMENT

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.



Home	About	Targets	Ligands	Lifecycle	Species	Resources	Guide to PHARMACOLOGY
----------------------	-----------------------	-------------------------	-------------------------	---------------------------	-------------------------	---------------------------	------------------------------

<h3>Targets</h3>  <ul style="list-style-type: none"> ▶ Antimalarial targets <p>Search for targets GO</p>	<h3>Ligands</h3>  <ul style="list-style-type: none"> ▶ All antimalarial drugs ▶ Approved antimalarial drugs <p>Search for ligands GO</p>	<h3>Latest Updates & Help</h3> <p>Latest updates:</p> <p>The first full release of GtoMPdb was made on 18th Sep 2019.</p> <p>GtoMPdb was presented at the EMBL BoMalPar XV meeting in Heidelberg, 28-30 May 2019. See our poster.</p> <p>Help</p> <p>View our help page for information about the data in and using the Guide to MALARIA PHARMACOLOGY.</p>
<h3>Parasite Lifecycle Stages</h3>  <ul style="list-style-type: none"> ▶ Plasmodium liver stage ▶ Plasmodium dormant liver stage ▶ Plasmodium asexual blood stage ▶ Plasmodium sexual blood stage ▶ Plasmodium mosquito host <p>View parasite lifecycle home page GO</p>	<h3>Target Species</h3>  <ul style="list-style-type: none"> ▶ <i>P. falciparum</i> ▶ <i>P. vivax</i> ▶ <i>P. knowlesi</i> ▶ <i>P. berghei</i> ▶ <i>P. cynomolgi</i> ▶ <i>P. yoelii</i> <p>View target species home page GO</p>	<h3>GtoPdb Twitter activity</h3> <p>Tweets by @GuidetoPHARM</p>  <p>Embed View on Twitter</p>
<h3>News</h3>  <ul style="list-style-type: none"> ▶ 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 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.

