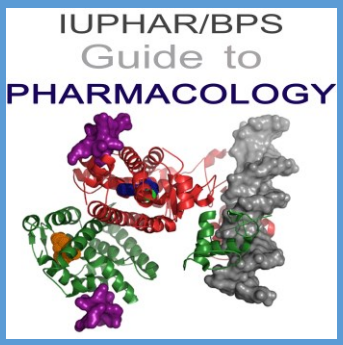
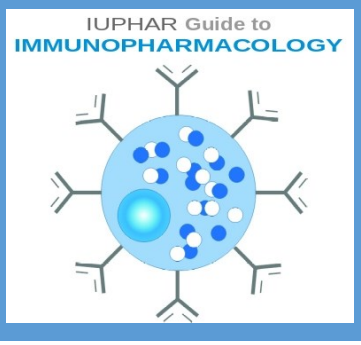
IUPHAR
International Union of Basic and Clinical Pharmacology

BRITISH PHARMACOLOGICAL SOCIETY





DATABASE Report

October 2017

enquiries@guidetopharmacology.org

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INTRODUCTION

This October 2017 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/GtoImmuPdb-focused meeting held in Edinburgh in April 2017.

We are now nearly 24 months into our 3-year Wellcome Trust funded project to develop the "The Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb): Integration of targets, diseases and therapies into an expert-driven database". This grant began on the 1st of November 2015. More details can be found in our blog, which includes technical blog posts highlighting aspects of the development of the resource.

This report (along with the accompanying slide set) will detail our progress on the GtoPdb and GtoImmuPdb projects. It is based on the April 2017 report as a reference. A few general sections have been left in for context but most have been updated with the April content cut back to reduce repetition. Please talk to us to follow-up any points raised in this document, issues and suggestions.

GENERAL OVERVIEW OF DATABASE TEAM ACTIVITIES

PUBLIC ENGAGEMENT – PROMOTING OUR RESOURCES

CONFERENCES/MEETINGS (SINCE APRIL 2017 AND UPCOMING)

- BioIT World, Boston, May 2017, Christopher Southan.
- Edinburgh Pharmacology 2017 symposium, Edinburgh, May 2017, Adam Pawson
- Edinburgh Infectious Diseases 6th Annual Symposium, Edinburgh, June 2017, Adam Pawson
- World Congress on Inflammation 2017, London, July 2017, Elena Faccenda
- Bioschemas Adoption Meeting, Hinxton, October 2017, Joanna Sharman
- International Conference on Trends for Scientific Information , Heidelberg, Oct 2017, Chris Southan
- ELIXIR-UK All Hands meeting, Edinburgh, Nov 2017, Joanna Sharman, Chris Southan, Simon Harding.
- Pharmacology 2017, London, December 2017, (team attendance depending on accepted abstracts)
- ELIXIR-UK SME industry meeting, January 2018, Chris Southan

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

PUBLICATIONS

PUBLISHED (SINCE THE APRIL REPORT)

- **Is systems pharmacology ready to impact upon therapy development? A study on the cholesterol biosynthesis pathway.** Benson H, Watterson S, Sharman J, Mpamhanga C, Parton A, Southan C, Harmar A, Ghazal P. *Br J Pharmacol*. 2017 Sep 14. doi: 10.1111/bph.14037, PMID: 28910500
- **Examples of SAR-centric patent mining using open resources**, Christopher Southan. Book chapter in: *Comprehensive Medicinal Chemistry III*, Andy Davies and Colin Edge, Eds, Elsevier, doi.org/10.1016/B978-0-12-409547-2.13814-4 July 2017 pages 464-487
- **Last rolls of the yoyo: Assessing the human canonical protein count.** Southan C, *F1000Res*. 2017 Apr 7;6:448. doi: 10.12688/f1000research.11119.1.2017. PMID: 28529709

IN PRESS/SUBMITTED/IN PREPARATION

- **The IUPHAR/BPS Guide to PHARMACOLOGY in 2018: Updates and expansion to encompass the new Guide to IMMUNOPHARMACOLOGY.** Harding, S.D., J. L. Sharman, Southan, C., E. Faccenda, A. J. Pawson, S. Ireland, A.J.G. Gray, L. Bruce, S. P. Alexander, S. Anderton, C. Bryant, A. P. Davenport, C. Doerig, D. Fabbro, F. Levi-Schaffer, M. Spedding, J. A. Davies and NC-IUPHAR (2017). Nucleic Acids Res. (Database Issue) submitted.
- **Accessing expert-curated pharmacological data in the IUPHAR/BPS Guide to PHARMACOLOGY.** Joanna L Sharman, Elena Faccenda, Simon D Harding, Adam J Pawson, C Southan, Jamie A Davies and NC-IUPHAR. *Current Protocols in Bioinformatics*, submitted Oct 2017.
- **Challenges of connecting chemistry to biology: perspectives from curating the Guide to Pharmacology.** Christopher Southan, Joanna Sharman (other authors TBC). ACS Omega. (Invited

Perspective due by end 2017).

- **Caveat usor: assessing differences between major chemistry databases.** Invited review for *ChemMedChem*, Chris Southan, in preparation.
- **SynPharm, a database of drug-responsive protein sequences**. Sam Ireland, Simon Harding, Joanna Sharman, Christopher Southan and Jamie Davies, in preparation
- **Virtual versus reality: An analysis of deuterated drugs** Chris Southan, in preparation
- **Will the real drugs please stand up**? Comparing approved structures in PubChem (Southan, et al.), in preparation.
- **Advances in proteases and alpha/beta hydrolases inhibition for human disease** (Turner, et al.) in preparation

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 major databases) aware of our activities. 5) establishing reciprocity with our key followers and collaborators (n.b. our strategic exploitation of Social Media and Scholarly Portals overlap in practice but the latter has its own section below).

FACEBOOK

The number of 'likes' increased to 3215 (September 2017), from 3204 in April 2017.

TWITTER

@GuidetoPHARM has just pipped 1,648 tweets, our followers have increased to 1216 (September 2017) from 1127 in April 2017 and our re-tweet rate is gradually increasing. This medium helps with rapid technical interchanges with teams from other resources. It is also an increasingly useful alerting system for our blog posts, key papers, including from BJP, other pharmacology journals, immunology, biochemistry and medicinal chemistry, weekly PDB structures etc. Consequently, most of our Hot Topics are now first picked up from Twitter. We also engage in a discrete level of diplomatic re-tweeting for reciprocal reach extensions (*e.g.* with @BritPharmSoc , @BrJPharmacol, @PharmRevJournal, @IUPHAR, @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 make connection requests from GtoPdb and IUPHAR scientists they know). Our own LinkedIN group page now has 156 followers, up 13 from Apr 2017. We are also now reciprocally cross-pointing to the IUPHAR LinkedIN page and the IUPHAR/ASPET Pharmacology Education Project page.

BLOGGING

Our Edinburgh blog (http://blog.guidetopharmacology.org/) is receiving over 480 views on average per month, which has increased because we are now posting more content. This is our primary news feed and includes database release updates, new features, technical items or articles. We also post all Hot Topics that have comments and announcements of IUPHAR reviews, which we announce on social media. This replaces our old RSS feed which we no longer maintain. Team member Chris Southan maintains his own (http://cdsouthan.blogspot.com/) where relevant posts include cross-pointers to GtoPdb.

HOT TOPICS

As an established and popular feature our Hot Topics are seeded in the form of new significant pharmacology, drug discovery and key human genomics papers. These are communicated to us from Subcommittee members or picked up from Twitter. We have introduced a CiteUlike tag, htopic, used for collation from which we move them to their own website page. For a selection, as before, we commission concise commentaries from our expert contacts. Our latest guest commentary in September is from Prof Gerald Chum on the Crystal structure of the LPA6 receptor.

SLIDESHARE

Our account (http://www.slideshare.net/GuidetoPHARM) allows the database team to share slide sets and posters with the community thereby extending the reach way beyond conference session direct attendees. Our slidesets received 3,243 views over the past year. We have also added 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.

PUBMED COMMONS

We continue our exploitation by adding comments on relevant PubMed IDs for cross-pointers either between our publications and/or to draw attention to particular database sets. Examples include pointing forwards from the 2013 NAR and 2014 to the 2016 NAR. This is useful because even in 2017 citing authors often cite the older 2014 NAR.

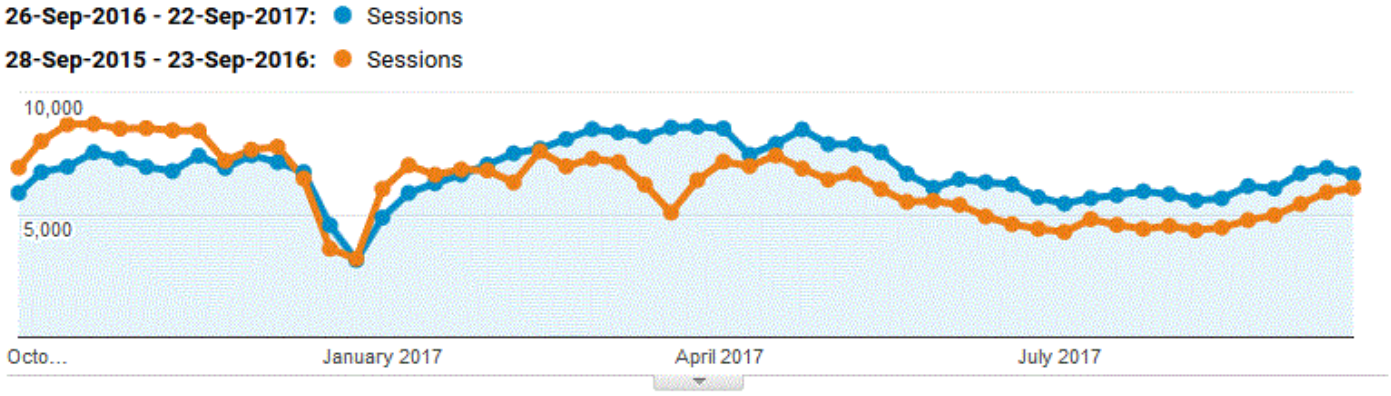
ENQUIRIES RECEIVED FROM USERS

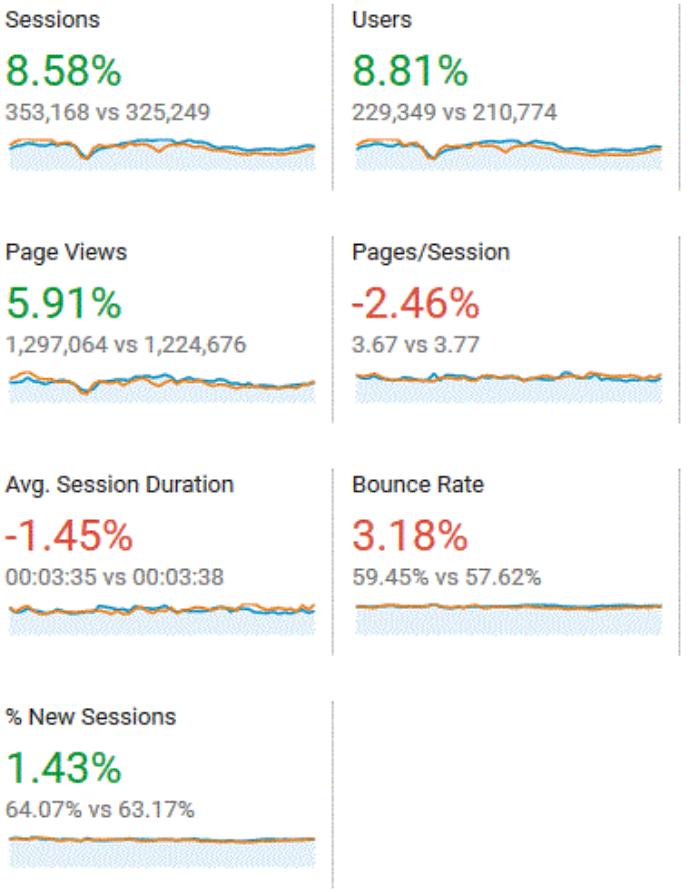
During 2016/2017 we had noticed more user communications coming in to enquiries@guidetopharmacology.org, This upswing has continued in 2017, currently up to about one a week, include our first one direct from a Dundee University Twitter follower. These pose a variety of questions, some of which are quite challenging. We have also had database errors pointed out (at a low frequency we should add), covering a spectrum from wrong names to disputed mechanism of action to complex stereochemistry issues. Fielding this feedback has had a number of positive consequences, including the included compliments and alerts to additional papers. We have also highlighted selected corrections in release notes. Note also from correcting these individual instances we can sometimes execute an internal consistency check to pick up other errors of the same type.

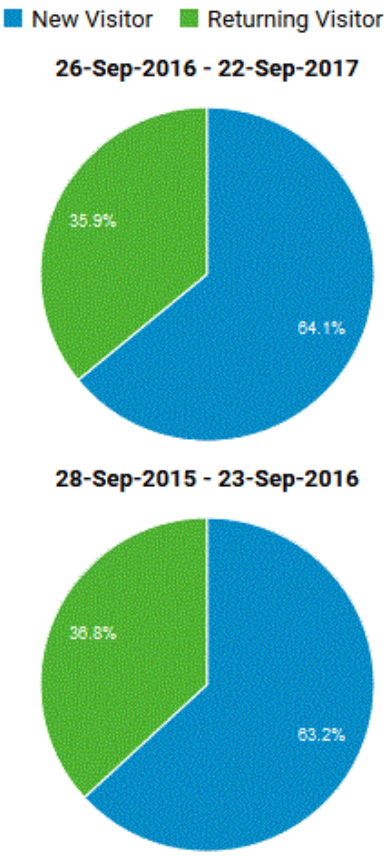
ENGAGING WITH US

As is implicit from the Social Media section above, it is crucial to extend our external “presence”. 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, new publications, meeting slide sets and blog posts. Note also that each time you either save one of our publications to your own Mendeley or CiteUlike accounts 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 (see below in Portals) notches up for that paper (n.b. we are only advocating professionally considered low-key engagement levels).

GtoPdb WEB SITE ACCESS STATISTICS







Graphs comparing visitors to guidetopharmacology.org for the 12 months from September 2016 to September 2017, with the previous 12 months.

Monthly statistics	*September 2016-September 2017 (previous 12 months)*
Sessions	29,669 (27,203)
Users	19,296 (17,643)
Page views	108,661 (102,345)
Pages / Session	3.66 (3.76)
Avg. Session Duration	00:03:35 (00:03:38)

GtoPdb CONTENT

These database statistics were compiled from our August 22nd 2017 release (v2017.5). All database statistics can be found at http://www.guidetopharmacology.org/about.jsp#content.

Targets	*Number of (Human) UniProt IDs*
7TM receptors	395
Nuclear hormone receptors	48
Catalytic receptors	243
Ligand-gated ion channels	81
Voltage-gated ion channels	144
Other ion channels	49
Enzymes	1182
Transporters	509
Other protein targets	174
Targets with ligand interactions	1684
Targets with quantitative ligand interactions	1431
Targets with approved drug interactions	563
Primary targets with approved drug interactions	313
Total number of targets	**2825**
Ligands	*Number of ligands*
Synthetic organics	5807
Metabolites	584
Endogenous peptides	782
Other peptides including synthetic peptides	1297
Natural products	247
Antibodies	223
Inorganics	38
Approved drugs	1334
Withdrawn drugs	67
Ligands with INNs	2114
Labelled ligands	607
PubChem CIDs (SIDs)	6822 (8978)
Ligands with target interactions	7663
Ligands with quantitative interactions (approved drugs)	6716 (824)
Ligands with clinical use summaries (approved drugs)	2089 (1332)
Total number of ligands	**8978**
Number of binding constants	46488
Number of binding constants curated from the literature	15281

DOWNLOAD STATISTICS

Yearly period 28th Sept Year 1 to 27th Sept Year 2.

GOOGLE ANALYTICS COMPARISON OF DOWNLOADS

Event Category: Downloads
Event Label: Downloaded

	Count
2015-2016	2,562
2016-2017	2,430
Change	-5%

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:

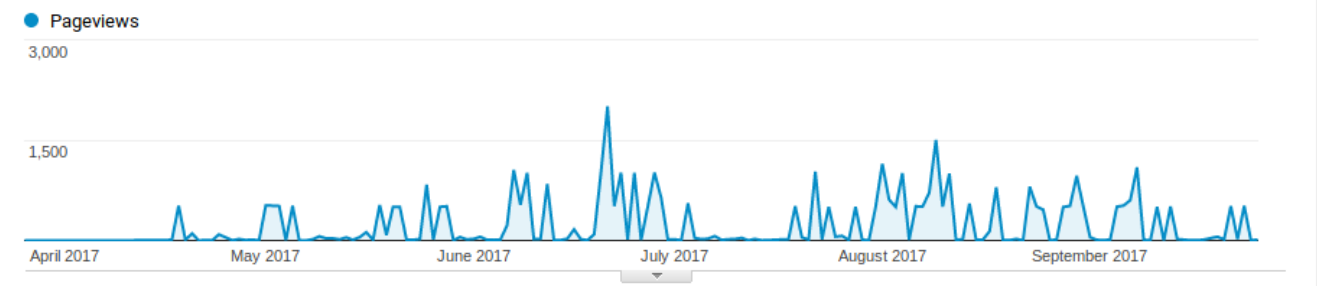
	2015-2016	2016-2017	Change
Targets CSV file	918	963	5%
Interactions CSV file	289	272	-6%
Ligands CSV file	237	230	-7%
UniProt Mapping file	169	155	-8%
HGNC mapping file	78	67	-14%
Peptides CSV file	75	97	29%
PostgreSQL*	141	182	29%
Generic slides (PPT & PDF)	253	221	-13%
Generic poster	117	115	-2%
Other files			
Tutorial	406	407	0%
Terms and Symbols	321	285	-11%

* Total downloads of PostgreSQL database dump files (versions 2015.3-2017.5)

WEB SERVICES

For the first time we are able to report web service access statistics. We introduced Google Analytics tracking in our March 2017.2 release. Since these are generally calls made from client computers to our server, they are not recorded in the same way as visits to our website (although you can view the JSON results in a web browser). 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 nearly **42,000** total hits over the <6 months since we've been recording them. The most popular pages are the target and ligand lists. Unfortunately, it doesn't include information about specific parameters that users can apply to the URLs, such as filters by target or ligand type. So we can't tell if users are loading all targets, or just GPCRs, for example. The most popular target is ID 1 (5-HT1A) and the most popular ligand is ID 1152 (VIP). Perhaps Target ID 1 is popular with people testing out the web services...



Primary Dimension: Page | Page Title | Other

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

	Page	Pageviews	Unique Pageviews	Avg. Time on Page	Entrances	Bounce Rate	% Exit	Page Value
		41,878 % of Total: 100.00% (41,878)	24,146 % of Total: 100.00% (24,146)	00:00:08 Avg for View: 00:00:08 (0.00%)	753 % of Total: 100.00% (753)	50.86% Avg for View: 50.86% (0.00%)	1.80% Avg for View: 1.80% (0.00%)	$0.00 % of Total: 0.00% ($0.00)
1.	/services/targets	2,944 (7.03%)	287 (1.19%)	00:00:20	221 (29.35%)	46.61%	5.43%	$0.00 (0.00%)
2.	/services/ligands	870 (2.08%)	198 (0.82%)	00:00:34	92 (12.22%)	69.57%	10.11%	$0.00 (0.00%)
3.	/services/targets/1/transduction	539 (1.29%)	6 (0.02%)	00:00:07	2 (0.27%)	0.00%	0.37%	$0.00 (0.00%)
4.	/services/ligands/exact	510 (1.22%)	5 (0.02%)	<00:00:01	4 (0.53%)	50.00%	0.59%	$0.00 (0.00%)
5.	/services/targets/1	409 (0.98%)	10 (0.04%)	00:00:05	1 (0.13%)	0.00%	0.73%	$0.00 (0.00%)
6.	/services/targets/1/interactions	316 (0.75%)	21 (0.09%)	00:00:09	1 (0.13%)	0.00%	0.32%	$0.00 (0.00%)
7.	/services/ligands/1152	314 (0.75%)	13 (0.05%)	00:00:00	0 (0.00%)	0.00%	0.00%	$0.00 (0.00%)
8.	/services/ligands/1152/synonyms	314 (0.75%)	13 (0.05%)	<00:00:01	0 (0.00%)	0.00%	0.32%	$0.00 (0.00%)
9.	/services/ligands/1152/databaseLinks	312 (0.75%)	13 (0.05%)	00:00:00	0 (0.00%)	0.00%	0.00%	$0.00 (0.00%)
10.	/services/ligands/1152/structure	312 (0.75%)	13 (0.05%)	<00:00:01	0 (0.00%)	0.00%	0.00%	$0.00 (0.00%)

Traffic to GtoPdb web services URLs over the past 5.5 months

GtoPdb INTERACTIONS WITH OTHER RESOURCES

For more details of the teams we collaborate with please see April 2017 and October 2016 reports. Only significant changes since April are reported below.

GPCRDB

With David Gloriam and his team at the University of Copenhagen we intend to harmonise our human GPCR numbers in 4Q2017. Antony Davenport and Chris Southan have been invited to Copenhagen in Feb 2018 to a meeting for the European PhD Training Network to identify selective serotonin receptor 5-HT2A agonists (SAFER) Chris continues to co-supervise PhD student Alex Hauser who's publication record indicates good progress.

ELIXIR

Engagements continue with this important Europe-wide initiative. As reported before, we have an entry in the ELIXIR tools and resources directory as one of the official UK ELIXIR Node Resources and part of the Excelerate initiative. This gives us local Edinburgh connections to Prof. Chris Ponting as Head of the UK ELIXIR Node and Prof. Richard Baldock the PI for the EMAP mouse expression database. We attend weekly UK node teleconferences. In Nov 2016 we completed an application to be promoted to a core European Node. While we were unsuccessful in this first round we were relatively close in the evaluation score (report available). We will thus use the feedback to optimise our reapplication early in 2018. Along with more impact measurement it was suggested we should constitute an SAB for GtoPdb which should not be too difficult.

INTEROPERABILITY, RDF AND OPENPHACTS

One of ELIXIR's aims is to promote interoperability and FAIR (Findable, Accessible, Interoperable, Reusable) compliance (see **FAIR** Guiding **Principles** for scientific data management and stewardship. Wilkinson MD et al. Sci Data. (2016)). Therefore, we have embarked on several initiatives to increase interoperability of the GtoPdb data, including creating a new RDF version, submitting our ligands to WikiPathways, working with the Bioschemas group to implement Schema.org mark-up (which helps search engines to find and analyse content), and setting up a new NC-IUPHAR Subcommittee on Data Interoperability.

We have set up collaboration with Alasdair Gray, a Linked data and RDF expert from Heriot-Watt University (who has also agreed to chair our Subcommittee on Data Interoperability). Alasdair's undergraduate student, Liam Bruce, completed his project to produce an RDF version of the GtoPdb data (focusing on interactions in the first instance) to facilitate eventual loading into the OpenPHACTS API. Other important direct consumers of our content, including pharmaceutical companies, increasingly prefer RDF format for data uptake. The RDF flat files are now available to download. There are 4 data files (one containing all the data, one describing just targets, one for ligands and one for interactions); these are provided in Notation3 (N3) format. We also provide 2 metadata files which include a general description of the dataset and specific information on the current version: 2017.5. The metadata have been generated in accordance with the W3C Health Care and Life Sciences Community (HCLS) Profile to ensure FAIR compliance. The RDF will be updated in line with each database release.

At the moment, users would need to download these flat files and load them into a local triplestore (a special type of database for semantic querying across RDF data). We are in the process of providing linked data pages for each resource in the RDF data, i.e. the URL used to identify each target, ligand, and interaction in the RDF will become dereferenceable to a specific, new URL on our site. Additionally, we will be providing a SPARQL endpoint with a set of example queries to help exploit the RDF data and enable deeper analysis of the GtoPdb data in conjunction with other linked data datasets. In the future, we plan to provide link-sets that capture the database cross-references contained in the GtoPdb as well as extend coverage of the data.

PUBCHEM

We continue to interact with Evan Bolton and Paul Theissen, from PubChem mainly around enhancing visibility and utility of our ligand entries (see ligand drug link section below). The PubChem team not only gave us a citation but also a detailed and important mention in their paper "Literature information in PubChem: associations between PubChem records and scientific articles" (PMID 27293485).

BINDINGDB

We continue to interact with Michael Gilson the PI for BindingDB where Christopher Southan is on their SAB. He has curated a selection of USPTO patents for GtoImmuPdb where extensive analogue SAR in the patent that exceeds that in the paper.

STRUCTURAL GENOMICS CONSORTIUM PROBE PORTAL

Christopher Southan is on the SAB for the SGC/Wellcome Chemical Probes Portal for which he continues to be assigned probe reports by Amy Donner the Portal Director. We now have links for 112 of their 148 probes.

RECIPROCAL JOURNAL-TO-DATABASE CONNECTIVITY

This important area is described in the April report. More recently we have investigated the statistics of our connectivity in some depth for inclusion in the draft version of our new NAR database paper. This established that we have 30,894 PubMed IDs in our system, of which 9,086 ligand-associated references provide "Depositor Provided PubMed Citations" (DPPMC) for our SID submissions to PubChem. Of these, 6,011 refer to quantitative interactions The key axis of connectivity that we facilitate is PubChem-to-PubMed reciprocal linking for our ligands and their curated references. The importance of this overall has been described by the PubChem team in some detail, including the contribution of GtoPdb as one of the mapping sources (PMID 27293485). This means that any user coming in to the NCBI Entrez system either via PubMed or PubChem can connect the paper to the structure (via the PubChem links on the lower RH

facet of PubMed entries). As described in April, in addition to curating selected ligands from BJP articles we have out-links for all their papers where GtoPdb entities are mentioned by authors. The transiition from tables to in-line links for GtoP entries is now complete and the XML format also gives us an easy way to count links for particular papers. For example, for BJP, Volume 174, Issue 18 September 2017, the 12 papers therein have 134 out-links to GtoPdb. We have also achieved our first “circular” example where GtoPdb team members are co-authors on a Systems Pharmacology study, partly derived from the database, (PMID 28910500) for which we have added 51 links “back in”. BJP and Wiley are now considering process options for us to capture key compounds not yet in GtoPdb prior to publication.

NEW GTOPDB WEBSITE FEATURES (SINCE APRIL 2017)

HOMEPAGE REORGANISATION

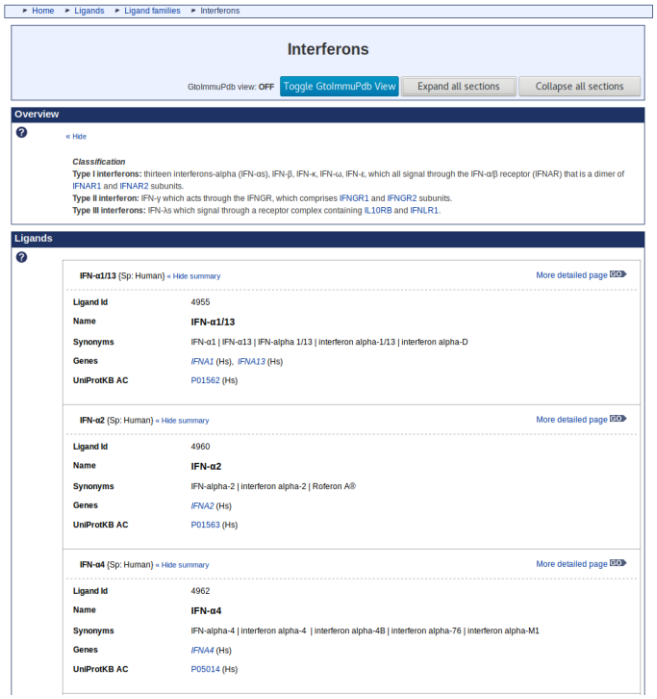
The GtoPdb homepage underwent a reorganisation in May 2017, which gives greater prominence to news items in a panel in the centre and moves the quick links to targets/ligands and key resources to the left. Links to the important associated resources (GtoImmuPdb and CGTP) remain in the panel on the right. IUPHAR reviews are highlighted in the panel below. Underneath this are links to other useful resources: the IUPHAR Pharmacology Education Project, SynPHARM, and ELIXIR. In the fourth panel on this row is a sign up box for our email newsletter, which has moved down from the top in the old design. We have removed the Facebook feed from our homepage and moved the Twitter feed up, because Facebook posts are always also sent out on Twitter (besides, this newsfeed preview is ideal for the shorter Tweet content), and we tend to post more often on Twitter due to the ease of “retweeting” other members’ content (see above section on Twitter engagement).

The new design should not feel too different from the old one, but we hope the new layout will quickly alert visitors to new content, which in the old version was hidden halfway down the page. Any feedback on the new design is welcome!

New GtoPdb homepage design

LIGAND FAMILIES

We have extended the database schema to group related ligands together into families, using the information on Hugo Gene Nomenclature Committee (HGNC) gene family pages (https://www.genenames.org/cgi-bin/genefamilies/). The full family listing page is available under the 'Ligands' sub menu of the main navigation bar, and also via the ligand list. Each family also has its own database page, modelled on the target family page, for example see the chemokines. Individual ligand summary pages also link back to the family pages. Furthermore, we have begun to explore adding in other types of ligand groups, for example Immune checkpoint modulators, which brings together a disparate group of ligands with common functionality. The ligand family page has options to add overview and comment text, longer introductions and further reading (similar to target families).



Ligand family page for the Interferons. The page is modelled on the target family layout, with links to the more detailed pages for individual ligands on the right.

DATABASE LINKS REVIEW AND ECOSYSTEM AWARENESS

This section updates the April 2017 report that included our important assessment of in-links as well as the review and removal of some out-links. In the wider context it should be appreciated we have relatively little control over in-links (indeed there are some we would rather not have) but there are occasions when we approach sources where we think reciprocal linking to us would add user value to them. While we obviously have control of out-links we choose to put in, these are difficult to balance in number vs user value vs curatorial overhead. We refer to this in/out balance as awareness of our position in the global bio-database ecosystem. More recently, after careful utility-based considerations, we have added out-links to 1) UniChem, which cross-references between chemical structure identifiers from different databases, 2) CATH/Gene3D structural domains and superfamily 3D alignments and 3) the Human Protein Atlas (HPA) tissue expression database. Note the latter two are now ELIXIR Core Data Resources. We have also ensured cross-links exist between GtoPdb and the Pharmacology Education Website (PEP), www.pharmacologyeducation.org/) and SynPharm (http://synpharm.guidetopharmacology.org/), the database of ligand-binding sequences. The current set of database link-outs from GtoPdb target and ligand pages can be viewed. We ensure that the cross-links are regularly refreshed through formal and informal contacts with database providers. Of note are the links to RCSB Protein Data Bank (PDB). The acceleration at which pharmacological targets are being co-crystallised with ligands (and regularly featured in our Hot Topic collections) meant it was necessary to introduce PDB InChIKey look-ups as part of our database update procedure, to ensure that links are up-to-date in each release. Consequent to the creation of peptide ligand family pages, we also updated our reciprocal HGNC links to include human genes encoding peptide ligands.

GRAPHS COMPARING LIGAND ACTIVITY DATA ACROSS SPECIES

In April we reported on the development of new ligand activity graphs comparing activity ranges across species using data extracted from GtoPdb and ChEMBL. The graphs are available *via* the ligand page biological activity tab and are described in this blog post: https://blog.guidetopharmacology.org/2017/03/23/database-release-2017-2/. Over the past few months we have fixed some bugs and tweaked the data content, some of which were due to quirks of the ChEMBL dataset. This included removing bloat caused by the PubChem Bioassay data which ChEMBL recycles. Some odd patent data (from BindingDB that is also extracted into ChEMBL) still remains, where assay results have been duplicated with slightly different descriptions, which makes it difficult for our tool to tell they are duplicates (ChEMBL generally suffers from a high proportion of duplicates as they don't usually distinguish between the original citation and authors repeating the figures in subsequent papers).

Originally these graphs were only available for ligands that we had links to in ChEMBL. However, we have now extended it to all ligands where GtoPdb records activity data, even if they don't have additional data from ChEMBL. Unfortunately, this still means that there may be cases where additional data does exist in ChEMBL but we have yet to map this to GtoPdb ligands, in particular for larger peptides or other molecules e.g. those with complex stereochemistry, due to the difficulty in identifying equivalent database entries for these structures.

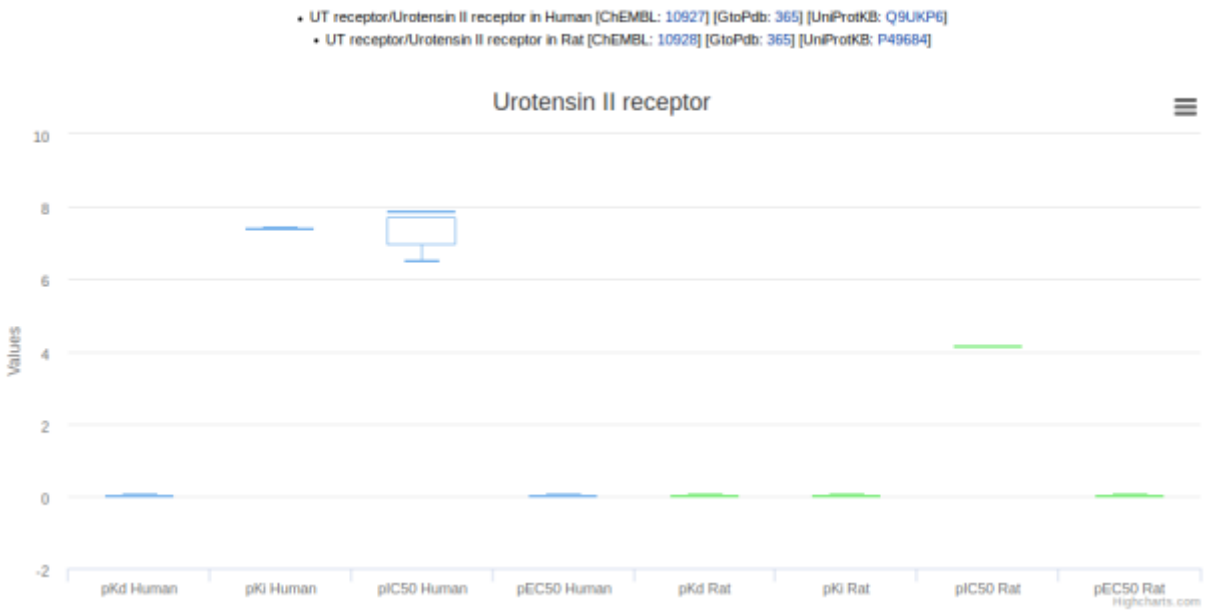


Chart showing palosuran activity at human and rat UT receptors.

OTHER WORK/SUGGESTED NEW FEATURES IN OCTOBER 2016 / APRIL 2017

Updates on other suggestions for new website features discussed at the October Paris meeting and April Edinburgh meeting are:

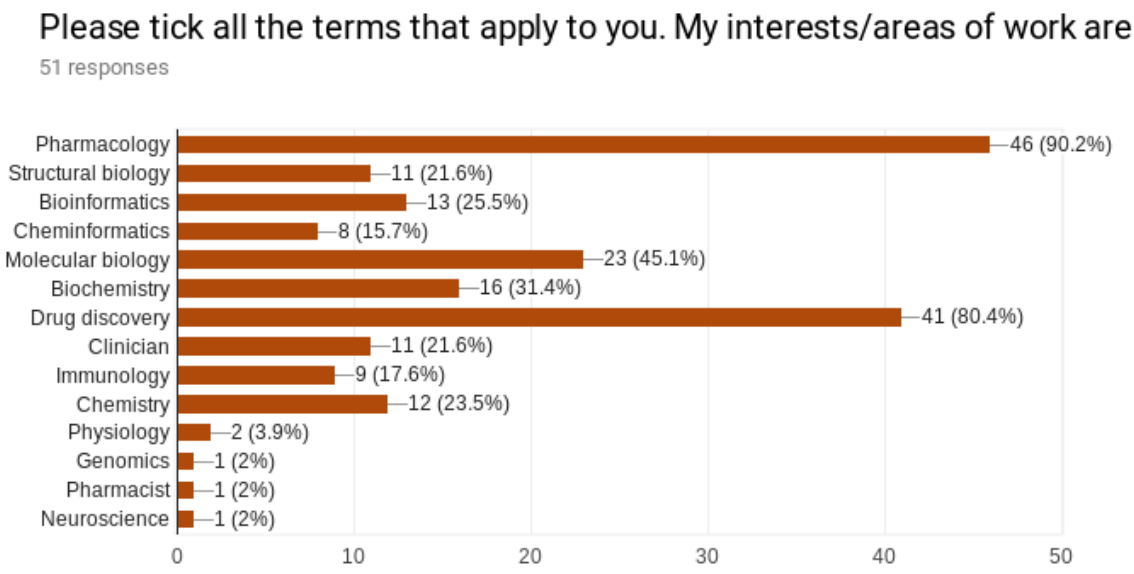
- **Converting to HTTPS:** Using HTTPS (secure connection) on websites is becomingly increasing important (browsers and search engines are starting to warn users when they access an insecure site). JS has been working with UofE Information Services to obtain security certificates from JISC which will allow us to install HTTPS on our web server, which we hope will be completed soon.
- **Upgrading our server software**: Our server is using older versions of Java and Tomcat (the web server) so we have submitted a request to the UofE Information Services hosting team to upgrade them to newer versions, which should happen soon. This will require us to test all our web applications with the new versions, but should hopefully not result in much disruption to users. We will notify users of any planned downtime via a message on the website and social media.
- **Creating a mobile application for the GtoPdb and CGTP**: There was enthusiasm at the April meeting for developing a mobile application for both GtoPdb and CGTP. It was felt that this might be easier to progress for the CGTP, as it's a subset of the data and it could be developed in collaboration with Wiley. Amrita Ahluwalia was going to follow this up with Wiley and BPS. Another option discussed was to produce a working offline version of the GtoPdb site (or part of it) that could be handed out on a memory stick. JS will talk to UofE IS about options here, but this cannot be done until the outstanding work above has been completed.

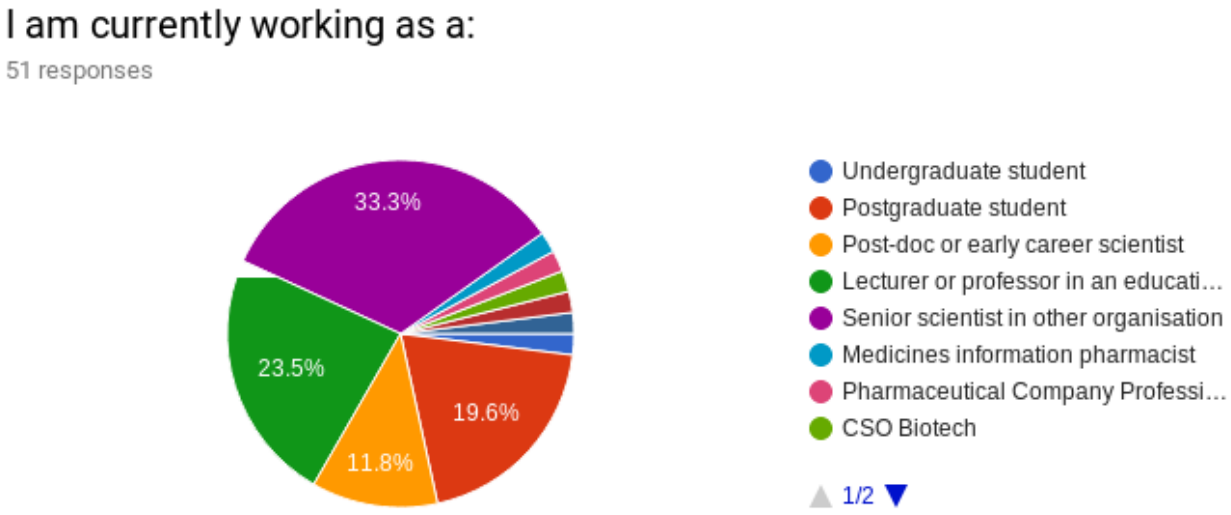
  Meanwhile, JS initiated a survey (not limited to current users of GtoPdb) to gather feedback and requirements for a GtoPdb mobile app, which has had 51 responses so far. This would be necessary for any future plan to build an app, whether this was outsourced or not (though current resources and team expertise would most likely mean that app development would need to be out-sourced, should suitable funding be found.) Below is a summary of the results from the survey:

  - Two-thirds of respondents said they had used the GtoPdb site (8% don't know) and over half saying they used it about once a month, and a quarter saying at least once a week.
  - Of those, ~40% said they sometimes or frequently access it on a mobile device.
  - Over a third of respondents said they had used the Concise Guide, and of those about 30% said they ever used it on a mobile device.
  - Over 75% of respondents said they would be likely to use a mobile application with data from GtoPdb, with the rest saying "maybe" - nobody said "no".
  - The features people thought would be important in an app in order of preference were:

1. Summary information for targets and ligands (94%)
2. Approved drugs and their targets (82%)
3. Key recommended ligands for experimental use (70%)
4. Search function (67%)
5. Links to further reading (65%)
6. Disease information (61%)
7. Images of ligand and target structures (53%)
8. Offline access to data (47%)
9. Links to online protein and chemistry databases, e.g. UniProt, PubChem (45%)
10. Extensive pharmacological information (43%)
11. Other suggestions: chemical structure search; export for further review on PC/Mac (1 person)

- About the respondents:





- Countries: UK (25%), US (8%), Brazil (8%), Sweden (6%), Switzerland (6%), France (4%), Greece (4%), Malaysia (4%), Spain (4%), and 16 other countries on 2% each (inc from Europe, South America, Asia, and Nigeria and Australia).
- All except 1 rated the internet access in their location as at least 3 on a scale of 1-5 with 1 being very poor and 5 being excellent, with almost 90% rating it 4 or 5.
- 40% have an Android phone, 20% have an Android tablet, 56% have an iPhone, 31% have an iPad, 6% have a Microsoft Windows phone and 4% have a Windows tablet.

- Other responses:
  - Easy access to every option, quiz for students, frequent updates
  - Great Idea. Add a dilutions calculator for lazy students.
  - Interested in gene variants (somatic or germline) in relation to treatment response, drugs, trials, and targets ranking.
  - If possible, the authors and year if publication.

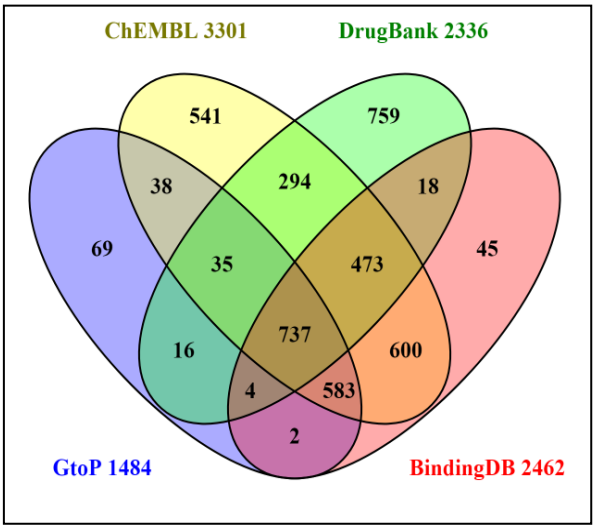
GtoPdb ENTITY GROWTH

Growth rates over the span of the previous Wellcome Trust grant are documented in earlier reports and our 2016 NAR paper. Notwithstanding, it is important to note that the staff changes associated with the new Wellcome grant resulted in the loss of one curatorial FTEs from the team as a whole, plus the effective transfer of two FTEs to GtoImmuPdb. We consequently cannot sustain the previous overall growth rate (*i.e.* 2013-15 below). While the subcommittees have submitted Concise Guide updates, most new entities are being added *via* the population of GtoImmuPdb. However, significant curation effort goes towards tagging pre-existing targets and ligands with GtoImmuPdb relevant comments and new references.

	Oct 2013	*Oct 2015*	*April 2016*	*Oct 2016*	*Apr 2017*	*Oct 2017*
Target protein IDs	2485	2761	2775	2794	2808	2825
Ligands total	6064	8024	8400	8674	8872	8978
Approved drugs	559	1233	1273	1291	1322	1334
Antibodies	10	138	172	205	212	223
Peptides	1776	1981	2007	2039	2063	2079
Synthetic small molecules	3504	5055	5363	5563	5729	5807
PubChem SIDs	3107	8024	8328	8674	8831	8978
PubChem CIDs	2694	6057	6163	6337	6813	6822
Binding constants	41076	44691	45534	45908	46287	46488
References	21774	27880	29247	30251	31239	31733

GtoPdb TARGET UPDATES (SINCE APRIL 2017)

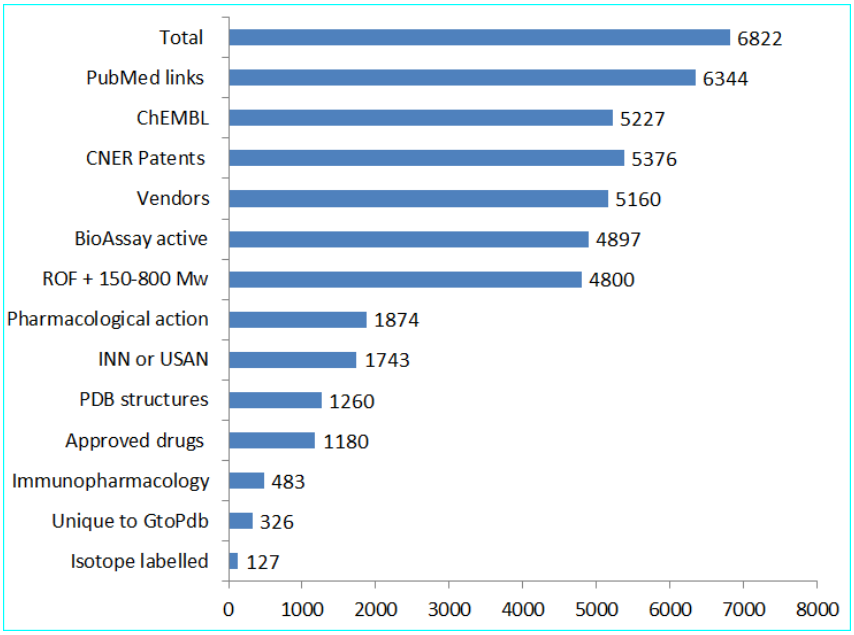
- New subcommittee chairpersons: Rejean Couture (Bradykinin), Eric Prossnitz (GPER), Steve Lolait (VP/OT), Dejian Ren (CatSper/Two Pore), Haoxing Xu (TRP), Jane Mitchell (Cox), Chen Yan (PDEs).
- The major part of the work to update the target family summary pages has been completed in advance of producing the Concise Guide to PHARMACOLOGY 2017/18 from the database (see below).
- GPCR updates: Dopamine receptors, Endothelin receptors, Glucagon receptors, Melanin-concentrating hormone receptors, Neuromedin U receptors, P2Y receptors, Prostanoid receptors, Succinate receptor.
- Ion channel updates: Epithelial sodium channel (ENaC), P2X receptors.
- Other protein targets updates: RGS proteins
- New targets:
  - Piezo channels
  - New family, Butyrophilin and butyrophilin-like proteins
  - Reorganisation and additions to Immune checkpoint proteins - contains Immune checkpoint catalytic receptors and Other immune checkpoint proteins
  - Ligand family Immune checkpoint modulators
- Relative target growth and coverage. This can be assessed by comparing our own UniProt cross-references (for targets with quantitative interactions) against the other major chemogenomic resources with UniProt cross-references, DrugBank, BindingDB and ChEMBL. The October 2017 updates are shown below.



These intercepts and differences in the above figure are informative, but note that DrugBank includes targets based on literature co-occurrence rather than data-supported mechanism of action. The main shifts from April are a modest increase in the 4-way consensus (722 < 737) and that ChEMBL has expanded human target coverage 448 < 541 in their new release 23. We have 69 targets not in the other three databases.

GtoPdb PUBCHEM STATS

As for 2016, most new ligands in 2017 have been added *via* GtoImmuPdb (see below). These add to our current substances (SID) that we submit to PubChem (refreshing previous submissions) giving us 8978 ligand entries from release 2017.5. Those that have defined chemical structures are merged into 6822 Compound Identifiers, CIDs. The new feature allowing the selection of just approved drugs was introduced in the last report. The select is "IUPHAR/BPS Guide to PHARMACOLOGY"[SourceName] AND approved [Comment] which can be pasted into the Substance query box to retrieve 1417 SIDs. Of these 1247 have CIDs (use the “Find Related Data” operator and select “same CIDs”. The chart below indicates selected PubChem overlap statistics for 2017.5.



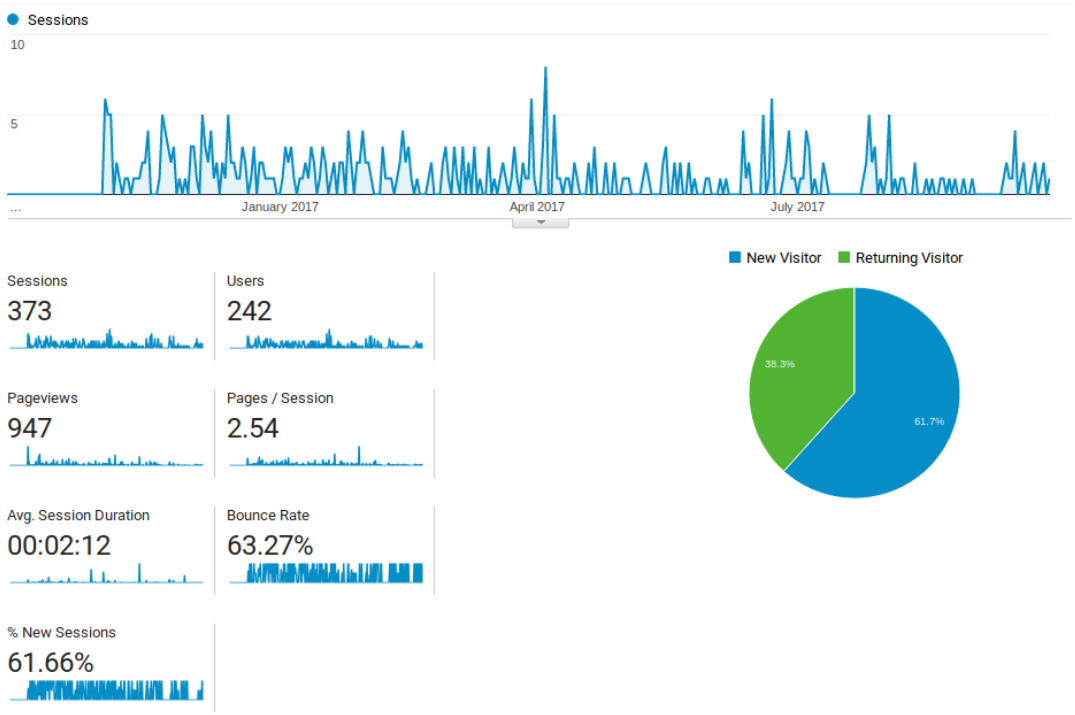
In terms of complementarity within the database ecosystem we have 1595 structures that ChEMBL does not have, 5451 not in DrugBank and 5540 not in DrugCentral. In addition we have 326 structures unique to us. Ensuring this complementarity of our content ensures that our integration by other resources (academic or commercial) becomes imperative rather than optional.

PRODUCING THE CONCISE GUIDE TO PHARMACOLOGY 2017/18

The major part of the work to update the target family summary pages has been completed in advance of producing the Concise Guide to PHARMACOLOGY 2017/18 from the database, which is now awaiting online publication (mid-October 2017). For the 17/18 version, we have been working towards trying to make the information more concise, and limiting both ligands and further reading to the 5 most useful in many cases. Obviously, there are some targets where it makes sense to have more or less than 5 displayed on the summary page, but in any case, all the ligands can still be viewed on the detailed target page, and the website contains more further reading references than are included in the published Concise Guide. Overall, we have included links to 1679 targets and 3524 ligands We are very grateful to all the contributors and the editors who have provided information.

SynPHARM: A NEW 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 is being drafted. The figure below shows the SynPHARM access statistics for the past year. About 13% of the hits come from Edinburgh, many of which are likely to be from our team or local UofE SynthSys institute colleagues. A further 12% are from London, which likely represents a lot of visits from Sam Ireland, the original developer of SynPHARM, who has now moved to London.



Demographics
Language
Country
City
System
Browser
Operating System
Service Provider
Mobile
Operating System
Service Provider

	City	Sessions	% Sessions
1.	Edinburgh	49	13.14%
2.	London	43	11.53%
3.	(not set)	22	5.90%
4.	Waltham	7	1.88%
5.	North Laurel	7	1.88%
6.	Berlin	6	1.61%
7.	Tunis	6	1.61%
8.	Hyderabad	5	1.34%
9.	Vienna	4	1.07%
10.	Montreal	4	1.07%

SynPharm access statistics for the past year (recording only began at the end of Oct 2016)

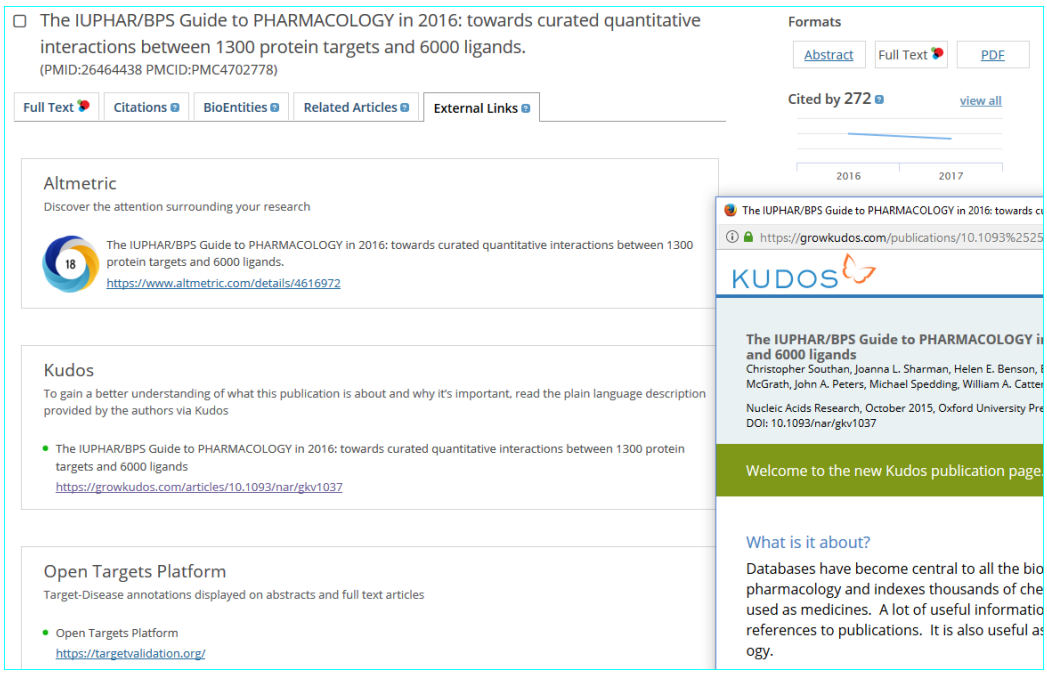
BIBLIOMETRICS AND SCHOLARLY PORTALS

- As outlined in April we track various impact metrics for the GtoPdb team and NC-IUPHAR affiliated papers in PubMed, PubMed Central , European Pub Med Central (EPMC) and Kudos entries. All team members now have ORCID IDs (from which an individual author citation graph can be generated in EPMC) as well as Edinburgh Research Explorer profiles.
- We also track our Altmetrics for our outputs since institutions and funders are taking increasing notice of the resulting interest "scores". Our team papers continue to be ranked around the 90th percentile.
- We continue to maintain our Google Scholar pages (*e.g.* Adam Pawson, Chris Southan and Joanna Sharman) as well as ResearchGate entries.

As of October 2017, these sources record the following; (n.b. any EPMC listing can be ranked by citation counts and total cites calculated from downloads. PubMed and WOS citation counts are generally higher)

- Database team member cumulative co-authored publications have increased to 153.
- IUPHAR reviews in BJP stand at 24.
- IUPHAR Pharmacological Reviews have reached 92.
- The BJP "Concise Guide" sets from 2013 and 2015 add up to 17 papers. We expect a jump from the publication of the 2017 set imminently.
- We still have five publications in the NAR Database issues but should shortly notch up to six
- We continue to get high citation rates in some grant-linked articles because the BJP and BJCP selected these as reference citations . These are topped by our NAR 2014 Database Issue (PMID 24234439) that now has 675 PubMed citations.
- The equivalent 2016 Database Issue (PMID 26464438) has now caught up at 518 PubMed citations.
- The Concise Guide to PHARMACOLOGY 2013/14 set PubMed citations continue to be led by G-Protein Coupled Receptors (PMID 24517644) at 425.

The latest EPMC mark-up features can be seen below for our 2016 NAR paper



MMV COLLABORATION ON ANTIMALARIALS

As some readers of this report will know our future funding strategic considerations have encompassed antinfectives. As a consequence, we have initiated a pilot phase of curating antimalarial drugs and lead compounds sponsored by Medicines for Malaria Venture (MMV). An initial set of anti infective pilot entries was reported on our blog at the end of August. We are pleased to report that Jane Armstrong (formerly from the Edinburgh GUDMAP database) has just joined the curation team for this new initiative. Further details and updates will be included in the April 2018 report.

THE GUIDE TO IMMUNOPHARMACOLOGY DATABASE (GtoImmuPdb)

GtoImmuPdb WEB INTERFACE & DATABASE DEVELOPMENT STATUS

The Guide to IMMUNOPHARMACOLOGY (GtoImmuPdb) has been developed as an extension to the existing Guide to PHARMACOLOGY (GtoPdb). The development of GtoImmuPdb aims to provide improved data exchange between immunology and pharmacology expert communities, so to better support research and development of drugs targeted at modulating immune, inflammatory or infectious components of disease. The underlying GtoPdb schema has been extended to incorporate new immune system specific data types (such as processes and cell types). It also means the existing GtoPdb website has been further developed to surface this new data and incorporate it into the existing search and browse mechanisms. GtoImmuPdb does not therefore have its own website, although it is being developed so that it can run from a unique domain (www.guidetoimmunopharmacology.org), with its own portal, which serves as a unique immunological access-point to the Guide to PHARMACOLOGY.

Our first public beta-release was made in May 2017 (GtoImmuPdb v1.0), alongside the general GtoPdb release 2017.4. This was followed in August with the GtoImmuPdb beta-release v2.0, in line with GtoPdb 2017.5. Full technical details on the development progress of GtoImmuPdb can be found on our blog.

GtoImmuPdb USER TESTING

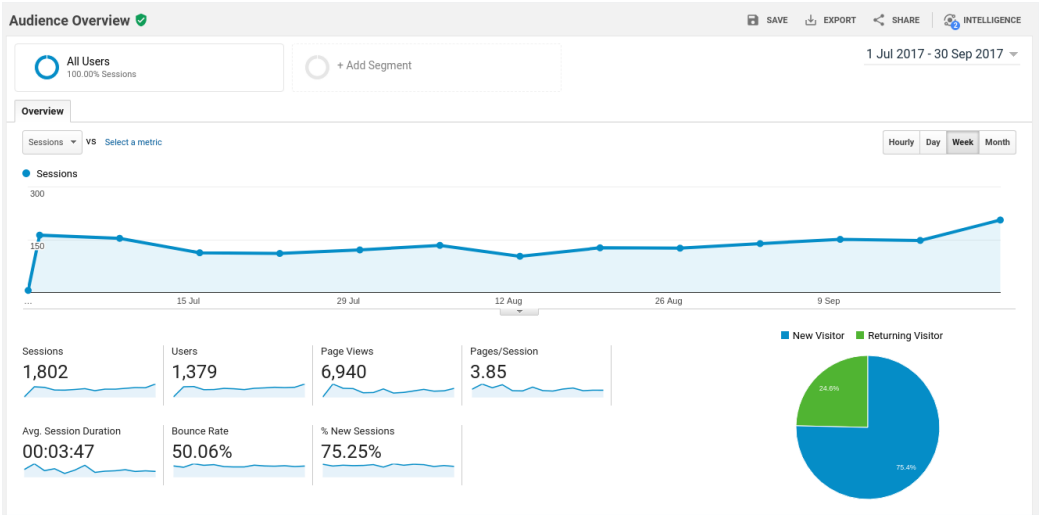
During July 2017, a user-testing exercise was undertaken to gather feedback on the GtoImmuPdb v1.0 beta-release. Testers were recruited by sending out emails to immunology research groups in Glasgow, Manchester & Dundee, as well as to the BSI Edinburgh Immunology Group, the London Inflammation Network and to the IUPHAR ImmuPhar Section. In total nine respondents completed the testing, which focussed on assessing the quality and coverage of the data, as well as the site style, layout and navigation. Those testing the site had a good range of research experience, from PhD students to Professors. Overall, the site was very well received. Users were asked to rate how easy it was to find and understand the different data types (on a scale of 1-7, with 1 being very difficult and 7 being very easy), and nearly all responses score 5 or more. The site received similar scores of data usefulness and credibility. There were though plenty of comments and suggestions to help us improve things

- The GtoImmuPdb portal layout was a positive, but some redundancy in items was noted, and a preference for alphabetical lists
- The immunological process data requires more explanation, particularly around GO terms and evidence. It was also noted that the process association comments were lacking or absent
- Cell type associations were easy to understand, but could do with more evidence about the associations, they also lacked data for some cell type categories (ILCs, stromal cells)
- Disease data layout quite clear, but could benefit from combining target and ligand data - disease summaries?
- Disease data requires more references, and information about how up-to-date drug information is.
- It is important to maintain definitions, descriptions and references - these are often the most useful
- Information about ligand-ligand interaction/interference and FDA pregnancy risks would be useful
- Navigation through the site was not always intuitive - this is due to inconsistent page naming, absence of obvious descriptions and/or help.

Our aim now is to incorporate this feedback into the next beta-release before running further user-testing in advance of the first full release of GtoImmuPdb in Spring 2018.

GtoImmuPdb ANALYTICS

In June 2017, after the first beta-release of GtoImmuPdb, analytics code was put into the site to track the usage of GtoImmuPdb. This tracks users who specifically access the www.guidetoimmunopharmacology.org URL. In the three-month period between July and September 2017 ~140 session are recorded on GtoImmuPdb each week.



Access statistics for GtoImmuPdb (July-September 2017)

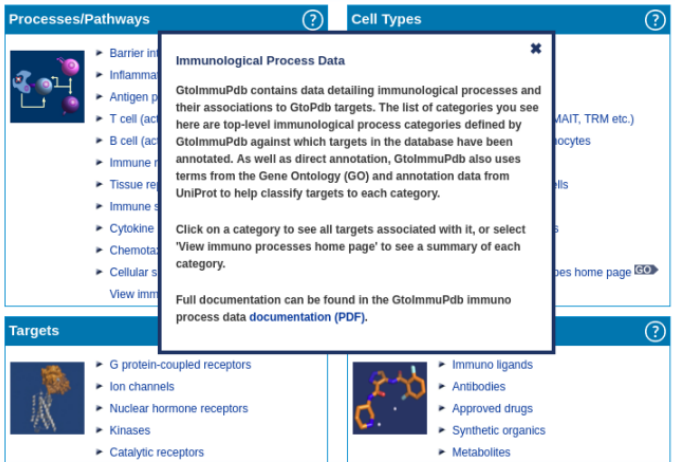
The majority of users accessing GtoImmuPdb have come from the USA and UK, together accounting for nearly 46% of all traffic to the site. The countries with the next highest users accessing GtoImmuPdb are China (9%), India (6%), Japan (4%) and Germany (4%).

	Country	Sessions	% Sessions
1.	United States	418	23.20%
2.	United Kingdom	236	13.10%
3.	China	162	8.99%
4.	India	112	6.22%
5.	Japan	78	4.33%
6.	Germany	76	4.22%
7.	Canada	51	2.83%
8.	Russia	45	2.50%
9.	France	41	2.28%
10.	Mexico	41	2.28%

The top ten countries ordered by number of sessions accessing GtoImmuPdb between July and September 2017

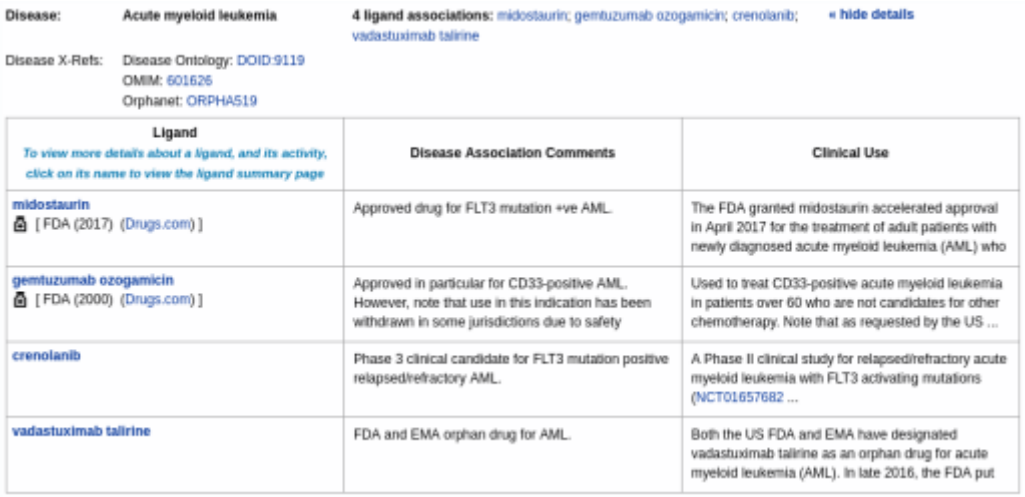
GtoImmuPdb PORTAL AND WEB-INTERFACE

Over the first two beta-releases a few changes have been made to the GtoImmuPdb portal and web-interface. Some of these are as a direct result of feedback from our user-testing. For example, we have now included help pop-up on the main panels of the portal. Having help available beside each panel should make it easier for users to find the help they need and to understand each data type.



New help pop-ups have been added to the GtoImmuPdb portal

The layout of both the process and cell type associations has had minor modification to help navigation, switch the position of drop-down menus and quick links. We have also included a back-to-top link for when the user scrolls down a long page.
Our user-testing highlighted the need to display more information on the disease association pages, particularly about why ligands are associated with some diseases. The information displayed has been extended to show whether the ligands are approved drugs (and which regulator it was approved by) and links to more info at drugs.com. We have also added the clinical use comments for the ligand. This is all data that can be found on the ligand summary pages, but we have also surfaced into on the disease association pages to bring added value and ensure the most relevant information is available in the right places.



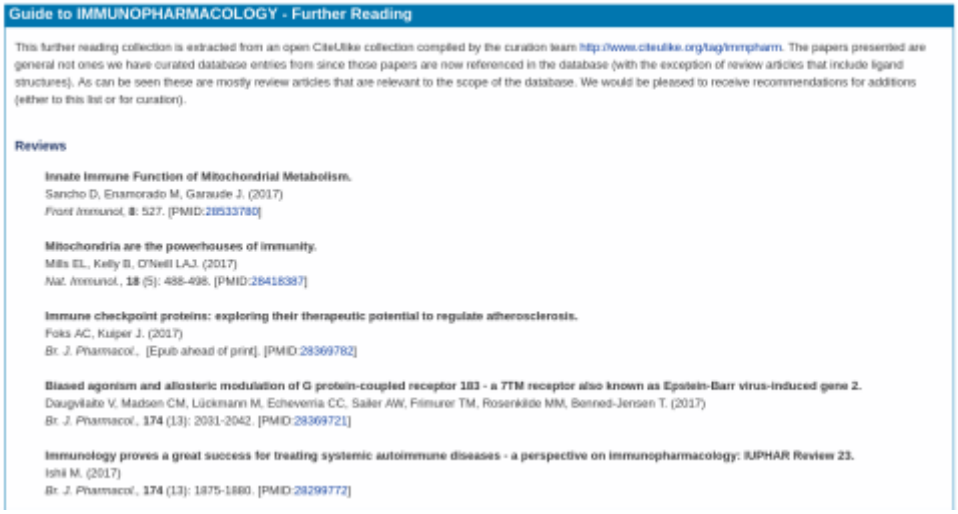
Disease: Acute myeloid leukemia — **4 ligand associations:** midostaurin; gemtuzumab ozogamicin; crenolanib; vadastuximab talirine — « hide details

Disease X-Refs: Disease Ontology: DOID:9119; OMIM: 601626; Orphanet: ORPHA519

Ligand *To view more details about a ligand, and its activity, click on its name to view the ligand summary page*	Disease Association Comments	Clinical Use
midostaurin [FDA (2017) (Drugs.com)]	Approved drug for FLT3 mutation +ve AML.	The FDA granted midostaurin accelerated approval in April 2017 for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) who
gemtuzumab ozogamicin [FDA (2000) (Drugs.com)]	Approved in particular for CD33-positive AML. However, note that use in this indication has been withdrawn in some jurisdictions due to safety	Used to treat CD33-positive acute myeloid leukemia in patients over 60 who are not candidates for other chemotherapy. Note that as requested by the US ...
crenolanib	Phase 3 clinical candidate for FLT3 mutation positive relapsed/refractory AML.	A Phase II clinical study for relapsed/refractory acute myeloid leukemia with FLT3 activating mutations (NCT01657682 ...
vadastuximab talirine	FDA and EMA orphan drug for AML.	Both the US FDA and EMA have designated vadastuximab talirine as an orphan drug for acute myeloid leukemia (AML). In late 2016, the FDA put

The disease association pages have been altered to show more information about why ligands are associated to a disease

A new page has been added that presents a further reading collection extracted from an open CiteUlike collection compiled by the curation team http://www.citeulike.org/tag/immpharm. The papers presented are general, not ones from which database entries have been curated. They are mostly review articles that are relevant to the scope of the database. We would be pleased to receive recommendations for additions (either to the further reading list or for curation).



Guide to IMMUNOPHARMACOLOGY - Further Reading

This further reading collection is extracted from an open CiteUlike collection compiled by the curation team http://www.citeulike.org/tag/immpharm. The papers presented are general not ones we have curated database entries from since those papers are now referenced in the database (with the exception of review articles that include ligand structures). As can be seen these are mostly review articles that are relevant to the scope of the database. We would be pleased to receive recommendations for additions (either to this list or for curation).

Reviews

Innate Immune Function of Mitochondrial Metabolism.
Sancho D, Enamorado M, Garaude J. (2017)
Front Immunol, **8**: 527. [PMID:28533780]

Mitochondria are the powerhouses of immunity.
Mills EL, Kelly B, O'Neill LAJ. (2017)
Nat. Immunol., **18** (5): 488-498. [PMID:28418387]

Immune checkpoint proteins: exploring their therapeutic potential to regulate atherosclerosis.
Foks AC, Kuiper J. (2017)
Br. J. Pharmacol., [Epub ahead of print]. [PMID:28369782]

Biased agonism and allosteric modulation of G protein-coupled receptor 183 - a 7TM receptor also known as Epstein-Barr virus-induced gene 2.
Daugvilaite V, Madsen CM, Lückmann M, Echeverria CC, Sailer AW, Frimurer TM, Rosenkilde MM, Benned-Jensen T. (2017)
Br. J. Pharmacol., **174** (13): 2031-2042. [PMID:28369721]

Immunology proves a great success for treating systemic autoimmune diseases - a perspective on immunopharmacology: IUPHAR Review 23.
Ishii M. (2017)
Br. J. Pharmacol., **174** (13): 1875-1880. [PMID:28299772]

GtoImmuPdb further reading page. Listing papers of relevance to immunopharmacology that are not already used in curated entries

IMMUNO PROCESS DATA

The main immunological process categories used in GtoImmuPdb underwent a revision following our April 2017 meeting. Targets are annotated to these categories based on their GO annotations to GO terms mapped to each of the categories

The revised categories summarised in the table below, showing unique targets (UniProtKB) annotated under each category and the total target-GO annotations.

Process Category	GtoPdb Human UniProtKB	Target-GO annotations
Barrier integrity	40	52
Inflammation	576	1277
Antigen presentation	158	226
T cell (activation)	172	345
B cell (activation)	136	222
Immune regulation	435	1072
Tissue repair	18	18
Immune system development	199	350
Cytokine production & signalling	390	979
Chemotaxis & migration	229	382
Cellular signalling	448	1079

IMMUNO CELL TYPE DATA

The top-level cell type categories have also been revised, and the table below shows these categories 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	32
T cells	CL:0000789 alpha-beta T cell CL:0000815 regulatory T cell CL:0000911 effector T cell	39
Dendritic cells	CL:0000451 dendritic cell	29
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	1
Macrophages & monocytes	CL:0000235 macrophage CL:0000576 monocyte	37 37
Granulocytes	CL:0000094 granulocyte	34
Natural killer cells	CL:0000623 natural killer cell	21
Mast cells	CL:0000097 mast cell	26
Innate lymphoid cells	CL:0001065 innate lymphoid cell	0
Stromal cells	CL:0000499 stromal cell	0

GtoImmuPdb TARGET AND LIGAND CURATION STATUS

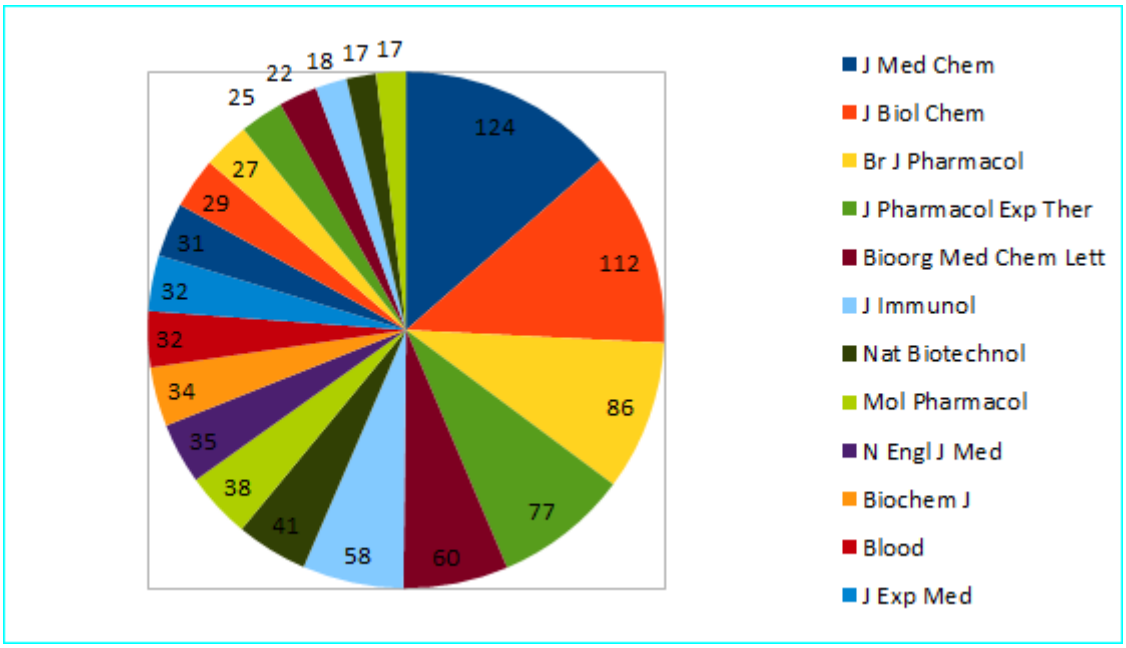
GtoImmuPdb CURATION STATS

- 455 targets tagged as in GtoImmuPdb:
  - 141 catalytic receptors
  - 135 enzymes
  - 86 gpcrs
  - 17 voltage-gated ion channels
  - 64 other proteins
  - 6 nuclear hormone receptors
  - 5 transporters
  - 3 ligand-gated ion channels
- 816 ligands tagged as in GtoImmuPdb:
  - 449 synthetic organic
  - 121 antibodies
  - 213 peptides
  - 9 natural products
  - 1 inorganic
- Detailed lists on:
  - dev.guidetoimmunopharmacology.org/immuno/immunoHelpPage.jsp

GETTING TO CONTENT: SEARCHING, COLLATION, EXTRACTION, ALERTING

The different strategies explored to retrieve papers have already been described in the April report. In CiteUlike, the curation team have now tagged 738 publications tagged as immphar" (N.B. this is a public collection so anyone can engage with us). A recent selection is shown below.

As reported before we follow news distillations from Immune Regulation News , Human Immune News British Society for Immunology, Edinburgh Centre for Inflammation Research as well as journals such as Nature Immunology and Journal of Immunology. While expansion and extraction continues we would really welcome committee evaluation of our immphar list and the database content to see if we had significant gaps and or biases in curation triage. In our recent analysis of PubMed links, we were able to specifically count the journals that contribute references to GtoImmuPdb, as shown below.


124
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J Med Chem
J Biol Chem
Br J Pharmacol
J Pharmacol Exp Ther
Bioorg Med Chem Lett
J Immunol
Nat Biotechnol
Mol Pharmacol
N Engl J Med
Biochem J
Blood
J Exp Med