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NC-IUPHAR news

The biannual newsletter from the IUPHAR Committee on Receptor Nomenclature and Drug Classification and the team developing the IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb)

A MESSAGE FROM NC-IUPHAR

By Stephen Alexander

Since I have taken over from Michael Spedding the reins of NC-IUPHAR, I have been even more in awe of the masterful way in which he organised meeting after meeting with a full program of presentations of cutting edge scientific achievements at our twice-yearly committee meetings.

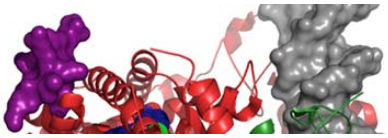
More than that, the breadth and depth of knowledge he was able to bring to bear allowed a continuing level of high achievement in terms of one of the major outputs of NC-IUPHAR – its publications. I'm looking forward to continuing our long collaboration even though our roles and titles have changed recently.

Our publications are a key feature of NC-IUPHAR, alongside the database, of course. Our long-term relationship publishing reviews in Pharmacological (more on the database is presented on Page 2 and 3). Reviews, together with the more recent link with the British Journal of Pharmacology, are vital elements of our profile since they provide a feedback mechanism whereby we have an objective measure of our usefulness for the pharmacological community (see Page 20). As Michael has noted on many occasions, an H-index close to 80 is a testimonial to the work of NC-IUPHAR over the last two decades. A major consideration for the Executive Group of NC-IUPHAR is the continuation of the pipelines which feed into those two journals. We are working with Eliot Ohlstein, the Editor for NC-IUPHAR, to ensure these retain the same strength and currency which we have enjoyed with previous publications from NC-IUPHAR. Part of the forward strategy will be to explore how we might increase our coverage of non-traditional areas. Thanks to the hard work of colleagues like Bill Catterall and Rick Neubig (Page 4), alongside Anthony Davenport, Tony Harmar, John Peters and many others (see the long list of subcommittees on Page 19), we have had really good in-depth coverage of GPCR, nuclear hormone receptors and ion channels. We are looking to identify the scope for representing the enzymes and transporters, which present distinct challenges for the online database and for NC-IUPHAR publications.

One of the milestones of last year was the successful application to the Wellcome Trust to fund a project termed "The Guide to Immunopharmacology", led by Jamie Davies in Edinburgh and bringing together collaborators from six countries as co-investigators on the application. This is highlighted on Page 2.

A further milestone of 2015 was the publication of the Concise Guide to PHARMACOLOGY 2015/16, discussed on Page 11. Amongst other properties of this publication, it represents the only remaining printed issue of the British Journal of Pharmacology. We anticipate another issue in this series in the summer of 2017; work towards this has already started.

I would like to welcome formally new colleagues to the membership of NC-IUPHAR (see Page 4) and to the database team in Edinburgh (Page 5) and to thank a number of colleagues for their contributions to NC-IUPHAR in the last year, some of whom have decided to step down from the committee (see Page 4 again). Their altruism and dedication to NC-IUPHAR and pharmacology in general has made a significant contribution to help maintain the profile of the discipline at a time when there is fragmentation in both the industry and academia. I see part of the future role of NC-IUPHAR being to continue a trend propounded by Michael in the championing of good science and, principally, good pharmacology. This particular role is definitely a challenge for NC-IUPHAR, but working together with other IUPHAR committees and the huge numbers of scientists worldwide which are represented through IUPHAR.



IUPHAR/BPS
Guide to PHARMACOLOGY

An expert-driven guide to pharmacological targets and the substances that act on them.

The IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb) is an open-access database with expert-curated summaries on a wide range of targets of approved and experimental drugs. It covers the key properties of each target family, nomenclature, selective ligands, and recommended background reading. More detailed information is provided for a subset of important targets. NC-IUPHAR oversees the development of the database, and its network of >650 international scientists contribute information and review the data.

Some developments since the January 2015 newsletter…

New project to develop "The Guide to Immunopharmacology"

We are very pleased to announce a new initiative (from 1st Nov 2015) to establish **"The Guide to Immunopharmacology: Integration of targets, diseases and therapies into an expert-driven database".**
This project will be supported by a 3-year grant awarded to Professor Jamie Davies at the University of Edinburgh by the Wellcome Trust (WT).

Immune/inflammatory/ infection responses and disorders have become an increasing focus of pharmacological R&D. We will enrich GtoPdb with kinome resources linking to diseases to assist selection of new targets, tool compounds and drugs. Suggested priorities are established (JAK, PI3K, IKK) and less validated (RIPKs, IRAKs, MAP3Ks) target kinases in innate immunity.
This will later extend to adaptive immunity and kinases in selected pathogens. New data will be linked according to the existing GtoPdb expert-curation model but with a strong focus on translational aspects (e.g. clinical benefit, biomarkers and biological endpoints). In addition an immunology-orientated portal will be developed.

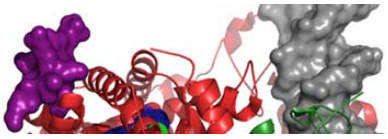
Co-applicants include kinase, immunity/inflammation and parasite biology experts: Dr Michael Spedding, Professor Francesca Levi-Schaffer, Professor Clare Bryant, Professor Christian Doerig, Professor Stephen Anderton, Dr Steve Alexander, Dr Doriano Fabbro and Dr Anthony Davenport. Data selection will be guided by new IUPHAR expert subcommittees set up for this task.
We owe thanks to many folk for the success of this proposal, including for their inputs to the preparation phase and letters of support (to whom we have already communicated our appreciation).

Further details will be surfaced in due course but we are also pleased that the British Pharmacological Society will continue to support the core Guide to PHARMACOLOGY resource during and after this project.
While technical decisions remain on exactly what interfaces and data structures are instantiated, we envisage both resources will be dovetailed into an expanded central database with different front-ends for users.
Any parties with Immunopharmacology interests we have not yet engaged with are welcome to make informal contact as we go forward.

Database statistics

Target class	Number of targets
7TM receptors	395
G protein-coupled receptors including orphans	389
Orphan G protein-coupled receptors	129
Other 7TM proteins	6
Nuclear hormone receptors	48
Catalytic receptors	239
Ligand-gated ion channels	81
Voltage-gated ion channels	141
Other ion channels	47
Enzymes	1168
Transporters	508
Other protein targets	139
Total number of targets	2769

Chemical class	Number of ligands
Synthetic organics	5303
Metabolites	582
Endogenous peptides	763
Other peptides including synthetic peptides	1236
Natural products	241
Antibodies	169
Inorganics	34
Approved drugs	1256
Withdrawn drugs	67
Drugs with INNs	1942
Labelled ligands	594
Total number of ligands	8328
Number of binding constants	14249
Number of binding constants from large-scale screens	31207
Number of references	29049



IUPHAR/BPS
Guide to PHARMACOLOGY

Some developments since the January 2015 newsletter…to be continued

GtoPdb website new features

- REST web services now provide computational access to the data.
- Data are now provided in JSON (JavaScript Object Notation) format. It is a lightweight data-interchange format which is easy for humans to read and write and for machines to parse and generate.
- It is easier to use than XML and can be readily integrated into other websites using JavaScript.
- There has been some uptake of the web services by external users already. We know that David Gloriam's group (GPCRDB) are using them and Sam Ireland, a new recruit in our team, is using them to develop a tool for exploring how druggable regions of existing targets can be synthetically engineered into other proteins.
- We now also provide downloadable structure-activity data CSV files from target pages.
- Sam Ireland has created a BLAST database for sequence-based searching of GtoPdb targets (protein or nucleotide sequences).

Database updates

- Family summary pages have been reviewed and updated in preparation for producing the Concise Guide to PHARMACOLOGY 2015/16 due out in November (see below).
- **GPCR updates:** Dopamine receptors, Chemokine receptors (CCR7, CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, ACKR3), NOP receptor, Relaxin family peptide receptors, TRH receptors, Vasopressin receptors.
- **Voltage-gated ion channel updates**: Members of the Transient Receptor Potential superfamily of channels.
- **Nuclear hormone receptors:** in progress; Retinoic acid-related orphans introduction, Liver X receptor-α and β, COUP-TF-like receptors, 3-Ketosteroid receptors.
- **Enzyme updates:** Added inhibitors for many proteinase enzymes, Enzymes involved in hydrogen sulphide synthesis (H2S is a signalling mediator).
- **Mutation information:** listed in the 'Clinical mutations and Pathophysiology' tables, has been standardised across the database. This builds upon earlier work to standardise the disease names used across the database to conform to Disease Ontology and Orphanet Rare Disease Ontology names where possible.
- **New TOADS** or targets of experimental compounds in clinical trials: B-cell lymphoma 2 (Bcl-2) protein family, Carrier proteins, Circadian clock proteins, EF-hand domain containing, Mitochondrial-associated proteins, Myosin binding proteins.
- **Ligand Updates:** Quantitative ligand interactions added for about 150 targets which previously had no chemical modulation information in the database (created over 140 new ligands in the process). As a consequence our total number of curated interactions now stands at 13859.

Latest content statistics are available on the right hand side and on the GtoPdb About page.

Changes in NC-IUPHAR

By Anthony Davenport, Michael Spedding and Adam Pawson

Three distinguished and long serving members of the NC-IUPHAR committee have recently stepped down but will continue as corresponding members, continuing the long standing tradition that you can check-out any time you like but you can never leave.

Sir Colin Dollery (GlaxoSmithKline) was a founder member of NC-IUPHAR and contributed an encyclopaedic knowledge of clinical pharmacology, based on over 40 years in academia and industry[1]. He has provided strategic guidance for the committee and has been a tireless fundraiser and advocate for NC-IUPHAR.

Tom Bonner (National Institute for Medical Health, Bethesda) has been a prolific contributor to G protein coupled receptor classification, particularly orphan receptors predicted to exist from the human genome and writes persuasively about new areas of classification most recently about splice variants [2].

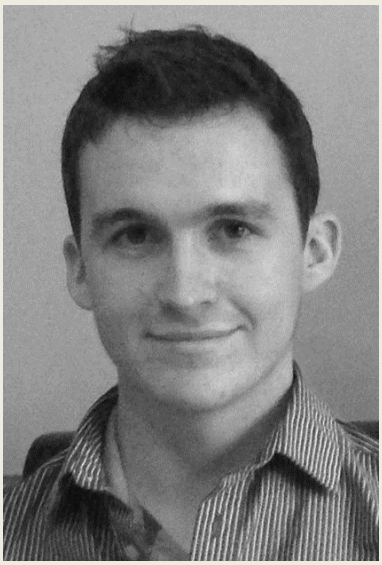
Tom Bonner and Sir Colin Dollery, here with past Chairman of NC-IUPHAR Michael Spedding (middle).

Bill Catterall (University of Washington) joined NC-IUPHAR in 1999 with the herculean task of gathering experts together to reach a consensus on ion channel classification and nomenclature, and populating a major element of the database (GtoPdb, http://www.guidetopharmacology.org). He has been remarkably successful. In autumn 2015, both Pharmacological Reviews with Bill as first author [3,4], received the accolade of Highly Cited paper from ISI Web of Science, having achieved 'enough citations to place them in the top 1% of their academic field'.

Rick Neubig (Michigan State University) has been a member of NC-IUPHAR since 2000, and has lead the crucial GPCR initiative, and was major contributor to the highly cited GPCR list. He also was the first author on the influential terms and symbols document, and a main contributor with Jean-Philippe Pin to the heterodimer document [5]. He therefore maintained NC-IUPHAR's reputation in analytical pharmacology. His incisive comments - and his dedication in travelling from the USA to work all weekend in Paris twice a year for 16 years, will be much missed.

We thank Colin, Bill, Tom and Rick for their major contributions to NC-IUPHAR and for their expertise and time freely given. We are delighted to welcome three new committee members. Mary Vore, Professor of Toxicology and Cancer Biology (University of Kentucky) brings expertise to the rapidly expanding new section in the database on drug transporters . Professor Jörg Striessnig, Chair of the Department of Pharmacology and Toxicology (University of Innsbruck) now leads on ion channels. Professor Francesca Levi-Schaffer (Dept of Pharmacy, Hebrew University of Jerusalem) strengthens the committee in immunopharmacology, which will be an exciting new area for NC-IUPHAR to research, following the award of a major Wellcome Trust grant in 2015.

1. Dollery CT (2014) Lost in Translation (LiT): IUPHAR Review 6. Br J Pharmacol 171:2269-2290.
2. Bonner TI (2014) Should pharmacologists care about alternative splicing? IUPHAR Review 4. Br J Pharmacol 171:1231-1240.
3. Catterall WA, Perez-Reyes E, Snutch TP and Striessnig J (2005) International Union of Pharmacology. XLVIII. Nomenclature and structure-function relationships of voltage-gated calcium channels. Pharmacol Rev 57:411-425.
4. Catterall WA, Goldin AL and Waxman SG (2005) International Union of Pharmacology. XLVII. Nomenclature and structure-function relationships of voltage-gated sodium channels. Pharmacol Rev 57:397-409.
5. Pin JP, Neubig R, Bouvier M, Devi L, Filizola M, Javitch JA, Lohse MJ, Milligan G, Palczewski K, Parmentier M, Spedding M. (2007) International Union of Basic and Clinical Pharmacology. LXVII. Recommendations for the Recognition and Nomenclature of G Protein-Coupled Receptor Heteromultimers. Pharmacol Rev. 59: 5-13.



"I am delighted to have joined a team where I can utilise so many aspects of my interests and background, and contribute to an already well-respected and professional endeavour such as the Guide to Pharmacology."

PROFILE

Sam Ireland

I'm a developer working with the Guide to Pharmacology team, having started in last September and due to complete the one-year project in September of this year.

My project is to create a database of 'transferable drug-binding elements' for the synthetic biology community, using data from the Guide to Pharmacology database. Many synthetic biology systems rely on external control in the form of small molecules which, among other requirements, have to be orthogonal to the system they are working within and ideally (if they are ultimately to be used in a mammalian/human system) their effects in that system should be well characterised.

The reasoning, therefore, was that the world of pharmacology could provide the synthetic biology community with a large catalogue of small molecules whose effects in vivo are well known, and which are known to bind to certain targets with a well characterised affinity. Instead of starting with a target and trying to identify a small molecule to bind it – traditional pharmacology – you would take a target and make it responsive to a small molecule of your choice, by splicing the specific polypeptide sequence which binds the ligand: inverse pharmacology.

As such, the project involves a lot of structural annotation of some of the Guide to Pharmacology's fifteen thousand documented target-ligand interactions, and then algorithmically determining the residues and continuous sequence which takes part in the interaction within these structures, as well as computational estimates of the foldability and stability of such a fragment. Of course, all final entries in the database will have been manually checked, and the final dataset will likely be a mix of algorithmically determined and manually curated entries.

There is also a more traditional software development aspect to the project – designing and creating the database itself, as well as the web interface that will be used by the synthetic biology community and tools/search capabilities that will be needed.

My own background is in Biotechnology/Synthetic Biology/Bioinformatics as an undergraduate, having pursued a number of personal non-Biological software development projects in parallel. I am delighted to have joined a team where I can utilise so many aspects of my interests and background, and contribute to an already well-respected and professional endeavour such as the Guide to Pharmacology.

The utility of expanding patent connectivity for GtoPdb users

By Christopher Southan

Compared to journal papers, patents have hitherto been a Cinderella data source in academic pharmacology. This is despite the fact that within the domain of medicinal chemistry, structure-activity relationship (SAR) data in patents exceeds that from papers by at least two-fold and may precede the latter by several years (PMID 24204758). In addition, lead chemical series against some proteins may remain patent-only and, while pharmaceutical companies are still the largest assignee type, filings by academic drug discovery groups are increasing. Note that we have briefly described our curation of patent links for selected GtoPdb ligand entries both in our FAQ (see data section) and in our recent NAR publication (PMID 26464438). The BACE2 example shown below is unusual in that nearly all the directed inhibitors (as opposed to BACE1 inhibitor cross-screening) are patent-only.

Ligand	Sp.	Action	Affinity	Units	Reference
verubecestat	Hs	Competitive	9.4	pK_i	8
example 41 (WO2012028563)	Hs	Inhibition	10.0	pIC_{50}	4
example 98 (WO2011020806)	Hs	Inhibition	9.0	pIC_{50}	9
example 2 (WO2013004676)	Hs	Inhibition	8.7	pIC_{50}	2
example 92 (WO2012095521)	Hs	Inhibition	8.4	pIC_{50}	7
example 20 (WO2010128058)	Hs	Inhibition	8.2	pIC_{50}	1
compound J [PMID: 21907142]	Hs	Inhibition	8.2	pIC_{50}	3
hydroxyethylamine transition-state inhibitor 1	Hs	Inhibition	6.2	pIC_{50}	6

Note we specify the location of the example compound in patents and some papers which can save users a lot of effort (n.b there is an interesting story around verubecestat). This report introduces GtoPdb users to wider aspects of patent linking utilities they may not have previously considered. These go beyond the small number we have captured directly (limited by curatorial capacity) and extends to potentially useful patent document links that now cover the majority of our small-molecule ligand set.

Accessing patents from GtoPdb ligand entries

Traditionally, medicinal chemistry patent mining has required licencing commercial products such as those from SciFinder, GVKBIO, Thomson Reuters, Elsevier and others. However, the last few years have seen a "big bang" in the public accessibility of both patent document full-text and extracted chemical structures (see PMID 26194581 and this slide set). The scale of this is indicated by PubChem including 17.8 million structures from patents (out of 72 million total by Jan 2016). Most of these come from SureChEMBL that automatically extracts ~80K novel structures a month (PMID 26582922). From our 6192 GtoPdb PubChem compound entries (CIDs) 4771 have patent matches (77%). The major utility is that users can now follow links out to patents from the substance (SID) links within the CID records we curate, without the need for subscription sources (PMID 26457120). Of these SID links SureChEMBL is particularly useful for patent document chemistry and to discern first-filings (i.e. earliest disclosure of structure exemplification). The utility of these arises from inclusion of SAR data sets, synthetic description of the examples and, occasionally, *in vivo* results. Locating these first-filings is challenging for older approved drugs since these are swamped by later name mentions (e.g. atorvastin is indexed against 10,027 patent document numbers in CID 6082).

Voltage-Gated Ion Channel Database in the IUPHAR/BPS Guide to Pharmacology

William A. Catterall, **Editor, Ion Channel Database**
IUPHAR/BPS Guide to Pharmacology

Voltage-gated ion channels and their structural relatives are crucial in electrical signalling in excitable cells and in physiological regulation in many other subtypes. They are the molecular targets for a large number of existing drugs and they are prime candidates for discovery of next-generation drugs for many clinical indications. There are more than 140 members of this large protein superfamily. The IUPHAR Nomenclature and Database Committee began to organise the nomenclature and the molecular, physiological, and pharmacological properties of these ion channels fifteen years ago and this work was presented in comprehensive form in the IUPHAR Ion Channel Compendium in 2002, in a revised and updated version of the IUPHAR Ion Channel Compendium in 2005 and in the IUPHAR Ion Channel Database that was launched online in 2009.

In the past two years, the content of the BPS Concise Guide to Pharmacology and the comprehensive IUPHAR Ion Channel Database have been merged to form the IUPHAR/BPS Guide to Pharmacology. The combination has resulted in a single comprehensive Ion Channel Database with an easily accessible opening page derived from the BPS Concise Guide to Pharmacology followed by a detailed presentation of ion channel properties from the IUPHAR Ion Channel Database. The information in the new Database has been updated in all dimensions, but special efforts were made to expand the sections on genetic variants, alternative splicing of genes, and ion channelopathies. Entries for many channel types were greatly expanded based on emerging scientific information. Particularly noteworthy in this regard are the Transient Receptor Potential (TRP) channels, whose structural features, physiological roles, and pharmacology have been greatly expanded. New nomenclature has been introduced for KCa channels. Drugs, toxins and other chemical entities can now be searched across full range of IUPHAR Databases on receptors, kinases and channels to identify primary and secondary molecular targets. This revised version of the Ion channel Database also has many additional search and retrieval capabilities as well as many new links to other databases. We believe that the new and updated IUPHAR/BPS Ion Channel Database will be of great value to the research community in universities, research institutes, biotech companies and pharmaceutical companies.

Expert input for the Ion Channel Database has come from eight Subcommittees whose efforts have been organised by Subcommittee Chairs. The broad international membership of these Subcommittees is given in full in each section of the Ion Channel Database. The Chairs of the Ion Channel Subcommittees are:

Voltage-gated Sodium Channels	NaV	William A. Catterall, Univ. of Washington
Voltage-gated Calcium Channels	CaV	William A. Catterall, Univ. of Washington
Transient Receptor Potential Channels	TRP	David E. Clapham, Harvard Univ.
CatSper and Two-Pore Channels	CatSper, TPC	
Cyclic Nucleotide Regulated Channels	CNG/HCN	Martin Biel, Ludwig-Maximilians Univ.
Voltage-gated Potassium Channels	KV	Lily Y. Jan, Univ. of California, San Francisco
Inwardly Rectifying Potassium Channels	Kir	Paul A. Slesinger, Mt Sinai Medical School
Two-Pore Domain Potassium Channels	K2P	Steve A. N. Goldstein, Brandeis Univ.
Calcium-activated Potassium Channels	KCa	Leonard K. Kaczmarek, Yale Univ.
Sodium-activated Potassium Channels	KNa	

I am very grateful to these Subcommittee Chairs for their excellent work on updating the Ion Channel Database. I am also especially grateful to the members of the Subcommittees on Voltage-gated Sodium Channels and Voltage-gated Calcium Channels, on which I serve as Chair. The success of the Ion Channel Database is entirely dependent on the expertise, organization and hard work of these exceptional scientists.

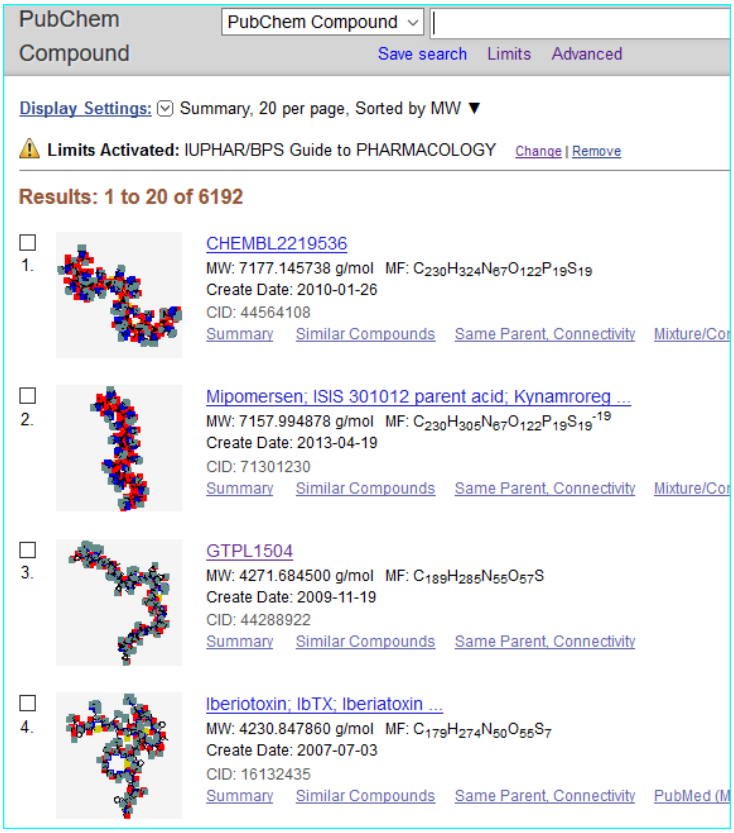
COLLATION AND ASSESSMENT OF GTOPDB IN-LINKS

by Christopher Southan

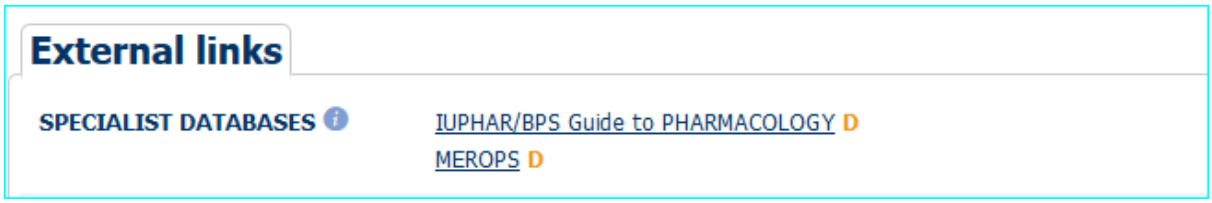
A valuable aspect of biological databases in general and the IUPHAR/BPS Guide to PHARMACOLOGY (GtoPdb) in particular are out-links to and in-links from other relevant resources. Not only do these facilitate manual navigation for users but, increasingly, sematic web linked-data queries as inter-database computational operations mediated by web services. The Edinburgh team engages extensively with other databases teams globally at many levels, including long-standing collaborations. Indeed, a component of our value is our expert selection of out-links for our GtoPdb entries, particularly since pharmacology spans the domains of bioinformatics, chemistry and genomics. Reciprocity of linking (a.k.a. cross-pointing) between any two databases becomes an enabling feature for both. This document reviews in-links to GtoPdb from public sources that have come to our attention. However, there may be others we are not aware of (e.g. inside pharmaceutical companies). Those resources that we specifically out-link to are listed in Table 5 in our NAR article PMID 26464438. There are other cases where reciprocal in-links are under consideration but not yet instantiated (e.g. NURSA , ESTHER BindingDB, DrugBank and Open PHACTS). As an open database we welcome in-links in the same way we add the value of curated out-links. Notwithstanding, there are caveats with the former, especially where these have been instigated without contact and/or our input at the technical level. The two main problems are associated firstly with automated parsing (e.g. the extent of manual post-linking specificity checks on their side) and secondly with update frequency w.r.t. our releases. To assess the latter we rely on source entity counts and loading dates but these are not always provided. We have been contacting any resources who (according to their source details) have not yet replaced deprecated IUPHAR-DB content superseded by GtoPdb.

The domain relevant in-links we know of are listed below (but please contact us if you are aware of others).

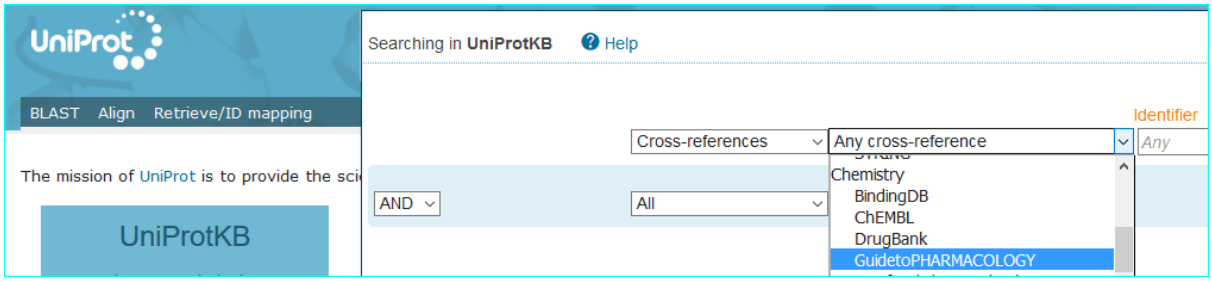
For PubChem (a global chemistry and bioactivity portal) we have 8201 ligand submissions as SIDs that each include a GtoPdb url. Of these, 6192 are merged into Compound identifiers (CIDs) with a defined chemical structure. Most of the SIDs 2009 SIDs without CIDs are large peptides, small proteins and antibodies that cannot form a CID. Note we have some SID duplicates structures where we have separate GtoPdb ligand IDs pointing to radiolabel citation data without specified substitution positions that have a CID. We also have 55 BioAssay entries for 5HT sub-family chemistry mappings.



HGNC is responsible for approving unique symbols and names for human loci, including protein coding genes, ncRNA genes and pseudogenes. We have a long-standing collaboration via NC-IUPHAR. An example out-link is shown below.

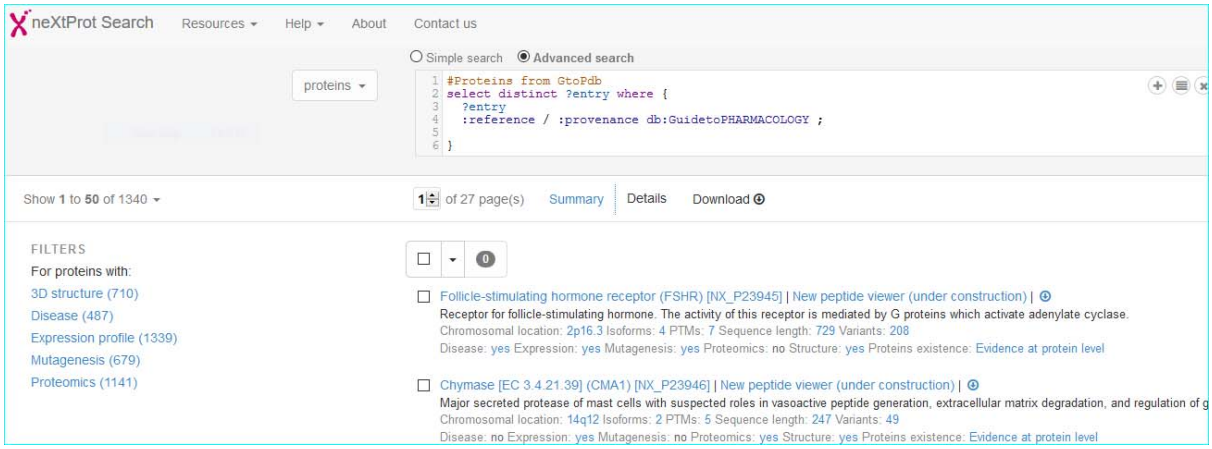


UniProtKB/Swiss-Prot: We are included in the Cross-References for protein entries. These can be selected using the menu. below.

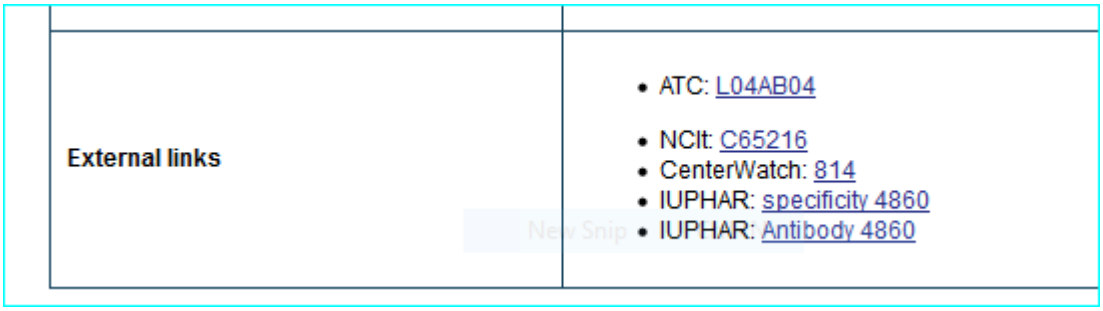


The query currently produces 2266 proteins with GtoPdb links as having ligand interactions.

neXtProt (PMID 25593349) is a protein-centric knowledgebase developed at the SIB Swiss Institute of Bioinformatics focused solely on human proteins. In a sense this is "forked" from Swiss-Prot but is technically distinct. It inherits our UniProt links.



IMGT/mAb-DB is a high-quality integrated information system focused on clinical antibodies. We have a long-standing collaboration. A link example is shown below.



ChEMBL, a database of bioactive drug-like small molecules with calculated properties and abstracted bioactivities. A target link example is below.

Target Cross References - Protein

Human Protein Atlas	ENSG00000186318
IntAct	P56817
Guide to Pharmacology	2330 (beta-site APP-cleaving enzyme 1)
PharmGKB	PA25232
UniProt	A0M8W7 B0YIU9 P56817 Q9BYB9 Q9BYC0 Q9BYC1 Q9UJT5 Q9ULS1

Our ligands get a nested link in the ChEMBL interface via UniChem.

UniChem Cross References

New View the UniChem Connectivity matches for CHEMBL1487

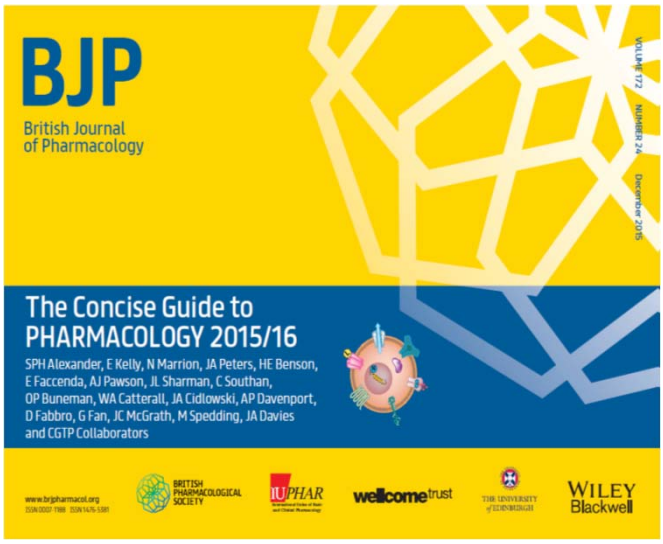
ACToR	134523-00-5
Atlas	atorvastatin
BindinDB	22164
ChEBI	39548
eMolecules	877278
FDA SRS	A0JWA85V8F
Guide to Pharmacology	2949
Human Metabolome Database	HMDB05006
IBM Patent System	65A247BC8DAC852F83CB85D0A6DC2511

UniChem produces cross-references between chemical structure identifiers from different databases within the EBI. We are listed as a source.

4	gtopdb	Guide to Pharmacology	The IUPHAR (International Union of Basic and Clinical Pharmacology)/BPS (British Pharmacological Society) Guide to PHARMACOLOGY database contains structures of small molecule ligands, peptides and antibodies, with their affinities at protein targets.	Standard InChIs and Keys available for download at http://www.guidetopharmacology.org/download.jsp

This was updated on 17-NOV-15 as 6006 chemical entities.

CONCISE GUIDE TO PHARMACOLOGY 2015/16



By Stephen Alexander

It's actually not that concise at all… It's 474 pages long. It's got over 1700 molecular targets described and over 6000 ligand interactions. Concise is a relative term. What the Concise Guide represents is a publication snapshot of a much more detailed website, www.GuidetoPHARMACOLOGY.org, which is continuously being updated.

The Concise Guide to PHARMACOLOGY 2015/16, as published in the last issue of the British Journal of Pharmacology in 2015, 172 (24), is a citable version of the website. Both the Concise Guide and the website are open access, with the information available to anyone with a computer and internet connection.

Purpose

The Concise Guide aims to provide for researchers, teachers and students a state-of-the-art source of accurate, curated information on the background to their work that they will use in the Introductions to their Research Papers or Reviews, or in supporting their teaching and studies.

The website is "an expert-driven guide to pharmacological targets and the substances that act on them". The aim of the website, as articulated in the Wellcome Trust-funded grant is to present ALL the human targets of medicinal drugs in use in the clinic currently and in the near future.

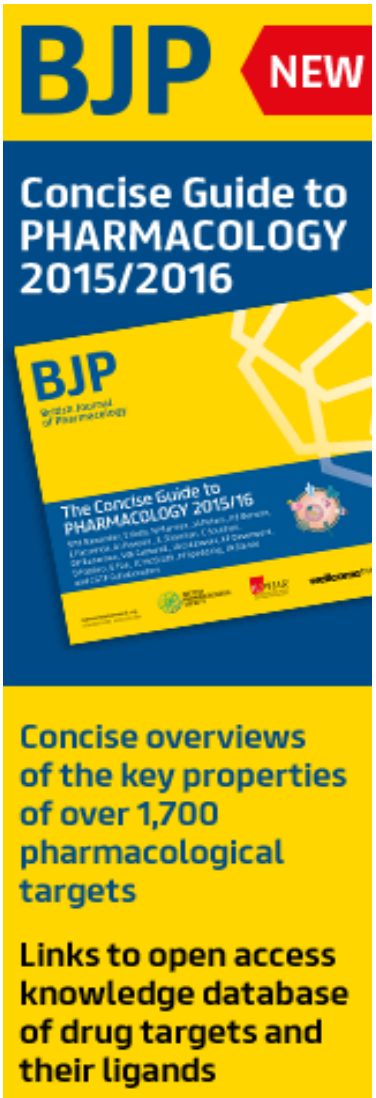
The Team

The authors of the nine articles which form the Concise Guide include the Editors of the Concise Guide (John Peters [Dundee], Neil Marrion [Bristol], Eamonn Kelly [Bristol] and myself Steve Alexander [Nottingham]) and Guest Editors who contributed to individual sections (Bill Catterall [Seattle], John Cidlowski [North Carolina], Anthony Davenport [Cambridge], Doriano Fabbro [Basel] and Michael Spedding [Paris]), and the Editor-In-Chief of BJP (Ian McGrath [Glasgow & Sydney]). Also included are the four curators of the database, who are based in Edinburgh and Göteborg (Helen Benson, Elena Faccenda, Chris Southan and Adam Pawson), as well as the database developer (Joanna Sharman) and the database project manager (Jamie Davies). In addition, there are two production editors based in Edinburgh (Peter Buneman and Grace Fan).

The Concise Guide makes use of collaborators, who for this edition numbered 141. The majority of these are chairs and members of the 90 subcommittees of the Nomenclature Committee of IUPHAR (NC-IUPHAR). These were invited to provide updates on their particular areas of expertise particularly for the Concise Guide.

Since the last edition

The Concise Guide to Pharmacology 2013/14 was published in December 2013 as eight sections over 419 pages. In the two years since then, there have been over 1400 citations to the CGTP2013/14. This equates to an apparent Impact Factor of 178, which is very impressive (if you believe in Impact Factors, of course). The additional pages in the CGTP2015/16 largely accrue from an expansion of information in the Enzymes and the 'Other targets'. In particular, the website has benefitted over the last two years from a concerted effort to expand the information on the protein kinases and proteases, much of which has been incorporated into the Concise Guide.



The Concise Format

The website has substantial links to other online databases (many of whom provide reciprocal links back to our database), including the Human Genome Nomenclature Committee, Ensembl, UniProt, PubChem, ChEMBL, OMIM and PubMed. Rather than present ALL the very detailed information listed on the website, the focus of the Concise Guide is a tabular approach (where possible) of molecular targets of similar structure/function. These are G protein-coupled receptors, ligand-gated ion channels, voltage-gated ion channels, other ion channels, catalytic receptors, nuclear hormone receptors, enzymes, and transporters, as well as a group of 'Other' proteins which do not fit into these subdivisions.

A new aspect of the Concise Guide 2015/16 is that each of these sections contains a complete listing of the families available for inspection on the online database, identifying those families reported in the Concise Guide by their page numbers.
The organisation of the data is tabular (where appropriate) with a standardised format, where possible on a single page, intended to aid understanding of and comparison within a particular target group. The Concise Guide is intended as an initial resource, with links to additional reviews and resources for greater depth and information. Pharmacological and structural data focus primarily on human gene products, wherever possible, with links to HGNC gene nomenclature and UniProt IDs. These links are active in both online text and pdf versions. In a few cases, where data from human proteins are limited, data from other species are indicated. Pharmacological tools listed are prioritised on the basis of selectivity and availability. That is, agents (agonists, antagonists, inhibitors, activators, etc.) are included where they are both available (by donation or from commercial sources, now or in the near future) AND the most selective.

The Concise Guide itself is the only form of the British Journal of Pharmacology which is available in hard copy. Given the size of the Concise Guide and its weight, there are unlikely to be many who will look forward to taking it with them on international flights. Fortunately, the publishers (Wiley) had an alternative solution for delegates at Pharmacology 2015, the annual meeting of the British Pharmacological Society in London, in December 2015. This attractive snapband is actually a USB drive with the nine sections of CGTP2015/16 already uploaded in pdf format.

CONFERENCES and WORKSHOPS

Attended by the Database team

- BPS Focused Meeting, April 2015, Edinburgh, GtoPdb team
- Joint ASCEPT-BPS Scientific Meeting, Hong Kong, May 2015; Adam Pawson
- 12th Basel Computational Biology Conference, June 2015; Chris Southan
- 23rd Annual International Conference on Intelligent Systems for Molecular Biology and the 14th European Conference on Computational Biology, Dublin, July 2015; Joanna Sharman
- American Chemical Society Meeting, Boston, August 2015; Christopher Southan
- International Conference on Trends for Scientific Information, Nice, October 2015; Christopher Southan
- Our slideshare account includes slide sets and posters presented by team members at the events listed above. Some are posted on Chris Southan's own slideshare.
- BPS Pharmacology 2015, London, December, Adam Pawson and Christopher Southan.

Upcoming

- The manager of PubChem, Evan Bolton has specifically invited a team representative to present at an American Chemical Society Special Symposium on "Chemistry, Data, & the Semantic Web: An Important Triple to Advance Science" in San Diego in March 2016 (abstract submitted).

SOCIAL MEDIA UPDATE

We have accounts on various sites to further the outreach of GtoPdb, keep existing users updated on new features or releases and enhance awareness of our publications.

FACEBOOK

The number of 'likes' increased to 3109.

TWITTER

Our followers have increased to 774. Our re-tweet rate is satisfactory, as demonstrated by our recent NAR paper reaching at least 2,500 users by this route. This medium is increasingly useful for rapid technical interchanges with teams from other resources. It also constitutes a de-facto alerting system for key papers, including the major pharmacology, biochemical and medicinal chemistry journals.

LINKEDIN

The Curation Team and Subcommittee Chairs have increased their reciprocal connectivity and have thereby significantly extended the collective inter-network outreach for posting updates.

BLOGGING

The blog (http://blog.guidetopharmacology.org/) is receiving about 180 views on average per month and we aim to post a new item at least once or twice per month. This includes details about database updates, new features, technical items, articles or events (guest posts are also welcome). The three most popular 2015 posts so far are 'The drug class of 2014', 'Database Update March 2015' and '21 years of NC-IUPHAR reviews and general publication updates'.

Team member Chris Southan maintains his own (http://cdsouthan.blogspot.com/) where relevant posts include GtoPdb cross-pointers.

ENGAGE WITH US

While not being out and out social media evangelists, we recognise the increasing importance for the team external profile, and for database resources to have a "presence".

Thus, the more readers of this document who "connect" with us, (via whichever of the channels above they engage with as part of their own professional profile) the better. This also has reciprocal mutual advantages. In particular re-tweets and LinkedIN likes are useful for extending the alerting network for 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 or blog (but make sure you specify a DOI or PubMed link for the auto-indexing) the Altmetrics score notches up for that paper.

GOOGLE ANALYTICS UPDATE

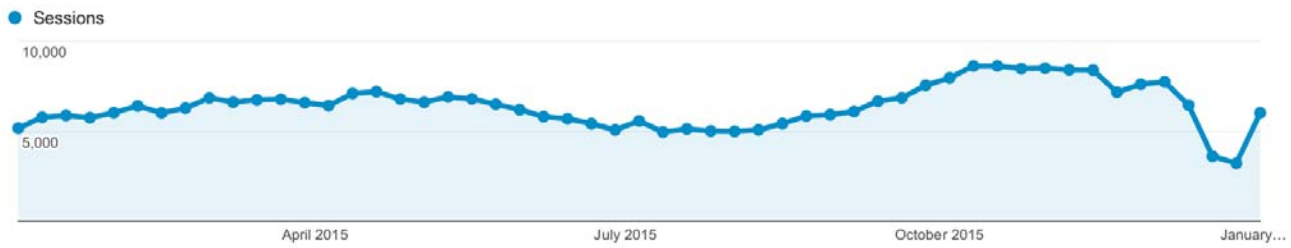
by Simon Harding

The Guide to Pharmacology website collects data on usage via Google Analytics. These analytics provide a reasonable guide to how many people are using the website and offers, to some extent, valuable information on site activity that can be used to help improve user experience.

The analytics are by no means perfect. They rely on cookies to track users, and given that users will often delete cookies – or similarly connect to GtPDB from multiple browsers and device, it makes tracking multi-session usage difficult. It has the effect of over-estimating the 'unique users' accessing the site. Despite these shortcomings, we can still glen interesting insight from them.

How well used is The Guide to pharmacology?

The following graph shows the number of sessions being run on the site per week during 2015. A session is counted as a single period of time a user is actively engaged with our website. So the same user can be responsible for multiple sessions.



On average we see ~ 28,200 session per month from ~ 19,000 unique users. Within all these session we see a figure of around 100,000 page views per month on average.

It is interesting to try and compare the usage statistics of GtPDB to other biological databases, although it isn't always easy to get accurate usage statistics from other resources. Our unique monthly users figure of ~ 19,000 is also likely to be an over-estimate, as previously mentioned.

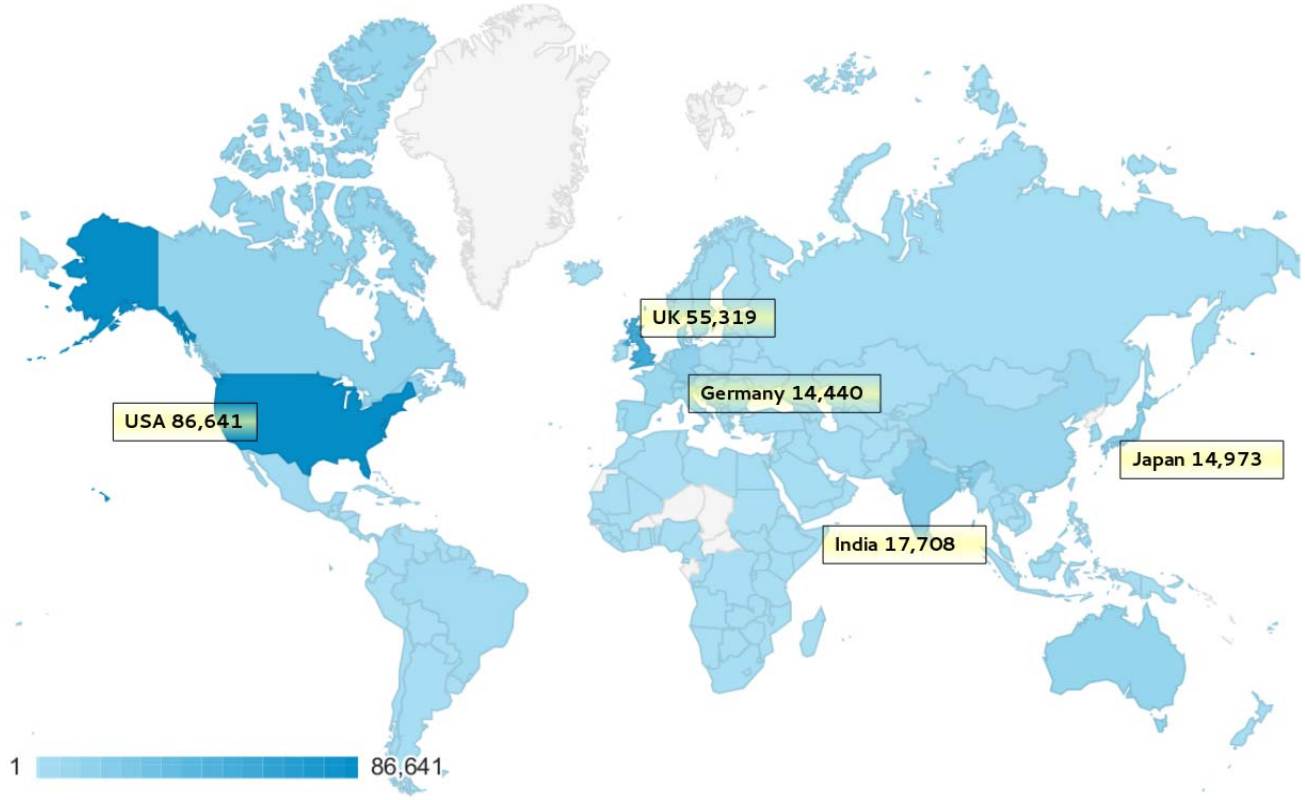
However, a recent report in Science (Kaiser J (2016). Funding for key data resources in jeopardy. Science, *351 (6268): 14*) provides some statistics against which we can compare the GtPDB.

Database	Unique Users Per Month (uupm)	2015 Funding ($)	Cost per unique monthly user ($) (Funding/12/uupm)
FlyBase	51300	4.2 million	6.8
GO Consortium	36000	3.7 million	8.5
MGI	53100	4.7 million	7.4
OMIM	300000	2.1 million (2014)	0.6
UniProt	433100	4.9 million	0.9
WormBase	25000	2.9 million	9.7
ZMOD	23300	3.1 million	11.1
GtPDB	19000	0.18 million (£125K)	0.8

Table 1. NHGRI funded databases usage statistics compared to GtPDB. Adapted from Kaiser J (2016), Science, 351

The GtPDB has slightly fewer unique users per month (uupm) compared to WormBase and ZMOD, about half as many as GO and around ~30,000 fewer compared to FlyBase and MGI. GtPDB's unique user count doesn't come close to that of either OMIM or UniProt. It is perhaps more interesting from the GtPDB perspective to take into account the level of funding when considering usage statistics. Here we see that the cost per unique monthly user is much more comparable to OMIM and UniProt (less than $1 per user), whereas the other resources cost's per monthly user are significantly higher. Of course comparisons such as these are somewhat cursory and include many caveats – we don't know from the report how the other databases user figures were calculate and we know that GtPDB's are likely to be overestimated. It is still interesting to try and gauge GtPDB relative usage.

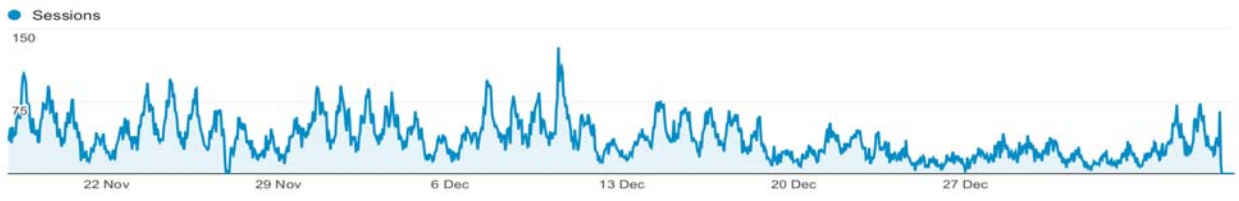
Who is using The Guide to pharmacology?



The analytics allows us to track where, geographically, users are based. Above is a map showing where traffic comes from to GtPDB, the darker the blue, the more sessions we see coming from that country. It maybe won't surprise us to see the USA and UK as being our most common users – contributing to ~ 40% of site traffic. This is followed by India, then Japan and Germany.

Effects of events

Something worthy of analysis is any effect on site traffic of external events. One such event of note was the release of the new Concise Guide to Pharamacology, which was published online ~9/10th December 2015. A look at the number of daily session hitting the site between 1st November 2015 and 23rd December shows a clear spike on 10th December 2015. Although this was encouraging, traffic to the site wasn't sustained in the following period. Perhaps there was an understandable 'Christmas' effect.



About NC-IUPHAR

The IUPHAR Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR), founded in 1987, is chaired by Michael Spedding (France). NC-IUPHAR has the objective of issuing guidelines for the nomenclature and classification of all the (human) biological targets, including all the targets of current and future prescription medicines; facilitating the interface between the discovery of new sequences from the Human Genome Project

and the designation of the derived entities as functional biological targets and potential drug targets; designating polymorphisms and variants which are functionally important; developing an authoritative and freely available, global online resource, the IUPHAR database, which is now accessible via the Guide to PHARMACOLOGY portal (**http://www.guidetopharmacology.org**), with a remit to provide access to data on all known biological targets; enable students and scientists in academia and industry, working in areas related to pharmacology and drug/target research, to exploit the full potential of the considerable amount of information on drug action available in the published literature; provide an entry point into the pharmacological literature for basic and clinical scientists from other disciplines; provide an integrated educational resource with access to high quality training in the principles of basic and clinical pharmacology and techniques; foster innovative drug discovery.

Membership

Executive Committee
Stephen Alexander, UK - Chair
Arthur Christopoulos, Australia - Deputy Chair
Doriano Fabbro, Switzerland - Industry Liaison
Adam Pawson, UK - Executive Secretary
Anthony Davenport, UK

Members
Stephen Alexander, UK
William Catterall, USA - VGICs Liaison
Arthur Christopoulos, Australia
John Cidlowski, USA - NHRs Liaison
Anthony Davenport, UK - Chair Evolving Pharmacology
Sir Colin T. Dollery, UK
Doriano Fabbro, Switzerland
Kozo Kaibuchi, Japan
Yoshikatsu Kanai, Japan
Francesca Levi-Schaffer, Israel
Eliot Ohlstein, USA - Editor
John Peters, UK - LGICs Liaison
Alex Phipps, UK

Past Chairs (ex officio)
Paul Vanhoutte, China
Robert Ruffolo, USA

Ex Officio
Sam Enna, USA - IUPHAR President
Michael Spedding, France - IUPHAR Secretary-General
Petra Thürmann, Germany - IUPHAR Treasurer

Simon Maxwell, UK - Educational Site Project Leader
Jamie Davies, UK - Database Chair/Principal Investigator
Joanna Sharman, UK - Senior Database Developer
Adam Pawson, UK - Senior Database Curator
Elena Faccenda, UK - Database Curator
Christopher Southan, Sweden - Senior Cheminformatician/Curator
Veronika Divincova, UK - Project Administrator
Elspeth Bruford, UK - representing HGNC

Corresponding members
Susan Amara, USA
Tom Bonner, USA
Michel Bouvier, Canada
Thomas Burris, USA
Steven Charlton, UK
Moses Chao, USA
Steven L. Colletti, USA
Graham Collingridge, UK
Richard Eglen, UK
Steven Foord, UK
David Gloriam, Denmark
Gillian Gray, UK
Debbie Hay, New Zealand
Allyn Howlett, USA
Franz Hofmann, Germany
Yu Huang, Hong Kong
Ad P. Ijzerman, The Netherlands
Michael F. Jarvis, USA
Bong-Kiun Kaang, Korea
Terry Kenakin, USA
Janos Kiss, Hungary
Stefan Knapp, Germany
Chris Langmead, Australia

Vincent Laudet, France
Margaret (Mandy) MacLean, UK
Fiona Marshall, UK
Alistair Mathie, UK
Ian McGrath, UK
Graeme Milligan, UK
Rick Neubig, USA
Stefan Offermanns, Germany
Richard Olsen, USA
Jean-Philippe Pin, France
Helgi Schiöth, Sweden
Graeme Semple, USA
David Searls, USA
Roland Staal, USA
Bart Staels, France
Georg Terstappen, Germany
Mary Vore, USA

Clinical Translational Pharmacology Group (core member Sir Colin Dollery)
Ed Bullmore, UK
Robert Dow, UK
Garrett Fitzgerald, USA
Alex Phipps, UK
Patrick du Souich, Canada
David Webb, UK
Don Birkett, Australia

A brief account of a historic Paris meeting.

By Michael Spedding and Steve Alexander

OCTOBER 2015 ATTENDEES

Stephen Alexander, UK
Amrita Ahluwalia, UK
William Catterall, US
Arthur Christopoulos, Australia
John Cidlowski, US
Anthony Davenport, UK
Colin Dollery, UK
Sam Enna, US
Doriano Fabbro, Switzerland
Graeme Henderson, UK
Kozo Kaibuchi, Japan
Stefan Knapp, Germany
Francesca Levi-Schaffer, Israel
Ian McGrath, UK
Christian Muchardt, France
Eliot Ohlstein, US
Ana Rath, France
Michael Spedding, France
Joerg Striessnig, Austria
Kathryn Wilson, UK

Database team

Jamie Davies, UK
Adam Pawson, UK
Elena Faccenda, UK
Christopher Southan, Sweden

This meeting marked the handover of chair from Michael Spedding to Steve Alexander, Michael, as secretary to Paul Vanhoutte (from the second year of the committee) and Bob Ruffolo, and then as chair from 2000, had been able to accompany the growth of NC-IUPHAR into a major organisation with >90 subcommittees (700 scientists) and a freely available database, the IUPHAR/BPS guidetopharmacology.org.

NC-IUPHAR has published more than 100 publications, and has an h-index of 78 and has contributed to the structuring of modern pharmacology. Steve, in a remarkable effort, has built up the Concise Guide to Pharmacology, from GRAC. Michael has been elected secretary general of IUPHAR. Furthermore, Bill Catterall handed over his dynamic leadership of the voltage-gated ion channels to Jorg Streissnig. The changes were celebrated appropriately in an emotional dinner. Jamie Davies was congratulated for his immaculate leadership of the database group, after the sad demise of Tony Harmar. The full list of the membership changes are in the document below.

However, the meeting also marked the change in Wellcome Trust funding with the grant associated with classifying all the drug sites in the human genome, terminating, and a new grant on immunological targets commencing. Financing of two senior curators by the British Pharmacological Society for five years is critical to the database, and its continuity.

During the meeting, Bill Catterall reviewed the current situation of the Chanome: New Structures, New Functions, prior to this immense task being taken on by Jorg Striessnig. A review article is in progress. We probably need to consider including information on splice variations that affect physiological function. Also note that splice variation may underlie gender differences in hormone actions (e.g. in stress response-possibly via set of genes that are only regulated by combinations of hormones). We should also curate phosphorylation affecting activity, trans-repression of genes (epigenetics).

A new database for kinase-oriented phospho-proteomics: KANPHOS (Kinase associated neural phospho signaling was presented by Kozo Kaibuchi which will be linked in to the guidetopharmacology.

The interactions of NC-IUPHAR and Orphanet were reviewed by Ana Rath. >80% of rare diseases are caused by genetic alterations. It is a major objective of modern medicine to correlate disease ontology with the molecular ontology. So can NC-IUPHAR with its target ontology associate with orphan disease ontology? A test case had been made with ~150 orphan diseases are associated with kinases.

Full listings obtained in a collaboration between GtoPdb and Orphanet (Elena Faccenda and Annie Orly). A problem is the degree of penetration of the kinases in the aetiology of the orphan diseases. Nevertheless the cross-talk between these lists seem very important, but deconvoluting is a lot of (important) work. Three lists have been prepared : 1. the rare orphan diseases with a kinase involvement 2 -the list of genes listed in table 1 and their relationships in Orphanet, 3. the list of diseases associated with the genes in table 2 (excluding the knowns in page 1) BUT all are officially orphan diseases. We will continue to define kinase and orphan disease ontology.

Christian Muchardt was invited to give his view on alternative splicing, whereby epigenetic control, particularly in inflammation may act at pivotal sites to change splicing and change a cell's proteome. JNK as example of alternative spliced protein- alternative splicing modulates the protein's ability to interact with other proteins. CD44- involved in cell-cell interaction- alternatively spliced in different cell types/tissues & in different types of cancer. Proinflammatory signals affect splicing - increasing the inclusion of variant exons & accumulation of RNA polymerase II. This translates into decreased elongation rate (nucleosomes cluster with transcription sites, as does lysine methylation (K9) which generates a binding site for HP1. Proinflammatory stimulation increases K9 methylation, & increases HP1gamma binding. And regulates formation of spliceosome. There was a debate as to how important this was, and how under-represented splice variants are in current research, compared to the purely genetic aspects.

John Cidlowski presented the nuclear hormone receptor update. Tom Burris & JC are writing a Pharm Rev article. Many of the orphans don't have much information as to their role - this situation may improve with generation of CRISPR knockouts with distinct phenotypes. Information on splice variations that affect physiological function will be covered : splice variation may underlie gender differences in hormone actions (e.g. in stress response- possibly via set of genes that are only regulated by combinations of hormones). John had previously presented the critical splice variants of the glucocorticoid response.

Eliot Ohlstein the editor, reviewed progress: 9 NC-IUPHAR reviews published in 2015. 6 are currently targeted for 2016. Steve Alexander reviewed the massive effort required to ensure that the Concise Guide to Pharmacology appeared on time. This remarkable publication covering a simplified, but expanded version of the Guide to Pharmacology is on time.

The excellent links with other pharmacological societies; Australian, French, Indian, Japanese, Chinese, PharfA, South African, were reviewed, as were potential future links with other societies (*e.g.* British Society for Immunology, Physiological Society, Biochemical Society). Thus another busy meeting ensured that the future of NC-IUPHAR and its role in structuring modern pharmacology is assured. Please note that we welcome any comments and activity - this is not an exclusive club, but a dynamic organisation to which YOU are welcome to contribute.

EXPERT *DRIVEN* ANNOTATION

The Guide to PHARMACOLOGY portal (which includes the IUPHAR Database) is maintained by a team of curators, with guidance from NC-IUPHAR and an international network of ~700 expert contributors, providing expert-driven annotation of the pharmacology of drug target systems from peer-reviewed primary literature sources.

A global knowledge environment for pharmacology students, academic and industrial scientists, and the interested public.

Subcommittees of NC-IUPHAR are responsible for developing the nomenclature for each drug target family and compiling data to be included in the database.
Where no relevant subcommittee exists, data are captured by the curators or individual experts and peer reviewed by at least two external referees.

Data are sourced from and referenced to the primary literature (peer-reviewed research publications rather than review articles), with links to citations in PubMed. Wherever possible, data are supported by more than one literature source. After review by the curators to ensure accuracy and consistency with the rest of the information in the database, the data are added to the development server.
After approval by NC-IUPHAR, the data are transferred to the public database. Data are reviewed at regular intervals (at least yearly) by subcommittees and other contributors and updated as necessary.

Our global network of expert contributors

NC-IUPHAR Subcommittee Chairs/Liaisons (>90 subcommittees; ~700 scientists)

G protein-coupled receptors Subcommittees
5-Hydroxytryptamine: Nick Barnes, John Neumaier
alpha$_1$-adrenoceptors: Dianne Perez
Apelin: Anthony Davenport
Bombesin: Robert Jensen
Calcium-sensing: Ed Brown, Hans Bräuner-Osborne
Cholecystokinin: Laurence Miller
Dopamine: Raul Gainetdinov
Formylpeptide family: Richard Ye
GABA$_B$: Bernhard Bettler
Glucagon receptor family: Laurence Miller
Histamine: Paul Chazot
Leukotriene: Magnus Bäck
Melanin-concentrating hormone: Jean-Louis Nahon
Metabotropic glutamate: Jean-Philippe Pin
Neuropeptide FF/neuropeptide AF: Jean-Marie Zajac
Neuropeptide Y: Dan Larhammar
Orexin: Christopher Winrow
Peptide P518: Jerome Leprince
Prolactin-releasing peptide: Helgi Schiöth
Relaxin family peptide: Roger Summers
Tachykinin: Susan Leeman, Steven Douglas
Urotensin: Hubert Vaudry

Ligand-gated ion channels Subcommittees
John Peters (Liaison for all LGIC subcommittees)
5-HT$_3$: John Peters
GABA$_A$: Richard Olsen
Glycine: Joseph Lynch
Ionotropic glutamate: Graham Collingridge
Nicotinic acetylcholine: Neil Millar
P2X: Charles Kennedy
ZAC: Timothy Hales

Antibodies Subcommittee
Alex Phipps

Adenylyl cyclases Subcommittee
Carmen Dessauer

Drug Target and Chemistry Curation Subcommittee
Christopher Southan

Epigenetics Subcommittee
Rabinder Prinjha

Acetylcholine (muscarinic): Arthur Christopoulos
alpha$_2$-adrenoceptors: VACANT
beta-adrenoceptors: Terry Hébert
Bradykinin: VACANT
Cannabinoid: Roger Pertwee, Allyn Howlett
Complement peptide: Peter Monk
Endothelin: Anthony Davenport
Free fatty acid: VACANT
Galanin: Andrew Gundlach
Glycoprotein hormone: Deborah Segaloff
Hydroxycarboxylic acid: Stefan Offermanns
Lysophospholipid (LPA): Jerold Chung
Melanocortin: Tung Fong, Helgi Schiöth
Motilin: Anthony Davenport
Neuropeptide S: Girolamo Calo'
Neurotensin: Jean Mazella
P2Y: Geoffrey Burnstock
Platelet-activating factor: VACANT
Prostanoid: Xavier Norel
Relaxin-like: Nick Barker
Trace amine: Janet Maguire
Vasopressin and oxytocin: Bernard Mouillac

Voltage-gated ion channels Subcommittees
William Catterall (Liaison for all VGIC subcommittees)
Calcium-activated potassium: George Gutman
CatSper and Two-Pore: David Chapman
Cyclic nucleotide-regulated: Martin Biel
Inwardly rectifying potassium: Yoshihiro Kubo
Transient Receptor Potential: David Clapham
Two-P potassium: Steven Goldstein
Voltage-gated calcium: William Catterall
Voltage-gated potassium: George Gutman
Voltage-gated sodium: William Catterall

Gasotransmitters Subcommittee
Andreas Papapetropoulos and Csaba Szabo

Guanylyl cyclases Subcommittee
Adrian Hobbs and Scott Waldman

Non-coding RNAs Subcommittee
Andrew Baker

Adenosine: Adriaan Ijzerman
Angiotensin: Sadashiva Karnik
Bile acid: Anthony Davenport
Calcitonin: Debbie Hay, David Poyner
Chemokine: Philip Murphy
Corticotropin-releasing factor: Richard Hauger, Frank Dautzenberg
Estrogen (G protein coupled): VACANT
Frizzled: Gunnar Schulte
Ghrelin: Birgitte Holst
Gonadotrophin-releasing hormone: Adriaan Ijzerman
Kisspeptin: Anthony Davenport
Lysophospholipid (S1P): Sarah Spiegel
Melatonin: Ralf Jockers
Neuromedin U: Gary Willars
Neuropeptide W/neuropeptide B: Anthony Davenport
Opioid: Larry Toll
Parathyroid hormone: Jean-Pierre Vilardaga
Prokineticin: Philippe Rondard
Protease-activated: Nigel Bunnett
Somatostatin: Stephan Schulz
Thyrotropin-releasing hormone: Marvin Gershengorn
VIP and PACAP: VACANT

Nuclear hormone receptors Subcommittees
John Cidlowski and Thomas Burris (Liaisons for all NHR subcommittees
NHR subcommittees are currently being reformed

Kinases Subcommittee
Doriano Fabbro

Pattern Recognition Receptors Subcommittee
Clare Bryant

Proteases Subcommittee
Anthony Turner

Transporters Subcommittee
Stephen Alexander

'Concise Guide to PHARMACOLOGY' Editors
Stephen Alexander, Eamonn Kelly, Neil Marrion, John Peters

A full list of NC-IUPHAR subcommittee members and contributors can be view at:
http://www.guidetopharmacology.org/GRAC/ContributorListForward

Recent publications

The collaboration between NC-IUPHAR, the American Society for Pharmacology and Experimental Therapeutics (ASPET) and the British Pharmacological Society (BPS) allows NC-IUPHAR subcommittees to publish nomenclature reports in *Pharmacological Reviews* and 'state-of-the-field' reviews in *British Journal of Pharmacology*. A selection of the most recent NC-IUPHAR related articles are listed below.

Pharmacological Reviews

Karnik SS, Unal H, Kemp JR, Tirupula KC, Eguchi S, Vanderheyden PM, Thomas WG. (2015) **International Union of Basic and Clinical Pharmacology. XCIX. Angiotensin Receptors: Interpreters of Pathophysiological Angiotensinergic Stimuli.** *Pharmacol Rev.* **67**: 754-819. [PMID:26315714]

Panula P, Chazot PL, Cowart M, Gutzmer R, Leurs R, Liu WLS, Stark H, Thurmond RL, Haas HL. (2015) **International Union of Basic and Clinical Pharmacology. XCVIII. Histamine Receptors.** *Pharmacol Rev.* **67**: 601-55. [PMID:26084539]

Prossnitz ER, Arterburn JB. (2015) **International Union of Basic and Clinical Pharmacology. XCVII. G Protein-Coupled Estrogen Receptor and Its Pharmacologic Modulators.** *Pharmacol Rev.* **67**: 505-40. [PMID:26023144]

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