

The 2015 *Nucleic Acids Research* Database Issue and Molecular Biology Database Collection

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Received November 10, 2014; Accepted November 11, 2014

ABSTRACT

The 2015 *Nucleic Acids Research* Database Issue contains 172 papers that include descriptions of 56 new molecular biology databases, and updates on 115 databases whose descriptions have been previously published in *NAR* or other journals. Following the classification that has been introduced last year in order to simplify navigation of the entire issue, these articles are divided into eight subject categories. This year's highlights include RNA-central, an international community portal to various databases on noncoding RNA; ValidatorDB, a validation database for protein structures and their ligands; SASBDB, a primary repository for small-angle scattering data of various macromolecular complexes; MoonProt, a database of 'moonlighting' proteins, and two new databases of protein–protein and other macromolecular complexes, ComPPI and the Complex Portal. This issue also includes an unusually high number of cancer-related databases and other databases dedicated to genomic basics of disease and potential drugs and drug targets. The size of *NAR* online Molecular Biology Database Collection, <http://www.oxfordjournals.org/nar/database/a/>, remained approximately the same, following the addition of 74 new resources and removal of 77 obsolete web sites. The entire Database Issue is freely available online on the *Nucleic Acids Research* web site (<http://nar.oxfordjournals.org/>).

NEW AND UPDATED DATABASES

The current *Nucleic Acids Research* (*NAR*) Database Issue is the 22nd annual collection of brief descriptions of bioinformatics databases, some of which are already well known, while others are described here for the first time. It includes 172 papers, of which 56 describe new databases (Table 1), 98 provide updates on the progress of the databases that

have been previously described in the *NAR* Database Issue, and 17 contain updates on the status of the databases whose descriptions have previously been published elsewhere (Table 2).

To simplify navigation within the issue, we introduced last year the division of the entire Database Issue into eight sections: (i) nucleic acid sequence and structure, transcriptional regulation; (ii) protein sequence and structure, motifs and domains, protein–protein interactions; (iii) metabolic and signalling pathways, metabolites, enzymes, protein modification; (iv) viruses, bacteria, protozoa and fungi; (v) human genome, model organisms, comparative genomics; (vi) genomic variation, diseases and drugs; (vii) plant databases and (viii) other molecular biology databases. After mostly positive feedback, this year's issue is again divided into the same sections. It must be noted, however, that many databases transcend the traditional borders between different areas of research and cannot be easily assigned to a single bin. In contrast, the *Nucleic Acids Research* online Molecular Biology Database Collection, <http://www.oxfordjournals.org/nar/database/a/>, still retains the same 15 categories and 41 subcategories as before.

The most notable feature of this year's issue is the increased number of databases that exploit RNA-seq data, using them for such diverse tasks as mapping transcription start sites (1), analysing gene co-expression data (2,3), and cataloguing chimeric transcripts (4). Co-expression data are naturally focused principally on model organisms, but the move away from microarray-based data sets allows a more objective sampling of transcripts that encompass newly discovered genes. RNA-seq data, cheaply obtained, also offer a convenient way to obtain valuable comparative information on non-model organisms. The non-human primate reference transcriptome resource [NHPRTR, (5)], for example, takes in relatives out to lemurs, enabling study of what is shared or distinct between us and our distant cousins. Similarly, DataBase of Apicomplexa Transcriptomes [DB-AT, formerly Full-Malaria, (6)] now includes RNA-Seq data for 14 species, shedding light on lesser known species with the context from the better studied apicomplexan parasites like *Plasmodium falciparum*.

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Table 1. Descriptions of new online databases in the 2015 *NAR* Database Issue

Database name	URL	Brief description
Addgene Vector Database ^a	http://www.addgene.org/vector-database/	Plasmid vectors from publications and commercial sources
ADReCS	http://bioinf.xmu.edu.cn/ADReCS	Adverse Drug Reaction Classification System
AHTPdb	http://crdd.osdd.net/raghava/ahtpdb/	Antihypertensive peptides database
APASdb	http://mosas.sysu.edu.cn/utr	Alternative poly(A) sites and downstream cleavage sites
BARCdb ^a	http://www.barcdb.org	Biobanking Analysis Resource Catalogue
BARD ^a	https://bard.nih.gov/	BioAssay Research Database
BCCTBbp ^a	http://bioinformatics.breastcancertissuebank.org	Breast Cancer Campaign Tissue Bank bioinformatics portal
Cancer3D	http://www.cancer3d.org	Mapping of cancer mutations to protein structures
CancerPPD	http://crdd.osdd.net/raghava/cancerppd/	Experimentally validated anticancer peptides
Candidate Cancer Gene Database	http://ccgd-starrlab.oit.umn.edu/	Cancer genes identified in transposon-based genetic screens in mice
CeCaFDB	http://www.cecafdb.org	Carbon flux data of central metabolism in various organisms
CFam	http://137.132.71.120/cfam	Similarity-based classification of chemical compounds
CMPD	http://cgcb.cgu.edu.tw/hmpd	Cancer Mutant Proteome Database
Coffee Genome Hub	http://coffee-genome.org/	Coffee genomics, genetics and breeding data and tools
ComPPI	http://compipi.linkgroup.hu	Protein–protein interactions linked to subcellular localization
DBTMEE	http://dbtmee.hgc.jp/	DataBase of Transcriptome in Mouse Early Embryos
DDMGD	http://www.cbrc.kaust.edu.sa/ddmgd/	Associations between gene methylation and disease
Digital Ageing Atlas	http://ageing-map.org/	Human ageing-related data
DoGSD	http://dogvb.big.ac.cn	Dog and wolf genome SNP database
EHFPI	http://biotech.bmi.ac.cn/ehfpi/	Essential Host Factors for Pathogenic Infection
EpilepsyGene	http://122.228.158.106/EpilepsyGene	Genes and mutations related to epilepsy
euL1db	http://euL1db.unice.fr	L1 retrotransposon insertions in humans
GBshape	http://rohsdb.cmb.usc.edu/GBshape/	Genome Browser for DNA shape annotations
i5k Workspace@NAL	http://i5k.nal.usda.gov/	Arthropod genome projects
iBeetle-Base	http://ibeetle-base.uni-goettingen.de	RNAi screen phenotypes in the red flour beetle <i>Tribolium castaneum</i>
ImmuCo	http://immuco.bjmu.edu.cn/	Gene coexpression in immune cells
KnotProt	http://biocomp.chem.uw.edu.pl/protop/	Proteins with topological knots and slipknots
LncRNA2Target	http://mlg.hit.edu.cn/lncrna2target	Differentially expressed genes after lncRNA knockdown or overexpression
lncRNASNP	http://bioinfo.life.hust.edu.cn/lncRNASNP/	SNPs in human lncRNAs
LncRNAWiki	http://lncrna.big.ac.cn	Wiki database of human lncRNAs
MeT-DB	http://compgenomics.utsa.edu/methylation/	N ⁶ -methyladenine in human and mouse mRNA
MethBank	http://dnamethylome.org	Nucleotide methylomes of gametes and early embryos
MethHC	http://MethHC.mbc.nctu.edu.tw	DNA methylation in human cancer
MoonProt	http://www.moonlightingproteins.org/	Moonlighting proteins
MyMpn	http://mycoplasma.crg.eu	<i>Mycoplasma pneumoniae</i> as a model organism
NRichD	http://proline.biochem.iisc.ernet.in/NRICH/D/	Sequence databases enriched with computationally designed protein-like sequences
NutriChem	http://cbs.dtu.dk/services/NutriChem-1.0	Nutritional and medicinal value of plant-based foods
Open TG-GATES	http://toxico.nibio.go.jp/english/	Gene expression and toxicology data for rat liver and human and rat hepatocytes
Organ System Heterogeneity DB	http://mips.helmholtz-muenchen.de/Organ_System.Heterogeneity/	Phenotypic effects of diseases and drugs on different organs
Plastid-LCGbase	http://lcbgase.big.ac.cn/plastid-LCGbase/	Plastid Lineage-based Conserved Gene-pair database
Platinum	http://structure.bioc.cam.ac.uk/platinum	Experimentally measured effects of mutations on protein-ligand complexes
PubAngioGen	http://www.megabionet.org/aspd	Public angiogenesis research portal
PyIgClassify	http://dunbrack2.fccc.edu/PyIgClassify/default.aspx	Clusters of conformations of antibody complementarity determining regions
RaftProt	http://lipid-raft-database.di.uq.edu.au/	Lipid raft-associated proteins
RiceVarMap	http://ricevarmap.ncpgr.cn/	Rice Variation Map, SNPs and indels
SASBDB	http://www.sasbdb.org/	Small Angle Scattering Biological Data Bank
SNP-Seek	http://www.oryzasnp.org/iric-portal/	Rice SNPs database
SuperFly	http://superfly.crg.eu	Spatio-temporal gene expression patterns in dipteran embryos
The Complex Portal	http://www.ebi.ac.uk/intact/complex	Macromolecular complexes from key model organisms
tRFdb	http://genome.bioch.virginia.edu/trfdb/	Short (14–32 nt) tRNA-related fragments
TrypanoCyc	http://www.metexplore.fr/trypanocyc/	Biochemical pathways of <i>Trypanosoma brucei</i>
TTSMI	http://tsmi.bii.a-star.edu.sg	Triplex Target DNA Sites in the human genome
VADE	http://bmi-tokai.jp/VaDE/	VarySysDB Disease Edition: disease-associated genomic polymorphisms
ValidatorDB	http://ncbr.muni.cz/ValidatorDB	Validation results for ligands and residues in the PDB
ViRBase	http://www.rna-society.org/vhncrnadb/	Virus–host interaction-associated ncRNAs
WDSPdb	http://wu.scb.pku.edu.cn/wdsp/	WD40 domain proteins and structure predictions

^aThis database is part of this issue's Resource Collection (see text for details).

Table 2. Previously published databases that are new for the *NAR* Database Issue

Database name	URL	Brief description
Araport	http://www.araport.org	<i>Arabidopsis</i> information portal
AraNet	http://www.inetbio.org/aranet/	Functional gene networks in <i>Arabidopsis</i> and other plants
ArrayMap	http://www.arraymap.org	Gene copy number profiling in human cancers
CODEX	http://codex.stemcells.cam.ac.uk/	ChIP-Seq, RNA-Seq and DNase-Seq data for haematopoietic and embryonic stem cells
DEPOD	http://www.depod.org	Human Dephosphorylation database
dbSNO	http://140.138.144.145/~dbSNO/index.php	A database of protein S-nitrosylation
diArk	http://www.diark.org/diark/	A database of eukaryotic genome sequencing projects
GeneFriends	http://www.genefriends.org	RNAseq based human gene and transcript co-expression map
GRASP	http://apps.nhlbi.nih.gov/grasp/	GWAS results
GenoBase ^a	http://ecoli.naist.jp/	<i>Escherichia coli</i> K-12 genes and single-gene knockout mutants
miRDB	http://mirdb.org	miRNA target prediction and functional annotation
MobiDB	http://mobidb.bio.unipd.it/	Intrinsically disordered and mobile proteins
PlasmoGEM ^a	http://plasmogem.sanger.ac.uk/	DNA vectors and data for genetic manipulation of malaria parasites
PLAZA	http://bioinformatics.psb.ugent.be/plaza/	Comparative genomics of monocot and dicot plants
ProteomeScout	https://proteomescout.wustl.edu/	Proteomics of post-translational modifications
RNACentral	http://rnacentral.org/	An international community portal for data on ncRNA sequences
sc-PDB	http://bioinfo-pharma.u-strasbg.fr/scPDB/	Potential drug-binding sites in protein structures from the PDB

^aThis database is part of this issue's Resource Collection (see text for details).

Among the nucleic acid sequence databases, the major new entry is RNACentral (<http://rnacentral.org>), an international community portal to various databases on noncoding RNA (7). This new web site collects the data from (and provides links to) 10 major ncRNA databases, including ENA, Rfam, RefSeq, tmRNA Website, and lncRNAdb, updates on which are presented as separate papers in this issue. The growing interest in lncRNAs led to the inclusion, in addition to an update on lncRNAdb (8), of four other lncRNA-related databases: lncRNA2Target, lncRNASNP, LNCipedia, and lncRNAWiki. The last is structured as wiki, attempting to encourage community annotation, as advocated in the 2012 *NAR* editorial by Finn and colleagues (9).

The protein database section includes two thought-provoking papers describing the recent changes and a new vision of the UniProt and InterPro databases (10,11). The InterPro article is an interesting narrative of attempts to efficiently deal with data that are challenging not only in quantity but also in heterogeneity (deriving from carefully curated to fully automatic sources), as well as reporting on a valuable domain architecture-based search tool. They are accompanied by regular updates on protein domain databases, such as CDD, SMART and SUPERFAMILY (12–14), and protein family/orthology databases, such as Inparanoid, OMA, OrthoDB, COG and MGD (15–19). While most of these databases have been featured in the *NAR* Database Issue in recent years, the COG database (18) receives its first update since 2003. The new version of COGs (whose description shares an author with this editorial) expands its coverage to 711 bacterial and archaeal genomes and provides improved annotations for more than 500 protein families (18). For two other databases in this issue, the tmRNA website and Islander (20,21), previous descriptions have been published in 2004.

Various aspects of the common goal of providing reliable and useful functional annotation are addressed by the updates of such well-known databases as GO, GOA, HAMAP, BRENDA, Rhea, Ensembl, FlyBase, XenBase, Mouse Genome Database, Rat Genome Database, neXtProt and the UCSC Genome Browser.

Functional annotation is often complicated by ‘moonlighting’, the ability of certain proteins to perform two or more unrelated functions depending, for example, on their localization inside or outside the cell, or expression in specific tissues. We expect MoonProt (22), a database of such ‘moonlighting’ proteins, together with MultitaskProtDB (23), published last year, to serve as guiding light in the analyses of this interesting phenomenon.

The protein structure category features an update on the status of the RCSB Protein Data Bank [PDB, (24)] and an update on a valuable collection of PDB-derived databases and structure-related tools (e.g., DSSP, HSSP, PDBReport, PDB-Redo) (25). Improvements to the CATH hierarchical database of structural domains include downloadable superpositions of superfamily representatives and improved parsing of ‘functional families’ (26). The Genome3D database also reports new developments (27) with sequences from 10 model organisms and from the Pfam database (28) now annotated with structural domain assignments from CATH, SCOP and several fold recognition programs. Four distinct methods now contribute structural models which

can be visualized online or downloaded (27). These papers are accompanied by a major new entrant in this area, the ValidatorDB (<http://ncbr.muni.cz/ValidatorDB>) database, which provides results of a thorough validation of the properties of bound ligands and non-standard residues (e.g. phosphoserine), reporting on various problems in the analysed structures, such as instances of missing atoms and incorrect chiralities (29).

Another important new arrival is SASBDB (<http://www.sasbdb.org/>), a repository for small-angle scattering data of proteins, nucleic acids, and various macromolecular complexes, obtained using beams of X-rays or neutrons (30). Improvements in both the brilliance of the latest synchrotrons and in instrumentation have considerably reduced the sample and time requirements of such experiments. Scattering experiments can address biologically important targets such as macromolecular complexes and intrinsically disordered proteins that can be difficult or even plainly intractable for other structural methods; and can span a huge target size range. Given these factors, it is not surprising that scattering experiments have seen a surge in popularity justifying a new, bespoke and (currently) curated primary database.

The importance of post-translational modifications (PTMs) of proteins is reflected in continued efforts to capture the diversity of PTMs and their biological significance. This issue includes dbDNO, which specifically deals with protein S-nitrosylation, and ProteomeScout, which neatly adds context to raw PTM data with context from various databases (31,32). The important involvement of PTMs in modulating protein–protein interactions is addressed by the PTMcode database, which combines different analytic routes to describe and predict functional associations between PTM sites in either the same protein or two interacting proteins (33).

A significant fraction of new and updated databases reflect the efforts to use the genomic data to advance human health. These include updates on such well-established databases as Online Mendelian Inheritance in Man[®] (OMIM[®]), Catalog of Somatic Mutations in Cancer (COSMIC), and the UCSC Cancer Genomics Browser (34–36). Several databases focus on diverse aspects of cancers, from identification of candidate genes in mice [Mouse Tumor Biology Database and the Candidate Cancer Gene Database, (37,38)] via the impact of DNA methylation (MethHC) or copy number variation (ArrayMap) in cancer cells, to the consequences of mutations at the protein sequence or structural level (Cancer Mutant Proteome Database, Cancer3D) (39–42).

While many databases featured in this issue have had a long and successful presence on the web, we are glad to note the 25th anniversary of BRENDA and the international ImMunoGeneTics information system [IMGT[®], (43)], the 15th anniversary of InterPro (11), and the 10th anniversary updates on BioModels and the Comparative Toxicogenomics Database (44,45). That said, the database with the most consistent presence in *NAR* is REBASE, a database of restriction-modification systems which has been featured in the first *NAR* Database Issue and described in *NAR* even before that. It now presents its 15th update (46), the first since 2010.

Finally, this year's issue also includes a selection of papers that, in addition to virtual resources (i.e. online databases), provide descriptions of tangible resources for molecular biology, which are linked to these databases. These include Addgene Vector Database, Biobanking Analysis Resource Catalogue, BioAssay Research Database, and Breast Cancer Campaign Tissue Bank (see Table 1). Among the updates on previously described resources (Table 2), it is worth mentioning GenoBase, a description of the renowned Keio collection of *Escherichia coli* K-12 single-gene knockout mutants and associated bioinformatics resources (47); PlasmogEM, a collection of DNA vectors and data for genetic manipulation of malaria parasites (48); Standard European Vector Architecture (SEVA), a database and a set of genetic tools for analysis and the engineering of Gram-negative bacteria for research or biotechnological purposes (49), and INFRAFRONTIER (formerly European Mouse Mutant Archive), which promotes the use of mouse models of disease by systemically phenotyping mouse mutants, as well as archiving and distributing mouse mutant lines (50).

NAR ONLINE MOLECULAR BIOLOGY DATABASE COLLECTION

This year's update of the *NAR* online Molecular Biology Database Collection (which is freely available at <http://www.oxfordjournals.org/nar/database/a/>), involved inclusion of the 56 new databases (Table 1) and 15 databases not described previously in the *NAR* Database Issue (Table 2). In addition, the Collection has been expanded by including such databases as the European Variation Archive (<http://www.ebi.ac.uk/eva/>), cBioPortal for Cancer Genomics (<http://www.cbioportal.org/public-portal/>), and the ExAC Browser from the Exome Aggregation Consortium (<http://exac.broadinstitute.org/>). On the other hand, 76 discontinued databases have been removed from the Collection, which kept its size almost unchanged. After contacting their authors, 177 database entries have been updated by their authors with respect to new URLs, new descriptions, and/or other kinds of metadata.

We welcome suggestions for inclusion in the Collection of additional databases that have been published in other journals. Such suggestions should be addressed to XMFS at xose.m.fernandez@gmail.com and should include database summaries in plain text, organized in accordance with the <http://www.oxfordjournals.org/nar/database/summary/1> template.

ACKNOWLEDGEMENTS

We thank Dr Martine Bernardes-Silva and the Oxford University Press team led by Jennifer Boyd and Caoimhe Ní Dhónaill for their help in compiling this issue.

FUNDING

The NIH Intramural Research Program at the National Library of Medicine [to M.Y.G.]. Funding for open access charge: Oxford University Press.

Conflict of interest statement. The authors' opinions do not necessarily reflect the views of their respective institutions. X.M.F.S. is an employee of Thermo Fisher Scientific Inc.

REFERENCES

- Suzuki,A., Wakaguri,H., Yamashita,R., Kawano,S., Tsuchihara,K., Sugano,S., Suzuki,Y. and Nakai,K. (2015) DBTSS as an integrative platform for transcriptome, epigenome and genome sequence variation data. *Nucleic Acids Res.*, **43**, D87–D91.
- Okamura,Y., Aoki,Y., Obayashi,T., Tadaka,S., Ito,S., Narise,T. and Kinoshita,K. (2015) COXPRESdb in 2015: coexpression database for animal species by DNA-microarray and RNAseq-based expression data with multiple quality assessment systems. *Nucleic Acids Res.*, **43**, D82–D86.
- van Dam,S., Craig,T. and de Magalhaes,J.P. (2015) GeneFriends: a human RNA-seq-based gene and transcript co-expression database. *Nucleic Acids Res.*, **43**, D1124–D1132.
- Frenkel-Morgenstern,M., Gorohovski,A., Vucenovic,D., Maestre,L. and Valencia,A. (2015) ChiTaRS 2.1 – an improved database of the Chimeric Transcripts and RNA-seq Data with novel sense–antisense chimeric RNA transcripts. *Nucleic Acids Res.*, **43**, D6–D7.
- Peng,X., Thierry-Mieg,J., Thierry-Mieg,D., Nishida,A., Pipes,L., Bozinoski,M., Thomas,M.J., Kelly,S., Weiss,J.M., Raveendran,M. *et al.* (2015) Tissue-specific transcriptome sequencing analysis expands the non-human primate reference transcriptome resource (NHPTR). *Nucleic Acids Res.*, **43**, D73–D743.
- Jakalski,M., Wakaguri,H., Kischka,T.G., Nishikawa,Y., Kawazu,S.-I., Matsubayashi,M., Kawahara,F., Tsuji,N., Cao,S., Sunaga,F. *et al.* (2015) DB-AT: a 2015 update to the full-parasites database brings a multitude of new transcriptomic data for apicomplexan parasites. *Nucleic Acids Res.*, **43**, D631–D636.
- The RNAcentral Consortium. (2015) RNAcentral: an international database of ncRNA sequences. *Nucleic Acids Res.*, **43**, D123–D129.
- Quek,X.C., Thomson,D.W., Maag,J.L., Bartonicek,N., Signal,B., Clark,M.B., Gloss,B.S. and Dinger,M.E. (2015) lncRNAdb v2.0: expanding the reference database for functional long noncoding RNAs. *Nucleic Acids Res.*, **43**, D168–D173.
- Finn,R.D., Gardner,P.P. and Bateman,A. (2012) Making your database available through Wikipedia: the pros and cons. *Nucleic Acids Res.*, **40**, D9–D12.
- The UniProt Consortium. (2015) UniProt: a hub for protein information. *Nucleic Acids Res.*, **43**, D204–D212.
- Mitchell,A., Chang,H.-Y., Daugherty,L., Fraser,M., Hunter,S., Lopez,R., McAnulla,C., McMenamin,C., Nuka,G., Pesseat,S. *et al.* (2015) The InterPro protein families database: the classification resource after 15 years. *Nucleic Acids Res.*, **43**, D213–D221.
- Marchler-Bauer,A., Derbyshire,M.K., Gonzales,N.R., Lu,S., Chitsaz,F., Geer,L.Y., Geer,R.C., He,J., Gwadz,M., Hurwitz,D.I. *et al.* (2015) CDD: NCBI's Conserved Domains Database. *Nucleic Acids Res.*, **43**, D222–D226.
- Letunic,I., Doerks,T. and Bork,P. (2015) SMART: recent updates, new developments and status in 2015. *Nucleic Acids Res.*, **43**, D257–D260.
- Oates,M.E., Stahlhacke,J., Vavoulis,D.V., Smithers,B., Rackham,O.J.L., Sardar,A.J., Zaucha,J., Thurlby,N., Fang,H. and Gough,J. (2015) The SUPERFAMILY 1.75 database in 2014: a doubling of data. *Nucleic Acids Res.*, **43**, D227–D233.
- Sonnhammer,E.L.L. and Östlund,G. (2015) InParanoid 8: orthology analysis between 273 proteomes, mostly eukaryotic. *Nucleic Acids Res.*, **43**, D234–D239.
- Altenhoff,A.M., Škunca,N., Glover,N., Train,C.-M., Sueki,A., Piližota,I., Gori,K., Tomiczek,B., Müller,S., Redestig,H. *et al.* (2015) The OMA orthology database in 2015: function predictions, better plant support, synteny view, and other improvements. *Nucleic Acids Res.*, **43**, D240–D249.
- Kriventseva,E.V., Tegenfeld,F., Petty,T.J., Waterhouse,R.M., Simão,F.A., Pozdnyakov,I.A., Ioannidis,P. and Zdobnov,E.M. (2015) OrthoDB v8: update of the hierarchical catalog of orthologs and the underlying free software. *Nucleic Acids Res.*, **43**, D250–D256.
- Galperin,M.Y., Makarova,K.S., Wolf,Y.I. and Koonin,E.V. (2015) Expanded microbial genome coverage and improved protein family annotation in the COG database. *Nucleic Acids Res.*, **43**, D261–D269.
- Uchiyama,I., Mihara,M., Nishide,H. and Chiba,H. (2015) MBGD update 2015: microbial genome database for flexible ortholog

- analysis utilizing a diverse set of genomic data. *Nucleic Acids Res.*, **43**, D270–D276.
20. Hudson, C.M. and Williams, K.P. (2015) The tmRNA website. *Nucleic Acids Res.*, **43**, D138–D140.
 21. Hudson, C.M., Lau, B.Y. and Williams, K.P. (2015) Islander: a database of precisely mapped genomic islands in tRNA and tmRNA genes. *Nucleic Acids Res.*, **43**, D48–D53.
 22. Mani, M., Chen, C., Amblee, V., Liu, H., Mathur, T., Zwicke, G., Zabad, S., Patel, B., Thakkar, J. and Jeffery, C.J. (2015) MoonProt: a database for proteins that are known to moonlight. *Nucleic Acids Res.*, **43**, D277–D282.
 23. Hernández, S., Ferragut, G., Amela, I., Perez-Pons, J.A., Jaime Piñol, J., Mozo-Villarias, A., Juan Cedano, J. and E., Q. (2014) MultitaskProtDB: a database of multitasking proteins. *Nucleic Acids Res.*, **42**, D517–D520.
 24. Rose, P.W., Prlc, A., Bi, C., Bluhm, W.F., Christie, C.H., Dutta, S., Kramer Green, R., Goodsell, D.S., Westbrook, J.D., Woo, J. *et al.* (2015) The RCSB Protein Data Bank: views of structural biology for basic and applied research and education. *Nucleic Acids Res.*, **43**, D345–D356.
 25. Touw, W.G., Baakman, C., Black, J., Te Beek, T.A., Krieger, E., Joosten, R.P. and Vriend, G. (2014) A series of PDB-related databanks for everyday needs. *Nucleic Acids Res.*, **43**, D364–D368.
 26. Sillitoe, I., Lewis, T.E., Cuff, A., Das, S., Ashford, P., Dawson, N.L., Furnham, N., Laskowski, R.A., Lee, D., Lees, J.G. *et al.* (2015) CATH: comprehensive structural and functional annotations for genome sequences. *Nucleic Acids Res.*, **43**, D376–D381.
 27. Lewis, T.E., Sillitoe, I., Andreeva, A., Blundell, T.L., Buchan, D.W., Chothia, C., Cozzetto, D., Dana, J.M., Filippis, I., Gough, J. *et al.* (2014) Genome3D: exploiting structure to help users understand their sequences. *Nucleic Acids Res.*, **43**, D382–D386.
 28. Finn, R.D., Bateman, A., Clements, J., Coggill, P., Eberhardt, R.Y., Eddy, S.R., Heger, A., Hetherington, K., Holm, L., Mistry, J. *et al.* (2014) Pfam: the protein families database. *Nucleic Acids Res.*, **42**, D222–D230.
 29. Sehnal, D., Svobodová Vařeková, R., Pravda, L., Ionescu, C.-M., Geidl, S., Horský, V., Jaiswal, D., Wimmerova, M. and Koča, J. (2015) ValidatorDB – database of up-to-date validation results for ligands and non-standard residues from the Protein Data Bank. *Nucleic Acids Res.*, **43**, D369–D375.
 30. Valentini, E., Kikhney, A.G., Previtali, G., Jeffries, C.M. and Svergun, D.I. (2015) SASBDB, a repository for biological small-angle scattering data. *Nucleic Acids Res.*, **43**, D357–D363.
 31. Chen, Y.J., Lu, C.T., Su, M.G., Huang, K.Y., Ching, W.C., Yang, H.H., Liao, Y.C., Chen, Y.J. and Lee, T.Y. (2015) dbSNO 2.0: a resource for exploring structural environment, functional and disease associations, and regulatory networks of protein S-nitrosylation. *Nucleic Acids Res.*, **43**, D503–D511.
 32. Matlock, M.K., Holehouse, A.S. and Naegle, K.M. (2015) ProteomeScout: an integrated repository and analysis resource for post-translational modifications and proteins. *Nucleic Acids Res.*, **43**, D521–D530.
 33. Minguez, P., Letunic, I., Parca, L., Garcia-Alonso, L., Dopazo, J., Huerta-Cepas, J. and Bork, P. (2015) PTMcode v2: a resource for functional associations of post-translational modifications within and between proteins. *Nucleic Acids Res.*, **43**, D494–D502.
 34. Amberger, J.S., Bocchini, C.A., Schiettecatte, F., Scott, A.F. and Hamosh, A. (2015) OMIM.org: Online Mendelian Inheritance in Man (OMIM®), an online catalog of human genes and genetic disorders. *Nucleic Acids Res.*, **43**, D789–D798.
 35. Forbes, S.A., Beare, D., Gunasekaran, P., Leung, K., Bindal, N., Boutselakis, H., Minjie, D., Bamford, S., Cole, C., Ward, S. *et al.* (2015) COSMIC: exploring the world's knowledge of somatic mutations in human cancer. *Nucleic Acids Res.*, **43**, D805–D811.
 36. Goldman, M., Craft, B., Swatloski, T., Cline, M., Morozova, O., Diekhans, M., Haussler, D. and Zhu, J. (2015) The UCSC Cancer Genomics Browser: update 2015. *Nucleic Acids Res.*, **43**, D812–D817.
 37. Abbott, K.L., Nyre, E.T., Abrahante, J., Ho, Y.Y., Isaksson Vogel, R. and Starr, T.K. (2015) The Candidate Cancer Gene Database: a database of cancer driver genes from forward genetic screens in mice. *Nucleic Acids Res.*, **43**, D844–D848.
 38. Bult, C.J., Krupke, D.M., Begley, D.A., Richardson, J.E., Neuhauser, S.B., Sundberg, J.P. and Eppig, J.T. (2015) Mouse Tumor Biology (MTB): a database of mouse models for human cancer. *Nucleic Acids Res.*, **43**, D818–D824.
 39. Huang, W.Y., Hsu, S.D., Huang, H.Y., Sun, Y.M., Chou, C.H., Weng, S.L. and Huang, H.D. (2015) MethHC: a database of DNA methylation and gene expression in human cancer. *Nucleic Acids Res.*, **43**, D862–D867.
 40. Cai, H., Gupta, S., Rath, P., Ai, N. and Baudis, M. (2015) arrayMap 2014: an updated cancer genome resource. *Nucleic Acids Res.*, **43**, D825–D830.
 41. Huang, P.J., Lee, C.C., Tan, B., Yeh, Y.M., Chu, J., Chen, T.W., Chang, K.P., Lee, C.Y., Gan, R.C., Liu, H. *et al.* (2015) CMPD: Cancer Mutant Proteome Database. *Nucleic Acids Res.*, **43**, D849–D855.
 42. Porta Pardo, E., Hrabe, T. and Godzik, A. (2015) Cancer3D: understanding cancer mutations through protein structures. *Nucleic Acids Res.*, **43**, D856–D861.
 43. Lefranc, M.P., Giudicelli, V., Duroux, P., Jabado-Michaloud, J., Folch, G., Aouinti, S., Carillon, E., Duvergey, H., Houles, A., Paysan-Lafosse, T. *et al.* (2015) IMGT®, the international ImMunoGeneTics information system® 25 years on. *Nucleic Acids Res.*, **43**, D413–D422.
 44. Chelliah, V., Juty, N., Ajmera, I., Ali, R., Dumousseau, M., Glont, M., Hucka, M., Jalowicki, G., Keating, S., Knight-Schrijver, V. *et al.* (2015) BioModels: ten year anniversary. *Nucleic Acids Res.*, **43**, D542–D548.
 45. Davis, A.P., Grondin, C.J., Lennon-Hopkins, K., Saraceni-Richards, C., Sciaky, D., King, B.L., Wiegiers, T.C. and Mattingly, C.J. (2015) The Comparative Toxicogenomics Database's 10th year anniversary: update 2015. *Nucleic Acids Res.*, **43**, D920–D926.
 46. Roberts, R.J., Vincze, T., Posfai, J. and Macelis, D. (2015) REBASE—a database for DNA restriction and modification: enzymes, genes and genomes. *Nucleic Acids Res.*, **43**, D298–D299.
 47. Otsuka, Y., Muto, A., Takeuchi, R., Okada, C., Ishikawa, M., Nakamura, K., Yamamoto, N., Dose, H., Nakahigashi, K., Tanishima, S. *et al.* (2015) GenoBase: comprehensive resource database of *Escherichia coli* K-12. *Nucleic Acids Res.*, **43**, D606–D617.
 48. Schwach, F., Bushell, E., Gomes, A.R., Anar, B., Girling, G., Herd, C., Rayner, J.C. and Billker, O. (2015) PlasmoGEM, a database supporting a community resource for large scale experimental genetics in malaria parasites. *Nucleic Acids Res.*, **43**, D1176–D1182.
 49. Martinez-Garcia, E., Aparicio, T., Goni, A., Fraile, S. and de Lorenzo, V. (2015) SEVA 2.0: an update of the Standard European Vector Architecture for de-/re-construction of bacterial functionalities. *Nucleic Acids Res.*, **43**, D1183–D1189.
 50. The INFRAFRONTIER Consortium. (2015) INFRAFRONTIER – providing mutant mouse resources as research tools for the international scientific community. *Nucleic Acids Res.*, **43**, D1171–D1175.